Proposed Econometric Strategy in Determining Thresholds of Levels of Diseases with Applications to Dengue Cases of a Highly Urbanized City

Hernan G. Pantolla*[1,2] and Alex C. Gonzaga[2]

[1]Mathematics and Statistics Unit, Kolehiyo ng Lungsod ng Dasmariñas, Cavite, Philippines
[2]Department of Physical Sciences and Mathematics, University of the Philippines Manila, Manila, Philippines

ABSTRACT

Disease thresholds of outbreaks are typically set at two standard deviations above the endemicity and are arbitrary in nature. For dengue, the potential effects of the lags in the rise of the reported number of cases, the complexity of the impacts of specific meteorological parameters, possible effects of climate change, and natural environmental anomalies, among others, also vary per geographical area which could further complicate the identification of disease thresholds. Common practice is to calculate the two standard deviations beyond the endemic level. Existing research typically focuses on calculating a reproduction number pertaining to the average number of people infected by a person with the infection in a population that is otherwise negative of the disease. This study, on the other hand, aimed to propose a novel approach by applying econometric procedures to identify thresholds of Levels of Disease that could be useful in drafting epidemiological surveillance guidelines and plans of action. The proposed strategy was done using the moving average (MA) of the weekly totals of confirmed dengue cases in Davao City in the Philippines, from January 2018 to December 2020, as the dependent variable. The study setting was selected since it is classified as a Highly Urbanized City, and hence, urbanization and globalization, which are among the primary drivers of dengue emergence, are observed. As regressors, meteorological variables, such as total rainfall, mean maximum temperature, mean minimum temperature, and relative humidity, which have been substantiated by the literature as widely utilized variables with varying impacts on the transmission of dengue cases, were used in this study. The proposed five-stage strategy includes (1) Optimal Lag selection, (2) Autoregressive Distributed Lag (ARDL) Model applicability assumption evaluation, (3) extracting the MA of the number of weeks identified as the optimal lag, (4) applying the ARDL Model to determine supplemental significant regressors and lags, and (5) implementing the Threshold Regression (TR) Model to determine the thresholds to differentiate the Levels of Disease for the study setting. The findings show the optimal lag is 2 weeks. The variables used were statistically proven to be a combination of stationary at the level and the first difference and

*Corresponding author
Email Address: hgpantolla@up.edu.ph
Date received: May 9, 2023
Date revised: June 30, 2023
Date accepted: September 4, 2023

KEYWORDS

Climate Change, Dengue, Econometrics, Epidemiology, Outbreak, Thresholds

hence, the ARDL Model was deemed applicable. Further, the ARDL Model retained (1) the first and (2) second lags of the dependent variable, as well as (3) the direct effects of mean maximum temperature. These three significant variables were used as fixed independent variables whereas the rainfall, minimum temperature, and humidity were used as region-varying regressors, for the dependent variable in the TR Model. Three Levels of Disease were recommended after optimally determining two threshold values which are 71.00 and 88.50. Hence, the three levels for the two-week MA of dengue cases are Endemic Level (below 71.00), Hyperendemic Level (71.00 to 88.50), and Outbreak Level (above 88.50) are recommended. This reproducible spatiotemporal strategy that combines epidemiology and econometrics can be applied to other geographical areas and diseases and be further improved with a longer time series.

INTRODUCTION

It is rare for infectious diseases to behave in simple dynamics. Due to overburdened healthcare systems, outbreaks (defined as an excess of cases beyond response capacity) have the potential to impose a disproportionately heavy dilemma according to Brady et al. (2015). The study of Brady et al. (2015) enumerated some of the characteristics of infectious diseases according to previous studies. To start with, significant progress has been made in the treatment of many infectious diseases and the reduction of their long-term burden (Lim et al. 2015). Nonetheless, unanticipated increases in cases beyond the seasonal expected average number of cases can frequently halt progress or strain the already hampered healthcare resources (Cotter et al. 2013; Garg et al. 2008; Hay et al. 2003a; Hay et al. 2003b). Multiple studies including that of the World Health Organization (WHO) stated that due to the absence of response skills, disease epidemics frequently spread quickly, are difficult or impossible to foresee, and place an excessively high burden on society (Garg et al. 2008; Grais et al. 2007; Najera 1999; WHO 2014). Research agendas and subsequent policy guidelines have heavily emphasized methods to predict outbreaks (early warning), how to identify them once they are occurring (early detection), how to respond to them appropriately (outbreak response protocols), and how to better plan for future outbreak occurrences (effective healthcare, surveillance, and control resource allocation) due to the clear importance of disease outbreaks to wider control efforts (WHO 2009, 2005, 1999; Farrar et al. 2007; Myers et al. 2000; Hutwagner et al. 2008). An explicit quantitative definition of exactly what the term *outbreak* refers to in terms of frequency, length, amplitude, and burden is necessary for the optimization of each of these distinct goals.

The study of Brady et al. (2015) continued that using epidemiological criteria, which classify common definition of outbreaks, is any temporal deviation from the expected prevalence of cases. (Wagner et al. 2001; Stroup et al. 1993). It can be challenging to identify between the expected number of cases (seasonal variation in frequency) and excessive incidents (outbreaks) for several infectious conditions with complex transmission patterns and limited surveillance by health systems. For instance, dengue is made up of four serotypes with intricate cross-immunity patterns in humans (Simmons et al. 2012; Wearing and Rohani 2006). Every serotype displays extraordinarily diverse environmental deviations in its distribution and infection prevalence. (Messina et al. 2014; Reiner et al. 2013). Additionally, it is challenging to interpret the seasonal patterns in reported case data because treatment, diagnosis, and reporting of dengue are all extremely varied (Simmons et al. 2012; Endy et al. 2011; Brady et al. 2014). This makes the task of interpreting seasonal patterns of reported dengue incidence difficult (Hay 2013). This may be exceptionally true also for smaller geographical levels.

Several factors lead to the emergence of dengue spread, but only three have been the most influential according to Gubler (2011). These are (1) urbanization, (2) globalization, and (3) ineffective vector management. In addition, dengue viruses (DENV) have completely adapted to a human-*Aedes aegypti*-human transmission cycle in densely populated tropical urban areas where both populations of humans and mosquitos are cohabiting. This environment is ideal for virus survival and the periodic production of epidemic strains. Typically, urbanized areas have modernized airports through which millions of travelers pass each year, providing pathways for the transfer of DENV to new cities, areas, and continents where mosquito control is nonexistent or minimal, if it exists at all. The result is a dengue epidemic (Gubler, 2011). The DENV exists among villagers and city dwellers. The European Centre for Disease Prevention and Control (ECDC) states that because its primary vector, *Aedes aegypti*, is prevalent in the peridomestic environment, dengue is primarily a village and urban disease. The species is a highly efficient vector since it feeds almost solely on people, reproduces in small man-made objects containing water, rests within structures, and seldom resides more than 50 meters away from human settlement. Its biting tendencies are typically diurnal (ECDC 2021).

Now an *epidemic threshold* (or *alert threshold*) is the incidence threshold at which a disease warrants immediate action. According to the United Nations High Commissioner for Refugees (UNHCR), the threshold for each disease varies depending on its spreading ability, other transmission mechanisms, and the extent of geographical endemicity (UNHCR 2023).

In general, outbreak thresholds are arbitrarily estimated to be two standard deviations (SDs) higher than the endemic level. (Wagner et al. 2001; Stroup et al. 1993; WHO 2009; Hutwagner 2003). The residual diversity for many diseases not taken into consideration by these methods makes it exceedingly uncertain to identify the endemic level and frequently, momentarily, and irregularly breach the outbreak threshold value (Badurdeen et al. 2013). Though there aren't many extra instances, even short epidemics could trigger the need for significant outbreak response measures. In terms of public health or operations, this would be considered a false alarm for an outbreak (Brady et al., 2015).

The topic of whether a pathogen introduced into a fully uninfected population will cause extinction or an outbreak has garnered significant attention. The outcome is impacted by the system's characteristics regarding the epidemic threshold condition. Growing evidence suggests that these limits exist in actual host-pathogen systems, indicating that they are not merely a theoretical concept (Dallas, Krkošek, and Drake 2018; Leitch, Alexander, and Sengupta 2019). The epidemic threshold is often specified in terms of the basic reproduction number, R_0, which is the average number of uninfected populations infected by a carrier (Diekmann and Heesterbeek 2000; Leitch et al. 2019). When R_0 is greater than 1, the disease may spread; when R_0 is less than 1, it dies off. The epidemic threshold can also be characterized as the critical value of at least one model parameter. Over the epidemic threshold, a finite proportion of the population is infected by the pathogen. Pastor-Satorras et al. (2015) found that in the limit of enormous networks, the prevalence (total number of infected individuals) remains infinitesimally small beneath the epidemic threshold. Exclusive reliance on a calculated R_0, though, poses major concerns too.

