# ASSOCIATION BETWEEN METEOROLOGICAL FACTORS AND DENGUE INCIDENCE IN GUANGDONG, CHINA: A TIME SERIES ANALYSIS USING DISTRIBUTED LAG NONLINEAR MODEL

Mai Liu, Yin Zhang, Lijuan Li and Lei Wang

Academy of Military Medical Sciences, Academy of Military Sciences, Beijing, PR China

**Abstract.** Climate variability greatly affects dengue prevalence; thus, further understanding of the relationship between weather conditions and dengue outbreaks is needed. We analyzed the association between meteorological factors (temperature and rainfall) and the incidence of dengue infection in Guangdong Province, PR China from 2018 to 2019, using weekly mean dengue cases and meteorological data. The nonlinear and delayed associations between dengue incidence and meteorological factors were assessed using a distributed lag nonlinear model. Overall, 9,447 dengue cases were recorded during the study period. The maximum lag-specific and cumulative percent change of dengue cases was 5.5% (95% confidence interval (CI): 3.1-7.9%; lag 0 week) and 28.3% (95% CI: 14.2-43.9%; lag 22 weeks) respectively per 1 °C increase in temperature, and 1.6% (95% CI: 0.6-2.6%; lag 0 week) and 9.4% (95% CI: 3.6-15.4%; lag 12 weeks) respectively for 1 mm increase in rainfall. The cumulative relative risk (RR) for a weekly mean temperature at 25.5°C over 22 weeks was 1.069 (95% CI: 1.031-1.151) relative to a weekly mean temperature at 22.8°C, and for a weekly mean rainfall over 12 weeks with a peak of 9.0 mm RR was 1.623 (95% CI: 0.91-3.40) relative to a weekly mean rainfall of 5.1 mm. However, the risk decreased significantly when rainfall exceeded 20.0 mm. We found a lag nonlinear relationship between meteorological factors and dengue incidence in Guangdong Province. Our findings can be used to develop climate-based early warning systems and provide insights for improving vector control of dengue outbreaks in Guangdong Province.

**Keywords:** dengue, rainfall, temperature, vector-borne disease

Correspondence: Lei Wang, Academy of Military Medical Sciences, Academy of Military Sciences, 27 Taiping Road, Haidian District, Beijing 100850, PR China
Tel: +86 66931045 E-mail: wangleienjoy@163.com

## INTRODUCTION

Dengue is one of the fastest-spreading mosquito-borne viral diseases of global public health concern. Its prevalence has increased 30-fold in the last 50 years (WHO, 2009), threatening more than half of the world's population (Messina *et al*, 2019; WHO, 2024). Over the past few decades, the prevalence of dengue has increased significantly in East and Southeast Asia, with approximately 75% of the global population at risk concentrated in the Asia-Pacific region (Bhatt *et al*, 2013; WHO, 2014). For example, the 2013-2014 dengue outbreaks in Fiji resulted in more than 25,000 cases (Kucharski *et al*, 2018). A dengue outbreak also occurred in Guangzhou, PR China in 2014 (Guo *et al*, 2017) and in the same year, Japan reported its first dengue outbreak in nearly 70 years (Kutsuna *et al*, 2015). The number of dengue cases in Taiwan reached a record high in 2014-2015 (Zhao *et al*, 2016; Wang *et al*, 2019). These phenomena highlight the rapid spread of dengue virus in the Asia-Pacific region.

Similar to dengue epidemics in many Southeast Asian countries, dengue prevalence in China has shown a trend of annual expansion, as well as a gradual spread from southeast coastal areas to inland provinces. Since 2010, the number of dengue cases in China has increased annually (Hu *et al*, 2022), with local cases of dengue reported in 13 provinces (Mu *et al*, 2020), thereby posing a serious disease and social burden on the country (Chen and Liu, 2015; Liu, 2021).

