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High relative humidity might trigger the occurrence of the second seasonal peak of dengue in the Philippines

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Highlights

1. Dengue incidence rate in the Philippines increased substantially in the past decade, particularly for the regions in south Philippines;
2. The association between mean temperature and dengue appeared J-shaped or upside-down-V-shaped;
3. The association between relative humidity (or rainfall) and dengue was heterogeneous across different provinces;
4. Relative humidity was the only factor associated with the second seasonal peak of dengue.

Abstract

Background: Dengue in some regions has a bimodal seasonal pattern, with a first big seasonal peak followed by a second small seasonal peak. The factors associated with the second small seasonal peak remain unclear.

Methods: Monthly data on dengue cases in the Philippines and its 17 regions from 2008 to 2017 were collected and underwent a time series seasonal decomposition analysis. The associations of monthly average mean temperature, average relative humidity, and total rainfall with dengue in 19 provinces were assessed with a generalized additive model. Logistic regression and a classification and regression tree (CART) model were used to identify the factors associated with the second seasonal peak of dengue.

Results: Dengue incidence rate in the Philippines increased substantially in the period 2013-2017, particularly for the regions in south Philippines. Dengue peaks in south Philippines predominantly occurred in August, with the peak in the national capital region (NCR) (i.e., Metropolitan Manila) occurring in September. The association between mean temperature and dengue appeared J-shaped or upside-down-V-shaped, and the association between relative humidity (or rainfall) and dengue was heterogeneous across different provinces (e.g., J shape, reverse J shape, or upside-down V shape, etc). Relative humidity was the only factor associated with the second seasonal peak of dengue (odds ratio: 1.144; 95% confidence interval: 1.023 – 1.279; threshold: 77%).

Conclusions: Dengue control and prevention resources are increasingly required in regions beyond the NCR, and relative humidity can be used as a predictor of the second seasonal peak of dengue in the Philippines.

Keywords: Dengue; Relative humidity; Second seasonal peak

1. Introduction

Dengue is the fastest-spreading mosquito-borne disease globally and it is transmitted through the bite of infected female *Aedes aegypti* or *Aedes albopictus* (Bhatt et al., 2013). Southeast Asia shoulders a considerable proportion of global dengue burden (Stanaway et al., 2016), and the Philippines accounts for 18% of the total dengue disease burden in Southeast Asia (Shepard et al., 2013). Despite the massive dengue burden in the Philippines, the epidemiological features (e.g., spatial and seasonal patterns) of dengue in the Philippines have rarely been characterized (Bravo et al., 2014). In particular, comprehensive data on the spatial and temporal patterns of dengue across different regions of the Philippines are lacking.

The life cycle and transmission of dengue virus as well as the growth and survival of *Aedes aegypti* and *Aedes albopictus* are inextricably linked to climate (Li et al., 2019; Morin et al., 2013; Xu et al., 2017). The association between climatic variables (e.g., temperature, rainfall and relative humidity) and the occurrence of dengue is complex and generally heterogeneous across different regions (Xu et al., 2019). Existing studies examining the association between climatic variables and dengue in the Philippines are limited in number and they have predominantly focused on Manila (Carvajal et al., 2018; Iguchi et al., 2018; Su, 2008; Sumi et al., 2016). Under the context of climate change, it is of increasing importance to better understand the climate-dengue association across different regions of the Philippines, given the fact that the dengue burdens of different regions of the Philippines are changing disproportionately (Bravo et al., 2014).

The occurrence of infectious diseases often has a distinct seasonal pattern, and the drivers behind the seasonal pattern of infectious diseases are multifaceted (Altizer et al., 2006). Some infectious diseases (e.g., dengue, and hand, foot, and mouth disease) have a bimodal seasonal pattern, with a first big seasonal peak followed by a second small seasonal peak (Miyazawa et al., 2008; Pascual and Dobson, 2005). Although an increasing number of studies have attempted to determine the reasons for the seasonality of dengue (Do et al., 2014; Hartley et al., 2002), the factors solely associated with the occurrence of the second seasonal peak of dengue have rarely been explored. This comprises an important omission in our current understanding because the second seasonal peak may, in and of itself, pose a considerable burden to the health of the population.

This study aimed to fill the abovementioned knowledge gaps and achieve three specific objectives: (1) to characterize the spatial and seasonal patterns of dengue in the Philippines; (2) to examine the associations of mean temperature, relative humidity, and rainfall with the occurrence of dengue in multiple provinces; and (3) to explore the factors associated with the second seasonal peak of dengue.

2. Material and methods

2.1. Data collection

2.1.1. Data for characterizing the spatial and seasonal patterns of dengue

The administrative division levels of the Philippines are region, province, municipality (city), and barangay. In total, the Philippines has 17 regions (16 administrative and one autonomous) and 81 provinces. Monthly data on dengue case number in the Philippines and all 17 regions of the Philippines from 2008 to 2017 were collected from the Philippine Department of Health. The Negros Island Region of the Philippines was distinct only from May 2015 to August 2017 and was not included in this study. Data on the populations of the Philippines and the 17 regions for year 2000 and year 2015 were obtained from the Philippine Statistics Authority. We used the compounded population growth rate (1.84%) to calculate the population for years 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2016 and 2017.

2.1.2. Data for examining the association between climate variables and dengue, and for exploring the factors associated with the second seasonal peak of dengue

Monthly data on dengue case number in the eight regions with the best quality dengue surveillance data, including NCR, Region II, Region III, Region IV-A, Region IV-B, Region V, Region VIII, and Region XII, were provided by the regional offices of the Philippine Department of Health. These eight regions included four of the five most populous regions in the Philippines (i.e., NCR, Region III, Region IV-A, and Region V). The specific time periods for different provinces were different (Table S1). Monthly data on average mean temperature, average relative humidity, and total rainfall for different provinces of the eight regions were collected from the Philippine Atmospheric, Geophysical and Astronomical Services Administration (PAGASA). Nineteen provinces (including NCR because its geographical size is smaller than an average province) with complete data on the three climatic variables were selected in the final analysis to quantify the association between climatic variables and the occurrence of dengue. These selected provinces were: NCR, Cagayan (Region II), Aurora (Region III), Nueva Ecija (Region III), Pampanga (Region III), Zambales (Region III), Batangas (Region IV-A), Cavite (Region IV-A), Quezon (Region IV-A), Rizal (Region IV-A), Palawan (Region IV-B), Albay (Region V), Camarines Norte (Region V), Catanduanes (Region V), Masbate (Region V), Eastern Samar (Region VIII), Northern Samar (Region VIII), Southern Leyte (Region VIII), and Cotabato (Region XII). The geographic locations of these selected provinces were presented in Figure S3 (supplementary material).