The systematic review of Liu et al. (2023) summarizes that depending on geographic location, the R_0 values for typical mosquito-borne diseases including dengue are clearly heterogeneous. The differences in R_0 estimates between temperate and tropical regions generalized that climate should be accounted for. They also found higher R_0 values in subtropical regions compared to tropical regions, which may indicate that other factors are also significant. For instance, socioeconomic differences between study locations may influence R_0 estimates, as locations with lesser capacities in managing public health may engage in less effective vector control or surveillance (Reiter et al. 2003; as cited in Liu et al. 2023).

Chowell et al. (2016; as cited by Liu et al. 2023), stated that the timing of interventions and the onset of an epidemic influence its scope. As such, a reactive intervention that is appropriately efficient may also underestimate the R_0. The *Aedes aegypti* as a vector thrives in urban settings (Weaver and Reiser 2010; as cited in Liu et al. 2023) as well and hence, overestimation of outbreaks in more urbanized areas may ensue. Additionally, the systematic review published by Leung et al. (2023) highlighted some expository information about modeling dengue cases. Meteorological parameters or a combination thereof were commonly used as regressors. The seriousness of the effects of lags especially in reporting delays of cases was also emphasized. Autoregressive time series modeling, moreover, appears to be an encouraging field to practice as some literature suggests. A summary of some of the common ways to calculate outbreak levels is given in Table 1.

Table 1: Common methods in setting a disease (dengue) threshold.

Method	Potential Bias(es)
2SDs above Endemic Level	• Arbitrarily set. • May not account for diversity of the disease. • Short epidemics (false alarm) may cause full-scale response.
Calculation of R_0	• Influenced by location and season. • The timing of intervention may cause underestimation.
Predictive Models	• Effects of lags are usually not accounted for. • Typically calculates the outbreak scenarios only.

This study, though, intends to proceed in a different and possibly novel direction. The objective of this is to use econometrics methods to generate dengue epidemiological thresholds for a specific urbanized locality in hopes to provide an alternative protocol for dengue surveillance and outbreak detection. It will also use meteorological parameters as regressors, account for potential effects of lags, and apply autoregressive modeling. It will also deviate from calculating an R_0 for a Highly Urbanized City located in the south of the Philippines and instead, directly estimate thresholds that could be used by the local government of the selected area for their localized dengue monitoring and surveillance.

MATERIALS AND METHODS

Variables used

The study will use local meteorological parameters as the initial set of regressors in hopes to capture some information on how the changing climate spatiotemporally affects a granular geographical location as summarized by Wilder-Smith et al. (2013). To start with, it is recognized that temperature influences adult vector survival, virus replication, and infectious periods (Wilder-Smith and Gubler 2008; Reiter 2001; Gubler et al. 2001; Patz and Reisen 2001).

The spread of Aedes mosquitoes is mediated by environmental, climatic, and meteorological parameters, which may provide insightful information for predictive models. The weather has been demonstrated to be a predictor of dengue activity (Patz and Reisen 2001; Earnest et al. 2011; Wu et al. 2007; Hii et al. 2009; Leung et al. 2023). The Intergovernmental Panel on Climate Change (IPCC) forecasts an increase in global mean temperatures (IPCC, 2007). This may produce climatic and environmental circumstances favorable to the spread of *Aedes* species into regions where they are not currently endemic. *Aedes aegypti* and *Aedes albopictus* could become established or reestablished soon due to the climatic appropriateness of numerous currently non-endemic regions and their climatic similarities to endemic regions (Reiter 2010). According to a study conducted in the southwestern Pacific, the rise in global temperature over the past four decades correlates with an increased likelihood of dengue outbreaks (Banu et al. 2011). Some research on climate change and dengue indicates a possible increase in transmission because of greater temperatures, humidity, and rainfall caused by climate change (Hii et al. 2009; Souza et al. 2010). This supports the theory that observable environmental changes, such as a rise in world average temperature and humidity, increase the possibility of dengue epidemics (Russel et al. 2009; Van Kleef et al. 2011). A Based on long-term average vapor pressure forecasts, temperature change, and population estimates, a study predicts that 50 to 60 percent of the world's population will live in dengue transmission risk areas by 2085 (Hales et al. 2002). If climate change did not occur or was not accounted for in the model, the hypothesis would be invalid only 35% of the population would be at risk (Van Kleef et al. 2011). Temperature increases may result in enhanced vector survival and/or migration into formerly non-endemic regions outside the tropics (Hales et al. 2002).

Although climate change may not be a sufficient and comprehensive factor in the current and ongoing spread of dengue, *global change* could potentially be (Sutherst 2004). The global change approach attempts to account for numerous contemporary elements that contribute to vector-borne communicable diseases (Sutherst 2004). Globalization factors, such as travel and commerce, trends in modern human settlement, and climatic conditions suitable to vectors all contribute to the accelerated spread of vector-borne transmissible diseases (Gubler, 2011). The main driver in explaining the contemporary increase in dengue transmission may be the increased mobility of both human populations and the vector, furthermore.

Study setting

Classified as a Highly Urbanized City (HUC), the selected study setting is Davao City. It is a first-class HUC on the island of Mindanao (National Economic Development Authority 2021). It has both an international airport and a seaport for global shipments. Davao City has a total land area of 2,444 square kilometers, making it the largest city in the Philippines by land area. Geographically, Davao City is in the southeastern portion of Mindanao, among the grid squares of 6°58′ to 7°34′ N latitude and 125°14′ to 125°40′ E longitude. The distance between Davao City Proper and Manila is roughly 946 kilometers by air (City Government of Davao 2019). Therefore, the city possesses two of the primary drivers of the spread of dengue cases, which are urbanization and globalization (Gubler 2011). The population is also mobile, and vectors could be the same too which could contribute to the spread of DENV. Figure 1, which was generated in ArcGIS 3.0.1 shows the location of Davao City.

Figure 1: Map of Davao City.

Davao City's climate, similar to the whole country, is tropical. The city receives substantial rainfall all during the year. Even the driest month (April is the warmest month of the year) receives significant amounts of rainfall (Weather Atlas, n.d.). Moreover, the climate of the city which is part of the Davao Region is oppressive, humid, and cloudy. The average annual temperature ranges from 23.9°C to 32.8°C, seldom falling below 22.8°C or rising above 34.4°C (WeatherSpark n. d.).

The confirmed weekly incidence of dengue cases is the dependent variable in this study. The data was requested from the Department of Health (DOH). The provided data by the DOH covers the morbidity weeks data from January 2018 to December 2020. On the other hand, the daily data was converted to the weekly total of rainfall (1, in mm), as well as the averages of maximum temperature (2, in °C), minimum temperature (3, in °C), and relative humidity (4, in %) are the initial set of independent variables which were all requested from the Philippine Atmospheric, Geophysical and Astronomical Services Administration (PAGASA). The meteorological parameters were collected from the PAGASA station in the city. The observation period is weekly frequency from January 01, 2018, to December 21, 2020, which makes up for 156 weeks to match the data of dengue cases provided by the DOH.

Statistical Methods

A five-stage strategy will be employed. Methods in econometrics shall be sequentially applied to come up with statistically valid results and eventually generate epidemic thresholds for the confirmed dengue cases in Davao City. The strategy starts with optimal lag selection (1). This is to account for the potential effects of lags on the reported number of confirmed cases. The optimal number of lags is then used to set the number of weeks for the calculated moving average (MA) of the variables (2). This will be done to minimize the effects of the delays in reporting data for various reasons, especially in the number of cases of dengue. Afterward, the applicability of the Autoregressive Distributed Lag (ARDL) Model shall be tested (3). All the variables must be either stationary at the level or at the first difference to match the assumptions and applicability of the ARDL Model. If any of the variables are neither stationary at the level nor the first difference i.e., stationary only at the second difference or higher, then the strategy cannot be implemented since ARDL Model estimates a linear regression model between the variables (Kripfganz and Schneider 2023). On the other hand, the ARDL Model shall be applied if applicable to discriminate the significant regressors with lags regardless of the magnitude of effects or direction (4). Lastly, the Threshold Regression (TR) Model shall be done using the significantly retained variables from the ARDL Model to identify the epidemic thresholds for confirmed dengue cases in Davao City (5). Figure 2 shows the visualization of the procedures.

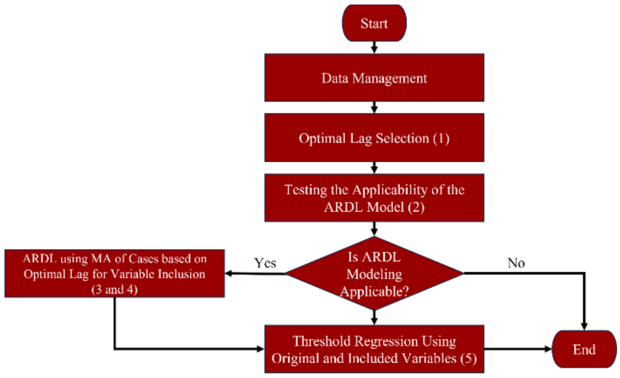

Figure 2: Flowchart of the statistical methods to be applied.

