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Demographic, Environmental, and Clinical Variables Associated With Dengue in Saint Lucia

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Abstract

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by

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DVM, University of the West Indies, 2001

MSc, University of London, 2006

MPH, University of Minnesota, 2010

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Dengue is the most important arboviral disease of public health concern on the world stage. In Saint Lucia, the disease has been endemic for years. Little research has been published on the specific epidemiology of dengue in Saint Lucia, and this study sought to identify the risk factors associated with the disease specific to the island. This study was underpinned by ecological theory, which is used to explain the possible relationships between risk factors and the occurrence of dengue. This three-manuscript study was used to evaluate the relationship between demographic, environmental, and clinical variables and the occurrence of dengue as individual studies. The data for the explanatory variables and dengue occurrence were accessed from the databases of Central Statistics Office of Saint Lucia, the Saint Lucia Tourism Authority, the Saint Lucia Meteorological Office, and the Ministry of Health and Wellness and analyzed using chi-squared and logistic regression tests. It was demonstrated that the adolescent age group, ages 13-18 years ($p < .001$, OR 4.339 [CI 2.731-6.891), the district of Laborie ($p = .05$, OR 3.371 [CI 1.459-7.792]), maximum daily temperature of $> 32^{o}$ C ($p = .05$, OR 3.350 [CI 1.312-8.555]) undifferentiated fever, ($p < .001$, OR 5.250 [CI 3.557-7.749]) acute respiratory infections or fever with respiratory signs and gastroenteritis 1.622 ($p < .001$, OR 1.622 [CI 1.038-2.535]) had significant, positive relationships with dengue in Saint Lucia. Findings may allow public health authorities to elicit social change by better targeting control programs, and further research is recommended to better understand the complex epidemiology of dengue in Saint Lucia. During periods of increased rainfall and temperature health care professionals should have a high index of suspicion for dengue.

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Dedication

I dedicate this manuscript to my parents Desmond and Lucia Lee, who always encouraged us to pursue education making personal sacrifice to ensure that we were able to pursue our dreams. I remember the late nights and early mornings that my father kept watch with me as I studied for one course or another, one exam or the other. Thank you for both for your unconditional love and support. I thank my brother Deale for his support and encouragement through the long and at times arduous course and dissertation process of this PhD. I also remember my oldest brother John and sister Beverly who have offered comfort and support at times during my educational journey when things were not the brightest. The love and support of family is paramount.

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Part 1: Overview

The Factors Associated With Dengue in Saint Lucia

Dengue is recognized as one of the most important arboviruses of global concern through its capacity for rapidly spreading from areas of endemicity to areas that were historically unfavorable for the explosion of *Aedes* mosquito vectors (Ahlawat & Kalra, 2017; Liebig et al., 2018). The Caribbean, including the island of Saint Lucia, is recognized as being hyperendemic for dengue because multiple strains of the dengue virus are found to circulate at the same time (Kumar et al., 2018). The prevalence of vector-borne diseases such as dengue are determined by the presence of the needed vector, in the case of dengue the *Aedes* mosquito, a susceptible population and the ability of the vector to attack this population. These parameters are further strengthened by the weakness of the public health structures to prevent and control associated outbreaks (Guzman & Harris, 2015). The limited resources available for public health in the region means that the burden of dengue in the region carries a tremendous cost to the population and economies of the region, especially because there are limited tools to control and manage dengue (Wilder-Smith et al., 2017). There is a dearth of published information on dengue in Saint Lucia, which I sought to address in this study.

Introduction

Dengue-Burden of Disease

Dengue is currently the most important arboviral disease affecting almost half of the entire world population, increasing more than 30 times in the past 50 years (Murray et al., 2013). The disease has become endemic in countries in Southeast Asia, the Americas, Africa, the Mediterranean, and Pacific (Guzman & Harris, 2015). The countries found to be endemic for dengue have historically been found between 35^{o}N and 35^{o}S, which typically included the tropical and subtropical regions with climates that could support the mosquito-vector populations (Souers et al., 2014). Transmission of dengue is now present in every World Health Organization (WHO) region of the world and more than 125 countries are known to be dengue endemic (Akter et al., 2017; Ebi & Nealon, 2016; Fritzell et al., 2018). In 2013, it was estimated that there were almost 60 million symptomatic cases and almost 14,000 associated deaths at a global cost of approximately US$9 billion (Shepard et al., 2016). Other researchers have suggested that approximately 390 million persons are infected with dengue every year though the majority of cases are asymptomatic and many of those exhibiting clinical signs recover (Bhatt et al., 2013a; Sanyaolu et al., 2017). Guo et al. (2017) reported that the global mortality rate associated with dengue between 1990 and 2015 was 1.3%.

Although the dengue associated fatality rate may be low, researchers attribute this to the lack of data or underreporting rather than an actual low mortality rate. The burden of dengue lies heavily on its associated medical costs and especially losses in productivity at work and school (Shepard et al., 2016). It is estimated that passive national surveillance systems may report cases up to 28-fold lower in Latin America than the actual caseload underscoring the severity of underreporting (Guzman & Harris, 2015; Sarti et al., 2016). In 2013, it was estimated that 1.14 million disability-adjusted life years (DALYs) were attributed to dengue (Castro et al., 2017). In 2019, the Americas recorded more than 3 million cases; more than the previous highest number of approximately 2.5

million in 2015 (Mitchell, 2020). This reflects how important dengue is within the region and the need to focus on it as a re-emerging disease. These losses in productivity have significantly influenced the world economy and are not well estimated because the majority of persons infected with dengue do not seek medical care and thus their absence from work or school is not correctly attributed to dengue. Dengue outbreaks can also affect tourism economies from decreased visitor arrival especially to mass events such as the Olympics or World Cup as well as travel for business, outcomes which are again challenging to correctly evaluate (Castro et al., 2017).

In a review of the literature by Cafferata et al. (2013) it was reported that between 2000 and 2007 the estimated cost associated with dengue was US$2.1 billion dollars per year in the Americas. The majority of dengue-endemic countries are low- or middle-income countries with limited resources to combat the disease, which is a global threat and researchers call on the public health community to raise the awareness of the larger world community to persuade donor agencies and countries to dedicate resources to address the challenge of dengue (Cafferata et al., 2013). Dengue is an important public health challenge to the countries of the Caribbean many of which are dengue endemic (Torres et al., 2017). The Caribbean islands with an estimated 2013 gross domestic product (GDP) of approximately US$66 billion and heavily reliant on service industries such as tourism are poorly equipped and lack the resilience to continually respond effectively to the public health challenge of dengue (Cannonier & Burke, 2018; Wright et al., 2018).

Saint Lucia and the other countries in the Americas have recently been facing the extraordinary crisis of the cocirculation of multiple arboviral diseases namely dengue, chikungunya and Zika, which are all transmitted by the *Aedes* mosquito (Carrillo-Hernández et al., 2018; Rodriguez-Morales et al., 2016). These viral diseases all share similar clinical signs, making early diagnosis based on clinical signs challenging and further exacerbating the public health burden of these diseases (Lowe et al., 2018). Chikungunya virus, which has circulated in the old world for decades since first being discovered in 1953, and Zika virus, which likewise has circulated in the old world since its discovery in 1947, both were first detected in the Americas in 2013 and 2015, respectively (Patterson et al., 2016). These new viruses, along with the ongoing circulation of dengue, quickly overwhelmed the public health services within the region, especially when the association between Zika infections and congenital microcephaly was reported which saw an increase of concerned mothers seeking treatment (Katzelnick et al., 2017; Rodriguez-Morales et al., 2016). The published data available on dengue and other arboviruses in the smaller Caribbean islands such as Saint Lucia are limited as a result of limited resources leading to inadequate surveillance and limited knowledge of the epidemiology of dengue (Schiøler & Macpherson, 2009; Torres et al., 2017). The rapid, uncontrolled spread of first chikungunya then Zika, emphasizes the deficiencies in public health systems across the Caribbean and the importance of investigating these diseases in an attempt to reduce the associated socioeconomic effects and provide public health agencies information that can be used to better prevent and control such diseases (Wilder-Smith et al., 2017). The 2020 COVID-19, pandemic devasted the public health systems of many countries across the world and in the Americas likely reduced the resources and focus applied to dengue (Lorenz et al., 2020; Zhu et al., 2020). Researchers also questioned the ability of clinicians to differentiate COVID-19 from dengue because the two diseases share similar clinical signs such as fever and rash (Yan et al., 2020).

Though there has been a significant amount of research on dengue, in some countries in the Caribbean and Latin America, there has not been a successful sustained program to control, reduce, or prevent the disease, which has a pattern of periodic outbreaks every 3 to 5 years (Cafferata et al., 2013). The failure of dengue programs is attributed to a wide range factors such as lack of efficient, accurate, bedside diagnostic tests and widely licensed vaccines, underreporting, effective therapeutics, lack of political will, and proper allocation of resources (Laughlin et al., 2012; Murray et al., 2013; Pang et al., 2017; Yousaf et al., 2018). There has been steady progress to the development of vaccines against dengue with one being licensed in 2016 in a limited number of countries, though there is considerable concern and debate over its efficacy and safety (Aguiar & Stollenwerk, 2018; Dans et al., 2018; Hadinegoro et al., 2015; Hadinegoro et al., 2018; Yousaf et al., 2018). There are numerous control and management options for the *Aedes* mosquito, which is the main vector of dengue, but these are often costly and require sustained resource appropriation which is challenging to many of the countries that are dengue-endemic given competing public health and other national needs (Horstick et al., 2015; Murray et al., 2013). The challenges of dengue are magnified in small-island states such as Saint Lucia where economic losses from loss of productivity are felt acutely through the tourism based economy and the limited resources restrict the scope of dengue surveillance and control activities (Jackman, 2014). Torres et al. (2017) noted that differences in the epidemiology of dengue exists between countries possibly because of differences in socioeconomic, demographic, geographic and cultural factors. A better understanding of the specific epidemiology of dengue in Saint Lucia will provide policy makers with information that can be used to maximize the use of limited resources and indicate areas that need additional focus.

Saint Lucia

Saint Lucia is a small, English-speaking island nation of the Eastern Caribbean archipelago of islands, which changed hands 14 times between the British and the French until 1814 when it was ceded to the United Kingdom. Its neighbors are Martinique to the north, Barbados to the east, and Saint Vincent and the Grenadines to the south. Saint Lucia is a volcanic, mountainous island with rain forests in the central region of the country (Malumphy, 2014). The estimated population of Saint Lucia is 165,000 with the majority, approximately 85%, being of African descent and life expectancy is estimated at 73 years for men and 78 years for women; the urban population was calculated at 18.7% in 2018 (WHO, 2012; WHO, 2018). The island is approximately 14 miles wide by 27 miles long (Gaspard & Yang, 2016). The population is divided 48.7 % and 51.3%, male and female respectively, as follows: 0-14 years: 20.02% (male 17,006/female 16,027), 15-24 years: 15.37% (male 12,870/female 12,492), 25-54 years: 42.97% (male 34,117/female 36,779), 55-64 years: 9.99% (male 7,608/female 8,881), 65 years and over: 11.65% (male 8,704/female 10,510, 2017 est.; *The World Factbook* — Central Intelligence Agency, 2018).

The rainy season typically starts in mid-June and continues to mid-November followed by a dry season mid-November to mid-June with the average daily maximum temperature varying from 27°C to 29°C and the average daily minimum temperature from 20°C (Malumphy, 2014). The January daily average high temperature is 27°C at the southwestern coastal capital city of Castries, with a nightly low of 20°C. The July daily average is 29°C and the nightly low is 20°C to 22°C in January and July, respectively (Malumphy, 2014).

Historically, Saint Lucia relied on agriculture as the mainstay of the economy, moving from sugar cane production to banana and coconut production. Currently, tourism has taken over as the main economic driver of the country with both cruise ship and stayover visitors contributing to this sector, welcoming almost 350,000 visitors during 2014. Saint Lucia's 2016 national gross domestic product (GDP) was estimated at US$ 2.4 billion, of which 6.7 % was spent on health care, a decrease from 7.4% in 2010 and 5.7% on education in 2016 (*The World Factbook* — Central Intelligence Agency, 2018). There are an average 1.3 beds per 1000 population with 0.1 physicians per 1000 population and an urbanization proportion of 18.7% (*The World Factbook* — Central Intelligence Agency, 2018). There are a number of public and private health care institutions on the island but there is no universal healthcare and many persons do not have health insurance, resulting in most of private health expenditure being out of pocket. There are four public hospitals, one private hospital, one public polyclinic and 38 primary care units and centers in Saint Lucia, with the addition of a new national hospital that is due to open in 2019 (Ministry of Health, Saint Lucia).

Saint Lucia has long harbored the *Aedes* mosquito, the vector for dengue though there have been a number of public health campaigns to eradicate or control the mosquito population. Until the 1950s when insecticide use became more common, control of mosquito vectors was achieved through an integrated approach that focused on reducing the breeding habitat of the mosquito. In 1953, the government of Saint Lucia, with the support of the World Health Organization (WHO), United Nations International Children Education Fund (UNICEF), and the Colonial Development and Welfare Scheme instituted a vector control program aimed at the eradication of *Aedes aegypti*. Under this initiative, the population of the *Aedes* mosquito dropped from 15% prior the start of the program to 0.14% in just more than a year by the end of 1954 (Bos et al., 1988). Nathan and Knudsen (1991) reported that in a survey of vectors in Saint Lucia that of 141 houses sampled, the mean number of artificial containers harboring mosquito larvae and pupae per house was 22, mean number of wet containers was 5.6, and a Breteau Index (number of containers harboring mosquito larvae or pupae per 100 houses) of 59.6 show that the mosquito had re-established itself on the island. The presence of the dengue vector increases the likelihood of transmission of the diseases and maintenance of local endemicity of the disease.

There has not been much research published on dengue in Saint Lucia, but Downs and Spence (1964) reported that 69 out of 90 persons, or approximately 77%, tested positive for dengue antibodies. At that time the authors found no evidence of antibodies to dengue in anyone age 14 or younger, indicating that there was diminished transmission of the virus at least 15-20 years prior to the study. There were also higher rates of immunity in urban areas than in rural ones.

Epidemiology of Dengue

Globally there has been a re-emergence and increased expansion of dengue during the past few decades, with autochthonous transmission occurring in geographic locations that were not traditionally known to experience the disease with a complexity of socioeconomic and environmental factors being strongly associated with these changes (Bhatt et al., 2013). This expanding geographical distribution of dengue has been associated with the globalization or the interconnectedness of countries, the increase in travel, and trade resulting in the movement of people, animals, and products. Climate change and the evolution of the dengue viruses have further added to the complexity of the disease (Murray et al., 2013). Small island states such as Saint Lucia are currently ill-equipped to deal with the challenges of climate change, so the effects on vectors of disease such as dengue are unlikely to be abated, leading to increased vector populations and as a corollary the increased risk of dengue outbreaks on the island (Chadee & Martinez, 2016; Karmalkar et al., 2013; Naish et al., 2014).

Dengue viruses have circulated for centuries in the Caribbean with epidemics being recorded at various times often involving multiple countries (Brathwaite Dick et al., 2012; Cafferata et al., 2013). The earliest recognized outbreak of dengue in the Caribbean region occurred in 1635 on the island of Martinique, which is the immediate northern neighboring island to Saint Lucia, more than a century later it was describe in Philadelphia in 1780 (Laughlin et al., 2012). The fluctuating occurrence of dengue in the

Caribbean region has been attributed to the attempts to eradicate its vector the *Aedes* mosquito in an attempt to control Yellow Fever. By 1962, there were nine Caribbean countries where the mosquito was eradicated (Brathwaite Dick et al., 2012; Murray et al., 2013). However, once these efforts ceased the mosquito population increased across the region and dengue became endemic. The early epidemics of dengue occurred at 10- to 40-year intervals, much longer than the recently reported 2 to 4 years periodicity that is currently experienced (Gubler & Clark, 1995).

After World War II, the geographic distribution and prevalence of dengue increased and currently many of the countries that are endemic for the disease are actually hyperendemic or having multiple serotypes of the virus circulating at the same time (Messina et al., 2014; Murray et al., 2013). DENV-2 was the only serotype found to be circulating in the Americas in 1970, with DENV-1 and DENV-4 being introduced in 1977 and 1981, respectively. DENV-3 was detected in 1994 and since then, all four serotypes have been found to circulate in many of the countries in the region (Brathwaite Dick et al., 2012; Murray et al., 2013; Ramos-Castañeda et al., 2017). It has been suggested that a change in the predominant serotype or genotype within a geographic area or country leads to outbreaks of dengue and coincides with the cocirculation of more than on serotype (Guzman & Harris, 2015). The occurrence of dengue epidemics in the Caribbean appear to follow a pattern of seasonality, occurring in the latter half of a year with increasing temperature and following the beginning of the rainy season (Kumar et al., 2018; Torres et al., 2017). These epidemics have been identified as occurring in the year following an episode of the El Niño weather phenomenon, or as it is referred to by many researchers El Niño+1 year (Lowe et al., 2018; Morin et al., 2013). In the Caribbean, years with the El Niño phenomenon tend to be warmer in the latter part of the year, whereas El Niño +1 years tend to have higher rainfall in the earlier part of the year, both of which positively affect vector populations and disease transmission (Lowe et al., 2018). The World Meteorological Organization has identified there was a weak La Niña for 2017/18 and it is predicted that there will be a weak El Niño for the winter season 2018/19, which means that the region may see increased cases of dengue as a result of this weather phenomena (World Meteorological Organization, 2018). Understanding the relationship between environmental variables and dengue specific to Saint Lucia will provide public health authorities with information that may effectively predict the occurrence of dengue on the island.

The Caribbean and Latin America have been overwhelmed by arboviral diseases especially in the last decade with a chikungunya epidemic starting in 2013 and a Zika epidemic in 2015, but dengue was still found to circulate at four times the combined prevalence rate of these two diseases (Rodriguez-Morales et al., 2016). The combined circulation of these viruses overburdened the health care systems across the regions with more than 1.5 million cases of these arboviral diseases occurring between 2015 and 2016 (Rodriguez-Morales et al., 2016). Overall, the incidence and prevalence of dengue in the Americas are on the increase, with the Americas reporting the most cases of any WHO region between 2000 and 2006 with a 4.6-fold increase dengue fever but an 8.3-fold increase in dengue hemorrhagic fever, the more life-threatening form of dengue, during this period. During this period though the Americas reported more cases, more dengue-related deaths were reported in the more populated Southeast Asia region which may indicate underreporting of cases in that region (San Martín et al., 2010). During the last few decades the Americas region transitioned from an area of low dengue endemicity to an area of hyperendemicity with all four serotypes of the DENV in circulation in almost every country in the region giving emphasis to the importance of the disease in the region (Cafferata et al., 2013; Murray et al., 2013).

Díaz-Quijano and Waldman (2012) reported that the number of endemic countries in the Caribbean and Latin America has moved from 5 to 15 during the last few decades with a concomitant increase in the deaths associated with the disease. The emergence and re-emergence of dengue has been related to poor or ineffectual vector control, urban migration leading to increased population density in urban areas, uncontrolled urban expansion, inadequate housing, lack of environmental modulators such as air-conditioning, water, sewage or waste disposal and increased movement of people because of business or tourism (Murray et al., 2013; Torres et al., 2017). In an ecological study by Díaz-Quijano and Waldman (2012), it was found that population density was strongly associated with dengue fatalities more so than dengue incidence, given that sustained dengue transmission requires at least a population of 10,000. A review by Akter et al. reported evidence that the type of housing, apartments, and interconnected buildings had a greater influence of the transmission of dengue than stand-alone housing suggesting the likelihood of infected mosquitoes interacting with a susceptible host was higher in interconnected buildings. In the Caribbean region, most of the countries are classified as middle-income countries, so the causally linked factors mentioned previously are expected challenges especially because of the difficult socioeconomic balances and lack of resources at the national level that can be directed at public health and dengue in particular (Cafferata et al., 2013).

The countries endemic for dengue have been forced to allocate limited public health resources to manage the threat of the disease, which most often results a reactive approach to outbreaks, rather than a comprehensive management strategy because most do not have active research programs to provide information to guide response planning (Cafferata et al., 2013; Morin et al., 2013; Murray et al., 2013; Runge-Ranzinger et al., 2016). Martinique, the neighboring island North of Saint Lucia, experienced a number of outbreaks in the last decade each characterized by one or two serotypes, suggesting the hyperendemic nature of dengue on the island. The DENV-1, -2 and -4 were the main serotypes involved with these outbreaks with DENV-2 most often being associated with secondary infections and severe dengue, whereas DENV-4 was associated with the mildest infections (Thomas et al., 2014). Díaz-Quijano and Waldman (2012) reported that DENV-2 was responsible for more almost 2.5 times higher mortality rate than the other serotypes and which agreed with the results of other studies that have found DENV-2 is most commonly associated with outbreaks at the global level (Guo et al., 2017; Murray et al., 2013). The change in the predominant serotype of dengue circulating was associated with the advent of an epidemic during a period of favorable environmental conditions such as the El Niño phenomenon which support amplification, replacement, and epidemic transmission (Guzman & Harris, 2015).

Most Caribbean countries have become hyperendemic for dengue, which increases the risk of heterotypic infections of dengue that lead to the more severe forms of dengue such as dengue hemorrhagic fever, which has been reclassified as severe dengue, and an increased burden of disease (Lowe et al., 2018). It has been suggested that most of the dengue outbreaks experienced in mainland countries such as Brazil, originate from the Caribbean representing the importance of the Caribbean to the global spread of the disease (Wilson & Chen, 2014). Kumar (2013) reported that all four serotypes have been circulating in the Caribbean region since 2001 and cocirculate in many countries. In a review of the literature, Murray et al. (2013) reported that more than 1.6 million cases of dengue were identified in the Americas, 49,000 becoming severe dengue. Researchers have identified that all four serotypes of the dengue virus have been circulating in Jamaica since 2007; and DENV-2, and DENV-4 were probably responsible for a dengue epidemic around the same time (Brown et al., 2011). It is believed that DENV-1 and -2 were the most prevalent serotypes in the Americas during the 1990s, which changed to DENV-2 and -3 in the 2000s.

In a study by Brown et al. (2011) examining dengue in Jamaica between 2003 and 2007, the authors were able to identify that most of the patients affected were infants, children younger than age of 3 years, and young adults. The regional emergence of new lineages of the dengue virus as other become extinct has been suggested as the pathway for continued dengue outbreaks and possibly the increased severity of the disease (Ramos-Castañeda et al., 2017). The evolution of the dengue virus differs between the human host and the mosquito vector, with less diversity occurring as a result of replication in humans. This means that with increases in the Aedes vector population mutation of the dengue viruses is more likely to occur leading to outbreaks of disease. Though scientists have been able to identify a number of mutations in the serotypes of the dengue virus circulating in the Caribbean region, they have not been able to conclusively link these mutations with changes in the epidemiology of the disease (Ramos-Castañeda et al., 2017). The understanding of the epidemiology of dengue at the local individual country levels is important to facilitate more successful control of the disease.

A study from 2000 to 2009 in Barbados identified a mean of 70 cases of dengue per year with the highest number 180 being recorded in 2007 (Kumar, 2013). Investigating the associated risk factors with the outbreaks during this 10-year period, epidemiologists were able to identify age as a major factor associated with confirmed cases of dengue, with the majority of cases occurring in children younger than 5 years (Kumar, 2013). The authors of the study also highlighted the significance of underreporting of dengue cases in the lack of accurate estimation of the burden of the disease in the region, with 10 to 27 symptomatic cases going unreported for every suspect case and 15 cases going unreported for each case of dengue hemorrhagic fever reported (Kumar, Gittens-St Hilaire, & Nielsen, 2013). This demonstrates that although researchers believe that the current burden of dengue is a major global concern at almost 400 million cases each year, it may even be a much more substantial number than estimated (Bhatt et al., 2013). Shepard et al. (2016) suggested that there may be a disproportionate number of cases of dengue in children reported because parents are more likely to seek medical care for children with symptoms of dengue out of fear of the possible fatal outcome.

In contrast to the results of the study by Kumar et al. (2013), a review by Sanyaolu, Ahmed, Okorie, and Kadavil (2017), reported that dengue fever most commonly affected children less than 15 years of age. Though in an earlier review by Chen and Vasilakis (2011), it was noted that although in hyperendemic regions such as Southeast Asia and Latin America, the trend as moving toward an increasing occurrence of dengue in adult populations. These contrasting data may be a result of differences in study methodology, local confounding factors, or differences in the epidemiology of dengue viruses in different populations and strengthen the argument for specific studies on dengue epidemiology at the local level.

This increased incidence in the Americas has also seen the increase in dengue-related deaths from approximately 242 in the 1980s to more than 2,000 in the 2000s, which is believed to be a reliable indicator of trends and outcomes of the disease (Díaz-Quijano & Waldman, 2012). The same study Díaz-Quijano and Waldman (2012) found that the Caribbean islands have the highest rates of dengue related mortality that may be a result of less robust public health systems to manage outcomes of the disease. The authors found that factors such as age to endemicity or the period from first emergence of a virus serotype to endemic-epidemic transmission of the virus and the calendar year in which the data is collected, annual rainfall, population density, Human Development Index which looks at measures such as health, education and standard of living and circulation of DENV-2 were associated with dengue-related mortality.

The explosive expansion of dengue into areas where the disease was not commonly found ultimately reflects the epidemiology of the disease, which as a vector-borne disease relies on the human-mosquito-human cycle (Weaver et al., 2018). The successful maintenance of dengue virus circulation requires the interaction of competent vectors and infected human hosts, this interaction heightened by the mobility of today's human population and the increasing population density and urbanization (Carrington & Simmons, 2014; Hagenlocher et al., 2013). The important role of the human host in the continued transmission of dengue further underscores the importance of socioeconomic factors that affect the likelihood of interaction of human hosts and mosquito vectors. The socioeconomic variables include social class, urbanization, unplanned urbanization, housing, waste management, water supply, education, employment, and income (Arauz et al., 2015; Mulligan et al., 2015).

The wide range of socioeconomic factors possibly associated with dengue fever and variety of methods by which they are measured makes it difficult to effectively compare the results of different studies into these phenomena (Mulligan et al., 2015). Socioeconomic factors influence the occurrence of dengue through the ability of members of the community to make informed decisions through education, on eliminating mosquito breeding habitats, seeking health care when ill and improving living conditions, other socioeconomic factors such as income level and employment contribute towards the ability to afford better decisions (Akter et al., 2017; Carabali et al., 2015; Murray et al., 2013; Quintero et al., 2014). Globalization and trade have spurred the movement of persons not only from rural to urban areas but also across national borders which facilitates the spread of the dengue virus through infected persons or even movement of infected mosquitoes (Murray et al., 2013).

Urban migration often results in unplanned housing development with poor water supply, unsafe water storage and poor waste management which provide good sites for oviposition and increases in vector populations (Murray et al., 2013; Neiderud, 2015). Unemployed persons and persons within low income brackets may not have access to healthcare because of lack of health insurance, unavailability of services in geographic area, or lack of out-of-pocket funds (Carabali et al., 2015; Neiderud, 2015; Zellweger et al., 2017). This causes a revolving cycle of disease, reduced productivity, increased poverty and therefore increased disease occurrence.

In a study by Depradine and Lovell (2004), it was determined that with some environmental variables, there is a lag between the peak of the element and the related peak in incidence of dengue. From the results of the study based in Barbados, Depradine and Lovell (2004) identified a strong correlation between vapor pressure and incidence of dengue at a lag of 6 weeks, minimum temperature at a lag of 12 weeks, maximum temperature at a lag of 16 weeks, and a weaker correlation with rainfall at a lag of 7 weeks. This correlation between incidence of dengue and temperature was also supported by Amarakoon et al. (2008). The authors also identified a negative correlation between windspeed and incidence of dengue at a lag of 3 weeks. Researchers looking at environmental data in Trinidad and Tobago identified a 6-month lag between temperature and morbidity associated with dengue and also a 6 month lag when including both temperature and rainfall in the model (Wegbreit, 1997). The difference in these studies may possibly be attributed to local phenomena, but also to differences in study design, the study in Barbados relied on monthly measures of climate variables, whereas the study in Trinidad and Tobago incorporated weekly measures that may have provided more detailed results. Depradine and Lovell (2004) identified that maximum incidence of dengue occurred at an average temperature of 27^{o}C. The importance of environmental variables draws attention to the need to identify which risk factors are most strongly associated with dengue occurrence.

Downs and Spence (1964), who reported a 77% prevalence rate for dengue antibodies in Saint Lucia, also found no evidence of antibodies to dengue in anyone age 14 years or younger, indicating that there was diminished transmission of the virus 15 to 20 years prior to the study. This phenomenon may support the theory that after 15 years of hyperendemicity the target population for the dengue virus changes from children to adults (Vicente et al., 2017). At the time of the study in 1964, there were also higher rates of immunity in urban areas than in rural ones, which may have reflected a higher viral challenge than in rural areas (Downs & Spence, 1964).

In the past, the Ministry of Health in Saint Lucia also set programs to address rodent and vector control in collaboration with the World Health Organization and other international agencies, with the primary target of this program being the *Aedes aegypti* mosquito (Bos et al., 1988). The earliest attempts to control this vector in Saint Lucia started in 1953 in conjunction with the regional initiative by the Pan American Health Organization (PAHO) to eradicate the mosquito from the region. Historically efforts had been made to control this vector but these efforts followed the pattern of many other countries where the control programs would lessen activity with the successful reduction of the numbers of the mosquito allowing for repopulation (Nathan & Knudsen, 1991). Specific challenges to the program included lack of awareness of the rural communities concerning the vector and the diseases it spread and lack of supplies as well as the significant cost to the Ministry of Health budget in maintaining the program (Bos et al., 1988). A major contributing factor to the successful expansion of the *Aedes* population in Saint Lucia was the presence of numerous breeding sites through old tires, drums, coconut shells and other forms of refuse.

In 1986, the Ministry of Health instituted a public health initiative to address the mosquito population once again, and under this program removed 530 tons of solid waste from one of the target communities on the island underscoring the abundance of larval breeding sites (Bos et al., 1988). The common larval habits included roof gutters, animal watering pans, tires, flower pots, buckets and tin cans with house plants being the main habitat recognized in the typical house (Chadee & Martinez, 2016). In Saint Lucia the most common habitat was house plants, which was followed by drums used for storing water, buckets and then used tires (Nathan & Knudsen, 1991). Understanding how vector populations affect dengue is also a key component of the successful control of the disease.

The number of dengue cases have increased within the Americas and Saint Lucia is one of the countries where this has been highlighted (Matysiak & Roess, 2017). In a seroprevalence study by Wood et al. (2014) it was reported that the seroprevalence of dengue in pregnant women in Saint Lucia was approximately 97% underscoring how much of a threat the disease is to the island. Shepard et al. (2016), reported that during the period 1990-2013 Saint Lucia reported 5,472 cases of dengue or an incidence rate of 3,002 per 100,000, with 162 being hospitalized, 3,930 ambulatory (persons who sought medical care but were not hospitalized) and 1,380 nonmedical cases, with 3 fatal cases reported. Saint Lucia's incidence rate was higher than the neighboring islands of Barbados at 662.19 per 100,000 (1885) and Saint Vincent and the Grenadines at 1,984.02 per 100,000 (2,170) for the same time period. In a shorter time period of 14 years, it was reported according to PAHO data that the incidence rate of classic dengue was 21.3 per 100,000, during an 11 year period 0.35 per 100,000 for hemorrhagic dengue incidence and classic dengue mortality 0.32 per 100,000 (Cafferata et al., 2013). The differences in these estimates may reflect the use of different data, different time periods, different methodologies, different classification of cases and underscores the difficulty in the availability of reliable estimates. Indeed, there is significant underreporting of dengue cases to regional agencies such as PAHO and this may lead to inappropriate policies that do not recognize the true severity of the dengue epidemic through the region (Torres et al., 2017).

The direct cost of associated with a hospitalized case of dengue in Saint Lucia was estimated at US$588, more than six times higher that than the estimated global average of US$70.10. Ambulatory and nonmedical cases were estimated at US$97 and US$9 respectively. The indirect cost of dengue was estimated at US$146 and US$82 for both ambulatory and non-medical cases. These indirect costs are important because these largely result from loss of productivity (Shepard et al., 2016). A major threat of dengue to the island of Saint Lucia is the effect that the disease can have on the important tourism industry, which would have devastating effect on the local economy (Bos et al., 1988). These combined factors outline the serious effect dengue within the island of Saint Lucia especially economic losses which may not be correctly attributed to the disease because of underreporting or underdiagnosing.

Variables

This study focuses on a combination of demographic, environmental and clinical variables that provide the opportunity to explore the epidemiology of dengue in Saint Lucia. The relationship between demographic variables that will include sex, age, geographic location, access to healthcare, urbanization based on population density and occurrence of dengue as the outcome variable will be investigated. Entomologic indices as well as the environmental variables temperature, wind speed and direction, humidity, and rainfall as recorded at the two weather stations on Saint Lucia, one each placed in the north and south of the island which be analyzed to identify possible relationships to dengue occurrence. Saint Lucia much like most countries around the world collects syndromic data through surveillance of hospitals and health centers across the island, and uses this data to direct the activities of the public health department and the ministry of health. The variables undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS) fever and neurological symptoms (fever and NS), gastroenteritis will be compared with the occurrence of dengue in Saint Lucia to determine which variables are best able to predict the occurrence of the disease.

Though epidemiologists have focused much research on the entomologic and epidemiologic factors that possibly affect the occurrence and severity of dengue Bowman, Runge-Ranzinger, and McCall (2014) suggest that these associations have not always provided useful predictive models. Identifying risk factors critical to the development of the correct predictive model and then determining the most effective way to assesses and measure these variables is a challenge that does not always lead to consensus among experts. For example, Morin et al. (2013) suggest that it is more prudent to use shorter time scales and more narrow geographic areas when investigating environmental factors associated with diseases because they are more likely to be sensitive to changes that occur at daily or weekly intervals than longer periods though other researcher use monthly intervals often because this is the format in which the data is available. This disagreement among researchers has led to the recommendation that better evidence linking possible risk factors to the occurrence of dengue is needed (Ebi & Nealon, 2016).

Environmental factors

Researchers suggest that environmental variables such as mean, minimum and maximum temperature, rainfall, relative humidity, and wind velocity and direction all have an effect on dengue outbreaks (Akter et al., 2017; Depradine & Lovell, 2004; Filho, 2017; Morin et al., 2013). Other factors that have been associated with dengue are the level of urbanization, number of artificial containers in the environment, socioeconomic variables such as education and employment, changing demographics and herd immunity (Morin et al., 2013; Murray et al., 2013; Stanaway et al., 2016). Though there are many factors that are involved in the risk of dengue transmission the large number also provides multiple avenues to address the control of the disease.

The strength of association between risk factors and the occurrence of dengue varies by location, temporality, study design and even dengue virus serotype (de Castro et al., 2018; Filho, 2017; Tseng & Chang, 2016; Velasco-Salas et al., 2014; Wong et al., 2015). Filho (2017) found that the strength of association in relation to the incidence of dengue for relative humidity was statistically significant at 7.3 (1.05-50.6) to 18.1 (1.6-206.2) at a lag of zero months and differing serotypes; rainfall was statistically significant at lags of 0 and 1 month ranging from 7.0 (1.05-46.4) to 10.1(1.4-73.7) respectively, and average temperature at a lag of 1 month and odds ratio of 26.7 (1.6-433.1). The odds ratios of the risk of dengue associated with minimum, maximum and average temperatures were found to be as high as 2.69 (2.44-2.97), 2.33 (1.89-2.42) and 2.84 (2.66-2.96) respectively (Fan et al., 2014). The vector indices commonly used to evaluate *Aedes* populations were found to have odds ratios that also differed by household density, with the Breteau index ranging from 1.03 (1.01-1.04) to 1.05; The Container Index from 1.02(1.01-1.03) to 1.08 (1.06-1.1) and the House Index from 1.03(1.01-1.06) to 1.04(1.02-1.06).

Demographic Factors

In a community-based study by Velasco-Salas et al. (2014) it was reported that age and sex were statistically associated with dengue infection with odds peaking in the 21-25 age group with an odds ratio14.50 (OR=14.50, 9.14-23.01) times the 5-10-year-old reference group and with women 1.53 (OR=1.53, 1.24-1.89) times more likely to be infected than men. A study by Aung et al. (2013) reported an odds ratio of 2.042 (1.143-3.648). for the association of the female gender with dengue fever whereas Nguyen et al. (2018) reported and odds ratio of 2.79 (1.61-4.83) linking women more frequently to secondary dengue infections. In the case of past infections persons who were employed were more likely to have dengue infections (OR=3.79, 2.71-5.31). De Castro et al. (2018) reported that the per capita income was associated with dengue epidemics (OR=1, 1.0-1.1). Education was also found to play significant role in the prevalence of dengue, with the presence of the disease decreasing as educational level increased with the odds as high as 3.62 (1.87-7.00) among persons with no formal education as compared to someone with a university education (Prayitno et al., 2017). Researchers have found an increased occurrence of dengue in lowland areas as compared to highlands (OR=5.07, 2.12-12.12; Dhimal et al., 2014). The occurrence of dengue in urban compared to rural areas has also been found to significantly differ with it being greater than three times more likely for it to occur in urban areas (OR=3.18, 2.21-4.69; Vairo et al., 2014). Wu et al. (2009) reported that the level of urbanization was significantly related to the risk of dengue fever (OR=3.875, 1.784- 8.770).

Clinical Factors

Huy et al. (2013) report an odds ratio of 4.66 (1.70-12.8) for neurological signs associated with the risk of severe dengue, whereas Zhang et al. (2014) report an association between with gastrointestinal symptoms such as vomiting or nausea (OR=1.69, 1.26-2.28) and abdominal pain (OR=2.28, 1.63-3.18). Among the key indicators of severe dengue infections is any bleeding, which has been found to have an odds ratio of 1.43 (1.10-1.85) to 5.58 (3.43-9.10) with the strength of the relationship increasing with the severity of bleeding (Pongpan et al., 2013). Brémond et al. (2015) report an odds ratio of 1.43 in dengue cases compared to unconfirmed cases. A study of undifferentiated fever by Mueller et al. (2014), found that dengue was identified more often among those patients with fever (OR=3.7, 1.5-9.3).

Problem Statement

This dissertation will address the lack of published data on the epidemiology of dengue in Saint Lucia, specifically exploring the relationship between demographic, environmental including vector prevalence and clinical factors, and their effect on the occurrence of dengue in Saint Lucia in an attempt to address the gaps that exist in the literature related to dengue in Saint Lucia. In a review of the literature on dengue in the Americas, Torres et al. (2017) noted that few articles were published on English-speaking countries of the Caribbean, and data on the smaller islands such as Saint Lucia, were either included in larger studies lacking the specificity at the island level or were lacking.

Dengue is a disease of great public health significance because of the severe effect of loss of productivity especially to a tourism-based economy and the lack of published research on dengue in Saint Lucia which may reduce the capacity of the Ministry of Health in prevention and control of the disease. Infectious diseases are more effectively managed when their occurrence can be prevented or minimized, but such programs are dependent on the knowledge and understanding of these diseases especially within the local context. The successful control of dengue continues to elude public health agencies not only in Saint Lucia but in many countries around the world.

Purpose

Although there is a large body of published literature on dengue, there is little that has been published on the disease and its specific local context in Saint Lucia. Researchers have called for the continued investigation into the epidemiology of dengue and other issues related to the disease such as the economic burned, specific therapeutics and vaccine technology (Cheong et al., 2013; Katzelnick et al., 2017; G. K.-K. Low, Ogston, Yong, Gan, & Chee, 2018; Runge-Ranzinger et al., 2016; Wilder-Smith et al., 2017). Many investigators have identified numerous risk factors that are associated with dengue, including age, sex, urbanization, rainfall, temperature, humidity, locality and vector indices, but there is no published work that investigates these relationships with dengue in Saint Lucia and the Saint Lucian population.

Many of the studies on various aspects of dengue have relied heavily on historical data especially using weather data that is routinely collected by meteorological agencies and public health surveillance data on incidence of the disease and outcomes (Bowman et al., 2014; Cafferata et al., 2013; Ganeshkumar et al., 2018; Guo et al., 2017; Naish et al., 2014). These data are also regularly collected in Saint Lucia, but no recent study has been published exploring the relationship between these variables and dengue. There is a large volume of data available that can be applied to provide an analysis of dengue and its epidemiology in Saint Lucia. Analysis of this data may also highlight other gaps in the literature on dengue that need to be addressed and increase research endeavors in Saint Lucia.

