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Correlation Analysis of Climatic Variables, Migration and Dengue Cases in Southeast Florida

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Walden University
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Abstract

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Brunilda Lugo

MS, University of Puerto Rico, 1987

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Dissertation Submitted in Partial Fulfillment

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Abstract

Dengue fever is a debilitating, viral, mosquito-borne disease occurring in tropical and subtropical areas in the world. The majority of dengue cases in the United States were acquired in endemic areas by travelers or immigrants. However, in recent years, autochthonous (locally acquired) dengue cases have been diagnosed in Florida. The purpose of this study was to find an association between potential risk factors and the expansion of dengue fever in the United States. Guided by the eco-bio-social framework, which offers a broad assessment of risk factors for the illness, a retrospective design was used with archival data to correlate changes in climatic variables and imported dengue cases with autochthonous dengue cases in Southeast Florida from 1980 to 2013. A Spearman correlation indicated weak correlations between temperature and autochthonous dengue cases ($r_s = .099$, $p = 000$) and imported dengue cases with autochthonous dengue cases ($r_s = .162$, $p = 000$). A negative binomial multivariate regression was used to analyze the expansion of dengue to each monthly unit of temperature, rainfall, and imported dengue cases over 34 years. The results indicated that temperature (IRR = 2.198; 95% CI [1.903, 2.538]) and precipitation (IRR = .991; 95% CI [.988, .994]) were predictors for the geographic expansion of dengue fever in Southeast Florida. The positive social changes include the use of the results to develop an understanding of how climatic variables and migration may influence the expansion of dengue fever to nonendemic regions. The results can be used by public health authorities to address risk factors and to formulate evidence-based decisions in regard to prevention and education concerning dengue fever.

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Dedication

“Once you make a decision, the universe conspires to make it happen.”

– Ralph Waldo Emerson

I want to dedicate this dissertation to the most important men in my life. First, this dissertation is dedicated to my husband, Dr. Orlando Nieves, who has been my rock, my support, and my cheerleader. Secondly, I dedicate this dissertation to my son, Orlando Javier Nieves-Lugo, who is the embodiment of the quote at the beginning of the dedication; he is my heart, and he is my life. Finally, I dedicate this dissertation to my father, Santos Lugo Santiago; he taught me the importance of higher education, and even though he is not with me anymore, I know he would be very proud of my accomplishment.

Acknowledgments

> "No one who achieves success does so without acknowledging the help of others.
> The wise and confident acknowledge this help with gratitude."
> – Anonymous

I need to acknowledge those who generously gave of their time to be part of this process and helped me to reach my goals. I recognize my husband, Dr. Orlando Nieves, who gave me his support, love, and patience. I also want to acknowledge my classmates and friends who were always present when I needed help or when I just needed to let out my frustrations: Dr. Idania Ayuso-Rodriguez, Dr. Juan Acevedo, and Dr. Luz Nieves. I also want to thank my friend Peggy Hammond, MA, who was my editor for the first three chapters; I am so grateful for her help. My sincere thanks to Dr. Dallas Alston, who was willing to share his valuable time and kindly edited the final document.

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Chapter 1: Introduction to the Study

Dengue is a systemic viral infection transmitted by its primary vector, the *Aedes aegypti* mosquito. According to Centers for Disease Control and Prevention (CDC, 2013), the burden of dengue is extensive, with more than 50 million cases recorded worldwide and 2.5 billion people living in areas at risk. The burden of this disease covers more than 100 countries, making it one of the world's most important vector-borne diseases (Racloz, 2012). Dengue is endemic in tropical and subtropical regions; therefore, countries in the regions of the Asia-Pacific, the Americas, the Middle East, and Africa are affected by this disease (Guzman & Isturiz, 2010).

In the Americas, the dengue incidence rate has experienced a 4.6-fold increase during the last three decades (San Martin et al., 2010). During the 1980s, the total number of dengue cases reported was 1,033,417 (16.4/100,000); in the 1990s, this number was 2,725,405 (35.9/100,000), and from 2000-2007, it was 4,759,007 (71.5/100,000). During this same period, cases of dengue hemorrhagic fever also increased from 1.3% to 2.1% to 2.4% (San Martin et al., 2010).

According to CDC (2013), the case fatality of dengue hemorrhagic fever (a complication of dengue fever) can be as high as 10%; however, it can be reduced to 1% with early recognition and primary treatment. The morbidity and mortality of dengue vary by region, and in the majority of countries where dengue occurs, children are most often affected (Murray, Quam, & Wilder-Smith, 2013).

The mosquito *A. aegypti* is the primary vector of the dengue virus (Eisen & Moore, 2013). In tropical and subtropical regions where dengue is endemic, cases occur every year (CDC, 2012). Several conditions need to be met for dengue cases to appear: enough precipitation for breeding grounds, warm temperature, a large number of vectors, and large numbers of people with no immunity to the four virus serotypes, and contact between vector and host (CDC, 2013).

The interaction of the factors mentioned above can be affected by climate changes, which can favorably influence the population of the vector and increase the transmission of dengue significantly (Herrera-Martinez & Rodriguez-Morales, 2010). Ferreira (2012) indicated that the spread of the mosquito and the virus has led to a global resurgence of epidemic dengue fever and of the most severe forms of dengue.

There has been increasing interest in climate variation and its effects on vector-borne diseases, mostly concerning dengue. During the 1950s, only nine countries had reported dengue cases; today, it is a public concern in more than 100 countries (Adelman, 2013). Although there is uncertainty about how climate change will affect the distribution and incidence of this disease, predictions have been made of increased vector-borne diseases and changing climatic variables (Adelman, 2013).

There is a need for more quantitative studies to elucidate the relationship among climate change, migration/imported dengue cases, and the spread of dengue fever. This information can be used to add to the body of knowledge on climate change and its impact on vector-borne infectious diseases. The study may also provide evidence to support the implementation of policies to prevent or mitigate the effects of the expansion of dengue to nonendemic regions. This chapter includes an introduction of the topic of the study, the epidemiology of dengue, and the factors that have influenced the emergence of dengue as the most common and fastest spreading vector-borne virus worldwide (Bouri, 2012). The background section has information about the association between climate change and dengue fever, as well as some background on research about precipitation, rainfall, migration, and dengue fever. The problem statement establishes the gap in literature that makes this study necessary. The purpose of the study, the research questions, and the hypotheses are included and explained, as are the conceptual framework, the course of action necessary to approach the study, and the nature of the study. This chapter also addresses the key concepts, assumptions, scope, delimitations, and limitations of the study. The chapter ends with the significance of the study and a summary.

Background

The National Oceanic Atmospheric Agency (NOAA, 2007) defined *climate change* as a long-term shift in the statistics of the weather indicating a change in climate normals for a given place and time of year from one decade to the next. The agency argued that global climate is presently changing, as evidenced in the data for the last decade of the 20th century and the beginning of the 21st, which was the warmest period in the entire global instrumental temperature record since the mid-19th century (NOAA, 2007). Thus, according to Costello (2009), climate change is the global health threat of the 21st century, and potential health threats related to climate change extend to food resources, ecosystems, and certain diseases.

Climate change was forecast to have diverse impacts on human health, including some infectious diseases, especially vector-borne infectious diseases (Mills, Gage, &

Khan, 2010). Dengue fever is one of the infectious diseases that are strongly influenced by climate change (Herrera-Martinez & Rodriguez-Morales, 2010). An increase in temperature and precipitation can increase the population of the vector of dengue fever, *Aedes aegypti*, and dengue incidence (Hsieh & Chen, 2009). Morin, Comrie, and Ernst (2013) stressed that climatic changes influence vector dynamics, virus development, and the interaction between vector and host. Increased precipitation (e.g., rainfall) and more containers that collect water produce more breeding grounds for mosquitoes; warmer temperature enhances breeding and accelerates the maturation phase of the virus inside the vector (Yang, Macoris, Galvani, Andrighetti, & Wanderley, 2009).

Saker, Lee, Cannito, Gilmore, and Campbell-Lendrum (2004) stated that dengue was limited to tropical and subtropical regions; however, climate change can favor the geographic expansion and increase transmission of this disease. Scientists on the Intergovernmental Panel on Climate Change (IPCC) anticipated that vector-borne diseases, including dengue fever, would expand their geographic distribution to higher latitudes and higher altitudes, with an extension of the transmission season (Saker et al., 2004).

Thai and Anders (2011) reported that the geographic range of dengue expanded from 15,000 cases reported annually in 10 countries in 2000 to 1 million cases annually in more than 60 countries during 2005. The authors stressed that many countries in the Americas were experiencing a re-emergence of dengue and the geographic expansion of dengue fever, which represented a challenge for national and regional health. They also indicated that warmer temperature and increased rainfall and humidity were important determinates for the geographic expansion of dengue fever into new regions (Thai & Anders, 2011).

Canyon, Muller, and Hii (2013) disregarded humidity as an important factor for dengue fever transmission. They argued that mosquitos survive and continue biting when hosts are available, even in the presence of low humidity.

Few quantitative studies have been conducted to associate climatic variables with the incidence of vector-borne infectious disease. Pecoraro et al. (2007) found that a correlation existed between the abundance of several species of West Nile virus mosquito vectors and mild climate in western Washington State, United States. Colon-Gonzalez, Lake, and Bentham (2011) found that the incidence of dengue fever was positively associated with the strength of El Nino in dengue endemic Mexico; they also found that warm temperature increases the number of infected mosquitos and the transmission rates. However, Colon-Gonzalez et al. found no statistical association between precipitation and dengue fever. The authors admitted that other factors may have impacted this finding; they indicated that, in the period of El Nino, enough rainfall was available to create ample breeding sites.

Huang, Clements, Williams, Milinovich, and Hu (2013) found that dengue fever was strongly associated with temperature, rain, and relative humidity; these weather variables have been shown to have different effects depending on the tropical or subtropical area. Colon-Gonzalez et al. (2011) argued that some studies had related climate variability to dengue fever during short periods, but few had analyzed this association during a 10-year period. The authors understood that analyzing short periods poses a problem of understanding overall associations between climate variability and dengue fever.

Few quantitative studies have focused on climate change and dengue fever in relation to geographic expansion due to migration. Lee et al. (2013) conducted a study of the effects of climate change on *Aedes albopictus* in Jeju Island, South Korea. The results suggested that the virus-bearing vector expanded its geographic distribution from Vietnam to Jeju Island due to the effects of migration and climate change. Studies revealed that the impact of climatic variables and other factors on dengue fever depended on the region (Morin et al., 2013); therefore, there was a need to study these factors in the areas where dengue fever was expanding.

Researchers have not conducted quantitative studies of climate variability and migration in relation to dengue fever in Southeast Florida, United States, where recent autochthonous dengue fever cases have been found. Therefore, there was a need to determine whether climate changes and migration were the primary factors for the expansion of dengue fever in this particular region.

Problem Statement

Dengue fever is a disease that is transmitted by a mosquito that continues to spread to other regions to become a risk for additional populations, making this disease a major public health problem (Madoff, Fisman, & Kass-Hout, 2011). Usually, patients with the disease manifest classic dengue fever symptoms similar to influenza symptoms including severe headaches; aching joints, muscles, and bones; and sometimes a rash (Schmidt, 2010). A portion of patients develop potentially lethal forms of dengue known as *dengue hemorrhagic fever* (DHF) and *dengue shock syndrome* (DSS; Schmidt, 2010). Dengue hemorrhagic fever (DHF) can occur when a patient is infected with a second dengue serotype; about 20-30% of patients with DHF will progress to DSS, which is the most severe form of dengue (Bouri et al., 2012). Intense supportive treatment can lower the fatality rate to 1%; nevertheless, if the disease is not treated, the fatality rate can be as high as 10% (CDC, 2012).

Prevention programs, which include vector control and removal of breeding sites, have been unsuccessful for most endemic countries (Simmons et al., 2012), and dengue vaccines are not yet available (Bouri et al., 2012). Additional data have convinced scientists that human activity is the leading cause of temperature increases in the earth's troposphere resulting in global climate change (Shuman, 2011). Because climate change may alter patterns of precipitation and temperature, scientists expect a significant impact on human health, mostly from vector-borne infectious diseases such as dengue (Shuman, 2011).

The global burden of dengue resulting from climate change is contemplated to affect 5 to 6 billion people (about 50% of the world population) by 2085, based on projections on the expected effect of climate change on humidity (Hales et al., 2010). As a result of climate change, combined factors such as higher temperature, increased precipitation, and migration may make dengue fever and its complications a major public health threat (Shuman, 2011). The threat will affect not only endemic areas, but also nonendemic areas where the vectors (e.g., *A. aegypti*) will be able to survive and proliferate (Shuman, 2011).

Recently, several quantitative studies have been performed to correlate climate change and other variables with dengue fever within endemic regions such as Mexico, Puerto Rico, Vietnam, Singapore, and South Korea (Colon-Gonzalez, Fezzi, Lake, & Hunter, 2013; Hii et al., 2009; Johansson, Cummings, & Glass, 2009; Lee et al., 2013). Few quantitative studies have been conducted on the correlation among climate change, imported dengue fever cases, and dengue fever in nonendemic regions.

One study was conducted in the subtropical regions of Taiwan (Shang et al., 2010), in which results indicated that imported dengue cases can trigger autochthonous cases when weather conditions are met. At present, no study has been conducted in southern nonendemic areas of the United States such as the Treasure Coast of Florida (including Palm Beach, Martin, St. Lucie, and Indian River Counties). According to Mills et al. (2010), reliable data on the effects of climate change on vector-borne zoonotic disease are scant; therefore, the author stressed that, while preliminary studies have accumulated some data, conclusions remain speculative until more studies are conducted.

Dengue has the potential of emerging as a public health threat in the United States as more regions experience outbreaks of this disease, which can have serious health and economic consequences (Bouri et al., 2012). Several positive social change implications may arise from this study, including increased scientific knowledge concerning the effects of climate change and other variables in relation to vector-borne infectious diseases such as dengue. Knowledge gained from the study may justify the development of preventive environmental management programs to control the expansion of the vectors and virus into nonendemic areas.

The evidence from this study and other studies may help policy makers to develop policies for communicating to the public how to prevent or mitigate the effects of dengue fever in regions at risk.

Purpose of Study

The purpose of this quantitative ecological study was to determine whether changes of local climate (precipitation and temperature) and migration in Southeast Florida are related to the expansion of the ranges of dengue fever within that area. This study used secondary data from the National Climatic Data Center (NCDC)/National Oceanic and Atmospheric Administration (NOAA) in Asheville, NC, as well as data from Florida's public health system, the CDC, and the U.S. Census Bureau for migration trends over 34 years (1980-2013).

The study's intent was to correlate temperature, precipitation, and migration with autochthonous (locally acquired) dengue fever cases in a specific region. The independent variables were temperature, precipitation, and migration, which may be important agents driving the geographic limits of dengue transmission to nonendemic regions. The dependent variable was the geographic expansion of the ranges of dengue fever, which was defined as the appearance of autochthonous dengue cases in nonendemic areas.

Research Questions and Hypotheses

Research Question 1: Was there a significant relationship between temperatures during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship of temperature during 34 years in Southeast Florida with the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship in temperature during 34 years in Southeast Florida with the geographic expansion of dengue fever within the region.

Research Question 2: Was there a significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

Research Question 3: Was there a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida?

$H_{0:}$ There was no relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida.

H_1: There was a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida.

The independent variables were climatic variables, temperature and precipitation, and migration, which were continuous variables. The dependent variable was the expansion of dengue fever using the number of autochthonous dengue cases in the region, which also was a continuous variable

Conceptual Foundation

Arunachalam et al. (2010) developed a conceptual framework to explore the ecological, biological, and social factors involved in the breeding of the *Aedes* mosquito and dengue virus transmission. Arunachalam et al. constructed the framework based on a comprehensive field study in four cities and two provincial towns in Asia. The authors developed the protocol to answer one research question: What ecological, biological, and social factors determine dengue vector densities and contribute to viral transmission?

Arunachalam et al. (2010) conducted their field study during a 2-year period in regions endemic to dengue fever, carrying out household surveys, background surveys, and entomological surveys. The authors understood that the variables influencing vector breeding were many and complex. According to their framework, rain and temperature influence vector ecology, including feeding opportunities and breeding sites, and dengue transmission is directly influenced by temperature. Migration is part of the social and ecological context, including urbanization, habits, and water supplies.

Eco-bio-social research on dengue was an appropriate framework for the study because it included the specific variables of interest and determined how these variables interacted with each other. In Chapter 2, the reader will find a more detailed explanation of the connection between the framework and the research questions.

Nature of Study

The study was a quantitative ecological study using secondary data in a retrospective approach. The ecological study design may be used to evaluate the relationship between exposure and disease at the population level instead of the individual level (Aschengrau & Seage, 2008). Ecological study design was suitable for important questions that could not be easily answered by other study designs, and ecological studies involve research where some or all of the variables are ecological in nature (Tu & Ko, 2008).

The objective of the study was to investigate the relationship of climatic variables (temperature and precipitation) and the migration of imported dengue cases on the geographic expansion of dengue fever in Southeast Florida. Because an ecological study focuses on the population level and its exposure to the disease, the population level for my specific study was the population of the Treasure Coast of Florida (e.g., Palm Beach, Martin, St. Lucie, and Indian River), which has more than doubled during the last 30 years from 787,904 to 1,886,235 (U.S. Census, 2014).

In this study, I used secondary data on climatic variables (temperature and precipitation) from land-based stations located in specific regions in Southeast Florida. The climatic independent variables, temperature and precipitation, were continuous variables that included 34 years of data. The data were collected from the National Climatic Data Center (NCDC), a branch of the National Oceanic and Atmospheric Administration (NOAA) located in Asheville, NC. The data on migration (independent variable) were retrieved from the U.S. Census and covered 34 years. The data on dengue cases were accessed through the websites of the Florida Department of Health and the Centers for Disease Control and Prevention (CDC); the data set included the years 1980 to 2013.

The goal of the study was to determine whether a correlation existed between the climatic variables and migration, and the variable geographic expansion of dengue fever in the subtropical region of Southeast Florida. Chapter 3 contains a detailed explanation of the methodology of the study.

Operational Definitions

The following operational definitions are important in this study.

Aedes aegypti: Scientific name of the primary mosquito that transmits viral diseases, mostly dengue fever, also known as the *yellow fever mosquito* (CDC, 2014a).

Autochthonous disease: A disease originating in the place in which it was found; in the study, it may be referred to as *locally acquired disease* (Bauman, 2013).

Baseline temperature/precipitation: Computed by averaging 30 or more years of temperature/precipitation data (NOAA, n.d.b).

Climate: The long-term trend of temperature and precipitation averages, including extremes, for specific regions. The climate definition includes different time intervals—

months, years, seasons, decades, or given dates of the year—and includes local regions and may be global in extent (NOAA, n.d.).

Climate normals: The latest three-decade averages of climatological variables, which include temperature and precipitation (NOAA, 2011).

Extrinsic incubation period: The time taken by an organism to complete its development in an intermediate host. In the mosquito, the term refers to the time span in which the mosquito takes a viremic blood meal and becomes infected (Tjaden, Thomas, Fischer, & Beierkuhnlein, 2013).

Geographic expansion of dengue: The appearance of autochthonous dengue cases (locally acquired) in areas where it was previously absent.

Hyperendemicity: Refers to multiple serotypes of dengue virus existing in an area (Oki &Yamamoto, 2012); these include the four serotypes of the dengue virus, Den 1, Den 2, Den 3, and Den 4.

Intrinsic incubation period: The time taken by an organism to complete its development in the definitive host. In humans, the term refers to the time span in which the human becomes infected and the onset of symptoms occurs (Tjaden et al., 2013).

Migration: Refers to the migration of imported dengue cases to nonendemic regions.

Precipitation: Precipitation normals that include rainfall and liquid water equivalent of freezing precipitation. Precipitation was measured by tenths of millimeter (mm) units (NOAA, n.d.).

Temperature: The numerical measure of detection of heat. Temperature was reported in degrees and tenths in Celsius (°C) units (NOAA, n.d.).

Temperature/precipitation anomaly: The difference from the average or baseline temperature/precipitation (NOAAb, n.d.).

Vector: In epidemiology, an animal (typically an arthropod) that transmits a disease from one host to another (Bauman, 2013).

Vector-borne disease: An illness caused by an infectious virus or other microbe transmitted by blood-sucking arthropods to a host (Bauman, 2013).

Zoonotic disease: Disease naturally spread from usual animal host to humans (Bauman, 2013).

Assumptions

The study used secondary data on dengue cases from the Public Health Department of Florida and the CDC; therefore, assumptions were made related to the data. First, the assumption was made that the cases of dengue reported followed the case definition and that the physicians had completed all the necessary documentation. This assumption was necessary because the analysis were based on this secondary data, so I assumed that all of the dengue cases were properly diagnosed.

A second assumption was made related to the immunity of the population of Southeast Florida. I assumed that the immunity of this population for all the serotypes was susceptible to the dengue virus; therefore, I assumed that the number of susceptible individuals in this region was high. This assumption was necessary to help explain the autochthonous (locally acquired) dengue cases in a nonendemic region.

Damal, Murrell, Juliano, Conn, and Loew (2013) researched the phylogeography of the dengue vector *A. aegypti* and found that Florida’s landscape was not a barrier for the human-aided dispersal of the mosquito. The researchers found *A. aegypti* in various locations of Florida such as West Palm Beach, Ft. Lauderdale, and Jensen Beach (part of the Treasure Coast) in 2006. Based on these findings, I had a third assumption: Mosquitos gradually spread from the Florida Keys, located in the extreme southern portion of Florida, northward to the Treasure Coast. This assumption was necessary to help explain that the landscape did not interfere with the expansion of *A. aegypti*.

Scope and Delimitations

According to FDH (2012), a dengue outbreak was reported in Martin County with a mixture of imported and autochthonous (locally acquired) dengue cases. The report was interesting because that region of Florida was a nonendemic area for dengue fever. The outbreak was one of several during recent years, potentially indicating the spread of dengue to this region; therefore, the scope of the study included the counties of Southeast Florida.

The Southeast Florida region, the Treasure Coast, has four counties: Palm Beach, Martin, St. Lucie, and Indian River Counties. During the last 10 years, these four counties have increased in population; resident growth from 2000 to 2010 in Palm Beach County was 16.7%, in Martin County was 15.5%, in St. Lucie County was 44.2%, and in Indian River County was 22.2%. The increase of population in these regions was due to natural increase (22%), international migration (41%), and domestic migration (37%). These numbers showed that the population was a mix of natural residents (American born) and foreign-born residents (SFRPC, 2012).

According to the South Florida Regional Planning Council (SFRPC, 2012), the foreign-born residents came from Latin America, mostly from the Caribbean (Cuba, Dominican Republic, Haiti, Jamaica, and Puerto Rico), Central America (Mexico and Nicaragua), and South America (Colombia, Honduras, Peru, and Venezuela). These demographic data gave an idea of the overall characteristics of the population in Southeast Florida, and these immigrants came from countries that were endemic for dengue fever. Groups not included were populations to the north, center, and east of Indian River County.

Several studies have researched the relationship among climatic variables, imported dengue cases, and dengue fever (Colon-Gonzalez et al., 2013; Huang et al., 2013; Shang et al., 2010). The findings indicate relationships among climatic variables, imported dengue cases, and dengue fever in different parts of the world. The findings from this study can be generalized to similar populations and geographies where dengue fever may have a high risk of spreading.

Limitations

The study had several limitations; the primary limitation was the lack of individual-level information that can lead to a bias known as *ecological fallacy*. Bias can occur when the relationship that exists between the variables at an aggregated level may not represent the real relationship that exists at the individual level (Tu & Ko, 2008). In other words, the inference of the population having the same characteristics in the region as the individual level may not necessarily be accurate. To avoid the ecological fallacy, the findings were analyzed and interpreted only at the levels at which they were measured; this meant that the findings were limited to the region of the Treasure Coast in Florida. These findings cannot be generalized to other areas where the climatic variables and the characteristics of the populations are different.

Another limitation was the possibility of underreporting or overreporting dengue fever cases in the area by the surveillance systems, in which case the estimation of the disease rate and mortality might be affected. The data reported were based on passive reporting by physicians, other health care staff, and laboratories in Florida (FDOH, 2012). The reporting was mostly dependent on when a person becoming ill sought medical attention, in which case the physician or authorized personnel reported the case after receiving a positive diagnosis of dengue fever from the laboratory (FDOH, 2012). Sometimes, steps were omitted in this process, so the number of reported cases may represent only a portion of the real number of cases of notifiable diseases occurring each year in Florida (FDOH, 2012).

Evaluations of reporting systems for notifiable diseases indicate that completeness can vary by disease (Doyle, Glynn, & Groseclose, 2002). These differences in report completeness for diseases’ occurrence at the local level may indicate, with certain variations, differences in the real occurrence of disease and in the rigor with which surveillance was executed (Doyle et al., 2002). Also, there was the possibility of large numbers of undetected asymptomatic cases; such cases might have been carriers that facilitated dengue transmission. In January 2010, dengue fever and viral hemorrhagic fever were added to the list of nationally notifiable infectious diseases (CDC, 2010); however, in Florida, dengue fever became a reportable disease around 2008 (FDOH, 2012).

A limitation to be considered is that the results of studies should not be assumed to be applicable to other nonendemic regions where outbreaks of dengue fever were observed. Application of the results may not be appropriate because of differences in local climate, human interactions with the environment, socioeconomic factors, and local geography or landscape. Finally, there was limited information about the presence of the dengue fever vector, *A. aegypti*, in Southeast Florida (e.g., Treasure Coast) before 2013. Information about autochthonous dengue fever in this area in 2013 is available, and some recent articles have addressed the situation.

Significance

In providing information on the impact of climatic variables (temperature and precipitation) and migration on infectious diseases, especially on vector-borne diseases, this study contributes to the body of knowledge for policy makers and scientists. This study may increase awareness of the effects of climate change and how it will affect the health of communities on a regional, national, and global scale. Changes in vector-borne diseases are being seen around the world, and more populations are vulnerable to these diseases (Shuman, 2011). Studies of this nature are needed to increase the evidence of climate change to prompt countries to join in an effort to minimize the factors that are affecting the world.

The social change implications of this study include not only adding to the body of knowledge about climate change and infectious diseases, but also contributing to a better understanding of the complexities of the transmission of the dengue virus and how it relates to climate change and migration. At the community level, this study may be useful for local policy makers seeking to develop programs to educate the community and to help prevent and mitigate the effects of dengue, especially in regions where this disease is not endemic. At the national level, the study contributes additional data about climate change and its effects on health for policy makers to use in developing programs that will benefit the environment and populations. At the global level, studies like this one offer data about the impact of climate change on the distribution of infectious diseases.

Summary

Scientists have formulated hypotheses concerning the effects of climate change on infectious diseases; their predictions include that vector-borne diseases such as dengue and malaria will re-emerge due to changes in temperature and precipitation. Many quantitative studies focus attention on these climatic variables in particular regions, based on studies that show that local or regional variation in climate and geographic factors affects the rate of disease. These variations limit the scientist to researching local regions and investigating how the variables impact certain diseases, mostly vector-borne infectious diseases, which are susceptible to temperature and precipitation.