Optimal Lag Selection

The Likelihood Ratio (LR) Test compares a Vector Autoregressive (VAR) framework, with say l^* number of lags, to another with $l^* - 1$ lags for a given lag l^*. Every coefficient on the l^*th lags of the endogenous variables is zero, according to the null hypothesis. The process will be done repetitively, and the optimal lag order is selected by this procedure when the first l^* that rejects the null hypothesis is obtained (StataCorp 2021a). More information can be taken from Lutkepohl (2005) regarding this procedure. The Final Prediction Error (FPE), Akaike Information Criterion (AIC), Schwarz-Bayesian Information Criterion (SBIC), and Hannan-Quinn Information Criterion (HQIC) may suggest different optimal lags. However, the identified higher optimal number of lags shall be selected for the objective of the study which is to evaluate the number of lags corresponding to the effects of prior weeks of the independent variables and their lags to the response variable, and the lag(s) of the response variable as well.

Stationarity

The Augmented Dickey-Fuller Test (Dickey and Fuller 1979) will be applied to determine the stationarity of the variables. The test will be used to determine whether a variable is (1) stationary at the level which does not require differencing or (2) follows a unit-root process i.e., stationary only at the first difference (StataCorp 2021b). All variables that are stationary without differencing or at first difference shall be used in the ARDL Model.

ARDL Model

The ARDL Model is an econometric procedure for a specified response variable that specializes in determining the short-term effects of the predictor(s) and its corresponding lags (Pesaran, Shin, and Smith 2001). The ARDL is appropriate for modeling a set of variables that are either wholly stationary at the level also known as $I(0)$, or purely stationary only after differencing for the first time referred to as $I(1)$ as well, or a combination of both types. In addition, the ARDL system applies a linear regression model that incorporates potential lags of the response and explanatory variables as additional regressors (Kripfganz and Schneider 2023). This method will be used in hopes to provide contributions in reducing the complexity of the combination of variables and lags that may have impacts on the thresholds of dengue cases in the study setting.

The fundamental form of the ARDL(h, m) where h and m represent the optimal lags of the response variable y_t and regressor x_t in succession is provided by

$$\Delta y_t = \beta_0 + \Theta t + \sum_{i=1}^{h} \beta_i(\Delta y_{t-i}) + \sum_{j=0}^{m} \Gamma_j(\Delta x_{t,i-j}) + \lambda_1 y_{t-1} + \lambda_2 x_{t,i-1} + \varepsilon_t \quad (1)$$

In Equation 1, the possibility of having lags and differences included in the model is denoted by Δ. The component β_0 defines the constant while the trend, if existing, is denoted by Θ. The error terms are denoted by ε_t. Additionally, β_i and Γ_j denote~~s~~ the coefficients of the short-run relationship while $\lambda_i; i = 1,2$ denotes the long-run relationship coefficients (Haq and Larsson 2016). The ARDL Model also features identifying variables with effects in the long run as well as an Error Correction Term that can be plugged into the current form of the ARDL Model and extend it into an Error Correction Model (ECM) via determining an Error Correction Term. However, building an ECM will not be necessary for this proposed procedure since the main concern is the identification of significant variables and lags only that can be used in the Threshold Regression (TR) Model.

Now for this study that deals with the multivariate case ARDL(h, m_i), $i = 1,2,\ldots,4$, Equation 1 is extended into

$$\begin{aligned}\Delta \text{cases}_t = \beta_0 &+ \sum_{i=1}^{h} \beta_i(\Delta \text{cases}_{t-i}) + \sum_{i=0}^{m_1} \Gamma_{1,i}(\Delta \text{rainfall}_{t-i}) + \sum_{i=0}^{m_2} \Gamma_{2,i}(\Delta \text{maxtemp}_{t-i}) \\ &+ \sum_{i=0}^{m_3} \Gamma_{3,i}(\Delta \text{mintemp}_{t-i}) + \sum_{i=0}^{m_4} \Gamma_{4,i}(\Delta \text{humid}_{t-i}) + \Gamma_0 \text{cases}_{t-1} + \Gamma_1 \text{rainfall}_{t-1} \\ &+ \Gamma_2 \text{maxtemp}_{t-1} + \Gamma_3 \text{mintemp}_{t-1} + \Gamma_4 \text{humid}_{t-1} + \varepsilon_t. \end{aligned} \quad (2)$$

In Equation 2, h and m_i denote the empirically pre-defined optimal lags of the dependent variable, and independent variables, in succession. Further, β_i and Γ_i are the coefficients of the variables with short-run relationships. The 0.10 level of significance will be applied herein for leniency in regressor selection.

Threshold Regression

The TR is an extension of least squares regression that allows coefficients to vary across *regions*. The regions are differentiated by a threshold variable that may fall below or exceed a threshold value. The TR Model could generate multiple thresholds and the least values of SBIC, AIC, and HQIC could be selected (StataCorp 2021c). This study will attempt to find two values that will be empirically calculated as the recommended thresholds for dengue in the city. This simplifies the procedure and reproducibility of the model for other locations and/or diseases that would use the same set of variables. Correspondingly, the regions that will be identified by the threshold, afterward, shall be referred to as *Levels of Disease* in epidemiological terms used in epidemiology as defined by the Centers for (CDC 2012).

The TR Model that will be implemented in this study with three Levels of Disease as discriminated by the two determined thresholds $\upsilon_j, j = 1,2$ is given by

$$y_t = \underline{x}_t \underline{\beta} + \sum_{j=1}^{2} \underline{v}_t \phi_j I_j(\upsilon_j, V_t) + e_t$$

where y_t is the dependent variable (two-week MA of cases), $\underline{x_t}$ is a covariates vector that may include lagged values of y_t empirically identified from the ARDL Model. In addition, $\underline{\beta}$ is a vector of parameters in any of the Levels of Disease that are invariant, $\underline{v_t}$ is a vector of exogenous variables specific that are specific to each Level of Disease denoted by $\underline{\emptyset_2}$ and $\underline{\emptyset_2}$, and V_t as the threshold variable which could be one of the variables in $\underline{x_t}$ and $\underline{v_t}$, too. Additionally, e_t denotes an independent and identically distributed residual with mean 0 and variance σ^2. Moreover, $\upsilon_1 < \upsilon_2$ are thresholds in succession having the indicator $I_1(\upsilon_j, V_j) = I_1(\upsilon_1 < V_t \leq \upsilon_2)$ for the j^{th} Level of Disease. The TR framework follows a linear regression system that is conditional on each estimated threshold $(\hat{\upsilon}_1, \hat{\upsilon}_2)$ and the remaining parameters also apply the least squares method to estimate (StataCorp 2021c).

RESULTS

Optimal Lag Selection

The optimal number of lags is a vital piece of information. This value determines how many lags shall be considered in modeling the dependent variable using the pre-determined independent variables. It is also the basis for the number of weeks in generating values for the MA of the variables. Table 1 shows the results of the optimal leg selection.

Table 2: The optimal number of lags from each information criterion.

Lag	FPE	AIC	HQIC	SBIC
0	~3,400,000	29.24	29.28	29.34
1	365,532	27.00	27.24*	27.60*
2	356,535*	26.97*	27.42	28.07
3	367,891	27.00	27.65	28.59
4	381,321	27.03	27.88	29.12

Table 2 shows that the lowest value indicating the plausibility of being selected as the optimal number of lags according to both HQIC and SBIC is 1 while the AIC and FPE are 2. To avoid underfitting, the optimal number of lags is set to 2. This would allow simultaneous testing of the effects of the first and second lag of the significant regressors. Essentially, the impacts of the previous week and/or the week prior of a significant variable to the confirmed dengue cases can be statistically assessed in consideration of the limitation in the length of the time series. This also supports the use of a two-week period in extracting the MAs of the variables.

Summary Statistics

Table 3 shows the summary statistics of the variables used. The mean of the confirmed cases of dengue is 58.90 with a standard deviation (SD) of 40.95 confirmed cases. It has the minimum in Week 18 of 2020 at 11.50 whereas the maximum was on Week 29 of 2019 at 216.50. Additionally, the mean rainfall amount is 35.85 millimeters (mm) with an SD of 29.86 mm, the mean maximum temperature is 32.81˚C with an SD of 0.83˚C, the mean minimum temperature is 25.00˚C with an SD of 0.54˚C, and the mean relative humidity is 76.02% with an SD of 3.24%.

The visualization of the variables (with means in black perforated lines) is presented in Figure 2.

Table 3: Summary statistics of the two-week MAs of the variables.