This study is used to investigate the relationship between demographic, environmental including vector prevalence and clinical factors and the occurrence of dengue in Saint Lucia. The new knowledge generated will provide information that the Ministry of Health can use to set policy related to dengue and develop additional targeted public health interventions. The outcomes of these studies will also foster the need for further investigation into the phenomenon of dengue in Saint Lucia. Manuscript one is used to investigate the relationship between demographic factors specifically gender, age, urbanization based on population density, hospital access, place of residence or location, employment, visitor arrivals and occurrence of dengue occurrence in Saint Lucia. Manuscript two is used to evaluate the effect of environmental factors specifically vector indices, temperature, wind speed, wind direction, relative humidity, and rainfall as measured at weather stations on the island and vector prevalence at the district level, on the occurrence of dengue cases in Saint Lucia. The third manuscript is used to investigate which relationship between clinical factors specifically undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS) fever with hemorrhagic symptoms (Fever with HS) fever and neurological symptoms (fever and NS), gastroenteritis had the strongest relationship with the occurrence of dengue in Saint Lucia. This study will provide analysis of data on dengue specific to the Saint Lucian context in an attempt to improve public health outcomes related to the disease.

Social Implications

The new knowledge generated from this study may provide additional information that the Saint Lucian public health authorities can use to help focus dengue prevention, control, and management in an attempt to leverage the limited resources available in providing the best health outcome for the population. This new information could possibly be used to create social change initially at the national level, but also through the wider Caribbean that faces similar challenges in managing dengue, thereby improving the health outcomes of the population.

One of the major challenges of dengue is the loss of productivity among ambulatory and hospitalized cases, which includes both loss of work days and school days (Constenla, Garcia, & Lefcourt, 2015). Such loss of productivity translates into economic losses which carry social consequences in an island that is heavily reliant on the service industry and loss of school days can have a significant effect on future potential of the student, leading to negative social consequences. The direct healthcare costs associated with treating symptomatic cases of dengue are a heavy burden to the population of Saint Lucia especially because the majority of the population does not have health insurance and depends on out of pocket payments to meet healthcare costs which is similar in many of the small Eastern Caribbean islands (Adams et al., 2015).

Another important social challenge experienced during dengue outbreaks is the overwhelming of local health services and general chaos that can ensue especially with the co-circulation of other arboviral diseases that can cause similar clinical signs as dengue and further serve to inundate the local hospitals and clinics (Rodriguez-Morales et al., 2016). The prevention of dengue and minimization of its effect may lead to positive socioeconomic outcomes to the population of Saint Lucia because the resources both direct and indirect, typically associated with dengue can be redirected to other important demands. The analysis provided at the end of this study can possible be used to create specific educational campaigns on dengue in Saint Lucia, as well as identify which specific segments of the population should be targeted.

Important to the control of dengue is action at both the community and individual levels to minimize the breeding of the *Aedes* vector by destroying and not providing breeding habitats (Andersson et al., 2015; Kolopack et al., 2015). Motivating the population to take these steps will be among the most important social changes that can result from the outcomes of this study. This will require raising the awareness of the community, and providing them with targeted messaging that will inform them about dengue in Saint Lucia, how it is spread and the danger of the disease but most importantly how it can be prevented as well as prevention programs specifically tailored to the individual Saint Lucian communities (Andersson et al., 2015). Although the preventive actions at the individual level is known and promoted, these actions are often not taken, and specifically in the Saint Lucian context, the information elicited as a result of this study could be used to support the message of prevention (McGraw & O'Neill, 2013). Another aspect of social change will be to foster the culture of seeking healthcare based on symptoms as well as the improving the culture of reporting within the medical fraternity (Bhatt et al., 2013; Tomashek et al., 2014). Surveillance programs will only be as strong as the information that is received, having the stakeholders understand the epidemiology of dengue in Saint Lucia could function to improve such action.

Background

Dengue virology

The dengue virus was first discovered in 1943 by Ren Kimura and Susumu Hotta and later by Albert Sabin in 1944 (Laughlin et al., 2012; Snow et al., 2014). The dengue viruses (DENVs) are members of the Flaviviridae, a group of single strand, positive-sense, RNA viruses (Arauz et al., 2015; Muller et al., 2017). The virus has three structural and seven non-structural proteins (Muller et al., 2017). These positive sense viruses are enveloped and target the monocytes, macrophages and dendritic cells mainly (Laughlin et al., 2012).There are four genetically similar serotypes of the dengue virus DENV-1, DENV-2, DENV-3, DENV-4 each with multiple genotypes, which though providing homologous life-long immunity, do not produce lasting cross-protection to infections of a heterotypic strain. In 2013 researchers reported the discovery of a fifth serotype of the dengue virus which was believed to circulate in mainly in a sylvatic cycle unlike the other four serotypes have transitioned into a mainly human cycle (Mustafa et al., 2015). Since this discovery in 2013 little information has been published on this fifth serotype with most authors still using the four serotype classification of the virus (Sanyaolu et al., 2017).

DENV-1 has been identified to have five genotypes, DENV-2 six genotypes, DENV-3 four genotypes, and DENV-4 also has been identified to have four genotypes (Chen et al., 2011). In the Caribbean DENV-1 circulates as genotype III as well as V, DENV-2 has undergone the most changes in the region with all genotypes having circulated at one point, though the most virulent genotypes Asian I and II are not the main genotypes in the region (Ramos-Castañeda et al., 2017). In a review of the global epidemiology of dengue, Guo et al. (2017) determined that DENV-2 was responsible for the highest number of dengue outbreaks between 1990 and 2015. It is believed that DENV-3 Asia genotype III has been in circulation in the Caribbean region since 1994, though many subclades of this genotype circulated it has not been detected in the region since 2010 (Ramos-Castañeda et al., 2017). Only one genotype of DENV-4 has been reported in the region which is attributed to the stability of the virus.

When an infected mosquito bites a human host the dengue virus is inoculated into the blood stream and surrounding skin. The surface E protein is modified to allow the release of viral RNA into the infected cell, the non-structural proteins NS1 and NS2A play a role in viral replication and possible activation of the complement cascade as part of the body's immune response. Successful transmission of the dengue virus relies on a competent vector biting an infected host during the period of viremia with a titer above 10^3 viral RNA (Mayer et al., 2017). Investigators have found that the longer the interval between primary and secondary infections the higher the risk of severe dengue and case related fatality (Guzman & Harris, 2015). Longer intervals between further heterotypic infections also predisposes to symptomatic versus asymptomatic infections. It has also been demonstrated that asymptomatic infected persons are more infectious to mosquitoes than people with clinical signs of the disease making them an important risk factor in the spread of dengue (Castro et al., 2017).

Infections may be asymptomatic if the host's immune system is able to neutralize the infection locally, if not any of the myriad of clinical manifestations associated with dengue may occur, with the most severe being thrombocytopenia, hemorrhage, plasma leakage and shock (Sanyaolu et al., 2017). One of the important theories in the pathology of dengue is the antibody-dependent enhancement (ADE) theory which suggests that a primary infection with a dengue serotype may lead to the production of antibodies that are able to bind to a second heterologous infecting dengue virus but unable to neutralize it (Chen et al., 2011; Patterson et al., 2016; Sanyaolu et al., 2017). Instead this antibody-virus complex leads to increased uptake of the antibody-virus complex and activation of T-cells that secrete tumor necrosis factor and other cytokines that affect vascular permeability (Katzelnick et al., 2017; Sanyaolu et al., 2017). This ADE pathway has been linked to cases of severe dengue in infants with persistent maternal antibodies when exposed to a heterologous serotype of dengue as a primary natural infection (Katzelnick et al., 2017; Patterson et al., 2016). Dengue specific antibodies target E, prM, and non-structural (NS1) viral protein which is secreted from infected cells allowing it to be used as an indicator of viremia (Katzelnick et al., 2017; Sanyaolu et al., 2017). NS1 is also a valuable marker because it can be detected at the same time as viral RNA and before antibodies (Muller et al., 2017).

Dengue is transmitted most often by its mosquito vectors of the *Aedes* genus. When a naïve mosquito bites an infected person it is able to transmit virus particle after four to ten days of incubation (Mood & Mardani, 2017; Muller et al., 2017). Humans are the main multiplying reservoir of the dengue virus though it has been recovered from non-human primates, and maintain a human-mosquito-human transmission cycle especially in heavily populated urban areas (Chadee & Martinez, 2016). Once infected a person normally incubates the dengue virus for four to ten days before clinical symptoms are experienced, with these initial febrile symptoms lasting for 2-7 days (Mood &

Mardani, 2017). Once infected the mosquito will remain infected for the duration of its approximately 30-day lifespan (McFee, 2018).

In persons infected with the dengue virus, symptoms of disease begin about four to seven days after the infective bite, and typically last almost two weeks. An infected person is only able to transmit the virus to a naïve mosquito on average for five days while the viral load is high with even asymptomatic persons being able to transmit the virus. The mosquito in turn requires up to 12 days before it can transmit the virus onwards when taking a blood meal and remains infected for the rest of its life (Mood & Mardani, 2017). Although dengue transmission mainly occurs through bites of the infected vector it has also been reported that transmission has also occurred through blood transfusion and organ donation from viremic donors (Castro et al., 2017).

Dengue diagnostics

One of the essential components of an effective public health program designed to control and prevent dengue outbreaks is effective diagnostic tests that allow early and accurate determination of dengue cases (Kumar, 2013; Murray et al., 2013). This rapid diagnosis of the dengue virus would ideally be able to differentiate between the different possible serotypes of dengue and identify if there was a coinfection of multiple strains (Ganguly et al., 2013). A big part of the lack of accurate testing at any stage of the dengue virus infection is that there is no biomarker that is present throughout the entire period of infection (Muller et al., 2017). Current early acute phase diagnostic tests rely on the detection of viral RNA, virus and non-structural (NS1) protein. The tests for viral RNA are applicable from onset of diseases whereas the IgM immunoglobulin ELISA tests which only become effective five days after the onset of clinical symptoms and reduces the clinical value of the test. Approximately 80% of all dengue infections will be IgM positive within five days whereas IgG levels can be detected seven days after the onset of clinical signs and continue to increase (Banerjee et al., 2018; Ganguly et al., 2013; Mood & Mardani, 2017). The reverse transcriptase PCR test used for dengue diagnosis are specific and sensitive but performs best when applied to samples taken within the first five days of the onset of symptoms however once this window has been exceeded the sensitivity and specificity of the PCR decreases because the patient has cleared the viremia (Santiago et al., 2013; Yacoub & Wills, 2015). NS1 tests are able to detect the protein up to nine days after the onset of disease. There has also been the suggestion that with a diagnostic test such as the NS1 test that a higher tire correlates with a higher likelihood of developing dengue hemorrhagic fever or severe dengue later on (Banerjee et al., 2018). Neutralization tests can identify virus-specific antibodies that will differentiate flavivirus infections but are only applicable six months post infection. Though these tests are all helpful in public health surveillance and the clinical management of dengue it is clear that no one test is ideal at any stage of infection, therefore the application of the most appropriate test is dependent on factors such as early recognition of an outbreak, skill of attending physicians and availability. The cost and quality of the various assays available restrict the application of these tests especially in an island such as Saint Lucia with limited financial resources for public health. Recognizing the clinical signs that are most likely to predict dengue infection would assist in earlier recognition of cases and assist public health officials to identify and control outbreaks earlier.

Generally, in the Caribbean, most diagnosis for dengue is performed at a centralized national laboratory with confirmatory tests being conducted at the regional laboratory at the Caribbean Public Health Agency (CARPHA) that has absorbed the Caribbean Epidemiology Center (CAREC). This slows the diagnostic process and reduces the public health and clinical value of testing in an attempt to control outbreaks when, the results are related to the clinician or public health practitioner past the period of disease or these medical personnel never receive the results of tested samples (Katzelnick et al., 2017). The gold standard in diagnosing dengue is virus detection, isolation or identification through cell culture, though real time reverse transcriptase polymerase chain reaction is becoming more widely used because it allows a more rapid diagnosis because virus isolation can take days to weeks (Muller et al., 2017). Viral RNA for these PCR tests can be recovered from blood, serum, plasma, tissues, urine and saliva making it easy to collect the appropriate sample which can be challenging in some diseases (Guzman & Harris, 2015). Previous exposure can be determined by using tests such as the IgG ELISA, hemagglutination inhibition, and neutralization assays such as the plaque reduction neutralization test (PRNT) which is the most specific assay for measuring antibodies to the dengue virus, though outcomes tend to vary from laboratory to laboratory.

Dengue vectors

The main vector of dengue is the *Aedes* mosquito of which there are two main species that are found in the region, *Aedes aegypti* and *Aedes albopictus,* though *Aedes polynesiensis and A. mediovittatus* can transmit the virus (Chouin-Carneiro et al., 2016; Mayer et al., 2017; Poole-Smith et al., 2015). There have been many attempts to eradicate or control the population of this vector across the Caribbean and Latin American region, one of the most notable was by the United States Army when constructing the Panama Canal in an attempt to reduce the occurrence of yellow fever which was hampering construction efforts (Morrison et al., 2008). The *A. aegypti* has adapted to living in an urban environment where it is able to breed in artificial collections of water such as garbage, tires, vases, buckets, flower pots and water storage such as drums (Anders & Hay, 2012; Fuller et al., 2009a). In a study on the *Aedes aegypti* and the effect of climate change in Trinidad, (Chadee & Martinez, 2016) identified brick holes, septic tanks, vases, buckets and drums as the main breeding sites of the mosquito. Often human behavior out of a lack of understanding of dengue, the role of vectors and artificial containers or negative attitudes, contribute substantially to providing breeding habitats for the *Aedes* mosquito.

The behavior of the *Aedes* mosquitoes are affected by temperature and humidity, shortening the mosquito's gonotrophic cycle time, population density, extrinsic incubation period and other behavioral traits, which contribute to the increased occurrence of dengue in susceptible populations (Pang et al., 2017). The mosquito has adapted its breeding behavior to lay eggs in tree-holes, rock-holes, artificial containers but more recently to septic and sewer systems, mainly driven by man-made pressures such as insecticide use and removal of artificial breeding sites but also environmental change that has increased temperatures beyond the point of survivability for the *Aedes* vector (Chadee & Martinez, 2016). Researchers suggest that meteorological variables such as temperature, humidity and precipitation are important risk factors in dengue outbreaks and may provide useful information because vector ecology is affected by these factors (Murray et al., 2013). *A. aegypti* preferentially feeds on humans, though it is easily disturbed leading to multiple feedings with consequently efficient transmission of the dengue virus, and therefore thrives in areas of high population density and inadequate water supply and waste management (Guzman & Harris, 2015; Pang et al., 2017; Sanyaolu et al., 2017). These vectors prefer to feed and rest indoors bringing them into contact with their target human hosts, typically feeding during the day or when the lights are on (Mood & Mardani, 2017; Sanyaolu et al., 2017).

Vector surveillance or the monitoring of adult or juvenile mosquito populations responsible for dengue transmission typically relies on measures such as house index, container index and Breteau index which assess larval stages, however the correlation with disease transmission and prevalence has not been clearly understood (Anders & Hay, 2012; Ebi & Nealon, 2016; Gómez-Dantés & Willoquet, 2009; Pang et al., 2017). Anders & Hay (2012), suggest that the most effective way to assess the *Aedes* population and its correlation to disease transmission would be to capture adult mosquitoes and use PCR to determine which ones carry the dengue virus but this is resource intensive and may be beyond the capacity of most countries in the Caribbean region.

Burden of dengue in the Caribbean

The Caribbean and Latin America experienced approximately 3 million cases of dengue between 2001 and 2005 a significant increase from 2.1 million cases during the period of 1995-1999, which demonstrates the historical upward trend in incidence of the disease (Halasa et al., 2011). However, in 2019 the region experienced more than 3 million cases of the disease, a record which demonstrates how important the disease is to these countries (Mitchell, 2020). Stanaway et al. (2016) estimated that incidence of dengue more than doubling every 10 years from 8.3 million apparent cases in 1990 to 58.4 million cases in 2013, accounting for 566,000 years lived with disability (YLD) and 1.14 million disability-adjusted life years (DALYs) in 2013. Epidemiologists have estimated that almost 400 million persons are infected with dengue, 250, 000 cases of dengue fever and 93 million cases with no symptoms each year, with approximately two thirds of the world's population living in areas with the *Aedes* vector present and yet the true burden of the disease is not known because of challenges such as underreporting, reliance on manual reporting and non-standardized ways to assess this burden (Chadee & Martinez, 2016; Fuller, Troyo, & Beier, 2009a; Guzman & Harris, 2015; Vicente et al., 2017). Stanaway et al. (2016), suggest that the actual number of symptomatic cases of dengue may be 60 million cases occurring and approximately 10,000 deaths. This disparity among the estimates of the burden and incidence of dengue, presents a challenge to public health officials in responding in an appropriate manner to control and prevent the disease. It may also limit the importance of the disease on national governmental agendas or international health agency agendas.

Dengue morbidity has been estimated to cause 1300/millions of disability-adjusted life years, which has a significant effect on the countries where the disease occurs, especially the endemic countries (Akter et al., 2017). The wide distribution of dengue has led to an increasing number of co-infections such as leptospirosis, Chagas disease, tuberculosis, measles, malaria and chikungunya (Rodriguez-Morales et al., 2016). The burden of dengue has a heavy toll on the governments of the Americas with cost of illness amounting to US$2.1 billion per year without the inclusion of vector control. The WHO Global Strategy for Dengue Prevention and Control 2012-20 was developed as a multinational strategy to reduce dengue mortality by 50% and dengue related mortality by 25% but little progress seems to have been made with the disease continuing to expand its geographical footprint (Fritzell et al., 2018; Guzman & Harris, 2015; Souers et al., 2014). This limited influence of current public health strategies on the occurrence of dengue gives emphasis to the necessity of investigating the epidemiology of dengue at the local level in countries such as Saint Lucia.

It has been suggested that the case fatality associated with dengue may be declining with the reduction in risk of mortality due to changes in the distribution of the disease in population age groups, improved medical management of dengue cases and changing numbers of lifetime infections (Stanaway et al., 2016). The incidence of the disease is increasing markedly but epidemiologists are unsure if this is a true increase in incidence compared to an increase in reporting of the disease. However overall the unreliability of reported data makes it difficult to determine with certainty true incidence and mortality figures (Stanaway et al., 2016). It is thought that overall dengue mortality related statistics are more accurate because the cause of death is often identified whereas incidence is dependent upon healthcare seeking behavior, reporting, diagnosis and public health surveillance though the decrease in mortality may also be a result of underreporting in countries of high incidence of the disease (Stanaway et al., 2016).

The economic impact of dengue

The widespread incidence of dengue has led to a tremendous economic burden that is attributed to the cost of hospital care and loss earnings. It is estimated that there are 390 million infections each yeah with approximately 14 million occur in the Americas (Constenla et al., 2015). During outbreaks the cost of public health activities at the community level including vector control and awareness program, are the costliest aspects of dengue programs. Direct cost associated with dengue outbreaks include inpatient costs, tests, procedures, drugs, outpatient costs, whereas indirect costs are transportation in the search of healthcare or other related activities, food lodging, loss of work or school days which contributes to loss of productivity (Constenla et al., 2015). In countries such as Saint Lucia, where a large percentage of the GDP is dependent on service industries such losses in productivity will have severe detriment to the economy and future economy of the country.

Researchers have estimated that the global cost associated with the estimated 58.4 million annual cases of dengue is approximately US$8.9 billion though limited accurate country-level data make it difficult for this estimate to be as accurate as desired (Castro et al., 2017). A significant proportion of these costs associated with the burden of disease are related to productivity costs or public health initiatives such as vector control measures, surveillance and awareness campaigns (Bhatt et al., 2013; Castro et al., 2017; Galera-Gelvez et al., 2016; Krisnian, Alisjahbana, & Afriandi, 2017; Shepard et al., 2016).

Shepard et al., (2016) suggest that the 2013 dengue disease burden was more than 58 million symptomatic cases, approximately 13,500 related fatalities leading to a cost of US$8.9 billion across 141 countries. Of the 58.40 million cases that occurred in 2013 approximately 10.5 million hospitalize, 28.1 million through outpatient care, and 19.7 million that received no treatment. The majority of the expenditure on dengue is attributed to non-fatal cases that are hospitalized some 46%, then 33.6% which have clinical signs but are not hospitalized, 8.5% of asymptomatic cases and 11.9% that were fatal. The estimated global average cost per hospitalized case of dengue was US$70.10, US$51.16 for out-patient cases, US$12.94 for asymptomatic cases and $84730 and $75820 for fatal juvenile and adult cases respectively. Shepard et al. (2016) estimated that the average cost per case of dengue was US$152, this was lower than previous estimates that put the cost per case at approximately US$414. Halasa et al. (2011) estimated that the annual total cost of dengue to the Americas was US$2.1 billion or with a range from US$1-4 billion during the period 2000-2007. The approximate costs of dengue in the Americas ranged from US$72 in Cuba to US$2,300 in Bermuda for outpatient or ambulatory cases and US$306 in Nicaragua to US$17,803 in the United States for a hospitalized case though the countries of the Caribbean have the highest per capita cost (Halasa et al., 2011). Approximately 60% of the costs associated with dengue in the Caribbean region are attributed to losses in productivity, underscoring the importance of the disease (Halasa et al., 2011). These are costs that the largely middle-income countries of the region can ill-afford as they attempt to foster growth and development within their individual economies (Cafferata et al., 2013; Lee et al., 2013; Stahl et al., 2013).

The costs associated with dengue cases are further broken down with 66% of the cost of hospitalized non-fatal cases going to direct costs and 23% going to indirect costs. The costs associated with ambulatory cases was divided 32 % to direct costs and 52% to indirect cost and with non-medical cases 3% to direct costs with 25% of the costs associated with indirect costs (Shepard et al., 2016). The direct cost of associated with a hospitalized case of dengue in Saint Lucia was estimated at US$588, more than six times higher that than the estimated global average of US$70.10. Ambulatory and nonmedical cases were estimated at US$97 and US$9 respectively. The indirect cost of dengue in Saint Lucia was estimated at US$146 and US$82 for both ambulatory and non-medical cases. These indirect costs are important because these largely result from loss of productivity (Shepard et al., 2016). In addition, it is estimated that each dengue-associated death costs US$211,000 and US$138,000 respectively. The estimated total aggregate cost of dengue in Saint Lucia, was US$1,303,186 (Shepard et al., 2016). This is a significant cost to the small island nation with no national health insurance program and a limited number of persons with private health insurance, the majority of the costs are borne out of pocket (Adams et al., 2015). A study by Dieleman et al. (2016) estimated that future health costs in Saint Lucia would represent a total health expenditure per capita of US$ 1940 (1575–2341), government health expenditure 55·5% (45·4–64·0), prepaid private health expenditure 2·7% (1·4–3·9), out-of-pocket health expenditure 39·7% (34·4–45·3), DAH=development assistance for health 2·2% (0·0–7·4) 2·9% (2·2–3·6). The out of pocket costs for Saint Lucia are above the average global estimate of 20·6% (18·4–23·3), which indicates the severity of healthcare cost in Saint Lucia, which in turn lead to significant public health challenges such as managing infectious diseases such as dengue. Researchers estimate that the cost of healthcare in 2013 was US$7.83 trillion and would approach US$ 18.28 trillion by 2040 on the current projected trajectory (Dieleman et al., 2016). The burden of dengue in Saint Lucia is clearly defined by these demonstrated costs.

Economic estimates for the burden of dengue have been found to vary across different studies which is a result of different methods of estimation, the use of different measures, the use of varied data, and also temporality (Shepard et al., 2016). These differences in estimates of the burden of dengue create difficulty for policy makers and public health officials to institute reliable policies and allocate the appropriate resources to sufficiently address the challenge of dengue (Castro et al., 2017). In the Caribbean and Latin America, the approximate annual cost of dengue was reported as US$1.73 billion slightly lower than previous estimates of US$2.15 billion in 2010, it is difficult to determine if the difference is a real reduction in expenditure versus differences in analytical processes (Shepard et al., 2016). It is important to note that the global costs associated with dengue are greater than other infectious diseases of concern such as cholera, Chagas disease and canine rabies. This illustrates the importance of the disease, and dictates the need for increased resources to be directed at reducing the associated burden of disease for dengue (Bhatt et al., 2013; Shepard et al., 2014, 2016; Stanaway et al., 2016).

The burden of dengue is assessed by researchers in a number of different ways including the number of infections, epidemiologic measures such as years of life lost (YLL), years lived with disability (YLD) and disability life years (DALYs). The global burden of Disease Study 2013, estimated that the number of clinical cases of dengue more than doubled each decade between 1990 and 2013 (Shepard et al., 2016). Along with this apparent increase in the incidence of dengue, the disease was associated with 1.14 million DALYs in 2013 an more than 60% increase from 1990 (Castro et al., 2017). It has been reported by some researchers that between 50-100 million clinical cases and 36 million asymptomatic cases of dengue occur each year, with almost 25,000 deaths and approximately 750,000 DALYs (Halasa et al., 2011).

Clinical dengue

The typical clinical signs associated with a dengue fever (DF) infection are flu such as symptoms, high fever of 40^0C or 104^0F, retro-orbital pain, severe headache, myalgia, arthralgia, nausea, vomiting, hematemesis, melena, restlessness, irritability, inflamed lymph nodes and a rash (Muller et al., 2017; Sanyaolu et al., 2017). Most countries, especially in endemic areas, conduct public heath surveillance for the clinical signs associated with dengue in an attempt to identify cases and linked outbreaks as early as possible.

The initial febrile phase may be accompanied by signs of hemorrhage such as petechiae, bleeding from the gums, nose, mucosa and gastrointestinal tract. Patients in this phase may be positive for the tourniquet test, which is used to identify capillary fragility by using a blood pressure cuff to apply pressure the forearm then counting petechiae created (McFee, 2018; Muller et al., 2017). Most patients may recover after the febrile stage but some patients go onto what is called the critical phase which is characterized by increased permeability of capillaries which leads to plasma leakage and eventually shock and typically have decreasing temperatures (Muller et al., 2017). If a patient can survive the critical period for approximately two days given the appropriate treatment, then recovery is usually rapid, moving into the recovery phase where the patients may exhibit a recovery rash and their clinical profile stabilizes (Muller et al., 2017).Though there are many persons infected with dengue each year, the majority,70-80% are asymptomatic infections , however the burden of disease associated with the symptomatic cases can be overwhelming especially in developing countries such as Saint Lucia (Bhatt et al., 2013). Typically a patient is able to transmit the virus to naïve mosquitoes from four to twelve days after infection(Guzman & Harris, 2015). Dengue hemorrhagic fever was once classified by the World Health Organization (WHO) as dengue hemorrhagic fever and dengue shock syndrome, but was reclassified by WHO in 2009 to severe dengue. Severe dengue is a sometimes-fatal sequelae to secondary infections by a heterotypic dengue virus serotype that can lead to plasma leakage, hemorrhage and organ failure (Guzman & Harris, 2015). The clinical symptoms associated with this syndrome include, a defervescence to temperatures below 38^0C or 100^0F, abdominal pain, persistent emesis, hematemesis, tachypnea, gingival hemorrhage, fatigue and restlessness (Guzman & Harris, 2015; Mood & Mardani, 2017). Patients experiencing dengue, may go through three phases, febrile, critical, and recovery stage (Guzman & Harris, 2015; Mood & Mardani, 2017; Thomas et al., 2014).

Dengue infections may manifest asymptomatically, with non-specific clinical signs and as severe dengue which may lead to life threatening complications (Yacoub & Wills, 2015). The difficulty in identifying dengue because of its non-specific clinical presentation at times may contribute to misdiagnosis or delayed diagnosis of cases and therefore inappropriate management of cases and remains a concern for medical practitioners (Phakhounthong et al., 2018). Researchers have documented dengue to be associated with many different clinical signs that include fever, sore throat, leukopenia, arthralgia, myalgia, cephalia, lymphadenopathy, retro-orbital pain, lumbosacral pain, nausea, vomiting, diarrhea, headaches, petechiae, thrombocytopenia, exanthema rash, and ocular manifestations including hemorrhage, renal dysfunction, hepatic dysfunction, anterior uveitis and retinal detachment, (Agarwal et al., 2018; Guo et al., 2017; Singh et al., 2017). The clinical manifestations of dengue can also manifest as hematochezia, hepatomegaly, low or high hematocrit, low or high white blood cell count, high blood urea, high creatinine, low platelet count, tachycardia, abdominal pain, hematuria, and high alanine aminotransferase (ALT; Phakhounthong et al., 2018). In accordance with the World Health Organization's 2009 revised classification, the severe form of dengue has been demonstrated to also have a rapid decrease in platelet numbers, elevated hematocrit, hypovolemia from plasma leakage leading to shock, which used to be known as dengue hemorrhagic fever and dengue shock syndrome respectively (Horstick, Martinez, et al., 2015; Thomas et al., 2014; Van Kleef et al., 2009; Yacoub & Wills, 2015). The wide range of clinical signs associated with dengue contributes to the difficulty in early recognition and rapid treatment of the disease.

Dengue is a disease that can be mistaken for other infectious diseases such as chikungunya,COVID-19, West Niles, yellow fever, Middle Eastern Respiratory Syndrome (MERS) influenza, leptospirosis, Rift Valley fever, Zika virus, Ross River fever and malaria, especially in the early stages of the disease (Castro et al., 2017; Chadee et al., 2004; Kleef, Bambrick, & Hales, 2009; Lorenz et al., 2020; Mood & Mardani, 2017; Muller et al., 2017; Stanaway et al., 2016). The difficulty in making an accurate diagnosis based on clinical signs means that the appropriate treatment may not be given and the patient may face preventable outcomes as well as the transmission of the virus may continue to other susceptible persons. Dengue has also been associated with comorbidities such as asthma, diabetes, sickle-cell anemia, ethnicity (black persons have a reduced risk severe dengue), human leukocyte antigen (HLA), and non-HLA genetic disorders (Guzman & Harris, 2015; Guzmán & Kourí, 2002). There is still the need for further investigation of comorbidities associated with dengue because in mainly endemic populations this information is unavailable and the true impact of these conditions are not known (Vicente et al., 2017). Epidemiologists have suggested that using clinical case data in investigating the transmission parameters of a dengue outbreak is limited because of the inconsistent reporting patterns, inconsistent case definitions, and especially underreporting of infected persons who do not seek healthcare or whose data are not reported to the public health authorities (Anders & Hay, 2012). The co-circulation of dengue viruses and other arboviral diseases in conjunction with comorbidities create a significant challenge to public health authorities through the complexity of these associations and the related burden of disease.

Transmission of dengue follows both seasonal patterns within a year and cyclical patterns with outbreaks occurring in specific years which may be a result of many possible risk factors including environmental, vector, viral and human host dynamics (Castro et al., 2017). It has been suggested by researchers that dengue outbreaks in the Americas follows a specific pattern of endemic cycles followed by epidemic cycles of every 3-5 years (Brathwaite Dick et al., 2012; Cafferata et al., 2013).

The underreporting of dengue cases leads to unreliable estimates of the burden of diseases and as such epidemiologists recommend the use of expansion factors where the number of reported cases is multiplied by the expansion factor to take into account the unreported cases of the disease and better be able to estimate the true burden (Stanaway et al., 2016; Undurraga et al., 2013). Underestimation of dengue cases occurs because of inadequate public health surveillance, limited access to private healthcare data, differences in health-seeking behavior, inaccurate diagnostic tests, difficulty by attending physicians to recognize clinical symptoms and lack of regulations to enforce mandatory reporting of cases (Castro et al., 2017). For example Constenla, Garcia, and Lefcourt, (2015) reported that in Brazil a range of expansion factors were used for different studies assessing disability adjusted life years (DALYs) from 0.3-10, whereas in Puerto Rico the expansion factor ranged from 6- 30. Other authors have used expansion factors of 14 to 28 in Nicaragua, 1-10 for Brazil, 6 in Panama and 27 in Puerto Rico (Halasa et al., 2011). In countries where no estimates for expansion factors are available epidemiologists recommend using an expansion factor of 2.3 for fatal or hospitalized cases and 15 for cases that were not hospitalized (Halasa et al., 2011). Stanaway et al. (2016) estimated that an expansion factor of 12.3 should be applied globally when assessing reports of dengue because most official reporting systems only captured approximately 8% of symptomatic infections whereas other authors suggest an expansion factor of 28 is more appropriate based on global estimates of the disease (Guzman & Harris, 2015). Though the WHO changed the classification of dengue in 2009, there remains great variation in the definition of classification of dengue in affected countries further contributing to the lack of consistency and accuracy in burden of dengue estimates (Horstick, Martinez, et al., 2015). Also when assessing global estimates on burden of dengue many small countries that are endemic for the disease are left out of the analysis often because of lack of data (Constenla et al., 2015). These wide variations in the suggested expansion factors for considering the incidence of dengue suggest the difficulty in successful disease control plans and the need for specific local information on the epidemiology of dengue.

Dengue risk factors

Pang et al. (2017) suggest that risk factors for developing severe dengue include, the serotype of the virus, underlying medical conditions, race, host genetics, age, and sex (Carabali et al., 2015; Mahmood et al., 2013; Toledo et al., 2016). Other epidemiologists have reported that demographic and societal changes such as urbanization, population growth, living between latitudes 15^o north and 15^o south which has been expanded to include 35^o North and South, living below 100 m elevation, health system access, education, income, lack of public health literacy, and poor surveillance are all factors that contribute to the prevalence of dengue (Carabali et al., 2015; Mahmood et al., 2013; Souers et al., 2014; Stanaway et al., 2016). It has also been suggested by other authors that in addition to urbanization and population growth; movement of viruses and vectors because of the speed of modern transport, the lack of effective vector control and inadequate vector control management also contribute the incidence of dengue (Akter et al., 2017; Sanyaolu et al., 2017). Guo et al. (2017) suggested that after evaluating the literature on dengue between 1990 and 2015, that living with uncovered water container was the most important risk factor for developing dengue, with hypotension being most strongly associated with developing dengue hemorrhagic fever and suffering from diabetes mellitus most strongly associated with death among dengue patients. The large and varied number of possible determinants of dengue, contribute to the difficulties that researchers face in accurately characterizing the epidemiology of dengue, especially considered the local differences of each of these factors within the geographic areas where the disease occurs (Bhatt et al., 2013).

Demographic determinants especially those influenced by human behavior have significant effect upon the transmission of dengue viruses and the outcomes associated with subsequent of dengue infections (Guzman & Harris, 2015). One of the greatest factors associated with the spread of infectious diseases is the rapidity with which it is possible to move from one country to another often long before the end of the incubation period of many diseases allowing infected persons to enter countries free of the disease and initiate local transmission of the disease (Pal, 2013). This is especially important in the case of vector-borne diseases such as dengue where the destination country of the infected individual has competent local vectors that can help to quickly establish local autochthonous disease cycles (Massad et al., 2018; Semenza et al., 2014). Globalization and the improvement in the rapid transport and movement of people and goods as well as technological advancement such as the manufacture of rubber tires also contribute to the movement and population growth of the *Aedes* mosquito thus the rise in dengue transmission (Rezza, 2014). In the Caribbean the movement of people through tourism, either cruise or stayover could be a source of the introduction of dengue viruses to a country (Oduber et al., 2014). This is important because even in an endemic or hyperendemic country it is possible to introduce new genotypes or non-circulating serotypes therefore potentially beginning an outbreak of the disease (Ramos-Castañeda et al., 2017).

Researchers suggest that during a period of 15 years the burden of dengue within a population will typically shift from adults to children, though there are populations where adults remain a major affected population even when dengue is considered a childhood phenomenon the phenomenon has not been described for the Saint Lucian population in published literature (Vicente et al., 2017). This is likely in endemic or hyperendemic countries where most of the adult population would have been exposed to the circulating viruses and have protective immunity. After conducting a cross-sectional study of dengue cases occurring in the Brazilian community of Vitória, Esperíto Santo State between 2007 and 2013 (Vicente et al., 2017) reported and increased prevalence of severe dengue in male and elderly populations but not in juvenile populations.

Singh et al. (2017) reported that in surveillance of dengue cases that were seen at a hospital in North India, the majority of cases occurred in males of the age group 18-35 years and again Singh et al. (2018) found in a cross-sectional study of acute viral febrile illness that male patients in the age group of 20-30 years. This finding of a high incidence of dengue in male patients was also supported by Mehta, Bafna, and Pokale (2018) who found that men in the age group 21-40 years was most likely to present with dengue in the Indian city of Pune. Morin et al. (2013) suggest that dengue outbreaks can be associated with the introduction of a new serotype, the re-introduction of an old serotype, changes in herd immunity and the change in the demographics of the population. Other authors report a wide range of age groups affected by dengue differing between and sometimes even within countries including the 15 to 59 year age group, 5 to9, 10 to 19, and 20 to 39 and also the under 5 age group (Cafferata et al., 2013; Kumar et al., 2013; Kumar et al., 2018). In a study by (L'Azou et al., 2015) the authors identified that the seroprevalence of dengue was greater in the population older than 40 years with it reaching 87-97% in the islands of Martinique and Guadeloupe, though only 30% of those surveyed remembered having dengue. These wide differences in the epidemiology of dengue across different countries and even within countries gives emphasis on the need for local investigation of dengue as much as is practical

Age has been associated with dengue and its outcomes particularly in relation the immunocompetence of the individual (Carabali et al., 2015). Though research seems to indicate that a higher level of mortality occurs among the adult population when infected with dengue, the general sensitivity of the population to death among children drew greater concern (Carabali et al., 2015). In analyzing the Global Burden of Disease data Stanaway et al. (2016) report that mortality rates attributed to dengue were highest in patients younger than 1 year old decreasing into adulthood but again increased greater than the age of 45 years which may be attributed to lower immunocompetence with most of these deaths occurring in Southeast Asia.

The effect of the various demographic determinants of diseases still requires further research as there remain conflicting views on the role of ethnicity in dengue occurrence and outcomes of infection, but part of this conflict may arise from studies not always considering other possible confounding factors such as socioeconomic status which may see disadvantaged persons living in high-risk areas with ideal mosquito breeding grounds and lower access to healthcare (Carabali et al., 2015). Education is also considered a significant social determinant of dengue occurrence and its outcomes because persons with higher levels of education are more likely to understand the risk of dengue infections and the education of health care providers on identification and management of dengue leads to better outcomes for patients (Carabali et al., 2015).

The attempts to control the vector of dengue, the *Aedes aegypti* mosquito, were begun as early as 1901, when William Gorgas suggested fumigation and destruction of mosquito breeding sites in an attempt to control the occurrence of yellow fever, a program that was adopted in other countries in the region. The Pan-American Health Organization (PAHO) furthered the fight to eradicate the mosquito and control yellow fever in 1947, by establishing the Continental *Aedes aegypti* eradication plan centered on the use of DDT an organochlorine insecticide (Brathwaite Dick et al., 2012). The efficacy of this program may have restricted the circulation of DENV to only the DENV-2 serotype, American genotype which was first isolated in Trinidad in 1943. The DENV-3 serotype, Asian genotype was found to circulate during a 1963-1964 outbreak in the Caribbean islands starting with Jamaica. Another outbreak in 1977 involved the DENV-3 virus for the first time again starting in Jamaica then spreading to other islands, following which the DENV-4 virus was introduced to the islands of the Eastern Caribbean in 1981 spreading to the other countries in the Americas afterward (Brathwaite Dick et al., 2012). The abundant population of the Aedes vector in the Caribbean and Saint Lucia specifically is a significant risk factor for the occurrence of the disease.

Human related factors such as urbanization and population density have proven to be important as well, especially because of the associated demands on water supplies that may lead to improper storage of water providing rich breeding places for mosquito vectors (Akanda & Johnson, 2018; Khan et al., 2018; Murray et al., 2013). Water insecurity is further exacerbated by climate change factors that cause extreme weather events such as droughts, increased major storms, changes in precipitation and precipitation patterns, these may reduce water supply in addition to human activities and therefore cause the need for additional water storage.