The ethical approval was granted by the University Human Research Ethics Committee of Queensland University of Technology prior to the data being collected.

2.2. Data analysis

A time series seasonal decomposition analysis was conducted to understand the seasonal pattern and long-term trend of dengue in the Philippines from 2008 to 2017 (Xu et al., 2015). The monthly incidence rate (per 100,000) of dengue for the same time period was also calculated through dividing the monthly dengue case number by the yearly population.

A generalized additive modelling was used to examine the associations of mean temperature, relative humidity, and rainfall with the occurrence of dengue (Li et al., 2019). Seasonality and long-term trend were controlled for by adding the categorical variables of "month" and "year" in the regression model, respectively. School holiday (i.e., April to June) was also controlled for in the model as a binary variable. As mean temperature, relative humidity and rainfall impact the occurrence of dengue through affecting dengue virus and mosquitoes, there is a lag time between the occurrence of ideal climatic conditions and the occurrence of dengue, generally ranging from one to three months (Naish et al., 2014; Xu et al., 2019). Biologically, the lag time accounts for the increase in the mosquito population through elevated breeding, and, the time for humans to become infected following this vector population expansion. In this study, we used a maximum lag of three months (as the climate and dengue data we used were monthly data), and for each province, we compared the values of Akaike information criterion (AIC) of models using different lags to identify the optimal lag for each climatic variable. Because relative humidity and rainfall were highly correlated with each other (The Spearman correlation coefficient between relative humidity and rainfall in each province was generally > 0.7), for each province, we compared the AIC value of the model using temperature and relative humidity with the AIC value of the model using temperature and rainfall to get the optimal model. Finally, one best model with the optimal-lag temperature and the optimal-lag relative humidity (or rainfall) was identified for each province.

To identify those provinces with a distinct second seasonal peak of dengue, we used a seasonal decomposition analysis for each province (Xu et al., 2015). This analysis decomposed the original time-series of dengue into seasonal pattern, long-term trend, and residuals. The provinces with a distinct second seasonal peak of dengue identified from this step were Cagayan, Zambales, Batangas, Cavite, Quezon, Rizal, and NCR. The original data of these provinces were double checked to make sure that the number of dengue cases of the second seasonal peak month was greater than the number of dengue cases at one month before the peak. For each of these provinces, there were some years with a second seasonal peak and some years without a second seasonal peak. To explore which factors were associated with the occurrence of the second seasonal peak, we created a binary variable, with "1" representing the years with a second seasonal peak and "0" representing the years without a second seasonal peak. This binary variable was used as the outcome variable of the logistic regression. Mean temperature, relative humidity, and rainfall at one month, two months and three months before the month of the second seasonal peak, as well as the size of the first dengue peak (i.e., number of dengue cases), were used as exposure variables of the logistic regression. To avoid multicollinearity, we put only one exposure variable in the logistic regression model each time.

To make sure that the results for the factors associated with the second seasonal peak of dengue are robust, we also used a machine learning approach, classification and regression tree (CART) model, to select the variables associated with the second seasonal peak. This model has been well used in our prior research (Xu et al., 2015), a key advantage being that it allows all exposure variables to be included in the same model while negating issues of multicollinearity. All spatial analyses were conducted in ArcGIS version 10.5 and other analyses were conducted in R package version 3.5.0.

3. Results

3.1 The spatial and seasonal patterns of dengue in the Philippines

Figure 1A presented the temporal trend of dengue case number in the Philippines from January 2008 to December 2017, suggesting that there were dengue outbreaks in 2010, 2011, 2012, 2013, 2015, and 2016. This figure also showed that there was a second seasonal peak of dengue following the first seasonal peak of dengue in most years. Figure 1B presented the monthly dengue incidence rate in the Philippines.

Figures 2A and 2B showed the monthly distribution of dengue case number in the Philippines and the 17 regions, suggesting that dengue case number in most regions peaked in August, except for ARMM (July), NCR (September), Region IX (July), and Region XI (July). The regions with dengue case number peaking in July were all located in the southern part of the Philippines. Figures S1A to S1D (supplementary material) showed the temporal trends of dengue case number in different regions from 2008 to 2017 and indicated that the seasonal patterns of dengue in the regions of the south part of the Philippines were less regular compared with those regions in the north part of the Philippines.

Figure 3 illustrated the spatial patterns of dengue incidence rate (per 10,000) in the Philippines in the study period and in the two five-year periods. It suggested that some regions in the south part of the Philippines with relatively low dengue incidence rate in the first period (2008-2012), including Region X, Region XII, and Region XIII, had a relatively high dengue incidence rate in the second period (2013 to 2017). Figure S2 (supplementary material) illustrated the spatial pattern of dengue incidence rate in the Philippines by year, suggesting that dengue incidence rate in the regions of the north part of the Philippines (CAR, NCR, Region I, Region II, Region III, and Region IV-A) had been consistently high over the latter eight years.

The stacked histogram (Figure 4) presented the percentage contributions of different regions in terms of dengue case numbers, revealing that the contribution of NCR to the total number of dengue cases in the Philippines varied considerably across different years. The contributions of Region III, Region IV-A, and Region VII were appreciable, and they were greater than the contribution of NCR in certain years (e.g., 2016). Figures 3 and 4 revealed that NCR, Region III, Region IV-A, and Region VII were the regions with both high dengue case number and high dengue incidence rate.

3.2 The association between climatic variables and dengue

Table S1 depicted the summary statistics of dengue case number, mean temperature, relative humidity, and rainfall in the 19 provinces. Table 1 showed the AIC values of the generalized additive models and the optimal model for each province. Figure 5A presented the association between mean temperature and dengue in the 19 provinces, and it suggested that in some provinces (e.g., NCR and provinces in Region III), the number of dengue cases increased with an increase in mean temperature but then started dropping when mean temperature reached a certain level. In other provinces (e.g., provinces in Region V), the number of dengue cases increased with the increase of mean temperature. Bantagas was an exception where the number of dengue cases decreased with an increase in mean temperature. Figure 5A also revealed the intra-region heterogeneity in the shape of the temperature-dengue relationship (e.g., Regions IV-A and VIII).

Figure 5B presented the association between relative humidity (or rainfall) and dengue in the 19 provinces. In most provinces except for Albay, the number of dengue cases increased with an increase in relative humidity but started dropping when relative humidity reached a certain level. In contrast, the shape of the rainfall-dengue association was more diverse (J shape, reverse J shape, and reverse V shape). In NCR, the shape of relative humidity-dengue relationship was similar to the shape of temperature-dengue relationship.