Variable	Mean	SD	Min	Max
MA of Cases	58.90	40.95	11.50	216.50
MA of Total Rainfall	35.85	29.86	0.00	124.00
MA of Maximum Temperature	32.81	0.83	30.44	35.04
MA of Minimum Temperature	25.00	0.54	23.16	26.46
MA of Relative Humidity	76.02	3.24	66.50	82.00

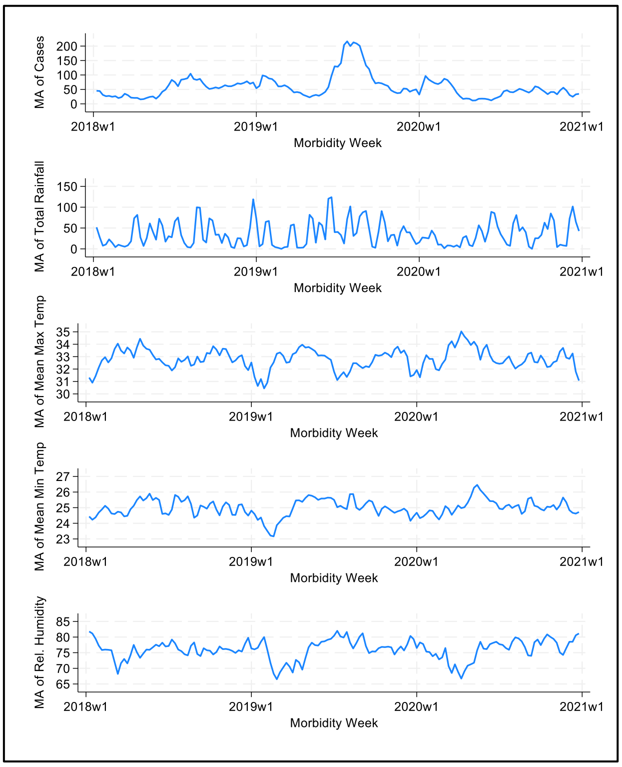

Figure 3: Time series plots of the variables.

A DOH official announced in early August 2019 that the city has the maximum number of dengue cases in the Davao Region, with 2,168 cases and 11 deaths since the beginning of the year (Philippine News Agency August 9, 2019). The data also showed that over 100 cases were confirmed between mid-June to mid-September 2019. The aggregated rainfall did not show much of any seasonality or trend. On the other hand, the deviations of maximum temperature and minimum temperature from the mean of the whole observation period have become slower especially for the latter in the mid to late 2021. The relative humidity has shown an increasing trend as well. The National Oceanic and Atmospheric Administration (NOAA) experts officially declared that 2020 was the second warmest year on record for the world, displacing 2019 to third place. Since records began, 2016 is still the warmest in terms of global averages (NOAA 2020). In addition, 2019 saw irregular weather patterns and averages in the Philippines (and globally), including the Davao Region, where Davao City, as a weak episode of El Niño occurred (PAGASA 2019a).

Stationarity of Variables

Table 4 shows the results of the Augmented Dickey-Fuller tests and that all the variables have p-values below the 0.05 significance level except for the confirmed dengue cases which are stationary only after the first difference. The combination of $I(0)$ and $I(1)$ variables substantiate the applicability of the ARDL Model.

Table 4: Stationarity of each variable.

Variable	Stationarity p-values: At level	Stationarity p-values: At first difference	Integration
Confirmed dengue cases	0.1119*	<0.0001*	$I(1)$
Aggregated rainfall	0.0131	-	$I(0)$
Maximum temperature	<0.0001*	-	$I(0)$
Minimum temperature	0.0051	-	$I(0)$
Relative humidity	0.0015*	-	$I(0)$

Application of the ARDL Model

The result of the ARDL Model with a 97.71% r-squared value is provided in Table 5. At the 0.10 level of significance for more lenient variable selection, the significant variables are (1) the first and (2) second lag of the MA of confirmed dengue cases, and (3) the direct effect of maximum temperature. These significant variables shall be plugged in as fixed independent variables into the TR Model as the independent variables – regardless of having a positive or negative coefficient. The MA of rainfall, MA of minimum temperature, and MA of relative humidity will then be used as time region-varying variables in the TR Model.

Application of the TR Model

The results of the TR Model that would provide the (1) thresholds that would be used for ranges of Levels of Disease and (2) coefficients of the effects of each regressor to the dependent variable are shown in Table 6 and Table 7, respectively, at the 0.10 significance level. The empirically identified thresholds of the two-week MA of the dengue cases for Davao City are 71.00 and 88.50 after setting its first lag as the threshold variable as seen in Table 6. The corresponding values for the AIC, SBIC, and HQIC for the threshold are 733.78, 779.24, and 752.25, respectively. From the calculations of the authors, this finding is also the result with the least values of the 3 criteria.

Three recommended Levels of Disease, for a more practical epidemiological surveillance approach for Davao City, are presented in Table 6. Following the definitions provided by the CDC, these three determined regions will be referred to as *Endemic, Hyperendemic,* and *Outbreak* (CDC 2012). The Endemic Level is the frequently expected level that is typically present in the area. This level is not necessarily the desired, which could be zero; rather, it is the level that is observable as the baseline. Assuming the level is not high enough to deplete the vulnerable populations and without intervention, the disease (which is dengue for this study) could persist indefinitely. The *Hyperendemic* level, on the other hand, refers to persistently higher levels of the disease whereas an *Outbreak* is defined as a rise in the number of cases of the disease that is normally observed in a smaller geographical area (as compared to an *Epidemic*). The results in Table 5 therefore show that the Endemic Level is expected is when the two-week MA of cases is sustained below the 71.00 threshold. A Hyperendemic Level occurs when the two-week MA of cases elevates from 71.00 to 88.50. Lastly, an Outbreak may be declared in the highly urbanized city if the two-week MA of cases has breached the 88.50 mark and has exceeded the third week.

Table 5: Results of the ARDL Model.

Variable	Effect	Coefficient	p-value	95% CI	
				LL	UL
MA of Cases	First Lag	1.23	<0.001*	1.07	1.39
	Second Lag	-0.33	<0.001*	-0.49	-0.17
MA of Rainfall	Direct	-0.04	0.444	-0.13	0.06
	First Lag	0.05	0.345	-0.05	0.15
	Second Lag	-0.05	0.276	-0.14	0.04
MA of Maximum Temperature	Direct	-5.25	0.099*	-11.50	0.99
	First Lag	-3.04	0.457	-11.09	5.02
	Second Lag	1.98	0.534	-4.30	8.27
MA of Minimum Temperature	Direct	3.75	0.307	-3.48	10.99
	First Lag	0.72	0.885	-9.13	10.57
	Second Lag	2.89	0.446	-4.59	10.38
MA of Relative Humidity	Direct	-0.43	0.625	-2.14	1.29
	First Lag	-0.56	0.607	-2.73	1.60
	Second Lag	0.71	0.376	-0.87	2.28
Constant		51.72	0.580	-132.43	235.87

* - significant at the 0.10 level; CI, LL, and UL denote Confidence Interval, Lower Limit, and Upper Limit, respectively

Table 6: Ranges of confirmed cases per Level of Disease

Alert Level	Range	AIC	SBIC	HQIC
Endemic	Below 71.00	733.78	779.24	752.25
Hyperendemic	71.00 to 88.50			
Outbreak	Above 88.50			

Table 7 shows the results of the TR Model at the 0.010 significance level. As shown, all three independent variables are significant. Particularly, the independent increases in the first lag of the MA of cases may increase by 1.37 on average, the second lag of the MA pf cases may decrease by 0.34 on average, and the direct effect of the MA of maximum temperature may decrease by 5.73 on average, the present value of the dependent variable holding other conditions constant.

Table 7: Results of the TR Model.

Components/ Level	Variables	Coefficient	p-value	95% CI	
				LL	UL
Independent Variables	First Lag of the MA of Cases	1.37	<0.001*	1.21	1.53
	Second Lag of the MA of Cases	-0.34	<0.001*	-0.47	-0.21
	MA of Maximum Temperature	-5.73	0.003*	-9.55	-1.91
Endemic	MA of Total Rainfall	0.07	0.087*	-0.01	0.14
	MA of Minimum Temperature	4.18	0.105	-0.88	9.24
	MA of Relative Humidity	-0.65	0.177	-1.61	0.30
	Constant	132.32	0.098*	-24.59	289.23
Hyperendemic	MA of Total Rainfall	-0.03	0.772	-0.20	0.15
	MA of Minimum Temperature	6.74	0.096*	-1.19	14.67
	MA of Relative Humidity	-0.72	0.610	-3.48	2.04
	Constant	68.29	0.557	-159.83	296.40
Outbreak	MA of Total Rainfall	-0.59	<0.001*	-0.84	-0.33
	MA of Minimum Temperature	5.13	0.406	-6.96	17.22
	MA of Relative Humidity	6.27	<0.001*	3.60	8.93
	Constant	-419.62	0.030*	-798.76	-40.47

* - significant at the 0.10 level; CI, LL, and UL denote Confidence Interval, Lower Limit, and Upper Limit, respectively

Table 7 further shows that in the Endemic Level, every increase in the MA of total rainfall may increase the dependent variable by 0.07 on average holding other conditions unchanged. When the Hyperendemic Level is reached, the MA of minimum temperature could increase the response variable by 6.74 on average while holding the other conditions constant. On the other hand, during an Outbreak, an increase in the MA of total rainfall may lessen by 0.59 on average while a rise in MA of relative humidity may increase by 6.27 on average, the dependent variable *ceteris paribus*.