The rapid expansion of urban areas due to increasing urban migration or population growth, leads to increased population density in areas with unplanned development with possible decreased waste management, poor water access, and improper storage of water perfect habitats for the mosquito vector to thrive (Castro et al., 2017; Gómez-Dantés & Willoquet, 2009; Gubler, 2011). Such unplanned development takes place particularly in low or middle income countries , typically in countries endemic to dengue, without proper planning for water access or storage and waste disposal (Murray et al., 2013). The *Aedes* mosquitoes have a limited flight range of up to 400m but are able to move further distances because of human transport, this along with climatic change has seen the expansion of the geographic range of both *A. aegypti* and *A. albopictus* (Casas et al., 2017). The limited flight range of the *Aedes* mosquito also suggests that viremic humans are more likely to have a significant effect on the transmission of the disease to new geographic locations than the mosquito itself (Casas et al., 2017). Other differences between *A. aegypti* and *A. albopictus* include *A. aegypti* lives for a maximum of 22 days compared to 65 days in the other, *A. aegypti* as a mainly indoor mosquito, lays its eggs in artificial containers indoors or in close proximity to households especially tree-holes or bamboo, occupies urban areas with or without vegetation and biting and movement impaired below 14^0C whereas *A. albopictus*, is an outdoor mosquito, prefers tree-holes and bamboo but can lay eggs in manmade containers also, typically thrives in vegetation and biting and movement are impaired below 13^0C (Ebi & Nealon, 2016; Padmanabha et al., 2012). Chadee & Martinez, (2016) determined that the *A. aegypti* exhibited a faster life-cycle 34^{o}C than at 32^{o}C though at 36^{o}C most larvae died. During the period of their study investigating the effect of climate change on the *A. aegypti* mosquito, (Chadee & Martinez, 2016) found that most breeding sites reaches temperatures in excess of 34^{o}C even as high as 49.5^{o}C resulting in the death of larvae and decreased mosquito populations. It has been reported that at warmer temperatures the larvae of *A. aegypti* remain smaller, and thus smaller adults which paradoxically are more efficient vectors of the dengue virus because these smaller mosquitoes feed more often to fuel the reproductive cycle (Wegbreit, 1997). Although having competent vectors is essential to the transmission of dengue, infected persons are more important for the geographic expansion of the disease, facilitated though movement of people for activities such as tourism (Oduber et al., 2014; Wilder-Smith, 2012).

A study by Schiøler & Macpherson, (2009) reported that during a dengue epidemic showed similar infestation levels of the *Aedes aegypti* mosquito across rural, peri urban and urban areas with average House Indices of 14%, and average Breteau Indices of 23%. These authors also indicated that during the epidemic period Saint Lucia also reported dengue cases though unlike other affected islands only one serotype of the dengue virus was found to circulate in Saint Lucia where severe dengue was reported. Each epidemic reported in Grenada was associated with the introduction of a new serotype of DENV, which suggests that new cases of dengue may indicate persons that were born after the last incursion of a new strain of DENV in 2002 (Schiøler & Macpherson, 2009).

As mentioned previously some of the major factors that have been associated with dengue occurrence worldwide are, globalization, tourism, trade, urban migration, urbanization, overpopulation, inadequate water supplies, inadequate waste management, and increasing temperature (Murray et al., 2013). These factors are seen as important to dengue epidemiology because they contribute to the size of the vector population, the ability of the vector to transmit the virus, the geographic distribution of the vector, and the increased contact of the vector with human hosts (Achee et al., 2015; Ebi & Nealon, 2016). Researchers have arrived at different outcomes when investigating the relationship between environmental variables and dengue with some finding an association between the these factors and the outcome and others finding no association (Depradine & Lovell, 2004). These differences in outcomes may be a result of differences in study methodologies, differences in data available, temporal differences, geographical difference as well as study populations and support the need for localized studies (Bowman, Donegan, & McCall, 2016; Bowman et al., 2014; Cafferata et al., 2013; Ganeshkumar et al., 2018; Horstick, Martinez, et al., 2015; Naish et al., 2014).

Many researchers have investigated the relationship between vector density and the occurrence of dengue, though the results have been mixed, some still relate the occurrence of the disease to the increases in the vector population as this is thought to make biological sense (Bowman et al., 2014; Getachew et al., 2015). In a systematic review of the literature exploring the relationship between vector indices an dengue, it was found that the majority of the studies included were unable to identify a conclusive link between vector indices and dengue (Bowman et al., 2014). Other, researchers found an association between dengue cases and the Breteau index (BI) of 20-46 during the rainy season, which was much higher than the accept BI of 5 thought to be the threshold for successful dengue transmission (Chadee et al., 2007). It is thought that tree cover or vegetation is an important factor in providing an adequate breeding environment for *Aedes* mosquitoes especially *Aedes albopictus* which preferentially breeds in arboreal environments. *Aedes aegypti* although preferring to breed in artificial containers will also breed in tree holes or other such spaces (Akter et al., 2017). In the past researchers have suggested that vector density, susceptible populations, and high virus circulation were essential to a high incidence of dengue cases. However, other authors have disputed this, citing other data that does not support the importance of vector density as a stand-alone factor rather noting the complex nature of dengue ecology suggests a complicated interaction of factors that contribute to dengue outbreaks (Guzmán & Kourí, 2002; Pang et al., 2017; Torres, Orduna, Piña-Pozas, Vázquez-Vega, & Sarti, 2017). Bowman et al. (2014) called for further investigation into the relationship between vector indices and dengue including better vector and dengue case data, coordinate multinational studies, local level investigation, unified threshold measures for vectors, and especially more widespread use of adult vector sampling. These differences in reported relationships with vector indices and dengue warrant investigation of these variables at the local Saint Lucian level.

The occurrence of dengue has also been associated with socioeconomic factors such as income, socioeconomic status, type of housing, number of people in household education and employment (Arauz et al., 2015; Fritzell et al., 2018; Velasco-Salas et al., 2014). These socioeconomic factors are suggested to affect where a person decides to or is able to afford to live and some of these areas may have poor water supply requiring water storage which may support oviposition of the mosquito vector and an increased likelihood of dengue transmission (Velasco-Salas et al., 2014). The *Aedes* vector of dengue lives in close proximity with its human hosts preferring to live and feed indoors, this means that unemployed persons that spend more time at home will have an increased likelihood of being bitten by a mosquito and exposure to dengue (Getachew et al., 2015;

Poole-Smith et al., 2015). Education level is also important, allowing persons at risk to understand the nature of the disease, what measures can be taken to prevent exposure to the disease and what action should be taken if on suspects exposure. Lower levels of educational attainment may lead to undesirable action such as improper storage of water, improper disposal of artificial containers that can providing breeding habitats for mosquitoes and failure to seek medical attention when necessary (Al-Dubai et al., 2013). Zellweger et al. (2017) suggested that the relationship between socioeconomic factors and dengue differ by location because the reasons for factors such as unemployment may differ, therefore any association identified has to be interpreted in the context of the specific population under study.

The Ministers of Health within the Pan American Health Organization region agreed to implement the Integrated Management Strategy for Prevention and Control of Dengue in 2003,with the intention of combining surveillance, vector and environmental control with clinical, and public health strategies to control dengue (Laughlin et al., 2012; San Martín et al., 2010). Pang et al. (2017) suggested that following the United Nations (UN) Sustainable Goals target 3.8 of the third goal the spread of dengue should be considered to be a result of economic development, population increase and globalization, necessitating a united global response. Though dengue has been approached at the local, regional and international levels the incidence of the disease continues to increase indicating the current practices have been unsuccessful and more must be done (Guzman & Harris, 2015; Katzelnick et al., 2017, 2017).

One of the greatest challenges in managing dengue is the lack of continuation of successful strategies, because there are often competing public health concerns that lead to the redistribution of resources away from dengue (Wilder-Smith et al., 2017; Wilder-Smith & Macary, 2014). Though dengue may exist as largely asymptomatic cases, when an epidemic occurs limited healthcare resources are easily overwhelmed, often by patients with similar clinical signs to dengue but suffering a different infection leading to severe public health crises (Ali et al., 2018). These overburdened public health systems often struggle to stem the spread of the disease, especially with the co-circulation of other arboviral diseases and may lead to tremendous economic loss, through decreases in productivity and associated costs of managing the disease as well as social upheaval (Bhatt et al., 2013; Shepard, Undurraga, Halasa, & Stanaway, 2016). In a review of the literature Murray et al., (2013) reported other researchers as predicting that up to 60% of the world's population would be living in areas where they would be at risk being infected by dengue by 2085.

The movement of people, animals and goods have been associated with the spread of infectious disease agents because the speed of transportation today often is shorter that the incubation period of diseases (Adda, 2016; Banks et al., 2015). In 2014 the number of tourists travelling internationally exceeded 1138 million a 45-fold increase from 25.3 million in 1950 and it is expected that this number will continue to increase (Baker, 2015). It has been reported that the tourism industry contributes a larger percentage to the GDP of the countries of the Caribbean than to any other country or region, suggesting any negative effect to this industry will have tremendous negative outcomes within the region (Cannonier & Burke, 2018). The tourism sector in the Caribbean contributed approximately US$49 billion to the region's economies and sustained more than 1 million jobs in 2013, and estimated to rise to greater than US$70 billion (Mycoo, 2017). Researchers estimated that more than 1 billion tourists travelled internationally in 2014 and was projected to grow at a rate of 4%, accounting for more than 10% of the global gross domestic product (GDP; Rosselló, Santana-Gallego, & Awan, 2017). Other authors put the number of persons travelling by air at almost 3 billion with many of them travelling to and from dengue endemic countries (Gubler, 2011). The relationship between tourism and dengue is two-fold, first tourists can serve as a vehicle for dengue transmission and secondly an outbreak that minimizes the productivity of the workers in the industry or dissuades visitors from traveling to the region could devastate the economy.

Tourism and other business or trade related movement of people have been associated with the spread of infectious diseases such as dengue (Massad et al., 2014; Shepard et al., 2014). Dengue has been recognized as the most common reported illness among travelers returning from any region with the exception of Central America and sub-Saharan Africa (Yacoub & Wills, 2015). Schiøler & Macpherson (2009) reported that in a 2001-2002 dengue epidemic was preceded more than 10 weeks by peak tourist arrivals from other countries experiencing dengue outbreaks. Khan et al. (2018) report that there has been a 40-fold increase in dengue that can be associated with increased travel in the twentieth century.

Researchers have determined that when the perception of risk to the traveler is high then the likelihood of travel is low (Baker, 2015). This means that notices of outbreaks can have significant potential effect on a country’s tourism industry as was predicted in Florida with the occurrence of Zika virus (Lee et al., 2017; Widmar, Dominick, Ruple, & Tyner, 2017).Tourists play many important roles in infectious disease ecology.They can assume the roles of sentinel, vector of disease or even the victim, which means they can have a significant role in dengue transmission, for example most cases of dengue in the United States have occurred as a result of returning tourists who have been infected (Baker, 2015; Neiderud, 2015). An important threat of dengue is to the 120 million travelers at risk each year. This is especially important to Saint Lucia and the other Caribbean countries all of which depend heavily on tourism, a market that could be devastated by dengue epidemics (Halasa et al., 2011). These 120 million at risk travelers also pose a significant threat to their home countries through the possible introduction of dengue to geographic locations that may not have local autochthonous transmission of dengue viruses and also introducing new genotypes of dengue viruses to even endemic countries such as Saint Lucia.

In the case of Saint Lucia, an eradication of such disease is expected to see an increase of more than 300,000 tourists an increase of 26% with the associated increase of more than US$ 300 million (Rosselló et al., 2017). In the Caribbean the close proximity of the islands and the movement of people between these islands has led to tourism being viewed as a significant factor in the transmission of dengue viruses across national borders primarily through the movement of viremic travelers especially those that are asymptomatic (Grange et al., 2014; Ramos-Castañeda et al., 2017). With the large number of cruise and stayover visitors that travel to Saint Lucia each year it is important to investigate the risk of dengue transmission through these routes.

In 2009 the WHO, revised its 1997 classification system for dengue of dengue fever, dengue hemorrhagic fever and dengue shock syndrome into dengue with or without warning signs and severe dengue, in an attempt to better address the severity of the disease and improve surveillance of the disease (Low et al., 2018). However, in 2018 many authors and researchers still use the 1997 definition or various modifications which limit the direct comparison of the data collected. Low et al. (2018) determined that there was no significant difference in case fatality rates when using the 2009 WHO classification as compared to the 1997 classification. In a review by Carabali, Hernandez, Arauz, Villar, and Ridde (2015) the authors reported that 82% of the papers included in their work still used the 1997 WHO dengue classification, 7.7% used the 2009 classification and the other 10.3% used various adaptations of these classifications that were specific for the area under consideration. It is hoped that by increasing the accurate recognition of dengue to improve treatment outcomes the burden of the disease and the effect of an epidemic will be reduced.

Another risk factor for dengue is the difficulty in clinical diagnosis, delaying recognition of outbreaks and public health responses. Researchers generally report dengue presenting with clinical signs of head-ache, retro-orbital pain, myalgia, arthralgia, malaise, and rash. but cases of dengue presenting with complications also demonstrated neurological disorders, cardiac disorders, hepatic disorders, gastrointestinal bleeding, thrombocytopenia and cavity effusion (Ahlawat & Kalra, 2017). Generally, the severe form of dengue is associated with secondary heterotypic infections however a certain number of infants experience severe dengue even with a primary infection which makes it even more important for a clinician to recognize the disease as early as possible. It has been demonstrated that secondary infections with a heterotypic serotype of dengue can lead to cases of severe dengue, whereas tertiary or quaternary infections with heterotypic serotypes can lead to clinical disease it is rarely severe (Katzelnick et al., 2017). Researchers have estimated that 5-10 percent of patients with dengue fever will develop dengue hemorrhagic fever and patients who develop dengue hemorrhagic fever have a 3-5 percent chance of death if they go on to develop the dengue shock syndrome (Mahmood et al., 2013).This wide range of clinical signs underscore how difficult it is for attending physicians to recognize and correctly diagnose dengue, which unfortunately contributes to the public health crisis in the face of an escalating epidemic.

Low, Ooi, and Vasudevan (2017), underscored the need for specific therapeutic interventions for dengue that will reduce the clinical symptoms of the disease and reducing the unwanted public health burden of the disease. Researchers in academia and private industry are currently working on potential therapeutic interventions that will meet this need, but as yet none have been brought to market (Whitehorn et al., 2014). These therapeutic modalities include inhibitors that target viral processes, viral protein, viral RNA and other structures, monoclonal antibodies, and viral fusion technology (Whitehorn et al., 2014). Though there are a number of potential therapeutic agents in development there are a number of challenges that continue to impede the success of researchers. This includes the lack of a suitable animal model, because non-human primates the closest model, do not exhibit signs of the disease; the lack of reliable epidemiology of the disease, and less than adequate clinical trials (Low et al., 2017). This lack of therapeutic tools, leaves physicians to employ symptomatic treatment of dengue cases. A major downside of this is that some of the public would not seek care unless suffering severe disease especially if they were treated previously (Elsinga et al., 2018; Wong & AbuBakar, 2013). The lack of affordable, effective diagnostic tools and treatment modalities places the emphasis on prevention in the control of dengue and the need for understanding the epidemiology of the disease.

Singh et al. (2017) suggest that the clinical profile of dengue has changed slightly during the decades of its occurrence this poses a serious challenge to clinicians and health departments responsible for managing the disease cases and outbreaks. The most common clinical sign reported in a study in Lucknow Province India, was fever, then headache, unlike other studies vomiting was also more common with fewer reported cases of rash and retro-orbital pain which are usually common markers of dengue (Singh et al., 2017). Vicente et al. (2017) reported that across a selected population in Brazil, among persons with dengue children presented more often with hemorrhage and plasma leakage than other groups. Female children mainly demonstrated hemorrhage and epistaxis whereas male children demonstrated plasma leakage more often. In the adolescent population females more often presented petechial hemorrhage, and males presented hemorrhage, cavity effusion and plasma leakage. Adults and elderly among the sampled population demonstrated lower proportions of hemorrhage overall than other segments of the population (Vicente et al., 2017). Researchers were able to identify an association between gender and the clinical manifestations of dengue, with males presenting more often with severe dengue (Vicente et al., 2017). These researchers also found that there is an association between ageing and the outcomes of dengue infections, with elderly more often presenting with severe dengue and children presenting less often with the severe form of the disease. There is also the possible association of the serotype of dengue virus in circulation and the segment of the population affected with disease, the elderly presented with severe dengue more often when DENV-2 was in circulation than when DENV-1 or -4 were in circulation (Vicente et al., 2017). The most common clinical signs identified on a review of the global epidemiology of dengue between 1990 and 2015 were headache, malaise, fever, and asthenia (Guo et al., 2017). Atypical signs such as acute kidney damage, hepatitis, acute respiratory disease syndrome, neurological signs, cholecystitis, disseminated intravascular coagulation, Guillain-Barré syndrome and transverse myelitis, may occur (Ahlawat & Kalra, 2017; Verma et al., 2014). The changing typical clinical presentation of dengue in some countries indicates the importance of discovering the most significant clinical risk factors of the disease that can be used for early diagnosis and public health surveillance.

The changes to the WHO dengue classification guidelines in 2009, led to the inclusion of neurological signs in identifying cases of dengue (Carod-Artal et al., 2013). The neurological symptoms include encephalitis, seizures, inattention, neuromuscular complications such as Guillain-Barré syndrome, neuro-ophthalmic disorders, headache, dizziness, lethargy, insomnia, confusion, memory impairment, encephalopathy, loss of sensation psychiatric disorders, and encephalopathy (Carod-Artal et al., 2013; Nadarajah et al., 2015; Verma et al., 2014). The recognition of the association of dengue with these neurological signs further complicates the early recognition of the disease and the dependent rapid control of outbreaks.

Researchers have reported that though chikungunya, Zika and dengue are commonly found in co-circulation, most patients seem to only test positive for only one of the viruses. Elsinga, Halabi, Gerstenbluth, Tami, and Grobusch (2018) reported that there were differences in clinical manifestation in cases where dengue infection preceded chikungunya infection as compared to an infection of chikungunya without prior dengue. Dengue infections have recently been demonstrated to occur in patients also infected with the chikungunya virus, though such a phenomenon has been reported in Africa and South-East Asia (Furuya-Kanamori et al., 2016). Singh et al. (2018) reported multiple cases of dengue and chikungunya coinfections but did not find any statistically significant additional clinical signs or increased severity of clinical signs. All of the patients with coinfection exhibited signs of headaches, body aches, weakness and joint pains. It is unclear if coinfection results in different clinical signs or outcomes of infection with some researchers reporting no differences whereas others have reported a higher rate of severe clinical signs and poor outcomes. There have been reports of increased occurrence of hepatic dysfunction and atypical hemorrhagic manifestations (Singh et al., 2018). In their systematic review of the literature on the global epidemiology of dengue Guo et al. (2017) determined that co-infections were detected in 47.7% of reported outbreaks. Identifying the differences in dengue manifestations may allow quicker more appropriate treatments for clinical cases of these diseases and rapid control and termination of outbreaks and epidemics. The co-circulation of arboviral diseases increases the likelihood that a patient may have concurrent infections making the correct diagnosis and appropriate treatment plan difficult for clinicians and possibly lead to unwanted outcomes and weakened public health surveillance (Elsinga et al., 2018).

Climate change is one of the greatest threats to the global populations and has significant effect on the dengue vector, virus and occurrence of the disease (Butterworth et al., 2017; Campbell et al., 2015; Larrieu et al., 2014). Scientists have determined that a rise in global temperature to 1.5°C above the levels of the pre-industrial era along with concomitant rise in greenhouse gases will have major negative effects on human life, the environment including increased risk of infectious diseases, and the vectors that they spread (Murray et al., 2013; Mycoo, 2017). Guzmán and Kourí (2002) reported that the WHO predicted a 1-2°C rise in temperature would be associated with an increase in the incidence of dengue leading to hundreds of millions of infections and up to 30,000 dengue related fatalities. Caribbean countries, the majority being small island developing states (SIDS) or countries with lowlands, are especially at risk to rising sea levels which threaten to destroy coastal areas and affect the availability of potable water leading to the increased need in water storage (Mycoo, 2017). These SIDS are also undergoing significant levels of informal urbanization often in vulnerable locations that may be suitable for mosquito breeding. The costs associated with the current environmental mitigation strategies of retreat, protect and accommodate are beyond the economic resources of the majority of SIDS calculated at up to 30% of their GDP and compared to

1% in developed countries, forcing the Caribbean countries rely on the assistance of donor countries and external agencies (Mycoo, 2017). These changing climatic conditions and the resulting efforts to combat them such as increased water storage may directly and inadvertently increase the incidence of vector-borne diseases such as dengue causing a significant social and economic burden in countries with struggling economies (Lowe et al., 2018).The economic losses attributed to climate change through increased catastrophic natural events such as hurricanes along with the loss of revenue from tourism in the Caribbean is projected to be US$22 billion by 2050 though this estimate does not include other risks associated with climate change (Mycoo, 2017). These countries do not have economies that are resilient enough to respond to these potential catastrophic losses.

Among the recognized climate changes to the Caribbean are the increases in temperature and the decreases in rainfall leading to drier conditions during the traditional rainy seasons of June to October, contributing to the further critical nature of water resources (Mycoo, 2017). Typically in the Caribbean the rainy season is identified as occurring from June to November (Depradine & Lovell, 2004). The difference in environmental parameters, as with the rainy and dry seasons which may be different at the local level, makes it challenging to compare studies and the outcomes of these studies. In Barbados, it has been established that there is a seasonal distributions of dengue cases, with them occurring 1-2 months after rainfall, peaking during October to January (Kumar et al., 2013). It has been predicted that with the increases of temperatures globally the geographic distribution of dengue and the incidence of the disease will also increase (Wegbreit, 1997).

Many researchers have identified the probable association of dengue with climatic variables such as rainfall, humidity, windspeed, vegetation, temperature, and even weather events such as El Niño Southern Oscillating (ENSO) events (Akter et al., 2017; Ebi & Nealon, 2016; Lowe et al., 2018; Morin et al., 2013). The ENSO events, both El Niño and La Niña are associated with changes in temperature and precipitation along with other changes in weather related variables which have been associated with changes in vector populations and therefore in the incidence of vector-borne diseases such as dengue (Lowe et al., 2018). Generally, the sea-surface temperatures are warm during the El Niño phenomenon and cold during the La Niña. In El Niño years, the weather patterns in the Caribbean typically demonstrate less rain and increased temperatures in the year with increased rain and temperatures in the early part of the following year (Lowe et al., 2018). Amarakoon, Chen, Rawlins, & Taylor (2004) were able to establish that dengue outbreaks in the Caribbean, had a periodicity of 2-3 years which was shorter than the previous decade which had been every 3-4 years though other researchers have suggested that the cycle is 3-5 years alternating from endemic to epidemic cycles (Brathwaite Dick et al., 2012; Cafferata et al., 2013). The researchers were able to identify a possible association between peaks in dengue epidemics within the Caribbean region with ENSO events in 1982/83, 1986/87, 1992/93, 1994/95, 1997/98, 2010/11, 2011/12, and 2014-2016 (Lowe et al., 2018). This periodicity was actually linked with below normal rainfall and higher temperatures, with the epidemics occurring in the later part of the year, peaking with the decrease in rainfall. The recognition that the relationship between weather patterns and dengue suggests the need to investigate such relationships in the context of Saint Lucia.

Hosein, Al-Tahir, & Ramlal, (2013) published a study which supports the rainy season having significant effect on the incidence of dengue in Trinidad and Tobago and that most of the associated dengue cases presented during the rainy season. Watts, Burke, Nisalak, Harrison, and Whitmire (1987) demonstrated that cases of dengue began to increase in the latter part of the dry season between the months of March to May, but peaked in the rainy season between June and November though the increase has not been associated with increased vector density. Singh et al. (2017), suggest that dengue outbreaks typically peak in September, just after the heavy rains experienced in India.

Heavy rains can also contribute to the increase in vector density by providing a greater number of suitable breeding habitats that did not exist otherwise (Butterworth et al., 2017). Researchers have been able to use environmental variables to inform models on dengue occurrence which allow the prediction of outbreaks as much as 40 weeks in advance which is a helpful tool for public health agencies to mitigate the consequences or avoid these outbreaks (Lowe et al., 2018; Morin et al., 2013). In countries where the appropriate local meteorological data may not be available, researchers suggest the use of substitute data such as sea-surface temperatures which are available from international agencies such as the Australian Bureau of Meteorology (Fuller et al., 2009).

Along with a rise in surface temperature; changes in temperature, rainfall, and humidity indirectly affects changes in the incidence and prevalence of dengue through the effect on the breeding cycle, survival rate, and biting rate of the *Aedes* vector. Higher temperatures can increase the frequency with which the mosquito feeds and also reduce the period from the mosquito becoming infected with the virus and the ability to pass it on in future feeding that is known as the extrinsic incubation period increasing the possible number of feedings or vectorial capacity of the mosquito (Chadee & Martinez, 2016; Lowe et al., 2018; Morin et al., 2013). Increasing temperatures can affect hatching and development time also increasing the vectorial capacity of the mosquito (Butterworth et al., 2017). Ebi and Nealon (2016) reported that local temperature, humidity, and high levels of precipitation were strongly associated with elevated levels of dengue risk. The ideal temperature for survival of all stages of *A. aegypti* mosquitoes is between 20 to 30^{0}C (Ebi & Nealon, 2016). Under experimental conditions, Watts, Burke, Nisalak, and Harrison, and Whitmire, (1987), were able to prove that the extrinsic incubation period for dengue was reduced from 12 to 7 days when incubation temperatures for *Aedes aegypti* mosquitoes increased from 30^{o}C to 32^{o}Cor 35^{o}C which suggests that as temperature increases *A. aegypti* becomes a more efficient vector of dengue. At 20^{o}C, though the virus could be recovered from the thorax-abdomen, none was recovered from the salivary glands, which suggests that the mosquito would be unable to transmit the dengue virus at this temperature (Watts et al., 1987).

Temperature affects the occurrence of dengue through a number of different pathways, mainly through its effect on vector and virus ecology. In a review by Morin et al., (2013) it was indicated that as temperature increased from 26^{o}C and 28^{o}C to 30^{0}C, the time it took for the dengue virus to appear in the salivary glands of the *Aedes aegypti* mosquito after feeding decreased from nine days to five days (Morin et al., 2013). This period known as the extrinsic incubation period (EIP) which reflects the time from the mosquito being infected to becoming infectious to a new host is an important measure of the efficacy of the vector. Decreases in the EIP may generally lead to the increased ability for the vector to infect naïve hosts (Morin et al., 2013). Increases in ambient temperature also increases the rate of viral replication in the vector. In the review other researchers were found to suggest that the EIP may decrease when the temperature changes from 30^{o}C to 32-35^{o}C from greater than 12 days to approximately 7 days but at approximately 26^{o}C no virus transmission occurred, and yet other researchers found that at 25^{o}C the EIP was 15 days whereas at 30^{o}C the EIP decreased to 6.5 days. This indicates that though there are differences in the results of different research studies the general outcome is that at colder temperatures mosquitoes were less effective as a vector (Morin et al., 2013).

In a review by Morin et al. (2013) the authors reported that temperature also affects, feeding, fertility the development of the ovaries and eggs, the development of the mosquito at each stage of development, and the overall survival of the *Aedes aegypti* vector with development rates increasing with increases in temperature up to 34^{o}C. The authors also indicate that research has shown that an adult female mosquito takes a blood meal 3 days after emerging as an adult and with an EIP of approximately 12 days takes about 15 days at most before being able to pass on the dengue virus to a host and only about 40% of mosquitoes survive to be able to become infectious. Temperature may also affect the mosquito’s behavior, preferring artificial containers for breeding that are in cooler shaded areas which is a reason that shade providing vegetation is important in the disease ecology of dengue. Increasing temperatures will lead to evaporation of water from unprotected breeding sites which in turn increases larval density and competition, reducing the survival rate of the mosquito. Artificial containers that contain organic material that the larvae can feed on are also favored by the *Aedes* mosquito (Morin et al., 2013). The eggs of *Aedes aegypti* are able to survive across a wide range of environmental conditions unlike those of *A. albopictus* which do not survive well at humidity less than 95% or temperatures greater than 22°C (Morin et al., 2013). Increases in humidity is also associated with more favorable conditions for vector survival and proliferation (Morin et al., 2013). The effect of environmental or climatological factors on the occurrence of dengue is multifaceted and creates a complex relationship. The lack of agreement among study results illustrates this complex relationship where it is unlikely that one factor directly influences the occurrence and outcomes of dengue infections and any predictive model for dengue would have to include multiple possible determinants.

Notwithstanding the focus on the effect of minimum, maximum and average daily temperatures on dengue occurrence, Lambrechts et al. (2011) insist that the diurnal temperature range (DTR) is just as important if not more important that other measures of temperature. They were able to prove that the daily temperature variation influences the transmission of the dengue virus by the *Aedes aegypti* mosquito. In their experiments they were able to demonstrate that DTR affects vector competence and vector survival. More specifically Lambrechts et al. (2011) suggested that a larger DTR will shorten the extrinsic incubation period (the time for the spread of the virus from the midgut to other tissues) in the mosquito at constant mean temperatures and hence increased viral transmission but this model did not reflect real life experiences and may suggest the interaction of other factors that affect this outcome. These authors also suggested that an increased DTR would likely decrease midgut infection by limiting viral entry or replication in midgut cells, with even short periods at high or low temperatures with a large DTR leading to decreased viral transmission. At a constant mean temperature of 26°C and at diurnal temperature ranges of 0°C, 10°C and 20°C the rate of viral infection dropped from 99% to 88% to 76% respectively. Since infection rates reach a maximum at temperatures past mean temperatures of 26°C the researchers suggest that exposure to lower temperatures will reduce transmission of DENV. Lambrechts et al. (2011) reported that at temperatures less than 18°C, a wider DTR results in increased transmission of dengue and with temperatures higher than 18°C a wider DTR leads to decreased transmission indicating a sensitive balance between temperature and disease transmission.

Butterworth et al. (2017) suggested through modeling that transmission of dengue is possible in Southeastern American states with highest rates occurring between July and September and even possible year-round transmission in the state of Florida. It was noted that the model had several limitations including not accounting for possible explanatory variables such as vegetation, herd immunity, human adaptation, humidity, viral evolution, socioeconomic factors, and insect resistance. Socioeconomic factors can include, income, education, use of air-conditioning, waste disposal and, water storage (Gómez-Dantés & Willoquet, 2009; Murray et al., 2013; Stanaway et al., 2016). Though rainfall has been associated with dengue by some, (Cafferata et al., 2013) researchers suggest that in the

Caribbean dengue cases are not associated with rainfall during the same month of occurrence, which matches with the time lag suggested by other researchers (Fuller, Troyo, & Beier, 2009). Chadee et al. (2004) suggested that dengue transmission peaks during the rainy season in the Caribbean Region. These cases and the associated outbreaks have been found to follow seasonal patterns in the Caribbean normally occurring during the months of heavy rainfall from June to October (Chadee et al., 2007). Heavy rainfall has also been associated with decreased incidence of dengue through the washing away of mosquito habitats and breeding sites and decreasing the vector population (Morin et al., 2013).

Researchers have identified that risk of dengue increased once the maximum rainfall reached>50 mm; and that minimum, maximum, and mean temperature, relative humidity and wind velocity were able to predict severity and timing of dengue outbreaks (Akter et al., 2017; Amarakoon et al., 2008; Ebi & Nealon, 2016). In Barbados researchers have found significant correlation between monthly cases of dengue and temperature lagged by 3 months (Amarakoon et al., 2008). Some authors suggest that the onset of dengue epidemics is more strongly associated with temperature changes than with rainfall, suggesting temperature is a strong risk factor dengue outbreaks (Amarakoon et al., 2008). Another possible factor for the onset of dengue epidemics is immunologically naïve population, which occurs when a new serotype, or a new genotype of a circulating serotype is introduced into the population (Amarakoon et al., 2008; Chen & Vasilakis, 2011; Schiøler & Macpherson, 2009). This phenomenon was demonstrated in 1977 with the introduction of DENV-1 and again in 1981 with the introduction of DENV-4

Challenges to the control of dengue

Currently there are no effective United States Food and Drug Administration (FDA) approved therapeutics for the treatment of dengue and only one recently approved vaccine is available in some countries (Wang & Gubler, 2018). The new, limited availability Dengvaxia vaccine from Sanofi Pasteur which was licensed first licensed in 2015, was reported to have an efficacy of 56-64% which is considered to be a moderate effect and may have benefits for public health with a dengue vaccine (Yousaf et al., 2018). Challenges with unequal immune response leading to different coverage of the individual stereotypes has led concerns of the vaccine potentiating secondary infections (Dans et al., 2018a, 2018b; Hadinegoro et al., 2018; World Health Organization, 2017a). These concerns have led the WHO to release recommendations that the vaccine should only be used in countries with high prevalence and burden of dengue, the target population should have at least a 70% primary dengue infection rate (WHO,2017). The recommended target age groups are between 9-45 years, with higher than 50% prevalence of dengue because there is a higher protentional for the occurrence of severe dengue in persons seronegative at vaccination.

There are two other vaccines that entered phase three trials in 2016; DENVax by Inviragen//Takeda which is a live attenuated vaccine. Another live attenuated vaccine TetraVax, is in development by National Institute of Allergy and Infectious Diseases, National Institute of Health/Butantan. Merck is also developing a vaccine called DEN1-

80E which will contribute to the widening variety of interventions possible to combat dengue (Constenla et al., 2015). Dengvaxia is a mixture of four DENV1-4 genes joined with non-structural genes of yellow fever 17D vaccine (Halstead, 2017). The lack of effective vaccines forces public health initiatives to focus on vector control, surveillance, education and clinical management to control dengue outbreaks and the outcomes associated with them (Laughlin et al., 2012).

Researchers have called for the increased funding for development of diagnostic tests because current technology is expensive, not as versatile as required and in some cases with questionable value. Development of point of service testing would greatly improve the ability of the clinicians to quickly provide the appropriate management of cases (Horstick et al., 2015). Though there are a number of vaccines under development, promising useful tools in dengue control strategies, scientists however have expressed concern about the ability to differentiate vaccinated persons from naturally infected persons once these vaccines are widely implemented (Pang et al., 2017). These lack of effective prevention and treatment options minimize the ability to quickly control dengue outbreaks, leading to increased public health related burdens of disease especially in a country such as Saint Lucia where the majority of health care costs are met by the government (Dieleman et al., 2016).

One of the challenges with the epidemiological surveillance and clinical management of dengue is the availability of bedside, versatile acute-phase diagnostics; as well as distinguishing flavivirus infections (Katzelnick et al., 2017; Laughlin et al., 2012). In 2002 Guzmán & Kourí, (2002) recommended the need for improved diagnostic tests that were accurate and non- expensive, more than 15 years later we see that this has not been achieved to the extent that would affect clinical diagnostics sufficiently (Wang & Gubler, 2018). Without these diagnostics which allow early accurate recognition of dengue, patients go undiagnosed with sometimes dire consequences and public health authorities do not have valid epidemiologic information to guide policy. Currently the best available diagnostics test for dengue is the reverse transcription-PCR (RT-PCR) which is both sensitive and specific and is held as the gold standard test for dengue (Wang & Gubler, 2018). Katzelnick et al. (2017) suggested the need for diagnostic test that rely on biomarkers associated with dengue to allow determination of the severity or possible severity of disease as compared to the current reliance on clinical manifestations to achieve the same outcomes. Mood and Mardani (2017), highlighted the need for developing a better understanding of dengue infections especially the associated clinical manifestation because the disease is one of the most rapidly emerging infectious diseases with significant morbidity and mortality worldwide. Part of the challenge to developing effective diagnostics is that there is no one biomarker that is present throughout the course of dengue as a disease. The laboratory diagnosis of dengue at the present time relies on RT-PCR as mentioned before, as well as virus isolation, IgM and IgG enzyme-linked immunosorbent assays (ELISA), non-structural protein 1 (NS1) antigen detection and neutralization tests, all of which require significant resources in reagents, laboratory facilities and trained personnel (Wang & Gubler, 2018).

The behavior patterns of the *A. aegypti* mosquito, resting and feeding indoors during the daytime make interventions such as insecticide-treated bed nets less effective than with other vectors, whereas insecticide-treated curtains, indoor residual insecticide spraying, and water-jar covers are preferred (Heydari et al., 2017; Quintero et al., 2015).In the urban setting *A. aegypti* is more likely to be active, feeding more than its counterparts in rural areas, where they are less likely to interact with human hosts. The activity of the mosquito and its preference of urban dwellings means that it is more likely to bite the young and elderly that may be at home during the day, though it has been reported that the *A. aegypti* feeds atypically at night in Trinidad and Tobago (Chadee et al., 2004). This difference in risk of being bitten between the extremes of age could possibly explain why the incidence of dengue is significantly high in children (Cafferata et al., 2013; Kumar et al., 2013). Rapidly increasing populations increase the likelihood of mosquito-human interaction and the spread of dengue viruses. At the same time increased population density and unplanned housing development make vector control challenging. A modern approach to vector control should include multiple strategies. This would include using biological controls such as larvivorous fish for example *Poecilia reticulata*, insecticides, access to pipe borne water to reduce inadequate water storage (Horstick, Tozan, et al., 2015; Horstick & Morrison, 2014; McGraw & O'Neill, 2013; Nathan & Knudsen, 1991). Pang et al. (2017), suggested that a useful intervention in dengue prevention is community-based intervention especially through social mobilization. This is likely to have direct effect at the level where the mosquito vector interacts with its target human hosts and may significantly reduce the risk of dengue.

Public health officials have historically relied on measures such as larvicides to control the vectors of dengue including organophosphates such as temefos, and bio-larvicides such as *Bacillus thuringiensis israelensis*. However the widespread use of organophosphate larvicides have been associated with negative environmental effects and the development of resistance which may reflect the continually increasing incidence rate of dengue (Cafferata et al., 2013; Pang et al., 2017). Some organophosphates such as pyriproxyfen have been used with less negative side effects than temefos or methoprene, and longer active than *Bacillus thurengiensis* (Wang et al., 2013). A focus on only education of the public and treatment of cases is likely to be unsuccessful, especially in situation where water shortage or diminished access to water will force inhabitants to store water and often in inadequate vessels (Akanda & Johnson, 2018).

Another biological control for mosquitoes is the use of Wolbachia bacteria to infect mosquitoes lowering the fecundity and lifespan as well as blocking the replication of the virus. Scientists are also able to genetically modify mosquitoes inserting the Release of Insects Carrying a Dominant Lethal (RIDL) which causes larval death (Pang et al., 2017). Though there are a number of vector control options available, the cost is prohibitive to some countries where as others are less than effective, these limitations undoubtedly contribute to the rising expansion of *Aedes* habitats and the incidence of dengue.

Constraints such as distance or lack of transportation are considered by some authors to be related to outcomes of dengue with some authors have indicated that there is a higher association of mortality related to dengue in rural areas (Carabali et al., 2015). Along with the physical barriers to health care access, healthcare coverage through insurance or ability to pay out of pocket could possibly affect dengue infections and associated outcomes. Further to access to healthcare and healthcare coverage, other healthcare related factors related to dengue included opportunity for receiving healthcare, quality of care, and knowledge of the healthcare provider (Carabali et al., 2015). It is also suggested that although gender may not play an overt role in dengue infections and related outcomes, healthcare seeking behavior may differ between sexes and therefore influence the likelihood of infections and outcomes. The challenge of access to healthcare is important to evaluate as such information can be used by policymakers to better allocate resources in an attempt to address these limitations.

Researchers suggest that the epidemiology and clinical presentation of dengue are not well understood or described and results in sometimes conflicting outcomes of the many research studies that are conducted (Katzelnick et al., 2017; Kumar, 2013; Laughlin et al., 2012; Runge-Ranzinger et al., 2016; Wilder-Smith et al., 2017). Though dengue is still characterized by most public health agencies such as the World Health Organization (WHO), the Centers for disease Control and Prevention (CDC) and the Pan American Health Organization (PAHO), as a neglected tropical disease (NTD); experts dispute this because it is a disease that affects high income countries that are not necessarily in the tropics (Horstick et al., 2015). There are significant research gaps in the area of vector control, therapeutics, integrated surveillance, vaccines, clinical management, and bed-side diagnostics (Horstick, Martinez, et al., 2015; Laughlin et al., 2012). A major reason contributing to the research gaps, is that the majority of funding for dengue research is driven by pharmaceutical companies and their main focus has been on developing needed vaccines for the disease. Unfortunately, many of the countries and regions that are affected by dengue do not have the funds to drive their own research and are therefore dependent on larger well-funded organizations. Of the top ten sources of funding for dengue research only Brazil represents an affected country (Horstick et al., 2015). These funding agencies collectively have spent billions of dollars on research without a ground-breaking product being developed which is underscored by the recent concerns about the dengue vaccine Dengvaxia produced by Sanofi Pasteur, (Dans et al., 2018a, 2018b). Researchers have also called for increased investigation of early warning signs of dengue infection which can help improve medical care of dengue cases (Horstick et al., 2015).

