Modelling Dengue Transmission Risk in Central and South America using Climate Data

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Abstract

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Objective:

The principal objective of this project was an assessment of the seasonal change in the geographical risk and human population at risk of dengue virus (DENV) infection, which causes dengue fever (DF). This was accomplished through the development of a DENV transmission suitability model, using the daily survival probability of the mosquito vector and the virus extrinsic incubation period as a function of temperature and humidity, and dengue case data in Brazil, Colombia, and Costa Rica.

Methods:

This descriptive study design was a secondary longitudinal data analysis of data for confirmed DENV infections and meteorological conditions in Brazil, Colombia, and Costa Rica from 2012 until 2018. The presence of dengue transmission was made binary in the study based on the human incidence rate within the countries.

A logistical regression was utilized to quantify the relationship between dengue incidence and the modeled probability that the DENV carrying mosquito, *Aedes aegypti*, will survive the extrinsic incubation period. This probability will be referred to as the risk index (RI) and was calculated using temperature and relative humidity. A logistic model was created by using the weekly RI and the dengue incidence rate at each respective Administrative Level 1 unit to calculate the probability that the conditions would support DENV transmission.

Results:

The output of the individual country models, as well as, the combined model provided several statistically significant findings. All the models had at least a 70% accuracy, except for Costa Rica. Each of the models quantified statistical significance among the dependent (human DENV cases) and independent variables (RI). For every 0.01 increase in RI (probability the mosquito will survive past the incubation period), the odds of dengue increased by 12.6% (Brazil), 23.6% (Columbia), 69.5% (Costa Rica), and 23% (Combined). Interpretation of the combined model was that for every 0.01 increase in RI, the odds of the presence of DENV increased by 23%.

Conclusions:

The model results suggest a positive association between favorable environmental conditions and DENV incidence, which is of public health importance for the general population and for the most vulnerable populations. The ability to forecast favorable environmental conditions may aid in appropriate future DENV resource allocation and planning not only in these countries but throughout the region. Applicable mitigation and adaptation strategies must be developed and implemented to address the increasing incidence of DENV.

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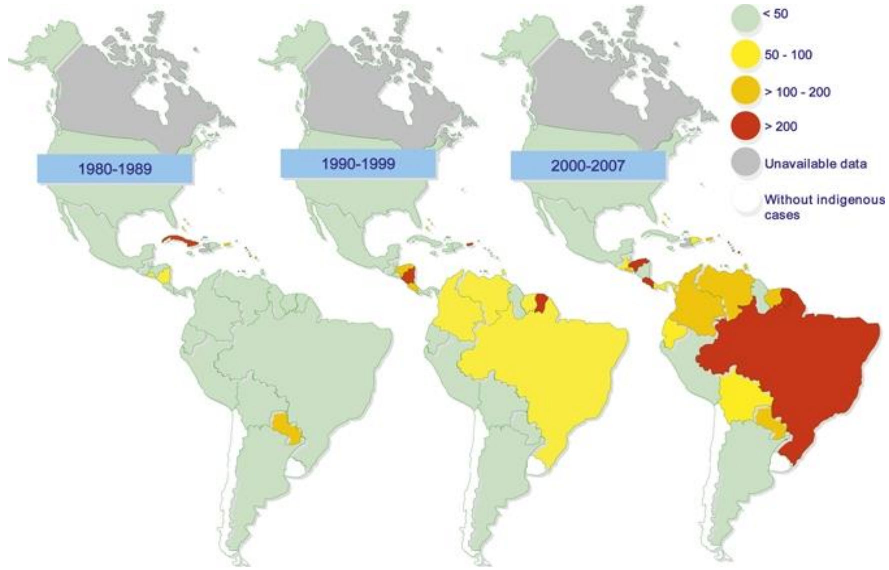
Background

Dengue fever (DF) is a mosquito-borne viral disease with a major impact on public health globally (Guzman et al., 2010). World Health Organization (WHO) data suggest that DF is endemic in at least 100 countries around the world. Dengue is abundant throughout the tropics, with local spatial variations in risk influenced strongly by rainfall, temperature and the degree of urbanization. Using cartographic approaches, there are estimated to be 390 million (95% credible interval 284-528) dengue virus (DENV) infections per year, of which 96 million (67-136) manifest apparently (any level of disease severity) (Bhatt et al. Year!). Symptoms of rash, vomiting of blood, and nose bleeding may indicate potentially fatal hemorrhagic manifestations, i.e. dengue hemorrhagic fever, with a 0.5-5.0% mortality rate (Lee et al. 2012).

Because there are four different serotypes of DENV and it can fluctuate from asymptomatic to requiring serious medical intervention, there is significant underreporting to health agencies. Latin America posts some of the highest incidences of DF in the world. Countries in the Americas experienced a three-fold increase in incidence from 1980-2007 (San Martín, J. L 2010) (Figure 1).