Although there are many factors, which affect the spread of dengue, climate change is generally considered to be the main driver of increased prevalence (Hales *et al*, 2002; Morin *et al*, 2013; Wu *et al*, 2018). Meteorological factors that impact the intensity and distribution of dengue outbreaks include temperature, precipitation, humidity, wind speed, air pressure, sunshine, and evaporation, which influence the distribution, density and reproductive rate of the mosquito vectors (Yang *et al*, 2009; Banu *et al*, 2014). Among these factors, temperature and rainfall are the two most important factors, each showing a nonlinear relationship with the risk of dengue (Morin *et al*, 2013; Xiang *et al*, 2017; Wang *et al*, 2022). Temperature and rainfall influence dengue prevalence by interfering with the development and reproduction of the Aedes mosquito vector (Hoeck *et al*, 2003). The prevalence of dengue is related to extreme weather conditions, such as high temperature, drought, flood, and El Nino event (Cheng *et al*, 2020; Li *et al*, 2023). Given that climate variability greatly affects dengue prevalence, an understanding of its relationship with weather conditions is needed.

Despite the urgent need to combat dengue, especially in endemic areas of the Asia-Pacific region such as China and Southeast Asia, up-to-date surveys of dengue outbreaks are still lacking. Guangdong Province is one of the major dengue endemic areas in China (Sun *et al*, 2020). Thus, this study analyzed the association between meteorological factors (temperature and rainfall) and the incidence of dengue in Guangdong Province from 2018 to 2019. The data should assist in the prediction and prevention of dengue outbreaks at an early stage, hence reducing the disease burden and economic costs to this region of the country (Bhatt *et al*, 2013; Stahl *et al*, 2013; Shepard *et al*, 2016).

## MATERIALS AND METHODS

### Study setting

The study was conducted in Guangdong Province, which lies in the southernmost part of mainland China and is located between 20° 09′ N to 25° 31′ N latitude and 109° 45′ E to 117° 20′ E longitude. It is approximately 800 km from east to west and 600 km from north to south, with an area of 179,800 km2. By the end of 2020, the permanent population of Guangdong Province reached 126 million, with a population density of 702.2 people per km2, making it the largest province with the largest permanent population in PR China (Yang, 2022). Guangdong Province has a subtropical monsoon and tropical climate in the north and south respectively, which provides a very suitable habitat for Aedes mosquito and conducive to the spread of dengue virus and dengue infection (Xu *et al*, 2017).

### Data collection

**Health data:** Dengue is classified as a Class B infectious disease in PR China and is monitored by the National Notifiable Infectious Diseases Surveillance Information System (Zhang *et al*, 2016). The diagnostic criteria for dengue infection follow the Diagnostic Criteria for Dengue Fever (WS216-2018) developed by the National Health Commission (Cheng *et al*, 2017). Here, we only included confirmed cases of dengue infection and excluded suspected cases. Dengue cases were classified into imported and locally acquired cases based on history of travel and mosquito bite. An imported case is defined as an infection in an individual who has traveled to a dengue-endemic area <15 days before symptom onset and was bitten by mosquitoes. Otherwise, a case is defined as locally acquired (Zhang *et al*, 2018). To exclude the impact of control policies enacted during the coronavirus epidemic in 2019, daily disease data on locally acquired and imported dengue cases were obtained from the Chinese Center for Disease Control and Prevention in Guangdong Province from 01 January 2018 to 31 December 2019, and compiled into weekly average data.

**Meteorological data:** Daily data on average temperature, precipitation, average humidity, average wind speed, average pressure, average sunshine, and average evaporation in Guangdong Province from 01 January 2018 to 31 December 2019 were obtained from the National Meteorological Information Center from its 86 ground monitoring stations (Fig 1) (Wu and Gao, 2013) and compiled into weekly average data.

**Data management and statistical analysis**

Dengue outbreaks are caused by a complex relationship among multiple meteorological factors, such as temperature, rainfall and vector ecology. These relationships are nonlinear and exhibit delayed effects (Lowe *et al*, 2018; Coalson *et al*, 2021). To simplify the problem and focus of the study, we assume that the population is homogeneous before modeling and, therefore, we ignore differences in age and sex. We apply a flexible modeling approach using a distributed lag nonlinear model (DLNM) (Gasparrini *et al*, 2010) to account for nonlinear and delayed associations between meteorological factors and dengue incidence using cross-basis functions.

Spearman's correlation coefficient is used to explore the correlation among meteorological factors. A quasi-Poisson DLNM is then applied to estimate the associations between weekly meteorological factors and dengue incidence. Concurrently, meteorological factors are included in the model to control for potential confounding effects, and time terms are included to control long-term trends.