No quantitative study has been conducted to research the effects of temperature, precipitation, and migration on the expansion of dengue fever in Southeast Florida. These regions, composed of four counties—Palm Beach, Martin, St. Lucie, and Indian River—were nonendemic regions for dengue fever; however, cases of autochthonous dengue fever had been observed during the past year. Therefore, the purpose of this quantitative ecological study was to determine if a correlation existed among temperature, precipitation, and migration with the expansion of dengue fever in nonendemic regions of Southeast Florida.

I used the conceptual framework of eco-bio-social research on dengue. Arunachalam et al. (2010) described links between ecological, biological, and social factors in the population of the *Aedes* vector and the dengue virus. For this study, I used secondary data from the NCDC, the Florida Health Department, and several studies about the expansion of dengue fever. This study has implications for positive social change in that it may promote a better understanding of the influence of climatic variables in vector-borne infectious diseases in nonendemic areas.

The evidence from this study adds to the body of knowledge about the impact of climatic variables and social factors on the population of vectors and vector-borne diseases. This study and other studies of this nature may help scientists to understand how these factors interact to result in the expansion of dengue fever to nonendemic regions.

Chapter 2 of this study provides more detailed information on the characteristics of the vectors, the dengue fever virus, and how the vector is affected by temperature and precipitation. Included are the search strategies used to conduct the literature review and more details about the theoretical base of the study. Additionally, I address quantitative research about dengue fever and the study designs and methodology used by other researchers.

Chapter 2: Literature Review

Introduction

Until recently, dengue fever was considered a disease that mostly affected populations from countries in the Caribbean, Central and South America, the Eastern Mediterranean, South-East Asia, and the Western Pacific (WHO, 2014). Dengue fever was not considered endemic to the continental United States; the dengue cases of U.S. citizens occurred in Puerto Rico, the U.S. Virgin Islands, Samoa, or Guam and were imported to the United States (Gentry, 2012). Dengue cases were also reported in travelers from dengue-endemic regions visiting the United States. (CDC, 2013). The disease was viewed as a neglected tropical disease affecting populations in developing countries and not typically affecting populations in the United States (Bouri et al., 2012).

However, after more than 50 years without local dengue occurrences, numerous autochthonous cases emerged on the Texas-Mexico border (2005-2006) and in Key West, Florida (2009-2011; Eisen, 2013). These outbreaks demonstrated the potential for the emergence of dengue fever in nonendemic regions of the United States (Radke, Gregory, & Carina, 2012). The cause of the reemergence of dengue in Florida is unknown (CDC, 2010); possibilities include the following: (a) the disease had been present and had started being detected, (b) environmental conditions were favorable, (c) there was an abundant presence of the mosquito, and (d) there was more opportunity for the mosquito to bite humans (CDC, 2010).

The vector of dengue, the *Aedes* mosquito, has been established in more than 100 tropical and subtropical countries (Hii, Zhu, Ng, Ng, & Rocklov, 2012). The mosquito has facilitated the reemergence or expansion of dengue fever in developed countries around the world in tropical and subtropical areas, and it is now a threat for the United States (Bouri et al., 2012).

The purpose of this study was to correlate the relationship between climatic variables and migration with the geographic expansion of dengue fever into the southeast region of Florida. The climatic variables used for the study were precipitation and temperature. Several studies have suggested that climate change may promote the geographic expansion of many vector-borne diseases such as yellow fever and dengue (Foley, 2001; Jetten & Focks, 1997; Johansson, Dominici, & Glass, 2009; Lee et al., 2013; Patz, Martens, Focks, & Jetten, 1998).

Several studies have suggested the influence of imported dengue cases and climatic variables as factors that may promote the expansion of this disease to nonendemic regions (Huang et al., 2013; Shang et al., 2010). During the last 50 years, studies have revealed unprecedented expansion in the geographic distribution of dengue fever globally, with nearly 400 million people infected and a quarter of these presenting the acute illness (Low & Ooi, 2013).

As mentioned before, multiple factors have been assumed to contribute to the demographic expansion of dengue fever. Some researchers have argued that factors such as increase in the global population, immigration of population from endemic areas, poverty, and lack of sustained pest control programs are important reasons for the expansion (Guzman & Isturiz, 2010). They have argued that the specific contribution of these factors is difficult to measure, but many researchers have agreed that temperature and precipitation are the most important factors (Alto & Bettinardi, 2013; Couret, Dobson, & Benedict, 2014; Morin et al., 2013; Yang et al., 2009). Gubler et al. (2002) explained the relationship between climatic variables and vector-borne diseases, stressing the importance of temperature, rainfall, and other climatic variables on the survival rate and behavior of the vector, and the decrease or increase of the probability of transmission of the virus. Shang et al. (2010) addressed the unknown role of imported cases in dengue epidemics in nonendemic areas; their study revealed that imported cases have a role in initiating autochthonous dengue cases once the meteorological conditions are favorable and the mosquito is present (Shang et al., 2010).

Although researchers have identified the primary climatic factors and some studies have identified migration or imported cases as facilitators of the expansion of dengue fever in endemic regions, there is a need to correlate the climatic variables, migration, and the expansion of dengue in nonendemic regions in the United States.

Chapter 2 contains information regarding the literature review search strategy, details of the theoretical foundation of the study, and reviews of the current literature on climate change, migration/imported cases, and dengue fever. The review section includes some of the categories of the conceptual framework: environment (temperature, precipitation); vector ecology; virus (replication, transmission); and social context (migration).

The study used current literature from Carrington, Armijos, Lambrechts, Barker, and Scott (2013); Chan and Johansson (2012); Hii et al. (2012); Morin et al. (2013); Tjaden et al. (2013); and Yang et al. (2009). Also seminal articles were used from

Christopher (1960); Gubler et al. (2002); Hanson (1936); Jetten and Focks (1997); Patz et al. (1998); and Watts, Burke, Harrison, Whitmire, and Nisalak (1987). These studies were related to climatic variables and migration and their effects on dengue fever, the vector, and the virus. A summary and conclusion is presented at the end of the chapter.

Literature Search Strategy

The search strategy for the literature review mostly involve use of Walden University Library's multiple database search tool, Thoreau, as well as Google Scholar, PubMed, and Science Direct. Google Scholar was linked with Walden's library, and the Document Delivery Service was used to request several articles not available in the library. "Related articles" in PubMed and Google Scholar and the "cited by" feature were used to search using the articles cited in both search engines.

Multiple open-access peer-reviewed articles were retrieved from PLOS Neglected Tropical Diseases, PLOS One, and Infection Ecology and Epidemiology. The program Mendeley was used to store articles and to search for articles using key words.

The search included traditional terms for *climatic changes* and *dengue fever*, terms used in articles related to these topics, and MESH terms found in some articles. The terms for climate changes included *temperature*, *precipitation*, *rainfall*, *relative humidity,* and *ENSO*. For dengue fever, the terms used included *vector-borne infectious diseases, dengue, Aedes species, Aedes aegypti, autochthonous dengue, imported dengue cases dengue serotypes, re-emerging diseases, geographic expansion, dengue epidemiology,* and *dengue transmission*. In addition to the terms mentioned, the search included combined terms such as *tropical and subtropical countries*, *dengue fever and*

Puerto Rico, *dengue fever and United States*, *dengue fever and climatic changes*, and *Florida and dengue fever*.

The primary sources for the literature review were peer-reviewed articles whose publication dates were between 2009 and 2013. There were some articles with publication dates prior to 2009, but these were kept to a minimum. The reason the search and literature review included articles older than 2009 was because such articles offered important context relevant to the conceptual framework, seminal work, and historical background. The search also included review articles and references from specialized websites such as the National Oceanic and Atmospheric Agency (NOAA) and the Centers for Disease Control and Prevention (CDC).

Conceptual Foundation

Arunachalam et al. (2010) developed a conceptual framework indicating a relationship among the ecological, biological, and social factors in dengue fever. The framework was developed based on a field study that the authors conducted in several countries in Asia. The objective of the framework was to answer several research questions, including questions concerning the identification of the ecological, biological, and social determinants of dengue vector density and its contribution to viral transmission. The study was conducted in several large cities, provincial areas, and peri-urban regions in dengue-endemic locations in Asia.

The authors researched the direct and indirect relationships among social and ecological context, vector ecology, and vector control in relation to *A. aegypti* population density and its relationship with dengue transmission. They emphasized the complexity of these relationships and how interaction and changes can affect each part of the system by either decreasing or increasing dengue transmission (Arunachalam et al., 2010).

The framework was the result of the following information:

- findings from field study conducted in six Asian cities or periurban areas;
- collection of information from household surveys, neighborhood background surveys, and entomological surveys;
- review of studies of climate variables, temperature, and rain, and their effects on dengue transmission and vector density;
- assessment of vector breeding sites; people's knowledge, attitudes, and practices related to dengue; and the characteristics of the study areas (Arunachalam et al., 2010).

The result was ecological, biological, and social research on dengue, a conceptual framework (Figure 1) that illustrates the factors influencing vector density that will influence dengue transmission.

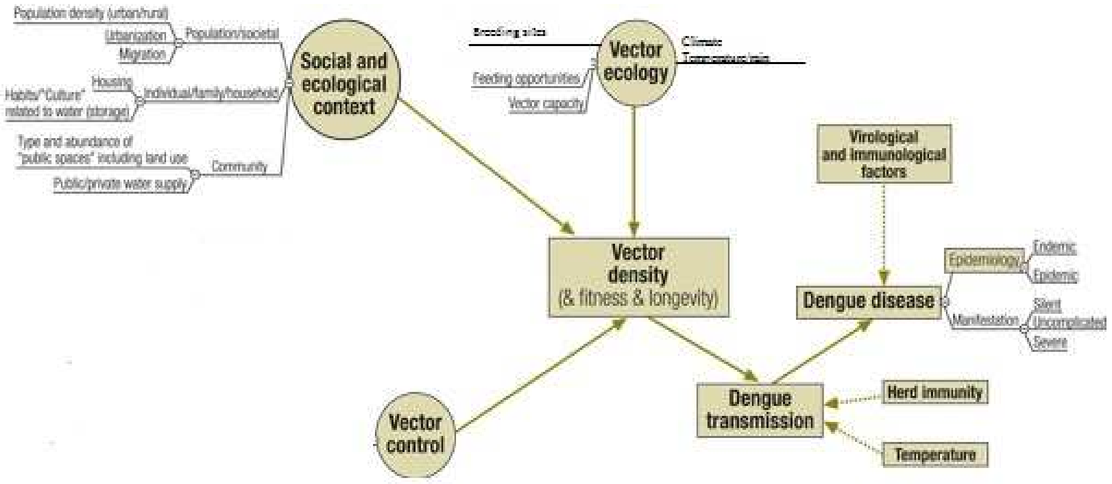


Figure 1. Eco-bio-social research on dengue, a conceptual framework. Adapted from "Eco-Bio-Social Determinates of Dengue Vector Breeding: A Multicountry Study in Urban and Periurban Asia," by N. Arunachalam et al., 2010, *Bulletin of the World Health Organization* 2010, *88*, 173-184. Reprinted with permission (see Appendix B).

This model shows how the social and ecological context, which includes human population density by immigration and urbanization, directly influences vector density. Also, vector ecology, which includes climate, rain, temperature, breeding sites, vector capacity, and feeding opportunities, directly influences vector density. Vector control influences the population and density of mosquitos if these procedures are used in the areas of study.

Ecological, biological, and social variables are interdependent factors for dengue vector production with a direct impact on dengue transmission and dengue transmission are influenced by temperature. Ecological factors are related to climatic variables (temperature, precipitation) and natural and manmade ecological conditions (Quintero et al., 2014). Biological factors include the behavior of the mosquito *A. aegypti* and the transmission dynamic of the dengue virus (Quintero et al., 2014).

The framework includes a climate variable, temperature, which has a direct influence on viral transmission and vector ecology. The other climate variable, precipitation, has a direct influence on vector ecology. In relation to vector ecology (Figure 2), according to Morin et al. (2013), an increase in temperature will increase the development and increase survival of the vector; an increase in temperature will also accelerate the reproductive rate of the vector (mosquitos). The accelerated reproduction of the mosquitos will increase the likelihood of transmission by increasing the number of blood feedings (Morin et al., 2013).

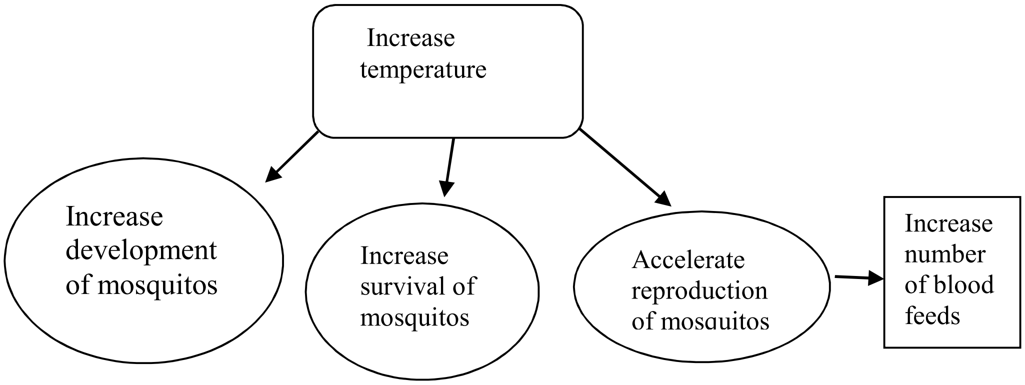


*Figure 2.*Effects of temperature on vector ecology. Adapted from "Climate and Dengue Transmission: Evidence and Implications," by C. W. Morin, A.C. Comrie, and K. Ernst, 2013, *Environmental Health Perspectives*, *121*, p. 1265. Reprinted with permission.

In relation to viral transmission, an increase in temperature will increase transmission by reducing the length of the extrinsic incubation period (EIP). Finally, increased temperature will increase the probability of survival of the adult mosquito and will raise the amount of viral replication inside the mosquito (Morin et al., 2013).

The effects of temperature on viral replication and transmission were documented in several studies. Watts et al. (1987) suggested that temperature influenced the replication rate of the dengue virus in *Aedes* vectors; however, the results also suggested that temperature has no effect on the establishment of infections in these vectors.

A more recent study indicated a shorter viral extrinsic incubation period (EIP) when the temperature increases. The data showed that at a temperature of 25°C, the EIPs ranged from 5 to 33 days, and at 30°C, the EIPs ranged from 2 to 15 days (Chan & Johansson, 2012). This means that an increase of 5°C in temperature will decrease the development time of the virus by one half. Patz et al. (1998) found that dengue transmission increased with a small increase in temperature. The authors explained that the findings indicated that fewer *Aedes* vectors would be necessary to spread and maintain dengue fever within a susceptible population.

Members of the genus *Aedes*, vectors for the dengue fever virus, are susceptible to temperature. Studies have shown that higher temperature increases the larval development rate, shortens the time span before the adult mosquito emerges, and increases the vector biting rate (Thai & Anders, 2011). Jansen and Beebe (2010) suggested that temperature and rainfall influenced larval abundance and development. Nevertheless, the association between rainfall and larval abundance and development varied greatly between regions and habitats.

Morin et al. (2013) suggested that the dengue virus can be found in *A. aegypti's* competitor, *Aedes albopictus*. Most of the research reviewed involved the assumption that *A. aegypti* was the primary vector for dengue fever (Akbari et al., 2013); Morin et al. understood that *A. albopictus* also has the potential to be a vector for the virus. Nevertheless, some studies have found evidence that *A. albopictus* is less susceptible to dengue fever infections and less susceptible to the virus disseminating to the salivary glands (Lambrechts, Scott, & Gubler, 2010).

The broad eco-bio-social conceptual framework was a tool developed by a research partnership between the Special Programme for Research and Training for Tropical Diseases at the World Health Organization and the Ecosystem and Human Health (EcoHealth) program of Canada's International Development Research Center (IDRC; Quintero et al., 2014).

The eco-bio-social framework has been used in several studies. Quintero et al. (2014) used the framework to identify the key factors associated with vector breeding in several countries in Latin America. Kittayapong et al. (2012) researched the application of eco-bio-social tools to control dengue vectors in Thailand. Quintero et al. argued that this tool has been used to understand the factors influencing the vector population; the author also stressed that areas or regions under study are different from each other. Differences include community dynamics, the ecology, geography of regions, urbanization, and vector control practices (Quintero et al., 2014).

The framework developed by Arunachalam et al. (2010) was suitable for the study because it includes the principal variables of research: temperature, precipitation, and migration. For this study, the social factor researched was the migration aspect of the framework.

***Aedes aegypti*, Vector of Dengue Fever**

Aedes aegypti is a small to medium sized mosquito, 4-7 mm long with a life span of a couple of weeks to months, depending on environmental conditions (Dengue Virus Net, 2014). According to Zettel and Kaufman (2012), *A. aegypti* is a polytypic organism with three different subspecies, domestic, sylvan, and peridomestic. Powell, and Tabachnick (2013) considered the mosquito as a monophyletic group, with the domestic form of the *A. aegypti* dominating tropical and subtropical regions of the world.

The domestic variety of the mosquito has evolved to live in close proximity with humans and their dwellings; they are active in the daytime and can bite indoors as well as outdoors (CDC, 2012). The close association with humans has provided opportunities for the mosquito to adapt and exploit a variety of sites for the oviposition of eggs and the development of the larvae (Eisen & Moore, 2013).

The mosquito is a holometabolous insect; in other words, it undergoes a complete metamorphosis with an egg, larval, pupal, and adult stage (Zettel & Kaufman, 2012). The female mosquito is larger than the male mosquito and the female requires a blood meal to produce eggs. The female mosquito will produce from 100 to 200 eggs, depending on the size of the blood meal, and can produce five batches of eggs during its lifetime (Zettel & Kaufman, 2012). According to Eisen and Moore (2013), the female can take multiple partial blood meals from different humans: this practice increases the probability of feeding on infected individuals with dengue and increases the probability of infecting many individuals during a short time.

The capacity of the mosquito to disperse over long distances was crucial for the geographic extension of dengue fever (Harrington et al., 2005). Liew and Curtis (2004) concluded that female *Aedes* species could disperse horizontally quickly and easily throughout areas with a radius of 320 m in search of sites to lay eggs. Harrington et al. (2005) found that *A. aegypti* moved from 50 to 100 m after release.

Liew and Curtis (2004) found that mosquitoes disperse horizontally and vertically. Mosquitoes ranged in apartment blocks from the 12th floor to the 21st floor and laid eggs on each floor. The ability of *A. aegypti* to disperse extensively horizontally and vertically allows the mosquito to lay eggs in apartments and neighboring communities (Hii, 2013).

Aedes aegypti **Lifecycle**

The *A. aegypti* lifecycle has two phases which consist of terrestrial and aquatic phases (Figure 3; CDC, 2012). In the terrestrial phase, the female mosquito will bite humans several times when seeking to lay eggs (Padmanabda, Durham, Correa, Diuk-Wasser, & Galvani, 2012). The female mosquito will feed twice a day, in the morning, and late afternoons (Hii, 2013). An important characteristic of the female *A. aegypti*, contrary to other mosquito-human systems, is that it feeds, rests, and lays eggs indoors or outdoors in proximity to humans and has adapted to prefer human blood for its energy source for reproduction (Padmanabha et al., 2012).

After the blood meal, the female will lay eggs on surfaces or containers that will likely be temporarily wet (Zettel & Kaufman, 2012) or just above the waterline (CDC, 2012). The female can lay a batch of around 100-200 eggs, and in her lifetime she can produce up to five batches (Denguenet, 2014).

The eggs resist desiccation for six or more months (CDC, 2012), are not laid all at once and are laid separately (CDC, 2012). The aquatic phase starts when the rain or water in natural or artificial containers floods the eggs; the larvae hatch and will feed on bacteria, algae or small particles of plants (CDC, 2012).

The larvae have various developmental stages three molts; these stages are called first to fourth instars (Nature Education, 2014a). When the larvae reach full growth (fourth instar) it goes through metamorphosis to form a pupae. The pupae will take two days to develop into an adult mosquito, which will break the exoskeleton of the pupa and will be able to fly to search for a terrestrial habitat (Nature Education, 2014a).

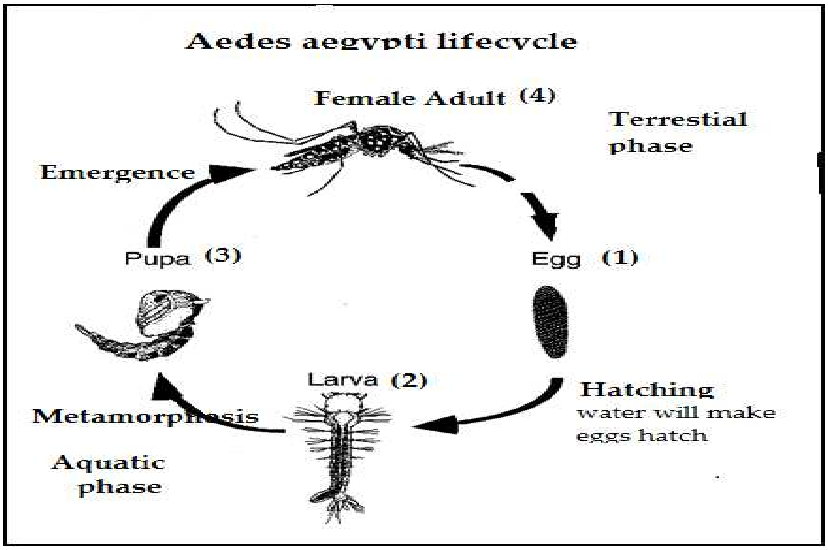


Figure 3. Aedes aegypti lifecycle. Female mosquito (4) after blood meal. Eggs (1) can withstand no water for more than 6 months. Larvae (2) hatch when in contact with water, and undergo a metamorphosis to form a pupa (3). Two days later, a mosquito emerges. The entire lifecycle lasts 8 to 10 days, depending on the environment.

Climate and *Aedes aegypti*

The entire *A. aegypti* mosquito lifecycle takes approximately 1 or 2 weeks to complete; it may be shorter or longer, depending on the temperature, water, and nutrients in the aquatic phase. Higher temperatures will shorten the duration of the lifecycle (Hii, 2013). Yang et al. (2009) researched and estimated the rates of mortality of the aquatic phase and the adult mosquito in relation to temperature. The results indicated the optimal range of temperature for development of the larva and pupa was 15 °C< T< 35 °C, and the optimal range for the survival of the adult mosquito was 15 °C < T < 30 °C.

At 26 °C, a quick transition occurs within the aquatic stage. These differences in temperature in the phases of the lifecycle may indicate that the effects of temperature on the mosquito's lifecycle are different for distinct stages (Yang et al., 2009). The authors also found that at lower temperatures the development of the larva to pupa to adult does not occur, nor does the female mosquito increase its oviposition. The optimal temperature which will yield the highest number of offspring was 29.2 °C.

Carrington et al. (2013) conducted laboratory studies that indicated immature development times were highly dependent and inversely related to temperature to a maximum of 35 °C. The researchers found that large diurnal temperature ranges will accelerate the development of the larva, but beyond the threshold of 35 °C, the development will begin to decline. An earlier study on the effects of temperature and larval development rates and survival found that the development from egg to adult inversely related to temperature, from 7.2 ± 0.2 days at 35 °C to 39.7 ± 2.3 days at 15 °C (Tun-Lin, Burkot, & Kay, 2000). The authors found the minimum temperature threshold for development was 8.3 ± 3.6 °C with a maximum survival rate (88% to 93%) at 20 °C to 30 °C.

Carrington et al. (2013) and Tun-Lin et al. (2000) researched and agreed on the maximum temperature threshold of 35 °C for the development of larvae; however, Tun-Li et al. (2001) conducted field studies and found greater variability for the development rates, when compared to the research done in laboratories. Both authors cautioned on the results of these studies because of unique circumstances of temperature and mosquito populations for the different regions where studies were conducted.

Couret et al. (2014) conducted a study where three different factors were analyzed: temperature, density of larvae, and diet. The findings showed that the temperature was the most significant factor impacting the immature cycle and the survival rate of larvae. However, the authors recommended that the larval density should be taken in account when predicting development rate and survival, but never excluding temperature.

Hii (2013) summarized the impact of temperature and rainfall on the rates of the development, feeding, and the population density. The author stressed that at higher temperatures, the lifecycle will decrease, and it will affect the size of the mosquito; if the lifecycle was reduced, the mosquito will be smaller and the feeding will increase. Dengue transmission rate will increase with increased feeding (Hii, 2013). Rainfall will provide for numerous natural and artificial breeding habitats, if the containers can hold at least 10 ml (20mm) of water the population density will increase rapidly (Hii, 2013). However, high temperatures above 35 °C or/and heavy rainfall can lower dengue transmission by reducing the survival rate of *Aedes* (Yang et al., 2009).

Aedes aegypti, as an adult, is considered the primary vector of dengue fever (Colon-Gonzalez, 2013). The mosquito lives in tropical and subtropical regions, mostly because the highest survival rate of the mosquito occurs in temperatures from 20°C to 30 °C. *Aedes aegypti* is considered as a poikilothermic organism (Brady et al., 2013); therefore, this mosquito is notably susceptible to changes in temperature, climate changes, and climate variability (Hopp & Foley, 2003). Distribution of *A. aegypti* historically has been limited by the 10 °C January and July isotherms (Christopher, 1960); although small variations in climate may not have a significant effect, temperature variations may result in detectable consequences at the local level (Canyon, Muller, & Hii, 2013).

Many articles have reported the influence of temperature and rainfall on the dengue distribution (Hii et al., 2009; Huang et al., 2013; Johansson et al., 2009), and on the development of the lifecycle, survival rates of vectors, biting rates, infective rates, and the incubation period of dengue virus (Hii et al., 2012; Maciel-de- Freitas, Torres Coceco, & Lourenco-de Oliveira, 2007; Tjaden et al., 2013; Tun-Lin et al., 2000; Yasuno & Tonn, 1970;). When temperature increases, *Aedes* mosquitos exhibit shorter periods of development in all stages of the life cycle, not only increasing population growth, but also increasing the mosquito feeding rate. The dengue viruses inside *Aedes* adult mosquitos require shorter incubation periods to migrate to salivary glands (Oki & Yamamoto, 2012; Yang et al., 2009).

Brady et al. (2013) found that the female adult *A. aegypti* will experience a reduction in mobility and decrease in capability to take a blood meal at a temperature below 14 °C to 15 °C; without a blood meal the mosquito will not survive longer than 3 days. Canyon et al. (2013) conducted a study that investigated if low and high relative humidity affected the biting rates of *A. aegypti*. The researchers found that host-biting did not decrease in low humidity; biting increased six times more than expected. The results were observed in a domestic arid strain of *A. aegypti* which will seek a host to bite multiple times to replenish its fluids and energy to lay eggs. Nevertheless, in high humidity and high precipitation where sugar was available, the host-biting rate decreased by half (Canyon et al., 2013).