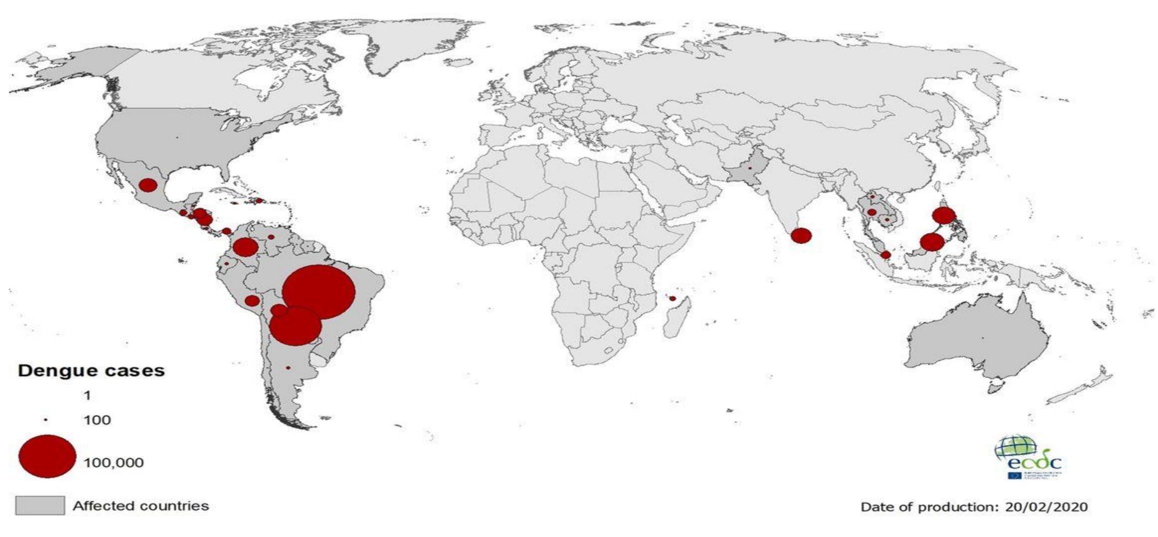
Figure 1: Average dengue incidence per 100,000 by country, Region of the Americas, 1980–2007.



Source: San Martín, J. L 2010

Those at highest risk reside in low income communities in tropical and subtropical climates where resources for vector control and prevention are limited (Spiegel et al. 2005). South and Central America currently have some of the highest numbers of DENV cases. Since the beginning of 2020, most of the cases were reported by Brazil, Paraguay and Colombia (ECDC 2020) (Figure 2). The ability to forecast time periods that pose the greatest risk of contracting dengue is beneficial for developing early warnings to underserved populations at risk.

Figure 2: Geographical distribution of dengue cases reported worldwide, January to February 2020



Source: ECDC (2020) https://www.ecdc.europa.eu/en/dengue-monthly

Understanding the optimal environmental conditions in relation to mosquito survival and the extrinsic incubation period of the virus are key in mitigating the risk of contracting dengue. The *Aedes aegypti* mosquito requires favorable temperature and humidity to survive. Their internal body temperature is not internally regulated, and they depend on optimal conditions to minimize the risk of heat and cold stress. The meteorological and environmental conditions (e.g. temperature, precipitation, humidity) associated with DF incidence in the Caribbean and Central America vary spatially (Arboleda et al. 2009).

The relationship between environmental conditions and DF occurrence is well studied by the scientific community. Modeling is an essential tool to support planning, decision making and dengue intervention assessments for public health. Public awareness must be promoted for prevention and control of DENV transmission. Understanding the threat and communicating the threat is imperative. Cooperation between governments, health agencies, and the general public ensures the broadest and most effective campaign to reduce DENV transmission. Communication and cooperation between different government sectors allows for distributing resources effectively and efficiently to combat DENV.

Local governments and public health agencies need the ability to conduct vulnerability assessments and optimally estimate the probability of local dengue transmission. There is a high need for accurate models to estimate local transmission initiation and propagation. Decision makers that have these DENV risk estimates can focus on interventions in preparation for the occurrences of DF. Having this knowledge based on probability of DF incidence is vitally important to assist in prevention, education, and control measures for long range planning.

Methods:

Study Design

This descriptive study design was a secondary longitudinal data analysis of data for confirmed DENV infections and meteorological conditions in Brazil, Colombia, and Costa Rica from 2012 until 2018. The presence of dengue transmission was made binary in the study based on the human incidence rate within the countries.

A logistical regression was utilized to quantify the relationship between dengue incidence and the modeled probability that the DENV carrying mosquito, *Aedes aegypti*, will survive the incubation period using temperature and relative humidity as inputs. Incidence rate was calculated as the number of DF cases per 100,00 population at Administrative Level One (1). The DF incidence was the dependent variable (categorized as 0 or 1) and the risk index (RI), defined as the probability that the female mosquito will survive the extrinsic incubation period, was the independent variable.

The ultimate goal of this study was to generate a model that can estimate the probability of DENV transmission occurring in the study area monthly or seasonally from climate data.