3.3 The factors associated with the second seasonal peak of dengue

Table 2 presented the results of the logistic regression, showing that relative humidity might be able to predict the second seasonal peak of dengue at a lag of two months (odds ratio: 1.144, 95% confidence interval: 1.023 – 1.279). The size of the first seasonal peak, mean temperature, and rainfall were not associated with the second seasonal peak of dengue. The CART model also yielded the same result as the logistic regression, suggesting that relative humidity at two months before the second seasonal peak of dengue was the only factor which stood out among all factors (Figure S4). The CART model result has also suggested that the second seasonal peak of dengue had a threshold relative humidity of 77%.

4. Discussion

This study, to the best of our knowledge, is the first multi-province study in the Philippines which examined the association between climatic variables and dengue, and it is the first attempt to identify the factors associated with the second seasonal peak of dengue. Several findings are note-worthy. First, the regions with dengue case number peaking in July were all located in south Philippines, and the seasonal patterns of dengue in the regions of south Philippines were less regular than those in north Philippines. Second, the incidence rate of dengue in the regions of north Philippines had been consistently high in the period 2010-2017. The percentage contribution of NCR to the dengue case number in the Philippines changed largely across different years. Third, the shape of the climate-dengue relationship was heterogeneous across different provinces of the Philippines. Fourth, relative humidity was associated with the second seasonal peak of dengue at a lag of two months.

Dengue has posed a substantial burden on households and government of the Philippines (Edillo et al., 2015), and vector control remains the most viable option for curbing the transmission of dengue virus, because there is no antiviral treatment and the implementation of a dengue vaccine had been halted in the Philippines due to safety concerns (Dyer, 2017). Understanding the peak month of dengue in different regions can help identify the optimal timing for intense and well targeted vector control. The most common dengue peak month (i.e., August) in different regions which we observed in our study period was consistent with the findings in earlier years (i.e., 2000 to 2011) (Bravo et al., 2014). Many factors might contribute to the August dengue peak, and one noteworthy factor is the school term. In the Philippines, summer holidays start in April and end in June. The school opening in June facilitates human movement and may play a role in the occurrence of the August peak (if ideal climatic conditions exist from June to August).

Another noteworthy factor in the southern part of the Philippines is the increasing human movement during the Ramadan celebration. As people in the southern part of the Philippines are mainly Muslims, they celebrate Ramadan generally from May to August (the celebration time changes across different years). Prior studies have reported that, from 2000 to 2011, the peak month of dengue in the Philippines ranged from July to November (Bravo et al., 2014), but we observed a narrower range (i.e., July to September) from 2008 to 2017, with the peak of dengue in NCR happening in September. NCR has been widely recognized as the focus of research and practice of dengue control and prevention in the Philippines due to its crucial role in the commerce of the country and its big population. However, in this study, we observed that, although the percentage contribution of NCR to the total number of dengue cases in the Philippines was large in the early years (e.g., 2008 and 2009), it varied considerably across different years and was not dominant in recent years (e.g., 2016). In contrast, the percentage contribution of Region IV-A has been consistently high in almost all years – a factor that has remained largely unacknowledged. The change of the percentage contributions of different regions across different years calls for more attention to be paid to those regions beyond NCR.

Rainfall has previously been asserted as the most important climatic factor associated with the occurrence of dengue in the Philippines (Su, 2008), partially because the peak of dengue generally occurs one or two months after the onset of rainy season. More recently, the roles of mean temperature and relative humidity in the occurrence of dengue have been increasingly explored and recognized in the Philippines (Carvajal et al., 2018; Iguchi et al., 2018; Sumi et al., 2016). The life cycle of dengue viruses and the growth and survival of mosquito vectors are strongly linked to temperature, relative humidity, and rainfall (Morin et al., 2013; Wongkoon et al., 2018). The existing evidence suggests that dengue transmission favors moderately high temperature, but extremely high temperature may increase the rate of mosquito mortality and hence decrease the risk of dengue transmission (Hii et al., 2009). There are optimal ranges of relative humidity and rainfall for dengue transmission also, below or above which dengue transmission would be restricted (Morin et al., 2013). One of the mechanisms behind the association between high humidity and the occurrence of dengue is that people who live in apartments may tend to walk outside more to get some fresh air during high humidity days, providing an opportunity for more mosquito bites. Although we observed that dengue case number increased with an increase in temperature in provinces of Region V and Region VIII, we found that the relationship between mean temperature and dengue was non-linear in most other provinces, which is consistent with our prior work in Thailand (Xu et al., 2019). This finding indicated that in the future, as climate change proceeds, the increasing ambient temperature may increase the burden of dengue only in some regions/provinces in the Philippines. Projection of the future burden of dengue in the Philippines under climate change scenarios needs to consider local factors (e.g., sociodemographic factors). For example, Hu et al. found that in Queensland, overseas-acquired dengue cases increased by 1% with a 1-unit increase in the socioeconomic index for areas (SEIFA) (Hu et al., 2012).

Apart from mean temperature, we have also found a non-linear relationship between rainfall (relative humidity) and dengue in some provinces. Abundant rainfall fills up the water containers of households, and these containers may become the breeding sites of *Aedes aegypti* (the main dengue vector in the Philippines), facilitating the transmission of dengue. However, very heavy rainfall may flush away larvae and pupae, restricting the transmission of dengue, although sometimes the water containers may remain flooded following heavy rainfall and thus still provide suitable breeding habitat for new eggs. Substantial heterogeneity in the relationship between rainfall (relative humidity) and dengue across different provinces was observed in this study. In particular, the optimal range of rainfall (relative humidity) which dengue transmission favored varied largely across different provinces. Climate change may disrupt the global water cycle, and local change in rainfall may alter the distribution of mosquitos (IPCC, 2014). Previous studies projecting the future burden of dengue under climate change scenarios have predominantly focused on the future change of temperature, with the future change of rainfall being neglected (Ebi et al., 2018; Messina et al., 2015). The findings of our study and prior studies (Naish et al., 2014) suggested that the change of rainfall anticipated for the future also needs to be incorporated into the projections of dengue burden under climate change scenarios.

Prior studies have endeavored to explore the climatic drivers of dengue outbreaks (Adde et al., 2016; Chuang et al., 2017) and predict dengue epidemic peaks using climatic factors (Li et al., 2019; Xu et al., 2017), but the second seasonal peak of dengue has rarely been considered. In our study, the results of the logistic regression and the CART model both suggested that high relative humidity was associated with the occurrence of the second seasonal peak of dengue in the Philippines. High relative humidity is generally caused by abundant rainfall and is typically followed by high temperatures, and thus it is a good indicator of warm feeling for human being particularly in the areas with dense population. Future studies exploring the reasons behind this relationship and identifying more factors (e.g., human movement) associated with the second seasonal peak of dengue are warranted.