DISCUSSION

Figure 4 shows the plot of the two-week MA of cases in Davao City. The plot also shows the segments named Segment A (S_A), Segment B (S_B), and Segment C (S_C) has breached the calculated threshold at $y = 88.50$ threshold for the Outbreak Level. The threshold was exceeded in (S_A) and in (S_B) but on both times, the MA of cases have only lasted for two weeks. There is no reason to declare an Outbreak for those periods since the MA of cases did not last for more than two weeks and went to Hyperendemic Level before lowering back to the Endemic Level after a few weeks. In contrast, (S_C) depicts 14 weeks with a sustained MA of cases that exceeded the Outbreak threshold. This coincides with the national dengue epidemic that was declared in 2019 by the national government. There was also an isolated week with a surge where the Outbreak threshold was breached but quickly went back to Hyperendemic Level and eventually to the Endemic Level.

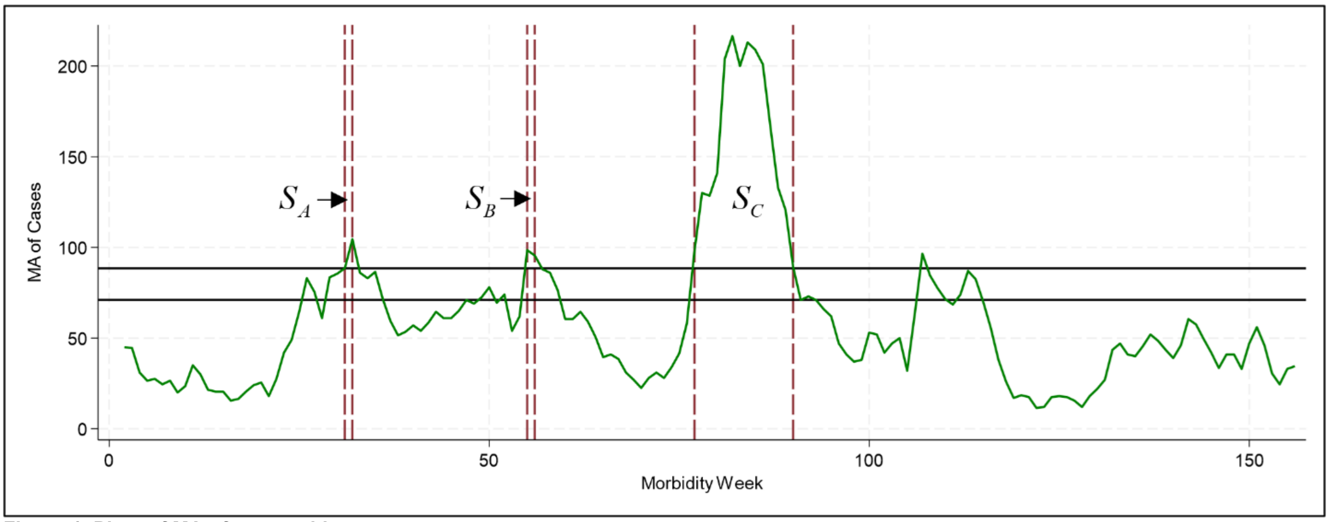

Figure 4: Plots of MA of cases with segments.

Curiously, S_C lasted from mid-June to mid-September in 2019. This covers the June-July-August seasonal quarter where the southwest monsoon (SWM) colloquially termed *habagat* is expected. The SWM transports a mass of substantially humid air during its season every year (Bouquet 2017; as cited in Espino et al. 2021). The El Niño episode in 2019 that was declared to have officially ended in August (PAGASA 2019a) may have also complexly affected the surge in cases due to its complex impacts on the transmission of dengue aside from the disruptions that it causes on the weather patterns of a geographical area.

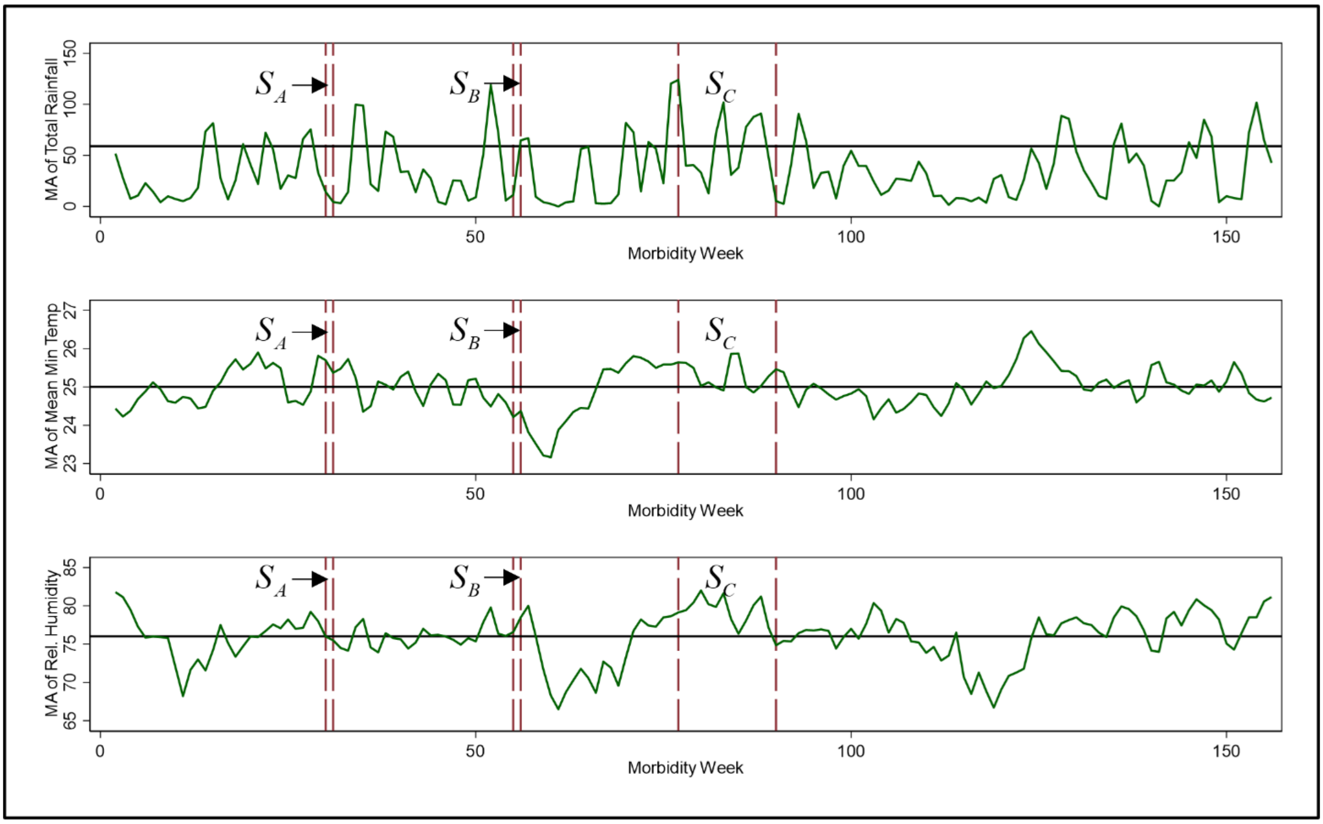

Figure 5: Plots of the MAs of Rainfall, Mean Minimum Temperature, and Mean Relative Humidity with their corresponding means S_C.

Given the effects of local meteorological parameters, such as humidity, rainfall, and temperature, on the Aedes vector, these parameters are proven statistically to be crucial in monitoring the spatial and temporal propagation of dengue (Naish et al., 2014). Seasonal variations in these meteorological parameters will play a significant part in determining the length of time and potential severity of the transmission of dengue in areas where these meteorological parameters are suitable to sustain transmission (Naish et al., 2014). It appears that several studies supporting the association of dengue epidemics to temperature (Chen and Hsieh 2012; Descloux et al. 2012; Earnest et al. 2012; as cited in Naish et al. 2014), rainfall (Hales et al. 2002; Johansson et al. 2009; as cited in Naish et al. 2014), and relative humidity (Chakravarti and Kumaria 2005; Gharbi et al. 2011; Thammapalo et al. 2005; as cited in Naish et al. 2014) in Davao City is consistent as well. Table 6 intuitively shows interesting new findings, too. Excessive rainfall could push the Endemic Level to Hyperendemic Level. The Hyperendemic Level through increased minimum temperature could then be elevated to an Outbreak. Seasons where the relative humidity is consistently high which could persist for more than two weeks, on the other hand, could trigger an Outbreak in the city.

According to several studies (Saifur et al. 2012; Southwood 1972; Moore et al. 1978), the survival and growth of many *Aedes aegypti* breeding sites depended more on human behavior than on rainfall. This may help to partially explain why rainfall and associated lags have negligible to no effects on the cases of dengue. The results of this study, i.e., the non-significance and marginal impact of mean aggregated rainfall and its lags, may have been influenced by the relatively short time series and included climatic anomalies of the occurrence of El Niño in 2019, along with the increasing trends in the temperature trend.