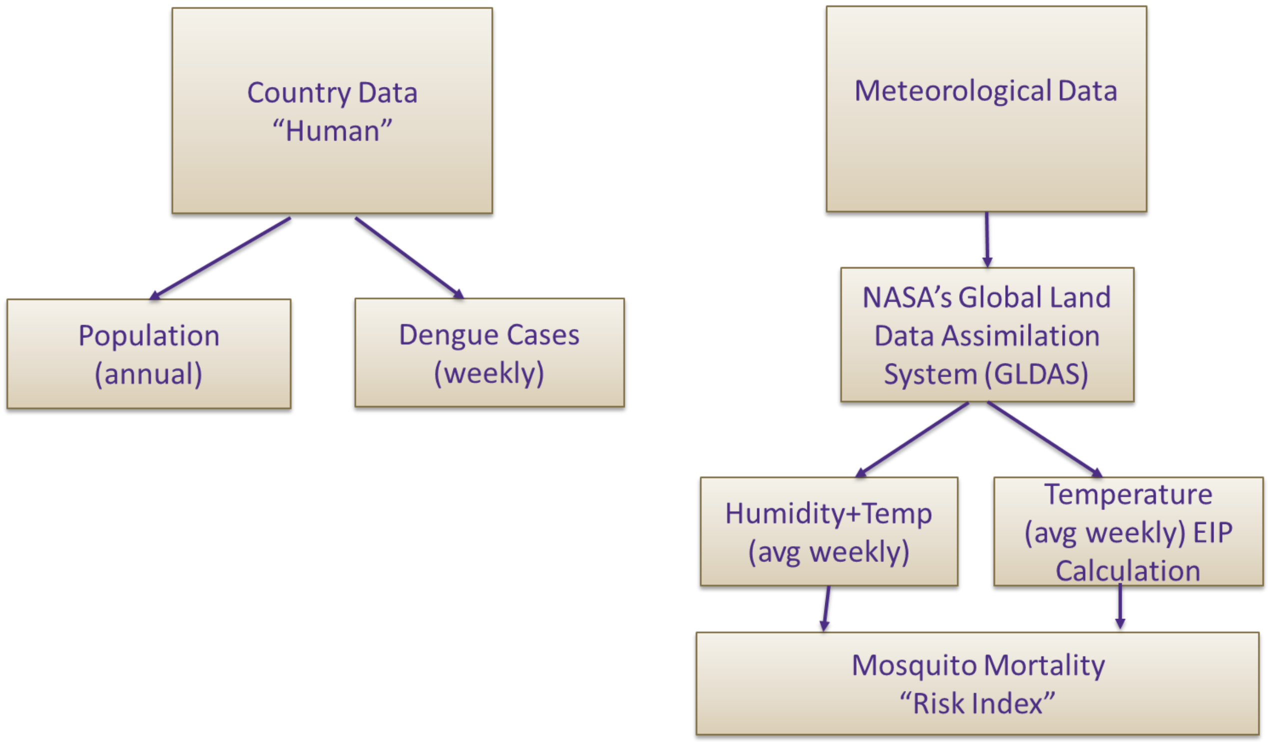
Study subjects

The study did not include any identifiable information for the confirmed cases of DENV. The data is from open sources published by the respective countries. The data was in raw numbers of confirmed cases at the Administrative One (1) level.

Data Collection

The data for this study were collected from reputable open sources found on the web. The data for confirmed cases of DF were collected from the respective national level public health reporting systems. The flow and frequency of data collection were dependent on the specific variables of human case rate, population, temperature, and humidity (Figure 3). The dependent variable of human cases of DENV and the dependent variables of temperature and humidity are summarized below.

Figure 3: Data Collection Flow and Frequency Diagram



Note: Figure 3 shows the data collection and frequncy of the study.

The public health departments of Brazil, Colombia, and Costa Rica primarily posted their number of confirmed DENV cases weekly. The data were analyzed at the Administrative 1 level, the governmental structure below national level. The following are the Administrative 1 levels for each country:

1) Brazil (State)

2) Columbia (Department)

3) Costa Rica (Provinces)

The confirmed human DF cases were collected at the weekly rate, as reported by the individual departments of health. The data years were collected and analyzed as follows:

1) Brazil- 27 States from 2014 until 2017

2) Columbia- 35 Departments from 2007 until 2018

3) Costa Rica- 9 Provinces from 2012 until 2018

This study used National Aeronautical Space Administration (NASA) Global Land Data Assimilation System (GLDAS) for all the climate/weather data. The data were gridded (0.5° resolution) and provided at 3-hour intervals and aggregated weekly. Data were averaged over the administrative units. The data was aggregated in this manner to facilitate analysis with the respective administrative unit's DF incidence rate.

Analyses

Temperature data were used to calculate the extrinsic incubation period (EIP) in days, which is the incubation period of DENV within the female mosquito. Temperature and relative humidity were used to calculate the daily survival probability of the adult female mosquito. From the results of these two calculations, the probability that a mosquito will survive the EIP at a given temperature and relative humidity is calculated as: (daily survival probability) ^EIP. The outcome is defined as the RI.

A logistic model was created by using the weekly RI and the dengue incidence rate at each respective Administrative Level 1 unit. The DENV incidence rate was calculated using logistic regression with a transformation of One (1) being the presence of DENV in the respective Administrative Level 1 unit and Zero (0) being little or no transmission. Based on the collected data and the initial analysis of the population data, the case rate was determined as follows

1) Presence of DENV "1" will be a case rate of $\geq$ 0.5 per 100,000 population at risk.

2) Absence of DENV "0" will be a case rate of < 0.5 per 100,000 population at risk.

The output of the logistic regression model provided a probability of DENV cases occurring given a specified RI value.

Results:

Country Characteristics:

The study year, total population for each Administrative 1 unit, number of human cases, and the case rate per 100,000 of the population at risk for each country are described in Table 1. The weekly RI was graphed for each country at the level of Administrative 1 units (Figures 4-6). The figures illustrate the seasonal/environmental requirements needed for the female *Ae. aegypti* to survive the EIP Different scales were used when plotting the weekly Admin 1 RI to show the seasonal distributions ((Figures (1) Brazil, (2) Colombia, Costa Rica (3)).

DENV risk was modeled individually and collectively for Brazil, Colombia, and Costa Rica; results are presented as Odds Ratios (OR) and p-value.