This study has two major strengths. First, we assessed the association between climatic variables and dengue in 19 provinces of the Philippines which covered multiple regions. Second, we identified the factor associated with the second seasonal peak of dengue. Several limitations of this study need to be acknowledged. First, due to data unavailability, we were not able to examine the association between climatic variables and dengue in all provinces of the selected regions. Second, we only included climatic factors and the size of the first seasonal peak of dengue in the model to identify factors associated with the second seasonal peak of dengue. Other factors such as human population density and travel across different provinces etc. should also be explored in the future analyses. Third, should they become available, daily instead of monthly data would provide more accurate estimates for the lag period in the climate-dengue association.

5. Conclusions

Dengue incidence rate in the regions of south Philippines has increased in recent years, and the seasonal patterns of dengue in these regions were less regular than north Philippines. Dengue control and prevention in the Philippines may need to expand its targeting to those regions beyond NCR (e.g., Region IV-A). The future change of dengue burden associated with climate change may vary between different provinces. Relative humidity might be a good predictor of the second seasonal peak of dengue in the Philippines.

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Table 1. The values of Akaike information criterion (AIC) of different models

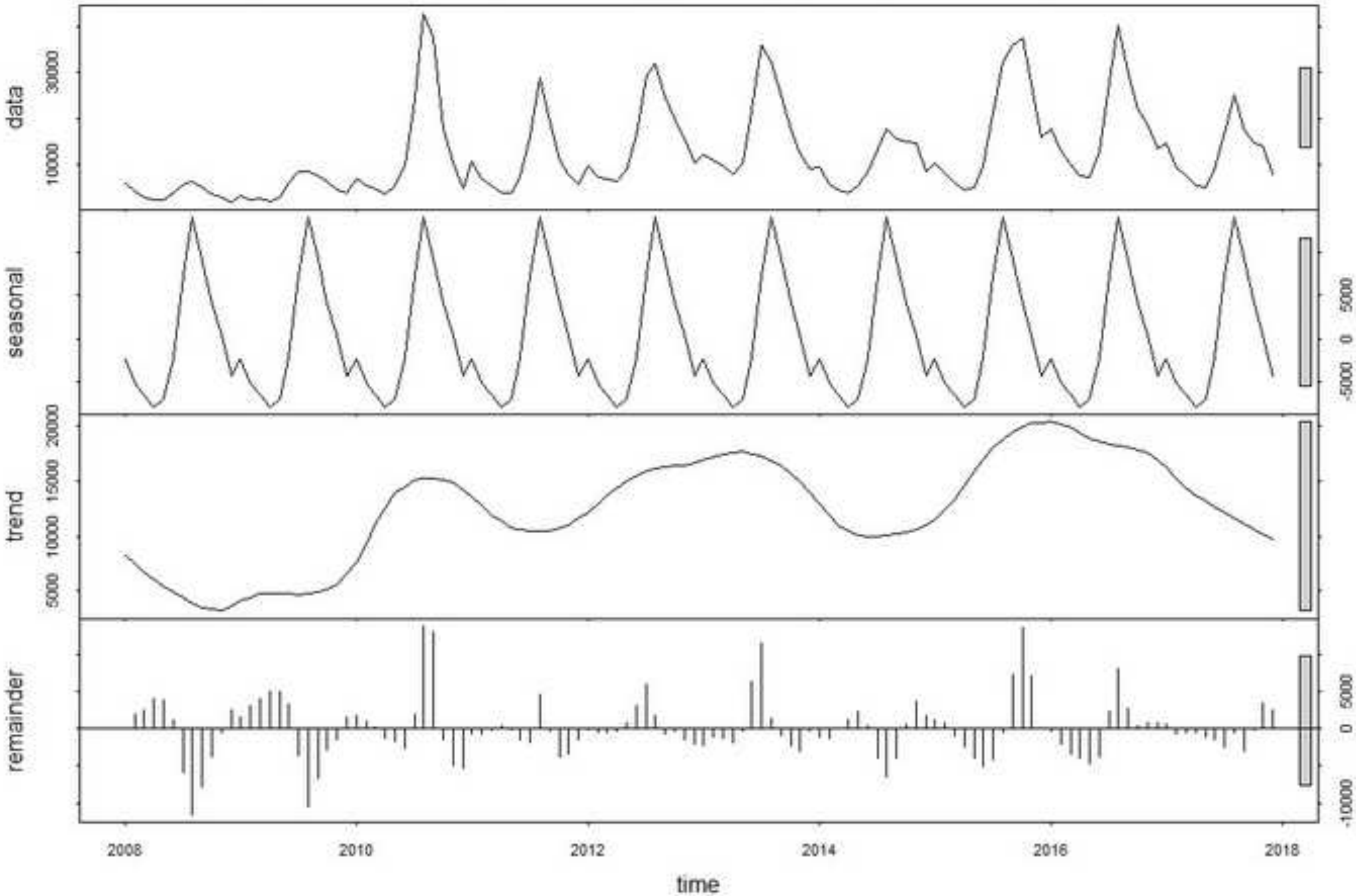
	Tmeanlag1	Tmeanlag2	Tmeanlag3	RHlag1	RHlag2	RHlag3	Rainfalllag1	Rainfalllag2	Rainfalllag3	Tmean+RH	Tmean+Rainfall
II_Cagayan	**4407.279**	4674.898	4418.3	4556.842	4608.679	**4532.198**	4564.567	4470.78	**4406.975**	4151.782	**3954.039**
III_Aurora	2315.072	2360.317	**2243.186**	**1964.455**	2118.932	2195.216	**2256.164**	2327.941	2333.514	**1787.095**	2021.926
III_Neuva Ecija	**5603.083**	6052.439	5832.417	5393.054	**5177.064**	5335.327	6002.55	**5719.401**	6120.632	**4907.163**	5083.403
III_Pampanga	6725.872	**6366.555**	6474.278	7146.133	**6932.537**	7361.542	7745.014	7558.528	**7365.84**	6107.296	**5947.837**
III_Zambales	2837.645	2854.25	**2748.486**	3040.63	2866.627	**2808.312**	2960.724	**2852.417**	2870.105	**2447.669**	2496.464
IVA_Batangas	**4100.547**	4162.112	4355.834	**4029.502**	4130.908	4503.945	4353.302	**3993.911**	4131.378	3674.144	**3563.891**
IVA_Cavite	6014.686	**5578.179**	5584.922	6267.769	**5700.381**	5912.297	6584.789	**5937.083**	5953.287	**4855.176**	5082.661
IVA_Quezon	**3639.178**	3982.125	4077.267	4080.599	3756.648	**3398.394**	**3907.182**	3978.8	4166.311	**3025.44**	3454.261
IVA_Rizal	3520.909	**3393.571**	3627.333	3546.416	**3347.207**	3380.62	**3476.842**	3535.501	3580.928	3225.512	**3214.619**
IVB_Palawan	3268.409	3357.097	**2928.201**	3458.468	3441.334	**3142.459**	**2324.385**	2519.844	3042.378	2770.216	**1935.99**
NCR	**17972.52**	18069.22	18291.59	17873.1	**15923.78**	18334.83	18522.34	**17113.52**	18476.72	**15174.2**	16173.43
V_Albay	1316.561	**1270.832**	1298.18	1436.271	1386.121	**1299.666**	1442.638	1440.59	**1417.185**	**1187.232**	1261.758
V_Camarines Norte	982.9032	921.46	**792.9302**	873.268	**730.9913**	862.0111	**803.1366**	825.6725	982.5861	**614.4225**	737.681
V_Catanduanes	1136.89	**1076.268**	1080.999	1155.368	1071.555	**1005.407**	**1061.641**	1140.51	1071.416	**941.8013**	998.8838
V_Masbate	779.9706	769.76	**741.4747**	785.7061	**772.0722**	775.5017	760.7627	**758.2315**	761.5564	730.6573	**708.5677**
VIII_Eastern Samar	**1496.325**	1571.33	1501.938	1570.839	1580.583	**1491.168**	1491.588	**1490.01**	1552.224	1374.294	**1333.195**
VIII_Northern Samar	**1399.11**	1571.677	1543.747	1561.406	1549.48	**1539.644**	**1504.459**	1561.591	1550.745	1319.657	**1229.084**
VIII_Southern Leyte	705.9911	698.1534	**675.1479**	672.5971	686.2389	**659.7557**	705.6201	**690.396**	695.8835	**594.2952**	670.0252
XII_Catabato	**5418.49**	5557.936	5642.77	5574.737	**5545.479**	5557.164	5836.534	5680.187	**5581.632**	5302.434	**5221.613**