The gonotrophic cycle, the time interval between two consecutive blood-meal feedings was temperature dependent (Lardeux, Tejerina, Quispe, & Chavez, 2008).

According to Hii (2013), higher temperature will reduce the gonotrophic cycle duration, increasing the feedings. Multiple feedings in the cycle will increase the risk of disease transmission by increasing the frequency of contact with the host (Farjana & Tuno, 2013). Eisen and Moore (2013) reported that a warmer climate could increase the propagation of the mosquito *A. aegypti*; however, the authors argued that this variable was not the only factor in the proliferation of the mosquito. The reproduction rates of the female mosquito will decline at temperatures over 35 °C and at temperatures of 16 °C or less. At these temperatures the mosquito will not reproduce; even though the mosquito will continue to bite, it will not lay eggs (Carrington et al., 2013).

The effect of rainfall was complex. Rainfall events can increment vector abundance by increasing the availability of immature stage habitat (Stewart-Ibarra, Ryan, Beltran, Mejia, Silva, & Munoz, 2013). However, heavy rainfall episodes can reduce mosquito abundance by washing out the larvae from breeding sites, and drought events can increase mosquito abundance by using more household water storage (Stewart-Ibarra et al., 2013). Rainfall and temperature were factors in influencing the incidence of dengue fever virus transmission. Huang et al. (2013) found thresholds for rainfall of 27 mm to be important in determining the rate of autochthonous dengue fever; if it was below this threshold the dengue fever cases will be restricted.

Barrera, Amador, and MacKay (2011) found that the number of adult mosquitoes were positively associated with the rainfall and temperature in Puerto Rico. Yasuno and Tonn (1970) correlated the rainy season in Thailand with the highest rate of dengue hemorrhagic fever. The authors also found that in the rainy season, there was an increase in the total time of biting during the day, and the biting was more spread out. During the cool months, the biting rate (number of female mosquitoes caught per man per hour) decreased to 1.48 and during the rainy season increased to 4.77. Temperature and rainfall were the most important predictors for *A. aegypti* abundance and oviposition activity, the rainfall factor depends on the region and the collection of rainfall (natural or artificial) (Stewart Ibarra et al., 2013).

Causative Agent: Dengue Virus

Dengue fever is caused by a virus that belongs to a larger designation known as the arboviruses, viruses transmitted by arthropods (e.g., mosquitoes, ticks, flies, mites, and lice; CDC, 2012). Specifically, the dengue virus belongs to the Flaviviridae family which are enveloped, icosahedral, positive, and single stranded RNA, and is the *Flavivirus* genus, dengue virus species (Bauman, 2013). An important characteristic of the RNA genome is that these were dynamic molecules; their structures change throughout the viral lifecycle, responding to the environment of the host cell (Iglesias & Gamarnik, 2011).

The *Flavivirus* genus includes other pathogens: West Nile virus (WNV), Japanese encephalitis virus (JEV), yellow fever virus (YFV), and tick borne encephalitis virus (TBEV). These viruses were transmitted by vectors and were classified as zoonosis; the JEV, WNV, and Saint Louis encephalitis virus (SLEV) have a cycle that includes the *Culex* mosquito and birds. The transmission stops with the human hosts, as dead-end hosts (Endy, Weaver, & Hanley, 2010). Yellow fever virus (YFV) has a cycle of transmission maintained in a sylvatic cycle that includes nonhuman primates and the

Aedes mosquito, but the virus has adapted to transmission in urban regions through the *A. aegypti* mosquito (Endy et al., 2010). The author explained that the virus no longer needs a nonhuman host, not like the other *Flavivirus* pathogenic viruses; therefore, the dengue virus is not classified as a zoonotic virus.

Phylogenetic studies of the dengue virus suggested that the dengue virus adapted differently from the other *Flavivirus*; the virus evolved into four antigenically and phylogenetically distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4 which was unique in the Flaviviridae family (Gubler, 2002). Each of the serotypes interact differently with the antibodies in the blood serum of humans; even though the four serotypes share 65% of the genome, there were still genetic differences among them (Nature Education, 2014b). Each serotype has emerged in an endemic cycle of transmission between the *A. aegypti* mosquito and humans.

Climatic Variables and Dengue Fever Virus

To determine the risk of dengue fever occurring in a specific region, the extrinsic incubation period (EIP) played a vital role (Tjaden et al., 2013). The EIP was the viral incubation period between the time when the mosquito takes a blood meal contaminated with dengue virus and the time when the mosquito became infectious (Chan & Johansson, 2012). The virus was ingested by a female mosquito, and time was required for the virus to replicate, move to the midgut, and spread through the mosquito's body until the virus reached the salivary glands.

In the salivary glands, the virus will pass to a host during the next blood meal of the infected female mosquito (Tjaden et al., 2013). The authors argued that the duration of the pathogen EIP was temperature dependent. Studies have shown that warmer air and water temperatures decrease the extrinsic incubation period, therefore increasing dengue virus titers in mosquitoes (Stewart Ibarra et al., 2013).

Rohani, Wong, Zamre, Lee, and Zurainee (2009) found that the EIP decreased, from nine to five days when the temperature increased from 26 °C to 30 °C. Higher temperatures facilitated a faster replication of the virus inside the mosquito *Aedes* and these were better able to transmit the virus. Campbell, Lin, Iamsirithaworn, and Scott (2013) agreed that the optimal temperature for transmission was 28 °C to 30 °C with a humidity of 80%, and with a humidity of 62% the optimal temperature was 24.5 °C to 26.5 °C; the maximum temperature for the highest transmission was 32.5 °C with the maximum humidity of 92%. The temperature has a regulatory role to trigger the viral transmission on or off, with a key threshold of 28 °C. Campbell et al. (2013) stressed that no dengue cases were found when the mean temperature was below 21 °C or minimum temperature of 14.5 °C.

These were important threshold temperatures because no virus was found in the salivary glands of the mosquito at 20 °C, and no larva reached the adult stage at 14 °C; these temperatures may represent barriers in weather for sustained transmission. Phillips (2008) suggested that in a cool climate, the virus will take a longer time to replicate inside the mosquito *A. aegypti*; therefore, the mosquito will die before it is capable of transmitting the virus to the host.

Clinical Overview of Dengue Fever

Dengue fever (DF), an acute febrile disease, was the most common arthropod-borne disease worldwide (Pye, 2012). An infective female mosquito transmitted the dengue virus which can be either *A. aegypti* (primary vector) or *A. albopictus* (secondary vector; CDC, 2014a). The disease was caused by any of the four closely related RNA virus serotypes classified as DENV 1, DENV 2, DENV 3, and DENV 4 (CDC, 2013). Each serotype can cause the classic dengue fever; nevertheless, if a recurrent infection occurred with a different serotype, the outcome could be the most severe form of dengue fever, dengue hemorrhagic fever (Khan et al., 2013). Even though an infection with one of the serotypes can produce lifelong immunity, no immunity was produced for the rest of the serotypes, although some studies have suggested short-term immunity (Pye, 2012).

The classical dengue fever symptoms are high fever, severe headache, severe joint, and bone pain, severe muscle pain, and sometimes a rash. According to the CDC (2012), in younger children and patients with first time dengue fever, these symptoms are milder in comparison with older children and adults. The symptoms usually are self-limiting and the duration of the primary infection is about seven days (Khan et al., 2013).

A reinfection with any dengue fever serotypes will cause dengue hemorrhagic fever which was the leading cause of viral hemorrhagic fever worldwide (Srikiatkhachorn et al., 2010). Dengue hemorrhagic fever (DHF) symptoms include high fever, hemorrhagic manifestations, skin bleeding, mucosa bleeding, gastrointestinal bleeding, plasma leakage, and thrombocytopenia associated with abnormal bleeding

(Srikiatkhachorn et al., 2010). Another clinical manifestation known as dengue shock syndrome (DSS) was defined as dengue hemorrhagic fever with circulatory failure.

The case definition of dengue fever has been changed since 1997 to accommodate a more complex classification for dengue severity (CDC, 2012). The classification was divided into dengue with no warning signs, dengue with warning signs, and severe dengue (CDC, 2012). The case definition for dengue with no warning signs was fever and two of the following: nausea, vomiting, rash, aches, pains, leukopenia (low white blood cell count), or positive tourniquet test (determines capillary fragility) (CDC, 2012).

Dengue with warning signs requires strict monitoring and medical mediation. Signs includes fever and any of the following: abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, liver enlargement, or thrombocytopenia (CDC, 2012). Severe dengue will require hospitalization and the signs and symptoms include: one of the following: severe plasma leakage, shock, fluid accumulation with respiratory distress, severe bleeding, or organ involvement such as enlarged liver, impaired consciousness, and failure of the heart and other organs (CDC, 2012).

No vaccine was available for any of the serotypes of dengue fever; no preventive treatment and no antiviral drug treatment existed for dengue fever. Patients were treated for their symptoms with appropriate management regimes (Hii, 2013). Patients who showed signs of dengue hemorrhagic fever were treated not only for the fever, but required intravenous or oral fluid replacement or blood transfusions (Srikiatkhachorn, 2010).

Nevertheless, treatments depend on the age and underlying conditions of the patient; usually children are vulnerable for plasma leakage than adults and adults that have pre-existing conditions are more vulnerable than healthier adults (Low & Ooi, 2013). Management of dengue hemorrhagic fever requires hospitalization and treatments are more effective with an early clinical diagnosis (CDC, 2012).

Epidemiology of Dengue fever

Dengue fever has a large burden on a global scale; it was estimated that 50 to 100 million infections occurred every year in more than 100 countries (Simmons, Farrar, Vinh Chau, & Wills, 2012). More than 100 countries were endemic for dengue fever, and 2.5 billion inhabitants in tropical and subtropical region were at risk for this disease, including the 120 million people that travel to these regions every year (Tuiskunen, Back, & Lundkvist, 2013).

The approximately 100 million annual infections include an estimate of 500,000 people with dengue hemorrhagic fever that required hospitalization, most of these patient being children (Tuiskunen et al., 2013) and 25,000 deaths every year (Hynes, 2012). Nevertheless, according to Murray et al. (2013), the real impact of dengue was difficult to ascertain because some countries have inadequate disease surveillance, inadequate reporting levels, and misdiagnosis. Some articles report a global burden of close to 400 million cases of dengue fever.

Dengue fatality rate has been reported from 0.5% to 5.0% (Lee, Liu, & Yang, 2012), although if dengue shock syndrome developed, the fatality rate increased 12% to 44% (Lee et al., 2012). However, effective and prompt case detection, appropriate management, which can include hospitalization and intravenous rehydration, will lower the case fatality of severe dengue to less than 1% (Murray et al., 2013).

Migration/Imported Dengue Cases

Shang et al. (2010) explained that several studies have established the link between imported dengue cases and autochthonous (e.g., locally acquired) dengue cases by phylogenetical analysis and viral sequence comparisons. However, the relationship among the imported dengue cases, the transmission dynamics, the local climatic variables, and autochthonous dengue cases needs to be quantitatively assessed (Shang et al., 2010). Huang, Clements, and Hu (2013) studied the relationship of imported dengue cases, weather variability, and the incidence of autochthonous dengue cases in nonendemic Cairns, Australia. The study revealed a positive association between imported dengue cases and autochthonous cases, but the occurrence of autochthonous cases were more associated with monthly temperature than imported cases.

Sang et al. (2014) studied the association between dengue occurrence and possible risk factors. The authors found that imported dengue cases play a critical role in local dengue fever transmission with influence of climatic variables. Shang et al. (2010) found that imported dengue cases may trigger autochthonous dengue cases when the appropriate weather conditions were met.

Imported dengue cases have been recorded in Florida and the reemergence of the disease have been accompanied by a continuous flow of human migration to the state (Rey, 2014). The last dengue epidemic was in 1934; this epidemic affected a large portion of the state (Rey, 2014). Hanson (1936) described the epidemic of 1934 as the

State Health Officer and admitted that an announcement of an unusual disease may result in enough reported cases to simulate an epidemic. The author also expressed doubts about the correct diagnosis of dengue when it could have been another disease and admitted to the inadequate medical force to investigate each case. Hanson (1936), who led the antimosquito campaign in 1934, did not specify if the cases were autochthonous or imported dengue cases.

In 2009, about 3.5 million Caribbean immigrants resided in the United States; of these, 69% reside in Florida and New York. The number of immigrants from endemic dengue region has increased more than 17-fold during the past 50 years and nearly four of every ten immigrants in Florida were born in the Caribbean (McCabe, 2011). According to Naish et al. (2014), climatic factors may contribute to changes in dengue incidence, however migration and human travel were among the important factors which can potentially influence dengue expansion.

Global Situation of Dengue Fever

Dengue fever (DF) has been present for centuries; this disease has been endemic in the tropical and subtropical regions of the world. Messina et al. (2014) explained that the transmission of the dengue virus to humans could have occurred hundreds of years ago; nevertheless, the isolation of the some serotypes of the dengue virus only occurred in 1943 in Japan and 1945 in Hawaii. According to Thai et al. (2011), this disease has spread over the last 50 years from an estimate of 15,000 cases, reported annually to the World Health Organization (WHO) from less than 10 countries in the 1960, to 50 to 100 million cases in more than 100 countries.

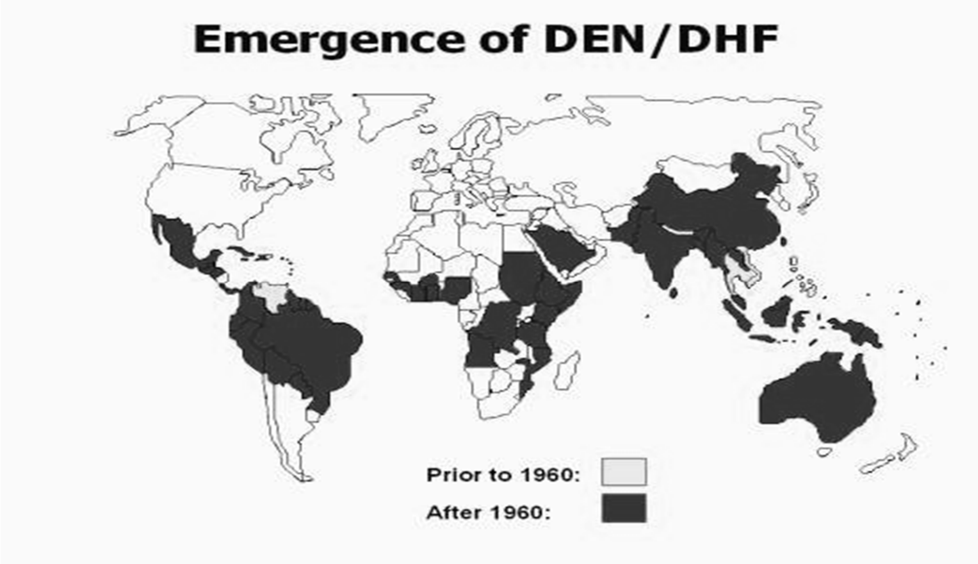


Figure 4. Geographic spread of dengue fever. From “Impact of Dengue,” by the World Health Organization, 2015, retrieved from http://www.who.int/csr/disease/dengue/impact/en

Dengue in the Americas has been documented with data sets from southern Brazil to the Mexico-United States border (Brady et al., 2012). In Central and South America, efforts from the Pan American Health Organization (PAHO) restricted the expansion of dengue fever (DF) throughout the American continent; nevertheless, the control of the vector *A. aegypti* was discontinued by the 1970’s. Estimates indicate that by 1995, the incidence levels of DF reached the levels that were found before the PAHO vector control campaign (Murray et al., 2013). In the United States, from 1946 to 1980, no dengue fever cases were autochthonous; the cases were imported from either U.S. territories or former U.S. territories, such as Puerto Rico, US Virgin Islands, American Samoa, and other regions endemic for dengue fever (Hynes, 2012). The author explained that a total of 1 million imported cases were reported during a ten year period from 1980 to 1989; however, a total of 4.5 million imported dengue cases were reported from 2000 to 2007.

In Asia, epidemic outbreaks of dengue fever and dengue hemorrhagic fever have been reported from Philippines and Thailand since the 1950s (Guzman & Isturiz, 2010). These countries and Vietnam were the ones with the highest number of dengue cases in Asia. India has reported dengue fever and dengue hemorrhagic fever cases since 1945. China had reported cases of dengue fever in the 1980s and 1990s, although the country had stopped reporting case of dengue fever to the World Health Organization (WHO) since 2003 (Guzman & Isturiz, 2010).

In Europe, most of the dengue cases were imported; a dengue fever outbreak was reported in Madeira, Portugal, in 2012, transmitted by the *A. aegypti* mosquito which involved around 2000 cases (Rogers, Suk, & Semenza, 2014). Finally, a handful of countries in Africa had reported some outbreaks of dengue fever, and it was known that the virus was circulating within this continent. Even though the surveillance system in Africa was lacking or inadequate, outbreaks were rare in comparison with Asia and the Americas (Guzman & Isturiz, 2010).

Geographic Extension of Dengue Fever

The Global Strategy and Public Health Advances in Dengue estimated that since 2000 to 2005, an increase of 110 million persons were at risk of dengue fever; the cases of dengue fever have grown exponentially by decade (Nathan & Dayal-Drager, 2006). According to Eisen and Moore (2013), established vector species had expanded their geographic ranges, potentially driven by climate changes and because of the introduction of vector species in new geographic areas.

Christopher (1960) established the broad geographic distribution of *A. aegypti,* mostly limited by cold temperatures, in the northern and southern hemispheres on the low-latitude areas of the equator of the average 10 °C winter isotherms (Figure 5). Eisen and Moore (2013) argued that the mosquito, *A. aegypti,* may expand its geographic range when conditions were favorable. The authors stated that the potential for expansion was demonstrated when *A. aegypti* recuperated lost territory after the Pan American Health Organization ceased the campaign to eliminate the mosquito.

Liew and Curtis (2004) found that the mosquito can fly vertically to buildings 21 stories high, indicating the potential of the mosquito to expand to higher altitudes. Lee et al. (2013) found a relationship between mean temperature and the quantity of precipitation on the distribution of mosquitos from endemic regions of Southeast Asia to Jeju Island (South Korea). Rohani et al. (2009) argued that climate variations and potential climate changes such as shifts in temperature, total precipitation, and rainfall patterns will alter the geographic range of mosquitos, their fecundity, biting rates, and longevity.

The expansion of dengue fever can be observed with several maps (Figures 5 to 7), indicating the advance of dengue in countries where this disease was absent. Figure 4 shows the geographic extension of dengue fever until 2006. World Health Organization (WHO, 2009) added Bhutan, Hawaii (United States), Galapagos Islands (Ecuador), Easter Island (Chile), Hong Kong (SAR, China), and Macao (SAR, China). In 2003, eight countries reported dengue cases, Bangladesh, India, Maldives, Myanmar, Sri Lanka, Thailand, Indonesia, and Timor-Leste, and in late 2006 Nepal reported the first autochthonous cases (WHO, 2009). During 2005 and 2006, outbreaks of dengue were been reported in Madagascar, Pakistan, Saudi Arabia, Sudan, and Yemen (Nathan & Dayal-Drager, 2006).

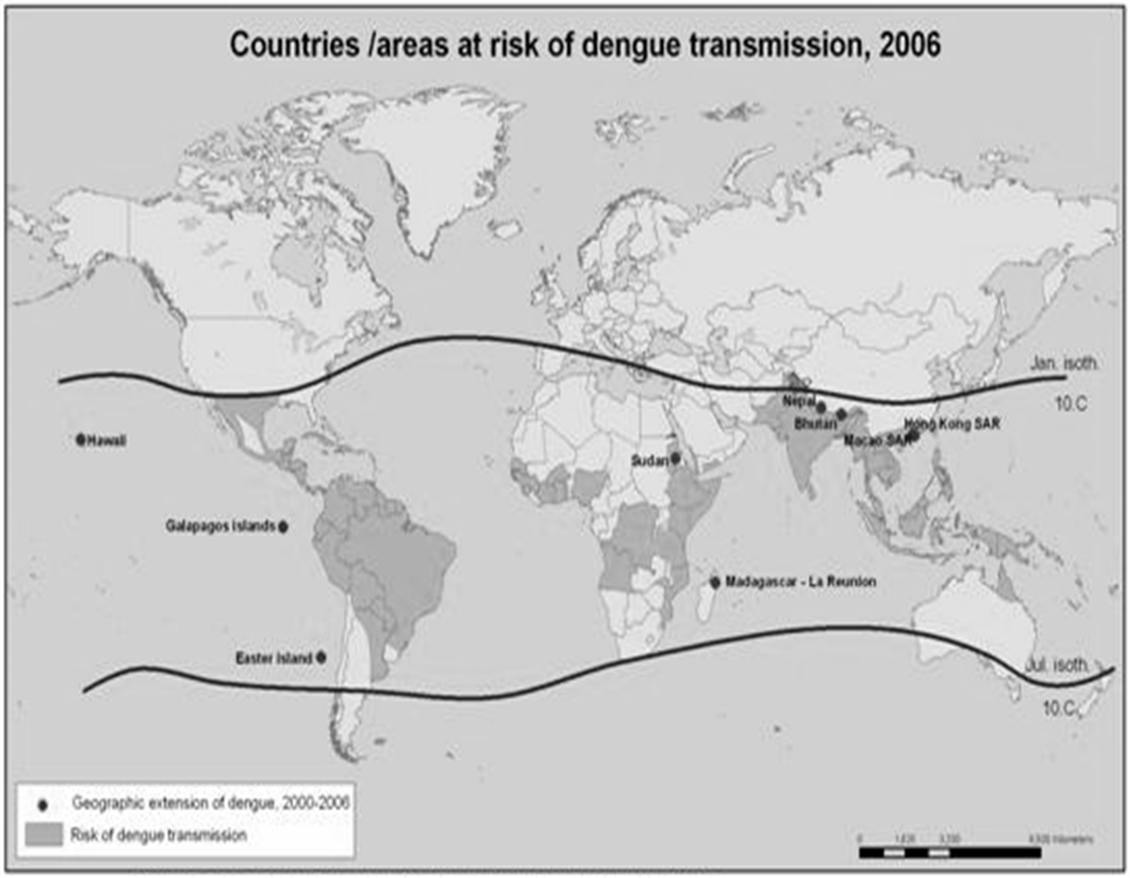


Figure 5. Geographic extension of dengue fever for 2006. From “Impact of Dengue,” by the World Health Organization, 2015, retrieved from http://www.who.int/csr/disease /dengue/impact/en

Figure 6 demonstrates the geographical extension of dengue fever until 2008. This map indicated the spread of dengue fever to areas where in 2006, no cases were reported, Madagascar reported an outbreak in 2006 and in 2008 the entire island was at risk for dengue fever.

By 2008, dengue fever cases were reported in Cambodia, Malaysia, Vietnam and Philippines; these four countries have the highest number of cases (1,020,333) and deaths (4,798) in the Western Pacific Region, The disease had also spread to Pacific island countries such as French Polynesia, New Caledonia, Cook Islands, American Samoa, Palau, and the Federal States of Micronesia (WHO, 2009).

In the Americas region, more than 30 countries reported dengue fever. Argentina, Brazil, Chile, and Paraguay reported dengue fever cases; Brazil had the highest fatality rate of these four countries. Bolivia, Colombia, Ecuador, Peru, and Venezuela also reported with Colombia having the highest fatality rate. In Central America, Mexico, Costa Rica, Honduras, and Nicaragua reported dengue cases; however, all countries in this region were at risk for dengue fever (WHO, 2009).

The Caribbean countries were considered at risk for dengue fever and were endemic for this disease; however, the Dominican Republic has the highest mortality rate. Finally, in North America, from 2001 to 2007, cases of dengue fever were reported, but most were in persons that had travelled from endemic areas (WHO, 2009).

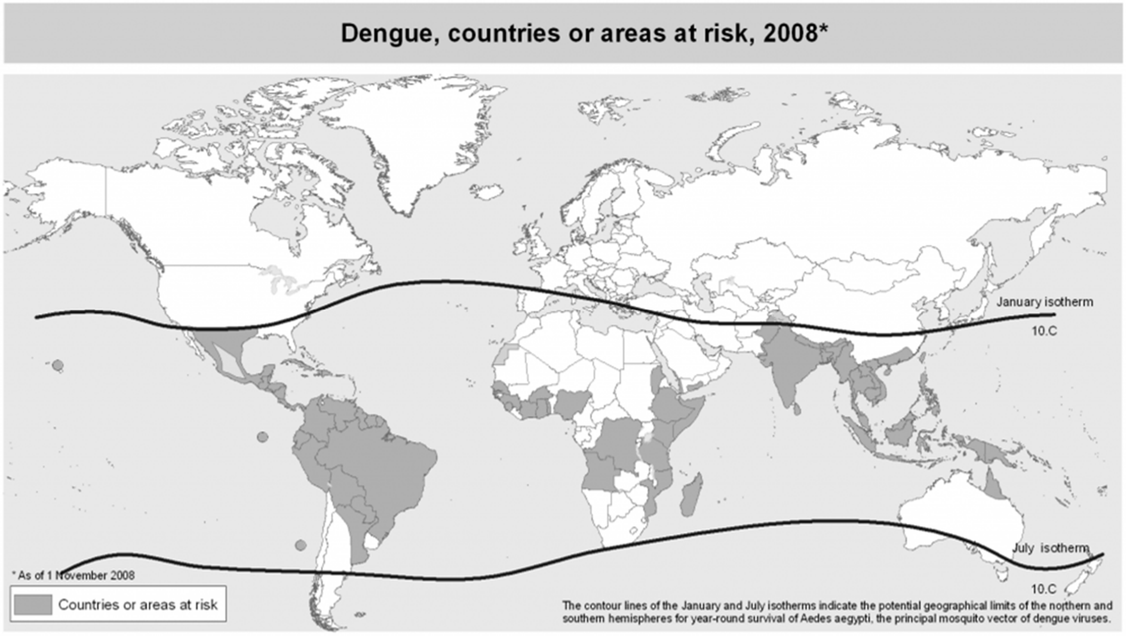
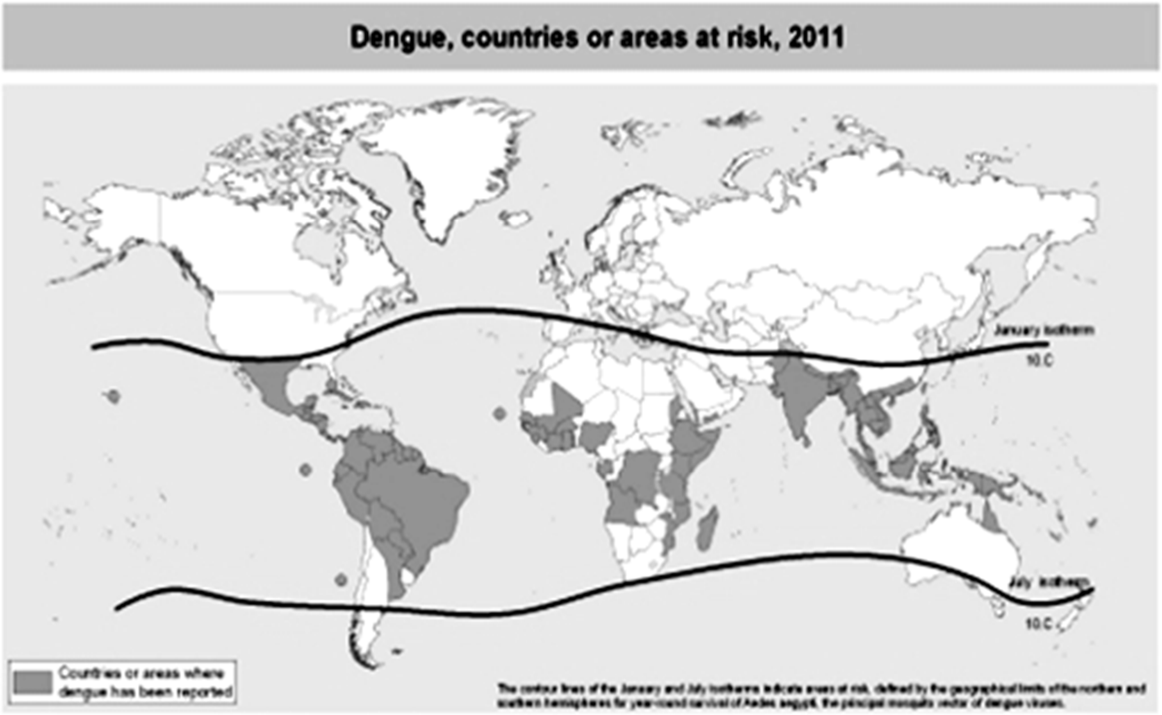


Figure 6. Geographic extension of dengue fever for 2008. From “Comprehensive Guidelines for prevention and Control of Dengue and Dengue Haemorrhagic Fever” by the World Health Organization, 2011, retrieved from www.abc.net.au/rn/backgroundbriefing/document/20100221_map.pdf

As shown in Figure 6, dengue fever was prevalent in the tropics and some subtropical regions of the world; nevertheless, the number of cases were increasing as the disease spreads to new regions. In the Americas, the Western Pacific, and Southeast Asia, the cases exceeded 1.2 million in 2008 and over 2.3 million in 2010 (WHO, 2014). Europe was threatened for possible outbreaks of dengue, although this possibility did not exist in years beforehand, and for the first time autochthonous cases appeared in France and Croatia in 2010. Madeira, Portugal experienced an outbreak of dengue in 2012 of autochthonous cases, and imported cases were reported in other 10 countries in Europe (WHO, 2014). In the United States, cases of dengue fever were reported in 2009 and 2013 in Key West Florida, even though dengue continued to impact South American countries mostly in Honduras, Mexico, and Costa Rica (WHO, 2014). Figure 7 indicates the expansion of dengue fever to Florida, United States and France.