Table 1: Characteristics of Brazil, Colombia, and Costa Rica

	Brazil			Colombia			Costa Rica		
Study Year	Population n=27 Admin 1	Cases	Case Rate[1] (per 100,000)	Population n= 33 Admin 1	Cases	Case Rate[1] (per 100,000 pop)	Population n= 9 Admin 1	Cases	Case Rate[1] (per 100,000)
2007	—	—	—	43,645,604.00	41,706.00	95.55601522	—	—	—
2008	—	—	—	44,059,386.00	36,915.00	83.78464466	—	—	—
2009	—	—	—	44,473,169.00	52,281.00	117.5562731	—	—	—
2010	—	—	—	44,886,952.00	156,874.00	349.486862	—	—	—
2011	—	—	—	45,300,735.00	30,176.00	66.61260573	—	—	—
2012	—	—	—	45,714,517.00	53,876.00	117.8531537	6,210,743.00	17,208.00	277.0682992
2013	—	—	—	46,128,300.00	125,521.00	272.1127811	6,375,837.00	40,891.00	641.3432464
2014	207,100,487.00	593,561.00	286.6053135	46,542,083.00	107,845.00	231.7150266	6,511,015.00	9,051.00	139.0105844
2015	205,594,836.00	1,700,323.00	827.0261224	46,955,866.00	96,367.00	205.2288845	6,533,227.00	14,145.00	216.5086258
2016	211,184,311.00	1,514,860.00	717.3165435	47,369,648.00	100,997.00	213.2103663	6,298,696.00	18,757.00	297.7917969
2017	213,105,475.00	239,395.00	112.3363912	47,783,431.00	25,233.00	52.80700752	7,096,369.00	4,824.00	67.97842671
2018	—	—	—	48,197,214.00	42,490.00	88.15862261	7,177,496.00	2,397.00	33.39604787

[1] Human case rate was calculated per Admin 1, by annual population at risk per 100,000.

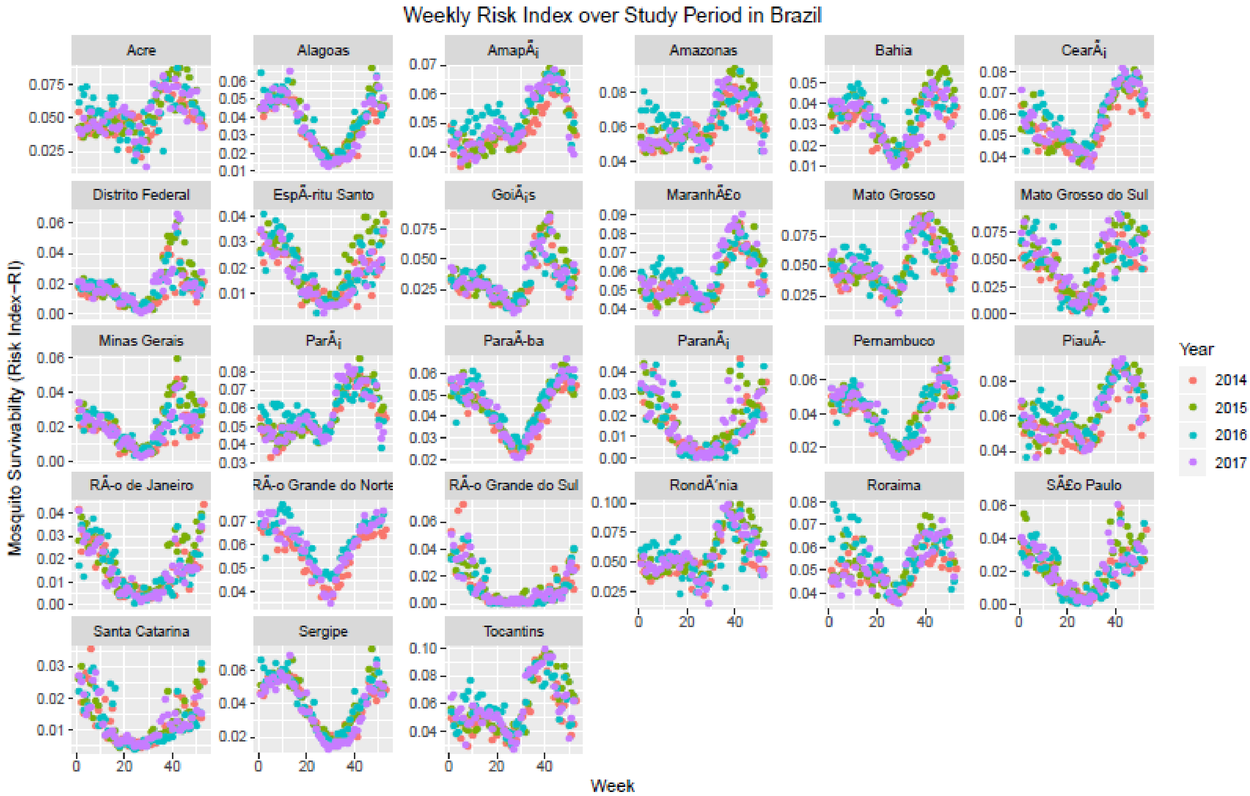


Figure 4: Weekly Mosquito Survivability across all Brazilian States.

Figure 5: Weekly Mosquito Survivability across Colombian Departments.