Tmeanlag1: mean temperature at lag one month; **Tmeanlag2**: mean temperature at lag two months; **Tmeanlag3**: mean temperature at lag three months; **RHlag1**: relative humidity at lag one month; **RHlag2**: relative humidity at lag two months; **RHlag3**: relative humidity at lag three months; **Rainfalllag1**: rainfall at lag one month; **Rainfalllag2**: rainfall at lag two months; **Rainfalllag3**: rainfall at lag three months

Table 2. Logistic regression of the second seasonal peak with the first seasonal peak and the climatic variables

	Odds ratio	95% confidence interval	Model AIC value
Size of the first seasonal peak	1.323	0.691 – 2.533	-
Temperature (lag one month)	0.759	0.511 – 1.127	-
Temperature (lag two months)	0.833	0.583 – 1.191	-
Temperature (lag three months)	0.910	0.653 – 1.269	-
Relative humidity (lag one month)	1.112	1.001 – 1.238	57.294
Relative humidity (lag two months)	1.144	1.023 – 1.279	56.895
Relative humidity (lag three months)	1.198	1.020 – 1.406	60.123
Rainfall (lag one month)	1.006	0.998 – 1.013	-
Rainfall (lag two months)	1.002	0.997 – 1.006	-
Rainfall (lag three months)	1.005	0.998 – 1.012	-

Figure 1A. The temporal trend of dengue case number in the Philippines from 2008 to 2017



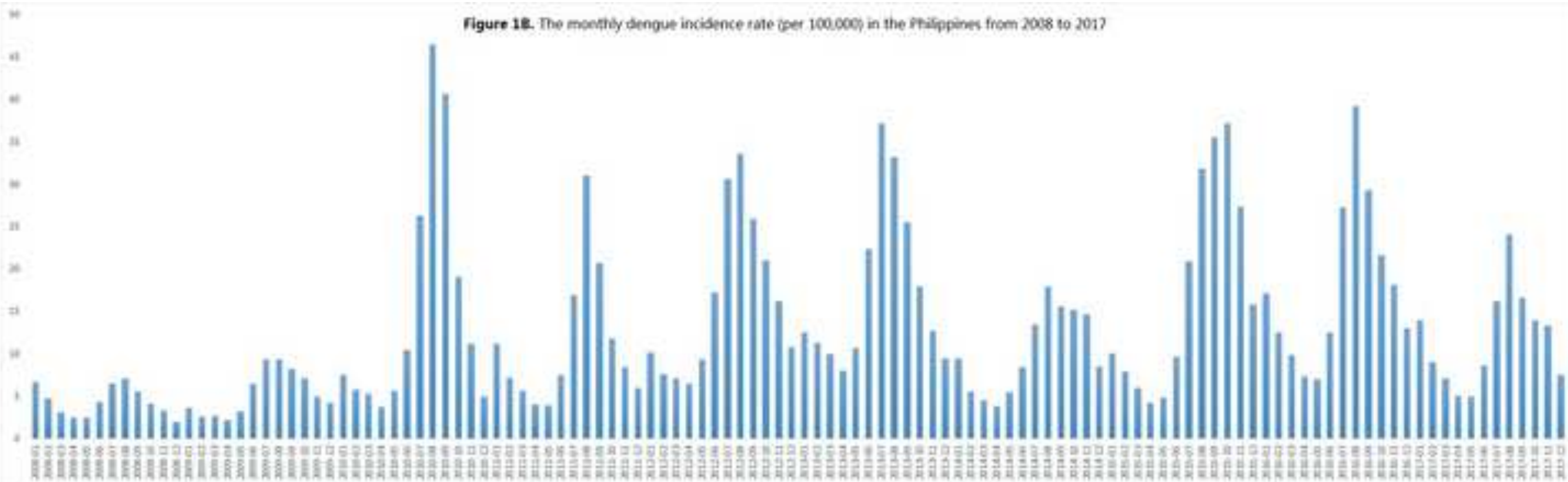


Figure 18. The monthly dengue incidence rate (per 100,000) in the Philippines from 2008 to 2017

Figure 2A. The monthly distribution of dengue case number in the Philippines and the 17 regions