Constenla et al., (2015) suggested the need for studies that provide accurate estimates of dengue occurrence as well as the economic burden of the disease that can be used for more effective disease transmission modeling as well as cost-effectiveness of dengue programs including vector control and immunization. The authors also recommended the need to assess the effect of dengue on the healthcare systems, tourism and other industries especially in the context of comorbidities. Clinicians have difficulty in making a diagnosis of dengue based on clinical signs especially depending on the patient's presentation which can be mistaken for measles, influenza, Zika, yellow fever or malaria (Muller et al., 2017). Identifying the segments of the population that bear the burden of dengue, is important to help policy makers allocate limited resources in a manner that provides the best outcomes for management of dengue (Castro et al., 2017).

Castro et al. (2017) suggested that passive surveillance systems are more appropriate for measuring trends in dengue incidence and sentinel surveillance better for seasonal outbreaks and they suggest that the combining of data from varying sources could provide greater insight into the ecology and epidemiology of dengue. The majority of national surveillance systems do rely on passive surveillance which is used to collect data applied to creating health policies. Early warning systems that rely on data from multiple sources across multiple years and geographic borders are usually limited because of the lack of available, uniform data (Fuller, Troyo, & Beier, 2009). These surveillance systems play an important part in collecting data that can be used to understand the entomological relationship between dengue and its vectors especially with regard to epidemics and control measures (Sarti et al., 2016). Indeed early warning systems may be the key to successful dengue control (Ramadona et al., 2016). The ability to correctly identify early warning signs of dengue infections and likelihood of progression to severe dengue will be beneficial in the clinical management of the disease (Singh et al., 2017). During a 1998 epidemic of dengue in the Caribbean island of Trinidad and Tobago, the health services were quickly overwhelmed by the acute nature of the outbreak (Chadee et al., 2004). Poor surveillance is also linked to the lack of cooperation of other industries such as the tourist industry, as well as the difficulty in assessing the true burden of the disease because of the fairly low case fatality rate (Gubler, 2011). Surveillance is often the first line of defense for public health systems in combatting disease, especially infectious diseases such as dengue and without effective surveillance systems that provide early warning as far prior to an epidemic as possible the spread of dengue is likely to continue unchecked.

Though many Caribbean countries have national vector control programs and have collected large amounts of data much of these have not been analyzed or published leading to a dearth of information that can be used to improve public health outcomes associated with vector-borne diseases (Nathan & Knudsen, 1991). It is important to understand the epidemiology of dengue at the country level because considerable differences exist between countries, because of differences in economies, public health infrastructure, and other local variables. Even within countries it would be preferable if data is available and analyzed at smaller community aggregations to determine if there may be significant differences at these levels which will allow the most appropriate use of resources in addressing threats of dengue (Nathan & Knudsen, 1991). It is unknown if patients with serial infections of dengue have increased severity of clinical signs or different outcomes (Schirmer et al., 2017). Rodriguez-Morales et al. (2016) suggest the need for further research into the epidemiology of arboviruses in the Caribbean and Latin America and an assessment of the clinical manifestations of these diseases especially as coinfections as well as with comorbidities such as sickle-cell anemia. It is unclear if infections by one of these arboviruses predisposes the patient to subsequent infections by other arboviruses because coinfections are likely to occur in the region with continued co-circulation of arboviruses (Rodriguez-Morales et al., 2016). The lack of data and uniformity in study methodologies make accurate comparison of dengue epidemiology among countries difficult.

Carabali et al. (2015), underscored that traditionally there has been little research directed at social science approaches to investigating dengue with research focusing on the biological aspect of the disease more often, and though there are guidelines for treatment of dengue still there are and management strategies, there are many avoidable deaths each year. Social science research may provide the additional information that is necessary for public health officials to have a greater success in minimizing or preventing the unwanted outcomes associated with dengue (Carabali et al., 2015). Murray et al. (2013) highlighted the need to improve the estimation of the burden of dengue in an effort to improve control of the disease through better informed policy making and allocation of resources. Dengue is classified as a neglected tropical disease and it is hoped that such a designation will increasingly open avenues for resources that are needed to fund research into necessary interventions such as vaccines and therapeutics as well as more accurate understanding of the epidemiology of the disease.

Though there has been research published on dengue in the Caribbean region the majority of it has been focused in Puerto Rico and Trinidad and Tobago, (Chadee et al., 2007). The data used to evaluate the incidence and prevalence of dengue is often inaccurate because it is subject to both under- and overreporting, the effect of changing case definitions, difference in diagnostic capacity and healthcare availability and access (Morin et al., 2013). The efforts to control dengue outbreaks also affect the incidence and prevalence of the disease and may affect the identification of possible causal factors through confounding. A lot of the research done on dengue has been focused on epidemics and not a lot has focused on investigating the burden of the disease during interepidemic periods (Gubler, 2002). It has been recognized that there are gaps in the knowledge on the relationship between environmental variables and infectious diseases such as dengue in the Caribbean (Depradine & Lovell , 2004). Akter et al., (2017) suggest for example the need for further evaluation of the joint effect of environmental variables and socioecological factors and the role they play in the transmission of dengue.

The foundation of an effective dengue public health surveillance program is an understanding of the epidemiology of the disease towards which this study will contribute.

Key Constructs

The key variables that will be investigated in this study are a combination of demographic, environmental and clinical factors specific to Saint Lucia which will provide the opportunity to investigate the local epidemiology of dengue in Saint Lucia. These three categories of variables have been cited by other authors when describing the epidemiology of dengue in other countries (Cafferata et al., 2013; Guzmán & Kourí, 2002; Murray et al., 2013; Sanyaolu et al., 2017; Torres et al., 2017). Dedicating each category to a separate manuscript allows the multifaceted investigation of the risk factors of dengue in Saint Lucia, which will provide a more comprehensive evaluation of the local dengue ecology. The relationship between demographic variables that will include sex, age, geographic location or place of residence, access to healthcare measured by district, urbanization, employment status, visitor arrival, and occurrence of dengue will be investigated. The environmental variables that will be considered are temperature, wind speed and direction, humidity, and rainfall as recorded at the two weather stations on Saint Lucia, one each placed in the north and south of the island along with entomological indices (Breteau, House and Container Indices). Saint Lucia much like most countries around the world collects syndromic data through surveillance of hospitals and health centers across the island, and uses this data to direct the activities of the public health department and the ministry of health. The variables undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS) fever with hemorrhagic symptoms (Fever with HS) fever and neurological symptoms (fever and NS), and gastroenteritis will be compared with the occurrence of dengue in Saint Lucia to determine which variables are best able to predict the occurrence of the disease. The results of each of these studies will provide analysis of targeted areas of the epidemiology of dengue in Saint Lucia.

Environmental Variables

Much of the research into dengue has focused on the effect of environmental factors such as precipitation and rainfall and this was brought more sharply into focus with the recognition of climate change and the occurrence of more severe weather events such as catastrophic hurricanes and severe droughts. Events such as the El Nino Southern Oscillation (ENSO) have been demonstrated to have significant effect on ocean surface temperatures which in turn affect local weather conditions in the countries in these regions (Ebi & Nealon, 2016; Lowe et al., 2018; Morin et al., 2013). Scientists are worried about global warming and possible increases in global temperature to greater than 1.5^{o}C over preindustrial levels (Mycoo, 2017).Though many researchers agree that environmental variables have an effect on dengue, there is still much debate on exactly how these variables affect the occurrence or severity of dengue outbreaks (Akter et al., 2017; Depradine & Lovell, 2004; Morin et al., 2013; Wegbreit, 1997). Some authors suggest that environmental variables influence vector ecology of the *Aedes* mosquito, increasing mosquito density, shortening the period to infectivity, the fecundity of the mosquito, and the feeding patterns. In a study by Wijayanti et al. (2016) the authors suggested that although it is widely accepted that environmental variables play a role in the occurrence and transmission of dengue, they are likely to vary at the local level and location specific research should be conducted to determine the effect of these variables on dengue, supporting work of previous researchers (Chang et al., 2015). Lowe et al. (2018) were able to create a model using environmental variables to correctly predict dengue outbreaks in Barbados 86% of the time using historical data. In some cases, researchers have not been able to find definitive associations between environmental variables and dengue outcomes. The differences between study outcomes may be a result of factors such as differences in study methodology, local country differences and time periods. These outcomes underscore the difficulty in drawing conclusions on the relationship between the described risk factors and dengue outcomes.

Temperature

Temperature as a variable associated with dengue has been widely studied, assessing its effect on the mosquito vector as well as the dengue virus and susceptible hosts. The *Aedes* mosquito successfully reproduced at temperatures around 30^{o}C and higher however if the temperature exceeds 36^{o}C larval survival rapidly decreases indicating that excessive temperatures does not support increases in vector density (Chadee & Martinez, 2016; Morin et al., 2013). The mosquitoes life cycle was found to be accelerated under experimental conditions at 32^{o}C and 34^{o}C, which would suggest that at these temperatures in nature, the vector will be able to spread disease within a shorter time frame (Chadee & Martinez, 2016; Morin et al., 2013). Chadee and Martinez (2016) found, while investigating the effect of climate change on the *Aedes aegypti* mosquito in Trinidad and Tobago, that water temperatures in water holding structures such as tree holes, plastic cups, eaves gutters and drums all exceed 34^{o}C most almost reaching 50^{o}C. This also suggests that mosquito density will decrease at these temperatures because the larvae do not survive or the mosquito will have to find alternative breeding sites protected from these temperatures. Though *A. aegypti* is a more efficient vector of dengue than *A. albopictus*, the latter is able to survive and reproduce at temperatures as low as 20^{o}C unlike *A. aegypti* which will not reproduce at those temperatures. Increases in ambient temperatures have also been demonstrated to increase viral replication within *Aedes* mosquitoes (Morin et al., 2013). The extrinsic incubation period (EIP, period from being infected to infectiousness) of the mosquito as found to shorten from greater than 12 days at 30^{o}C to approximately seven days at temperature ranges from 32-35^{o}C and no transmission was found to occur at temperatures of 26^{o}C (Watts et al., 1987). Temperature also affects ovarian development, egg laying; egg, larvae, pupa and immature mosquito development. In addition to these effects, the mosquito's blood feeding pattern is also affected by temperature, ceasing below 15^{o}C and also curtailed at temperatures greater than 36^{o}C (Morin et al., 2013). All of these factors serve to improve the *Aedes* vectorial capacity within a defined temperature range an may therefore contribute to the occurrence of cases and epidemics of dengue.

Cheong et al. (2013) found that with an increased minimum temperature from 25.4 °C to 26.5 °C, the risk of the occurrence of dengue increased, underscoring the importance of the relatively cooler temperatures as compared to daily maximum temperatures which are likely to result in water temperatures at breeding sites being high enough to prohibit larval survival. Many researchers have also investigated the effect of lagged temperature values on dengue outcomes suggesting that temperature has delayed effect as do the other environmental variables on the transmission of dengue (Amarakoon et al., 2008; Depradine & Lovell , 2004; Lambrechts et al., 2011; Ramadona et al., 2016; Wegbreit, 1997). These lag times vary from between 3-7 months on average (Amarakoon et al., 2008; Cheong et al., 2013; Depradine & Lovell , 2004; Wegbreit, 1997). Tosepu, Tantrakarnapa, and Worakhunpiset (2018), report that there is a relationship with temperature and dengue hemorrhagic fever (DHF), with the average monthly temperature being associated with DHF by a lag of 2, 3 and 4 months, maximum temperature by a lag of 3 and 4 months and minimum temperature a lag of 0,1, 2, and 3 months. Lowe et al. (2018) reported that dengue outbreaks were found to increase with increasing minimum temperature up to 25 °C peaking at a lag of 2-3 months after. The lags noticed between changes in temperature and the occurrence of dengue are probably accounted for by the time it takes for first by the mosquito breeding cycle, then the adult mosquito biting a viremic person, then extrinsic incubation period, biting a susceptible person and then the incubation period in that host. It is unlikely that any of the factors that affect the vector will lead to immediate increases in dengue occurrence requiring time for the vector or virus to change reproduction rates.

Scientists have used many different variations of the temperature variable to investigate its relationship with dengue outcomes including mean daily temperature, minimum daily temperature, maximum daily temperature, diurnal temperature range, moving average temperature (Amarakoon et al., 2008; Morin et al., 2013). The measure to be used in this study will depend on the data that is available on this environmental variable. Temperature has been most often studies using secondary historical data typically meteorological data and experimental studies where animal models were used or mosquito colonies (Depradine & Lovell, 2004; Ebi & Nealon, 2016; Morin et al., 2013; Ramadona et al., 2016; Watts et al., 1987; Wegbreit, 1997). The differences in outcomes observed by researchers in investigating the effect of temperature on dengue may be attributable to local geographical differences, methodological differences as well as temporal differences.

Wind

Wind is an environmental variable that has not undergone the same level of scrutiny as temperature but Depradine and Lovell (2004) found that there a negative correlation with windspeed and the occurrence of dengue with a lag of about 3 week and Cheong et al. (2013) also found that windspeed had an inverse relationship with dengue occurrence. These researchers have suggested that strong winds minimize the *Aedes* vector's ability to seek a suitable host, which will minimize the risk of disease transmission but also reduces the likelihood of having a blood meal that stimulates the ovary and egg laying will be decreased leading to a decrease in mosquito population and also decrease risk of transmission. Windspeed is likely to have little effect on mosquitoes already living indoors in close proximity to their hosts and may even have a positive effect if the wind is excessive as in storm strength restricting inhabitant's ability to leave the house and allowing greater possibility of interaction with mosquitoes within the home. Filho (2017) investigated the relationship between both wind speed and wind direction and the occurrence of dengue among other environmental variables but was unable to find a significant association though that may be a result of the complex nature of dengue occurrence which involves human, vector and environmental factors.

Rainfall

Rainfall similar to temperature has been explored extensively in relation to its association with dengue outcomes and its association has repeatedly confirmed by numerous studies though with different strengths of association from weak to strong (Cheong et al., 2013; Depradine & Lovell , 2004; Ebi & Nealon, 2016; Ramadona et al., 2016; Tosepu et al., 2018). Increased rainfall has been suggested to provide a suitable environment where mosquitoes are able to breed and stimulates egg hatching, this leads to an increase in vector density and risk of dengue transmission (Guo et al., 2017; Wijayanti et al., 2016). Wegbreit (1997) found a negative correlation of precipitation and incidence of dengue, suggesting that precipitation decreased incidence 6 months later. Limper et al. (2016) found that rainfall was associated with an immediate increase in the incidence of dengue incidence after a 10-mm increase, reaching a maximum after a lag of 1.5 month. In a study exploring predictive models of dengue in Barbados excess rainfall exhibited a lag of 1-2 months in dengue incidence whereas droughts were positively associated with the risk of dengue with a lag of five months (Lowe et al., 2018). In a study investigating the influence of climatic factors on dengue fever in Indonesia, Tosepu et al. (2018) reported that dengue hemorrhagic fever was positively correlated with above average rainfall in the same month, exhibiting no time lag. Overall it has been suggested that heavy rainfall can wash away mosquito breeding sites which will lead to a decrease in dengue transmission, in other experiences rainfall collected in artificial containers can provide ideal breeding sites and therefore increase vector density and transmission of disease (Wegbreit, 1997). An explanation for the positive correlation recognized between heavy rainfall and dengue occurrence by Tosepu, Tantrakarnapa, and Worakhunpiset (2018) may be persons remained indoors for longer periods therefore increasing the risk of bites form infected mosquitoes. Drought situations may force individuals to store water if there is not a reliable supply, if this water storage is not done in safe and mosquito proof systems it can lead to an increase in suitable mosquito breeding sites, increases in mosquito density and eventually increased dengue transmission (Morin et al., 2013). In the Caribbean region where there are two distinct rainfall seasons, this factor not surprisingly plays an important role in the life cycle of the dengue vector population and therefore dengue itself.

Humidity

Temperature, rainfall and relative humidity have been identified by some researchers as the main environmental variables that are risk factors of dengue and contribute to the seasonal occurrence of dengue and the *Aedes* mosquito (Ramachandran et al., 2016). Relative humidity a combination of rainfall and temperature also has a significant effect on the lifespan of mosquitoes (Ramachandran et al., 2016). Relative humidity is defined as the ratio of the amount of moisture in the air or the water vapor pressure, compared with the maximum amount of moisture air could hold at a defined temperature or the saturated vapor pressure (Zhang et al., 2014). Increases in relative humidity have been associated with increased in mosquito fecundity and egg hatching rate especially in *Aedes aegypti* (Costa et al., 2010). Increases in fecundity and hatching rate can lead to increased vector density, increasing the risk of dengue transmission. Dengue outbreaks have been positively associated with relative humidity (Limper et al., 2016; Sumi et al., 2017). Humidity has been associated with a lag increased transmission of dengue at up to 3 months (Chen et al., 2010) though Tosepu et al. (2018) found humidity to be positively related to DHF at a time lag of zero but negatively correlated at time lag five.

Entomological indices

Dengue is a vector-borne disease and the ecology of the main host *Aedes* mosquito plays a significant role in the transmission and severity of dengue infections and though attempts have been made to eradicate the vector from the Caribbean region in the past, the discontinuation of these programs because of lack of resources or political will has seen the mosquito population survive and thrive in most of the Caribbean countries including Saint Lucia (Brathwaite Dick et al., 2012; Downs & Spence, 1964; Morrison et al., 2008). The presence of these mosquito vectors increases the likelihood of dengue transmission to a susceptible population and understanding the local effects these vectors have on dengue transmission in the Saint Lucian context is important for the successful control of the disease. Vector surveillance is recommended by the WHO and is conducted in most dengue endemic countries, however most indices focus on the larval and pupal stages which are not considered to be reliable indicates of future adult populations by some researchers (Bowman et al., 2014). Researchers use many entomological tools or indices to describe the mosquito population within a geographical area including house index, contain index and the Breteau index which are indices that measure larval immature stages of the mosquito (Anders & Hay, 2012; Wijayanti, Sunaryo, et al., 2016). The House Index represents the proportion of houses having larvae or pupae, the Container Index indicates the proportion of containers with water that are infested with larvae or pupae, and the Breteau Index which evaluates the quantity containers with larvae or pupae per 100 houses surveyed though sampling protocols may vary (Bowman et al., 2014; Chadee, 2009; Wijayanti et al., 2016). A review of the literature by Bowman et al. (2014) suggested that there is a positive association between entomological indices used for vector surveillance and the occurrence of dengue whereas other studies in the review failed to identify this relationship which may have resulted from weaknesses in study design. In a study comparing the efficacy of traditional larval indices, and other possible indices of mosquito populations such as pupae indices, collected mosquitoes for species identification and vector population density, Wijayanti et al. (2016) found that the traditional indices did not successfully predict dengue transmission even though the Breteau and Housing Indices were higher during the rainy season. The pupae index identifies the number of pupae per container and also quantifies the variety of containers generating the highest number of adult mosquitoes (Chadee, 2009; Wijayanti et al., 2016). The short coming of these surveillance techniques is that they do not determine which species of mosquito is present, nor do they reliably indicate how many larvae will survive to become adult mosquitoes capable of transmitting dengue viruses (Bowman et al., 2014). Some researchers recommend that the use of such indicators should be validated at the local level in endemic countries that still rely on traditional larval indices to quantify mosquito populations and use this data to predict dengue transmission (Bowman et al., 2014; Wijayanti et al., 2016).

Identifying and quantifying adult mosquitoes are seen as the most reliable methods of estimating true mosquito abundance and possible risk associated with dengue transmission, because the adult mosquito is responsible for the actual transmission of dengue (Chadee, 2009; Wijayanti et al., 2016). Identification of the mosquitoes prevalent and species composition help to determine which mosquito is in abundance and if it is the vector most closely linked with the spread of a disease such as dengue. The studies used to investigate the relationship of entomological indices and dengue include cross-sectional and prospective studies as well as literature reviews (Bowman et al., 2014).

Demographic Variables

Movement of people

Many authors have suggested that the most important factor in the introduction of dengue to a population is the movement of viremic persons rather than infected mosquitoes which have a limited flight range of up to 400 m (Casas et al., 2017; Gubler, 2011). Visitors, travelling for business, leisure or otherwise contribute to the spread of dengue, not only in acquiring the virus but also by transmitting it to susceptible populations (Horstick, Tozan, et al., 2015; Neiderud, 2015; Wilder-Smith, 2012). The Caribbean and Saint Lucia are vulnerable to introduction of dengue viruses that may be of a different serotype or genotype currently circulating because of heavy reliance on tourism. Most countries around the world track visitor arrivals either through air or seaport in the case of an island or land border checkpoints in other cases. These statistics can be used to investigate dengue outbreaks and the likelihood of visitor introduced cases of disease. Peaks in visitor arrival may also coincide with peaks in mosquito populations again increasing the likelihood of viable mosquitoes feeding on viremic visitors which may lead to the occurrence of an outbreak of disease.

Age

Researchers have identified that age especially through immunocompetence is a risk factor for dengue infection and the outcomes of infection (Carabali et al., 2015). Guo et al. (2017) determined that between 1990 and 2015 the mean age of persons infected with dengue was 30.1 years with the mean becoming older after 2010, from an average of 27.2 years to 34 years after 2010. There have been many research studies focused on the occurrence of dengue and the age groups affected and the results have differed both according to time and geographical location. Kumar et al. (2013) reported that the incidence of dengue in children Barbados between 2000 and 2009 was 1.14/1,000 children years compared to that of Trinidad and Tobago of 2.46/1000 population or 7.7/1,000 population because there was no data available on another population of children in the region. When the age groups were further stratified Kumar et al. (2013) found that the incidence of dengue was high in the 12-16 year old age group compared to the under five year age group. A systematic review of dengue in the dengue epidemiology by Cafferata et al. (2013) found that the 15-59 year age group was most often affected by dengue using data from Bolivia, Brazil, Colombia, and

Mexico. A review of the literature on the epidemiological characteristics of dengue in the Caribbean showed that the incidence amongst age groups differed by country with some countries recording the highest incidence in children in the 5-9 year old age group, others the age of fifteen years, others in the 15-44 age group, and yet other countries underscoring the inconsistency in the epidemiological data on dengue and age in the region (Torres et al., 2017). In Southeast Asia where the disease has been endemic for many more years the epidemiology shows that the prevalence of dengue is higher in the adult age groups (Torres et al., 2017). Singh et al. (2017) in a retrospective study of an epidemic in Lucknow, India identified the most affected group as those 18-35 years. In systematic review and meta-analysis by Guo et al. (2017) it was reported that mean age of patients infected with dengue was 30.1 years. Other authors suggest that both children and the elderly are highest at risk for dengue (Mood & Mardani, 2017). In a review of the literature by Fritzell et al. (2018), the authors report that the analysis of the data available suggests an increase in the seroprevalence of dengue in older persons. Sanyaolu et al. (2017) reported that there is a higher incidence of dengue among children particularly the 4-9 month age group and the 5-9 year age group. Yet other authors have suggested that the effects of dengue transition from adults to children after about 15 years though the evidence of outbreaks have proven it is difficult to predict the population that will be affected (Vicente et al., 2017). Knowing the specific age groups most greatly affected by dengue in Saint Lucia will allow the Public Health Department and the Ministry of Health to design target intervention plans for these populations.

Sex

In a systematic literature review to investigate the global epidemiology of dengue between 1990 and 2015, Guo et al. (2017) determined that 54.5% of the patients infected with dengue during the period of the study were male. Singh et al. (2017), also reported that in a study of a dengue epidemic at a tertiary care hospital in Lucknow, India the majority of the infected patients were male. It was reported by Casas et al. (2017) that males were more likely to go further distances to seek healthcare during a dengue outbreak, and this may account for differences in documented cases of disease between males and females this was also supported by a meta-analysis conducted by Guo et al. (2017) which found that between1990 and 2015, 54.% of the global cases of dengue were male. There is some inconsistency in the research on sex and dengue occurrence with other studies evaluating the phenomenon in the Caribbean and Latin America found a higher prevalence in females (Torres et al., 2017). Stanaway et al. (2016) also report that there is a higher prevalence of dengue among the female population when reviewing the Global Burden of Disease Study 2013. Fritzell et al. (2018), suggest that there is a sex related difference in the occurrence of dengue and that further research is need to investigate this epidemiological phenomenon. The differences in reported outcomes of the relationship between sex and occurrence of dengue indicate the need to determine the local relationship in Saint Lucia.

Location or place of residence

The physical location where the human host population for the dengue virus lives has been found to affect the risk of transmission and the occurrence of the disease. The effect of location may be related to such variables as the movement of people in and out of the area, land use of the area, the presence of vegetation, inadequate water sources and the number of viable mosquito breeding sites in the area which may contribute to specific areas being at risk of recurrent outbreaks (Akter et al., 2017; Burattini et al., 2016; Ramadona et al., 2016). The higher likelihood for specific regions to experience dengue outbreaks or even recurring dengue outbreaks can also be related to socioeconomic factors such as level of income, education level, and public health infrastructure (Delmelle et al., 2016; Mulligan et al., 2015). The outcomes of the study may suggest further investigation to identify what within specific districts is associated with dengue. Epidemiologist can use the knowledge of the association of specific locations or regions and the incidence of dengue to target resources that allow the more efficient control of dengue through interventions that are best suited to the characteristics identified (Sommerfeld & Kroeger, 2015). Saint Lucia is divided into 11 districts, Gros Islet, Castries, Anse la Raye, Canaries, Soufriere, Choiseul, Laborie, Vieux Fort, Micoud, Dennery, and Babonneau, comparison of the occurrence of dengue across these districts, will help the Public Health Department target dengue programs and limited resources where it is most needed and most likely to have effect (Cherry et al., 2014).

Urbanization

Urbanization refers to the shift of a population from a rural area to a built-up environment and the increase in the number of cities and populations they contain. This often leads to large numbers of people living in close proximity with each other and results in social, psychological and economic changes (Neiderud, 2015; Srivastava, 2009). The migration of persons to these urban centers many times in search of employment, may see the unplanned development of areas which may lead to inadequate water availability or waste management. It is not uncommon to find in urban areas two vastly different conditions of living because slums are often associated with urban centers. These slum areas reflect unplanned housing with little access to safe water, sanitation and inadequate housing conditions that are often not vector-proof (Neiderud, 2015). The lack of water availability may cause inhabitants of these urban and peri-urban centers to implement water storage which inadvertently may create suitable breeding habitats for the *Aedes* mosquito, the vector of dengue and subsequently increase the risk of transmission of dengue and as a result urbanization has been recognized as important contributor to the increased incidence of dengue (Neiderud, 2015).

In the urban setting there is likely to be an increased number of artificial water containers that are capable of trapping water including things such as steel drums for water collection, uncovered garbage cans, old tires, discarded bottles, cups or other receptacles and other refuse which the mosquito can use for oviposition. The increased population density and vector density increases the likelihood that mosquitoes come into contact with viremic persons and then go on to bite susceptible persons creating a sustainable transmission pathway (Bowman et al., 2014). Researchers, in exploring the relationship between geographic distribution, climate change, and dengue reported that urbanization was an important risk factor for the occurrence of dengue (Morin et al., 2013; Neiderud, 2015; Weaver, 2013; Xu et al., 2016). Urbanization has been associated with the occurrence of dengue but authors suggest that the association with mortality has not been clearly defined (Carabali et al., 2015). There are a number of metrics to evaluate urbanization and often differ by country and researcher, in the U.S metropolitan areas are considered urban even if there is greenery present, in other countries it is based on living in the capital, aggregate population or population density (Chauvin et al., 2017; Neiderud, 2015). Dengue is considered to be mainly an urban health problem and as the population within urban centers expand so is the likelihood that the incidence of dengue will also increase. Saint Lucia follows this trend with most of the locally available jobs causing migration from outer districts to the Castries and Gros Islet.

Healthcare access

The epidemiology of dengue has indicated that of the almost 400 million cases that occur annually, the majority are asymptomatic, and of the remaining 96 million that develop clinical signs not all seek healthcare nor have ready access to such care. Díaz-Quijano & Waldman (2012) reported a greater association of dengue mortality rather than incidence of dengue with increased population density, and suggested that this was a result of lack of access to appropriate healthcare in some urban settings with large populations or because of underreporting of the disease. In a review by Carabali et al. (2015) it was reported that difficulty in transportation to a health center and geographical limitations such as distance to health services this was also supported in a qualitative study by (Krisnian et al., 2017). Access to healthcare is measured by a number of variables such as travel time or distance to the nearest health facility, population-to-provider ratio, distance decay algorithms and catchment sizes (Casas et al., 2017).

Employment

Employment as a socioeconomic variable has been associated with the occurrence of dengue in a number of ways, the outcomes of which are also affected by the reason for unemployment and the duration of unemployment (Al-Dubai et al., 2013; Wijayanti, et al., 2016). Importantly unemployed persons may spend more time at home and indoors, which means that there is and increased likelihood of bites from infected mosquitoes (Zellweger et al., 2017). Another important factor is the relationship between unemployment and poverty, which further affects where someone may be able live. Unemployed persons may be forced to live in areas of overcrowding, unplanned urbanization, inadequate water sources, improper water storage, and improper waste disposal (Hagenlocher et al., 2013). These factors provide suitable breeding environments for the *Aedes* vector, leading to increases in the vector population and increased mosquito-human contact. Unemployment may limit the ability of persons to afford vector preventatives such as aerosol sprays and air-conditioning (Dirrigl & Vitek, 2013; Tither, 2014). In countries such as Saint Lucia where a large percentage of the population is uninsured, unemployment may also reduce the likelihood that someone may seek healthcare if infected with dengue (Wijayanti, et al., 2016).

Education

Level of education as a socioeconomic variable has also been related to the occurrence of dengue (Al-Dubai et al., 2013; Wong et al., 2016). Level of education has been related to socioeconomic status, income, and employment, all of which could affect a person’s living conditions and exposure to dengue-infected mosquitoes (Corak, 2013). Level of education has also been linked to health seeking behaviors and the understanding of the epidemiology and burden of dengue within the population (Elsinga et al., 2018). The attitudes and beliefs of a population that may lead to the engagement in negative behaviors related to dengue such as improper water storage, the keeping of artificial containers around the household that serve as breeding sites, and improper waste management have been associated with level of education (Al-Dubai et al., 2013; Dhimal et al., 2014).

Clinical variables

In many cases the presumptive diagnosis of dengue is made based upon the history and clinical signs of the patient because bedside tests may not always be available or accurate but allows when correct allows the early initiation of treatment protocols and minimization of unwanted outcomes (Katzelnick et al., 2017; Phakhounthong et al., 2018). It is not unusual for atypical manifestations of dengue to be overlooked which minimizes the early response to the disease which may escalate into an epidemic and a larger public health challenge (Nimmagadda,et al., 2014). The common clinical signs attributed to dengue encompass a wide range of variables including fever, headache, retro-orbital pain, nausea, vomiting, weakness, stomach pain, decreased appetite malaise, myalgia, arthralgia, rash, and respiratory distress (Sanyaolu et al., 2017; Singh et al., 2018). The hemorrhagic form of dengue, is characterized by petechial hemorrhages, ecchymosis, epistaxis , gastrointestinal bleeding, vaginal bleeding , bleeding gums, thrombocytopenia , and plasma leakage possibly leading to shock (McFee, 2018). It is not uncommon for persons to be infected with dengue to be also exposed to other co-morbidities both infectious and non-infectious such as leptospirosis, chikungunya, Zika, diabetes, hypertension, asthma, and cardiac disease (Badawi et al., 2018; Carrillo-Hernández et al., 2018; Guo et al., 2017; Pang et al., 2017). Most hospitals and public health surveillance systems have transitioned to syndromic surveillance using algorithms that collect data based on the clinical signs with which the patients present. These by themselves are non-diagnostic but allow early recognition of diseases by clinicians and public health agencies to track diseases that affect the population (Henning, 2004; Morse, 2012). Some of the variables commonly collected at hospitals include undifferentiated fever, upper and lower respiratory tract infections with fever, gastroenteritis with or without vomiting, diarrhea abdominal pain, and rash with fever (Fleischauer et al., 2004; Kumar et al., 2013). Undifferentiated fevers have been associated with diagnosing dengue in the mild form which could result from the infection by any of the four serotypes (Guzman et al., 2013). Analyzing the relationship between the variables collected regularly by health agencies and dengue will possibly provide an algorithm that will assist clinicians in the earlier recognition of disease and also provide epidemiological data that can be used to track disease. These variables are studied using a wide variety of study methods including literature reviews, retrospective studies, prospective studies, and cross-sectional studies (Katzelnick et al., 2017; Mehta et al., 2018; Mood & Mardani, 2017). Identifying which of the common syndromic surveillance disease symptoms are most closely related to dengue in Saint Lucia, will allow for the early recognition and prompt treatment of dengue cases, identification of epidemics, and reduction of the burden of disease related to dengue outbreaks.

Conceptual framework and theories.

Epidemiologists have recognized that the occurrence of diseases in a population is a result of multiple factors such as host, agent and environmental variables as represented by the epidemiologic triad. (Paillard, 2016). Moving beyond the simple epidemiologic triad, researchers have recognized that the occurrence of disease is based on a complex interaction of variables with influences and outcomes constantly changing (Zuckerman et al., 2014). A more modern theory is the ecological theory of disease which incorporates genetic, molecular, biological, social, political, and environmental variables in an attempt to accurately represent real-life complex relationships between variables associated with disease (Jousimo et al., 2014). This theory is applicable to dengue because it takes into consideration how multiple factors such as the *Aedes* mosquito, demographic, clinical, and environmental variables affect the occurrence and outcome of dengue as a disease. Ecological theory focuses on the evolution of the causative agent of the disease of interest as well as changes in external variables that affect the outcomes of infection (Jousimo et al., 2014; Smith et al., 2005). The theory focuses on the affect changes in external factors such as environmental conditions, population demographics such as age and sex, and biological factors as demonstrated through clinical signs will affect or interact with the causative agent of a disease changing the occurrence of the disease. Ecological theory has been used to investigate the effect of host characteristics on the outcome of disease, the use of ecological factors to predict the outcomes of disease as well as the effect of biological factors on disease. The strength of this theory is that is recognizes the complexity of relationships between variables and how a change in any one of these relationships can cause a shift in observed outcomes (Smith et al., 2005).

Ecological theory provides the foundation for the investigation of the demographic, environmental, and clinical variables as risk factors of dengue in Saint Lucia. The differences in these variables in Saint Lucia as compared to other countries may lead to the unique epidemiology of the disease in this location which supports the need for this study because there is limited published data on these phenomena. The theory supports the inclusion of multiple factors in statistical models such as the logistic regression models used in this study to predict the occurrence of dengue. The inability to successfully control and prevent dengue may be as a result of these evolutionary changes to any of the independent factors that contribute to the spread and occurrence of the disease.

Specific Knowledge Gap

Though there has been extensive research into dengue and its ecology, the discrepancies in data collection methods and the study methodologies used to investigate this disease has led to widely varying information on the disease. It has been suggested that localized investigations should be conducted to provide specific information on the disease for the targeted geographic location and its associated population (Wijayanti, 2016). There is little data published on the risk factors of dengue in Saint Lucia and what little that has been published has been as part of larger studies which do not guarantee the results are specific to Saint Lucia (Torres et al., 2017). I sought to provide the analysis of possible risk factors for dengue in Saint Lucia, which can be used by the local Ministry of Health to create a model that can anticipate dengue outbreaks, and provide targeted interventions to prevent and minimize the effect of dengue on the island.

Overview of the Manuscripts

These three studies are needed to identify what factors are most important to understanding the epidemiology of dengue in Saint Lucia and what variables are best able to predict dengue outbreaks. Identifying the risk factors of dengue in Saint Lucia would allow health authorities to focus limited resources and achieve the best public health outcomes possible. Using three studies allowed the evaluation of a large number of variables. A regression model with too many variables is open to error or identifying erroneous significant associations, but by first using separate models the factors most strongly associated with dengue outcomes can then be included in a separate model that may more accurately predict possible dengue epidemics in future studies. The three manuscripts evaluated groups of similar variables in an attempt to identify the variables that are the strongest risk factors of dengue in Saint Lucia. These studies were conducted in parallel and used to provide a comprehensive description of the relationship between the occurrence of dengue and possible risk factors in Saint Lucia.

Meteorological variables have been associated with dengue and their relationship has been investigated by numerous authors particularly temperature and rainfall (Díaz-Quijano & Waldman, 2012; Estallo et al., 2015; Filho, 2017; Hosein et al., 2013; Khan et al., 2018; Matysiak & Roess, 2017; Ramadona et al., 2016; Tosepu et al., 2018). The meteorological services in Saint Lucia also collect, relative humidity, wind speed, and wind direction at two weather stations on the island as part of their regular monitoring of local weather conditions. These were included in the model investigating the relationship between meteorological variables and the occurrence of dengue on the island.

Demographic and socioeconomic variables play integral roles in the epidemiology of any disease, infectious or non-communicable, and understanding their relationship with dengue in Saint Lucia is critical to the successful prevention and management of the disease. Key variables such as sex, age, and place of residence are important to public health officials trying to target the most vulnerable sections of the population. The literature is not unanimous in identifying the relationship between these variables and the occurrence of dengue, and it is suggested that local investigations are conducted to describe this interaction within specific populations (Amaya-Larios et al., 2014; Castro et al., 2017; Laserna et al., 2018). In addition to age, sex and place of residence, the model also included employment, urbanization, access to hospital, and visitor arrivals which have been shown to be associated with the risk of dengue (Akter et al., 2017; Huang et al., 2013; Oduber et al., 2014; Shepard et al., 2014; Yung et al., 2016).

The early identification of dengue cases is critical to public health efforts to control the spread of the disease. The limited availability of accurate and affordable bedside tests limits the ability of public health surveillance programs at healthcare institutions. Using the clinical observations that form part of the syndromic surveillance programs of the Ministry of Health can provide additional tools to assist in early detection of dengue cases if significant associations are found to exist between these variables. The main variables included in this syndromic surveillance are undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis. Undifferentiated fever has been found to be associated with dengue in other studies and it is important to identify if this variable has the same relationship with dengue in Saint Lucia (Mueller et al., 2014).

The Walden IRB number for this study is 03-19-19-0675142.

Manuscript 1

Specific problem. Manuscript one was used to explore the problem of which demographic variables are most important in understanding the epidemiology of dengue in Saint Lucia.

Research question. What is the relationship between sex, age, geographic location or place of residence, employment status, urbanization, hospital access, visitor arrivals, and occurrence of dengue in Saint Lucia?

Nature of study and design. This study followed a quantitative, non-experimental, retrospective design in exploring the relationship between demographic variables and the occurrence of dengue in Saint Lucia (Anglemyer et al., 2014). I used data previously collected through regular surveillance activities in Saint Lucia to answer the research question. The sample consisted of cases from the Saint Lucian population that were identified with having clinical signs consistent with dengue through syndromic surveillance. The use of secondary data reduced the time necessary to conduct this study, while providing the researcher the ability to minimize contact with the subjects of the study. This information was analyzed using logistic regression to evaluate the relationship between the possible risk factors and their relationship with the dependent variables. The hypotheses for the research question posed previously were

H_0: There is no significant relationship between sex, age, geographic location or place of residence, employment status, urbanization, hospital access, visitor arrivals, and occurrence of dengue in Saint Lucia.

$H_{1:}$ There is a significant relationship between sex, age, geographic location or place of residence, employment status, urbanization, hospital access, visitor arrivals, and occurrence of dengue in Saint Lucia.

Sources of data. The data that I used to answer the research question included secondary data from national health syndromic surveillance database that is managed by the Ministry of Health which is information at the individual level from infectious disease surveillance activities during the period 2008-2017. This data was a combination of hospital and other health-center information that the government collects on infectious diseases. I also used demographic and socioeconomic data from the government Central Statistics Office of Saint Lucia, and data on visitor arrivals from the Saint Lucia Tourist Authority. There were no available code books to these databases. Nominal data were coded as low, medium, and high based on a tertile distribution of the data across its range.

Variables: Sex. This variable represented the sex that is ascribed to the subjects involved in the study and is measured on a categorical scale having two levels male and female with males coded as 1 and female 0.

Age. This variable represented the age of the Saint Lucia population during the study time period. Age was measured level with the values Age was measured at the individual level according to Medical Subject Headings (MeSH), Infant (age 0-

23months), Pre-school child (age 2-5 years), Child (age 6-12 years), Adolescent (age 13-18 years), Adult (age 19-44 years), Middle Aged (age 45-64), Aged (age 65-79 years), and Aged 80 and over (Kastner et al., 2006).