Dengue, countries or areas at risk, 2011

The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of Aedes aegypti, the principal mosquito vector of dengue viruses.

Figure 7. Geographic extension of dengue fever for 2011. From "Public Health Information and Geographic Information Systems Organization" by World Health Organization, 2012, retrieved from http://www.who.int./mapLibrary/Files/Maps/ Global_DengueTransmission_ITHRiskMap.pn

Overall, the areas where dengue fever was most prevalent and endemic were Africa, Australia, the Caribbean, Central and South America, Hawaii, Mexico, the Pacific Islands, and Southeast Asia (WHO, 2014).

Summary and Conclusion

Dengue fever in its endemic areas was a major public health problem and was among the most threatening emerging infectious disease that may expand its geographic range (Madoff, Fisman, & Kass-Hout, 2011). Even though the historical range of dengue fever was limited by the 10°C January and July isotherms (to 15° in South America) (Christopher, 1960), dengue fever has been re-emerged globally with intensified epidemic and geographic expansion since the 1980s (Hii, 2013). Recently, the frequency of dengue epidemics has increased and dengue cases were being reported for the first time in regions such as Nepal, France, and Madeira, Spain (Hii, 2013).

This disease was transmitted by a highly domesticated vector, *A. aegypti*. The *A. aegypti* mosquito was the principal vector of dengue fever; it has evolved to feed mostly on human blood and has adapted to the urban environment using artificial containers for larval habitat (Gubler & Clark, 1996). *Aedes aegypti* was strongly influenced by temperature; for example, an increase of temperature increases the competence of the mosquito for propagation and viral replication (Oki & Yamamoto, 2012). An increase of temperature can shorten the duration of the lifecycle, the adult will emerge in less time (Hii, 2013), can increase the population growth, and the mosquito's feeding rate (Yang et al., 2009).

Precipitation (e.g., rainfall) also influenced *A. aegypti*; rainfall can increase the mosquito population by increasing the accessibility of immature stage habitat (Huang et al., 2013). For female mosquitos, precipitation can increase the total time of biting during the day and the biting was more spread out (Yasuno & Tonn, 1970). Numerous researchers argued that the most important climatic factors for the re-emerging of the vector of dengue fever were temperature and precipitation (Alto & Bettinardi, 2013; Couret et al., 2014; Morin et al., 2013; Yang et al., 2009).

The conceptual framework eco-bio-social research on dengue will be used to guide the study focused on the principal climatic variables, temperature and precipitation, and the social factor of migration. Researchers found that temperature was the primary factor that directly impacts the vector of dengue, *A. aegypti* (Carrington et al., 2013; Couret et al., 2014; Lambrechts et al., 2010; Watts et al., 1987); many agreed that rainfall influences the vector as well (Hii et al., 2012; Hii, 2013; Huang, 2013). However, there was disagreement concerning other variables and their impact on the vector. Some researchers suggested that humidity was more important than rainfall (Canyon et al., 2013; Chakravarti & Kumaria, 2005) and others such as Campbell et al. (2013) suggested that humidity does not have a direct or indirect impact on *A. aegypti.*

Depradine and Lowell (2004) disagreed that precipitation was an important factor for the vector. Other factors that researchers have studied were socio-ecological (Stewart Ibarra, 2013), vector competition, *A. albopictus* (Lambrechts et al., 2010), El Niño-Southern oscillation (ENSO) events (Foley & Hopp, 2001; Johansson et al., 2009), imported dengue by migration (Huang et al., 2013), and population density (Schmidt et al., 2010).

Numerous studies have been conducted on the climatic variables and the vector of dengue fever, *A. aegypti*; most of the studies concentrate on dengue fever endemic regions such as Puerto Rico, Thailand, South Korea, and Vietnam (Barrera et al., 2011; Campbell et al., 2013; Lee et al., 2013; Schmidt et al., 2010). However, few studies were conducted in nonendemic areas, such as the study relating temperature and dengue fever in Argentina (Carabajo, Cardo, & Vezzani, 2012). Presently, no recent study has been conducted correlating temperature, precipitation, and migration with autochthonous dengue fever cases in nonendemic area of southeast Florida, United States

Given the clear gap in the literature and the importance on understanding climate change and its impact on vector-borne infectious diseases, I will contribute to the existing body of knowledge by providing updated information on climatic variables and dengue fever in the United States. In the study, Arunachalam (2010) conceptual framework focused the study by mapping the climatic variables in the specific region of southeast Florida and evaluating how migration will influence the vector, *A. aegypti*. Chapter 3 had information related to the methods that will guide the analysis of the study. Chapter 3 identified the target population, access data, explained operationalization of variables, determined threats to validity, and discussed ethical problems if any.

Chapter 3: Research Method

Introduction

The purpose of this quantitative ecological study was to find an association among migration (imported dengue fever cases), climatic variables (temperature and precipitation), and autochthonous dengue cases in the nonendemic southeast region of Florida. Climatic data were collected from NOAA from land-based stations in specific regions in Southeast Florida. Data on dengue cases (imported and autochthonous) were retrieved from the Florida Morbidity Reports from the Florida Health Department (FHD) and the CDC. The data used ranged from 1980 to 2013, a total of 34 years. This amount of time and data were chosen in keeping with NOAA's recommendation to study a period of at least 30 years because this is the standard time period used to ensure that a researcher covers climatic variability (NCDC, 2014).

The main sections of this chapter address the study's research design and rationale, methodology, and threats to validity; the chapter concludes with a summary. The section on the research design and rationale presents information regarding the study design and the dependent and independent variables. The methodology section includes information about archival data, the data analysis plan, the target population, sampling, sampling procedures, instrumentation, and operationalization of variables. The section regarding threats to validity includes the ethical considerations of the study. At the end of the chapter, a summary provides an abbreviated version of Chapter 3.

Research Design and Rational

The dependent variable of the study was the geographic expansion of dengue fever, defined as the appearance of autochthonous dengue fever (locally acquired) in areas where this disease was previously absent. The three independent variables were two climatic factors—temperature and precipitation (e.g., rainfall)—and a third independent variable of social context—human migration, defined as imported dengue cases in specific areas of Southeast Florida.

The study used an ecological design, which is an observational or nonexperimental design like most epidemiological study designs (Aschengrau & Seage, 2008). The ecological study design made it possible to understand of the effects of ecological variables for which there was no correlation at the individual level; with this design, I examined rates of disease at the population level (Lengerich, 2015). Three types of ecological variables were recognized: aggregate, environmental, and global; this study used the environmental and global variables. The environmental variable was defined as a "measure of the physical characteristics of the environment in which people reside, work, recreate or attend school" (Lengerich, 2015, para. 6.2). This design allowed the analysis of environmental measures or environmental variables such as temperature and precipitation and allowed the description of the geographic location where the population lives or works (Aschengrau & Seage, 2008).

The global variable, which was one of the ecological variables, was defined as "a measure of the attributes of groups, organizations, or places for which there was no analogue at the individual level" (Lengerich, 2015, para. 6.2). The study included the variable of human migration, which fit the definition of global variable.

This study involved analysis of data on climatic variables and human migration for a period of 34 years because time was an important component of this study; a time-trend design was included. This type of design is a form of longitudinal ecological study that can provide a dynamic view of a target population's health status when exposed to climatic variables such as temperature and precipitation and imported dengue cases.

According to Coggon (2009), a common approach in ecological-design studies is geographical correlation between the prevalence of risk factors and disease incidence. In this study, I attempted to correlate the risk factors of changing temperature, precipitation, and imported dengue cases with the number of autochthonous dengue fever cases in a nonendemic region for a period of 34 years. However, Coggon stressed caution concerning the interpretation of findings, strongly advising that researchers make allowances for potential confounding effects of other variables using appropriate standardization.

Several studies using the ecological study design have found associations between climate change and increased dengue fever cases (Colon-Gonzalez et al., 2011; Hii et al., 2013; Johansson et al., 2009; Patz et al., 1998; Thai & Anders, 2011; Watts et al., 1987). Most of these studies have used local meteorological data and confirmed dengue fever cases to understand the correlation between these variables. Few ecological studies have addressed the relationship among imported dengue cases, climatic variables, and autochthonous dengue cases in nonendemic regions (Shang et al., 2010; Huang et al., 2013).

The ecological design seemed the most suitable for the study because the variables analyzed were ecological variables (temperature and precipitation) and imported dengue cases, with the study designed to determine how these risk factor influenced the health of the target population.

The data sets used were composed of secondary data. Data on the climatic variables, temperature and precipitation (e.g., rainfall), were provided by the National Climatic Data Center in Asheville, NC. The climate data were downloaded through the NCDC website. There were some time constraints on the retrieval of data on dengue cases (local and imported) from the Florida Public Health Department and the CDC for the years 1980-2013. The data, which contained some confidential information, had to be specifically requested.

Methodology

The methodology section presents information regarding the population, sampling and sampling procedures, archival data, instrumentation, materials, operationalization of variables, and data analysis plan.

Population

A target population is defined as the entire group on which a researcher seeks to draw conclusions. For the study, parameters were established that described the target population that was at risk of the disease in question (Crosby, DiClemente, & Salazar, 2006). In this study, the target population was the communities of Southeast Florida, specifically the region known as the Treasure Coast. This region extends across four counties—Palm Beach, Martin, St. Lucie, and Indian River—and 53 municipalities totaling more than 1.4 million residents (Treasure Coast Regional Planning Committee [TCRPC], 2010). According to the United States Census Bureau (USCB, 2014), of the almost 1.5 million residents in the Treasure Coast, 69% are White (nonHispanic), 16% are Hispanic, and 14% are Black. Females make up 51% of the population of the Treasure Coast, 24% of the residents are under 18 years of age, and 26% are 65 years of age or over (USCB, 2014).

The target population lives in a region where the geography may be suited for mosquitos. The Treasure Coast of Florida covers an area of 11,395.95 km^2 and has a significant number of natural resources such as lakes, rivers, lagoons, savannas, and marshes, including the Indian River and Indian River lagoon system (Merritt, 2010). The region is shielded from the Atlantic Ocean by barrier islands and sandbars, which protect the shallow lagoons, rivers, and bays (Merritt, 2010). Beginning in the north and moving southward, Florida's southeastern Treasure Coast has four counties: Palm Beach, Martin, St. Lucie, and Indian River. The lagoon system and the Atlantic coast are the most dominant physiographic aspects of the area (Merritt, 2010). The area has nearly 160 km of Atlantic coastline, and excluding the southern part of Palm Beach County, the area has a coastal barrier island system. The area's barrier island coastline is composed of beach, approximately 25% of which is in the public domain (TCRPC, 2010).

The Indian River lagoon south to Jupiter inlet lies west of the barrier island toward the northern boundary of the area. This estuary is a 32 km-long region positioned in the center along the east coast of Palm Beach County, and it is designated an Estuary of National Significance. Lake Worth lagoons, as well as the Indian River, interconnect with the Atlantic Intracoastal Waterway, which is an inland navigation passage that along the east coast of Florida (TCRPC, 2010)

The area's estuaries are critical because they contain nutrient-rich ecosystems and communities, such as beds containing sea grass, algae, and oysters, in addition to tidal marshes with exposed sand and shell bottoms, mud flats, tidal marshes, and mangrove swamps. The type of wetland that is most dominant is the mangrove swamp, which has exposed vegetation bordering the estuaries of the area (Merritt, 2010). This region also provides a nutrient base that is important in supporting the region's commercial and sport fish populations. The marine industries, as well as recreational boaters, rely on this region (Merritt, 2010). Most of the municipalities are located in Palm Beach County, which has 38 incorporated municipalities (Palm Beach County, 2014), in comparison to Martin County with four municipalities (Martin County, 2011), St. Lucie County with three municipalities (St Lucie County, 2015), and Indian River County with five municipalities (Indian River County, 2014). Table 1 contains the estimated population of each county for the year 2013.

Table 1

Population per County of the Treasure Coast District

County	Population
Indian River County	141,994 (estimates 2013)
Martin County	151,263 (estimates 2013)
St. Lucie County	286,832 (estimates 2013)
Palm Beach County	1,372,171 (estimates 2013)

Note. From “Quickfacts: Palm Beach County, Florida,” by U.S. Census Bureau, 2014, retrieved from http://quickfacts.census.gov/qfd/states/12/12099.html

Sampling and Sampling Procedures

The “goal of a sampling technique is to maximize the generalizability of the sample of the population” (Crosby et al., 2006, p. 290). The term *population* can refer to the possible elements of a defined group; elements can be people or units that have importance in public health (Crosby et al., 2006). In this study, the research question involved well-defined units: temperature, precipitation, and human migration during a specific period of about 34 years.

The first step in sampling was selecting land-based stations in areas where autochthonous (locally acquired) dengue fever cases were found and where data on precipitation and temperature had been collected for more than 30 years. In the United States, more than 6,000 observation stations have been recording data for various periods of time (Rennie et al., 2014.). However, with the improvement of technology, the land-based stations dedicated to measure temperature had been modernized and reduce in numbers to around 1,500 stations (NOAA, 2009).

In the State of Florida, a total of 844 stations that collect data for different elements have been undergoing modernization, and some of these stations are no longer accessible in real time (NOAA, 2009). The Treasure Coast and the coastal part of the County of Palm Beach have a total of 13 stations that collect data only for temperature and precipitation (NCDC, n.d.). Of these 13 stations, four land-based stations are located in the area where the autochthonous dengue fever cases were identified, and of these four stations, three stations have collected data for more than 30 years. The data from these three stations, which contain readings for both temperature and precipitation for more than 34 years, were used for the study.

In this study, a data set was collected containing information on all of the dengue fever cases (autochthonous and imported) from the area of study over 34 years. All records of dengue cases were included unless there were duplicate records or missing important values. The inclusion criteria were as follows:

- date of onset and date of diagnosis;
- laboratory results;
- city and state;
- determination of imported dengue fever or autochthonous dengue fever.

Records without all the inclusion criteria were excluded from the analysis. The rest of the information on the Florida Department of Health Practitioner Disease Report Form was excluded (Appendix A).

Using the computer software program Minitab® 17, I conducted an estimation of sample size and power analysis for Poisson regression. The two-sample Poisson rate was chosen because it was useful to determine whether the rate differed across two groups, to determine whether one group had a higher rate of occurrence than another group, and to determine whether the difference might be too small to have practical importance (Evans, 2013). Raw data on dengue cases in Florida were tabulated in the worksheet provided by Minitab® 17 (Minitab 17, 2015). The inputs were the baseline = 130, comparison rate = 135, alpha = .05, and the lengths of observation for Sample 1 and Sample 2 = 1, 1; the resulting curve showed three scenarios (Figure 8):

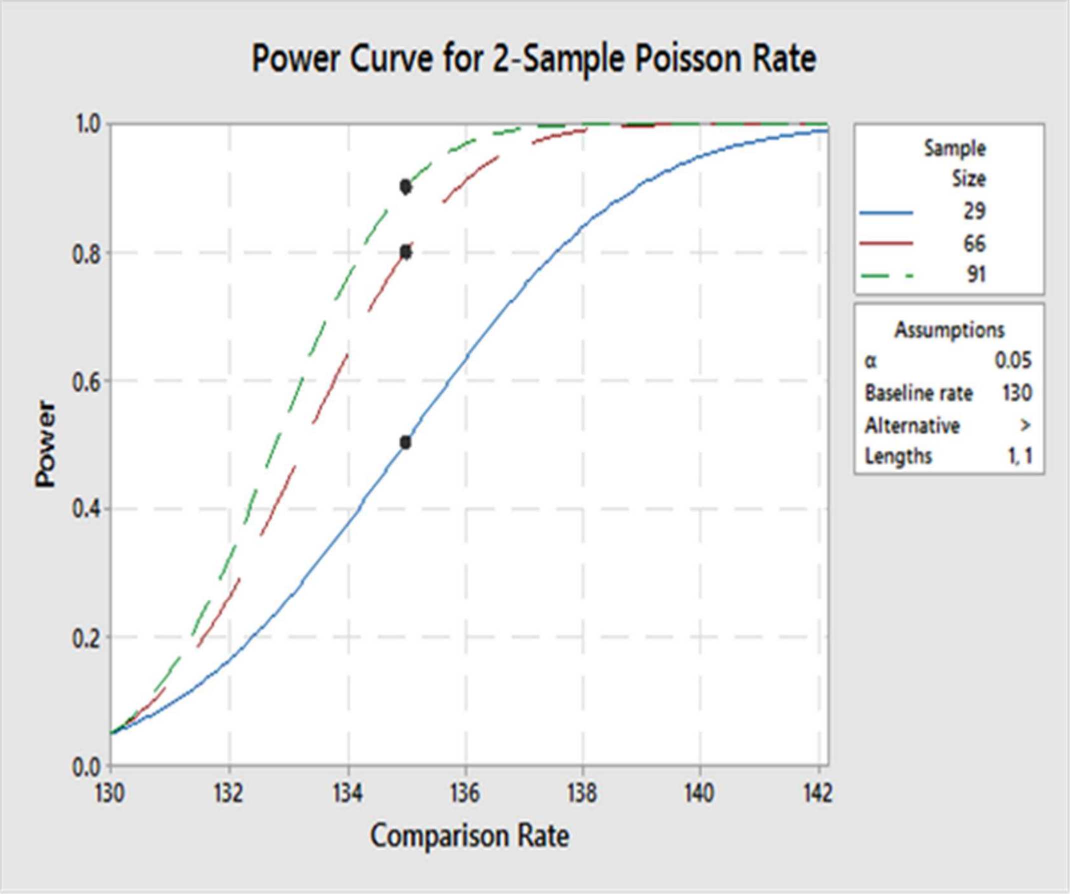


Figure 8. Sample size and power analysis for two-sample Poisson rate.

Table 2

Different Scenarios of Sample Size and Power

Comparison rate	Sample size	Target power	Actual power
135	29	.5	.503665
135	66	.8	.802456
135	91	.9	.900630

Note. Minitab output (Minitab® 17.1.0, 2015).

At a comparison rate of 135 dengue cases (with the highest number of imported dengue cases in 5 years estimated at 137), with a target power level of .8, a sample size of 66 cases per year was appropriate to detect a change between imported dengue cases and autochthonous dengue cases. A power level of .5 requires a sample of 29 dengue cases per year; therefore, using the power level of .8 would increase the sample size to gain more discrimination power (Table 2). In summary, the calculations indicated detection of five cases with a target power level of .8 with 66 dengue cases per year.

Archival Data

The study used archival or secondary data for the statistical analysis; data of this type were collected by others such as organizations or governmental agencies (Jones, 2010). The data on climatic variables were collected from the National Climatic Data Center (NCDC); this government agency is part of the National Oceanic and Atmospheric Administration (NOAA) and is "responsible for preserving, monitoring, assessing, and providing public access to the Nation's climate and historical weather data" (NCDC, 2014, para.1). The center is the largest climate data archive in the world and provides data and climatological services to the public, government, industries, and researchers (NCDC, 2014).

Global Historical Climatology Network (GHCND) Monthly Summaries was a database that addresses the critical need for historical precipitation, temperature, and snow records over global land areas (NCDC, n.d.). The GHCND-Monthly Summaries database includes 18 meteorological elements such as temperature (means and extremes), precipitation (totals, extremes and number of days when parameters were reached), snowfall, maximum snow depth, and degree days (NCDC, n.d.). The data was collected by land-based observation stations and these stations (e.g., land-based) contained observations of the meteorological elements mentioned above in more than 40,000 stations around the world (NCDC, n.d.).

The center provides data of several climatic variables such as average temperature, maximum temperature, minimum temperature, and precipitation for each state or region of the country. Some of the data start as early as the year 1865 to the present and offers time scales from months, year to date, annual, and previous 12 months (NCDC, 2014). In addition, specific climate variables such as temperature and precipitation, can be searched for division or city of specific states. Depending on the data, it can be offered in graphs and in tables to search at a glance.

The data from specific land-based stations was facilitated by the Program Manager of Global Observing Systems Information Center (GOSIC), lead of NOAA and NCDC Metadata Working groups, and lead of NCDC Master Archive Collection Inventory (MACI). Data was also facilitated by the Director World Data Center for

Meteorology (NOAA/NCDC). Additional data was downloaded through the NCDC website.

The data for cases of imported dengue cases and autochthonous dengue fever cases in Southeast Florida was sourced from the Florida Department of Health (FDH) or the Centers for Disease Prevention and Control (CDC). Some of the dengue cases were found in the Florida Morbidity Statistics Report from the FDH, which was the official record of the incidence and prevalence of reportable disease in Florida. The data contained in this report were final, unless otherwise noted (FHD, 2012). A reportable disease or condition was "one for which regular, frequent, and timely information regarding individual cases is considered necessary for the prevention and control of the disease" (CDC, 2014b, p. 2).

According to Florida Statutes Section 381.003, "The Department shall conduct a communicable disease prevention and control program as part of fulfilling its public health mission" (FHD, 2012, p. 3). Public health participants' work together to identify and characterize emerging trends of disease. The partners in these surveillance systems were physicians, nurses, laboratorians, hospital infection preventionists, and public health nurses who collaborate in reporting notifiable diseases (FHD, 2012).

The Florida Morbidity Statistics Report compiled the following:

- summary of annual morbidity data from notifiable infectious and environmental diseases in Florida;
- descriptions of trends of disease surveyed over time, and correlated with patterns from other states, which helps in guiding future

disease prevention and control efforts; and

- resources to medical and public health authorities at county, state, and national levels available from the summary (FHD, 2012).

The county and health department obtain the morbidity report data from medical staff, hospitals, and laboratories throughout Florida. The agencies received this data by passive and active surveillance (FHD, 2012). The state of Florida requires, under Section 381.0031, Florida Statutes and Florida Administrative Code (FAC), each of these participants to report suspicious and confirmed notifiable diseases and conditions (FHD, 2012). The state also requires from the personnel in charge of laboratories, hospitals, medical facilities or other facilities providing health service, for them to inform notifiable diseases and conditions, including the confirmed laboratory test results included in the Table of Notifiable Diseases or Conditions to be Reported, Chapter 64D-3, FAC.

Even though the laboratory result was included, the physician was required to disclose the disease. "These data are the basis for providing useful information on reportable diseases and conditions in Florida to health care workers and policymakers, and would not be possible without the cooperation of the extensive network involving both private and public sector participants" (FDH, 2012, p. 3).

Data were obtained in diverse ways:

- passive surveillance depending on assigned medical staff, laboratories, and other health care providers to inform diseases to the Florida Department of Health (FDH) confidentially in any of three forms (electronically, telephone, or facsimile);

- active surveillance involving the assigned health-care providers to frequently contact hospitals, laboratories, and medical staff to report cases of a given disease or condition;
- information about cases of notifiable diseases reported from medical staff, especially laboratories, to FDH electronically, which is collected automatically, without the intervention of medical personnel (FDH, 2012).

When a disease was identified (i.e., patients were exposed, became ill, diagnosed, or hospitalized), the cases were designated by the county of residence. Cases involving nonresidents of Florida were not included as a Florida case, even if they were hospitalized, diagnosed, or became ill in Florida. These cases were not included in the Florida Morbidity Statistic Report. The out-of-state "cases are referred through an interstate reciprocal notification system to the state where the person resides" (FDH, 2012).

The remaining dengue fever cases were obtained from the Florida Department of Health website for mosquito-borne diseases surveillance. Permission for the Walden University Institutional Review Board and agreement from the Florida Health Department was obtained to collect the necessary data for analysis.

Instrumentation and Materials

Dengue fever is a reportable disease; licensed practitioners or physicians must report diseases or conditions included in the Table of Notifiable Diseases or Conditions (Appendix A), Chapter 64D-3.029, F.A.C., (FDH, 2012). The public health system relies on reporting to survey the health of the community and to contribute to the evidence for preventive action (FDH, 2012). Medical officers are mandated to supply specific information with laboratory orders at the time the sample is sent or received by the laboratory (FDH, 2012).

The reporting of these diseases is crucial for prevention and to implement programs related to infectious diseases. The Notifiable Infectious Disease Report is the archival count of cases, and is approved by the chief epidemiologist of every state or territory before sending the reports to the *Summary* (CDC, 2014b). The surveillance and reporting systems connect public health departments to physicians, public health nurses, and clinical laboratories. These health-care practitioners report patients with reportable infectious diseases, unexplained diseases, and severe problems. Laws and regulations mandate every state and territory to report diseases, but some states require reporting other diseases that are not nationally notifiable (Silk & Berkelman, 2005).