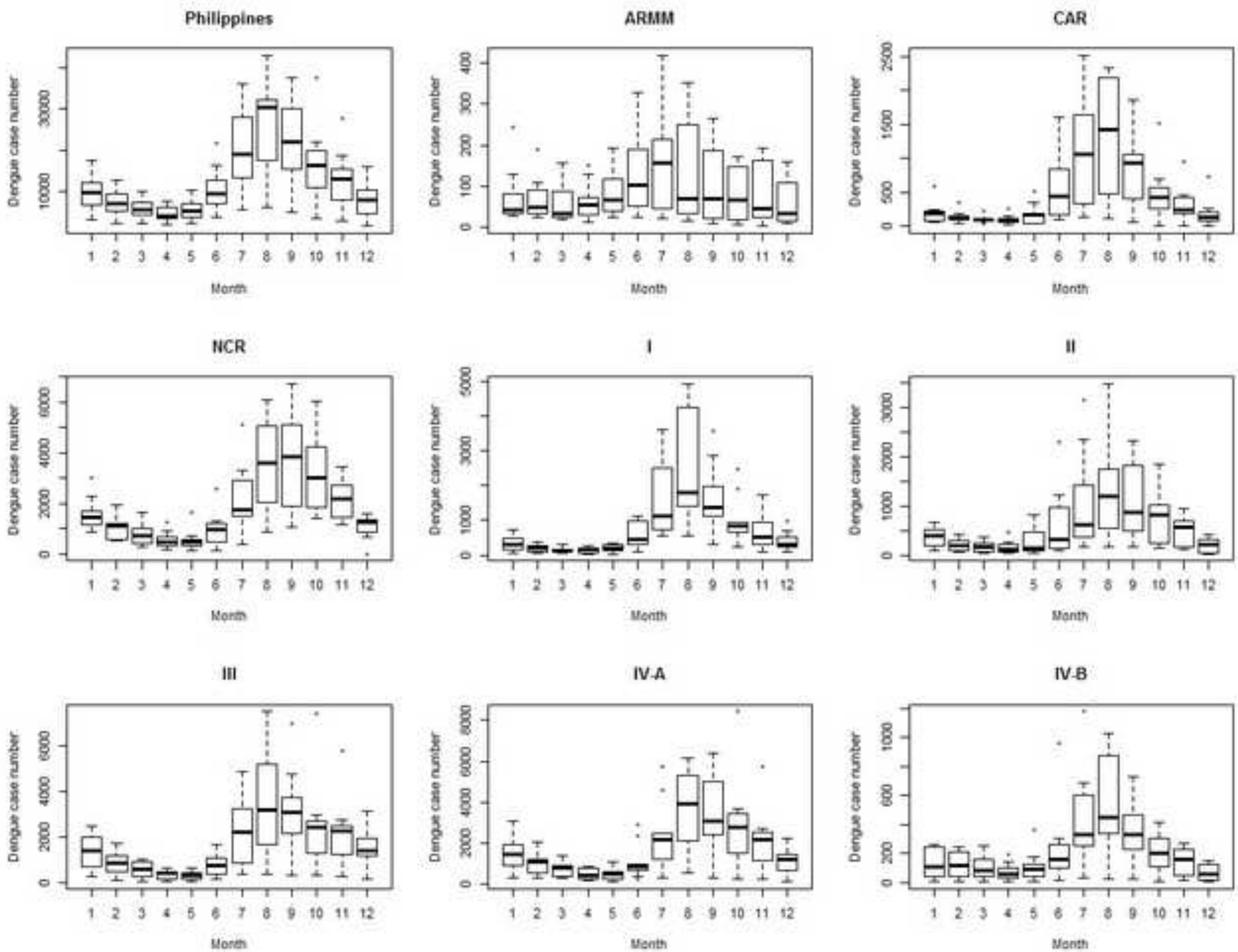


Figure 2B. The monthly distribution of dengue case number in the Philippines and the 17 regions