Geographic location or place of residence. This variable was measured as a categorical variable on a nominal level. The island of Saint Lucia is broken up into 11 districts Gros Islet, Castries, Anse-la- Raye, Canaries, Soufriere, Choiseul, Laborie, Vieux Fort, Micoud, Dennery, and Babonneau (Cherry et al., 2014) but the national census combines the districts of Babonneau with Castries and this was reflected in the present study for a total of 10 districts.

Employment status. Unemployed, this was a population level variable at the district level and was measured as a categorical variable at the annual district level. This nominal variable had 3 levels low (≤2,500 persons), medium(>2,500-5,000 persons), and high(>5,000 persons), Employed, also a population variable on a nominal scale measured at the annual district level with 3 levels, low (0-11,000 persons), medium (>11,000-22,000 persons), and high (>22,000 persons).

Urbanization: This variable was based on the population density within the geographic districts of Saint Lucia and was measured as a ratio variable as the number of persons per square mile. This variable was calculated for each district using their population numbers per year. The population density variable was divided into three categories low (≤1,000 persons/sq. mile), medium (>1,000-1,500 persons/sq. mile), and high (>1,500 persons/sq. mile).

Hospital access. This variable was based on the number of health facilities in comparison to population within the eleven districts identified in Saint Lucia and were measured as a ratio variable. This variable was calculated based on the population of each district per medical facility for each year of the study. The hospital access variable was divided into three categories low (≤3,000 persons/health facility), medium (>3,000-4,500 persons/health facility), and high (>4,500 persons/health facility).

Visitor arrivals. This variable represented the number of visitors entering Saint Lucia either through cruise ship or airlift. This variable was measured as a categorical variable on the nominal level based on groupings of arrivals per month for each year of the study period, for cruise visitors low (≤30,000 persons/month), medium (>30,000 – 60,000persons/month), and high (>60,000persons/month); and for stayover visitors low (≤25,000 persons/month), medium (>25,000-30000 persons/month), and high (>30,000 persons/month).

Education. Education represented the highest level of education attained. This variable was a population level statistic and was measured as a categorical variable on a nominal level at the national level per year of the study period, with the categories of no education, less than secondary, secondary, and tertiary education. The category of no education was measured at low (≤6,000 persons), medium (>6,000 ≤7,000 persons) and high (>7,000 persons); less than secondary education low (≤61,500 persons), medium(>61,500-65,000 persons), and high (>65,000 persons); secondary low (≤58,000 persons), medium (>58,000-61,000 persons), and high (>61,000 persons) and tertiary low (≤12,500 persons), medium (>12,500-14,000 persons), and high (>14,000 persons).

Statistical analysis: The data used in this study were analyzed through bivariate analysis using the chi-square test followed by logistic regression by the IBM SPSS Statistics 25 software. The analyses conducted consisted of descriptive analysis of the data, chi square tests of independence between the categorical variables in this study, followed by logistic regression models because the outcome variable the occurrence of dengue was a nominal variable denoting the presence or absence of the disease. Chi-square analysis was used to investigate the strength of association between each risk factor and the dengue outcome variable on an individual level and then the relationship between the independent variables and the outcome variable were explored using logistic regression. This combination of statistical tests has been employed by prior researchers to provide a more comprehensive analysis of the relationship between variables (Akboğa Kale & Baradan, 2020; Kumar et al., 2014; Shrestha, 2019). Logistic regression was the most appropriate statistical model to evaluate the relationship of independent variables and categorical outcome variables (Liu et al., 2014). The dependent or outcome variable for this study occurrence of dengue, was a categorical variable measured on a nominal scale, dengue positive or dengue negative. The independent predictor variables in this model were gender, age and place of residence, employment status, urbanization, hospital access, and visitor arrivals, which were all be measured as categorical variables on a nominal scale.

Power Analysis: Sample size estimation for this study was determined by power analysis using G*Power 3 (software, http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3/). In this study, assuming two-tailed, z-test, an alpha level of .05, a power of 0.80 and 0.90, for a logistic regression model, the required sample size using G*Power 3 is 355 (80% power) and 468 (90% power) with a medium effect size of 0.3. The number of persons examined for possible dengue infection represents the sample for this study. The power analysis with effect size of 0.3 was chosen because earlier studies investigating the relationship between gender and the occurrence of dengue have reported odds ratios of 2.042 (1.143-3.648) to 2.79 (1.61-4.83), however because each location may have different outcomes I have been conservative using a medium effect size (Aung et al., 2013; Nguyen et al., 2018).

Manuscript 2

Specific problem. Saint Lucia like other countries collects regular weather information and entomological data which has been proven to be associated with the incidence of dengue and useful in predicting outbreaks of the disease. This information, which would be helpful to public health agencies in predicting and averting dengue outbreaks, has not been published for Saint Lucia to the author's knowledge.

Research question. What is the effect of temperature, wind speed, humidity, and rainfall as measured at weather stations on the island and vector prevalence at the district level, on the occurrence of dengue cases in Saint Lucia?

Nature of study and design. This study followed a quantitative, non-experimental, retrospective design in exploring the relationship between the variables temperature, wind speed, humidity, and rainfall as measured at weather stations on the island and vector prevalence at the district level, and occurrence of dengue (Anglemyer et al., 2014). I used data previously collected through regular surveillance activities in Saint

Lucia to answer the research question. I combined multiple data sets accessed from government agencies to address this research question. The use of secondary data reduced the time necessary to conduct this study, while providing the researcher the ability to minimize contact with the subjects of the study. This information was analysed using logistic regression to evaluate the relationship between the possible risk factors and their relationship with the dependent variables. The hypotheses for the research question posed previously were

H_0: There is no effect of temperature, wind speed, humidity, and rainfall as measured at weather stations on the island and vector prevalence at the district level, on the occurrence of dengue cases in Saint Lucia.

$H_{1:}$ There is an effect of temperature, wind speed, humidity, and rainfall as measured at weather stations on the island and vector prevalence at the district level, on the occurrence of dengue cases in Saint Lucia.

Sources of data. This study required the combination of data from the Saint Lucia Meteorology Office on environmental factors such as rainfall, temperature, and humidity which was collected at two weather stations on the island providing average rainfall for these areas, the Department of Environmental Health with conducts group level vector surveillance, and the Ministry of Health individual level infectious disease surveillance during the period of 2008 to 2017. These data sources provided the information that was analysed to answer the research question of interest.

Variables: Rainfall was measured as a continuous variable but I transformed this data into categorical data for ease of analysis. This data represented the average daily rainfall per month, the highest daily rainfall per month and the cumulative monthly rainfall in Saint Lucia during the period of the study, 2009-2017. The categories for average daily rainfall low(≤10mm/day), medium (>10-20mm/day) and high (>20mm/day), and highest daily rain fall were 0-45mm, >45-90mm, and >90mm. The categories for cumulative monthly rainfall were low (0-100mm/day), medium(>100-200mm/day), and high (>200mm/day).

Relative humidity. The relative humidity was measured as a proportion on a continuous scale but I also transformed this data into categories for ease of analysis and interpretation. This data represented the daily relative humidity were recorded in Saint Lucia during the period of the study, and were identified in the following categories low (0-75%), medium (>75-80%), and high (>80%),

Windspeed. Windspeed represented the daily recorded windspeed in Saint Lucia during the period of the study, measured in miles per hour (mph). This was a continuous variable but I transformed it into a categorical variable for ease of analysis. The categories for analysis were low (0-9mph), medium (>9-11mph) and high (>11mph),

Wind direction. Wind direction measures the direction from which the prevailing wind is coming from at the time windspeed is measured. This variable was measured in the following categories accounting for the azimuth bearings N (0^0) NNE(0-44^0), NE (45^0),ENE (46-89^0), E (90^0), ESE (91-134^0),SE(135^0), SSE (136-179^0), S(180^0),SSW (181-224^0), SW(225^0),WSW(226-269^0),W (270^0),WNW (271-314^0),NW (315^0), and NNW (316-359^0).

Minimum Temperature. The minimum temperature is measured every day as a meteorological variable in Saint Lucia, and represents the lowest temperature recorded for the day. This daily measurement is a continuous variable measured in degrees Celsius but I transformed this data into categorical data for ease of analysis, low (0^0C -16^0C), medium (>16^0C-20^0C), and high (>20^0C).

Maximum Temperature. The maximum temperature is measured every day as a meteorological variable in Saint Lucia, and represents the highest temperature recorded for the day. This daily measurement was a continuous variable measured in degrees Celsius but I transformed this data into categorical data for ease of analysis, low (0^0C -30^0C), medium (>30^0C -32^0C), and high (>32^0C).

Average Daily Temperature. The average daily temperature is measured every day as a meteorological variable in Saint Lucia, and represents the arithmetic mean of the temperature recorded for the day. This daily measurement was a continuous variable measured in degrees Celsius but I transformed this data into categorical data for ease of analysis, low (0^0C -26^0C), medium (>26^0C-28^0C), and high (>28^0C).

Daily Sunshine. The daily sunshine represents the daily duration of sunshine experienced in Saint Lucia during the study period. This continuous level variable was measured in hours and I converted it to categories to facilitate ease of analysis. These categories are Category low (0-8hrs of sunshine/day), Category medium (>8-9) hrs. of sunshine/day), and Category high (>9 hrs. of sunshine/day),

Vector Surveillance. Vector surveillance relies on the use of three larval indicators Breteau index (number of positive containers per 100 houses inspected), House

Index (percentage of houses infested with larvae and/or pupae) and Container index (percentage of water-holding containers infested with larvae or pupae) measured as ratio variables.

Statistical analysis: The data used in this study was analyzed through bivariate analysis using chi-square analysis followed by multivariate logistic regression using the IBM SPSS Statistics 25 software. The analyses conducted consisted of descriptive analysis of the data, chi square tests of independence between the categorical variables in this study, followed by multivariate logistic regression models because the outcome variable the occurrence of dengue is a nominal variable denoting the presence or absence of the disease. Chi-square analysis was used to investigate the strength of association between each predictor variable and the dengue outcome variable on an individual level and then the relationship between the independent variables and the outcome variable were explored using logistic regression. This combination of statistical tests has been employed by prior researchers to provide a more comprehensive analysis of the relationship between variables (Akboğa Kale & Baradan, 2020; Kumar et al., 2014; Shrestha, 2019). Logistic regression was the most appropriate statistical model to evaluate the relationship of independent variables and categorical outcome variables (Liu et al., 2014). The dependent or outcome variable for this study occurrence of dengue, was a categorical variable measured on a nominal scale, dengue positive or dengue negative. The independent predictor variables in this model were rainfall, minimum temperature, maximum temperature and average daily temperature, relative humidity, windspeed, wind direction, daily sunshine, and vector surveillance, which were all be measured as categorical variables on a nominal scale.

Power Analysis: Sample size estimation for this study was determined by power analysis using G*Power 3 (software, http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3/). In this study, assuming two-tailed, z-test, an alpha level of .05, a power of 0.80 and 0.90, for a logistic regression model, the required sample size using G*Power 3 is 248 (80% power) and 325 (90% power) with a medium effect size of 0.3. This medium effect was used because previous studies investigating meteorological variables and dengue report high odds ratios such as relative humidity 7.3 (1.05-50.6) to 18.1 (1.6-206.2) at a lag of zero months and differing serotypes; rainfall was statistically significant at lags of zero and one month ranging from 7.0 (1.05-46.4) to 10.1(1.4-73.7) respectively, and average temperature at a lag of one month and odds ratio of 26.7 (1.6-433.1). The odds ratios of the risk of dengue associated with minimum, maximum and average temperatures were found to be 2.69 (2.44-2.97), 2.33 (1.89-2.42), and 2.84 (2.66-2.96) respectively (Fan et al., 2014).

Manuscript 3

Specific problem. One of the of most important control methods for dengue epidemics is through the early recognition of the disease because there is a deficiency of accurate bedside tests that can be used for rapid diagnosis. Most public health surveillance systems have moved towards syndromic surveillance, as is done in Saint Lucia. Identifying which of the common syndromic surveillance variables are associated with dengue will allow quicker identification and control of dengue cases and thus epidemics.

Research question. What clinical symptom undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis has most significant relationship with dengue fever in Saint Lucia?

Nature of study and design. This study followed a quantitative, non-experimental, retrospective design in exploring the relationship between the variables undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis and occurrence of dengue (Anglemyer et al., 2014). I used data previously collected through regular surveillance activities to answer the research question. The use of secondary data reduced the time necessary to conduct this study, while providing the researcher the ability to minimize contact with the subjects of the study. This information was analyzed using logistic regression to evaluate the relationship between the possible risk factors and the dependent variables. The hypotheses for the research question posed previously were

H_0: Clinical symptoms undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis are not associated with dengue fever in Saint Lucia.

$H_{1:}$ Clinical symptoms of undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis are associated with dengue fever in Saint Lucia.

Sources of data. The data that was used to answer the research question are secondary data from national surveillance data that is managed by the Ministry of Health individual level infectious disease surveillance activities. This data were a combination of hospital and other health center information that the government collected on infectious diseases from 2008 to 2017.

Variables: Undifferentiated fever, represents persons in an acute (sudden) febrile illness (> 38.0ºC or 100.4ºF) in a previously healthy person of less than 7 days duration with two or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting, jaundice – and without any particular symptoms fitting another syndrome definition. Children < 5 years of age: case management and specimen collection will vary according to the evolution of the clinical presentation. This variable was measured as a categorical variable on a nominal scale indicating presence or absence of the clinical sign.

Acute respiratory infection or fever and respiratory symptoms (ARI or FRS) represents people with an acute respiratory infection with measured fever of ≥ 38 C°, and cough, with onset within the last 10 days. This was a categorical variable measured on a nominal scale.

Fever with hemorrhagic symptoms (Fever with HS). This variable was measured on the categorical scale and a nominal level. Fever with hemorrhagic symptoms represents subjects presenting with acute (sudden) onset of fever (> 38.0ºC or 100.4ºF) in a previously healthy person, presenting with at least one hemorrhagic (bleeding) manifestation with or without jaundice (e.g. purpura, epistaxis, hemoptysis, melena).

Fever and neurological symptoms (fever and NS). This was a categorical variable measured on a nominal scale. Fever and neurological symptoms represent subjects presenting with any acute (sudden) onset of fever (> 38.0ºC or 100.4ºF) with or without headache and vomiting in a previously healthy person presenting with at least one of the followings signs: meningeal irritation, convulsions, altered consciousness, altered sensory manifestations, paralysis except AFP.

Gastroenteritis. This variable was measured on a categorical scale at a nominal level. Gastroenteritis identifies subjects presenting with acute (sudden) onset of diarrhea, with or without fever (> 38C or 100.4F) and presenting with 3 or more loose or watery stools in the past 24 hours, with or without dehydration, vomiting and/or visible blood.

Statistical analysis: The data used in this study was analyzed through bivariate analysis using chi-square followed by multivariate logistic regression using IBM SPSS Statistics v.25 software. Chi-square analysis was used to investigate the strength of association between each risk factor and the dengue outcome on an individual level and then the relationship between the predictor variables and the dependent variable was be explored using logistic regressions. This combination of statistical tests has been employed by prior researchers to provide a more comprehensive analysis of the relationship between variables (Akboğa Kale & Baradan, 2020; Kumar et al., 2014; Shrestha, 2019). Logistic regression was the most appropriate statistical model to evaluate the relationship of independent variables and categorical outcome variables (Liu et al., 2014). The dependent or outcome variable for this study occurrence of dengue, was a categorical variable measured on a nominal scale, dengue positive or dengue negative. The independent predictor variables in this model were undifferentiated fever. Other covariate variables included acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS) fever, and neurological symptoms (fever and NS), and gastroenteritis, which were all be measured as categorical variables on a nominal scale.

Power Analysis: Sample size estimation for this study was determined by power analysis using G*Power 3 (software, http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3/). In this study, assuming two-tailed, z-test, an alpha level of .05, a power of 0.80 and 0.90, for a logistic regression model, the required sample size using G*Power 3 is 68 (80% power) and 84 (90% power) with a medium effect size of 0.3. This medium effect was used because in a study by Mueller et al. (2014), it was reported that dengue was identified more often among those patients with fever (OR=3.7, 1.5-9.3).

Significance

This dissertation provided new knowledge on the epidemiology of dengue in Saint Lucia, a small English-speaking island in the Caribbean of which there is limited published work. It identified what variables, commonly collected through routine surveillance and monitoring on the island, are significantly associated with the occurrence of dengue. This increased understanding of dengue in Saint Lucia may stimulate the need for further research in more specific areas that will further contribute to refining predictive models of dengue or other important considerations in the outcome, diagnostics, treatment or burden of the disease. The knowledge generated in this study may also be applicable to other populations with similar characteristics as Saint Lucia for example the other island of the Organization of Eastern Caribbean States.

The identification of the factors associated with dengue in Saint Lucia will provide the Ministry of Health and other agencies with information that can be used to more efficiently utilize the limited resources available to address public health challenges. The information generated through this dissertation may allow the development of more targeted educational campaigns for both the public and the healthcare practitioners involved in prevention and response to dengue outbreaks. The outcomes of the study may encourage members of the public to seek healthcare more frequently and in a timelier manner as well as encourage healthcare providers to report disease in an effort to reduce underreporting.

Social Change

An important aspect of social change is the ability to change the knowledge, attitudes, beliefs and behavior or action of a population. An important social change that may result from this study is the preventive action at the individual level to reduce the occurrence of dengue which may include removing or better securing artificial containers that may serve as breeding sites for the *Aedes* mosquito, which will inadvertently reduce the incidence of other arboviral diseases that have been highly prevalent in Saint Lucia such as chikungunya and Zika. Raising the awareness of the population with special messaging based on the identified risk factors of dengue in Saint Lucia will provide the knowledge that will allow the public to take the necessary actions to reduce the occurrence of dengue (Neiderud, 2015). Another important social change that can occur is the improvement in the socioeconomic outcomes of the Saint Lucian population through the decreased loss of productivity commonly associated with dengue that is a significant burden to the population and the country's economy which is heavily dependent on service industries and the human resource. The decrease in dengue will also lead to a decrease in economic spending on healthcare which is important to a country that does not have a universal healthcare program resulting in the majority of the population paying for healthcare out of pocket. This reduction will allow for reallocation of these personal finances to other aspects of the individual's needs and have direct influence on their everyday life. The outcomes of the study could be used in applying for aid from donor countries or international agencies to address arboviral diseases and dengue specifically, which in turn will improve the living conditions and life experiences of the population of the island.

Summary

Dengue is the most important and wide spread arboviral disease currently in circulation and it is accredited with causing almost 400 million cases of disease each year, with approximately 96 million symptomatic cases and 500,000 requiring hospitalization (Bhatt et al., 2013). Dengue also has a significant economic burden associated with direct costs including surveillance, medical expenses, medication, diagnostic test, hospitalization, vector control and professional training. Indirect costs such as lost wages, loss of productivity, costs associated with travel to and from healthcare institution by patient and family, disruption of trade and business, decreased quality of life, temporary disability and loss of life are also important (Mayer et al., 2017). The dollar cost associated with these outcomes are difficult to correctly assess because not every case is reported and may not be attributed to dengue when they are reported but the global annual cost of dengue was estimated to be almost $US 40 billion (Castro et al., 2017). The countries of the Caribbean and Saint Lucia in particular can ill-afford these costs which supports the importance of this study.

Dengue is endemic in more than 125 countries, and it is estimated that almost have the world’s population is at risk (Murray et al., 2013). Most of the Caribbean countries are included in the groups of dengue endemic countries and Saint Lucia is no exception. There has however been little information published on dengue in Saint Lucia, and most of it published more than five years ago (Bos et al., 1988; Downs & Spence, 1964; Nathan & Knudsen, 1991). Public health practitioners largely have to rely on published information from other external sources which do not also accurately predict the local experience based on nuances (Wijayanti et al., 2016). The provision of information specific to Saint Lucia addresses this gap in the literature.

The large body of research on dengue contains numerous factors that have been associated with the occurrence and severity of dengue including sex, age, place of residence or location, urbanization, visitor arrival, rainfall, temperature, humidity, windspeed, and clinical factors such as undifferentiated fever as well as fever with neurological symptoms (Cheong et al., 2013; Hii et al., 2016; Khan et al., 2018; Murray et al., 2013; Neiderud, 2015; Ramadona et al., 2016; Sanyaolu et al., 2017; Singh et al., 2018; Verma et al., 2014). The relationship between dengue and the previously mentioned factors have not been analyzed specific to Saint Lucia, in the author's knowledge and this body of work is designed to address this gap in the literature.

The outcomes of this study can be utilized by the Public Health Department and the Ministry of health to create targeted interventions that will maximize the limited resources available for public health and reduce the burden of dengue on the island. Specific programs can be created to raise the awareness of any groups specifically associated with dengue. This would foster social change within communities and at the individual level in actions that can be taken to reduce favorable breeding sites for the *Aedes* vector, minimize contact with the vector improve health seeking behavior, improve reporting and minimize overall losses of productivity.

Each of the three studies were designed to analyze historical data in order to provide information of various aspects of the epidemiology of dengue in Saint Lucia namely the association of demographic, environmental and clinical risk factors with the occurrence of dengue. The studies were all retrospective, non-experimental studies using historical data collected by various agencies in Saint Lucia.

Part 2: Manuscripts

Demographic Variables as Predictors of Dengue in Saint Lucia

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Outlet for Manuscript

The *International Journal of Tropical Disease & Health* is well suited for the publication of this manuscript because it is an international journal with a focus on the control, prevention, and epidemiology of diseases that circulate in tropical areas. One of the diseases that meet this criterium is dengue. As such, it is an appropriate outlet to publish data on dengue and its epidemiology in Saint Lucia.

Abstract

Dengue remains one of the most important, if not the most important, vector-borne diseases. It has expanded its geographical range over time and as a result almost 400 million cases occur every year, contributing significant economic burden to affected countries through the associated health-care costs and loss of productivity. This study is the first published research examining the relationship between demographic variables and dengue in Saint Lucia, and such information is crucial to low- and middle-income countries that have limited budgets to apply to the management and control of such health risks. The current study involved the retrospective analysis of surveillance data on dengue and the relationship to general demographic variables in Saint Lucia.

The largest prevalence of dengue from the sample was found in the district of Castries (29.6%) and 25% of the cases occurring in the adult group (ages 19-44 years). It was found that more than 40 % of the dengue cases occurred in the population when between 12,500 to 14,000 persons had tertiary education. Logistic regression of the data allowed the demonstration of strong significant relationships between age, the 13- to 18-year age group ($p < .001$, OR 4.091 [CI 2.628-6.369]) and tertiary education ($p < .001$, OR 4.785 [CI 2.896- 7.905]) and occurrence of dengue. Further research is needed to better characterize the relationships identified between demographic variables in Saint Lucia and dengue. The health authorities can use the information generated to ensure that control and prevention programs target the groups that are at greatest risk in an effort to maximize the resources available for health programs.

Introduction

Dengue is the most widespread arboviral disease with estimates that 40% to 60% of the earth's population at risk of developing the disease when exposed to the infected Aedes mosquito vector (Bhatt et al., 2013; Khan et al., 2018; Pang et al., 2017). The greatest burden of the disease is arguably the loss of productivity in days absent from work or school especially to countries where the human resource is the main support of the economy (Laserna et al., 2018; Murray et al., 2013). More than 125 countries have been found to experience dengue cases of local origin with many of these countries being endemic and the Caribbean is no exception (Cafferata et al., 2013; Díaz-Quijano & Waldman, 2012; Stanaway et al., 2016). Unfortunately, most of the published work on the disease has focused on the Central and South American countries along with a handful of the Caribbean islands. Saint Lucia, one of the islands of the Eastern Caribbean, has not been the recent focus of published research on dengue which reduces the potential of public health agencies to effectively manage the disease and its burden within the country especially because it has been recommended that the local epidemiology of the disease should be studied because it has been found to vary across countries and even within some of the larger countries (Bowman et al., 2014; Castro et al., 2017; Chadee & Martinez, 2016; Laserna et al., 2018; Schiøler & Macpherson, 2009).

Saint Lucia is a small, tropical, English-speaking island in the Eastern Caribbean with a population of approximately 165,000 (Gaspard & Yang, 2016). Each year, the island welcomes more than 1 million visitors as both cruise and stayover visitors, which are all potential reservoirs of disease The island is volcanic and mountainous, with rain-forests in the interior of the island and most of the heavily populated areas situated in coastal areas around the island (Bégin et al., 2014; Malumphy, 2014; Walters, 2016b). The tropical, dense land cover provides ideal environments for mosquito oviposition and proliferation of the various stages of its lifecycles, whereas the concentration of population in relatively limited centers increases the likelihood of mosquito human interaction leading to possible transmission of dengue. These factors contribute to providing the suitable habitat for oviposition of the Aedes mosquito vector of dengue and well as the human-mosquito interaction that lead to disease transmission. There are 11 districts across the island Gros Islet, Castries, Anse la Raye, Canaries, Soufriere, Choiseul, Laborie, Vieux Fort, Micoud, Dennery, and Babonneau, though for the purpose of this study Babonneau was combined with Castries, because some local agencies record data in that manner creating 10 districts (Cherry et al., 2014). The capital city is found in Castries and there are three towns, Gros-Islet, Soufriere, and Vieux Fort. Tourism has replaced agriculture as the main economic industry on the island with both cruise and stayover visitor sectors being important to the island (Gabriel et al., 2013). Annually, Saint Lucia welcomes more than 1 million visitors, the majority of which are cruise and stayover visitors each serving as a possible source of the introduction of the dengue virus. The population is divided 48.7 % and 51.3% male and female, respectively; 0-14 years: 20.02% (male 17,006/female 16,027), 15-24 years: 15.37% (male 12,870/female 12,492), 25-54 years: 42.97% (male 34,117/female 36,779), 55-64 years: 9.99% (male 7,608/female 8,881), and 65 years and over: 11.65% (male 8,704/female 10,510) (*The World Factbook—Central Intelligence Agency*, 2018) . Life expectancy is estimated at 73 years for men and 78 for women and the urban population was calculated at 18.7% in 2018 (*Global Regions*, 2020). There are six hospitals, one polyclinic and 31 health centers on the island (Ministry of Health, 2018).

Much research has centered on identifying possible risk factors for dengue that could be used by public health authorities as points of focus in a prevention and control program. As a result of these endeavors researchers have identified statistically significant relationships between demographic variables such as sex, age, population density (Alok, Kumar & Nielsen, 2015), place of residence and socioeconomic variables such as economic status, employment, education level, urbanization, and income (Bhatt et al., 2013; Díaz-Quijano & Waldman, 2012; Prayitno et al., 2017). The effects of each of these variables on dengue occurrence and severity has been found to vary across geographic locations and time, and suggestions have been made that the specific local epidemiology should be investigated in an effort to provide applicable data and analysis useful to identified populations (Castro et al., 2017; Chadee & Martinez, 2016; Constenla et al., 2015; Khan et al., 2018; Laserna et al., 2018; Runge-Ranzinger et al., 2016).

The difference recognized in the occurrence of dengue between sexes has be related to socioeconomic factors such as employment, where being a housewife, unemployed, below school-age or older adult subject may lead to greater risk of exposure to dengue-infected mosquitoes that typically prefer to rest and feed indoors (Velasco-Salas et al., 2014; Vicente et al., 2017). In other societies a higher risk of dengue is seen among the population of working-age males who are more likely to be exposed outdoors during the active period pf the mosquito if the environment supports this behavior of the mosquito (Prasith et al., 2013). Age as a variable has also been found to vary (L'Azou et al., 2014), with researchers suggesting that circulating serotypes of the dengue virus have a major effect in that the longer a serotype has circulated the more likely it is for a population to have been infected or infections could have occurred from previous outbreaks and epidemics leading to high prevalence of these serotypes and the associated immunities (Ramadona et al., 2016; San Martín et al., 2010). The introduction of a different serotype, especially through visitors to the country may lead to secondary cases of dengue in persons previously infected with a heterologous serotype or primary cases in younger members of the population if it is a homologous serotype (Alok, Kumar & Nielsen, 2015; Thomas et al., 2014). This is a major risk to Saint Lucia, which receives visitors from other countries that are also endemic for dengue and could serve as a possible source of introduction of new strains of the virus. Nunes et al., (2014) suggested that many of the new strains of dengue introduced in Brazil come from Caribbean islands. Tourism accounts for approximately 65% of the GDP of Saint Lucia with the island welcoming approximately 1 million cruise and stayover visitors each year, which underscores the importance of the industry to the island (Mycoo et al., 2017; Walters, 2016a).

Location or place of residence has also been associated with the occurrence of dengue through factors such as land use, tree-cover, rural or urban setting, water supply, population density, housing quality, access to health care and general environmental factors such as presence of artificial containers that provide breeding sites for Aedes mosquitoes (Ali et al., 2013; Alvis-Guzman et al., 2015; Morin et al., 2013).

Traditionally, it was thought that the incidence of dengue was greater in urban areas because of the higher likelihood of high population densities, improper waste management and lower quality of housing in unplanned urban areas, however some studies show that it is possible to have a higher incidence of dengue in rural areas because of factors such as poor water supply leading to inappropriate water storage (Bhatia et al., 2013). Hospital access as determined by how quickly a person can access healthcare based on the proximity of a healthcare institution affects the outcome of dengue epidemics. In countries such as Saint Lucia where there is no nationalized health care and the majority of the population does not have health insurance, the cost of health care is borne out of pocket and this may also limit access to care.

Socioeconomic factors such as level of education, employment and level of income have been widely associated with the transmission of infectious diseases including dengue. The risk is normally higher in those of lower socioeconomic strata because of higher level of exposure to the infected vector either through low standard of housing or more exposure time in habitats where the mosquitoes rest and feed, the inability to live in an area with better water supply and waste management, and the lack of knowledge about the disease including routes of transmission, clinical signs of disease, treatment and prevention measures (Al-Dubai et al., 2013; Bhatt et al., 2013; Kenneson et al., 2017; Mulligan et al., 2015; Murray et al., 2013; Quintero et al., 2014). It has been found in some circumstances that knowledge of the disease and preventive measures does not translate into action leading to the occurrence of the dengue across all economic strata which may relate to perception of risk (Diaz-Quijano et al., 2018). Urbanization has also been linked to the risk of dengue occurrence mainly because of unplanned urban developments with poor waste management and water supplies and high population densities (Banu et al., 2014; de Brauw et al., 2014; Murray et al., 2013; Neiderud, 2015). These urban areas provide many sites for oviposition as well as a greater chance that an infected mosquito will come into contact with a susceptible person causing higher rates of disease transmission in these areas.

The understanding of the epidemiology of dengue in Saint Lucia is important in maximizing the use of the limited resources available for public health. Though socioeconomic factors have been associated with dengue as noted previously, no published data are available on which, if any predictors are related to the disease in Saint Lucia. The identification of possible associations with socioeconomic factors with dengue in Saint Lucia may allow the public health authorities to develop more target prevention and control strategies. This study is based upon ecological theory that posits that changes in external factors such as demographics of a population will affect the occurrence of diseases such as dengue (Zuckerman et al., 2014). I therefore sought to evaluate the hypothesis that there is a significant relationship between sex, age, geographic location or place of residence, employment status, education, urbanization, hospital access, visitor arrivals and occurrence of dengue in Saint Lucia. This will possibly address the gap in literature on local epidemiology of dengue.

Materials and Methods

The relationship between demographic variables and the occurrence of dengue in Saint Lucia was tested through a retrospective, quasi experimental study using descriptive analysis of the data, bivariate analysis using chi-square tests of independence followed by multivariate logistic regression of secondary data. The significance level for both the chi - squared and logistic regression analysis was set at 0.05. The individual level variable sex was measured having two levels male and female, whereas geographic location or place of residence of each case represented the 10 districts found in Saint Lucia; Anse La Raye, Canaries, Castries, Choiseul, Dennery, Gros-Islet, Laborie, Micoud, Soufriere, and Vieux Fort. Age was measured at the individual level according to Medical Subject Headings (MeSH), Infant (age 0-23months), Pre-school child (age 2-5 years), Child (age 6-12 years), Adolescent (age 13-18 years), Adult (age 19-44 years), Middle Aged (age 45-64), Aged (age 65-79 years), and Aged 80 and over (Kastner et al., 2006). A number of data were only available at the population level as collected by the responsible agencies. These data were transformed into nominal data, low, medium and high based on tertiles for the range of data. Employment was measured at the population level employed and unemployed as separate variables within each district and by year based on the manner of data collection. Unemployment was measured at 3 levels, low (≤2,500 persons), medium (>2,500-5,000 persons), and high (>5,000 persons). Employed, also a population variable on a nominal scale was measured at the annual district level with 3 levels, low (0-11000 persons), medium (>11,000-22,000 persons), high (>22,000 persons). Urbanization was based on the population density within the geographic districts of Saint Lucia and measured as a ratio variable as the number of persons per square mile being measured at the population level. The population density variable was divided into three categories low (≤1,000 persons/sq. mile), medium (>1,000-1,500 persons/sq. mile), and high

(>1,500 persons/sq. mile). Similarly, the population-level variable hospital access was based on the number of health facilities in comparison to population within the ten districts identified in Saint Lucia. The hospital access variable was divided into three categories low (≤3,000 persons/health facility), medium (>3,000-4,500 persons/health facility), and high (>4500 persons/health facility). Visitor arrivals represented the number of visitors entering Saint Lucia either throughcruise visitors low (≤30,000 persons/month), medium (>30,000 – 60,000 persons/month), high (>60,000 persons/month), and for stayover visitors low (≤25,000 persons/month), medium (>25,000-30,000 persons/month), high (>30,000 persons/month). Both variables were measured at the population level. Education represents the highest level of education attained in the categories of no education, primary, secondary, and tertiary level education all measured at the population level. The category of no education was measured at low (≤6,000 persons), medium (>6,000 ≤7,000 persons), and high (>7,000 persons); less than secondary education low(≤61,500 persons), medium(>61,500-65,000 persons), and high (>65,000 persons); secondary low (≤58,000 persons), medium (>58,000-61,000 persons), and high (>61,000 persons); and tertiary low (≤12,500 persons), medium (>12,500-14,000 persons), and high (>14,000 persons). This study design was most practical because large datasets of the relevant information exist, minimizing the study time and eliminating the need to interact directly with patients and included variables at the individual and population levels. These data were accessed from the Ministry of Health infectious disease surveillance database, census data from the Central Statistics office and visitor arrival from the Saint Lucia Tourism Authority, covering the period from 2011 to 2017. Ethical approval was granted from Walden University and the Medical and Dental Saint Lucia Council, Saint Lucia.

Results

During the period of observation for this study in Saint Lucia 1869 cases were investigated for possible dengue infections. Between 2011 and 2017 the population of Saint Lucia steadily increased from 167,366 to 177,301. The overall number of male cases to female cases were similar 979 to 890, and occurred in every age group under consideration infant to >80 years. Of the confirmed dengue cases 667 were male and 643 were female. Confirmed cases were reported in each of the 10 districts with the greatest number of confirmed cases occurring in Castries 529 and Gros Islet 239. During the seven-year period of observation covered in this study the incidence of confirmed dengue cases was on average 1.104 cases/1,000 persons, with the highest incidence recorded in 2011, 4.475 cases/1000 persons, and 2013, 1.165 cases/1000 persons. On average the highest incidence was found in the age groups from 0-44 years. Table 1. displays the prevalence of dengue across the different variables and their categories. It should be noted that proportion of dengue cases were highest when the level of unemployment was also highest at 30% of sample at level when more than 5,000 persons were unemployed, and lowest when visitors to the island was the lowest with less than 30,000 cruise ship visitors and less than 25,000 stayover visitors at 54%, and 30.9% respectively. The highest percentage of dengue cases were found in the adult age group (19-44 years) and the highest proportion of cases occurred in the district of Castries.

Table 1

Distribution of Variables Within Population at the Time Sample Cases Occurred, 2011-2017 Saint Lucia

Variable	Dengue positive		Dengue negative	
	Count	Percentage	Count	Percentage
Population level data				
Unemployed				
Low	405	22.70%	149	8.30%
Medium	305	17.10%	113	6.30%
High	537	30.00%	279	15.60%
n = 1788	1247		541	
Employed				
Low	464	26.00%	197	11.00%
Medium	252	14.10%	72	4.00%
High	531	29.70%	272	15.20%
n = 1788	1247		541	
Cruise visitors				
Low	1006	54.00%	336	18.00%
Medium	27	1.40%	38	2.00%
High	272	14.60%	185	9.90%
n = 1864	1305		559	
Stayover visitors				
Low	576	30.90%	169	9.10%
Medium	465	24.90%	248	13.30%
High	264	14.20%	142	7.60%
n=1864	1305		559	
Population density				
Low	636	35.60%	236	13.20%
Medium	82	4.60%	39	2.20%
High	529	29.60%	266	14.90%
n = 1788	1247		541	
Hospital access				
Low	149	8.30%	59	3.30%
Medium	275	15.40%	121	6.80%
High	822	46.00%	361	20.20%

n = 1787	1246		541	
Education				
No education				
Low	399	21.30%	226	12.10%
Medium	94	5.00%	97	5.20%
High	817	43.70%	236	12.60%
n = 1869	1310		559	
Less than secondary				
Low	1180	63.10%	426	22.80%
Medium	68	3.60%	65	3.50%
High	62	3.30%	68	3.60%
n = 1869	1310		559	
Secondary				
Low	784	41.90%	212	11.30%
Medium	282	15.10%	109	5.80%
High	244	13.10%	238	12.70%
n = 1869	1310		559	
Tertiary				
Low	189	10.10%	205	11.00%
Medium	782	41.80%	197	10.50%
High	339	18.10%	157	8.40%
n = 1869	1310		559	
Individual level data tied to each case				
Districts				
Laborie	51	2.90%	33	1.80%
Castries	529	29.60%	268	15.00%
Canaries	2	0.10%	5	0.30%
Soufriere	44	2.50%	9	0.50%
Dennery	62	3.50%	35	2.00%
Anse La Raye	239	13.40%	74	4.10%
Gros-Islet	44	2.50%	10	0.60%
Choiseul	82	4.60%	39	2.20%
Vieux Fort	53	3.00%	12	0.70%
Micoud	141	7.90%	56	3.10%
n = 1788	1247		541	

Age				
Infant (0-23 months)	105	5.70%	98	5.30%
Preschool Child (2-5 years)	90	4.90%	76	4.10%
Child (6-12 years)	209	11.30%	83	4.50%
Adolescent (13-18 years)	209	11.30%	46	2.50%
Adult (19-44years)	462	25.00%	175	9.50%
Middle Aged (45-64years)	151	8.20%	52	2.80%
Aged (65-79 years)	51	2.80%	18	1.00%
Aged 80 years and older	12	0.60%	11	0.60%
n = 1848	1289		559	
Sex				
Male	667	35.70%	312	13.20%
Female	643	34.40%	247	16.70%
n = 1869				

Note. Table 1 displays the number/percentage represent cases that occurred under the variables of interest included in this study.

Chi-square analysis of the data indicated that there was a significant relationship between confirmed cases of dengue and all of the variables with the exception of sex and hospital access as indicated in Table 2.

Table 2

Pearson's Chi-Square Analysis of Factors Associated With Dengue in Saint Lucia

Variable	Value	*df*	Significance	Cramer's V
Age[a]***	77.057	7	.000	0.204
Cruise[b]***	64.733	2	.000	0.186
Stayover[b]***	31.544	2	.000	0.130
Pop. Density[c]*	8.299	2	.016	0.068
No Education[a]***	79.588	2	.000	0.206

Variable	Value	*df*	Significance	Cramer's V
Less than Secondary Education[b]***	62.696	2	.000	0.183
Secondary Education[a]***	123.251	2	.000	0.257
Tertiary Education[a]***	137.419	2	.000	0.271
Unemployed[c]**	11.010	2	.004	0.078
Employed[c]**	14.952	2	.001	0.091
Hospital Access[d]	0.407	2	.816	0.015
District[b]***	33.980	9	.000	0.138
Sex[d]	3.768	1	.052	0.045

Note. [a]Strongest significant association on Cramer's V, [b]More moderate significant association on Cramer's V, [c]Weak significant association on Cramer's V, [d] Non-significant result not included in further analysis.

$p < .05$*, $p < .01$**, $p < .001$***

The variables age, no education, secondary education, and tertiary education had a strongest association with confirmed dengue cases having a Cramer's V of more than 0.20; the other variables significantly associated with confirmed dengue cases had a weaker relationship with values of Cramer's V less than 0.20 Only cases with complete data sets were included in building logistic regression models which included 1763 cases.