NOAA's National Climatic Data Center collects, maintains, and preserves climate data archive to provide climatological services to the public, business, industry, government, and researchers (NOAA, n.d.). The precipitation and temperature data are collected by land-based observation stations sited at locations nationwide (Menne, Williams, & Palecki, 2009). Land-based stations adhere to established monitoring principles. These stations are closely monitored and are subject to rigorous calibration procedures (NOAA, 2009). The land-based stations have detailed station history which helps to identify and correct discrepancies (NOAA, 2009).

The stations collect data, including temperature, dew point, relative humidity, precipitation, and atmospheric pressure. However, not all stations collect all climatic variables; some stations collect only precipitation and others collect temperature and precipitation (NOAA, 2009). The specific stations that gathered the data for this study are known as cooperative observation stations and the instrumentation is faily simple. These stations are calibrated on a regular schedule (H. Diamond, personal communication, August 26, 2014).

Reliability and validity are the primary indicators of the quality of the measuring instruments (Kimberlin & Winterstien, 2008). Reliability estimates evaluates the stability of measures, and internal consistency of measurements by instruments over time (Kimberlin & Winterstien, 2008). The data used in the study is secondary data; the first consideration for reliability is to assure if the secondary data measures the variables required to answer the research question (Kimberlin & Winterstien, 2008). Validity is the indicator of how findings accurately represent measurements (Kimberlin & Winterstien, 2008).

Reliability and validity of the data compiled by FHD. The data of dengue fever cases was collected from the Notifiable Infectious Disease Report form of the regions of interest. The data reported by the physician and the laboratory complement each other. Laboratory reporting must be paired with the practitioner's report for disease or condition (FDH, 2012). Personnel with reporting responsibilities must verify the steps of the process to report this data (FDH, 2012).

The report content is required by Florida Statutes to include the patients' name, complete address, social security, and personal information. The personal information includes age, sex, race, and ethnicity. In relation to the disease, the physician or health provider includes the date of onset, symptoms, and diagnosis. The laboratory section includes the type of diagnostic test, type of specimen, date, and site of collection. Diagnostic test results include information related to quantitative procedures performed, and all available results including the characterization of the organism. Finally, the health provider reports the treatment given, the provider's name, and other important epidemiological information (Appendix A, FDH, 2014).

The Table of Notifiable Diseases or Conditions provides the timeframe for reporting. If the institution was electronically operational, the report can be sent electronically or if by telephone, the notification must be accompanied by a report no more than 72 hours in the form of facsimile or another method that was confidential (FDH, 2014). For example, dengue fever can be reported the next business day, but if the disease was autochthonous it must be reported by phone upon diagnosis (FDH, 2014).

The reported cases were collected in Merlin, Florida's web-based reportable disease surveillance system and codes were assigned to each disease. Codes can be added, old codes can be deleted, and some diseases have more than one code identifying different clinical manifestations (FDH, 2014).

Completeness, an important reliability factor for disease reports, refers to the percentage of the diagnosed patients with a reportable disease disclosed to relevant public health jurisdiction (Doyle et al., 2002). The ability to detect outbreaks or epidemics depends on the sensitivity of the surveillance systems and on the completeness of the reports (Silk & Berkelman, 2005).

Completeness was more important for infrequently occurring diseases, which was crucial to understanding the occurrence accurately and to generate national and global comparisons among public health administrations (Doyle et al., 2002). According to Doyle et al., variation in completeness of the reporting of infectious diseases varied in the United States from a range of 9% to 99%. The variation seems to be linked or related to the severity of the disease (CDC, 2014). For example, reporting completeness seems to be higher for sexually transmitted diseases or tuberculosis. The reasons for this were not clear, but may be associated with the notion that some of these diseases are more serious or there are more resources assigned to treat and preventing them, including sending case workers in the community (Doyle et al., 2002).

Another reporting problem is that for some reportable diseases, the data is sent independently to different CDC programs (CDC, 2014b). This surveillance data might differ from data reported in the *Summary.* The cause of the discrepancies may be because (a) differences of the date used to aggregate data such as date of report or date of disease occurrence, (b) different timing in reporting, (c) different source of the data, d) different case definitions, and (e) policies regarding case ownership (i.e., which state should report the case to CDC; CDC, 2014b). Other factors that influence the completeness of data includes awareness of a specific disease in the community, state, and local resources, control measures implemented, state and local priorities, availability of diagnostic facilities and public health surveillance.

Completeness of data reporting can also be affected when there are changes in disease reporting which are independent of the incidence of the disease. Some of these factors can be the discovery of new emerging diseases, introduction of new diagnostic test, and changes on the methods for public health surveillance (CDC, 2014b). The lack of some demographic data (e.g., socioeconomic levels) affects the estimation on demographic-specific rates in the *Summary* (CDC, 2014b).

Lazarus, Klompas, and Platt (2009) analyzed studies which suggested that manual reporting provide delayed and inaccurate data, accompanied with many errors and omissions. The authors stressed that an automated system, based on a comprehensive source of electronic data, can contribute available details from the source. The system can make the job easier for the provider and minimize transcription errors. To maintain reliability and validity, surveillance and measurements activities periodically should be evaluated (CDC, 2001).

Guidelines have been established to increase the susceptibility of the systems, which includes diagnosis, disease-reporting, and case elements (CDC, 2001). The secure web-based disease surveillance system, Merlin, was used by 67 county health departments in Florida. The large amount of users and thousands of cases, which were not reviewed individually, brings a challenging task to maintain data quality (Eisenstein, 2014). The system was programed for automated logic checks to prevent unreasonable data from being entered; however, improbable scenarios were not addressed such as patients older than 100 years of age (Eisenstein, 2014).

In 2013, these concerns were addressed and, data quality checks were added to Merlin. The results were a reduction in the number of data errors in submitted cases, improvement in data quality, decreased time spent on cases review, and a reduction of time of county health department spent updating cases (Eisenstein, 2014). By implementing early checks, improvements to Merlin yielded a 92% reduction in selected data quality errors (Eisenstein, 2014).

Reliability and validity of the data compiled by NOAA/NDCD. NOAA issued an administrative order (202-735D) for continuation of scientific excellence and integrity and to strengthen the confidence of researchers, policy makers, and public in general in the reliability, quality, and validity of NOAA science (NOAA, 2011). The scope of the order is to established NOAA's principle of scientific integrity and the NOAA policy of integrity of Scientific Activities (NOAA, 2011).

The order applies to all employees engaged in supervising, managing, analyzing, and communicating information resulting from scientific activities, including contractors. The order, which is detailed and specific for scientific integrity, stresses that employees preserve the integrity of the data record by adhering to NOAA data management standards (NOAA, 2011).

The Global Historical Climatology Network (GHCN-Monthly) data base contains historical precipitation, temperature, and other climatic data collected by hundreds of land-based stations nationwide and globally (NOAA, 2014). The period of data collecting differs from station to station, with hundreds dating from the 1950s and hundreds being updated every month through CLIMAT reports (NCDC, 2002). NCDC land-based stations observations supplies a high level of service associated with the data that is collected (NCDC n.d.)

The data is rigorous scrutinized with quality assurance reviews, both the historic and the GHCH near real time data (NOAA, 2014). The quality reviews include time series checks which analyze bogus changes in the variance and means, audits on source data, spatial comparisons that checks the veracity of the climatological mean, and neighbor audits that pinpoints outliers from a spatial and serial viewpoint (NOAA, 2014).

A peer-reviewed study computed the possible bias in trends caused by inefficient station exposure. The findings found only a small subset of stations with this condition and these had their exposure corrected at the time of the study. The study found no bias in long-trends (Peterson, 2006). Another peer-reviewed study provided an overview of the sources of bias and the process of removal which includes urbanization and nonstandard exposures (Menne, Williams, & Vose, 2009). The removal of some bias included the evaluation of urban bias and once the data was adjusted from these stations they found the same trend as the remaining rural stations (NOAA, 2009a).

NCDC have been leaders in developing methods of detection as well as quantifying biases in station time series, since 1980s. The detection and removal of the bias is crucial so that the time series are consistent with respect to its actual instrumentation and exposure (NOAA, 2009a). NOAA’s field office personnel trained volunteers and these volunteers are subject to periodic visits to provide support and ensure instrumentation is working correctly. Any inconsistencies or difficulty found by the field officer are investigated, corrected, and worked on to ensure that daily and monthly measurements are being taken correctly (NOAA, 2009). In addition to the monitoring, the calibration, and the training, the NCDC provides data checks of the measurements, in search of discrepancies.

Study Variables

The variables selected and presented in the section were based on the research questions, literature review, and the availability of the data sets.

Dependent variable. The dependent variable of the study was the geographic expansion of dengue fever to southeast Florida, United States. Geographic expansion of dengue fever refers to the appearance of autochthonous dengue cases (locally acquired) in areas where it was previously absent. The variable was a continuous variable with the number of autochthonous dengue cases monthly during 34 years in southeast Florida.

Independent variables. This study had independent variables associated with climatic characteristics precipitation, temperature, and a social context variable which was migration, as defined below.

Precipitation: refers to the fall of rain and the liquid water equivalent of frozen precipitation (snow, sleet, and hail), on the earth's surface, measured by tenths of millimeters (mm). The precipitation dataset, includes extreme maximum monthly precipitation and total precipitation. This variable was used as a continuous variable and the dataset included 34 years of monthly values per each element per one station, with a total of three stations.

Temperature: refers to the numerical measure of detection of heat. NOAA land based stations measure the temperature by degree and tenths Celsius (°C). Temperature readings, with a precision of tenths of degree of Celsius (°C), included extreme minimum temperature, and extreme maximum temperature, monthly mean minimal temperature, monthly mean maximum temperature, and monthly mean temperature (NOAA, 2009).

The variable was a continuous variable and the dataset had 34 years of monthly values per each element per one station, with a total of three stations.

Human migration: For this study, migration referred as imported dengue cases as defined as laboratory-confirmed dengue cases with a migration or travel history from dengue endemic countries (Shang et al., 2010). These movements may partially explain the risk of introducing the dengue virus in nonendemic zones; human migration and travel by those infected with dengue may help drive the expansion of the disease (Murray et al., 2013).

This variable, imported dengue cases, was used as a continuous variable with the number or counts of imported dengue cases monthly for 34 years in southeast Florida.

Data Analysis Plan

General information. In this study, descriptive statistics, bivariate analysis, and a Poisson regression were used in the statistical software IBM SPSS, version 21. A Poisson regression applied the dependent variable using the number of autochthonous dengue cases per month, as a count variable. All statistical test results were evaluated using an overall significance level of $p < .05$ and 95% confidence interval.

Temperature and precipitation data were downloaded from NOAA/NCDC in Microsoft Excel format, from the land-based stations where the autochthonous dengue cases were located. The data from NOAA/NCDC was retrieved clean with no missing values, no repetition, and adjusted by NCDC employees (H. Diamond, personal communication, August 29, 2014).

The imported and autochthonous dengue cases were retrieved from the Florida Department of Health or the CDC. The data was screened for completeness, missing data, unknown values and duplication. Data analysis was performed to address the research questions restated as follows:

Research questions and hypotheses. The research questions and hypotheses of the study were the following:

Research Question 1: Was there a significant relationship between temperature during 34 years in southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship of temperature during 34 years in southeast Florida with the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship of temperature during 34 years in southeast Florida with the geographic expansion of dengue fever within the region.

Research Question 2: Was there a significant relationship between precipitation during 34 years in southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship between precipitation during 34 years in southeast Florida and the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship between precipitation during 34 years in southeast Florida and the geographic expansion of dengue fever within the region.

Research Question 3: Was there a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to southeast Florida?

H_0: There was no relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to southeast Florida.

H_1: There was a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to southeast Florida.

Table 3

Variables and Research Questions

Variable name	Type	Measurement	Research question
Temperature	Independent	Continuous	RQ1: Was there a significant relationship between temperature during 34 years in southeast Florida and the geographic expansion of dengue fever within the region?
Precipitation	Independent	Continuous	RQ2: Was there a significant relationship between precipitation during 34 years in southeast Florida and the geographic expansion of dengue fever within the region?
Migration	Independent--------	Continuous------	RQ3: Was there a significant relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and geographic expansion of dengue fever to southeast Florida?

Descriptive analysis. Descriptive statistics were used to organize and summarized the data in a meaningful and effective manner (Frankfort-Nachmias, & Nachmias, 2008). Measures of central tendency and dispersion for each continuous variable included mode, median, and mean to determine the distribution of the observations (Frankfort-Nachmias, & Nachmias, 2008). Measures of dispersion included range, variance, and standard deviation.

Bivariate analysis. Several correlation test analyses were performed between the independent and dependent variables to examine the magnitude of the relationship. Wang (2005) performed bivariate correlation between dengue outbreaks (dependent variable) in Puerto Rico and each of the climate factors studied were temperature, precipitation, sea surface temperature, and relative humidity. The author found positive correlations between sea surface temperature and dengue outbreaks on the endemic island. A Pearson correlation was conducted for each climate factor and imported dengue cases against autochthonous dengue cases.

Pearson correlation. Pearson correlation was a parametric measure used to measure the strength and direction of linear relationship between two continuous variables (Kent State, 2015). The measure produces a sample correlation coefficient, *r*, and can range from -1, indicating a perfect negative linear relationship, and 1, indicating a perfect positive linear relationship. An "*r*" of 0 will indicate no relationship between the two continuous variables (Kent State, 2015).

For Pearson's correlation, the data should meet the following assumptions: the two variables should be continuous, the relationship needs to be linear, there should be no significant outliers, there should be no relationship between the variables, and the variables should be approximately normally distributed (Laerd Statistics, 2013).

To verify if there was a linear relationship between the variables, a scatterplot was plotted to visually examine for linearity. Pearson's *r* was sensitive to outliers; using SPSS, a criteria was included to detect the outliers. To detect bivariate normality, a Shapiro-Wilk test of normality was conducted using SPSS (Laerd Statistics, 2013). The Spearman rank correlation, a nonparametric alternative, was used because the assumptions of Pearson's correlation were not met.

Multivariate analysis. The multivariate analyses performed were the Poisson regression analysis and, in case of overdispersion, the negative binomial regression.

Poisson regression analysis. Poisson regression was a parametric test that was useful when counting a number the occurrences of an event over time, area, distance, or any type of measurement (UMass, 2013). This test was useful when the events were independent, this means that one event neither deceases nor increases the chances of another event. The average probability of the event for the period was known so it was possible to calculate how many events have occurred in a given time frame (UMass, 2013).

The Poisson regression analysis was used when the count of occurrences were rare events. For example, in this study the rare events were the number of autochthonous dengue fever cases in a nonendemic region. Sang et al. (2014) conducted a time-series Poisson regression analysis to quantify the relationship among imported dengue fever cases, mosquito density, and weather variables to local dengue transmission in nonendemic Guangzhou, China. The authors found that imported cases, mosquito density, and weather variables play a critical role in the local transmission of dengue.

Naish et al. (2014) conducted a systematic review focusing on quantitative methods for assessing the potential impacts of climate changes on dengue transmission. The authors found that several researchers used the Poisson regression for multivariate statistical analysis (Chen, Lin, Wu, Wu, Lung, & Su, 2012; Earnest, Tan, & Wilder-Smith, 2012; Pinto et al., 2011). Chen et al. (2012) utilized the Poisson regression to examine the relationship between extreme precipitation (heavy, torrential, extreme torrential) and the number of reported cases of eight different climate related diseases, including dengue fever. The authors found a statistical significance between extreme precipitation (heavy and torrential) and dengue fever cases ($p < 0.0001$) in endemic Taiwan.

Earnest et al. (2012) used a Poisson regression model to determine the relationship among temperature, relative humidity, rainfall, and dengue activity, accounting for the variability of long term climate (El Nino Southern Oscillation Index) in endemic Singapore. The authors found interaction effects between climatic variables and dengue outbreaks. Periods when El Nino was present did not control the association between climatic variables and dengue fever warnings. Pinto et al. (2011) conducted the Poisson regression, utilizing the number of dengue cases as the outcome variable and rainfall, relative humidity, and temperature as predictor variables. Pinto et al. (2011) found a positive correlation between dengue cases and temperature in dengue endemic Singapore.

The authors suggested that Wilder-Smith et al. (2011) used a different statistical model than Poisson regression to determine that no significant association was found between temperatures and dengue cases. Pinto et al. (2011) argued that a different statistical model was used, and not the multivariate model as the Poisson regression model, therefore a different result was obtain in the Wilder-Smith study.

This statistical analysis assumed the data followed a Poisson distribution. The Poisson distribution has several assumptions. The first assumption was that the distribution was skewed; traditional regression assumes a symmetrical distribution of errors. The second assumption was that the distribution was nonnegative, in contrast with other regression that can produce negative values. The third assumption was the variance increases as the mean increases in contrast with other traditional regressions which assume a constant variance (Nussbaum, Elsadat, & Khago, 2007).

The Poisson distribution specified the mean incidence rate of a rare events per unit of exposure. The unit of exposure may be time, space, distance, or population size (Stat Trek, 2015). When the probability of developing a rare disease (dengue fever in southeast Florida) might be low (one in a thousand) and the population quite large, the number of people who contract the disease per year (or some other period or space) might be described by the Poisson distribution (Nussbaum et al., 2007).

The distribution was skewed because for several years the dengue cases were zero and began to appear later, so the distribution was skewed to the right, and it was nonnegative because counts cannot be less than zero and we cannot have 1.5 dengue cases. A variable with a skewed distribution can reduce statistical power, compared with normally distributed variables, skew can increase standard errors, making it harder to achieve statistical significance (Nussbaum et al. 2007).

The Poisson regression was used to analyze the relationship among the counts or rates of autochthonous dengue fever cases, the counts of imported cases, and the quantitative data of each climatic variables per month. An assumptions of the Poisson model was the equality of the mean and variance function; if the variance exceeds its mean, the data may be overdispersed (Rodriguez, 2013). Overdispersion was observed in the data, therefore an alternative approach was used in count data known as the negative binomial regression. According to Rodriguez (2013), the approach was to start from the

Poisson regression and add a multiplicative random effect Θ to represent unobserved heterogeneity, thus leading to the negative binomial regression model.

Threats to Validity

Internal validity of the study refers to the capacity of the design to test the hypothesis it was designed to test (Crosby et al., 2006). The threats to internal validity jeopardize confidence in interpreting that an association exists between the outcome and predictor variables.

This particular study used secondary data collected by two or three government agencies, FDH, CDC, and NOAA/NCDC, therefore some threats to internal validity such as maturation, history, attrition, and regression to the mean were not present (Peterson, Baker & McGaw, 2010). Selection bias was more likely to occur in case-control and retrospective cohort studies (Aschengrau & Seage, 2008).

Therefore, because this study was an ecological design where the climatological variables, imported dengue cases and expansion of dengue fever were compared; selection bias will be unlikely to occur. Repeating testing, diffusion, and experimenter bias were threats to internal validity that uses subjects and control groups. Because the study did not include selective subjects or control groups these were not threats to this particular study (Peterson et al., 2010).

The factual validity threats to the study were instrumentation and temporal ambiguity. Temporal ambiguity was formally defined as the inability of the researcher (based on the data) to specify if the independent variable really came before the dependent variable (Johnson, n.d.). In correlational studies, demonstrating that the cause precedes the effect can be a problem (Long & Hart, n.d.). Two strategies to control the threat of temporal ambiguity was to understand the variables of the study and to inspect the temporal precedence of data periods (Bergh, Hanke, Balkundi, Brown, & Chen, 2004). Temporal ambiguity arises when study designs consist of data collected at the same exact time (Bergh et al., 2004); however this particular study had reviewed data during 34 years to verify if the disease (autochthonous) was not present before the climatic changes and migration of imported cases.

Instrumentation threat was caused by inconsistencies with the testing instrument, interviewer, grader, or the test (Bergh et al., 2004). In this particular study, the researcher did not control instruments measuring the variables, however verification of the reliability of the measurements or reports explained the validity of the instruments.

External validity threats emerge when researchers describe incorrect inferences from a sample population to other populations, times or settings (Creswell, 2009). One way to improve external validity was to learn about the procedures used by the people who collected the data to assess the generalizability of the results (Smith et al., 2011). According to Zinser (2010), NOAA has established procedures to improve the data collection by implementing quality control steps and algorithms and having these documents peer reviewed. Several experts were contacted to state their professional views about the dataset and their opinion about the dataset was excellent. However, the experts also agreed that a modernized climate reporting system will terminate the need for data modification (Zinser, 2010).

The implemented algorithms corrected several concerns from the NCDC scientists, such as time of observation issues, documented and undocumented station changes, urbanization issues, and missing data (Zinser, 2010). According to NOAA (n.d.), the modifications to the historical and current data allows customers to compare data for any given period in a land station's record without external influences, such as undocumented station location moves, biasing results.

Zinser (2010) explained that, before publishing the adjusted dataset, some measure of quality control were included such as several steps of quality assurance; daily datasets were converted to monthly datasets and another round of quality checks were performed. Once all the reviews were in place, the data adjustments from the algorithms were applied, resulting in the new reviewed dataset version. NCDC scientists compared both versions for the same time period and the results found the old version and the adjusted version were similar (Zinser, 2010). According to the procedures followed by NOAA/NCDC to ensure a quality dataset for its clients, the results were a high-value dataset which can assess the generalizability of the results.

The dengue cases dataset was obtained from the Florida Department of Health (FDH) or the CDC. Because dengue was a notifiable disease, the cases from Florida were collected and compiled to the National Notifiable Diseases Surveillance System (NNDSS) operated by the CDC (CDC, 2014b). Healthcare providers, laboratories, and other designated staff were required to report these diseases by legislation or regulation (CDC, 2014b).

In Florida, collecting disease data follow the same format with specific information for some diseases. For example, autochthonous dengue fever has to be reported immediately to authorities. The form that health practitioners fill for the notifiable diseases consists of straightforward, standard demographic fields not open to a range of interpretations.

However, Smith (2011) suggested that available measures may not capture exactly what the researcher was trying to determine. The "existing dataset are often good enough to answer the research question with proper interpretation to account for what the measures actually assesses and how they differ from the underlying constructs" (p 927).

Other threats that must be addressed include the statistical conclusion validity. This threat arises when the researcher reach inaccurate inferences from the data because of inadequate statistical power or from not observing statistical assumptions (Creswell, 2009). To follow the statistical assumptions, normality was checked before conducting the parametric test, if normality was not met, several alternative statistical testing were used. One alternative was either to transform some of the results using SPSS or use nonparametric tests.

Statistical power was calculated using several scenarios with the Minitab software (table 2). Finally, ecological study design has limitations. Ecological study designs can only find relationships between variables; the study's result was reported as associations using the appropriate statistical analysis. Causation was not reported as a result of the study.

Ethical Procedures

The finalized research study was submitted for revision and approval of the Institutional Review Board (IRB) of Walden University, approval number for the study was 5-29-15-0183973.

An advantage of most secondary studies using public access datasets was the short time to IRB approval (Smith et al., 2011). Many public access large datasets contained unidentified information and were eligible for expedited review or exempt status. If the researcher can obtain the dataset from the web, it was probably exempt. The IRB made this determination (Smith et al., 2011). NOAA's NCDC provides services and data to the public, government agencies, and researchers.

A request for the dengue cases (autochthonous and imported) was submitted to the Florida Health Department. After approval, signing a Data User Agreement should have proceeded, which may include the following: (a) not use or disclose information other than the one permitted by the agreement, (b) use of appropriate safety measures that will prevent the disclosure of information, (c) no data sharing, and (d) no attempt to identify the individuals (CDC, 2011). According to the HIPAA privacy rule, the data provided has to be de-identified data and the data must be stored in a personal computer with a password protection. The data must be destroyed upon completion of the dissertation. However, after a conference call with the vector-borne diseases surveillance coordinators, it was concluded that the data needed was found in the Florida Department of Health website, which was a website with public access.

Summary

The study was a retrospective ecological design research which was useful for establishing a correlation among climatic variables, social variable, and the expansion of dengue fever in a nonendemic area. The region of study was southeast Florida which includes the counties of Palm Beach, Martin, St. Lucie, and Indian River. The dependent variable was the expansion of the dengue fever in the nonendemic area, defined as the appearance of locally-acquired dengue cases in areas where it was previously absent. The independent variables were temperature, precipitation, and migration (imported dengue cases).

After receiving the approval of the IRB, the data for the study were downloaded from the NCDC and the Florida Health Department websites. The period extended from 1980 to 2013, a time range of 34 years. IBM SPSS Statistics version 21 was used to conduct statistical analyses. Chapter 4 includes information related to the data collection procedures and results of the study. Descriptive analysis incorporated measures of central tendency and dispersion for continuous variable, bivariate analysis and because counts or rates were used, the multivariate analysis was the Poisson regression or the negative binomial regression. The findings were reported using the appropriate probability values and confidence intervals. The chapter concludes with a summary of the answer to the research questions.

Chapter 4: Results

Introduction

The purpose of this quantitative ecological study was to identify a relationship between climatic variables and human migration/imported dengue cases with the geographic expansion of dengue fever in nonendemic Southeast Florida. The research questions and hypothesis of the study were as follows:

Research Question 1: Was there a significant relationship between temperatures during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship of temperature during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship in temperature during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

Research Question 2: Was there a significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region?

H_0: There was no significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

H_1: There was a significant relationship between precipitation during 34 years in Southeast Florida and the geographic expansion of dengue fever within the region.

Research Question 3: Was there a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida?

$H_{0:}$ There was no relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida.

H_1: There was a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to Southeast Florida.

Information of the data collection process and the results of the study are presented in this chapter. The chapter includes descriptive analyses of the variables, evaluation of the assumptions of the statistical testing, and the findings of the bivariate analysis. For the bivariate analysis, the assumptions for the Pearson correlation were tested for the parametric analysis. If the assumptions were not fulfilled, the Spearman rank correlation was used for the nonparametric analysis. The findings are reported using the appropriate probability values and confidence intervals. The findings of the multivariate testing, the negative binomial regression analysis, are included. The chapter ends with a summary of the findings of the study.

Data Collection

After obtaining Walden's IRB approval number 5-29-15-0183973, data on dengue cases were extracted from a public assess website of the Florida Department of Health. These data consisted of the imported and autochthonous dengue cases in the State of

Florida for specific counties or regions. The data also included some of the years when imported dengue cases began to emerge (1997 to 2013) and years when autochthonous dengue cases began to emerge (2009 to 2013). The rest of the information in the dataset consisted of the county where the autochthonous dengue cases originated and some of the counties where the imported dengue cases originated. All the dengue cases (imported and autochthonous) had been diagnosed by a physician with laboratory confirmation.

The dataset on temperature and precipitation was obtained directly through the NCDC website. However, the dataset obtained from the Florida Department of Health was needed to localize the appropriate land-based stations. The chosen land-based station data included the climatic variables of temperature and precipitation, with a data set of more than 30 years and in the counties where the autochthonous dengue cases originated. A total of four counties and one region were selected: Monroe County, Miami-Dade County, Broward County, Palm Beach County, and Treasure Coast Region. The NCDC provided a mechanism to search for the land-based station that fulfilled the requirements described above.