This paper demonstrates that, at least for the datasets used and in Davao City, the impacts of minimum temperature and relative humidity are statistically significant in the rise of dengue cases for the Hyperendemic and Outbreak levels. This study is generally consistent with the findings that the mean (maximum) temperature could make dengue transmission slower which could be due to its impact on the life cycle of *Aedes aegypti* (CDC 2022; Thai and Anders 2011; Southwood et al. 1978; McMichael 1996) which is also seen in Table 6 where the mean maximum temperature used as a fixed covariate could decrease the dengue cases. This study also contributes to the literature on the effects of temperature, as evidence was discovered supporting the benefits of separating maximum and minimum temperatures and evaluating their lags, as factors in modeling dengue-confirmed cases. Moreover, the delays in the actual confirmed dengue cases should be accounted for (Dhiman et al., 2010), particularly before declaring a local outbreak to avoid false alarms and wasteful resource expenditure.

The selection of a base period for climate data is crucial as well. The relationship between climate and dengue in the same location can be quite distinct between decades (Naish et al. 2014). Changes in socioeconomics, demography, and urbanization could account for differences. This study conforms with the literature that recommends using long-term climate historical data to estimate values which are less affected by climate variability when modeling climate-based diseases (McMichael et al., 2001; Dinse, 2009). Updating the model whenever data is available could also be critical, especially with the changing climate.

The spatiotemporal scale of analysis, furthermore, is an additional aspect to consider when modeling. This is due to the temporal and geographical spatial features that provide valuable information on risk assessments that local or national dengue control and prevention initiatives can use to anticipate and react to dengue outbreaks, particularly during spikes. Dengue may be sensitive to differences in local, regional, and global climatic conditions. There is also the potential for climate-related global dengue transmission. Dengue may become endemic in areas that are currently only at risk and not endemic due to climate change, particularly temperature change (Naish et al 2014), too, and active dengue epidemic surveillance may become more of a necessity in the future. With varying impacts between the three Levels of Disease, it appears that the surge in dengue cases in Davao City is similarly affected by seasonality. Monitoring changes in the season is critical in anticipating potential upgrading of Levels of Disease. Specifically, based on meteorological parameters alone, (1) rainfall should be regularly monitored at the Endemic level, (2) a rise in minimum temperature is critical at the Hyperendemic Level, and (3) sustained relative humidity for more than two weeks could intensify the spread of DENV which may cause for a declaration of an Outbreak.

CONCLUSIONS AND RECOMMENDATIONS

This paper used 156 two-week MAs of the weekly data points of dengue cases and meteorological parameters from Davao City aiming to provide an alternative to existing methods before declaring a local outbreak. Dengue thresholds were determined using econometric methods. These thresholds are 71.00 and 88.50. The thresholds were then used to recommend three Levels of Disease, namely Endemic Level for MA of cases below 71.00, Hyperendemic Level for MA of cases from 71.00 and 88.50, and Outbreak Level for MA of cases exceeding 88.50 for more than two weeks in the locality. The findings further suggest that monitoring the fluctuations in the increased rainfall is crucial at the Endemic Level, elevated minimum temperature may sustain Hyperendemic Level, and relative humidity for more than two weeks could trigger an Outbreak Level. This suggests continuous epidemiological surveillance in the city while monitoring the seasons where the specified meteorological parameters are expected to be more intense. It is still recommendable to use at least several decades of climate baseline data in modeling climate-sensitive diseases such as dengue to generate results that have lesser biases attributed to climate variability (Dinse 2009; Harrington et al. 2013). This empirical finding, however, is not entirely proposed to supersede the current procedure of the WHO and DOH in declaring an outbreak. It is rather a recommendation that can be used as an alternative for localized actions via a playbook for policies in minimizing the effects spread of dengue and actions whenever the local dengue epidemiological surveillance shows a remarkable spike in the reported cases. The developed strategy in this paper could also be improved and/or used in dengue surveillance in Davao City and other locations using spatiotemporally collected data. The proposed strategy may be applied for dengue surveillance and declaration of a local outbreak especially to other localities since different geographical areas and states have varying protocols before declaring an outbreak based on their employed definitions (Harrington et al. 2013; Badurdeen et al. 2013). With the appropriate selection of the set of variables, the strategy in this paper that combines epidemiology and econometrics may be further developed for other diseases, too, for localized epidemiological surveillance.

ACKNOWLEDGEMENT

This study is part of the dissertation of Hernan G. Pantolla, who is a recipient of the Thesis and Dissertation Grant Program of the Philippines Statistical Research and Training Institute.

REFERENCES

Badurdeen S, Valladares DB, Farrar J, Gozzer E, Kroeger A, Kuswara N, et al. Sharing experiences: Towards an evidence-based model of dengue surveillance and outbreak response in Latin America and Asia. BMC Public Health. 2013;13(1). Available from: https://pubmed.ncbi.nlm.nih.gov/23800243/

Banu S, Hu W, Hurst C, Tong S. Dengue transmission in the Asia-Pacific region: Impact of climate change and socio-environmental factors. Trop Med Int Health. 2011;16(5):598–607. Available from: https://pubmed.ncbi.nlm.nih.gov/21320241/

Boquet Y. A Tropical Archipelago. Springer Geography. 2017;37–59. doi:10.1007/978-3-319-51926-5_3

Brady OJ, Messina JP, Scott TW, Hay SI. Mapping the epidemiology of Dengue. Dengue and dengue hemorrhagic fever. 2014;:30–49. Available from: https://cabidigitallibrary.org/doi/10.1079/9781845939649.0030

Brady OJ, Smith DL, Scott TW, Hay SI. Dengue disease outbreak definitions are implicitly variable. Epidemics. 2015;11:92–102. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4429239/

CDC. Dengue [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2022 [cited 2022 Sep]. Available from: https://www.cdc.gov/dengue/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdengue%2Fentomologyecology%2Fclimate.html

CDC (2012) *Principles of Epidemiology*, *Centers for Disease Control and Prevention*. Available at: https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section11.html.

Chakravarti A, Kumaria R. Eco-epidemiological analysis of dengue infection during an outbreak of Dengue Fever, India. Virology Journal. 2005;2(1). doi:10.1186/1743-422x-2-32

Chowell G, Sattenspiel L, Bansal S, Viboud C. Mathematical models to characterize early epidemic growth: A Review. Physics of Life Reviews. 2016;18:66–97. doi:10.1016/j.plrev.2016.07.005

City Government of Davao @davaocitygov · September 2. Life is here [Internet]. City Government of Davao. 2019 [cited 2022 Sep]. Available from: http://www.davaocity.gov.ph/

Cotter C, Sturrock HJW, Hsiang MS, Liu J, Phillips AA, Hwang J, et al. The Changing Epidemiology of Malaria Elimination: New Strategies for New Challenges. Lancet. 2013;382(9895):900–11. Available from: https://pubmed.ncbi.nlm.nih.gov/23594387/

Dallas TA, Krkošek M, Drake JM. Experimental evidence of a pathogen invasion threshold. R Soc Open Sci. 2018;5(1):171975. Available from: https://pubmed.ncbi.nlm.nih.gov/29410876/

Descloux E, Mangeas M, Menkes CE, Lengaigne M, Leroy A, Tehei T, et al. Climate-based models for understanding and forecasting dengue epidemics. PLoS Negl Trop Dis. 2012;6(2). Available from: https://pubmed.ncbi.nlm.nih.gov/22348154/

Dhiman RC, Pahwa S, Dhillon GP, Dash AP. Climate change and threat of vector-borne diseases in India: Are we prepared? Parasitol Res. 2010;106(4):763–73. Available from: https://pubmed.ncbi.nlm.nih.gov/20155369/

Dickey DA, Fuller WA. Distribution of the estimators for autoregressive time series with a unit root. JASA. 1979;74(366):427. Available from: https://www.jstor.org/stable/2286348

Diekmann O, Heesterbeek JAP. Mathematical epidemiology of infectious diseases model building, analysis and interpretation. zbMath Open. Chichester: Wiley; 2000. Available from: https://academic.oup.com/ije/article/30/1/186/619068

Dinse K. Climate Variability and Climate Change: What is the Difference. Michigan Sea Grant; 2009. Available from: https://www.michiganseagrant.org/wp-content/uploads/2018/10/11-703-Climate-Variability-and-Climate-Change-2013update.pdf

Earnest A, Tan SB, Wilder-Smith A. Meteorological factors and El Niño Southern Oscillation are independently associated with dengue infections. Epidemiol Infect. 2011;140(7):1244–51. Available from: https://pubmed.ncbi.nlm.nih.gov/21906411/

ECDC. Factsheet About dengue [Internet]. European Centre for Disease Prevention and Control. European Union; 2021 [cited 2022 Sep]. Available from: https://www.ecdc.europa.eu/en/dengue-fever/facts

Earnest A, Tan SB, Wilder-Smith A. Meteorological factors and El Niño Southern Oscillation are independently associated with dengue infections. Epidemiol Infect. 2011;140(7):1244–51. Available from: https://pubmed.ncbi.nlm.nih.gov/21906411/