In the exposure-response dimensions of temperature and rainfall, the natural cubic spline function (df = 3) is used to fit the exposure-response relationship. Based on previous studies (Wang *et al*, 2021), we extend the maximum lag to 22 and 12 weeks for temperature and rainfall respectively. Log-transformed dengue cases from the previous week are also added to reduce serial autocorrelation in the residuals. The model used is as follows (using temperature as an example):

$$\log[Y_t] = \alpha + cb(temp, lag) + ns(rh, df = 3) + ns(win, df = 3) + ns(ss, df = 3) + lag1 + time$$

| | | | |
|---|---|---|---|
| where | t | = | day of observation, |
| | $Y_t$ | = | number of dengue cases, |
| | $\alpha$ | = | model constant term, |
| | cb | = | cross basis function, |
| | ns | = | natural cubic spline function, and |
| | df | = | degree of freedom |

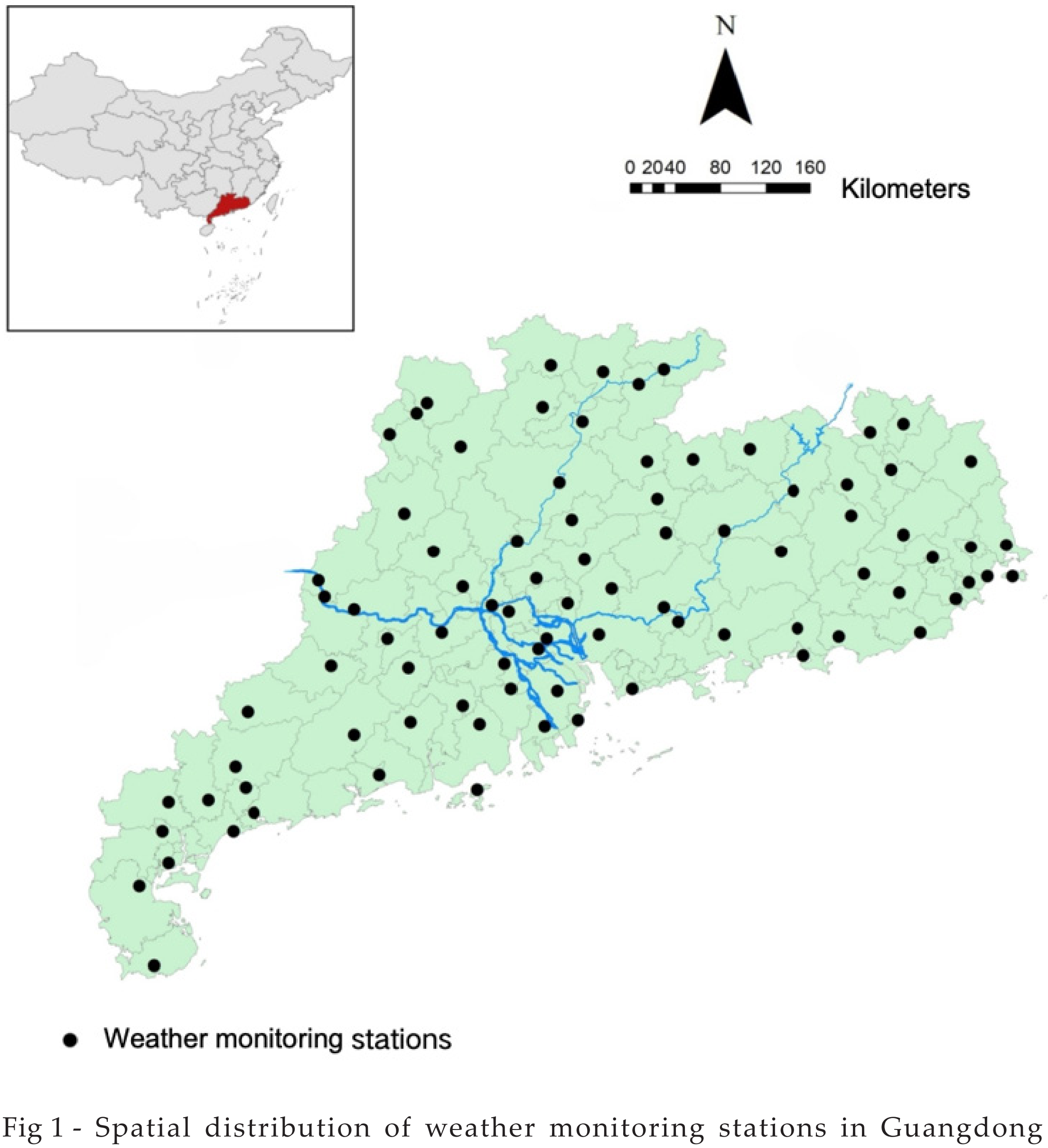


Fig 1 - Spatial distribution of weather monitoring stations in Guangdong Province, PR China

The map depicts locations of the 86 ground monitoring stations of the National Meteorological Information Center, Guangdong Province (inset).

Confounders considered for modeling include mean relative humidity (rh), wind speed (win), sunshine (ss), autocorrelation with a lag of 1 week (lag1), and long-term trend (time). All statistical analyses are conducted using the "dlnm" and "splines" packages in R software version 3.6.3 (https://www.R-project.org).

**Sensitivity analysis**

A sensitivity analysis is performed to identify the robustness of the results. First, the autocorrelation term (log-transformed dengue cases in the previous week) is excluded from the main model. Subsequently, a week-of-year variable is incorporated into the model to adjust for seasonality, using a natural cubic spline function with varying degrees of freedom of three, four and five in each model.