After finding the land-based station that fulfilled the requirements, data on temperature and precipitation for 34 years and the data on the dengue cases of the targeted counties were imported to IBM SPSS version 21. The NCDC took steps to clean the data before releasing the data to me. In total, four counties and one region were included; each county had one land-based station, and the Treasure Coast region consisted of three small counties with one land-based station. The counties and the land-based stations were the following: Broward County (Fort Lauderdale GHCND:

USC00083163); Miami-Dade County (Miami International Airport GHCND: USW00012839); Treasure Coast Region, which includes Martin County, St. Lucie County, and Indian River County (Stuart GHCND: USC00088620); Palm Beach County (West Palm Beach International Airport GHCND: USW00012844); and Monroe County (Key West International Airport GHCND: USW00012836). A land-based station for the county of Monroe, even though this county was located in the southwest region of Florida, was included because that was where the first autochthonous dengue cases were diagnosed in 2009 after more than 75 years of no local dengue cases.

The climatic variables extracted from the dataset of each land-based station included 34 years of temperature, which included the following variables: extreme minimum temperature (EMNT), extreme maximum temperature (EMXT), monthly mean minimal temperature (MMNT), monthly mean maximum temperature (MMXT), and monthly mean temperature (MNTM). The variable used to analyze the data was the MNTM (monthly mean temperature) because the mean was calculated using all the temperatures of the month. The rest of the variables were a repetition of the same temperature for every month. The precipitation dataset came with two variables: extreme maximum precipitation (EMXP) and total precipitation (TPCP). The variable used was total precipitation because it included the sum of the precipitation that occurred during the month.

The dataset from NCDC was joined with the data of the dengue cases extracted from the website of the Florida Health Department. The dengue cases only included the laboratory diagnosed dengue cases, autochthonous and imported, from each of the targeted counties. Detailed information was obtained from the years 2009 to 2013; before these years, data on imported dengue cases only came as yearly cases per county, and for some years, no data were found.

The population of each target county was collected directly through the Census Bureau website; the dataset consisted of the population numbers from the period from 1980 to 2013 for each of the regions. The data included numbers for the foreign-born population of the counties, including the numbers of Hispanics and Asians in the targeted regions. All of the data were extracted from public assess websites.

An offset variable was computed using the total number of years in which the imported and autochthonous dengue cases occurred (17 years) and multiplying these by the population of the counties throughout the 34 years. Temperature, precipitation, autochthonous dengue cases, and imported dengue cases were continuous variables. The variables of temperature and precipitation were adjusted using IBM SPSS version 21 to show the measure of the units correctly.

Population of Selected Counties of Southeast Florida

The areas targeted in this study were Monroe County (Key West, southwest Florida), Miami-Dade County, Broward County, Palm Beach County, and the Treasure Coast region; these counties and region are located in the southeastern tip of Florida (Figure 9). The population of the targeted counties and of the Treasure Coast region, which includes Martin County, St. Lucie, and Indian River Counties, increased and changed during the 34 years examined (Table 4).

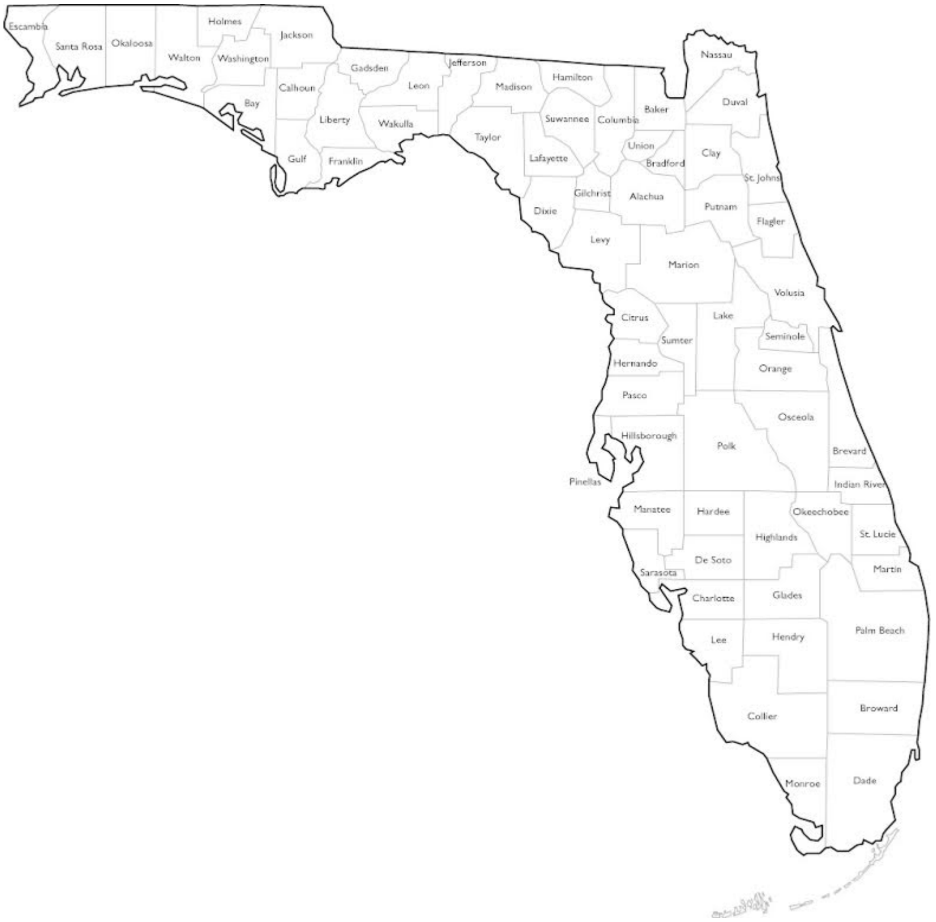


Figure 9. Florida counties. Retrieved from www.rillmzks.tk/florida-county-map/

Table 4

Population Increase of Southeast Florida

County	1980	1990	2000	2010	2013
Broward	1018257	1255488	1631445	1753578	1838844
Miami-Dade	1625509	1937194	2262902	2505379	2617176
Treasure Coast	211092	342412	435247	563350	580089
Monroe	63188	78024	79721	73269	76351

The population of Broward County increased 80% during the 34 years examined, while Miami-Dade County increased 61%, Palm Beach County increased 58%, the Treasure Coast region increased 174%, and Monroe County increased 21%. One reason for the increase in population for these counties was migration, and a portion of migration consisted of foreign-born immigrants (Table 5).

Table 5

Foreign-Born Percentage from Total Population per County

County	1990 (%)	2000 (%)	2009 to 2013 (%)
Broward	15.8	25.3	31.5
Miami-Dade	45	50	51.3
Treasure Coast	6	8.6	17
Palm Beach	12	17	22.6
Monroe	10	15	23

The category *foreign-born immigrants* includes people from all over the world, not only dengue endemic regions, but also nonendemic dengue regions. However, a high percentage of the foreign-born immigrants came from dengue endemic Latin America and Asia. For example, Miami-Dade County has the highest percentage of Latin American immigrants; in 2013, the size of this population was 2,617,176 (Table 4), with over 50% of foreign-born Latin Americans immigrating to this county (Table 6).

Table 6

Foreign-Born Latin American and Asian Population

County	2010	2011	2012	2013
Broward	485,807	488,582	497,492	500,612
Miami-Dade	1,263,139	1,261,832	1,268,187	1,342,492
Palm Beach	248,355	237,893	255,863	272,121

These numbers indicate a rapid increase of migrants whose origins were dengue endemic countries and U.S. territories (Puerto Rico). These immigrants may carry the dengue virus to nonendemic regions such as Florida. Additionally, there is a risk of infection among U.S. residents traveling to dengue endemic areas and returning with the virus to their homes. All of these cases were classified as imported dengue cases. Imported dengue cases have been diagnosed in Florida since 1997; these are individuals with a recent history of travel from dengue endemic countries. Several studies have linked autochthonous dengue outbreaks with introduction of the dengue virus from the imported dengue cases (Huang et al., 2013; Sang et al., 2014). Figure 10 shows the increase in population in all targeted counties and regions.

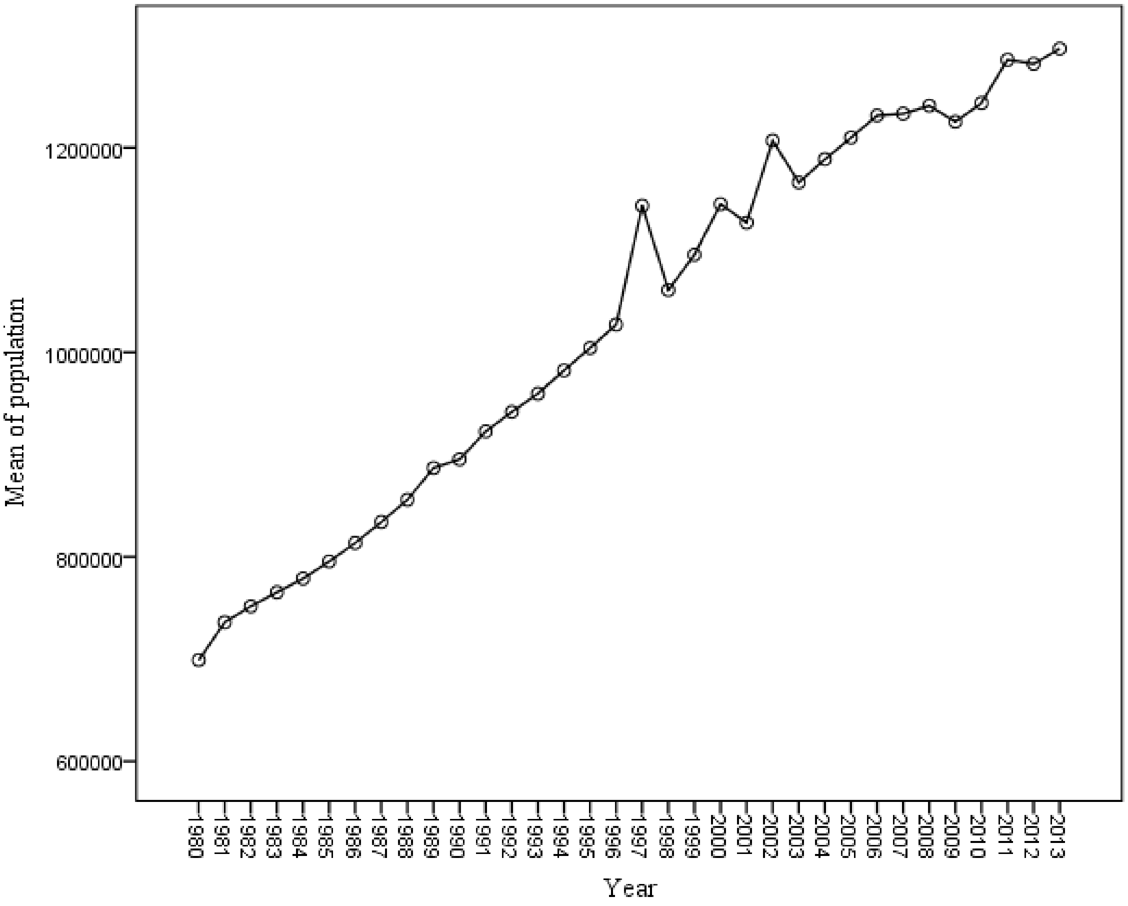


Figure 10. Mean of population over time.

Aedes aegypti Distribution

According to the CDC (2015), the approximate distribution of *A. aegypti* was concentrated mostly in the southern counties of the state of Florida and other southern U.S. states (Figure 10).

Figure 11. Approximate distribution of *Aedes aegypti* mosquito for the United States. Retrieved from "Chikungunya: Information for Vector Control Programs," by Centers for Disease Control and Prevention, 2015, retrieved from http://www.cdc.gov/chikungunya /pdfs/CHIKV_vectorControl.pdf

However, the distribution of the mosquito was developed using current available information, and it may not be consistently found in all shaded areas (CDC, 2015). In the State of Florida, finding the actual mosquito population is more difficult because the traps that many of the counties use (light traps) do not really target *A. aegypti* or *A. albopictus* (Eisen & Moore, 2013).

Results

This section contains the findings of the study, starting with the descriptive statistics and followed by the correlation results for the each of the research questions. The multivariate analysis of the negative binomial regression during 34 and 13 years is included.

Descriptive Analyses

In the year 2009, the first autochthonous dengue cases (locally acquired) were diagnosed in Key West, Florida. After those cases, more autochthonous dengue cases were diagnosed and these cases were found in counties east and north east from Key West such as Broward County and Martin County (Figure 9). These events indicated a possible geographic expansion of dengue fever. In total, 113 autochthonous dengue cases were found in the five selected counties or regions from 2009 to 2013. The mean of the autochthonous dengue cases was .06 with a mode of 0, and a median of 0. More autochthonous dengue cases were found in other counties, however these counties were not targeted in this study. In those five years a total of 362 imported dengue cases were diagnosed in these five counties. The mean of the imported dengue cases was .18 with a mode of 0, and a median of 0.

The total precipitation variable represented the sum of the precipitation during each month during 34 years for each of the five counties. The mean for total precipitation was 122.95 mm, the mode was 22.60 mm, and the median was 97.40 mm. The temperature variable used was the monthly mean temperature (MNTM). The mean was 24.58 °C, the mode was 28.4 °C, and the median was 25.10 °C.

For all the variables, the minimum and maximum number was included, to examine any number that were unrealistic. For example, the maximum temperature for all the five counties was 30.80 °C, however this number represented the mean per month for 35 years. There may have been temperatures higher than 30.80 °C but the number that was used to calculate was the monthly mean (Table 7). Figures 12 to 16 are plots for each variable (MNTM, total precipitation, imported dengue cases, autochthonous dengue cases, and yearly rate of autochthonous dengue cases) over time. These plots show the trend of each variable over time.

Table 7

Descriptive Statistics of Variables and Yearly Rate (Autochthonous)

		Autochtonousdenguecases	Importdenguecases	Total precipitation	Monthly mean temperature	Yearlyrate
N	Valid	2020	2020	2020	2020	2020
	Missing	0	0	0	0	0
M		.06	.18	122.9551	24.5884	.0564
Mdn		.00	.00	97.4000	25.1000	.0000
Mode		0	0	22.60[a]	28.40	.00
SD		.700	1.016	102.08416	3.47936	.83887
Variance		.491	1.033	10421.177	12.106	.704
Skewness		17.128	8.882	1.361	-.453	19.497
Std. error of skewness		.054	.054	.054	.054	.054
Kurtosis		333.827	102.230	2.521	-.735	437.303
Std. error of kurtosis		.109	.109	.109	.109	.109
Range		17	17	746.80	18.40	23.20
Min		0	0	.00	12.40	.00
Max		17	17	746.80	30.80	23.20
Sum		113	362	248,369.40	49,668.50	113.96

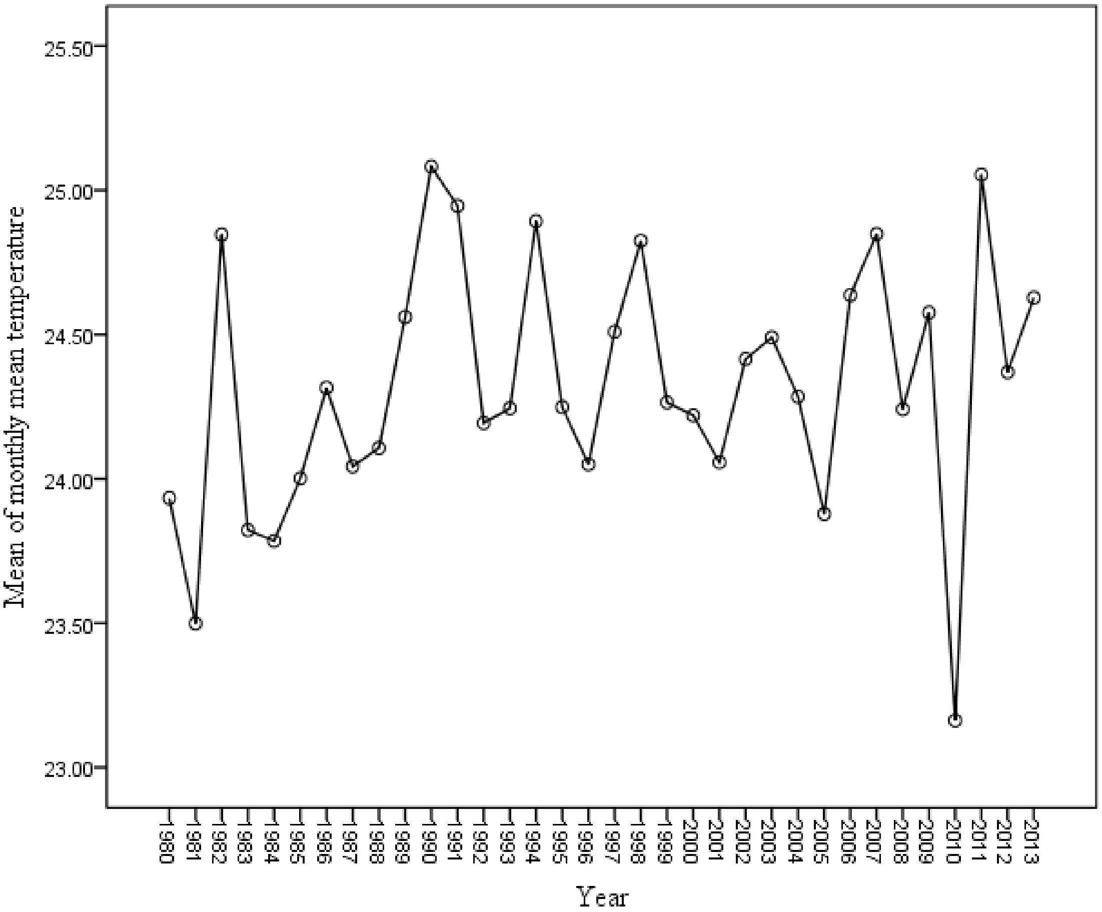


Figure 12. Mean of temperature over time.

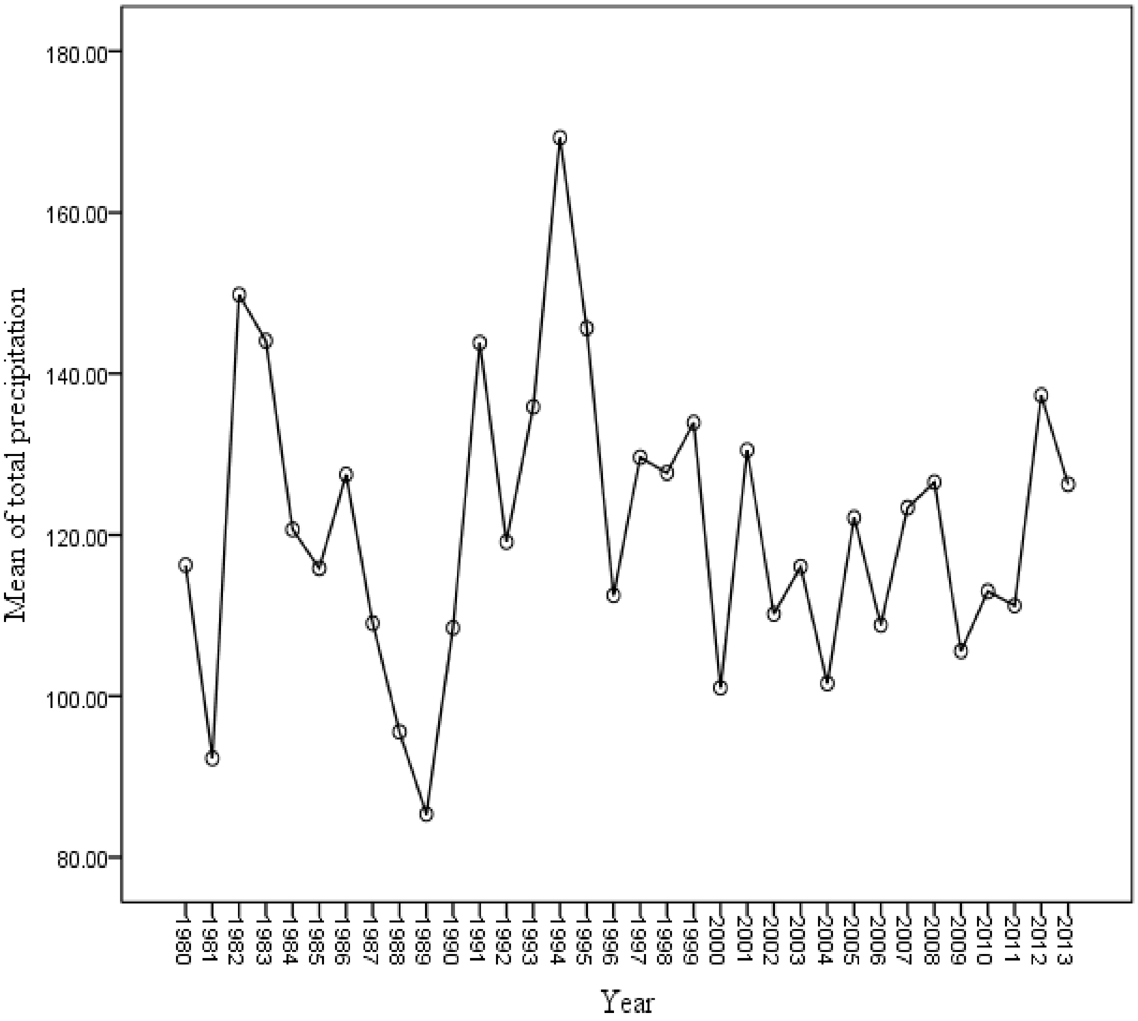


Figure 13. Mean of total precipitation over time.

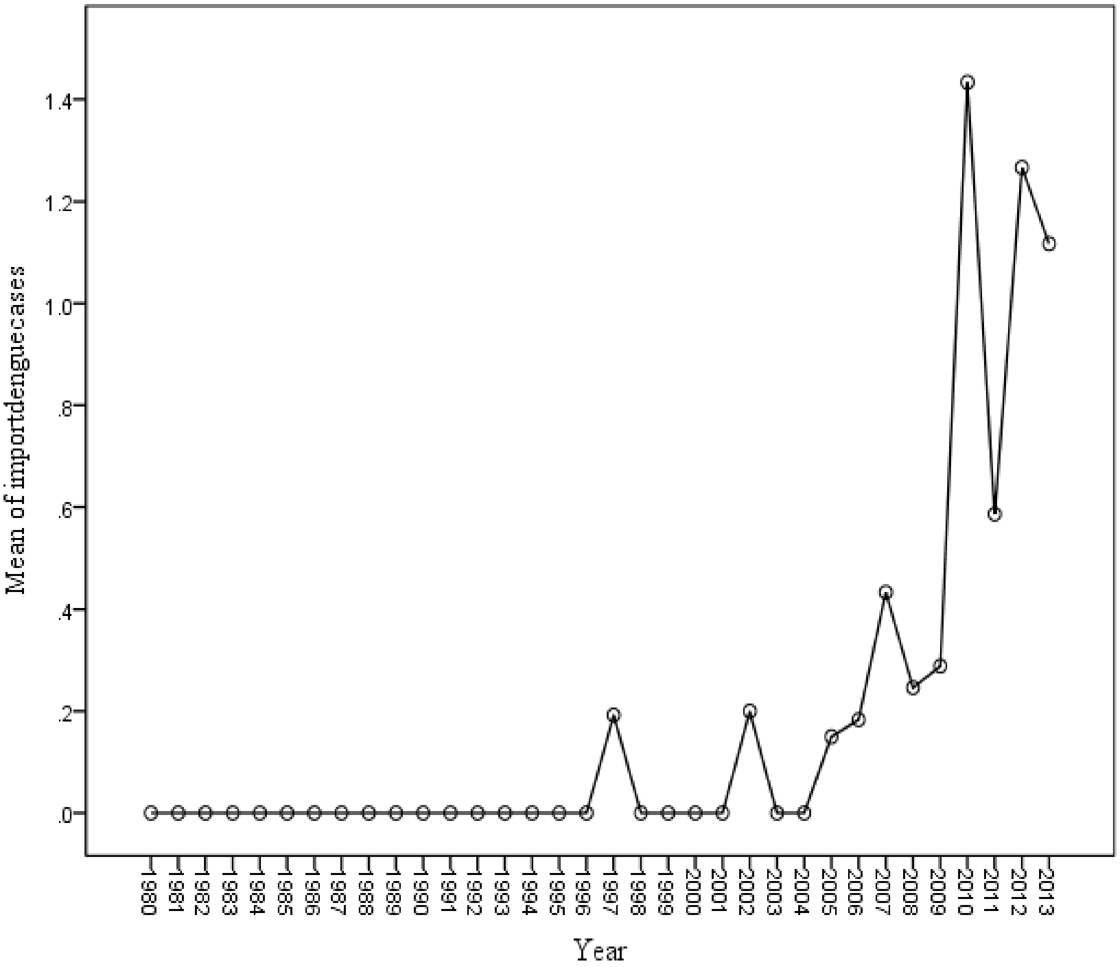


Figure 14. Mean of imported dengue cases over time.

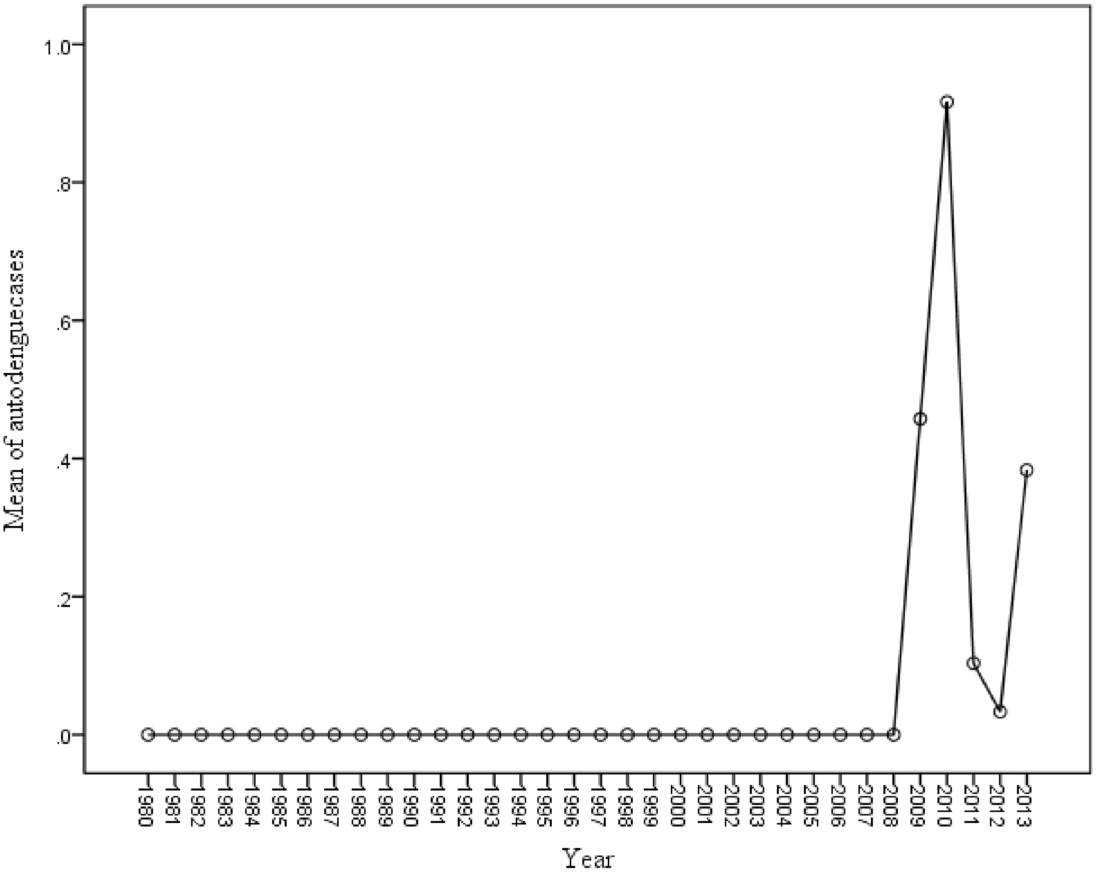


Figure 15. Mean of autochthonous dengue cases over time.