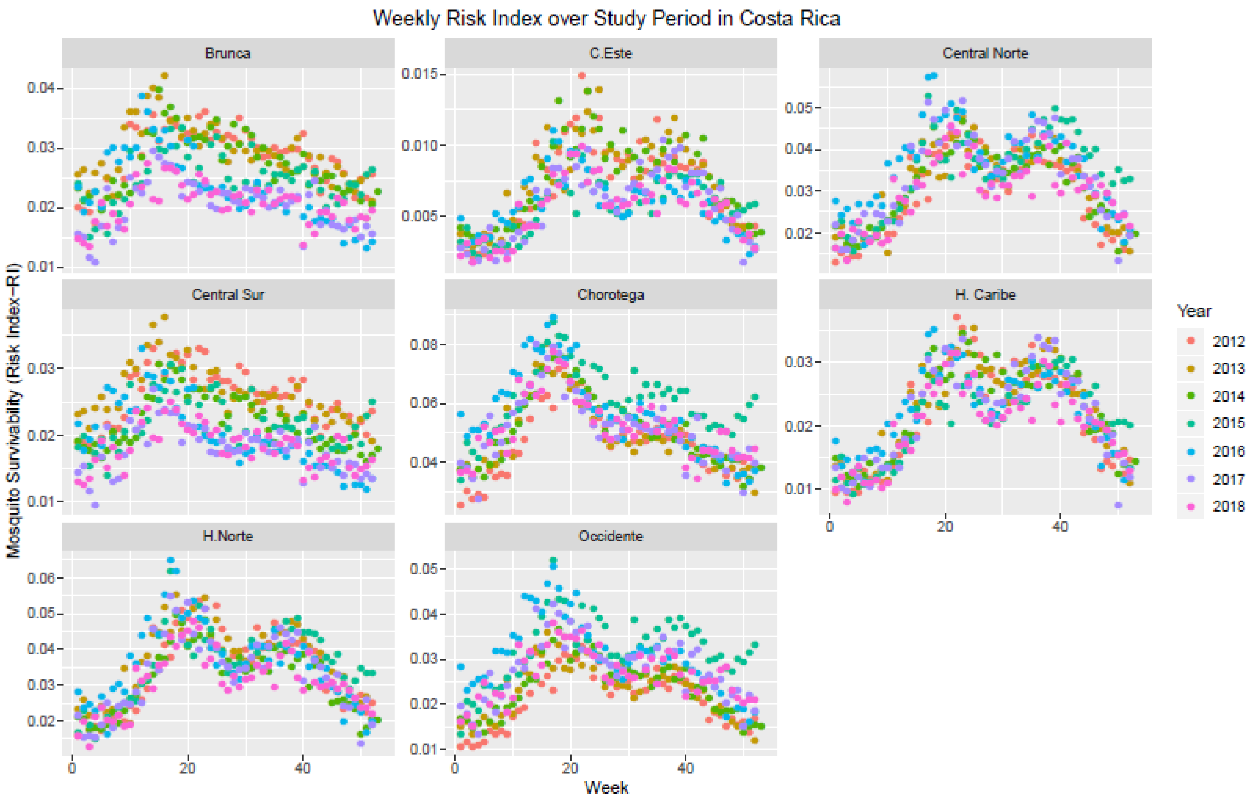


Figure 6: Weekly Mosquito Survivability across Costa Rica's Provinces.

Brazil Model:

The Brazil model had an average accuracy rate of 84.5%, which means the model successfully forecast the association 84.5% of the time over the four-year study period. The p-value was highly significant at ≤ 0.00072. The log odds of DENV without the impact of RI was 2.51, with an OR 12.2. This means that the data showed the odds of transmission was 12.2 to 1. This was expected in Brazil with a RI favorable most of the year for dengue transmission. Based on the model, for every 0.01 increase in RI or the probability the mosquito will survive past the incubation period, the odds of dengue increased by 12.6%. This outcome indicated the larger the RI, the greater likelihood of DENV transmission (Figure 7).

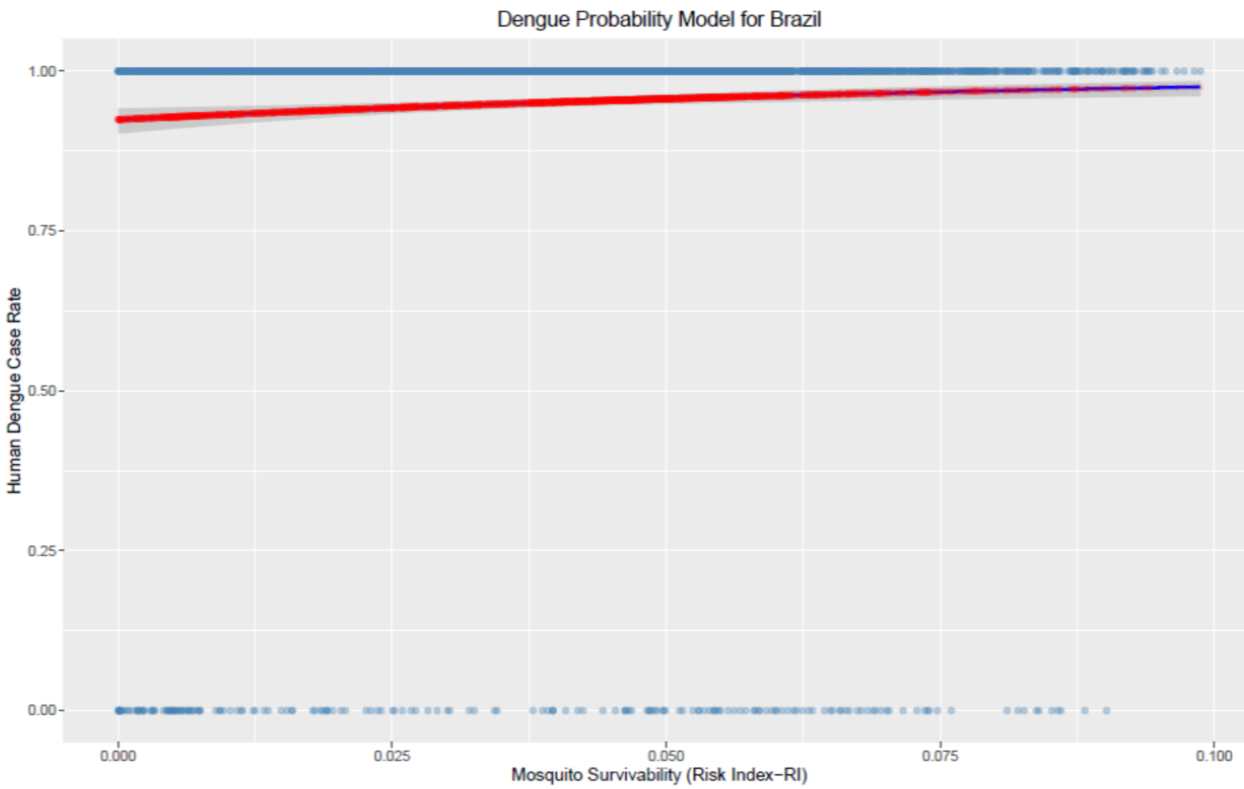


Figure 7: Model depicts the association between human dengue cases and the RI in Brazil.