## RESULTS

**Dengue cases and weather conditions**

Dengue cases (*n* = 9,447) were reported during the study period, with a weekly average of 13 (range = 0-69) dengue cases (Table 1). The weekly average temperature was 22.8°C (range: 7.5-29.7°C) and the weekly average rainfall was 5.1 mm (range: 0-3.4 mm) (Table 1).

**Correlation between meteorological factors and incidence of dengue fever**

Previous studies have shown that temperature, rainfall, relative humidity, wind speed, air pressure, sunlight, and evaporation may increase the risk of dengue fever (Faruk *et al*, 2022). Therefore, the above seven meteorological factors were included in the analysis, and the correlation among them was examined. To avoid collinearity, variables with correlation coefficients >0.7 of meteorological factors were excluded (Yan, 2023), and only temperature, rainfall, humidity, wind speed, and sunshine were finally included.

Disease outbreaks in 2019 were more severe than those in 2018 (Fig 2). The peak incidence of dengue fever and the peak of meteorological factors (temperature and rainfall) did not overlap completely; there was a lag (Fig 2). The peak incidence of dengue

Table 1

Distribution of weekly mean dengue cases and meteorological factors, Guangdong, PR China January 2018 - December 2019

| Variable | Number of valid days | Minimum | 25th percentile | Mean | Standard deviation | 75th percentile | Maximum |
|---|---|---|---|---|---|---|---|
| Weekly mean dengue cases | 730 | 0 | 1 | 13 | 19 | 15 | 69 |
| Weekly mean temperature (°C) | 730 | 7.5 | 18.4 | 22.8 | 5.4 | 27.7 | 29.7 |
| Weekly mean rainfall (mm) | 730 | 0 | 0.5 | 5.1 | 6.1 | 7.9 | 31.4 |