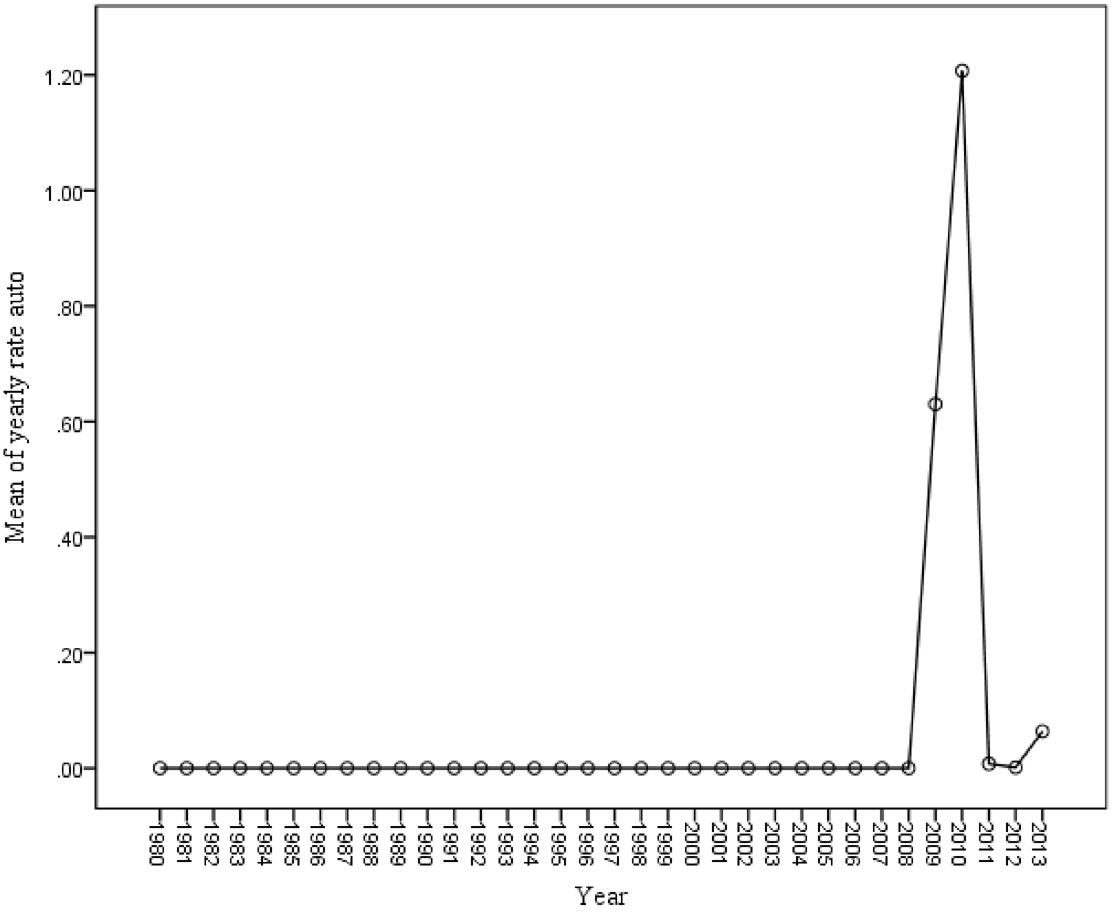


Figure 16. Mean of yearly rate of autochthonous dengue cases over time.

Research Question 1

Was there a significant relationship between temperature during 34 years in southeast Florida and the geographic expansion of dengue fever within the region?

Pearson's correlation. The first step was to test for the assumptions to assure that the data could be analyzed using the Pearson's correlation. The variables were continuous, and a scatterplot was made to visualized linearity. The scatterplot showed a positive association for cases when autochthonous dengue fever increased as the temperature increased, the scatterplot also showed all the zeros as a line across the graph.

To use the Pearson correlation, another assumption needed to be fulfilled, to determine if the data was normally distributed. This assumption was verified using the Shapiro-Wilk for normality test (Table 8). The histograms were included to visualize normality for the dependent variable (autochthonous dengue cases; Figure 17) and the independent variable (monthly mean temperature; Figure 18).

Table 8

Shapiro Wilk Results for Monthly Mean Temperature and Dependent Variable

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	*df*	Sig.	Statistic	*df*	Sig.
autochthonousdenguecases	.518	2020	.000	.054	2020	.000
Temperature (mean monthly, MNTM)	.109	2020	.000	.949	2020	.000

[a] Lilliefors significance correction.

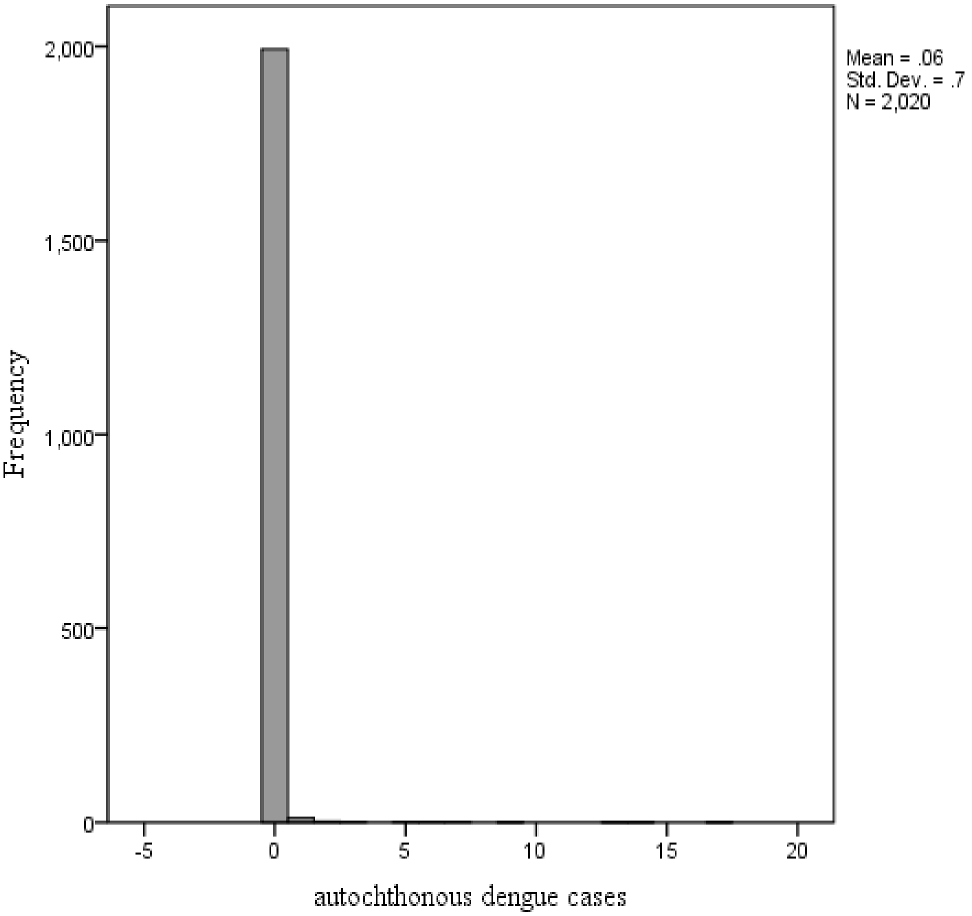


Figure 17. Histogram of autochthonous dengue cases.

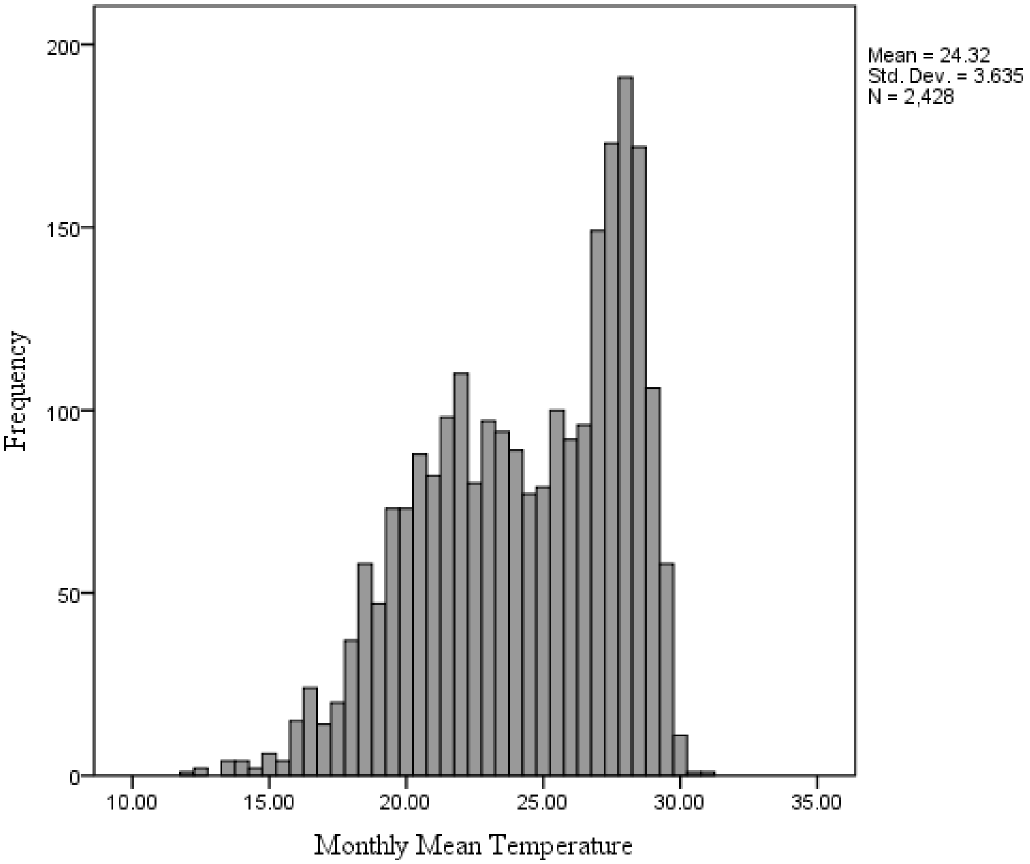


Figure 18. Histogram of monthly mean temperature.

For both variables, autochthonous dengue cases and monthly mean temperature, the results were statistically significant, *p* = .000. These results indicated that the data was not normally distributed, for this reason a Spearman rank correlation coefficient was more appropriate for the data.

The Spearman's correlation was used to determine the relationship between monthly mean temperature and autochthonous dengue cases. Table 11 shows the results of the Spearman's correlation. There was a statistically significant association between the independent variable (monthly mean temperature) and the dependent variable (autochthonous dengue cases), with a weak correlation, $r_s = .099$.

Research Question 2

Was there a significant relationship between precipitation during 34 years in southeast Florida and the geographic expansion of dengue fever in the region?

Pearson's correlation. The first step was to test for the assumption to assure that the data could be analyzed using the Pearson's correlation. The variables were continuous, and a scatterplot was made to visualize for linearity. The scatterplot showed no linear relationship between the independent variable (monthly total precipitation) and the dependent variable (autochthonous dengue cases).

A Shapiro Wilks test was run to determine normality (Table 9) and a histogram was included to visualize normality for total precipitation (Figure 19).

Table 9

Shapiro Wilk Results for Total Precipitation and Dependent Variable

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	*df*	Sig.	Statistic	*df*	Sig.
autochthonous denguecases	.518	2020	.000	.054	2020	.000
Total precipitation	.114	2020	.000	.890	2020	.000

[a] Lilliefors significance correction.

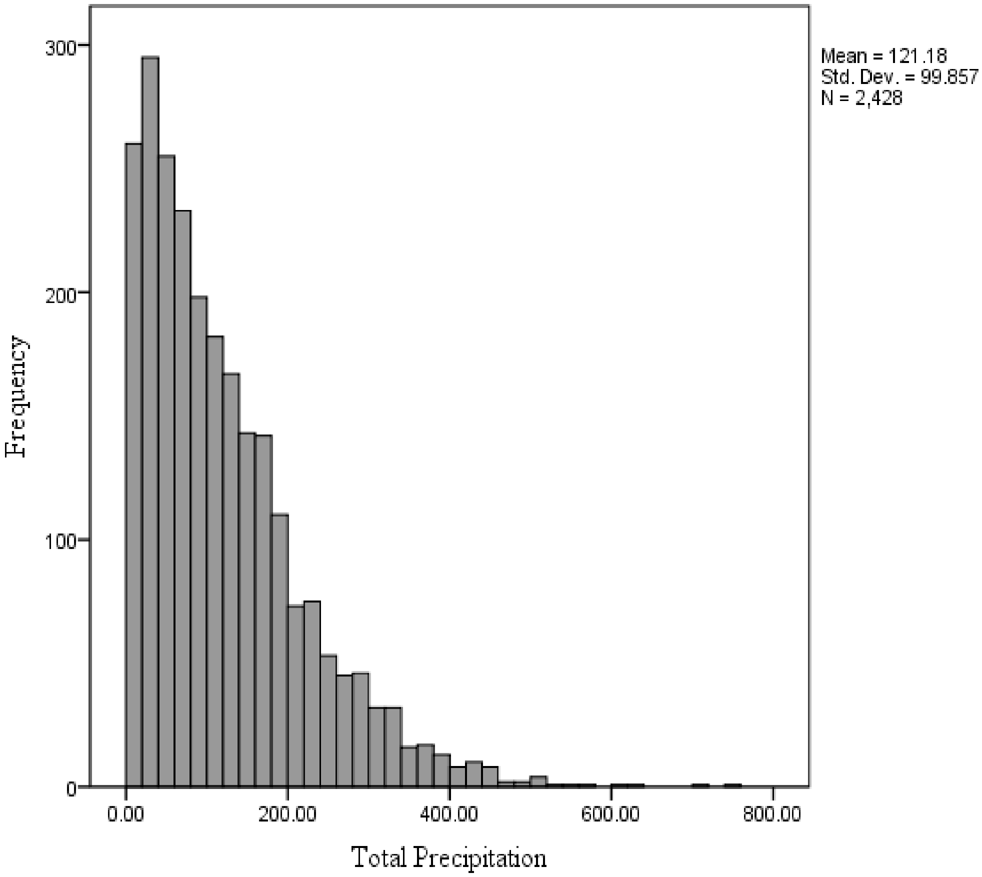


Figure 19. Histogram of total precipitation.

The results of the Shapiro Wilk test indicated that the data was not normally distributed; for this reason, a Spearman correlation test was run to determine correlation. Table 11 shows the results of the Spearman correlation between the independent variable (monthly total precipitation) and the dependent variable (autochthonous dengue cases), $p = .306$ with $r_s = .023$. These results indicate no correlation between precipitation and autochthonous dengue cases.

Research Question 3

Was there a relationship between human migration from dengue endemic areas to nonendemic areas during 34 years and the geographic expansion of dengue fever to southeast Florida?

Pearson correlation. The first step was to test for the assumptions to assure that the data could be analyzed using the Pearson's correlation. The variables were continuous, and a scatterplot was made to visualized linearity. The scatterplot showed no linear relationship between the independent variable (imported dengue cases) and the dependent variable (autochthonous dengue cases). In addition a Shapiro Wilk test was run to determine normality (Table 12) and a histogram was included to visualize normality for imported dengue cases (Figure 20).

Table 10

Shapiro Wilk Results for Imported Dengue Cases and Dependent Variable

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	*df*	Sig.	Statistic	*df*	Sig.
autochthonous denguecases	.518	2020	.000	.054	2020	.000
importdenguecases	.514	2020	.000	.173	2020	.000

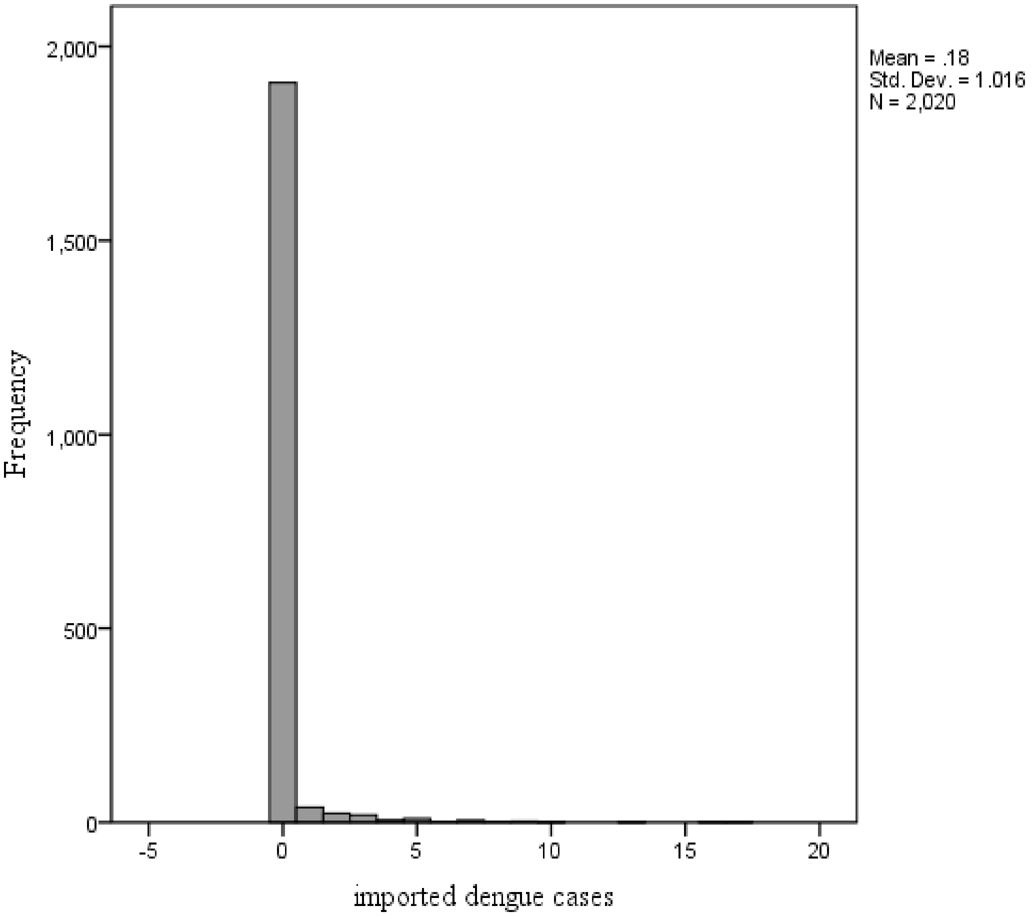


Figure 20. Histogram for imported dengue cases.

The results of the Shapiro Wilk test indicate that the data was not normally distributed, because the assumptions were not met to run a Pearson correlation, a Spearman correlation was ran to determine correlation. Table 11 shows the results of the Spearman correlation test. There was a statistical significant relationship between the independent variable (imported dengue cases) and the dependent variable (autochthonous dengue cases) p = .000, with a weak correlation, r_s =.162.

Table 11

Spearman Correlation Results

			Autoch dengue cases	Monthly mean temperature	Total precipitation	Import denguecases
Spearman's r_s	Autochthonous denguecases	Correlation coefficient	1.000	.099**	.023	.162**
		Sig. (2-tailed)	.	.000	.306	.000
		N	2020	2020	2020	2020
	Monthly mean temperature	Correlation coefficient	.099**	1.000	.487**	.061**
		Sig. (2-tailed)	.000	.	.000	.006
		N	2020	2020	2020	2020
	Total precipitation	Correlation coefficient	.023	.487**	1.000	.068**
		Sig. (2-tailed)	.306	.000	.	.002
		N	2020	2020	2020	2020
	importdenguecases	Correlation coefficient	.162**	.061**	.068**	1.000
		Sig. (2-tailed)	.000	.006	.002	.
		N	2020	2020	2020	2020

**Correlation is significant at the 0.01 level (2-tailed).

Multivariate Analysis

Poisson regression was used to predict which independent variables (imported dengue cases, total precipitation, and temperature) had statistically significant effects on the dependent variable (autochthonous dengue incidence). To analyze the data using the Poisson regression, the data needed to fulfilled several assumptions. The descriptive statistics of the data indicated the variance of the dependent variable was greater than the means of this variable. This indicated an overdispersion, which violated one of the assumptions of the Poisson distribution. Because this assumption was not fulfilled, a negative binomial regression analysis was performed for a better fit of the data to the model.

The data of the imported dengue cases and the autochthonous dengue cases were inconsistently reported in the FDOH website. This resulted in an inability to determine the exact month for when some imported dengue cases were diagnosed. For some imported dengue cases, the data were reported as yearly totals and for other cases some were reported as monthly totals. Due to the limitations of the data, an offset variable was added to adjust for the different periods. The offset variable was computed as the follows: Ln (population x the years of counted dengue cases (imported and autochthonous). The offset variable was named Ln_peryacquiredimported.

A negative binomial regression test was performed for 34 years of observations to determine the effects of the independent variables (temperature, total precipitation, and imported dengue cases) on the dependent variable (autochthonous dengue incidence). Each variable had 2,020 valid observations ($N = 2{,}020$).

Table 12 shows the results of the negative binomial regression test which included the coefficients for each predictor variable including standard error. One of the independent variables or predictors, imported dengue cases, was not statistically significant, $p = .429$, therefore, we failed to reject the null hypothesis.

The other two independent variables, temperature (MNTM), and total precipitation, were statistically significant for predicting autochthonous dengue incidence. Temperature (e.g., MNTM) had a p value of .000, 95% C.I. [1.903, 2.538];

and precipitation (totalprecipitation) had a *p* value of .000, 95% C.I. [.988, .994]; for these two predictors we rejected the null hypothesis

Table 12

Results of Negative Binomial Regression for 34 years

Parameter	B	*SE*	95% Wald confidence interval		Hypothesis test			Exp(B)	95% Wald confidence interval for Exp(B)	
			Lower	Upper	Wald chi-square	*df*	Sig.		Lower	Upper
(Intercept)	-39.242	2.0174	-43.196	-35.288	378.353	1	.000	1.000E-013	1.000E-013	1.005E-013
Importdenguec	.050	.0636	-.074	.175	.626	1	.429	1.052	.928	1.191
Totalprecip	-.009	.0014	-.012	-.006	41.218	1	.000	.991	.988	.994
Monthly mean temperature	.787	.0735	.643	.931	114.777	1	.000	2.198	1.903	2.538
(Scale)	1[a]									
(Negative binomial)	1[a]									

Note. Dependent variable: autochthonousdenguecases. Model: (Intercept), importdenguecases, totalprecip, MNTM, offset = Ln_peryacquiredimported.
[a]Fixed at the displayed value.

The results of this analysis indicated that there was an inverse or negative relationship between precipitation (totalprecip) and the outcome variable (autochthonous dengue incidence). For each 1 unit (mm) increase in precipitation, the rate of the autochthonous dengue incidence decreased by .9%. However, there was a positive relationship between temperature (MNTM) and the outcome variable (autochthonous dengue incidence). For each 1 unit (°C) increase in temperature, the rate of the outcome variable increased by 120%.

A negative binomial regression was performed for the last 10 years of observation to determine the effects of the independent variables (temperature, precipitation, and imported dengue cases) for the dependent variable (autochthonous dengue cases). Each variable had 773 valid observations (*N* = 773).

Table 13 shows the results of the negative binomial test which included the coefficients for each predictor variables along with their standard errors. One of the independent variables or predictors, imported dengue cases, was not statistically significant, *p* = .249, therefore, we failed to reject the null hypothesis. The other two independent variables, temperature (MNTM), and total precipitation, were statistically significant for predicting autochthonous dengue incidence. Temperature (e.g., MNTM) had a *p* value of .000, 95% C.I. [1.158, 1.503]; and precipitation (totalprecipitation) had a *p* value of .000, 95% C.I. [.991, .999]; for these two predictors we rejected the null hypothesis.

Table 13

Results of the Negative Binomial Regression for 10 years

Parameter	B	*SE*	95% Wald confidence interval		Hypothesis test			Exp(B)	95% Wald confidence interval for Exp(B)	
			Lower	Upper	Wald chi-square	*df*	Sig.		Lower	Upper
(Intercept)	-26.432	1.6842	-29.733	-23.131	246.308	1	.000	3.417E-012	2.222E-013	9.011E-011
Importdenguecases	.074	.0641	-.052	.200	1.331	1	.249	1.077	.950	1.221
Totalprecip	-.005	.0020	-.009	-.001	6.664	1	.010	.995	.991	.999
MNTM	.277	.0665	.147	.407	17.344	1	.000	1.319	1.158	1.503
(Scale)	1[a]									
(Negative binomial)	1[a]									

Note. Dependent variable: autochtonousdenguecases. Model: (Intercept), importdenguecases, totalprecip, MNTM, yearlyrate, offset = Ln_peryacquiredimported.
[a] Fixed at the displayed value.

The results of this analysis indicated that there was an inverse or negative relationship between precipitation (totalprecip) and the outcome variable (autochthonous dengue incidence). For each 1 unit (mm) increase in precipitation, the rate of the autochthonous dengue incidence decreased by .5%. However, there was a positive relationship between temperature (MNTM) and the outcome variable (autochthonous dengue incidence). For each 1 unit (°C) increase in temperature, the rate of the outcome variable increased by 32%.

Summary

In Chapter 4, the analysis of the research questions were tested through bivariate analysis and multivariate analysis. The bivariate analysis tested the relationship between each independent variable against the dependent variable. The negative binomial regression tested the effect of the predictors against the dependent variable to describe the relationship between statistically significant predictors and autochthonous dengue incidence.

The results provided in Chapter 4 answered the research questions; there was relationships among the temperature, precipitation, and autochthonous dengue incidence in the counties under study. The first research question was if there were significant relationship between temperature in the past 34 years in southeast Florida and the geographic expansion of dengue fever (e.g., autochthonous dengue cases) in the region. According to the bivariate analyses, Spearman correlation, there was a weak relationship between temperature and geographic expansion of dengue fever (e.g., autochthonous dengue cases), thus rejecting the null hypothesis.