Colombia Model

The Colombia model had an overall accuracy rate of 73.5% over the twelve-year study period, with a highly significant p-value of <0.0001. The log odds of DENV without the impact of RI was 0.603, with an OR of 1.83. This means that the data showed the odds of presence of dengue was 1.83 to 1. Based on the model, for every 0.01 increase in RI, or the probability the mosquito will survive past the incubation period, the odds of the presence of dengue increased by 23.6%. This outcome indicated the larger the RI, the greater likelihood of DENV transmission (Figure 8).

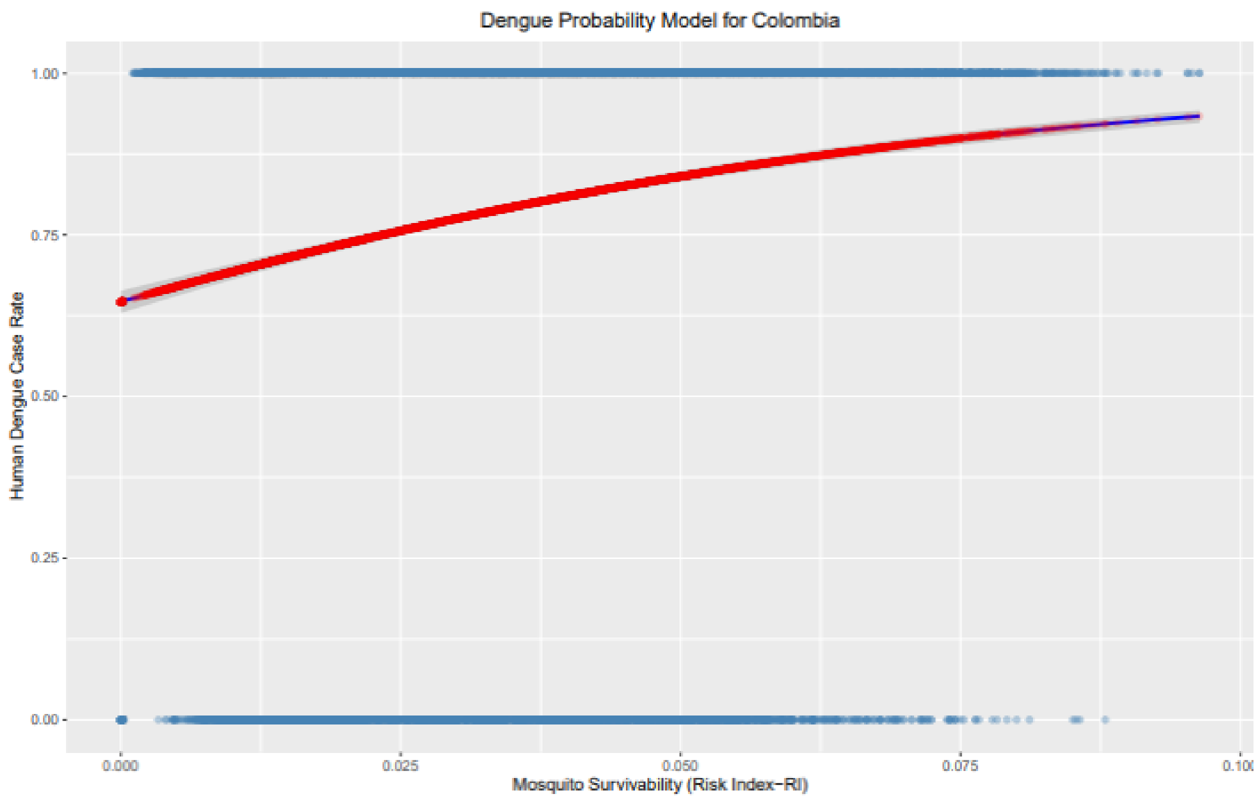


Figure 8: Model depicts the association between human dengue cases and the RI in Columbia.

Costa Rica Model

The Costa Rica model had an overall accuracy rate of 57.3% over the seven-year study period, with a highly significant p-value of <0.0001. The log odds of DENV without the impact of RI was -0.64, for an OR of 0.53. This means that odds of dengue presence was 0.53 to 1. Based on the model, for every 0.01 increase in RI or the probability the mosquito will survive past the incubation period, the odds of dengue presence increased by 69.5%. This outcome also indicated the larger the RI, the greater likelihood of DENV transmission (Figure 9). The model was not an acceptable standalone model due to the overall low accuracy. Inaccuracy in human case reporting and population could have skewed the model.