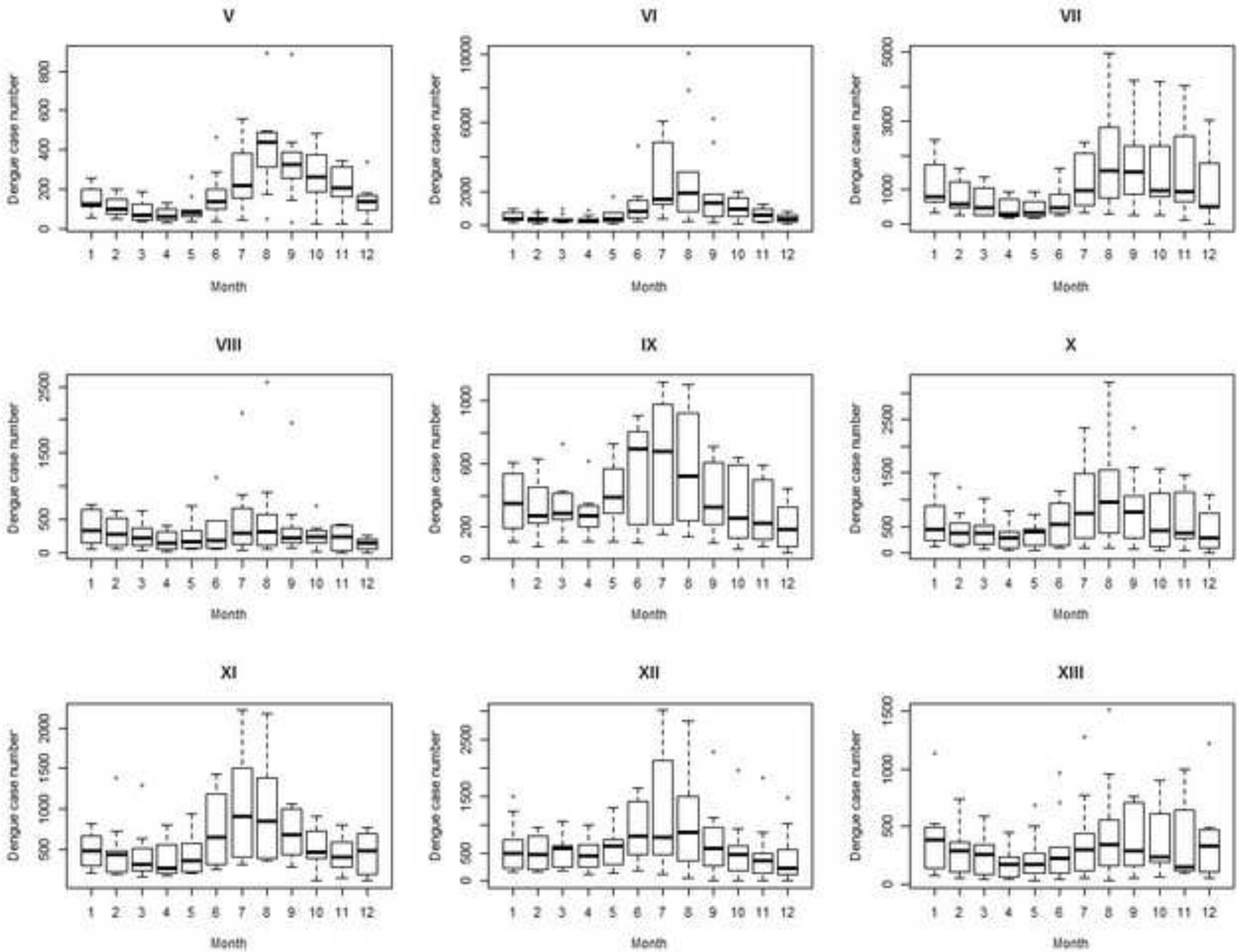


Figure 3. The spatial patterns of dengue incidence rate (per 10,000) in the Philippines during 2008 to 2017 and the two time periods (2008-2012 and 2013-2017). The 17 regions are Autonomous Region in Muslim Mindanao (ARMM), Cordillera Administrative Region (CAR), National Capital Region (NCR, also named as Metropolitan Manila), Ilocos Region (Region I), Cagayan Valley (Region II), Central Luzon (Region III), Calabarzon (Region IV-A), Mimaropa (Region IV-B), Bicol Region (Region V), Western Visayas (Region VI), Central Visayas (Region VII), Eastern Visayas (Region VIII), Zamboanga Peninsula (Region IX), Northern Mindanao (Regopm X), Davao Region (Region XI), Soccsksargen (Region XII), and Caraga Region (Region XIII).

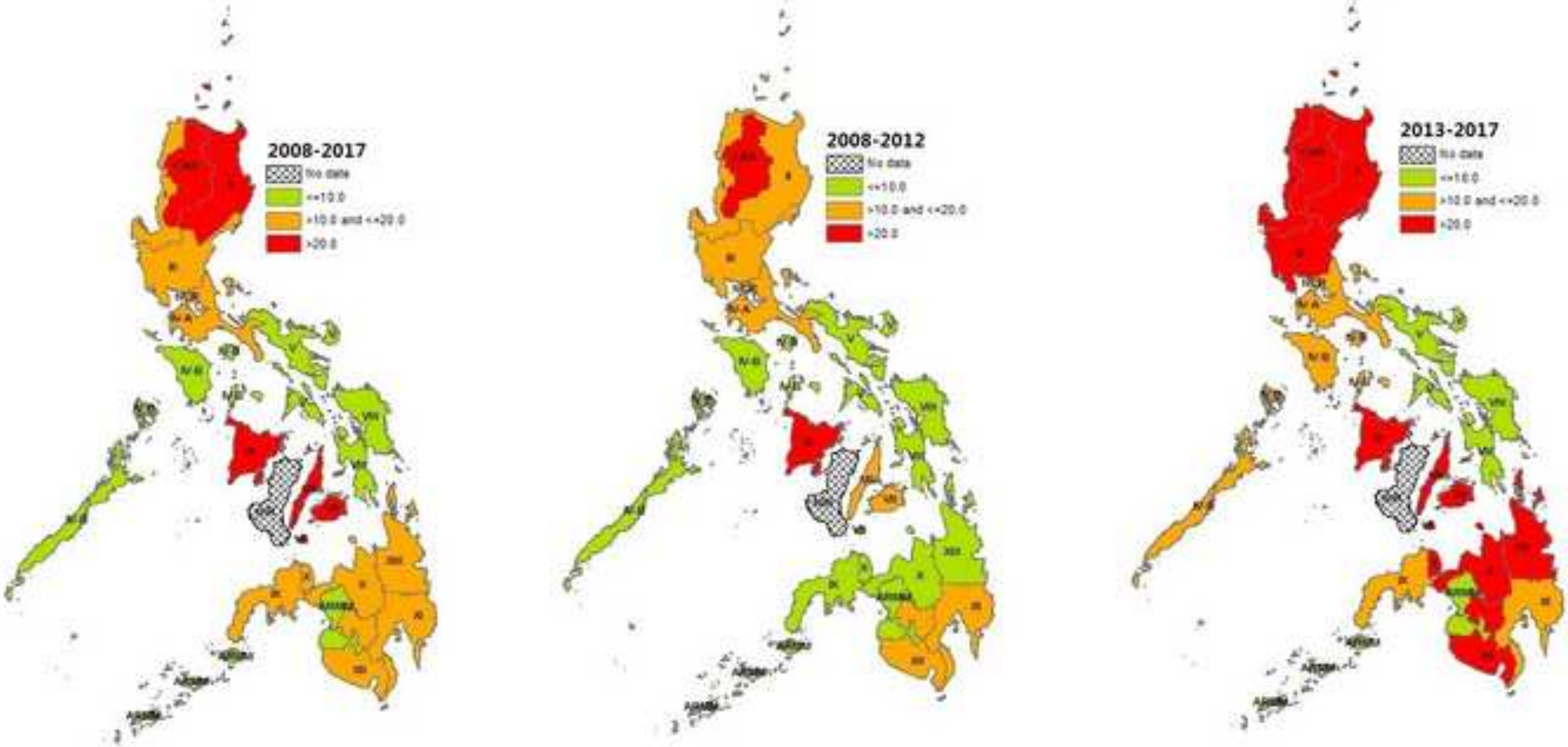


Figure 4. The percentage contributions of different regions in terms of dengue case number