A logistic regression model shown in Table 3., of all of the variables under analysis indicated that age, district, cruise visitors, and number of employed were significantly associated with confirmed dengue cases at different levels. The adolescent age group 13-18 (*p*<.001, OR 4.336 [CI 2.731-6.885) was most strongly associated with confirmed dengue cases when compared to the reference age group of 0-23 months but there was no proportionate increase or decrease with an increase of age. The district of Laborie was most strongly associated with confirmed dengue cases (*p*=.05, OR 3.211 [CI 1.302-7.918]) when compared to the Anse la Raye reference group. The number of employed persons was also significantly associated with confirmed dengue cases at the medium level >11,000-22,000 persons (*p*=.05, OR 18.343 [CI 3.323-101.239]) compared to the 0-11000-person reference group. The number of cruise visitors was most strongly associated with confirmed cases of dengue at the medium level >30,000-60,000 persons (*p* = .05, OR 0.408 [CI 0.221-0.754]) when compared to the 0-30,000 reference group though this association was a negative relationship.

Table 3

Logistic Regression Model of Predictive Factors of Dengue in Saint Lucia 2011-2017

								95% C.I. for O.R.	
		B	**S.E.**	**Wald**	***df***	**Sig.**	**Odds Ratio**	**Lower**	**Upper**
	Unemployed								
Ref.	Low								
	Medium	0.184	0.247	0.555	1	0.456	1.202	0.740	1.953
	High	-0.457	0.646	0.501	1	0.479	0.633	0.178	2.245
	Employed								
Ref.	Low								
	Medium**	2.909	0.872	11.142	1	0.001	18.343	3.323	101.239
	High	1.356	1.312	1.068	1	0.301	3.879	0.297	50.741

	Cruise Visitors								
Ref.	Low								
	Medium**	-0.896	0.313	8.172	1	0.004	0.408	0.221	0.754
	High***	-0.534	0.143	13.899	1	0.000	0.586	0.443	0.776
	Stayover Visitors								
Ref.	Low								
	Medium	-0.161	0.143	1.274	1	0.259	0.851	0.643	1.126
	High	0.081	0.177	0.211	1	0.646	1.084	0.767	1.533
	Population Density								
Ref.	Low								
	Medium*	0.786	0.331	5.638	1	0.018	2.194	1.147	4.196
	High	21.936	28413.603	0.000	1	0.999	3361789819.484	0.000	
	Less than Secondary Education								
Ref.	Low								
	Medium	-0.204	24574.785	0.000	1	1.000	0.815	0.000	
	High	19.846	28282.630	0.000	1	0.999	415776999.525	0.000	
	Tertiary Education								
Ref.	Low								
	Medium	1.138	24574.785	0.000	1	1.000	3.122	0.000	
	High	20.188	28282.630	0.000	1	0.999	585389891.462	0.000	
	No Education								
Ref.	Low								
	Medium	20.254	28282.630	0.000	1	0.999	625157556.441	0.000	
	High	19.712	40195.089	0.000	1	1.000	363644216.589	0.000	
	Secondary Education								
Ref.	Low								
	Medium	0.152	24574.785	0.000	1	1.000	1.164	0.000	
	High	-0.771	24574.785	0.000	1	1.000	0.463	0.000	

	Age								
Ref.	Infant								
	Pre-school Child	0.123	0.234	0.274	1	0.601	1.131	0.714	1.790
	Child**	0.692	0.211	10.771	1	0.001	1.998	1.322	3.021
	Adolescent***	1.467	0.236	38.659	1	0.000	4.336	2.731	6.885
	Adult***	1.156	0.187	38.289	1	0.000	3.176	2.203	4.581
	Middle Aged***	1.305	0.240	29.697	1	0.000	3.689	2.307	5.898
	Aged***	1.259	0.342	13.558	1	0.000	3.523	1.802	6.888
	Aged 80 and above	0.712	0.498	2.044	1	0.153	2.037	0.768	5.405
	District								
Ref.	Anse La Raye								
	Castries	-22.430	28413.603	0.000	1	0.999	0.000	0.000	
	Canaries	-1.048	0.903	1.345	1	0.246	0.351	0.060	2.061
	Choiseul*	1.167	0.460	6.418	1	0.011	3.211	1.302	7.918
	Dennery	0.303	0.346	0.770	1	0.380	1.355	0.688	2.668
	Gros Islet*	-2.189	0.916	5.714	1	0.017	0.112	0.019	0.674
	Laborie**	1.385	0.458	9.129	1	0.003	3.996	1.627	9.815
	Soufriere*	0.977	0.427	5.234	1	0.022	2.655	1.150	6.129
	Vieux Fort*	0.843	0.344	5.987	1	0.014	2.323	1.183	4.562

**p*=.05, ***p*<.01, ****p*<.001

A logistic model as reported in Table 4 containing the four variables that had the strongest association with confirmed dengue cases on chi-square analysis based on Cramer’s V; age, no education, secondary education, and tertiary education, indicated that every level of age was significantly associated with confirmed cases with the exception of the pre-school and 80 year old and over group; and the group with the strongest association was the adolescent age group (*p*<.001, OR 4.091 [CI 2.628- 6.369]) when compared to the infant reference group. The largest no education group >7,000 persons, was found to have a negative significantly associated relationship with confirmed cases (*p*=.05, OR 0.382 [CI 0.170- 0.861]) when compared to the reference group 0-6,000. Similarly, the largest group of the population with secondary education also had a negative significant relationship with confirmed dengue cases (p<.001, OR 0.315 [CI 0.179-0.553)] compared to the reference group 0-58,000. When compared to the reference group 0-12,500 persons with tertiary education, the fourth variable tertiary education was also found to be significantly associated with confirmed cases (p<.001, OR 4.785 [CI 2.896- 7.905]).

Table 4

Logistic regression model of strong significant demographic predictors of dengue in Saint Lucia 2009-2017

								95% C.I. for O.R.	
		B	**S.E.**	**Wald**	**df**	**Sig.**	**O.R.**	**Lower**	**Upper**
	Age								
Ref.	Infant								
	Pre-school Child	0.073	0.223	0.108	1	0.742	1.076	0.695	1.666
	Child**	0.614	0.201	9.307	1	0.002	1.848	1.246	2.743
	Adolescent***	1.409	0.226	38.922	1	0.000	4.091	2.628	6.369
	Adult***	1.069	0.177	36.480	1	0.000	2.914	2.059	4.123
	Middle Aged***	1.294	0.229	32.050	1	0.000	3.648	2.331	5.710
	Aged***	1.199	0.325	13.599	1	0.000	3.316	1.754	6.271
	Aged 80 and above	0.421	0.471	0.796	1	0.372	1.523	0.605	3.837
	No Education								
Ref.	Low								
	Medium	0.138	0.235	0.342	1	0.559	1.147	0.724	1.820
	High*	-0.961	0.414	5.396	1	0.020	0.382	0.170	0.861
	Secondary Education								
Ref.	Low								
	Medium	-0.216	0.369	0.344	1	0.558	0.806	0.391	1.659
	High***	-1.155	0.287	16.175	1	0.000	0.315	0.179	0.553

		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Tertiary Education								
Ref.	Low								
	Medium***	1.565	0.256	37.352	1	0.000	4.785	2.896	7.905
	High	0.227	0.273	0.697	1	0.404	1.255	0.736	2.142

*p=.05, **$p<.01$, ***$p<.001$

Table 5 demonstrated a third regression model including only the variables that were found to have a more moderate relationship with confirmed dengue cases indicated that both cruise tourism and stayover tourism were negatively associated with confirmed cases of dengue for the group >30,000-60,000 visitors/month ($p<.001$, OR 0.331 [CI 0.188-0.581]) and the group >25,000-30,000 visitors/month ($p<.001$ OR 0.703 [0.544-0.909]) when compared to the reference groups 0-30,000 and 0-25,000 visitors/month respectively. The education level less than secondary was found to be negatively associated with confirmed cases most strongly at the level of >65,000 persons ($p<.001$, OR 0.330 [CI 0.223 – 0.490]) compared to the reference group 0-61,500 persons. The variable district was found to be significantly associated with confirmed cases at multiple levels though without a continually increasing or decreasing pattern across the levels. The level which was most strongly associated with confirmed dengue cases was Laborie (p=.05, OR 3.371 [CI 1.459-7.792]) compared to Anse la Raye as the reference group.

Table 5

Logistic regression model of moderately significant demographic predictors of dengue in Saint Lucia 2011-2017

	B	S.E.	Wald	df	Sig.	O.R.	95% C.I. for O.R. Lower	Upper
Cruise Visitors								

Reference	Low								
	Medium***	-1.107	0.287	14.822	1	0.000	0.331	0.188	0.581
	High***	-0.521	0.131	15.770	1	0.000	0.594	0.459	0.768
	Stayover Visitors								
Reference	Low								
	Medium**	-0.352	0.131	7.243	1	0.007	0.703	0.544	0.909
	High	-0.180	0.155	1.354	1	0.245	0.835	0.616	1.131
	Less than Secondary Education								
Reference	Low								
	Medium***	-0.736	0.194	14.382	1	0.000	0.479	0.327	0.701
	High***	-1.108	0.201	30.379	1	0.000	0.330	0.223	0.490
	Districts								
Reference	Anse La Raye								
	Castries	0.300	0.242	1.534	1	0.215	1.350	0.840	2.171
	Canaries	-1.309	0.885	2.189	1	0.139	0.270	0.048	1.530
	Choiseul**	1.145	0.437	6.853	1	0.009	3.143	1.333	7.408
	Dennery	0.365	0.320	1.295	1	0.255	1.440	0.768	2.698
	Gros Islet**	0.796	0.268	8.846	1	0.003	2.217	1.312	3.746
	Laborie**	1.215	0.427	8.082	1	0.004	3.371	1.459	7.792
	Micoud	0.562	0.311	3.264	1	0.071	1.754	0.953	3.226
	Soufriere**	1.131	0.400	8.000	1	0.005	3.099	1.415	6.785
	Vieux Fort**	0.732	0.287	6.489	1	0.011	2.080	1.184	3.653

*p<.05, **p<.01, ***p<.001

The relationship between the variables with the weakest association with dengue cases was modeled through logistic regression as demonstrated in Table 6. Population density was significantly associated with confirmed dengue cases at the high population density level of >1,500 persons/sq. mile (p=.05, OR 5.966 [CI 1.196-29.760]) compared to the reference category 0-1,000 persons/sq. Mile. The variable unemployed was found to have a negative significant association with confirmed dengue cases that was highest at the level of >5,000 persons (p=.05, OR 0.314 [CI 0.104-0.954]) compared to the reference low unemployment level group of 0-2,500 persons. In contrast the variable employed was found to have a positive significant relationship with confirmed dengue cases at the medium level of >11,000-22,000 (P=.05, OR 1.827 [1.217-2.741]).

Table 6.

Logistic Regression Model weak significant demographic predictors of dengue in Saint Lucia 2011-2017

								95% C.I. for O.R.	
		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Unemployed								
Reference	Low								
	Medium*	-0.395	0.189	4.375	1	0.036	0.674	0.466	0.975
	High*	-1.157	0.567	4.172	1	0.041	0.314	0.104	0.954
	Employed								
Reference	Low								
	Medium**	0.603	0.207	8.471	1	0.004	1.827	1.217	2.741
	High	-0.944	0.988	0.914	1	0.339	0.389	0.056	2.697
	Population Density								
Reference	Low								
	Medium	-0.198	0.218	0.824	1	0.364	0.820	0.535	1.258
	High*	1.786	0.820	4.745	1	0.029	5.966	1.196	29.760

*p<.05, **p<.01

DISCUSSION:

The most significant finding was the positive relationship with dengue and tertiary education, which was also among the strongest relationships between any of the risk factors tested here and dengue. Previously authors have linked increased educational levels to better knowledge of dengue, better health-seeking behavior and better preventive actions and therefore with few cases occurring within this segment of a population (Dhimal et al., 2014; Louis et al., 2014). Within the Saint Lucian context, the positive significant relationship with persons with tertiary education may therefore reflect a better knowledge of the clinical signs of the disease and the ability to seek appropriate health-care. Tertiary education also includes students enrolled in the local community colleges and this coincides with the positive relationship with the adolescent group 13-18 years old. Another possible contributing factor to the strong association of tertiary education and dengue cases is this section of the population is more likely to live and work in more densely populated areas such as the city center and therefore come into greater contact with the mosquito vectors, which is supported by the positive associations of population density and employment with confirmed dengue cases (Wijayanti et al., 2016). Persons with tertiary education are more likely to have office or indoor jobs which may put them at higher risk of exposure to the indoor dwelling Aedes aegypti mosquito and in addition these persons are also more likely to be able to afford healthcare than persons with lower levels of education and consequently higher paying jobs. Having no education, less than a secondary school education or secondary education were found to all be negatively predict confirmed dengue cases in Saint Lucia, and this may be as a result of being uncertain of the clinical signs of the disease therefore increased reporting or seeking medical care for cases that were not dengue. Education has been established by other authors as predictors of the disease and are likewise important in the Saint Lucian context.

Age of persons infected with dengue has been previously established as a significant predictor of dengue within a population, however authors differ on which age groups seem to have the strongest association with dengue (Fritzell et al., 2018; Guzmán & Kourí, 2002; A Kumar et al., 2013, 2015; L'Azou et al., 2015; Torres et al., 2017). In this study the adolescent age group 13-18 had the strongest association with confirmed dengue cases which may be as a result of exposure and lack of immunological protection. The introduction of new serotypes or genotypes of the dengue against which the adolescent age group have no protection may also explain this relationship (Torres et al., 2017). The stronger association among this group may also be related to parents ensuring that children that are unwell receive medical care. However, the lack of a discernible pattern of increase or decrease in strength of association between age and dengue cases may reflect the introduction of varying serotypes or genotypes of the virus which would minimize the likelihood of a resistant population. The relationship to dengue occurrence in this group may reflect differences in behavior to other groups, that may put the adolescents at higher risk of dengue. These adolescents may possibly remain indoors for longer periods of time, related to studying and academic work, recreational playing of video games, computer use or sleep (Bucksch et al., 2016; Casey et al., 2016; Gross, 2004). A significant relationship was also found to exist across most age groups except the 0-23month and 80+ age groups, which may indicate that dengue affects a wide cross section of the population, but the greatest strength of association with the adolescent age group suggests that preventive measures should target this age group. The disparity across researches may suggests that there are multiple factors influencing the role of age in the occurrence of dengue in Saint Lucia, including immature immunity in infants, increased risk of exposure based on activity, increased risk of comorbidities with increased age, and decreased immunity in geriatric populations.

The negative significant relationships with tourism, may seem counter-intuitive initially, because the influx of persons to a geographical location is often related to the introduction of disease agents, however a number of factors may explain this phenomenon. The highest number of visitor arrivals for both cruise and stayover visitors, occurs mainly during the dryer, cooler parts of the year when mosquito population numbers are apt to be lower, reducing the disease transmission cycle. Additionally, during the busy tourist season, seasonal industry workers are likely to be employed and less likely to take opportunity to seek medical care, therefore potential dengue cases may go unidentified. The increased activity during peak visitor periods may also serve to decrease opportunities for exposure to infected mosquitoes. The increased activity during peak tourist season, also possibly decreases the amount of time at home for the members of the population employed within the industry and therefore potentially decreases the risk of exposure to the dengue mosquito vector.

Population density was also found to be positively associated with confirmed dengue cases and supports previously established outcomes by other authors, suggesting that the anthropophilic mosquito thrives in areas of dense populations (Wijayanti et al., 2016; Yung et al., 2016). This may be as a result of persons living in surroundings that support mosquito populations with water-holding receptacles, or without appropriate mosquito preventive measures. Unemployment was found to have a negative significant relationship with dengue possibly reflecting unemployed persons, may be less likely to seek medical care for dengue related symptoms because of the costs associated with such care. Employment on the other hand was found to have a positive significant relationship with dengue and an increased risk of exposure to dengue related to employment has been established by other authors with persons working outdoors at higher risk of transmission by *A. Albopictus* and conversely by *A. aegypti* indoors (Wijayanti et al., 2016; Yung et al., 2016). This positive relationship with dengue may reflect persons working in areas that exposes them to infected mosquitoes either outdoors or in indoor environments. It is also likely that employed persons are more likely to seek medical care and be diagnosed with dengue than unemployed persons. Dengue preventive plans should take into consideration the associations highlighted here, and include messaging specific to the subsets of the population affected. It would also suggest that greater surveillance or targeted surveillance should seek to determine the true epidemiology of the disease among persons with lower educational levels and the unemployed.

District or the geographical place where persons lived was also found to be significantly associated with confirmed dengue cases with Laborie having the strongest association followed by, Choiseul and Soufriere having the strongest association with dengue when compared to the Anse La Raye as the reference group. The population densities in these districts are low, and this is unlikely to be the explanation for the positive relationship with dengue because increased population density has been established as a risk factor for the disease (Salje et al., 2017). The unemployment level in these three districts were the lowest in Saint Lucia during the period of the study but as previously described unemployment was found to have a negative significant relationship with dengue. The rate of employment in these districts were among the highest across the island during the period of the study, which may mean that the population may have greater resources to seek healthcare increasing detection rates. Employment may also increase the risk of exposure to infected mosquitoes and help explain the strong significant relationship between district and dengue. These communities are also more rural and there is a possibility that there are more suitable environmental conditions to support mosquito populations and also the preventive programs by the Ministry of Health may have less uptake in these regions. In addition, the strong association of these rural communities with the occurrence of dengue supports the earlier finding of Downs and Spence (1964) which demonstrated higher levels of immunity to dengue in urban areas.

Hospital access was not found to be associated with confirmed dengue cases and this may reflect the fact that the number of health facilities has not changed greatly during the period of the study and also because of the size of the island persons have the ability to visit health facilities outside of their geographic place of residence.

Researchers have found the relationship between dengue and sex has been found to differ with some finding no relationship, and others finding either males or females have a stronger relationship to the disease; in this study sex was not associated with dengue in Saint Lucia (Ahmed and Broor, 2015; Chakravarti et al., 2016; Fernández et al., 2016; Torres et al., 2017). The lack of a difference between genders my indicate equal exposure to mosquito vectors as well as equal access to healthcare on the island.

The analysis of the data demonstrates that most of the demographic variables included are associated with dengue cases in Saint Lucia, which is important in establishing their local relevance. However, further analysis of these variables is necessary to better understand their relationships to dengue. The best model was only able to predict 73.1% of cases and this may be because the majority of variables were measured at the population level and lacked the specificity of individual level data. However, this data does not exist at the individual level and will require additional research to better explain these relationships.

There were a number of limitations with this study, including the limited detail on dengue and dengue suspect cases which did not include the individual's employment status or education level and limited date of onset information, as well limited information on visitors. With the exception of age, sex, and geographic location, the other variable was measured at the population level and result in a lack of specific detail for individual cases. The operationalization of the variables included in the study may also have led to incorrect outcomes and the continued analysis of the available data and collection of additional more specific data is warranted. Further studies should be conducted to investigate the high association of district with dengue to determine why there is a strong association with Laborie, Choiseul, and Soufriere with dengue. Also, the risk factors of age and employment should be further investigated to better understand how these variables are associated with dengue in Saint Lucia. It may be helpful to also conduct a behavior, attitudes, and knowledge study within the working population to specifically investigate these phenomena amongst employed persons. The accurate identification of dengue cases due to lack of understanding the disease or lack of economic resources to seek healthcare may also limit the true depiction of the relationship of predictors and dengue in Saint Lucia. The outcomes of this current study may provide additional background that can be used by the Ministry of Education to tailor its preventive program for dengue targeting the age groups and districts identified as being strong risk factors of dengue as well as the employed labor force to reduce the incidence of dengue in Saint Lucia.

Any disease that causes significant morbidity and therefore loss of days at work or at school will have significant social impact on a country; in particular at the lower levels of society that often cannot afford healthcare and the life outcomes of members of this section of the society can be negatively affected. Dengue affects almost 400 million persons per year, many within the lower economic levels of society because of living conditions that often support mosquito vector populations (Bhatt et al., 2013). The author was able to demonstrate that tertiary education, age, population density, employment, and geographic location are positively associated with dengue cases in Saint Lucia, whereas education less than tertiary level, visitor arrival, and unemployment was negatively associated. If public health authorities are able to target these sections of the population most at risk, the incidence of dengue might be reduced, minimizing the associated healthcare costs, the days lost at work or school, and consequent loss in productivity. This would minimize the social impact the disease would have in Saint Lucia and indeed possibly in other countries to which dengue maybe exported from Saint Lucia by the movement of infected persons or infected mosquito vectors.

Conclusions

This study allowed the author to test the study hypothesis, demonstrating that a number of demographic variables of the Saint Lucian population are associated with dengue in the specific local context However further studies should be conducted to understand these relationships more clearly. Although age had a moderate association and positive significant relationship with dengue, the lack of a discernible pattern to this relationship requires additional analysis to determine what is the true relationship in the Saint Lucian context. Similarly, also, education although being associated with dengue, the nature of the relationship is unclear and bears further investigation. These factors will play an important role in the successful design of prevention programs and also the uptake these preventive measures. Dengue remains a public health challenge in, Saint Lucia, the Caribbean and globally, research into risk factors especially at the local level is critical to successful control of this disease.

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Environmental Predictors of Dengue in Saint Lucia

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Outlet

International Journal of Environmental Health Research (*IJEHR)* is a journal dedicated to scientific research on the natural environment, built environment, and communicable disease and the impact of vectors. The scope of the journal is suited to publishing this study investigating the impact of environmental variables on the occurrence of dengue as a vector-borne disease in Saint Lucia.

Abstract

Dengue remains one of the most prevalent vector-borne viral diseases worldwide, accounting for almost 400 million cases, which can take a severe toll on the population and economy of the affected countries. This vector-borne disease is especially challenging in tropical regions where the environment supports the expansion of the vector population. This retrospective study is the first published research investigating the effects of environmental factors on the occurrence of dengue in Saint Lucia. Included were data on temperature, rainfall, wind, sunshine, relative humidity, and vector prevalence indices. Logistic regression demonstrated that maximum daily temperature has the strongest positive prediction with dengue cases >30-32^{0}C ($p < .05$, OR 2.905 [CI 1.223-6.902]). Further research is necessary to further explore the relationships between environmental data and dengue in Saint Lucia, but this study provides information that can be used by public health authorities to target control and management strategies.

Introduction

Infectious diseases such as dengue still pose a tremendous challenge to developing countries through the associated mortality, morbidity, loss of productivity, and the economic effects of the disease often because of the limited resources that are available for public health systems (Bhatt et al., 2013; Hotez et al., 2014). Globally, more than 2.5 billion people are at risk of developing dengue each year, with clinical cases estimated to be between 50 and 100 million annually, and many of these cases are in tropical, developing countries (Mehta et al., 2018). In 2019, the Pan American Health Organization reported more than 3 million cases of dengue in the Americas, the highest number ever recorded in that region (Mitchell, 2020). Vector-borne diseases such as dengue thrive in these countries because of favorable environmental conditions both natural and built (Chadee & Martinez, 2016; Prayitno et al., 2017). The vector of dengue is able to find abundant artificial water containers and structures for oviposition as a result of improper urban planning, improper disposal of waste, and changes to environmental conditions leading to increases in standing water (Matysiak & Roess, 2017). The subsequent increases in the mosquito population is an important factor in the increased geographic spread of the dengue virus into areas not traditionally associated with the endemic circulation of the virus (Khan et al., 2018). The burden of morbidity and loss of productivity associated with dengue infections can cause a catastrophe in endemic countries such as Saint Lucia that is heavily dependent on its human resource.

Saint Lucia is a small, mountainous island in the Eastern Caribbean island chain with a population of more than 160,000 people (Walters, 2016). A large proportion of the population does not have health insurance and medical costs are typically met out of pocket, which emphasizes the effects of any disease outbreak on both the population and the island's economy. There are 11 districts across the island, but for census and other data collection the country is reorganized into 10 districts: Gros Islet, Castries, Anse la Raye, Canaries, Soufriere, Choiseul, Laborie, Vieux Fort, Micoud, and Dennery (Cherry et al., 2014).

The capital city is found in Castries and there are three towns, Gros-Islet, Soufriere, and Vieux Fort. The rainy season typically starts in mid-June and continues to mid-November followed by a dry season mid-November to mid-June with the average daily maximum temperature varying from 27°C to 29°C and the average daily minimum temperature from 20°C (Malumphy, 2014). The January daily average high temperature is 27°C at the southwestern coastal capital city of Castries, with a nightly low of 20°C. The July daily average is 29°C and the nightly low is 20°C to 22°C in January and July respectively (Malumphy, 2014).

The dengue virus has been endemic in the Caribbean region for decades and though research has been conducted surrounding the disease in other islands and countries around the world there is a dearth of published literature on the disease in Saint Lucia. Laserna et al. (2018) suggested that the epidemiology of the disease differs across geographic locations and underscores the need of research specific to the locale of interest in that way providing stakeholders with information that may be unique. Saint Lucia and the other islands in the Caribbean are extremely vulnerable to environmental changes as small island states. Many of these environmental factors affect the dengue viruses indirectly or indirectly through its vector the Aedes mosquito and understanding the epidemiology of the disease in those contexts is important to public health officials.

Increases in environmental factors such as temperature have been associated with increases in mosquito populations by making the environment where mosquito eggs are deposit more favorable for egg survival, as well as reducing the time taken to develop into adults (Larrieu et al., 2014). A shorter life cycle may lead to increased numbers of the vector but also may result in smaller mosquitoes, which leads to an increase in blood meals and consequently the increased number of hosts that may be exposed to infected mosquitoes. Temperatures in excess of 40^{o}C may lead to decreased hatchability of mosquito eggs and decreased survival of larvae and pupae in aquatic environments (Chadee & Martinez, 2016). This leads the mosquito to find protected areas for oviposition of which there are many as a result of the built environment bringing the mosquito which preferentially feeds on humans, in even closer contact with its hosts. The increased temperatures also cause changes in the virus shortening its replication cycle and decreasing the extrinsic incubation period or the time from when the female mosquito is infected to the time she is able to infect a susceptible host (Larrieu et al., 2014)

Rainfall is another environmental variable that is associated with dengue and its vectors especially in an environment that has water-holding containers such as improperly disposed garbage, improperly covered water tanks or drums, improperly sealed septic tanks, and indoor vases (Chadee & Martinez, 2026). The increase in stagnant water after rainfall increases the available places for mosquito eggs to be laid which may in turn lead to increases in the population of the vector and increases of dengue in a susceptible population (Chanprasopchai et al, 2017; Tosepu, Tantrakarnapa, and Worakhunpiset 2018). Chanprasopchai et al, found a direct correlation between increases in rainfall and increases in dengue because of increase in mosquito populations following rainfall. Increases in other environmental factors such as humidity which is directly related to moisture in the air and temperature, also shorten the length of the vector's lifecycle and through similar mechanisms as described before will lead to more frequent feeding by the mosquito and increased potential dengue transmission (Akter et al., 2017).

Extremes in environmental variables can also have a negative effect on vector populations through decreased hatchability of eggs or decreased survival of the individual life stages of the mosquito. Extreme temperatures either below 13^0C or above 38^0C leads to the decreased feeding behavior of adult mosquitoes, which decreases the potential of disease transmission but also shortens the lifespan of the mosquito (Carrington & Simmons, 2014). High environmental temperatures, especially as a result of direct sunlight leads to high temperatures of standing water that is not shaded. Mosquito eggs and larvae in this water do not survive temperatures greater than 40^0C, which forces the Aedes mosquito to adapt and lay eggs in sheltered sites (Chadee & Martinez, 2016). Low humidity also decreases the hatchability of the mosquito eggs and decreases population size. Heavy rainfall has also been known to wash away oviposition sites leading to lower mosquito numbers and lessening the probability of disease transmission (Ramadona et al., 2016). Strong winds decrease the mosquitoes flight distance, oviposition, and time inhibiting feeding habits thus contributing to fewer opportunities for disease transmission

(Estallo et al., 2015). Light has also been found to be important for mosquito fecundity, hatchability, and adult survival, decreases in sunlight contributes to decreased positive outcomes for the vector population (Chadee & Martinez, 2016). These negative effects of extreme environmental variables suggest the need to determine the parameters within the local context of Saint Lucia that predict the occurrence of dengue.

Most countries regularly collect environmental data such as daily rainfall, sunshine, humidity, and wind speed and direction which have been used to predict the occurrence of dengue. Though scientists have expended considerable effort to investigate these relationships between climatological variables along with vector indices and the occurrence of dengue, there is great variation in the description of these relationships (Bowman et al., 2014; Fan et al., 2014; Hii et al., 2016; Morin et al., 2013). Research into the specific environmental predictors of dengue has not been conducted in Saint Lucia leaving a lack of detailed information on the effect of climatological variables on the occurrence of dengue on the island. This study addresses this critical gap in the literature. I hypothesize that temperature, rainfall, wind speed, wind direction, humidity, and vector prevalence are associated with the occurrence of dengue in Saint Lucia.

Materials and Methods

A retrospective non-experimental, quantitative study using secondary data on dengue cases, vector surveillance generated by the Ministry of Health and climatological data generated by the Meteorological Office of Saint Lucia was undertaken to evaluate the relationship between temperature, rainfall, wind speed, wind direction, and humidity, as measured at weather stations on the island and vector prevalence at the district level, on the occurrence of dengue cases in Saint Lucia. The dependent or outcome variable for this study occurrence of dengue, was a categorical variable measured on a nominal scale, dengue positive or dengue negative, with suspect case not confirmed as dengue positive on PCR included in the negative case group. The environmental data included in this analysis represents the data collected regularly in Saint Lucia as part of normal environmental monitoring, The independent predictor variables in this model were monthly averages of daily rainfall, highest daily rainfall, cumulative monthly rainfall, no of rainy days, daily minimum temperature, daily maximum temperature, average daily temperature , relative humidity, windspeed, wind direction, daily sunshine; and monthly vector surveillance using the Breteau index (number of positive containers per 100 houses inspected), House Index (percentage of houses infested with larvae and/or pupae), and Container index (percentage of water-holding containers infested with larvae or pupae). The data for each environmental variable was matched with the month of case identification. The weather data in Saint Lucia is measured at two locations, one in the North and the in the south of the island, and the data used for the analysis was the arithmetic average of the respective values. The data was first analysed using descriptive statistics then the variables were subjected to chi-square analysis to test for independence, finally the data were analysed using logistic regression which was most appropriate statistical model to evaluate the relationship of independent variables and categorical outcome variables (Liu et al., 2014). Authors have used this methodology of combining chi-square analysis and logistic regression to provide a more thorough analysis of data (Akboğa Kale & Baradan, 2020; Kumar et al., 2014; Shrestha, 2019). To reduce overfit of the model, the variables were grouped into low, moderate, and high significance based on Cramer's V and the analysis of the moderate and high variables is presented here (Sun, Pang & Wang, 2010). The data were grouped on a nominal scale based on tertiles for the range of data. The full tables of analysis reports are presented in the appendix.

Results

During the period of 2009-2017, the Ministry of Health and Wellness Saint Lucia, recorded more than 2000 cases of disease that warranted investigation for dengue. Out of the 2035 reported cases, 1426 were confirmed as being dengue positive. Amongst the variables discussed in this manuscript the high percentages of dengue cases were observed during periods when the relative humidity fell between 75-80% (50.6%), the maximum daily temperature was greater than 32^{o}C(42.5%), maximum daily rainfall less than 45mm (40.5%) and the House Index was >10-20 % (64.4%) as seen in Table 1.

Table 7

The distribution of dengue cases and non-cases against environmental variables in Saint Lucia 2009-2017

Variable	**Dengue Positive**		**Dengue Negative**	
Wind Direction				
NNE Wind	1301	63.90%	492	24.20%
n = 2035				
Wind Speed (mph)				
Low (0-9)	433	24.10%	97	5.40%
Medium (>9-11)	541	30.10%	181	10.10%
High (>11)	328	18.30%	215	12.00%
n = 1795				

Sunshine (hours)				
Low (0-8)	741	36.50%	189	9.30%
Medium (>8-9)	484	23.80%	241	11.90%
High (>9)	196	9.70%	179	8.80%
n = 2030				
Highest Daily Rainfall (mm)				
Low (0-45)	823	40.50%	398	19.60%
Medium (>45-90)	554	27.30%	182	9.00%
High (>90)	44	2.20%	29	1.40%
n = 2030				
Monthly Cumulative Rainfall (mm)				
Low (0-100)	218	10.70%	189	9.30%
Medium (>100-200)	629	31.00%	227	11.20%
High (>200)	574	28.30%	193	9.50%
n = 2030				
Monthly Average Rainfall (mm)				
Low (0-10)	1370	67.60%	579	28.60%
Medium (>10-20)	43	2.10%	25	1.20%
High (>20)	7	0.30%	4	0.20%
n = 2028				
Number of Rainy Days				
Low (0-10)	82	4.00%	88	4.30%

Medium (>10-20)	973	48.00%	416	20.50%
High (>20) *n* = 2028	365	18.00%	104	5.10%
Minimum Daily Temperature (ºC)				
Low (0-16)	2	0.10%	0	0.00%
Medium (>16-20)	27	1.30%	9	0.40%
High (>20) *n* = 2030	1392	68.60%	600	29.60%
Maximum Daily Temperature (ºC)				
Low (0-30)	72	3.5%	37	1.80%
Medium (>30-32)	487	24.0%	314	15.50%
High (>32) *n* = 2030	862	42.5%	258	12.70%
Average Monthly Temp (ºC)				
Low (0-26)	2	0.10%	0	0.00%
Medium (>26-28)	349	17.20%	253	12.50%
High (>28) *n* = 2031	1071	52.70%	356	17.50%
Relative Humidity (%)				
Low (0-75)	142	7.0%	131	6.50%
Medium (>75-80)	1027	50.6%	417	20.50%
High (>80) *n* = 2030	252	12.4%	61	3.00%

House Index (percentage of houses infested with larvae and/or pupae)				
Low (0-10)	91	5.40%	41	2.40%
Medium (>10-20)	1079	64.40%	385	23.00%
High (>20)	39	2.30%	40	2.40%
n = 1675				
Container Index (percentage of water-holding containers infested with larvae or pupae)				
Low (0-15)	826	49.30%	222	13.30%
Medium (>15-30)	382	22.80%	240	14.30%
High (>30)	1	0.10%	4	0.20%
n = 1675				
Breteau Index (number of positive containers per 100 houses inspected)				
Low (0-25)	420	25.10%	214	12.80%
Medium (>25-50)	783	46.70%	241	14.40%
High (>50)	6	0.40%	11	0.70%
n = 1675				

The trends of the environmental conditions are shown in Figure 1 and rainfall is compared to dengue cases during the period of the study in Figure 2.

Figure 1. Key environmental data for Saint Lucia, from 2009-2017

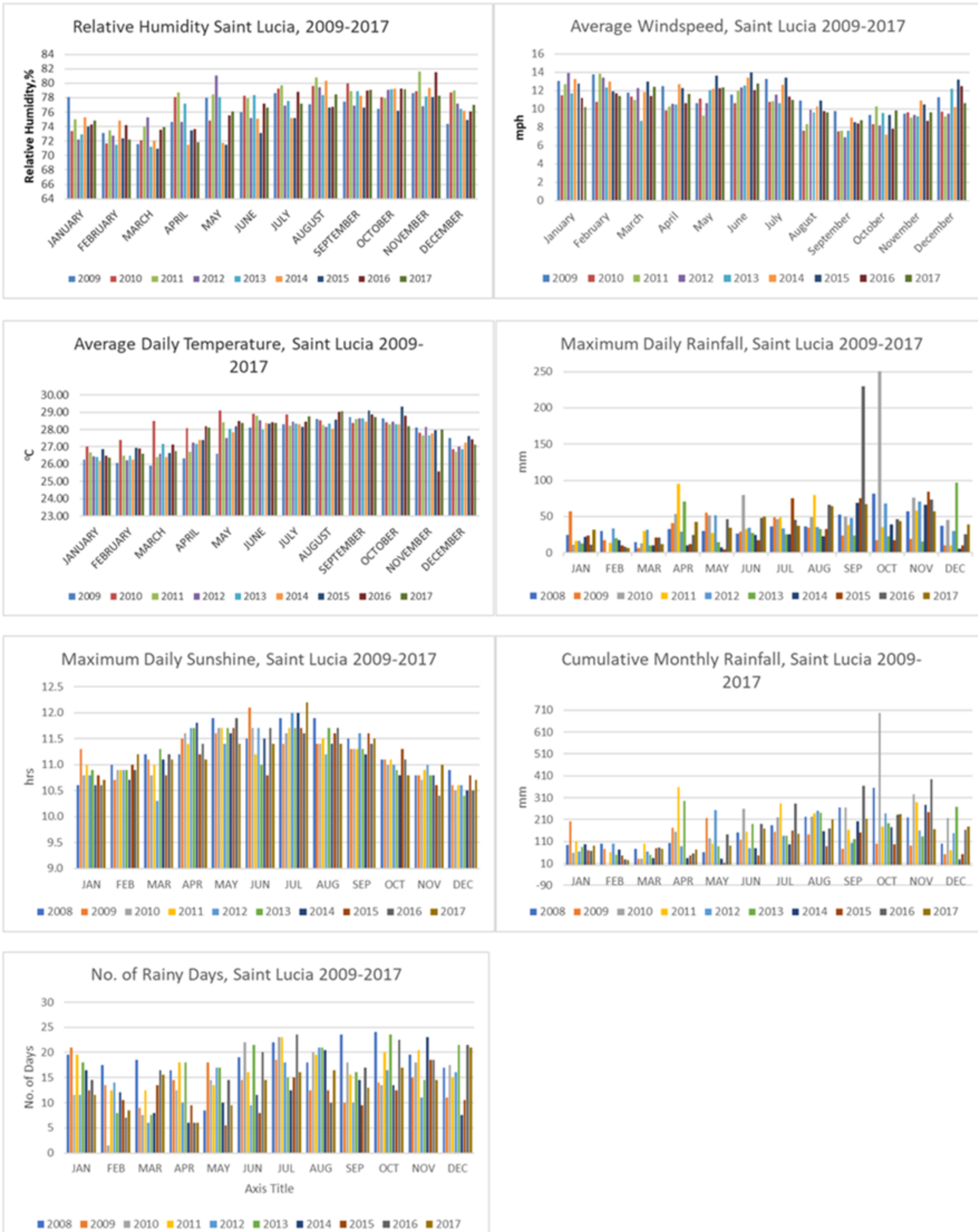
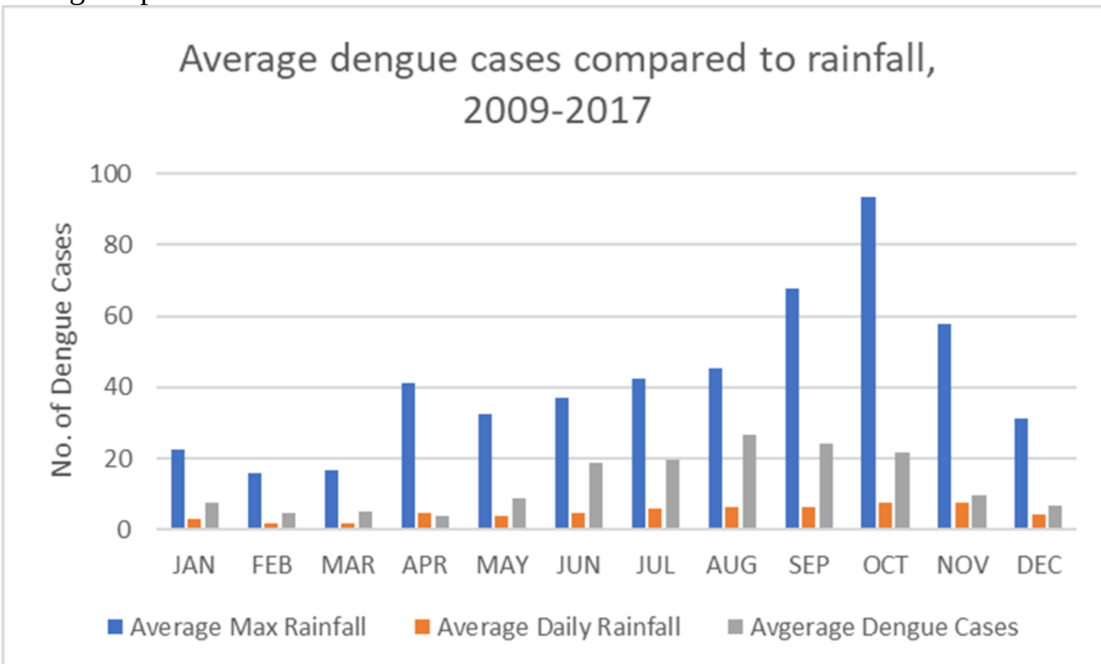
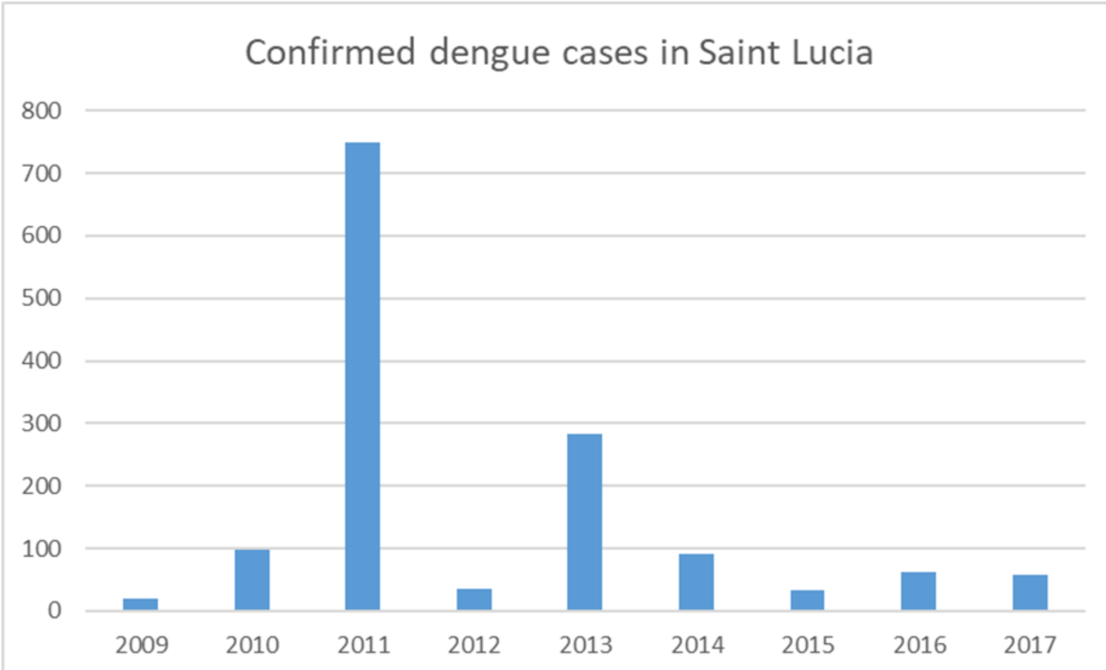


Figure 2. Average number of dengue cases in Saint Lucia compared to rainfall indices during the period 2009-2017



The highest number of confirmed cases occurred in 2011 with all of the districts across the island individually registering the highest number of cases that year with a total of 749 confirmed cases. There was also a second large outbreak in 2013 with 275 confirmed cases as demonstrated in Figure 3.