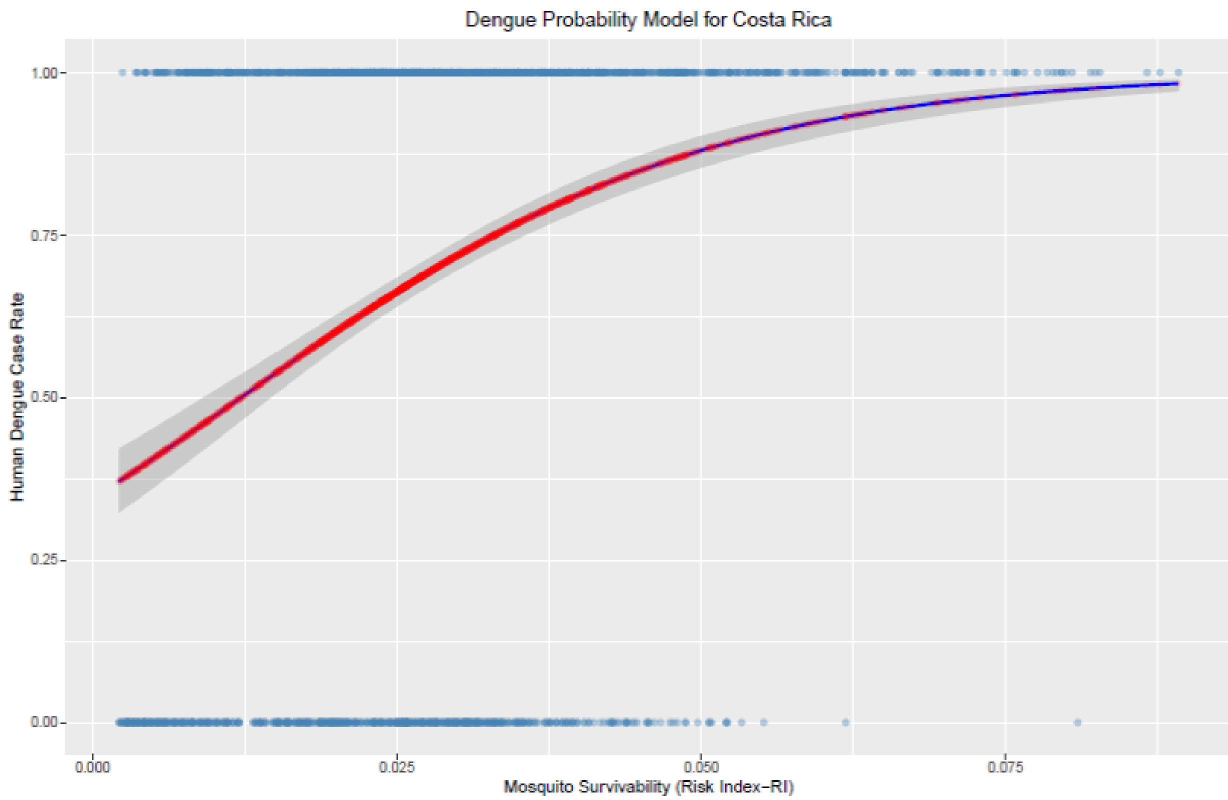


Figure 9: Model depicts the association between human dengue cases and the RI in Costa Rica.

Combined Model: Brazil, Colombia, and Costa Rica

The combined model had an overall accuracy rating of 70.2% over the combined twelve-year study period, with a highly significant p-value of <0.0001. The log odds of DENV without the impact of RI was 0.84, or an OR of 2.31. This means that the data showed the odds of dengue presence was 2.31 to 1. Based on the model, for every 0.01 increase in RI or the probability the mosquito will survive past the incubation period, the odds of dengue presence increased by 23%. This outcome had the same trend as the independent country models, and confirmed the larger the RI, the greater likelihood of DENV transmission (Figure 10). The combined model proved to be the best model to be used in other regional countries due to the combined country characteristics and data.

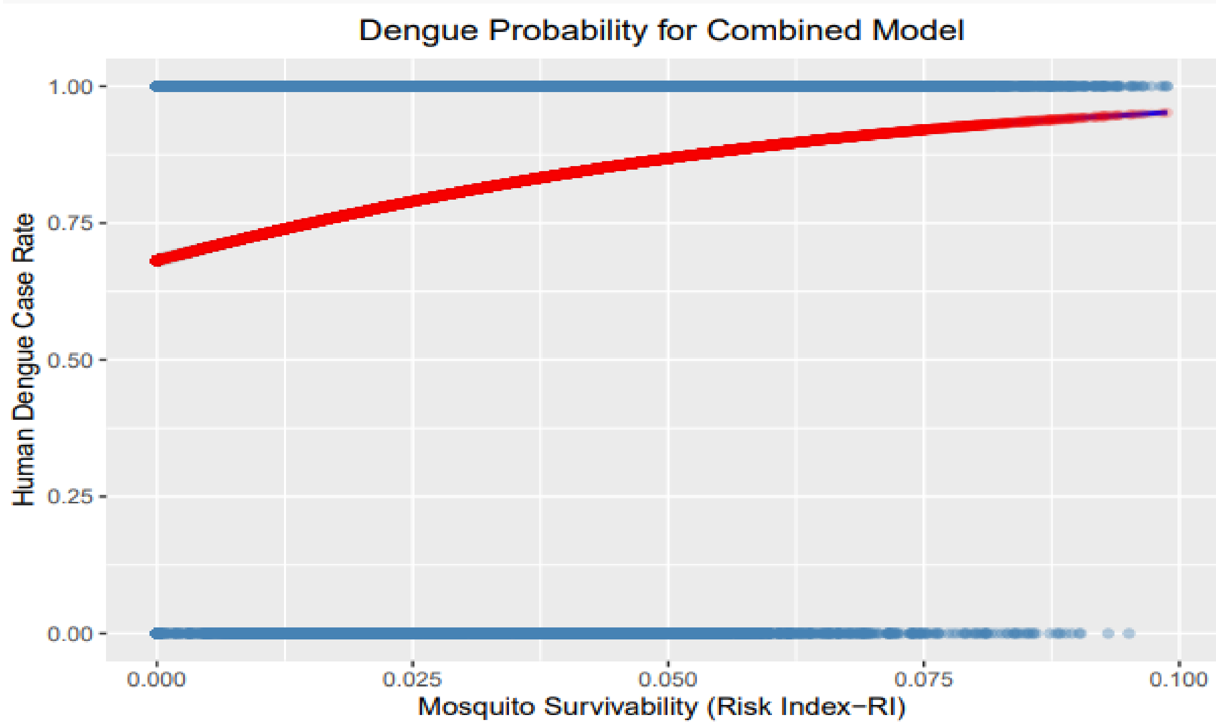


Figure 10: Model depicts the association between human dengue cases and the RI in Brazil, Colombia, and Costa Rica combined.