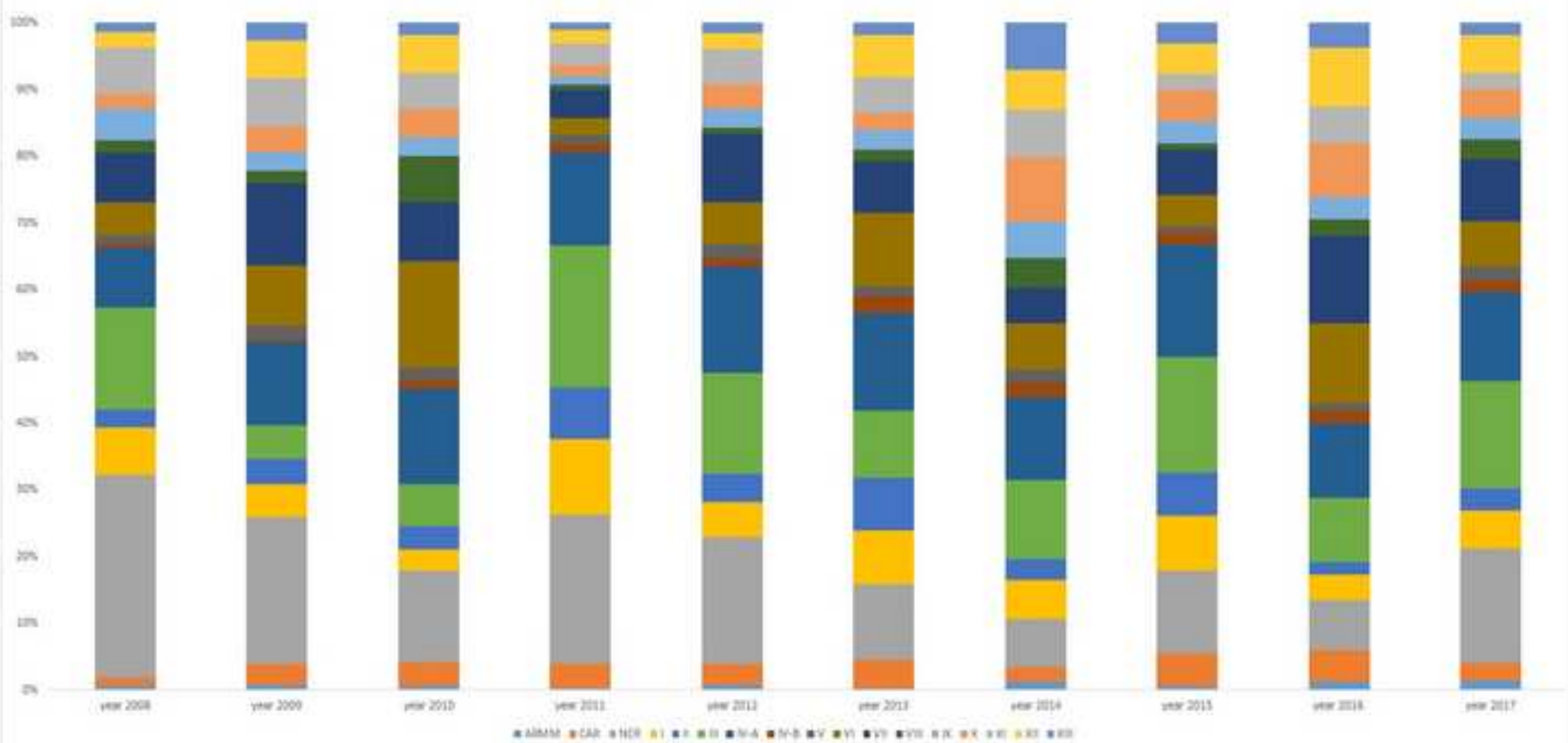


Figure 5A. The association between mean temperature and dengue in the selected provinces. The solid lines represent the relative risk of dengue under certain temperature value (relative to the mean value of temperature), and the black dash lines represent the 95% confidence interval of the relative risk. The red dash lines represent the 5th and 95th percentiles of temperature value.

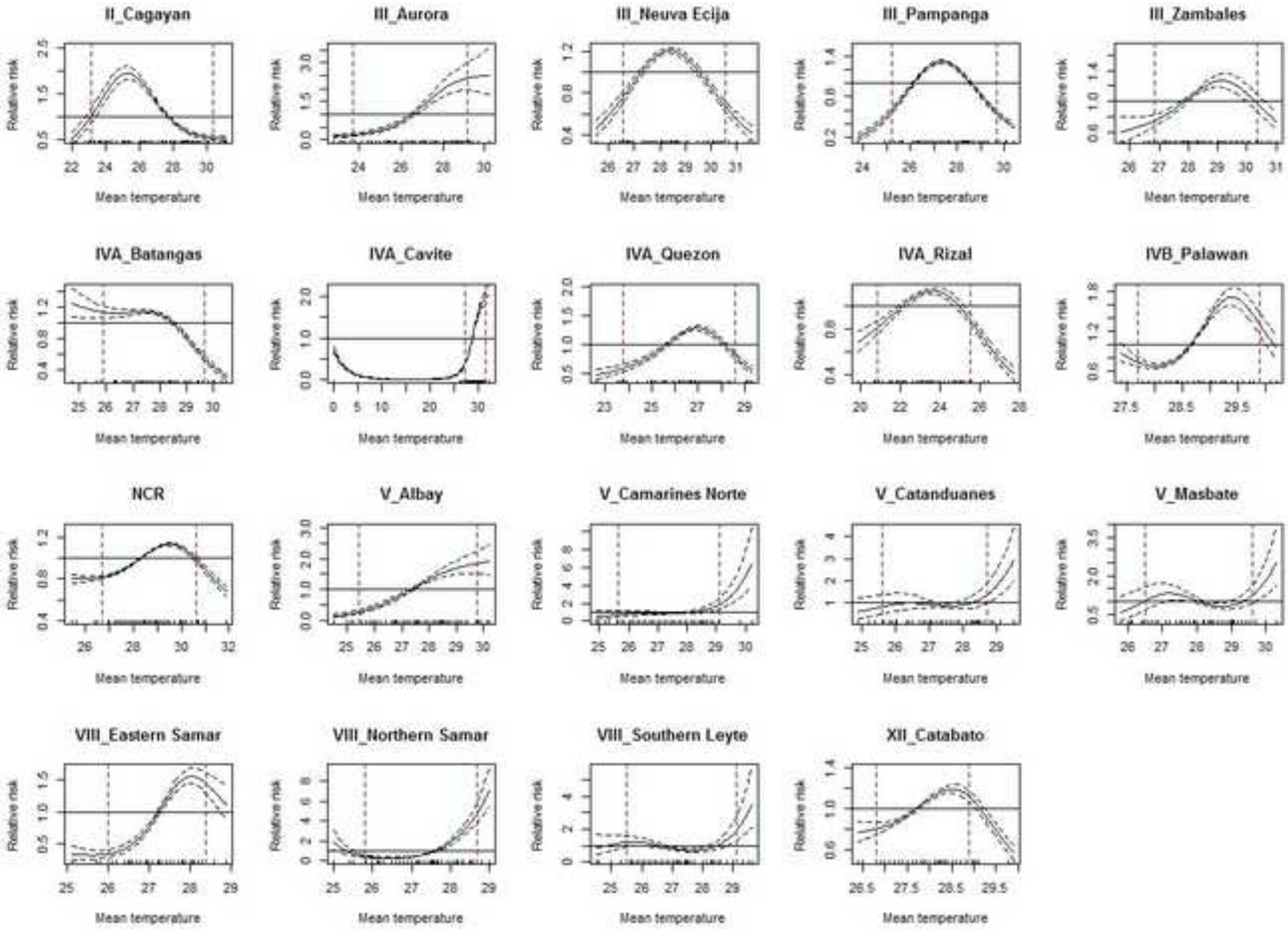


Figure 5B. The association between relative humidity (or rainfall) and dengue in the selected provinces. The solid lines represent the relative risk of dengue under certain relative humidity (or rainfall) value (relative to the mean value of relative humidity (or rainfall)), and the black dash lines represent the 95% confidence interval of the relative risk. The red dash lines represent the 5th and 95th precentiles of relative humidity (or rainfall) value.