Figure 3. Confirmed dengue cases in Saint Lucia for the period 2009-2017



The peak in dengue outbreaks in the Americas were recorded 2015, 2013,2016, 2010 in descending order of magnitude, each year recording more than 1.5 million cases (Mitchell, 2020). This demonstrates that dengue has a different epidemiology in Saint Lucia compared to the rest of the Americas. The greatest number of dengue cases on average occurred during September and October each year if the two largest outbreaks are not included, including all the years during the study period shows the highest number of cases peaking in August, then September, and October respectively. The average monthly rainfall for the period of observation was 5.88 mm (Std 2.86), with an average high of 44.68 (Std 45.73) mm. Average daily temperatures of 28.03 ^{0}C (Std 0.074), average maximum temperatures of 29.40 ^{0}C (Std 0.85), and average minimum temperatures of 25.90 ^{0}C (Std 0.85). During the same period the monthly average relative humidity was 77.44% (Std 2.46) and the monthly average sunshine 8.33 hours (Std 0.66).

The monthly average wind direction was from an NNE direction and the monthly average 10.15 mph (Std 1.87). The vector indices recorded were limited to only 2011-2014 and 2017; during this time the monthly average Breteau Index of 27.67 positive containers per 100 houses (Std 12.35), House Index of 14.94% (Std 5.08), and Container Index 17.33 % (Std 6.31). In Saint Lucia during the period of observation the highest average rain fall occurred in the months of October and November, with the highest average and maximum temperatures occurring in September whereas the lowest average minimum temperature but highest average windspeed occurring in February. The highest average relativity humidity was measured during the month of August. The period of highest average daily sunshine occurred during the month of July.

The chi-square analysis of the data with zero lag indicates that most of the variables are associated with confirmed dengue cases as demonstrated in Table 2. This is valuable as this data is already collected as a part of the normal duties of the meteorological office and department of environmental health and is readily available for inclusion in future analyses.

Table 8

Chi-square of independence analysis of environmental variables and dengue in Saint Lucia

Variable	Value	Significance	Cramer's V
Zero Lag			
Wind Direction***[b]	44.446	0.000	0.148
Wind speed***[b]	64.521	0.000	0.19

Sunshine***[c]	16.948	0.000	0.223
Highest Daily Rainfall***[a]	16.948	0.000	0.091
Cumulative Monthly Rainfall***[b]	65.85	0.000	0.18
Monthly Average Rainfall[a]	1.774	0.412	0.030
Number of Rainy Days***[b]	52.044	0.000	0.160
Minimum Daily Temperature[a]	1.299	0.522	0.025
Maximum Daily Temperature***	58.966	0.000	0.170
Average Monthly Temperature***[b]	59.684	0.000	0.171
Relative Humidity***[b]	59.384	0.000	0.171
Monthly House Index***[b]	22.854	0.000	0.117
Monthly Container Index***[b]	65.664	0.000	0.198
Breteau***[b]	31.998	0.000	0.138
One Month Lag			
Wind Direction[a]	0.388	0.534	0.014
Wind Speed***[b]	75.733	0.000	0.194
Sunshine**[a]	12.024	0.002	0.077
Highest Daily Rainfall[a]	0.806	0.668	0.020
Cumulative Monthly Rainfall***[b]	49.048	0.000	0.156
Monthly Average Rainfall[a]	1.867	0.393	0.030
Number of Rainy Days***[b]	23.675	0.000	0.108
Minimum Daily Temperature[a]	1.559	0.459	0.028

Maximum Daily Temperature***[b]	63.945	0.000	0.178
Average Monthly Temperature**[a]	12.771	0.002	0.080
Relative Humidity***[a]	16.067	0.000	0.089
Monthly House Index**[a]	11.989	0.002	0.084
Monthly Container Index***[b]	28.853	0.000	0.131
Breteau**[a]	12.204	0.002	0.085

*p<.05, **p<0.01, ***p<.001

The table contains the chi-square analysis of the variables at a zero-lag and 1-month lag time interval.
[a]low significance, [b]moderate significance, [c]high significance, [d] non-significant result not considered in further analysis.

A logistic regression model indicated that windspeed, sunshine, cumulative rainfall, average daily temperature, and the vector indices House Index, Container Index and Breteau Index were good predictors of dengue cases. In an effort to reduce model over-fit the predictor variables were grouped as low, moderate, and high association based on a Cramer's V in this context of less than 0.100, between 0.100 and 0.200 or greater, and separate logistic models were run for each (Sun, Pang & Wang, 2010). These four logistic models generated had predictive capacities of 76.2% for the model with all of the variables, 70.0% for the model with variables of low association, 76.0% for variables with moderate association and 70.0% for the model with the variable of high association. A regression model without the vector indices had a predictive capacity of 73.9%. This indicates that vector indices help to better explain the occurrence of dengue in Saint Lucia.

The logistic model of variables at zero-lag with a moderate association with dengue demonstrated that maximum daily temperature of > 32^{o} C had the strongest positive significant relationship (*p*= .011, OR 3.350 [CI 1.312-8.555]). The other significant positive values were monthly House Index >10-20% and Breteau Index >25-50 positive containers per 100 houses. Windspeed >11mph had the strongest significant negative relationship (*p*< .001, OR 0.222 [CI 0.133-0.370]). The other significant negative variables were monthly cumulative rainfall increasing across categories with highest association >200mm, average monthly temperature >28^{o}C, and Container Index >15-30% as seen in Table 5. Daily Sunshine was the only variable with a high association with dengue based on Cramer's V, 0.223. The logistic regression model with sunshine revealed a negative significant relationship that increased as the number of hours of sunshine increased with >9 hrs. sunshine per day having the strongest relationship (p<.001, OR 0.279 [CI 0.216-0.361]).

Table 9.

Logistic regression of environmental predictive variables with moderate and high association with dengue at zero- and one- month lags Saint Lucia 2009-2017

								95% C.I. for EXP(B)	
		B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(B)**	**Lower**	**Upper**
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	-0.081	0.263	0.095	1	0.757	0.922	0.550	1.544
	High (>11)***	-1.507	0.262	33.132	1	0.000	0.222	0.133	0.370
	Monthly Cumulative Rainfall (mm)								
Ref.	Low (0-100)								

	Medium (>100-200)**	-1.110	0.359	9.546	1	0.002	0.330	0.163	0.666
	High (>200)**	-1.234	0.430	8.261	1	0.004	0.291	0.125	0.675
	Number of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)	-0.021	0.284	0.005	1	0.941	0.979	0.562	1.707
	High (>20)	0.567	0.411	1.907	1	0.167	1.763	0.788	3.943
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)								
	Medium (>30-32)	-0.110	0.333	0.110	1	0.741	0.896	0.467	1.719
	High (>32)*	1.209	0.478	6.389	1	0.011	3.350	1.312	8.555
	Average Monthly Temperature (ºC)								
Ref.	Medium (>26-28)								
	High (>28)**	-0.911	0.274	11.074	1	0.001	0.402	0.235	0.688
	Relative Humidity %								
Ref.	Low (0-75)								
	Medium (>75-80)	0.522	0.316	2.735	1	0.098	1.686	0.908	3.129
	High (>80)	-0.167	0.396	0.177	1	0.674	0.846	0.389	1.841
	House Index %								
Ref.	Low (0-10)								
	Medium (>10-20)**	0.907	0.285	10.151	1	0.001	2.476	1.417	4.324
	High (>20)	0.044	0.484	0.008	1	0.928	1.045	0.404	2.699
	Container Index %								
Ref.	Low (0-15)								

	Medium (>15-30)***	-1.166	0.197	34.933	1	0.000	0.312	0.212	0.459
	High (>30)	-1.021	1.347	0.575	1	0.448	0.360	0.026	5.049
	Breteau Index								
Ref.	Low (0-25)								
	Medium (>25-50)***	0.872	0.211	17.114	1	0.000	2.392	1.583	3.617
	High (>50)	0.105	0.754	0.019	1	0.890	1.111	0.253	4.872
	1 Month Lag								
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	0.068	0.211	0.106	1	0.745	1.071	0.709	1.618
	High (>11)	-0.396	0.239	2.740	1	0.098	0.673	0.421	1.076
	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)								
	Medium (>100-200)	0.216	0.216	0.994	1	0.319	1.241	0.812	1.897
	High (>200)	0.201	0.243	0.685	1	0.408	1.223	0.759	1.969
	Number of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)	0.227	0.258	0.773	1	0.379	1.255	0.757	2.081
	High (>20)	-0.044	0.313	0.019	1	0.889	0.957	0.518	1.768
	Maximum Daily Temperature (ºC)								

Ref.	Low (0-30)								
	Medium (>30-32)	0.240	0.251	0.915	1	0.339	1.272	0.777	2.08
	High (>32)**	0.832	0.304	7.495	1	0.006	2.297	1.267	4.167
	Container Index %								
Ref.	Low (0-15)								
	Medium (>15-30)**	-0.411	0.129	10.187	1	0.001	0.663	0.515	0.853
	High (>30)*	-1.603	0.666	5.797	1	0.016	0.201	0.055	0.742
	High Significance								
	Sunshine (hours)								
Ref.	Low (0-8)								
	Medium (>8-9)***	-0.669	0.113	34.810	1	0.000	0.512	0.410	0.640
	High (>9)***	-1.276	0.132	93.886	1	0.000	0.279	0.216	0.361

*p<.05, **p<.01,***p<0.001

The data with a lag of one month was first analyzed using chi-square analysis as seen in Table 2. The regression model of the environmental data at a lag of one month as represented in Table 3 shows that relative humidity >80% when compared to the reference category of 0-75%, had the strongest significant relationship with dengue cases (p<.001, OR 0.100 [CI 0.046-0.214]). This was a negative relationship. The model of moderately associated variables demonstrated that maximum daily temperature > 32^{o}C (p=0.006, OR 2.297 [1.267-4.167]) had a positive relationship with dengue whereas Container had an increasingly negative relationship with dengue, as seen in Table 3.

The environmental variables were also analyzed without the vector indices because this data was limited to five of the nine years under analysis, The logistic regression for this data demonstrated that at the zero-lag time frame none of the variables had a positive relationship with dengue and sunshine had the strongest negative relationship with the strength increasing as the number of hours of sunshine increased. The strongest relationship occurred at >9hrs (*p*< .001, OR 0.154 [0.086-0.276]). At the 1-month time lag interval relative humidity was found to have a strong negative relationship with the occurrence of dengue >80% (*p*<.001, OR 0.197 [0.104-0.371]). Maximum daily temperature had a positive relationship with dengue occurrence (*p*=.022, OR 2.120 [1.114-4.035]).

The analysis of the variables without vector indices of moderate significance on Cramer's V as seen in Table 4 demonstrated that at the zero-lag time interval maximum daily temperature had the strongest positive relationship with dengue outcomes at >30-32^{o}C (*p*=0 .010, OR 2.014 [1.180-3.437]). The number of rainy days >20 had a significant negative relationship with dengue outcome at a zero-lag time interval as seen in Table 4. Windspeed was found to have a positive relationship with dengue outcomes at the zero-lag tie interval >11 MPH (*p*=0.004, OR 1.817 [1.204-2.742]) but a negative relationship at 1-month lag time interval >11MPH (*p*=0.003, OR 0.543 [0.365-0.807]).

Table 10

Logistic regression of environmental predictive variables with moderate significance (without vector indices) and dengue at zero- and 1- month lags in Saint Lucia 2009-2017

							95% C.I. for OR	
	B	**S.E.**	**Wald**	**df**	**Sig.**	**OR**	**Lower**	**Upper**
Wind Direction								

Ref.	ENE								
	NNE	-1.031	1.441	0.511	1	0.475	0.357	0.021	6.015
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	0.184	0.205	0.802	1	0.370	1.202	0.804	1.798
	High (>11)**	0.597	0.210	8.086	1	0.004	1.817	1.204	2.742
	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)								
	Medium (>100-200	-0.151	0.251	0.364	1	0.546	0.860	0.526	1.406
	High (>200)	-0.063	0.268	0.056	1	0.814	0.939	0.555	1.588
	Number of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)	-0.360	0.237	2.311	1	0.128	0.698	0.439	1.110
	High (>20)**	-0.957	0.309	9.579	1	0.002	0.384	0.210	0.704
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)								
	Medium (>30-32)*	0.700	0.273	6.585	1	0.010	2.014	1.180	3.437
	High (>32)	0.060	0.360	0.027	1	0.869	1.061	0.524	2.150
	Average Monthly Temperature (ºC)								
Ref.	Low (0-26)								
	Medium (>26-28)	21.531	28517.096	0.000	1	0.999	2243258150.428	0.000	
	High (>28)	21.479	28517.096	0.000	1	0.999	2129047833.398	0.000	
	Relative Humidity (%)								
Ref.	Low (0-75)								
	Medium (>75-80)	0.005	0.257	0.000	1	0.986	1.005	0.607	1.662
	High (>80)	-0.241	0.342	0.495	1	0.482	0.786	0.402	1.537
	1 Month Lag								

	Windspeed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	-0.098	0.177	0.307	1	0.579	0.907	0.642	1.282
	High (>11)**	-0.611	0.202	9.121	1	0.003	0.543	0.365	0.807
	Cumulative Monthly Rain (mm)								
Ref.	Low (0-100)								
	Medium (>100-200)	0.300	0.183	2.691	1	0.101	1.350	0.943	1.931
	High (>200)	0.216	0.205	1.106	1	0.293	1.241	0.830	1.856
	No of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)	0.277	0.215	1.665	1	0.197	1.319	0.866	2.010
	High (>20)	0.056	0.262	0.046	1	0.831	1.058	0.632	1.769
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)								
	Medium (>30-32)	-0.143	0.228	0.396	1	0.529	0.867	0.555	1.354
	High (>32)	0.287	0.267	1.155	1	0.282	1.332	0.790	2.247

p*<.05, ***p*<.01,**p*<0.001

Discussion

This author identified that windspeed had the strongest significant relationship with dengue cases. This relationship, as identified in the model of variables with moderate association with dengue including vectors at zero-lag time interval, was negative which suggests that as wind speeds increase there is a reduced likelihood of dengue cases which is probably related to the unfavorable conditions for mosquito host interaction because the small insects would unlikely to be able to fly in such conditions. High sustained winds may also serve to reduce suitable habitats for mosquito reproduction and survival, decreasing both humidity and moisture and thus serve to lower the incidence of dengue through decreased vector populations. The model without vector indices indicated positive relationship with wind at a zero-lag interval but then a negative relationship at the 1-month lag interval. This may underscore that dengue outcomes in Saint Lucia are truly a result of the interaction of multiple factors and that the results of the analysis including vector indices may obscure the true relationships of dengue because there was limited data in this instance. If so, the positive relationship at the zero-lag interval may indicate the driving of the mosquito indoors to avoid unfavorable conditions noting that the Aedes aegypti prefers to remain indoors close to their target hosts (Carrington & Simmons, 2014). Cumulative rainfall also had a similar negative relationship with dengue and may again suggest that too heavy a rainfall may reduce mosquito host interaction in the inclusive model. Interestingly the relationship between Container Index and dengue was found to be negative in both the zero and one month lag models, which may suggest that if persons identify containers infested with mosquito life stages, these are likely removed, therefore eventually leading to a decrease in the mosquito population within the home and reduced risk of disease transmission.

Environmental variables have been extensively linked to the epidemiology of dengue including temperature and rainfall, temperature being linked to both the mosquito vector and the dengue virus itself (Amarakoon et al., 2008; Banu et al., 2014; Cheong et al., 2013; Estallo et al., 2015). The peak occurrences of dengue appear earlier in Saint Lucia than represented in previous research, August to October as compared to October to December (Amarakoon et al., 2008). In the current study evaluation of the relationship of environmental variables and vector indices yielded mixed results to the nature of their relationship with dengue. The chi-square analysis of the data revealed that all of the variables included in this study were significantly associated with confirmed dengue cases with the exception of average daily rain fall and minimum daily temperature. Since no published work was identified analyzing such data for Saint Lucia, this author first investigated the relationships with zero lag and a lag of one month which would account for the vectors average three week cycle, future studies should include various lag intervals that would accommodate possible alterations in mosquito reproductive cycles due to environmental factors though other authors have suggested a variety of lag times (Amarakoon et al., 2008; Hii et al., 2012; Ramachandran et al., 2016). The analysis of data with one a one month lag indicated a slight change with the variables having an association with dengue, in the zero lag model minimum daily temperature and average monthly rainfall were not found to have a significant association with dengue, in the one month lag model more of the variables were not found to have a significant relationship with dengue. Both daily sunshine and monthly cumulative rainfall also had negative relationships with the strength of association increasing as the measure increased. This may indicate that the more harsh the condition the less hospitable it is to the vector population either through destruction of mosquito habitats or the eggs and the juvenile forms of the vector which are more sensitive to environmental conditions (Chadee & Martinez, 2016). The positive relationship with House Index and Breteau Index demonstrates that the presence of the different life stages of the vector can be used to predict the occurrence of dengue in member of the house hold. The relationship could also be a result of a lack of adequate data, future studies will require greater data collection to give an accurate reflection of this relationship in Saint Lucia.

The increased cumulative rainfall and monthly temperatures may negatively affect the mosquito vector population similar to the effect of increased windspeed discussed previously, because eggs and larvae exposed to these elements may be washed away or destroyed by the high temperatures to which they are sensitive (Chadee & Martinez, 2016). The negative relationship between windspeed and container index support the outcomes of the first model incorporating all of the variables. The logistic model with sunshine as the only variable with a strong association with dengue outcome provided support for the first model which incorporated all of the variables, showing a negative relationship with dengue, underscoring that large amounts of sunshine may lead to decreased mosquito populations because of the effect of ultra violet (UV) radiation (Swain et al., 2008). However, some authors suggest it is not necessarily the light but rather the accompanying heat and general dry conditions that lead to decreases in mosquito populations during increased periods of sunlight. Also Aedes, prefer to oviposition in low light environments so increased sunlight may directly decrease ovipositioning behavior (Blasius et al., 2019).

The maximum daily temperature was found to have a positive relationship with dengue and is supported by the scientific research which demonstrates that heat is important to the mosquito vector’s life cycle (Amarakoon et al., 2004; Marinho et al., 2016; Watts et al., 1987). Ideal environmental conditions have been found to shorten the life cycle of the mosquito, allowing greater fecundity of the vector and increased temperature can possibly lessen the extrinsic incubation period (Thai & Anders, 2011; Watts et al., 1987).Though authors have suggested a correlation between El Niño events and dengue outbreaks of the 2010/11, 2011/12, and 2014-2016 El Niño events in the Caribbean only 2011 event matches with a large outbreak of dengue in Saint Lucia, which was also the largest outbreak during the period of study.

The logistic regression model with a lag of one month showed similar relationships as the zero-lag mode with some exceptions. Maximum daily temperature which was not significant in the zero-lag logistic regression model became a positive predictor, which may demonstrate the effect on the vector life-cycle and delayed increase in dengue cases. Likewise cumulative rainfall changed from a negative to positive predictor and number of rainy days from no relationship to positive one both again supporting the effect of environmental factors on the life cycle of mosquitoes and subsequent disease transmission (Kajeguka et al., 2017; Zellweger et al., 2017). Further studies should be done describe the biology of the Aedes mosquito in Saint Lucia. Container index moved from negative to no relationship and House Index moved from positive to no relationship which may indicate their limited use in lagged models.

The relationships between environmental variables and the occurrence of dengue continue to be of a mixed nature with rainfall and temperature variables shown to have a positive relationship with dengue at a lag of one month whereas sunshine, and the vector indices House Index and Breteau index having a negative relationship with dengue supporting the assumptions made earlier in this manuscript. Maximum daily temperature had the strongest positive association with dengue, which may support the supposition that temperature has a positive effect on vector biology such as decreases hatching time, and shorter life cycles along with a positive effect on the virus extrinsic incubation period leading to increased risk of dengue transmission as demonstrated by Watts et al., (1987). Likewise average monthly rainfall also had a positive relationship with dengue cases, which reflects the concept that moisture or rainfall is an important factor to the development through the different stages of the mosquito life cycle by providing the appropriate habitat (Valdez et al., 2017). Rainfall was significant at >45-90mm but >90mm was not significantly associated with dengue, and this would suggest that higher levels of rainfall could see the destruction of habitats for oviposition and maturation of the mosquito vector.

This study had a number of limitations, the data on the vector indices were limited in the number of years of observation, having more detailed data, and expansive vector data would allow better analysis of their relationships with dengue in Saint Lucia. In addition, there were limitations of the case data that did not allow each case to be tied to exact environmental conditions experienced by the individual at time of infection. Also, environmental data was available only at two physical locations on the island which limits the ability to link cases to specific environmental conditions. The non-randomized identification of cases may also affect the analysis of the true relationship between predictors and dengue in Saint Lucia. The operationalization of variables may introduce error in the outcomes realized, and warrants continued analysis of the relationship between environmental variables and dengue outcomes. The significant association with all three vector prevalence indices and dengue even though limited data from these were available should encourage authorities to expand their vector surveillance program. I would also suggest that the results of this surveillance be made public because this information seemingly generates attention among the population and positive action to remove the different life stages of the vector. Additional research to determine the effect of lag-time on the relationship between environmental variables and dengue is to determine the Saint Lucian context of this relationship.

Whereas, there has been significant data published on this phenomenon, none has focused on Saint Lucia, and as shown within this study there are local variations which would necessitate slightly different approaches than provided by generalized data; it was demonstrated that the specific range of rainfall >45-90mm and temperatures warmer than 32^{o}C were associated with dengue cases. Prevention of dengue cases through the application of these data, will have a significant social implication by reducing the morbidity, mortality and loss of productivity from persons withing the population becoming infected. In a small-island developing state minimizing healthcare costs because general public healthcare is not provided, is a major winning outcome because these resources can be redirected to other challenges withing the country.

Conclusions

This study has demonstrated that some environmental variables including windspeed >11MPH, and rainfall >100mm are negatively linked to the occurrence of dengue in Saint Lucia whereas temperature >32^{o}C has a significant positive relationship. Further analysis with more granular data is needed to better understand these relationships and how this information can be used to improve public health outcomes related to dengue.

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Syndromic Health Surveillance Markers Associated With Dengue Fever in Saint Lucia

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Outlet

Emerging Infectious Disease journal is a resource dedicated to promoting the significance of emerging and re-emerging infectious diseases and also focuses on the epidemiology and management of these diseases. Dengue has been recognized as an important infectious disease and as such the outcomes of the study investigating the clinical risk factors associated with the occurrence of dengue is well aligned with the purpose of this journal.

Abstract

Vector-borne diseases are becoming more important in the face of climate change and conditions that favor the wider spread of their vectors and their endemicity in naïve populations. One of the most important vector-borne diseases is dengue, accounting for almost 400 million cases each year. This study provides an analysis of the relationship between regularly collected surveillance data and dengue cases in Saint Lucia, which may contribute to earlier diagnosis of these cases. It was found that undifferentiated fever 2.53 ($p < .001$, OR 2.060 [CI 1.623-2.597]), acute respiratory infections or fever with respiratory signs 5.250 ($p < .001$, OR 5.250 [CI 3.559-7.745]), and gastroenteritis 1.622 ($p < .001$, OR 1.617 [CI 1.036-2.526]) were significantly more likely to have positive cases of dengue. This data can be used to help clinicians more quickly identify suspect dengue cases specifically in the Saint Lucian context, potentially leading to improved health outcomes.

Introduction

Dengue remains one of the most significant public health challenges in the developing world and its global footprint continues to grow with an estimated 2.5 billion persons at risk of infection every year with an estimated 390 million cases occurring each year (Bhatt et al., 2013; Zhang et al., 2015). The Pan American Health Organization reported more than 3 million cases of dengue in the Americas in 2019, the highest number ever recorded in that region (Mitchell, 2019; Mitchell, 2020). Though many rapid bed-side diagnostic tests have been developed, these remain expensive with questioned sensitivity leading to a slow uptake of this technology. The most reliable methods of diagnosing dengue remain laboratory testing such as reverse transcription-PCR (RTPCR), which also poses a challenge due to the resources required to implement such testing and as such most clinical diagnosis remains the foundation of the management of the disease in most endemic areas (Bhatt et al., 2013; Gan et al., 2014; Wang & Gubler, 2018) .

The small islands of the Eastern Caribbean are among the countries that are endemic for the arboviral disease, dengue. Though the disease is not normally associated with a high level of mortality, its burden of disease is typically associated with loss of productivity from missing work or school days and the associated costs of outbreak response (Karunakaran et al., 2014; Laserna et al., 2018; Murray et al., 2013) . These costs are substantial to the economies of small island developing states such as Saint Lucia, with economies largely dependent upon tourism and facing the effects of climate.

Saint Lucia is a small, English-speaking island nation of the Eastern Caribbean. It is neighbored by Martinique to the north, Barbados to the east, and Saint Vincent and the

Grenadines to the south. The island is approximately 14 miles wide by 27 miles long (Gaspard & Yang, 2016) and is volcanic with rugged mountain features and rain forests in the central region of the country (Malumphy, 2014). The estimated population of Saint Lucia is 165,000. The population is divided 48.7 % and 51.3% male and female respectively, with ages as follows: 0-14 years: 20.02% (male 17,006/female 16,027), 15-24 years: 15.37% (male 12,870/female 12,492), 25-54 years: 42.97% (male 34,117/female 36,779), 55-64 years: 9.99% (male 7,608/female 8,881), 65 years and over: 11.65% (male 8,704/female 10,510, 2017) (*The World Factbook—Central Intelligence Agency*, 2018). Outbreaks of dengue pose a severe threat to the island that is heavily dependent on its human resource. Any outbreak of disease is further compounded because large numbers of the population do not have private health insurance nor is there a national insurance program, which forces most persons to pay for health care out of pocket.

Dengue fever is manifested as a flu-like illness with high fever, pain behind the eyes, headache, myalgia, and arthralgia, nausea, vomiting, swollen lymph nodes, or rash (Kumar et al., 2018; Muller et al., 2017). The disease on average will last for 2 to 7 days following an incubation period of 4 to 10 days after being infected by the mosquito vector (Morin et al., 2013; Patterson et al., 2016). In 2009, the World Health Organization revised the classification of dengue from dengue fever, dengue hemorrhagic fever, and dengue shock syndrome into dengue fever with and without warning signs, and severe dengue in an attempt to reduce misclassification of dengue cases that led to inappropriate case management.

There is still debate about the effectiveness of the new classification, which is used in Saint Lucia, though globally many researchers and public health officials still use the older classification or have adjusted the 2009 classification to meet individual local needs (Horstick et al., 2015). Severe dengue is described by persistent vomiting, abdominal pain, rapid breathing and respiratory distress, bleeding gums, hematemesis, tiredness, plasma leaking from blood vessels, fluid accumulation, severe bleeding, and organ failure (Aung et al., 2013; Naish et al., 2014; Van Kleef et al., 2009; H. Zhang et al., 2014). The wide variety of clinical signs that could be associated with dengue sometimes leads to delays in diagnosis or even misdiagnosis, and identifying those clinical indicators associated with dengue in Saint Lucia potentially mitigates such occurrences.

Public health agencies rely upon the early detection of dengue cases by clinicians in an attempt to recognize possible outbreaks and initiate management and control measures. Current rapid diagnostic tests rely on identification of antibodies through ELISA tests or the recognition of nonstructural proteins such as NS-1. These tests along with newer genetic based test such as microfluidic or microarray tests are expensive or have limited accuracy, which reduces their effectiveness (Bhatt et al., 2013; Gan et al., 2014; Muller et al., 2017).

In Saint Lucia, the diagnosis of dengue relies upon a clinical diagnosis which then triggers laboratory testing, first using rapid test for NS-1 antigens secreted from infected cells, which is done locally, then PCR testing which is done at the regional CARPHA laboratory. According to CARPHA recommendations, the NS-1 test has to be done within 7 days of onset of dengue, and the PCR must be done within 3 days of onset. This underscores how important it is to identify a suspect case based on clinical presentation. After 7 days, antibody testing is recommended because IgM should be in production by the body, and likelihood or recovering the virus is decreased (Guzman & Harris, 2015). The clinical diagnosis of a probable case of dengue is based on a person presenting with acute onset of fever and two or more other symptoms including, headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, and supportive serology.

The dengue preventive practices implemented in Saint Lucia are integrated focusing heavily on vector control through fogging to kill adult mosquitoes, larvicides, and also a public health awareness campaign that is run from May to November each year. The general public awareness campaign which starts off with a vector awareness week that has been adopted by CARPHA because of its success after first starting in Saint Lucia, as well as a focus on dengue as a disease (G. Chery, personal communication April 26, 2020).

This underscores the importance of accurate clinical diagnoses of dengue cases based upon recognition of clinical signs. In an attempt to improve surveillance programs many public health agencies have transitioned to syndromic surveillance where individual and population health data are collected and analyzed to identify diseases as quickly as possible, and facilitate the appropriate management strategies. Some of the health indicators collected regularly through syndromic surveillance in Saint Lucia are undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis. These clinical indicators are nonspecific to any one disease, however identifying which indicators are associated with dengue will allow clinicians to place the disease higher on the differential diagnoses list therefore possibly facilitating the early initiation of the correct treatment when dengue is involved. Data on the relationship between clinical indicators used in syndromic surveillance specific to Saint Lucia has not been published. Therefore, the analysis of clinical data from Saint Lucia allows the determination between these clinical indicators and the occurrence of dengue specifically in the local context of the island and potentially provides information that will improve patient outcomes related to dengue.

Researchers have recognized that infectious diseases are affected by the complex relationship of factors including host, agent and environmental, from the genetic level to higher level interactions such as economic and social (Zuckerman et al., 2014). The ecological theory provides the foundation for this study allowing the framework to answer if there are relationships between the clinical indicators undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis and the occurrence of dengue in Saint Lucia. The theory treats all relationships as equally important improving the ability to analyze complex relationships of sometimes disparate variables (Ngonghala et al., 2014).

The purpose of this study is to provide analysis of data that potentially will address the current gap in the literature that does not provide information on clinical risk factors specific to Saint Lucia using syndromic data. I hypothesize that there is a significant relationship between the clinical variables undifferentiated fever, acute respiratory infection or fever and respiratory symptoms (ARI or FRS), fever with hemorrhagic symptoms (Fever with HS), fever and neurological symptoms (fever and NS), and gastroenteritis and dengue fever in Saint Lucia.

Materials and Methods

The relationship between clinical variables; undifferentiated fever; acute respiratory infection or fever and respiratory symptoms (ARI or FRS); fever with hemorrhagic symptoms (Fever with HS); fever and neurological symptoms (fever and NS); and gastroenteritis and the occurrence of dengue in Saint Lucia was evaluated using a quasi-experimental study using descriptive analysis of the data, chi-square tests of independence followed by logistic regression of secondary data. These variables were measured as presence or absence of the condition. This retrospective study design was especially appropriate in this instance negating the need to interact with patients in addition, such a design help to accelerate the study process. These data were accessed from the Ministry of Health infectious disease surveillance database, 2009 to 2017. Ethical approval was granted from Walden University, the Medical and Dental Saint Lucia Council, Saint Lucia and the Ministry of Health and Wellness, Saint Lucia. For the purpose of analysis, the data was separated into confirmed dengue cases and non-dengue cases which included negative cases and suspect cases that did not test positive then subjected to chi-square and logistic regression analysis.

Results

The data from the Ministry of Health and Wellness contained 2035 cases of persons that were tested for dengue from 2009 to 2017, in Saint Lucia. Of these 2035 cases 1426 were confirmed as being dengue positive the prevalence of dengue during the study period is demonstrated in Figure 1. From the clinical presentations included in regular surveillance of patients the proportion confirmed with dengue were , 67.3% of those presenting with Undifferentiated Fever, 41.2% of those with ARI/FRS, 62..5% of those with Fever with Hemorrhagic Signs, 80.o% of those with Fever with Neurological Signs and 60% of those with Gastroenteritis as represented in Table 1.

Table 11 *Distribution of Syndromic predictors across cases in Saint Lucia 2009-2017*

Variable	Dengue Positive		Dengue Negative	
Undifferentiated Fever *n* = 1394	938	67.3%	456	32.7%
Acute Respiratory Illness/Fever with Respiratory Signs *n* = 131	54	41.2%	77	58.80%
Fever with Hemorrhagic Signs *n* = 16	10	62.5%	6	37.5%
Fever with Neurological Signs n = 15	12	80.0%	3	20.0%
Gastroenteritis *n* = 90	54	60.0%	36	40.0%

Chi-square analysis of the data revealed that there was an association with confirmed dengue cases α=0.05 with undifferentiated fever $\chi(1)$ = 16.732, p = .000, acute respiratory infections or fever with respiratory symptoms $\chi^2(1) = 55.581$, $p = .000$ and gastroenteritis $\chi^2(1) = 4.557$, $p = .033$; whereas fever with hemorrhagic symptoms $\chi^2(1) = 0.441$, $p = .507$, and fever with neurologic symptoms $\chi^2(1) = 0.710$, $p = .399$ did not demonstrate any association with confirmed dengue cases seen in Table 2. The logistic regression model was statistically significant, $\chi^2(5) = 94.381$, $p < .0005$ with a Hosmer and Lemeshow Goodness of Fit Test $\chi^2(3) = 4.30$, $p =.231$ indicating that the model was a good fit. The model explained 4.5% (Cox & Snell R2) to 6.4% (Nagelkerke R^2) of the variance in dengue cases and correctly classified 71.2% of cases. Though the current system identifies approximately 70%, not all of the cases are definitively classified based on PCR. The study model indicates the accuracy of the system can be improved. Dengue cases, as demonstrated in Table 3., were 2.53 (*p*<.001, OR 2.060 [CI 1.623-2.597]) times more likely to have undifferentiated fever, 5.250 (*p*<.001, OR 5.250 [CI 3.559-7.745]) times more likely to have acute respiratory infections or fever with respiratory signs and 1.622 (*p*<.001, OR 1.617 [CI 1.036-2.526]) times more likely to have gastroenteritis than negative cases of dengue.

Table 12 *Chi-square Analysis of clinical risk factors for dengue in Saint Lucia 2009-2017*

Variable	**Value**	**Significance**	**Cramer's V**
Undifferentiated Fever***	16.372	0.000	0.090
Acute Respiratory Illness/Fever with Respiratory Signs***	55.581	0.000	0.165
Fever with Hemorrhagic Signs[d]	0.441	0.507	0.015

Fever with Neurological Signs[d]	0.71	0.399	0.019
Gastroenteritis*	4.557	0.033	0.047

*p<.05, **p<.01, ***p<.001

[d] Non-significant result not included in further analysis

Table 13

Logistic regression model of clinical risk factors and dengue in Saint Lucia 2009-2017

							95% C.I. for O.R.	
	B	**S.E.**	**Wald**	**df**	**Sig.**	**O.R.**	**Lower**	**Upper**
Undifferentiated fever ***	0.719	0.120	36.033	1	0.000	2.053	1.623	2.597
ARI or FRS Positive***	1.658	0.198	69.875	1	0.000	5.250	3.559	7.745
Gastroenteritis Positive*	0.481	0.227	4.468	1	0.035	1.617	1.036	2.526

References for each category are negative cases

*p<.05, **p<0.01, ***p<.001

Discussion

Of the clinical variables regularly documented by the health services in Saint Lucia acute respiratory infections or fever with respiratory signs (ARI/FRS) had the strongest significant association with confirmed dengue cases. Respiratory symptoms and pulmonary involvement though possible with severe dengue because of vascular leakage are not among the most common clinical sign of the disease and the high association in this data-set is an important outcome that suggests further investigation is warranted (Beltrán-Silva et al., 2018; Prusty & Momin, 2019; Rodrigues et al., 2014). These non-pathognomonic clinical signs present a significant challenge during the flu-season when dengue cases may go undiagnosed and untreated leading to severe and even life threating outcomes. Under the current syndromic disease diagnosis flowchart in Saint Lucia, dengue is not included among the suggested differentials, and the result of this study suggests that dengue should be on this list (National Communicable Disease Manual, 2006). Undifferentiated fever is one of the most commonly clinical symptoms attributed to dengue, and the Saint Lucia data supports this clinical relation. This is important in the local context and gives clinicians confidence to include dengue in the differential diagnosis list and supports further evaluation of cases in an attempt to institute early management where possible. The data also indicated that gastroenteritis is a significant predictor of dengue in Saint Lucia, which could be related to nausea, vomiting, and diarrhea that have been associated with dengue cases in other countries (Guzman & Harris, 2015; Muller et al., 2017; Woon et al., 2016). According to the syndromic diagnosis flow chart from the National Communicable Disease Manual, dengue is not listed as one of the suggested differential diagnoses for cases presenting with gastroenteritis; the results of this study suggest that it should be a consideration (National Communicable Disease Manual, 2006). Fever with hemorrhagic symptoms and fever with neurological symptoms did not prove to be significantly associated with dengue in Saint Lucia though other studies have indicated these clinical signs to be associated with dengue infections (Carod-Artal et al., 2013).

In the Caribbean the restricted availability of the diagnostic platforms such as DENV multiplex RT-qPCR assays, pose a challenge to rapid diagnosis of dengue cases. These restricted resources means that physicians rely on the symptomatic diagnosis of the disease to initiate early treatment (Choi et al., 2017; Cleton et al., 2015; Tang & Ooi, 2012). The more common clinical signs of dengue include fever, skin rash, headache, vomiting, diarrhea and flu-like symptoms including cough, sore throat, and malaise (Guzman & Harris, 2015; Muller et al., 2017). Although these clinical signs are among common symptoms associated to dengue, local variation is known to exist, and this study supports signs important within the Saint Lucian context (Laserna et al., 2018; Wijayanti et al., 2016). Identifying those variables that are associated with dengue in Saint Lucia may provide additional benefits to clinicians in managing patients. Acute respiratory failure, though not common, has been associated with dengue in particular the severe form of the disease and may be a particular characteristic of dengue in Saint Lucia (Cheng et al., 2017; Yacoub et al., 2017).That neither clinical presentation of fever with hemorrhagic or neurological signs were found to be associated with confirmed dengue cases in Saint Lucia may be attributed to the difficulty to diagnose these symptoms when patients presented. The lack of association with fever with hemorrhagic signs may also indicate the difficulty in identifying such clinical signs in persons of darker skin. The reduced description of these clinical signs may suggest the need to remind physicians of their association with dengue and encourage their heightened observations during clinical exams for these less recorded signs (Waterman et al., 2015).