Model Statistical Summary

The output of the individual country models, as well as the combined model, provided several essential statistical findings that highlight the accuracy (Table 2). The accuracy rating presented the initial validation potential of the models. All the models performed above 70% accuracy, except for Costa Rica, which had an accuracy rating of 53%. Each of the models found statistically significant associations among the dependent and independent variables. The table displays the intercept and coefficient (independent variables) values. Finally, in the results showed that for every 0.01 increase in RI (probability the mosquito will survive past the incubation period), the odds of dengue presence increased by 12.6% (Brazil), 23.6% (Columbia), 69.5% (Costa Rica), and 23% (Combined). Interpreting the combined model row and the OR increase column, it can be inferred that for every 0.01 increase in RI, the odds of DENV presence in the model increased by 23%.

Table 2: Model Summaries

	Accuracy[1]	p-value	Significance	Intercept[2] Coefficient	RI Coefficient[3]	Log Odds OR w/o RI (0.1)[4]	OR per ↑1 Risk Index (.01)[5]
Brazil	84.50%	≤ 0.00072	High	2.51	11.9	12.2	12.6
Colombia	73.50%	<0.0001	High	0.603	21.16	1.83	23.6
Costa Rica	53.70%	<0.0001	High	-0.64	52.76	0.53	69.5
Combined	70.20%	<0.0001	High	0.84	20.67	2.31	23

[1] Accuracy depicts % the model correctly predicted the outcome. [2]Intercept coefficient is the log odds=0. [3] RI coefficient is the expected change in log odds for a one-unit increase in RI. [4] Log odd odds ratio without RI).01. [5] Odds ratio with RI increase per 0.01.

Discussion:

Strengths:

The study outcome displayed considerable potential for future use in public health monitoring. The models have the ability, with further refinement and more extensive data sets, to be regionally generalizable. Even with limited data, the models, apart from Costa Rica, had high predictability. Countries within the region should be able to apply the DENV human case rates and RI with similar accuracy.

The combined model using data from all three countries, had an accuracy rating of 70.2%, and could be used for seasonal predictions. With a broader data set and country characteristics, this model has the potential to be a great foundation model within the region.

This study was a substantial starting point for additional studies to be conducted. Future studies could use the collected long-term monthly climatology, gridded temperature, and relative humidity, the RI could be calculated for the entire region. The monthly gridded RI could then be used as input into the logistic regression model. The output would provide the gridded probability of the presence/absence of DENV for each month. Gridded human population data then could be overlaid on the dengue presence/absence maps to determine an approximate number of people at a specific location at risk for DENV each month.

Limitations

The study had a few limitations that potentially impacts the models' accuracy and utility. First, the reporting periods of confirmed DENV cases vary by country. For example, Colombia reported confirmed weekly DENV cases from 2007 to 2018, whereas Brazil has reported them from 2014 to 2017. Second, the use of secondary open-source data assumed the data are accurate with a similar case definition of confirmed cases across all countries, which is likely not the situation due to under-reporting and varying case definitions. Third, the scope of the study only includes a few countries where data were available. Assuming that these countries are representative of the entire region is problematic but necessary given data availability constraints. Next, the Costa Rica model did not perform well, which may be due to inconsistencies in case reporting and coupled with in-country Administrative 1 district realignment. Furthermore, some of the Administrative 1 units are very large and the environmental variation can get lost when we average across them. making predictability challenging. Lastly, the study did not include non-climate related factors, such as localized social determinants of health. Region-specific social determinants of health such as socioeconomic conditions, health system capabilities, education, community context, and neighborhood, and the built environment also impact DENV infection risk. Further research is needed to explore the impacts of both non-environmental determinates of health and environmental conditions regarding the actual risk of DENV to the population at risk.

Public Health Implications

Changes in weather conditions, climate change, and other environmental factors will continue to have profound impacts on DENV transmission and human health. This study analyzes DF and meteorological conditions and addresses the issues of increasing ambient temperature and humidity impacting the RI and the actual risk of contracting DENV. Continual increases in RI are associated with a shortened extrinsic incubation period and greater survival of the mosquito vector and, consequently, increased transmission of DENV.

The results show that more suitable temperatures and humidity have increased the reported cases of patients suffering from DF. DENV is a climate-sensitive virus that proliferates in warmer temperatures (to a point) and higher humidity. The study shows that the EIP is shorter at higher temperatures, due to faster viral replication and increased dissemination to the mosquito salivary glands. A shorter EIP results in mosquitoes becoming infectious sooner.

Continuous change in the global environment and the increased burden of DF incidence emphasize the importance of evaluating the significance of these changes. The ability to forecast favorable environmental conditions may aid in determining appropriate resource allocation and planning to prevent DENV transmission not only in these countries but throughout the region.

In conclusion, applicable population health intervention strategies must be developed and implemented to address the increasing incidence of DF. For example, governmental entities could reduce the burden of disease incidence by investing in climate-resilient health systems and surveillance that includes meteorological monitoring. Additionally, establishing an educational campaign targeted during seasonal periods of increased risk is imperative to ensure governmental entities and the population at risk have the knowledge needed for effective action.

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