Endy TP, Anderson KB, Nisalak A, Yoon I-K, Green S, Rothman AL, et al. Determinants of inapparent and symptomatic dengue infection in a prospective study of primary school children in Kamphaeng Phet, Thailand. PLoS Negl Trop Dis. 2011;5(3). https://pubmed.ncbi.nlm.nih.gov/21390158/

Espino PS, Ong AM, Yorac DJ, Libo-on JB. Climatological analysis of the Southwest Monsoon (Habagat) in Type 1 Climate Areas in the Philippines from 1949–2018. Publiscience [Internet]. 2021;4(1). Available from: http://www.publiscience.org/wp-content/uploads/2021/08/Climatological-analysis-of-the-Southwest-Monsoon-Habagat-1.pdf

Farrar J, Focks D, Gubler D, Barrera R, Guzman MG, Simmons C, et al. Editorial: Towards a global dengue research agenda. TM &IH. 2007;12(6):695–9. Available from https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-3156.2007.01838.x

Garg P, Nagpal J, Khairnar P, Seneviratne SL. Economic burden of dengue infections in India. Trans R Soc Trop Med Hyg. 2008;102(6):570–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18402995/

Gharbi M, Quenel P, Gustave J, Cassadou S, Ruche GL, Girdary L, et al. Time series analysis of dengue incidence in Guadeloupe, French west indies: Forecasting models using climate variables as predictors. BMC Infect Dis. 2011;11(1). Available from: https://pubmed.ncbi.nlm.nih.gov/21658238/

Grais RF, Dubray C, Gerstl S, Guthmann JP, Djibo A, Nargaye KD, et al. Unacceptably high mortality related to measles epidemics in Niger, Nigeria, and Chad. PLoS Medicine. 2007;4(1). Available from: https://pubmed.ncbi.nlm.nih.gov/17199407/

Gubler DJ. Dengue, urbanization and globalization: The unholy trinity of the 21st Century. Trop Med Health. 2011;39(4SUPPLEMENT). Available from: https://pubmed.ncbi.nlm.nih.gov/22500131/

Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R, Patz JA. Climate variability and change in the United States: Potential impacts on vector- and rodent-borne diseases. Environ Health Perspect. 2001;109(suppl 2):223–33. Available from: https://pubmed.ncbi.nlm.nih.gov/11359689/

Hales S, de Wet N, Maindonald J, Woodward A. Potential effect of population and climate changes on global distribution of dengue fever: An empirical model. Lancet. 2002;360(9336):830–4. Available from: https://pubmed.ncbi.nlm.nih.gov/12243917/

Hales S, Weinstein P, Souares Y, Woodward A. El Niño and the dynamics of Vectorborne disease transmission. Environ Health Perspect. 1999;107(2):99–102. Available from: https://pubmed.ncbi.nlm.nih.gov/9924003/

Haq S, Larsson R. The dynamics of stock market returns and macroeconomic indicators: An ... [Internet]. KTH Industrial Engineering and Management; 2016. Available from: https://kth.diva-portal.org/smash/get/diva2:950080/FULLTEXT01.pdf

Harrington J, Kroeger A, Runge-Ranzinger S, O'Dempsey T. Detecting and responding to a dengue outbreak: Evaluation of existing strategies in Country Outbreak Response Planning. J Trop Med. 2013;2013:1–9. Available from: https://pubmed.ncbi.nlm.nih.gov/24222774/

Hay S. Football fever could be a dose of Dengue. Nature. 2013;503(7477). Available from: https://pubmed.ncbi.nlm.nih.gov/24284696/

Hay S, Renshaw M, Ochola SA, Noor AM, Snow RW. Performance of forecasting, warning, and detection of malaria epidemics in the highlands of western Kenya. Trends Parasitol. 2003;19(9):394–9. Available from: https://pubmed.ncbi.nlm.nih.gov/12957515/

Hay SI, Were EC, Renshaw M, Noor AM, Ochola SA, Olusanmi I, et al. Forecasting, warning, and detection of malaria epidemics: A case study. Lancet. 2003;361(9370):1705–6. Available from: https://pubmed.ncbi.nlm.nih.gov/12767739/

Hii YL, Rocklöv J, Ng N, Tang CS, Pang FY, Sauerborn R. Climate variability and increase in intensity and magnitude of dengue incidence in Singapore. Glob Health Action. 2009;2(1):2036. Available from: https://pubmed.ncbi.nlm.nih.gov/20052380/

Hutwagner L, Thompson W, Seeman GM, Treadwell T. The bioterrorism preparedness and response Early Aberration Reporting System (EARS). J Urban Health. 2003;80(2 Suppl 1):89–96. Available from: https://pubmed.ncbi.nlm.nih.gov/12791783/

IPCC. Climate change 2007: The Physical Science Basis [Internet]. Cambridge: Cambridge University Press; 2007 [cited 2022 Sep]. Available from: https://books.google.com.ph/books?hl=en&lr=&id=8-m8nXB8GB4C&oi=fnd&pg=PA339&ots=hBkoA3rfIX&sig=tjcVoOsCp68PFOv4iWifIRMngqs&redir_esc=y#v=onepage&q&f=false

Johansson MA, Cummings DA, Glass GE. Multiyear climate variability and dengue—El Niño Southern Oscillation, weather, and dengue incidence in Puerto Rico, Mexico, and Thailand: A Longitudinal Data Analysis. PLoS Med. 2009;6(11). Available from: https://pubmed.ncbi.nlm.nih.gov/19918363/ .

Kripfganz S, Schneider DC. ardl: Estimating autoregressive distributed lag and equilibrium correction models. Stata Journal, forthcoming. 2023.

Leitch J, Alexander KA, Sengupta S. Toward epidemic thresholds on Temporal Networks: A review and Open questions. Appl. Netw. Sci. 2019;4(1). Available from: https://appliednetsci.springeropen.com/articles/10.1007/s41109-019-0230-4 1.

Leung XY, Islam RM, Adhami M, Ilic D, McDonald L, Palawaththa S, et al. A systematic review of dengue outbreak prediction models: Current scenario and Future Directions. PLOS Neglected Tropical Diseases. 2023;17(2). doi:10.1371/journal.pntd.0010631

Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the global burden of disease study 2010. Lancet. 2012;380(9859):2224–60. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61766-8/fulltext

Liu Y, Lillepold K, Semenza JC, Tozan Y, Quam MBM, Rocklöv J. Reviewing estimates of the basic reproduction number for Dengue, Zika and Chikungunya across global climate zones. Environmental Research. 2020;182:109114. doi:10.1016/j.envres.2020.109114

Lütkepohl H. New introduction to multiple time series analysis [Internet]. SpringerLink. Berlin: Springer; 2005 [cited 2022 Sep]. Available from: https://link.springer.com/book/10.1007/978-3-540-27752-1

McMichael A, Haines A, Sloof R, Kovats R. Climate Change and Human Health: an Assessment by a Task Group on Behalf of the World Health Organization [Internet]. World Health Organization;1996 [cited 2022 Sep]. Available from: https://apps.who.int/iris/handle/10665/62989

McMichael AJ, Haines A, Kovats RS. Methods to assess the effects of climate change on health. Health Effects of Climate Change in the UK. London, UK: UK Department of Health; 2001.

Messina JP, Brady OJ, Scott TW, Zou C, Pigott DM, Duda KA, et al. Global spread of dengue virus types: Mapping the 70 year history. Trends Microbiol. 2014;22(3):138–46. Available from: https://pubmed.ncbi.nlm.nih.gov/24468533/

Moore CG, Cline BL, Ruiz-Tibén E, Rivera-Correa E, Lee D, Romney-Joseph H. Aedes aegypti in Puerto Rico: Environmental determinants of larval abundance and relation to dengue virus transmission. Am J Trop Med Hyg. 1978;27(6):1225–31. Available from: https://pubmed.ncbi.nlm.nih.gov/727328/

Myers MF, Rogers DJ, Cox J, Flahault A, Hay SI. Forecasting disease risk for increased epidemic preparedness in Public Health. Adv Parasitol. 2000;:309–30. Available from: https://pubmed.ncbi.nlm.nih.gov/10997211/

Naish S, Dale P, Mackenzie JS, McBride J, Mengersen K, Tong S. Climate change and dengue: A critical and systematic review of Quantitative Modelling Approaches. BMC Infect Dis. 2014;14(1). Available from: https://pubmed.ncbi.nlm.nih.gov/24669859/

Najera JA. https://europepmc.org/article/med/10697881 [Internet]. Europe PMC. 1999 [cited 2022 Sep]. Available from: https://europepmc.org/article/med/10697881

National Economic Development Authority. Davao City: NEDA Region XI: Davao Region [Internet]. NEDA Region XI | Davao Region. 2021 [cited 2022 Sep]. Available from: https://nro11.neda.gov.ph/davao-region/davao-city/

NOAA. 2020 was Earth's 2nd-Hottest Year, just behind 2016 [Internet]. National Oceanic and Atmospheric Administration. 2021 [cited 2022 Sep]. Available from: https://www.noaa.gov/news/2020-was-earth-s-2nd-hottest-year-just-behind-2016#:~:text=It%27s%20official%3A%202020%20ranks%20as,an%20analysis%20by%20NOAA%20scientists.