The second research question was if there was a significant relationship between precipitation in the last 34 years in southeast Florida and the geographic expansion of dengue fever in the region (e.g., autochthonous dengue cases). According to the bivariate analyses, Spearman correlation, there was no relationship between precipitation and the geographic expansion of dengue fever (e.g., autochthonous dengue cases), thus accepting the null hypothesis.

The third research question was if there was a significant relationship between imported dengue cases in the last 34 years in southeast Florida and the geographic expansion of dengue fever in the region. According to the bivariate analyses, Spearman correlation, there was a weak relationship between imported dengue cases and the geographic expansion of dengue fever (e.g., autochthonous dengue incidence), thus rejecting the null hypothesis.

The multivariate analysis, negative binomial regression, included the effects of the covariates temperature, precipitation, and imported dengue fever cases on the dependent variable. The variables that contributed significantly in predicting dengue incidence rates were temperature and precipitation. The variable that was not statistically significant in predicting the dengue incidence rates was imported dengue cases.

These findings were interpreted in Chapter 5 by comparing them with the findings in the literature. Included in Chapter 5 were the limitations of the study, the recommendations for future studies, and the implications for positive social change. A conclusion is included at the end of the chapter.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this ecological retrospective quantitative study was to identify a relationship among climatic variables, human migration/imported dengue cases, and the geographic expansion of dengue to nonendemic South Florida. The dependent variable of the study was the geographic expansion of dengue fever to nonendemic South Florida. The dependent variable was defined as the appearance of autochthonous dengue fever cases (locally acquired) in areas where it was previously absent. The independent variables were two climatic variables, temperature and precipitation, and a social context variable, migration (e.g., imported dengue cases). The dependent variable was coded as a continuous variable, specifically as a rate; the independent variables were also continuous variables.

This study was conducted to address the lack of studies regarding the relationship among climatic variables, imported dengue cases, and the expansion of dengue fever to South Florida, which was a nonendemic dengue fever region.

Interpretation of the Findings

To the best of my knowledge, this is the first study that has incorporated temperature, precipitation, and imported dengue cases to find an association with the expansion of dengue fever in a nonendemic region in the United States. The results showed that temperature and precipitation could be used to predict dengue incidence rates (autochthonous dengue incidence) in Southeast Florida. The results also showed that there could be a geographic expansion of dengue fever in this region of Florida.

The independent variables have opposite effects on the outcome variable. The independent variable, temperature, showed a positive association with dengue incidence rates. Temperature was positively correlated with dengue incidence rates in the bivariate analysis as well as the regression analysis. This variable could serve as a predictor for dengue incidence rates in Southeast Florida. Temperature has been found to influence dengue fever incidence rates in several endemic regions of the world, such as Puerto Rico (Johansson, Dominici, & Glass, 2009), Thailand (Johansson, Cummings, & Glass, 2009), and Singapore (Pinto et al., 2011). Sang et al. (2014) found a positive association between temperature and autochthonous dengue cases in the nonendemic region of Guangzhou, China. Huang et al. (2013) found the same association in a similar study in Cairns, Australia. The authors mentioned suggested that temperature was the main determinant for dengue fever transmission and for the positive influence on the life cycle of *A. aegypti*. Increasing temperature reduces the time of the extrinsic incubation period, the gonotrophic cycle, and the mosquito lifecycle (Hii, 2013) and increases the mosquito population (Yang et al., 2009).

According to the descriptive statistics, the minimum (mean) was 23 °C, and the maximum (mean) temperature was 30.80 °C. This range fell within the optimal ranges for the faster development of the mosquito lifecycle (Hii, 2013), for the faster development of the larva and pupa (Yang et al., 2009), for the quick transition of the pupa to adult (Yang et al., 2009), and for the highest survival rate of the adult mosquito (Colon-Gonzalez et al., 2013). In addition, the replication and the transmission of the virus are temperature dependent (Adelman et al., 2013). According to Campbell et al. (2013), no dengue cases were found at a mean temperature of 21 °C, and no virus was found in the salivary glands of *A. aegypti* at a temperature of 20 °C. The temperatures of below 14.5 °C and over 21 °C may represent a weather barrier for the sustainability of dengue transmission (Campbell et al., 2013). These extreme temperatures were not observed in the data of monthly mean temperature for the length of the study. The results indicated a favorable temperature for the proliferation of the adult mosquito as well as the faster development of the pupa and for the replication and transmission of the dengue fever virus.

The independent variable, precipitation, has a negative association with autochthonous dengue incidence rates. The results indicated that increased precipitation decreased autochthonous dengue incidence rates. Precipitation was needed to increase the number of larval breeding places. Several studies indicated that increased precipitation increased breeding sites, increased the mosquito population, and enhanced the risk of dengue fever transmission (Sang et al., 2014). However, other studies reported a negative association of precipitation and local dengue incidence, suggesting that an increased amount of rainfall affected the larva and the eggs because they were washed away (Huang et al., 2013).

Some studies have discarded the influence of precipitation and local dengue incidence because of lack of statistically significant correlation between these two variables (Pinto et al., 2011). Precipitation was a predictor for local dengue incidence but in an amount that could create breeding grounds without disturbance. An increase of rainfall will affect breeding grounds and wash away the larva and eggs, decreasing local dengue incidence. Huang et al. (2013) found that 27 mm of rainfall was an important threshold for determining the incidence of local dengue fever. Huang et al. also found that rainfall was an important limiting factor mostly in Australia. Local dengue fever cases were restricted if rainfall was below a required amount in tropical regions. According to the 34 years of data analyzed for Southeast Florida, this threshold (27 mm) was reached 87% of the time throughout the counties. However, according to Hii (2013), only 21 mm were necessary to create a breeding site for the *Aedes* eggs to develop, and this threshold was reached 90% of the time within 34 years. These results suggest that there was enough precipitation for the development of the eggs in Southeast Florida for the study period.

The independent variable, imported dengue cases, had no association with autochthonous dengue incidence. The results indicated that this variable was not a predictor for local dengue case incidence. Shang et al. (2010) found no significant long-term effect of the imported dengue cases on local dengue incidence. Shang et al. suggested that the imported dengue cases may be the initial facilitator for local dengue case outbreaks in regions with low immunity; however, the relationship disappeared once the outbreak reached a threshold. Sang et al. (2014) found the same relationship in his study in nonendemic Guangzhou, China. The author found an association of local dengue cases with imported cases until a certain time frame within favorable weather conditions. Huang et al. (2013) found a strong influence of imported dengue cases with local dengue cases incidence, but also under favorable weather conditions.

The findings indicated that for an onset of dengue epidemic, the imported dengue cases had a significant quantitative relationship; the results of the bivariate analysis indicated a weak but positive relationship. Once the virus was in the vector ecology, the main determinants for spread and more local dengue cases were favorable weather conditions—in this study, temperature and precipitation.

Eco-bio-social research on dengue was the conceptual framework for the dissertation. As described in Chapter 2, the eco-bio-social model focuses on finding the determinants influencing the ecology of the dengue vector (Arunachalam et al., 2010). The framework includes a broad spectrum of factors that influence the *A. aegypti* mosquito. Ecological, biological, and social variables are interdependent factors for dengue vector development with a direct and complex impact on prevention and control measurements (Quintero et al., 2014). The framework has portions that were used in the study: ecological factors included temperature and rainfall; biological factors included behavior of the mosquito and transmission of the virus; and social factors included the migration of imported dengue cases. The broad conceptual framework guided the study of the factors and the complexities influencing the vector ecology and viral transmission of dengue fever.

Limitations of Study

There were limitations to the study regarding the use of a secondary dataset from the Florida Health Department, lack of data, and the study design. One of the limitations was the reliability and completeness of secondary data from the Florida Department of Health. Dengue fever was considered a neglected tropical disease not seen in Florida since 1934. The first patients with dengue began to be diagnosed in 1997, and these were imported dengue cases. Throughout the years, more imported dengue cases were diagnosed, but the data found were yearly, with no monthly cases reported. Not until the outbreak on Key West in 2009, when autochthonous dengue cases were first diagnosed, did the data begin to be reported on a monthly basis and with more detail.

The second limitation of the study was the lack of data concerning the population of the mosquitos responsible of transmitting dengue fever, and several other infectious viral diseases. According to Eisen and Moore (2013) the *A. aegypti* mosquito required a unique collection methodology. Current efforts were more focused on mosquitos such as *Culex* (West Nile virus vector), using light traps that did not yield useful surveillance data for the *Aedes* mosquito. The lack of *Aedes* sp. population data prevented the determination of the changes in population throughout the 34 years and impeded correlating this variable with the climatic variables of temperature and precipitation.

The third limitation was the possibility of under-reporting or overreporting of dengue fever in a region where the health providers were not familiar with this uncommon disease. Under-reporting can be likely if infected people did not seek medical attention because of subclinical symptoms of dengue fever. Another limitation could have been misclassification of dengue cases for other infectious diseases. These limitations were not under the control of the researcher.

The fourth limitation was other potential confounders such as mosquito population and other social factors affecting the assessment of the association among incidence of autochthonous dengue cases, climatic variables, and imported dengue cases.

However, past studies have found that temperature and precipitation can be predictors for autochthonous dengue fever cases. This study examined the relationship between these climatic variables and accounted for imported dengue fever cases and excess zeros.

Although there were benefits to the correlation and regression studies, such as convenience and low-cost, there were limitations of the study's design. The inherent weakness of the ecological design was the difficulty to detect complicated exposure-outcome relationships, so causation cannot be established. To address this limitation in this study, the results were reported as associations, not causations. In addition, the use of the appropriate statistical analyses helped address this limitation.

Recommendations

The results of this study contributed to the limited body of knowledge regarding autochthonous dengue fever cases, climatic variables, and imported dengue cases in nonendemic southeast Florida. However, there are opportunities for further research in this area.

More studies are needed to understand the factors influencing the mosquito and the dengue virus in the specific region of Southeast Florida. The regions that will benefit in future research are not only the vulnerable regions of Florida, but also Texas and Hawaii, which have had past outbreaks of dengue fever (Adalja et al., 2012). Utilizing the eco-bio-social research on dengue framework, which covers a broader spectrum of factors on the ecology of the mosquito and dengue transmission, will help researchers create a specific picture in the different vulnerable regions.

It is necessary to gather data on the population of the *Aedes* mosquito. This data could help to assess the changes in the population of this vector and be used to assess its relationship to the incidence and prevalence of dengue fever. Studies have found that the *Aedes* sp. was a highly adaptable vector for diverse ecological conditions (Bonizzoni et al., 2012). The *A. aegypti* mosquito was not only the vector of dengue fever virus, but also the vector of yellow fever virus and chikungunya virus (CDC, 2012). Leaving this vector unchecked will place multiple communities at risk.

An open communication between public health agencies, clinical and laboratory personnel, immediately as imported or autochthonous dengue fever are diagnosed, will help provide accurate and efficient information. This will provide an early opportunity for the community shareholders to be involved in vector control, dengue fever identification, and accurate reporting.

Implications

The findings of this study have the potential to trigger more studies in vulnerable regions of the United States and to encourage research on neglected diseases such as dengue fever in Florida, Texas, and Hawaii. This study has provided a better understanding of the influence of changing climatic weather on vector-borne infectious diseases in nonendemic regions. The implications for positive social changes include the use of these results by public health agencies and environmental agencies to formulate evidence-based decisions regarding resource allocations for prevention and mitigation of dengue fever outbreaks and possible geographic expansion of dengue fever

Another implication for social change is to update the actual knowledge about dengue fever in vulnerable regions. The knowledge of the risk factors associated with autochthonous dengue fever can promote future public health actions. There is limited data on the population of the *Aedes* mosquito which will be needed for more studies that will required this type of data to analyze the changes and behavior of the mosquito population in an evolving environment.

Another implication for social change is the possible open communication between public health agencies and clinical and laboratory facilities which can promote early identification of dengue cases for a better management from the health care providers and from the public health agencies. An important implication for social change is the development of strategies to inform, educate, and empower the community about the prevention and elimination of breeding sites and about the signs and symptoms of dengue fever in nonendemic regions such as Southeast Florida.

Since this study may be the first to research dengue fever and some of its risks factors in Florida, there may be other factors that can be contributing to the geographic expansion of dengue fever in the region. The final implication for social change is the promotion of more research regarding the social determinants and how they influence autochthonous dengue fever incidence.

Conclusions

To the best of my knowledge, this study is the first to correlate and regress the relationship between autochthonous dengue incidence with climatic variables and imported dengue incidence in nonendemic Southeast Florida. The results of this study suggest that temperature and precipitation are the principal predictors of the geographic expansion of dengue fever in Southeast Florida (e.g., autochthonous dengue incidence). The increase of temperature, along with an appropriate amount of precipitation may influence the geographic expansion of dengue fever in Florida.

The data has shown a movement of autochthonous dengue fever incidence from Monroe County (southwest Florida) to Miami-Dade County (southeast Florida) to Broward County (north of Miami-Dade County) to Palm Beach County (north of Broward County) to the Treasure Coast Region (Figure 9). This suggests that a change in temperature and adequate precipitation in those counties may have favored the proliferation of the *A. aegypti* mosquito and the rapid replication and transmission of the dengue fever virus, hence the appearance of autochthonous dengue fever cases.

Even though imported dengue fever incidence is not a predictor for autochthonous dengue fever cases; the high migration of people from dengue endemic regions to Southeast Florida suggests that the virus may have entered the mosquito ecology through migration. According to Shang et al. (2014) imported dengue fever cases facilitated the initial outbreaks of autochthonous dengue fever outbreaks; however, this influence disappeared once the outbreak reached a threshold. These outbreaks only occurred under favorable climatic conditions of temperature and precipitation.

Some studies found precipitation as an important determinant for autochthonous dengue incidence (Johansson et al., 2009, Huang et al., 2013). In this study, the conclusion is that with high precipitation, the larva, pupa, and eggs will be washed away and the dengue incidence will decrease, the same result was found by Sang et al. (2014) and Shang et al. (2013).

The results of a negative association between precipitation and autochthonous dengue incidence and a reverse relationship in other studies may seem inconsistent; however, we must take in consideration the amount of precipitation and general climate of the region that was being studied. The diversity of the climates and also the habits of the population makes it necessary to study each region because of its uniqueness.

There is a tremendous potential for the geographic expansion of the *A. aegypti* mosquito in areas where the climatic conditions are favorable, including regions of the United States. Dengue fever should not be considered a neglected disease anymore, especially when the highly adaptable *Aedes* mosquito has demonstrated resiliency and had reclaimed territory where it was considered eradicated.

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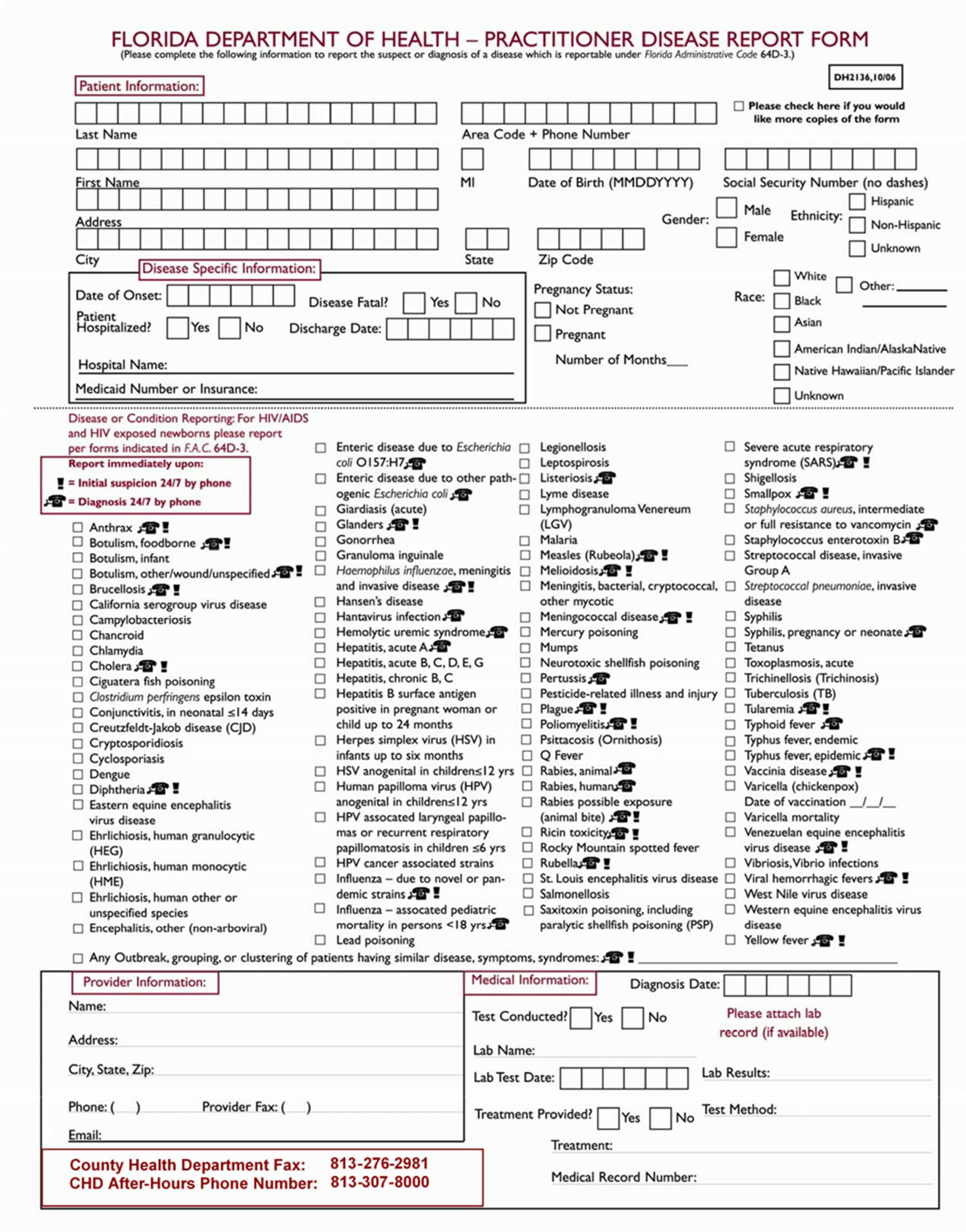
Appendix A: Practitioner Disease Report Form



FLORIDA DEPARTMENT OF HEALTH – PRACTITIONER DISEASE REPORT FORM

(Please complete the following information to report the suspect or diagnosis of a disease which is reportable under *Florida Administrative Code* 64D-3.)

DH2136,10/06

Patient Information:

☐ **Please check here if you would like more copies of the form**

Last Name

Area Code + Phone Number

First Name

MI

Date of Birth (MMDDYYYY)

Social Security Number (no dashes)

Address

Gender: ☐ Male ☐ Female

Ethnicity: ☐ Hispanic ☐ Non-Hispanic ☐ Unknown

City

State

Zip Code

Disease Specific Information:

Date of Onset:

Disease Fatal? ☐ Yes ☐ No

Patient Hospitalized? ☐ Yes ☐ No

Discharge Date:

Hospital Name:

Medicaid Number or Insurance:

Pregnancy Status:
☐ Not Pregnant
☐ Pregnant
Number of Months___

Race: ☐ White ☐ Other: ________
☐ Black
☐ Asian
☐ American Indian/AlaskaNative
☐ Native Hawaiian/Pacific Islander
☐ Unknown

Disease or Condition Reporting: For HIV/AIDS and HIV exposed newborns please report per forms indicated in *F.A.C.* 64D-3.

Report immediately upon:

❗ = Initial suspicion 24/7 by phone

☎ = Diagnosis 24/7 by phone

- ☐ Anthrax ☎ ❗
- ☐ Botulism, foodborne ☎ ❗
- ☐ Botulism, infant
- ☐ Botulism, other/wound/unspecified ☎ ❗
- ☐ Brucellosis ☎ ❗
- ☐ California serogroup virus disease
- ☐ Campylobacteriosis
- ☐ Chancroid
- ☐ Chlamydia
- ☐ Cholera ☎ ❗
- ☐ Ciguatera fish poisoning
- ☐ *Clostridium perfringens* epsilon toxin
- ☐ Conjunctivitis, in neonatal ≤14 days
- ☐ Creutzfeldt-Jakob disease (CJD)
- ☐ Cryptosporidiosis
- ☐ Cyclosporiasis
- ☐ Dengue
- ☐ Diphtheria ☎ ❗
- ☐ Eastern equine encephalitis virus disease
- ☐ Ehrlichiosis, human granulocytic (HEG)
- ☐ Ehrlichiosis, human monocytic (HME)
- ☐ Ehrlichiosis, human other or unspecified species
- ☐ Encephalitis, other (non-arboviral)
- ☐ Enteric disease due to *Escherichia coli* O157:H7 ☎
- ☐ Enteric disease due to other pathogenic *Escherichia coli* ☎
- ☐ Giardiasis (acute)
- ☐ Glanders ☎ ❗
- ☐ Gonorrhea
- ☐ Granuloma inguinale
- ☐ *Haemophilus influenzae*, meningitis and invasive disease ☎ ❗
- ☐ Hansen's disease
- ☐ Hantavirus infection ☎
- ☐ Hemolytic uremic syndrome ☎
- ☐ Hepatitis, acute A ☎
- ☐ Hepatitis, acute B, C, D, E, G
- ☐ Hepatitis, chronic B, C
- ☐ Hepatitis B surface antigen positive in pregnant woman or child up to 24 months
- ☐ Herpes simplex virus (HSV) in infants up to six months
- ☐ HSV anogenital in children≤12 yrs
- ☐ Human papilloma virus (HPV) anogenital in children≤12 yrs
- ☐ HPV assocated laryngeal papillomas or recurrent respiratory papillomatosis in children ≤6 yrs
- ☐ HPV cancer associated strains
- ☐ Influenza – due to novel or pandemic strains ☎ ❗
- ☐ Influenza – assocated pediatric mortality in persons <18 yrs ☎
- ☐ Lead poisoning
- ☐ Legionellosis
- ☐ Leptospirosis
- ☐ Listeriosis ☎
- ☐ Lyme disease
- ☐ Lymphogranuloma Venereum (LGV)
- ☐ Malaria
- ☐ Measles (Rubeola) ☎ ❗
- ☐ Melioidosis ☎ ❗
- ☐ Meningitis, bacterial, cryptococcal, other mycotic
- ☐ Meningococcal disease ☎ ❗
- ☐ Mercury poisoning
- ☐ Mumps
- ☐ Neurotoxic shellfish poisoning
- ☐ Pertussis ☎
- ☐ Pesticide-related illness and injury
- ☐ Plague ☎ ❗
- ☐ Poliomyelitis ☎ ❗
- ☐ Psittacosis (Ornithosis)
- ☐ Q Fever
- ☐ Rabies, animal ☎
- ☐ Rabies, human ☎
- ☐ Rabies possible exposure (animal bite) ☎ ❗
- ☐ Ricin toxicity ☎ ❗
- ☐ Rocky Mountain spotted fever
- ☐ Rubella ☎ ❗
- ☐ St. Louis encephalitis virus disease
- ☐ Salmonellosis
- ☐ Saxitoxin poisoning, including paralytic shellfish poisoning (PSP)
- ☐ Severe acute respiratory syndrome (SARS) ☎ ❗
- ☐ Shigellosis
- ☐ Smallpox ☎ ❗
- ☐ *Staphylococcus aureus*, intermediate or full resistance to vancomycin ☎
- ☐ Staphylococcus enterotoxin B ☎
- ☐ Streptococcal disease, invasive Group A
- ☐ *Streptococcal pneumoniae*, invasive disease
- ☐ Syphilis
- ☐ Syphilis, pregnancy or neonate ☎
- ☐ Tetanus
- ☐ Toxoplasmosis, acute
- ☐ Trichinellosis (Trichinosis)
- ☐ Tuberculosis (TB)
- ☐ Tularemia ☎ ❗
- ☐ Typhoid fever ☎
- ☐ Typhus fever, endemic
- ☐ Typhus fever, epidemic ☎ ❗
- ☐ Vaccinia disease ☎ ❗
- ☐ Varicella (chickenpox) Date of vaccination __/__/__
- ☐ Varicella mortality
- ☐ Venezuelan equine encephalitis virus disease ☎ ❗
- ☐ Vibriosis, Vibrio infections
- ☐ Viral hemorrhagic fevers ☎ ❗
- ☐ West Nile virus disease
- ☐ Western equine encephalitis virus disease
- ☐ Yellow fever ☎ ❗

☐ Any Outbreak, grouping, or clustering of patients having similar disease, symptoms, syndromes: ☎ ❗ ____________________

Provider Information:

Name:

Address:

City, State, Zip:

Phone: (   )

Provider Fax: (   )

Email:

County Health Department Fax: 813-276-2981

CHD After-Hours Phone Number: 813-307-8000

Medical Information:

Diagnosis Date:

Test Conducted? ☐ Yes ☐ No

Please attach lab record (if available)

Lab Name:

Lab Test Date:

Lab Results:

Treatment Provided? ☐ Yes ☐ No

Test Method:

Treatment:

Medical Record Number:

Appendix B: Permission to Use World Health Organization Materials

ID: 154792 - Form to request permission to reproduce or reprint WHO copyrighted material

permissions <permissions@who.int> Mar 13

to me

Dear Brunilda,

Thank you for completing the online form and for your interest in WHO published materials.

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Kind regards,
Joelle Jacquier
WHO Press

-----Original Message-----
From: internet
Sent: vendredi 13 février 2015 16:14
To: permissions; brunilda.lugo@waldenu.edu
Subject: [DataCol Web] Form to request permission to reproduce or reprint WHO copyrighted material

DataCol Web: Form to request permission to reproduce or reprint WHO copyrighted material
==
ID: 154792

Appendix C: Permission to Use DENV Ecology Diagram

From: Brunilda Lugo brunilda.lugo@waldenu.edu
Date: August 20, 2014 at 9:11:59 PM EDT
To: Cory W Morin <cmorin@email.arizona.edu>
Cc: Kacey Ernst <kernst@email.arizona.edu>, Andrew Comrie <Comrie@arizona.edu>
Subject: Re: Permission to use the Biophysical Influence on DENV Ecology Framework

Dr. Morin:
Thank you for your prompt reply and permission for using the framework. I went to the Environmental Health Perspective website; this particular journal is a publication of the U.S. Federal Government so it lies in the public domain and it is copyright free.
Thank you very much!

Sent from my iPad

On Aug 18, 2014, at 2:17 PM, "Cory W Morin" <cmorin@email.arizona.edu> wrote:

Hi Brunilda,

Thank you for taking an interest in my work, the topic of your research is very interesting. You certainly have my permission to use the figure (I have cc'd the other authors of the paper as well), however, because this figure was published (Environmental Health Perspectives) you will probably require permission from the journal. Good luck with your dissertation!

Cory Morin, PhD
NASA Postdoctoral Fellow
NSSTC