In addition to the important continuing education programs for members of the health care profession focusing on the epidemiology of dengue in Saint Lucia, it would be prudent to also provide educational programs for the public geared at raising awareness of what are likely local clinical signs of dengue especially ARI/FRS and gastroenteritis thereby allowing for earlier individual case detection but also the recognition of outbreaks. This earlier outbreak detection may allow the Ministry of Health and other partners to maximize the efficient use of resources to control one of the most prevalent infectious diseases globally. Runge-Ranzinger et al., (2016) recommend the need for integrated preparedness planning for dengue which incorporates clinical care, epidemiology environmental controls with risk communication. The data from the current study can be used to tailor such preparedness plans specifically to Saint Lucia and the Saint Lucian population, which is important because the disease can manifest with different clinical signs based upon circulating serotypes and genotypes but also geographically (Rocha et al., 2017; Torres et al., 2017). The center of most disease response plans is the early recognition of the target disease, and in the case of dengue this relies heavily on clinical or symptomatic diagnosis because laboratory confirmation can be limited. Knowing the local epidemiology of the disease is critical to effective response plans and the current syndromic surveillance by the Ministry of Health and Wellness provides an excellent core for such programs, such as expanding the suggested syndromic differential diagnosis list to include dengue for ARI/FRS and gastroenteritis.

There are a number of limitations to this study which are related to the use of secondary data. The data was collected during a nine-year period and there may be other factors that affected the occurrence of dengue across this time span. There were also many physicians involved in examining the patients during this period of time which will inherently introduce information bias and may explain why there was no association seen with the variable fever with hemorrhagic signs. Ultimately there are a number of the suspected cases of dengue that may have been real infections though they were unable to be confirmed. The correct identification of these cases may have influenced the outcomes of the analysis and allowed a different insight to the relationship between clinical variables and dengue in Saint Lucia.

It is important for the effective management of diseases and individual patient cases to have information as specific as possible for the population in question. The previous lack of data specific to Saint Lucia meant that physicians had to rely on data generated from other populations. This study has allowed the author to identify that undifferentiated fever, ARI/FRS, and gastroenteritis are key risk factors for dengue in Saint Lucia and therefore physicians should pay closer attention to these patients If this data is appropriately used within the clinical setting it may mean earlier diagnosis of cases and possibly more favorable resolutions, which will minimize the effect to society by loss of productivity and decreased health-care costs which in turn contribute to the improvement of social conditions in Saint Lucia.

Further research should be conducted to identify if the cases of fever with respiratory signs or acute respiratory infections are related to pulmonary involvement pulmonary alveolar hemorrhage, pleural effusion or other pathologic changes related to the dengue infection or indeed are related to a comorbidity such as influenza or pneumonia (Beltrán-Silva et al., 2018; Prusty & Momin, 2019). This manifestation of dengue is not common and but with such a strong association among the Saint Lucia cases additional research may change this perception. Similarly, an investigation into the cases of gastroenteritis would help to determine if these clinical variables are related to dengue infections or to a comorbidity. The clinical signs of dengue infections have also been found to vary with the serotype and genotype associated with the infection, and further evaluation of the Saint Lucia data could reveal similar which can be used to strengthen diagnostic capacity by alerting physicians to expected clinical signs based upon the circulating serotype and genotype during outbreaks. Suppiah et al., 2018 demonstrated that clinical signs such as vomiting were more common with DENV 2 and diarrhea with DENV 3. This study should also encourage research in the other small islands of the Caribbean, where the epidemiology of the disease may prove to be different but the combined data would provide a better understanding of the disease within this subset of the region, where inter-island travel is important and the risk of introducing circulating strains of the virus is high.

Conclusion

Dengue in Saint Lucia is significantly associated with gastroenteritis, undifferentiated fever and acute respiratory infections. This information should be used to improve the early diagnosis of dengue in patients presenting with these symptoms especially when there is an ongoing dengue outbreak. Though clinical signs such as fever with hemorrhagic signs or fever with neurological signs were not found to be significantly associated with dengue, this may be as a result of underdiagnosis or misdiagnosis and provides the avenue for continuing education training for local physicians on dengue to include less-common symptoms as well. An appropriate multifaceted dengue preparedness plan for Saint Lucia would include the significance of identifying clinical symptoms associated with the disease specific to the island and ensure a broad stakeholder focus including health and environmental health partners but also even more importantly, the public. With increasing climate changes, there will likely be continued increased in favorable habitats for the dengue mosquito vector and the prevalence and incidence of outbreaks of dengue are likely to continue underscoring how important it is to understand the epidemiology of the disease within local populations. This is the first study in decades to focus on dengue in Saint Lucia and has emphasized the need to conduct more locale-specific research into the disease.

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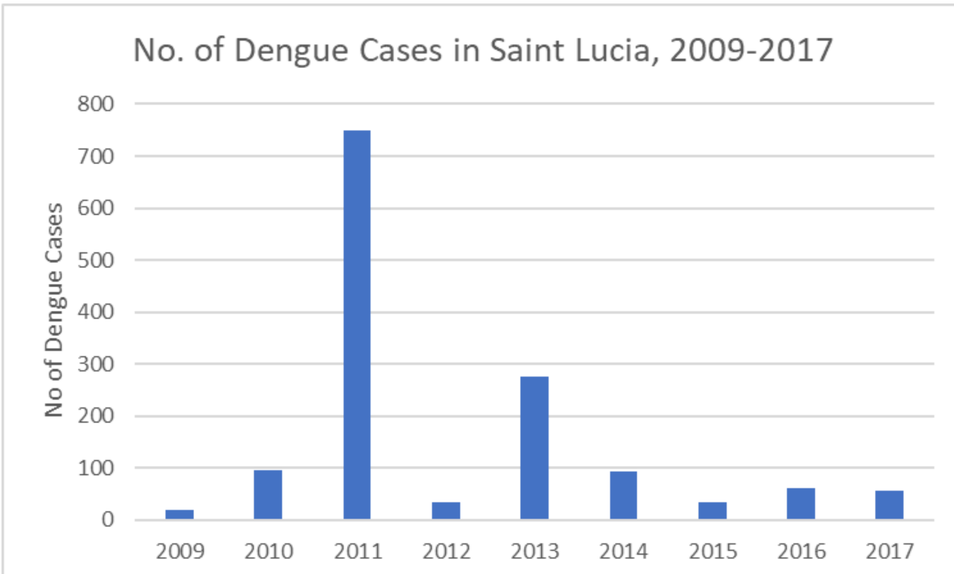
Figures.

Figure 1. Identified dengue cases in Saint Lucia during the period 2009-2017



Part 3: Summary

Integration of the Studies

Dengue remains a disease of immense importance globally and the Caribbean region also is an area of significant prevalence of the disease experiencing a spike in cases in 2019 that led to outbreaks in a number of the Americas (de Jesus et al., 2019). The Caribbean situation is critical, having the highest incidence rate in the Americas and prompting The Caribbean Public Health Agency (CARPHA) to issue a warning to the region for 2019 (Stewart-Ibarra et al., 2019). The importance of dengue as a re-emerging disease is underscored by the fact that the region went on to record more than 3 million cases, the highest figure on record. The largest epidemics of more than 1.5 million cases across the Americas region were recorded in 2015, 2013, 2016, and 2010 in descending order of magnitude (Mitchell, 2020). However, in Saint Lucia, the largest outbreaks between 2008 and 2017 were in 2011 and 2013, speaking to a somewhat different local experience.

The current study, divided into three individual bodies of work, was designed to evaluate a variety of epidemiologic characteristics of dengue in Saint Lucia, providing for the first-time information specific to the island. The major outcomes of the three works included that there are significant relationships between age, education level, temperature, rainfall, vector prevalence indices, and the clinical signs of undifferentiated fever, or fever with respiratory signs and gastroenteritis

I was able to successfully investigate the epidemiology of dengue in Saint Lucia. The three individual papers generated from this research provide information that can be used in unison by public health practitioners to aid in the prevention and control of dengue in Saint Lucia. Also important are the outcomes of this research, which provide a platform for further research studies to continue to explore the relationship between the variables included in this study. The outcomes of the study also demonstrate that there are differences in the epidemiology of dengue in Saint Lucia and that in the rest of the Caribbean. When the peak number of dengue cases occurred, and also the time of year in which these cases normally occurred (September to October in Saint Lucia), differs in comparison with other countries, in which cases typically occurred from October to December. There was similarity in the age groups affected, and the environmental factors, temperature, and rainfall were important factors associated with dengue (Amarakoon et al., 2008; Chadee et al., 2007; de Jesus et al., 2019; Kumar et al., 2018).

The information generated from the three individual studies can be used to identify the most likely sections of the population that would be most affected by a dengue outbreak and when this outbreak could possibly occur based on particular climatic conditions. This specific local approach could be of immense benefit to the health practitioners allowing the earlier initiation of treatment for dengue cases especially when the individual clinical symptoms are not pathognomonic for the disease (Guzman & Harris, 2015; Muller et al., 2017; Schiøler & Macpherson, 2009). This local model may be especially important because reliance on regional data or regional experience could lead to erroneous outcomes, and in appropriate management strategies and therefore unwanted and unexpected dengue outcomes, because it was demonstrated that the disease in Saint Lucia does not always mirror the regional experience.

Combining the outcomes of these studies will also allow public health officials to craft prevention campaigns that can specifically target the segments of the population most at risk particularly the 13- to 18-year-age group, which was identified as the age group most strongly associated with dengue, at times of the year when they are most vulnerable using the environmental variables and vector prevalence indices as forewarning beacons. By appropriately implementing these programs when needed, it would be possible to reduce message fatigue that may occur if the programs ran year round (So & Popova, 2018). Message fatigue is just as important to the public as to health care practitioners who may stop taking the appropriate dengue management steps in the face of other diseases and their other daily responsibilities.

Effective disease management is centered on preventive medicine and strategies to eliminate or minimize the incidence of the disease, in the case of dengue the elimination of the mosquito vector as well as early identification (Achee et al., 2015; McGraw & O'Neill, 2013; Nathan & Knudsen, 1991; Sanyaolu et al., 2017). Education is one of the most important aspects, if not the most important aspect, of any preventive disease management program because even if the measures and resources are available to combat the disease, the stakeholders, the lay public, and the medical professionals will not follow the recommendations and guidelines if they do not understand the reasons and necessities for doing so (Freimuth et al., 2000; Han et al., 2016; Paz-Soldán et al., 2015).

When the data from the three studies are reviewed collectively, the need for a more robust and multifactorial approach to understanding the epidemiology of dengue and also the need to ensure the local nuances of the disease, the agent, the vector, and the population becomes clear. Although the current literature supports the association of the variables included in this study with the occurrence of dengue, there are differences in the Saint Lucian experience. There is a need for more granular data both from the disease surveillance and demographic data that would provide a greater opportunity for better analysis of the relationship between these variables and dengue.

Theoretical Framework

This study was based upon the theoretical underpinnings of the ecological theory of disease, which suggests that disease occurrence is affected by multiple varying factors, including disease agent, environmental, and host factors. The outcomes of this study can be used to support the principles of this theory because associations were identified between demographic, environmental, vector, and clinical factors and dengue. This theoretical framework is critical to understanding the epidemiology of dengue and to the design and implementation of any prevention and control programs. It may not always be economically feasible to target every factor that affects the occurrence of a disease such as dengue, but by recognizing that there are multiple risk factors allows alternative avenues for management and control to be considered. For example there is a positive significant association between Container and Breteau Indices but it may not be possible to remove the receptacles holding the life stages of the mosquito, therefore by notifying the clinicians that there are high levels of mosquito populations, they can then pay attention to the clinical signs such as undifferentiated fever, fever with respiratory signs, and gastroenteritis in an attempt to identify dengue cases earlier and minimize the effects of a possible outbreak.

Unexpected Findings

There were a number of unexpected findings that need further research to better analyze the extent of the relationships. In the study, I focused on the demographic variables possibly associated with dengue in Saint Lucia and I discovered that no education and secondary education had significant negative relationships with dengue, whereas tertiary education had a significant positive relationship with dengue. Other research has demonstrated that persons with higher education levels have a lower incidence of dengue (de Mattos Almeida et al., 2007; Sriprom et al., 2010). This may require further research to better understand this relationship.

I suggest it may be related to occupational risk, because persons with tertiary education are more likely to be employed in offices where there may be a great risk of mosquito bites because the *Aedes aegypti* prefers to enter buildings where its hosts are located to feed (Crawford et al., 2017). In addition, the difference in educational level may result in different levels of seeking health care when feeling unwell or being able to afford health care because generally persons with higher education levels have higher-paying jobs and may be more likely to have a better understanding of dengue, thus seek health care more appropriately. The level of the employment data was not available at the individual case level and that lack of granularity may have led to ecologic bias, where the conclusions made on a group level is incorrectly inferred to apply to the individual. Another unexpected finding was that there was a significant negative relationship between tourist arrivals and dengue. This may result from increased employment, removing persons from environments where exposure to dengue may occur. Likewise, the decrease in dengue cases may have occurred because persons were too busy with activities related to tourism to seek medical care when feeling unwell.

In the study examining the relationship between environmental and vector prevalence variables and dengue, I discovered that there were significant negative relationships between Container Index, and Breteau Index and dengue cases. This relationship may be explained that when persons recognize high levels of the different mosquito life stages, they are more likely to take action to get rid of the receptacles or eliminate the habitat. This is turn may result in lower cases of dengue because the juvenile forms of the vector are not involved in the transmission of the disease so if their elimination ultimately reduces the adult vector that is involved in disease transmission. Generally it has been reported that the mosquito prevalence indices increase with dengue occurrence (Chadee et al., 2007).

There was limited data available for the mosquito prevalence indices, which may lead to incorrect outcomes of analysis. This supports the need for more widespread and regular vector surveillance that would provide more data for analysis and correct characterization of the relationship between vector indices and dengue in Saint Lucia, alternatively the operationalization of these indices or the data collected could be flawed. This suggests the need for additional research to build the volume of information on dengue in Saint Lucia and other Caribbean countries.

The third study, focusing on the relationship between clinical signs and dengue allowed the revelation that undifferentiated fever, fever with respiratory signs, and gastroenteritis had significant positive relationships with dengue; whereas fever with hemorrhagic signs and fever with neurological signs did not. It was unexpected that fever with hemorrhagic signs was not found to have a relationship with dengue because this can be one of the hallmarks of the disease (Guzman & Harris, 2015; Sanyaolu et al., 2017). The lack of a significant relationship between dengue and fever with hemorrhagic signs could have resulted from reduced identification of these signs or a true absence of these signs in the Saint Lucia context. Though dengue does have a hemorrhagic syndrome it does not mean that every case of dengue progresses to this stage, what is of greater concern is what other diseases on the island account for the cases of fever with hemorrhagic signs.

Disease Prevention Programs That Lead to Public Health Readiness

Most countries that experience the threat of dengue have implemented dengue prevention programs that generally are multifaceted including strategies such as vector control; bait programs, spraying, bed nets, elimination of vector habitats; vector and disease surveillance; healthcare resources such as diagnostics and treatment; and educational programs targeted at improving the overall knowledge and understanding of the disease (Achee et al., 2015; Heydari et al., 2017; Mitchell-Foster et al., 2015). These programs may function subtly in the background through the monitoring of case incidence which then generates the required response from the Ministry of Health and other stakeholders. With challenges from multiple infectious diseases it is both resource limiting and fatiguing to continue with public health educational programs constantly, and as such these programs are often implemented seasonally for example the influenza educational programs that are initiated just prior to the start of the flu season each year.

The Ministry of Health also produces media campaigns particularly directed at reducing the mosquito populations on island and thereby the risk associated with insects as vectors of disease such as dengue.

An integral part of disease prevention and public health readiness in Saint Lucia and the wider Caribbean is the reliance on agencies such as the Caribbean Public Health Agency (CARPHA) and the Pan-American Health Organization (PAHO) who provide, regional coordination in response to public health challenges such as dengue, training for both the public and private sectors, diagnostic capacity, as well as funding for local disease response programs and general epidemiology (Aarons, 2018; Stewart-Ibarra et al., 2019). These collaborations can provide early warning to Saint Lucia, based on the incidence of dengue in neighboring countries, though the results of this study have indicated that this must be taken in context of the local situation. These collaborations and linkages are essential for the success of public health programs in Saint Lucia and many other Caribbean countries where the limited resources including economic, infrastructural and personnel capacity, restrict the format and scope of prevention programs and readiness to respond to public health challenges.

The programs that are implemented to address diseases such as dengue are varied and undoubtedly have different outcomes. One of the measures implemented is that of fogging using an insecticide such as a pyrethroid which though having questionable efficacy within houses, serves also to remind the public of the threat of mosquitoes. Other disease prevention initiatives that lead to improved readiness are public health info adverts that are geared towards raising awareness, knowledge of the disease especially clinical signs and transmission, and to encourage healthcare seeking behavior. Additional programs include workshops for healthcare professionals that aim to ensure that public and private healthcare practitioners are aware of the threat of the disease, the current medical guidance on diagnosis and treatment and also the need for reporting. It is informative that with the threat of the Coronavirus Disease 2019 (COVID-19)(Zhu et al., 2020) the ministry of health has implemented a comprehensive approach in developing its preventive and management plan that is specifically designed to target all of the relevant stakeholders from the lay public to the medical professional. The aim is to build readiness and capacity ahead of the introduction of cases. The Ministry of Health in Saint Lucia, typically conducts annual public health awareness campaigns beginning with a vector awareness campaign in May through the rainy season ending in November and during any outbreaks outside this period. In addition to the vector awareness campaign, media infomercials on dengue and its symptoms are also conducted during this period (G. Chery, personal communication April 26, 2020). It is important to note the control and management of dengue within Saint Lucia is an integrated approach, and the outcomes of this study may help support these measures.

Potential Implications for Social Change

The outcomes of this study can be used to generate social mobilization where the community is provided with information that provides knowledge and motivation for members to take action to eliminate or minimize the risk of dengue. Such empowerment of a community, when they are given the opportunity and responsibility to directly affect their life circumstance is a powerful tool that can then be applied to other issues in the community (Asri et al., 2017). By having data that is specific to Saint Lucia, the importance of dengue can be highlighted to the local community and it is more likely that the Ministry of Health will be able to generate interest in preventing the disease. True success of public health interventions and programs are steeped in social mobilization, if a community is not involved as participatory partners such initiatives are likely to fail.

Another potential social change is one of improved life outcomes by minimizing days lost at school or at work. As such members of the Saint Lucian population who are prevented from contracting dengue, or are diagnosed and successfully treated earlier, are more likely to be productive members of society. Such a reduction in loss of productivity because of the application of the information generated in this study may mean that these individuals are able to improve their life outcomes by retaining work, attaining higher education levels that ultimately may lead to upward economic mobility. The loss of life with dengue, though lessened with advances in treatment and management, is also an important part of the burden of the disease (Bhatt et al., 2013; Cafferata et al., 2013) and the effect on society from loss of productive years of life and may be further minimized by the use of the information generated from this study.

Saint Lucia is a small-island developing state and as such has limited resources available to address all of the challenges that may face the population. Currently the island does not enjoy universal healthcare and diseases such as dengue place a tremendous burden upon the individual and the state. The resources that have to be allocated to healthcare at both the individual level and the state level increase the opportunity where these resources could have been applied to other challenges such as education, addressing crime, poverty, and other such social needs. The results of this study can be incorporated into dengue prevention and control management strategies, which may improve their efficiency and therefore reduce the burden of dengue in Saint Lucia.

It was found that there is a significant negative relationship between both stayover and cruise ship visitors, which may indicate that persons are more active through increased season employment related to the tourist industry, therefore decreasing the potential exposure to dengue carrying mosquitoes. The important social implication here is that if there is increased employment there may be a decrease in a disease such as dengue and maybe other infectious diseases as well. Another aspect of increased employment is that in a society such as Saint Lucia where there is no universal healthcare, persons with employment may be able to afford healthcare and additionally afford better living standards that may decrease exposure to dengue.

Areas of Future Research

This research has underscored the need for increased and more standardized data collection in Saint Lucia that can be used to better understand the relationship between possible clinical risk factors of dengue in Saint Lucia. The first studies addressing demographic variables dengue was limited in that most of the variables included only allowed for analysis at the community or population level because the individual case data available did not include these variables. Future research should seek to further explore the relationship of the variables that were identified as significant in the first study namely between age, education, and dengue. A number of age groups were identified as being significantly associated with dengue but there were no clear trends indicating that the association with dengue increased or decreased as age increased. It would be important to understanding this relationship to better determine if there actually is a discernible trend. In the case of the education again there was no clear trend and the outcomes of the study contradicted the general accepted belief that as educational level increases the occurrence of dengue decreases. In this study it was found that there was a significant positive relationship between dengue and tertiary education. This should be further investigated to determine if this is a real relationship and if so, why does that occur within the Saint Lucian population. The limited ability to identify the specific educational level of individual cases reduces the ability to successfully explore this relationship and a cross-sectional or prospective study may be required to better understand this relationship. A significant negative relationship was also found between tourist visitors and dengue and further research should be conducted to better characterize this relationship and understand the mechanism through which increased tourist arrivals led to a decrease in dengue cases.

The results from the second study demonstrate that there are relationships between environmental variables and dengue cases in Saint Lucia, especially with temperature and rainfall. Additional studies should be conducted to better understand these relationships. Previous research has demonstrated that incorporating time lags into research relating to dengue and environmental variables may better describe and explain these relationships (Cheong et al., 2013; Depradine & Lovell, 2004; Méndez-Lázaro et al., 2014; Ramachandran et al., 2016; Ramadona et al., 2016). Exploring this data at the individual level and with a variety of time lags would be necessary to truly understand these relationships in the local Saint Lucian context which may differ from other countries and locations. The relationship between vector prevalence indices and dengue require further investigation, because Container Index and Breteau Index were found to have a significant negative relationship with dengue whereas House Index was found to have a positive index, research has shown that all three typically have a positive relationship with the occurrence of dengue(Bowman et al., 2014; Chadee et al., 2007; Chang et al., 2015; Tseng & Chang, 2016; Wijayanti et al., 2016). This difference may be peculiar to Saint Lucia or as a result of deficient data because the vector indices data were limited in the number of years of data available as compared to the other environmental data. It was demonstrated that logistic models including vector data somewhat better explained the occurrence of dengue in Saint Lucia. It would be beneficial for a specific study to be designed to investigate these relationships, including more universal vector sampling across the entire island and tying dengue cases within a household to vector indices. All of the environmental data was measured at the population level and this as well as the operationalization of the data could have led to erroneous outcomes and as such it is necessary for additional analysis to be conducted for comparison of outcomes.

The third study yield results showing that at least three of the categories under regular surveillance in Saint Lucia were associated with dengue in Saint Lucia, undifferentiated fever, fever with respiratory signs, and gastroenteritis. A prospective study using these clinical presentations as markers of dengue should be undertaken to determine how useful these signs are in identifying cases of dengue in a clinical setting.

Similar research should also be conducted using the common clinical signs commonly monitored in disease surveillance with other diseases in an effort to better understand the epidemiology of these diseases in the local Saint Lucian context. In this study fever with hemorrhagic signs was not found to be significantly associated with dengue, this suggests that there may be other causes of this clinical presentation and research should be conducted in an effort to identify the most common disease associated with these signs. Such research would be extremely beneficial to the clinician faced with a patient presenting with these symptoms, especially when the research is conducted in the local context.

Overall, prospective research should be conducted with the variables identified as having significant relationships with dengue to determine how useful various models are in predicting the occurrence of dengue. If they are found to be accurate then these models can be used by the health authorities to better control the occurrence of dengue in Saint Lucia. In addition, similar research should be conducted into other infectious diseases such as influenza, leptospirosis, gastrointestinal diseases, and parasitic diseases such as schistosomiasis. It cannot be overstated how important it is to have data and information analyzed from this data that is specific to Saint Lucia(Bowman et al., 2014; Laserna et al., 2018). The reliance on information from sources external to the island may not take into account factors that are peculiar to the island, which may lead to ineffective disease prevention, management and control programs.

Another important research study would be to compare the epidemiology of dengue in Saint Lucia to other countries, especially in the Caribbean region, with an aim to identifying similarities and differences, and understanding them. None of this work has been conducted before to this author's knowledge. Such research would provide detailed epidemiological information that may help reduce the burden of dengue and other infectious diseases in Saint Lucia and the wider Caribbean. It would also inform the literature if research is conducted to determine the effect of interaction, modification and mediation that occurs between the possible risk factors of dengue because these phenomena do not occur in isolation and understanding these aspects of their relationship to dengue can be helpful in control of the disease (Corraini et al., 2017)**.**

The Process

One of the most challenging aspects of conducting this study was finding literature on dengue in Saint Lucia and other related information on Saint Lucia. There is a dearth of published research on almost any aspect of Saint Lucia and its people. This means a fair amount of extrapolation and supposition was needed in creating a foundation for the importance of a disease such as dengue in Saint Lucia. Indeed a review of the literature on dengue in the Caribbean produced papers focused on a limited number of countries, and as demonstrated there are differences in the epidemiology of the disease in Saint Lucia as compared to other countries and it is likely differences will also exist across the other countries of the Caribbean and further research and publication on phenomena within the Caribbean region should be encouraged.

It was challenging combining data from multiple disparate sources, especially as the consistency of the data varied in that not all cases provided complete records and had to be removed from analysis. The level at which the data was measured also varied making it challenging to truly link all of the environmental and demographic information to individual cases. It may be beneficial to limit the number of variables assessed in a study, not only from the need of an increased sample size as the number of explanatory variables increase but also to reduce the complexity of relationships that must be analyzed (Bujang et al., 2018).

Personal lessons learned were to exercise patience in collecting, collating and analyzing data. It was necessary to create multiple databases to determine the best way to combine the data from varied sources and many failed attempts at analyzing them. Although using fewer disparate sources would minimize this experience it is questionable if such omission would generate as rich an analysis of the problem as was possible. The iterative process of this study generated a large number of files, and a more detailed storage plan may have minimized the confusion that unfortunately occurred at times. In retrospect spending time in careful contemplation of the data available, the problem and the best way to approach the analysis before even attempting to do so may also have reduced the challenges faced in conducting this study. The detailed dissertation checklist was extremely helpful in focusing the study and meeting the expectations of the dissertation committee. Overall a positive lesson learned is that conducting research is both interesting and fulfilling even though it can be fraught with challenges along the way.

Conclusion

Through this study a number of demographics, environmental, and clinical variables were shown to have significant relationships with dengue in Saint Lucia. The adolescent age group, 13-18 years, tertiary education, living the districts of Laborie, Choiseul and Soufriere, maximum daily temperature > 32^o C, undifferentiated fever, ARI/FRS, and gastroenteritis all had a positive significant relationship with the occurrence of dengue in Saint Lucia. There is a limited amount of published data on dengue in the Caribbean, focused on only a few countries, and published data on any phenomena in Saint Lucia is extremely limited. The outcomes of this study can be applied to addressing this knowledge gap and serve as a stimulus to conduct further research. Standardization of data collection strategies across government organizations would lead to more complete data that could be used for the analysis of relationships between factors and outcomes of interest, there is a need for additional research and data collection to more comprehensively analyze the relationship between dengue, and possible explanatory variables. Such public health tools could be applied in an effort to reduce the burden of dengue within Saint Lucia; both in terms of the human impact through a reduction in morbidity and mortality, and through the economic and related social challenges as a result of the reducing the healthcare costs associated with managing the disease. The current study provides a foundation for future research to further characterize the epidemiology of dengue in Saint Lucia.

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Appendix

Tables

Table A1.

Logistic regression of environmental variables and dengue at zero- and 1-month lags in Saint Lucia 2009-2017

								95% C.I. for O.R.	
		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Zero Lag								
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	-0.174	0.297	0.343	1	0.558	0.840	0.470	1.503
	High (>11)***	-1.692	0.311	29.637	1	0.000	0.184	0.100	0.339
	Sunshine (hours)								
Ref.	Low (0-8)								
	Medium (>8-9)**	-0.746	0.283	6.958	1	0.008	0.474	0.272	0.825
	High (>9)*	-0.991	0.393	6.346	1	0.012	0.371	0.172	0.803
	Highest Daily Rain (mm)								
Ref.	Low (0-45)								
	Medium (>45-90)	0.796	0.498	2.557	1	0.110	2.217	0.836	5.882
	High (>90)	0.413	0.608	0.463	1	0.496	1.512	0.459	4.975

	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)								
	Medium (>100-200)**	-1.082	0.383	7.982	1	0.005	0.339	0.160	0.718
	High (>200)**	-1.829	0.625	8.572	1	0.003	0.161	0.047	0.546
	Number of Rainy Days								
Ref.	Low (0-10)			0.134	2	0.935			
	Medium (>10-20)	0.017	0.348	0.002	1	0.961	1.017	0.514	2.012
	High (>20)	0.133	0.524	0.065	1	0.799	1.143	0.409	3.191
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)								
	Medium (>30-32)***	-0.409	0.367	1.245	1	0.264	0.664	0.323	1.363
	High (>32)	0.712	0.557	1.632	1	0.201	2.037	0.684	6.068
	Average Monthly Temperature (ºC)								
Ref.	Medium (>26-28)								
	High (>28)**		0.286	8.283	1	0.004	0.439	0.250	0.769
	Relative Humidity (%)								
Ref.	Low (0-75)								
	Medium (>75-80)	0.464	0.325	2.041	1	0.153	1.591	0.841	3.009
	High (>80)	-0.709	0.431	2.706	1	0.100	0.492	0.212	1.145
	House Index %								
Ref.	Low (0-10)								
	Medium (>10-20)**	0.789	0.301	6.889	1	0.009	2.201	1.221	3.968
	High (>20)	-0.134	0.515	0.068	1	0.795	0.875	0.319	2.401
	Container Index%								
Ref.	Low (0-15)								
	Medium (>15-30)**	-0.782	0.233	11.249	1	0.001	0.458	0.290	0.723
	High (>30)	-1.213	1.397	0.754	1	0.385	0.297	0.019	4.594
	Breteau Index								

Ref.	Low (0-25)								
	Medium (>25-50)*	0.570	0.232	6.056	1	0.014	1.768	1.123	2.783
	Medium (>50)	-0.205	0.778	0.070	1	0.792	0.815	0.177	3.740
	1-month lag								
	Sunshine (hours)								
Ref.	Low (0-8)								
	Medium (>8-9)***	-0.977	0.223	19.264	1	0.000	0.376	0.243	0.582
	High (>9)	-0.302	0.294	1.049	1	0.306	0.740	0.415	1.317
	Average Monthly Temperature (ºC)								
Ref.	Medium (>26-28)								
	High (>28)	-0.323	0.221	2.139	1	0.144	0.724	0.469	1.116
	Relative Humidity (%)								
Ref.	Low (0-75)								
	Medium (>75-80)**	-0.936	0.275	11.562	1	0.001	0.392	0.229	0.673
	High (>80) ***	-1.961	0.366	28.758	1	0.000	0.141	0.069	0.288
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	0.072	0.263	0.074	1	0.786	1.074	0.641	1.799
	High (>11)	-0.348	0.284	1.497	1	0.221	0.706	0.405	1.233
	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)								
	Medium (>100-200)	0.510	0.300	2.883	1	0.090	1.666	0.924	3.002
	High (>200)*	0.761	0.373	4.167	1	0.041	2.140	1.031	4.444
	Number of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)**	0.951	0.344	7.653	1	0.006	2.588	1.319	5.077
	High (>20)	0.560	0.473	1.401	1	0.237	1.751	0.692	4.429
	Maximum Daily Temperature (ºC)								

		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
Ref.	Low (0-30)								
	Medium (>30-32)*	0.768	0.336	5.221	1	0.022	2.154	1.115	4.161
	High (>32)***	1.987	0.489	16.513	1	0.000	7.293	2.797	19.014
	House Index %								
Ref.	Low (0-10)								
	Medium (>10-20)*	0.622	0.261	5.679	1	0.017	1.863	1.117	3.107
	High (>20)	0.139	0.450	0.096	1	0.757	1.149	0.476	2.775
	Container Index%								
Ref.	Low (0-15)								
	Medium (>15-30)**	-0.504	0.191	6.968	1	0.008	0.604	0.416	0.878
	High (>30)	-0.302	0.941	0.103	1	0.748	0.739	0.117	4.672
	Breteau Index								
Ref.	Low (0-25)								
	Medium (>25-50)**	-0.661	0.213	9.632	1	0.002	0.516	0.340	0.784
	High (>50)	-1.127	0.691	2.659	1	0.103	0.324	0.084	1.256
	Constant	0.145	0.625	0.054	1	0.816	1.156		

*p<.05, **p<.01, ***p<0.001

Table A2.

Logistic regression of environmental variables with low association with dengue at zero- and 1-month lags in Saint Lucia 2009-2017

								95% C.I. for O.R.	
		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Zero Lag								
	Highest Daily Rain (mm)								
Reference	Low (0-45)								
	Medium (>45-90)***	0.387	0.105	13.558	1	0.000	1.472	1.198	1.808
	High (>90)	-0.310	0.247	1.573	1	0.210	0.734	0.452	1.190
	One Month Lag								
	Sunshine (hours)								
Reference	Low (0-8)								
	Medium (>8-9)***	-0.707	0.167	17.927	1	0.000	0.493	0.356	0.684
	High (>9)***	-1.030	0.219	22.186	1	0.000	0.357	0.233	0.548

		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Average Monthly Temperature (ºC)								
Reference	Medium (>26-28)								
	High (>28)***	0.643	0.162	15.753	1	0.000	1.903	1.385	2.614
	Relative Humidity (%)								
Reference	Low (0-75)								
	Medium (>75-80)	0.038	0.213	0.032	1	0.859	1.039	0.684	1.578
	High (>80)	0.144	0.295	0.240	1	0.624	1.155	0.648	2.060
	House Index %								
Reference	Low (0-10)								
	Medium (>10-20)	-0.207	0.225	0.846	1	0.358	0.813	0.523	1.264
	High (>20)	-0.577	0.389	2.202	1	0.138	0.562	0.262	1.203
	Breteau Index								
Reference	Low (0-25)								
	Medium (>25-50)	-0.207	0.161	1.666	1	0.197	0.813	0.593	1.113
	High (>50)	-1.192	0.601	3.939	1	0.047	0.304	0.094	0.985

*****p<.05, **p<.01, ***p<0.001

Table A3

Logistic regression of environmental variables without vector indices and dengue at zero- and 1-month lags in Saint Lucia 2009-2017

								95% C.I. for O.R.	
		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Zero Lag								
	Wind Direction								
Ref.	ENE								
	NNE	1.265	1.561	0.657	1	0.418	3.542	0.166	75.442
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)*	-0.528	0.211	6.237	1	0.013	0.590	0.390	0.893
	High (>11)***	-1.240	0.240	26.631	1	0.000	0.290	0.181	0.464
	Sunshine (hours)								
Ref.	Low (0-8)***			48.826	2	0.000			
	Medium (>8-9)***	-1.139	0.189	36.408	1	0.000	0.320	0.221	0.464

	High (>9)***	-1.661	0.254	42.773	1	0.000	0.190	0.115	0.312
	Highest Daily Rain (mm)								
Ref.	Low (0-45)*			6.345	2	0.042			
	Medium (>45-90)	0.184	0.329	0.314	1	0.575	1.202	0.631	2.289
	High (>90)	-0.658	0.445	2.190	1	0.139	0.518	0.217	1.238
	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)			2.352	2	0.309			
	Medium (>100-200)	-0.108	0.270	0.161	1	0.689	0.897	0.528	1.524
	High (>200)	-0.616	0.457	1.817	1	0.178	0.540	0.221	1.322
	Number of Rainy Days								
Ref.	Low (0-10)			0.515	2	0.773			
	Medium (>10-20)	0.068	0.280	0.058	1	0.809	1.070	0.618	1.851
	High (>20)	0.216	0.374	0.334	1	0.563	1.242	0.596	2.586
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)***			16.876	2	0.000			
	Medium (>30-32)**	-0.934	0.288	10.506	1	0.001	0.393	0.223	0.691
	High (>32)	-0.525	0.401	1.717	1	0.190	0.592	0.270	1.297
	Average Monthly Temperature (ºC)								
Ref.	Low (0-26)			0.810	2	0.667			
	Medium (>26-28)	-21.660	28436.286	0.000	1	0.999	0.000	0.000	
	High (>28)	-21.853	28436.286	0.000	1	0.999	0.000	0.000	
	Relative Humidity (%)								
Ref.	Low (0-75)			5.168	2	0.075			
	Medium (>75-80)	-0.017	0.267	0.004	1	0.950	0.984	0.582	1.661
	High (>80)	-0.616	0.369	2.789	1	0.095	0.540	0.262	1.113
	Constant	23.773	28436.286	0.000	1	0.999	21117436777.955		
	One Month Lag								

	Sunshine (hours)								
Ref.	Low (0-8)								
	Medium (>8-9)***	-0.754	0.161	21.847	1	0.000	0.471	0.343	0.646
	High (>9)**	-0.587	0.184	10.190	1	0.001	0.556	0.388	0.797
	Average Monthly Temperature (ºC)								
Ref.	Low (0-26)								
	Medium (>26-28)	0.122	0.534	0.052	1	0.819	1.130	0.397	3.217
	High (>28)	-0.357	0.529	0.456	1	0.499	0.700	0.248	1.973
	Relative Humidity (%)								
Ref.	Low (0-75)								
	Medium (>75-80)*	-0.480	0.228	4.438	1	0.035	0.619	0.396	0.967
	High (>80)***	-1.279	0.302	17.898	1	0.000	0.278	0.154	0.503
	Wind Speed (MPH)								
Ref.	Low (0-9)								
	Medium (>9-11)	-0.315	0.187	2.841	1	0.092	0.730	0.506	1.053
	High (>11)***	-0.900	0.219	16.947	1	0.000	0.407	0.265	0.624
	Cumulative Monthly Rainfall (mm)								
Ref.	Low (0-100)								
	Medium (>100-200)	0.421	0.219	3.673	1	0.055	1.523	0.991	2.341
	High (>200)	0.226	0.249	0.821	1	0.365	1.253	0.769	2.043
	Number of Rainy Days								
Ref.	Low (0-10)								
	Medium (>10-20)*	0.575	0.253	5.172	1	0.023	1.777	1.083	2.916
	High (>20)	0.291	0.310	0.877	1	0.349	1.337	0.728	2.456

		B	S.E.	Wald	df	Sig.	O.R.	Lower	Upper
	Maximum Daily Temperature (ºC)								
Ref.	Low (0-30)								
	Medium (>30-32)	0.015	0.243	0.004	1	0.952	1.015	0.630	1.633
	High (>32)*	0.767	0.312	6.037	1	0.014	2.154	1.168	3.974

*****_p_<.05, **_p_<.01, ***_p_<0.001

Table A4

Logistic regression of environmental variables with low significance (without vector indices) and dengue at zero- and 1-month lags in Saint Lucia 2009-2017

		B	S.E.	Wald	df	Sig.	O.R.	95% C.I. for O.R. Lower	Upper
	Zero Lag								
	Highest Daily Rain (mm)								
Ref.	Low (0-45)								
	Medium (>45-90)***	0.387	0.105	13.558	1	0.000	1.472	1.198	1.808
	High (>90)	-0.310	0.247	1.573	1	0.210	0.734	0.452	1.190
	One Month Lag								
	Sunshine (hours)								
Ref.	Low (0-8)								
	Medium (>8-9)	-0.176	0.131	1.813	1	0.178	0.839	0.649	1.084
	High (>9)	-0.293	0.153	3.684	1	0.055	0.746	0.553	1.006
	Average Monthly Temperature (ºC)								
Ref.	Low (0-26)								
	Medium (>26-28)	-0.382	0.491	0.604	1	0.437	0.683	0.261	1.788
	High (>28)	-0.188	0.491	0.146	1	0.702	0.829	0.316	2.170
	Relative Humidity (%)								
Ref.	Low (0-75)								
	Medium (>75-80)	0.312	0.160	3.789	1	0.052	1.366	0.998	1.871
	High (>80)	0.174	0.230	0.574	1	0.449	1.190	0.758	1.868

*****_p_<.05, **_p_<.01, ***_p_<0.001