PAGASA. [Internet]. El Niño Advisory No. 7 (Final) Quezon City: PAGASA; 2019 [cited 2022 Sep]. Available from: https://pubfiles.pagasa.dost.gov.ph/pagasaweb/files/climate/elninolanina/ENAdvisory_7.pdf

PAGASA. Onset of Rainy Season [Internet]. PAGASA. 2019b [cited 2022 Sep]. Available from: https://bagong.pagasa.dost.gov.ph/press-release/50

Palicte C. Philippine News Agency [Internet]. 2019 Aug 9 [cited 2022 Sep]; Available from: https://www.pna.gov.ph/articles/1077489

Pastor-Satorras R, Castellano C, Van Mieghem P, Vespignani A. Epidemic processes in complex networks. Rev. Mod. Phys. 2015;87(3):925–79. Available from: https://journals.aps.org/rmp/abstract/10.1103/RevModPhys.87.925

Patz JA, Reisen WK. Immunology, climate change and vector-borne diseases. Trends Immunol. 2001;22(4):171–2. Available from: https://pubmed.ncbi.nlm.nih.gov/11274908/

Pesaran MH, Shin Y, Smith RJ. Bounds testing approaches to the analysis of level relationships. Journal of Applied Econometrics. 2001;16(3):289–326. doi:10.1002/jae.616

Reiner RC, Perkins TA, Barker CM, Niu T, Chaves LF, Ellis AM, et al. A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970–2010. J R Soc Interface. 2013;10(81):20120921. Available from: https://pubmed.ncbi.nlm.nih.gov/23407571/

Reiter P. Climate change and mosquito-borne disease. Environ Health Perspect. 2001;109(suppl 1):141–61. Available from: https://pubmed.ncbi.nlm.nih.gov/11250812/

Reiter P. Yellow fever and dengue: A threat to Europe? Euro Surveill. 2010;15(10). Available from: https://pubmed.ncbi.nlm.nih.gov/20403310/

Reiter P, Lathrop S, Bunning M, Biggerstaff B, Singer D, Tiwari T, et al. Texas lifestyle limits transmission of dengue virus. Emerging Infectious Diseases. 2003;9(1):86–9. doi:10.3201/eid0901.020220

Russell RC, Currie BJ, Lindsay MD, Mackenzie JS, Ritchie SA, Whelan PI. Dengue and climate change in Australia: Predictions for the future should incorporate knowledge from the past. Med J Aust. 2009;190(5):265–8. Available from: https://pubmed.ncbi.nlm.nih.gov/19296793/

Saifur RG, Dieng H, Hassan AA, Salmah MR, Satho T, Miake F, et al. Changing domesticity of Aedes aegypti in northern Peninsular Malaysia: Reproductive consequences and potential epidemiological implications. PLoS ONE. 2012;7(2). Available from: https://pubmed.ncbi.nlm.nih.gov/22363516/

Simmons CP, Farrar JJ, van Vinh Chau N, Wills B. Dengue. N Engl J Med. 2012;366(15):1423–32. Available from: https://pubmed.ncbi.nlm.nih.gov/22494122/

Souza SS, Silva IG, Silva HH. Association between dengue incidence, rainfall and larval density of Aedes aegypti, in the State of Goiás. Rev Soc Bras Med Trop. 2010;43(2):152–5. Available from: https://pubmed.ncbi.nlm.nih.gov/20464144/

Southwood TR, Murdie G, Yasuno M, Tonn RJ, Reader PM. Studies on the life budget of Aedes aegypti in Wat Samphaya, Bangkok, Thailand. Bull World Health Organ. 1972;46(2):11–26. Available from: https://pubmed.ncbi.nlm.nih.gov/4537483/

StataCorp LLC. dfuller — Augmented Dickey–Fuller unit-root test. In: Stata Time-Series Reference manual: Release 17 [Internet]. College Station, TX: StataCorp LLC; 2021b [cited 2022 Sep]. Available from: https://www.stata.com/manuals/ts.pdf

StataCorp LLC. threshold — Threshold regression. In: Stata Time-Series Reference manual: Release 17 [Internet]. College Station, TX: StataCorp LLC; 2021c [cited 2022 Sep]. Available from: https://www.stata.com/man\uals/ts.pdf

StataCorp LLC. varsoc — Obtain lag-order selection statistics for VARs and VECMs. In: Stata Time-Series Reference manual: Release 17 [Internet]. College Station, TX: StataCorp LLC; 2021a [cited 2022 Sep]. Available from: https://www.stata.com/manuals/ts.pdf

Stroup DF, Wharton M, Kafadar K, Dean AG. Evaluation of a method for detecting aberrations in Public Health Surveillance Data. Am. J. Epidemiol. 1993;137(3):373–80. Available from: https://pubmed.ncbi.nlm.nih.gov/8452145/

Sutherst RW. Global change and human vulnerability to vector-borne diseases. Clin Microbiol Rev. 2004;17(1):136–73. Available from: https://pubmed.ncbi.nlm.nih.gov/14726459/

Thai KT, Anders KL. The role of climate variability and change in the transmission dynamics and geographic distribution of Dengue. Exp Biol Med (Maywood). 2011;236(8):944–54. Available from: https://pubmed.ncbi.nlm.nih.gov/21737578/

Thammapalo S, Chongsuwiwatwong V, McNeil D, Geater A. The climatic factors influencing the occurrence of dengue hemorrhagic fever in Thailand. Southeast Asian J Trop Med Public Health. 2005;36(1).

Van Kleef E, Bambrick H, Hales S. The geographic distribution of dengue fever and the potential influence of Global Climate Change. Environ. Health Perspect. 2011;2011(1). Available from: https://ehp.niehs.nih.gov/doi/10.1289/isee.2011.00337

UNHCR. Emergency handbook: Disease surveillance thresholds [Internet]. UNHCR. United Nations; [cited 2022 Sep]. Available from: https://emergency.unhcr.org/entry/38802/disease-surveillance-thresholds#:~:text=An%20%27alert%20threshold%27%20(or,which%20it%20is%20locally%20endemic

Wagner MM, Tsui F-C, Espino JU, Dato VM, Sitting DF, Caruana RA, et al. The emerging science of very early detection of disease outbreaks. J Public Health Manag Pract. 2001;7(6):51–9. Available from: https://pubmed.ncbi.nlm.nih.gov/11710168/

Watts DM, Whitmire RE, Burke DS, Nisalak A, Harrison BA. Effect of temperature on the vector efficiency of Aedes aegypti for dengue 2 virus. Am J Trop Med Hyg. 1987;36(1):143–52. Available from: https://pubmed.ncbi.nlm.nih.gov/3812879/WHO. Dengue: Guidelines for diagnosis, treatment, prevention and control. Geneva: World Health Organization; 2009 [cited 2022 Sep].

Wearing HJ, Rohani P. Ecological and immunological determinants of dengue epidemics. Proc Natl Acad Sci U S A. 2006;103(31):11802–7. Available from: https://pubmed.ncbi.nlm.nih.gov/16868086/

Weather Atlas. Davao City, Philippines - weather forecast & hourly temperature - Today [Internet]. Weather Atlas. ezoic; [cited 2022 Sep 7]. Available from: https://www.weather-atlas.com/en/philippines/davao-city

WeatherSpark. Weatherspark.com [Internet]. Davao Climate, Weather By Month, Average Temperature (Philippines) - Weather Spark. [cited 2022 Sep]. Available from: https://weatherspark.com/y/141485/Average-Weather-in-Davao-Philippines-Year-Round

Weaver SC, Reisen WK. Present and future arboviral threats. Antiviral Research. 2010;85(2):328–45. doi:10.1016/j.antiviral.2009.10.008

Wilder-Smith A, Gubler DJ. Geographic expansion of dengue: The impact of international travel. Med Clin North Am. 2008;92(6):1377–90. Available from: https://pubmed.ncbi.nlm.nih.gov/19061757/

Wilder-Smith A, Murray, Quam M. Epidemiology of Dengue: Past, present and future prospects. Clin. Epidemiol. 2013;:299. Available from: https://pubmed.ncbi.nlm.nih.gov/23990732/

WHO Ebola Response Team. Ebola virus disease in West Africa — the first 9 months of the epidemic and forward projections. N Engl J Med. 2014;371(16):1481–95. Available from: https://pubmed.ncbi.nlm.nih.gov/25244186/

WHO. Malaria Control Today. Geneva; 2005.

WHO. WHO Guidelines for Epidemic Preparedness and Response to Measles Outbreaks [Internet]. WHO. 1999 [cited 2022 Sep]. Available from: https://apps.who.int/iris/bitstream/handle/10665/66034/WHO_CDS_CSR_ISR_99.1.pdf

Wu P-C, Guo H-R, Lung S-C, Lin C-Y, Su H-J. Weather as an effective predictor for occurrence of dengue fever in Taiwan. Acta Trop. 2007;103(1):50–7. Available from: https://pubmed.ncbi.nlm.nih.gov/17612499/