mm: millimeter; °C: Degree Celsius

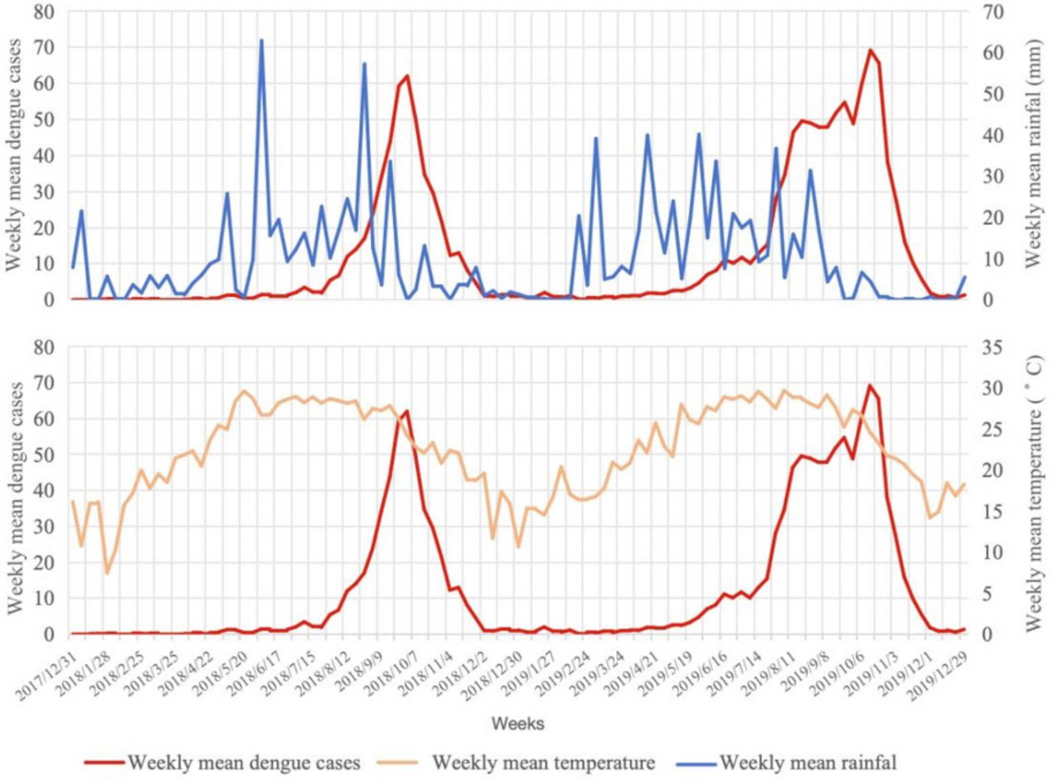


Fig 2 - Time series of meteorological factors and dengue incidence in Guangdong Province, PR China in 2018 and 2019

mm: millimeter; °C: Degree Celsius

cases occurred after the average weekly temperature peak. The peak incidence of dengue cases only coincided with the peak average temperature when precipitation was at a low peak. This suggested that the above meteorological factors were correlated with the incidence of dengue infection. Spearman's correlation analysis showed that the weekly incidence of dengue cases is significantly correlated with the weekly mean temperature (rs = 0.05, $p$-value <0.001) and weekly mean precipitation (rs = 0.149, $p$-value <0.001) (Table 2).

Table 2

Spearman's correlation coefficients between meteorological factors and dengue cases

| Variable | Temperature-hao | Rainfall | Relative humidity | Wind speed | Atmospheric pressure | Sunshine | Evaporation | Dengue case |
|---|---|---|---|---|---|---|---|---|
| Temperature | 1.00 | | | | | | | |
| Rainfall | 0.51** | 1.00 | | | | | | |
| Relative humidity | 0.33** | 0.76** | 1.00 | | | | | |
| Wind speed | -0.31** | -0.08 | -0.17 | 1.00 | | | | |
| Atmospheric pressure | -0.89** | -0.67** | -0.53** | 0.29* | 1.00 | | | |
| Sunshine | 0.46** | -0.27 | -0.52** | -0.15 | -0.24* | 1.00 | | |
| Evaporation | 0.55** | -0.14 | -0.51** | 0.01 | -0.35** | 0.86** | 1.00 | |
| Dengue case | 0.56** | 0.25* | 0.06 | -0.24* | -0.38** | 0.43** | 0.43** | 1.00 |

*$p$-value <0.05; **$p$-value <0.01

**Relationship between meteorological factors and dengue cases**

Temperature and rainfall are significantly associated with dengue cases (Fig 3). In the single-week lag structures, exposures to temperature (lag 0-6 weeks and lag 17-22 weeks) and rainfall (lag 0-6 weeks) were associated with increased dengue cases. The maximum lag-specific percent change per 1°C increase in temperature and 1 mm increase in rainfall was 5.5% (95% confidence interval (CI): 3.1-7.9%; lag 0 week) and 1.6% (95% CI: 0.6-2.6%; lag 0 week) respectively. In the cumulative lag structures, the unfavorable

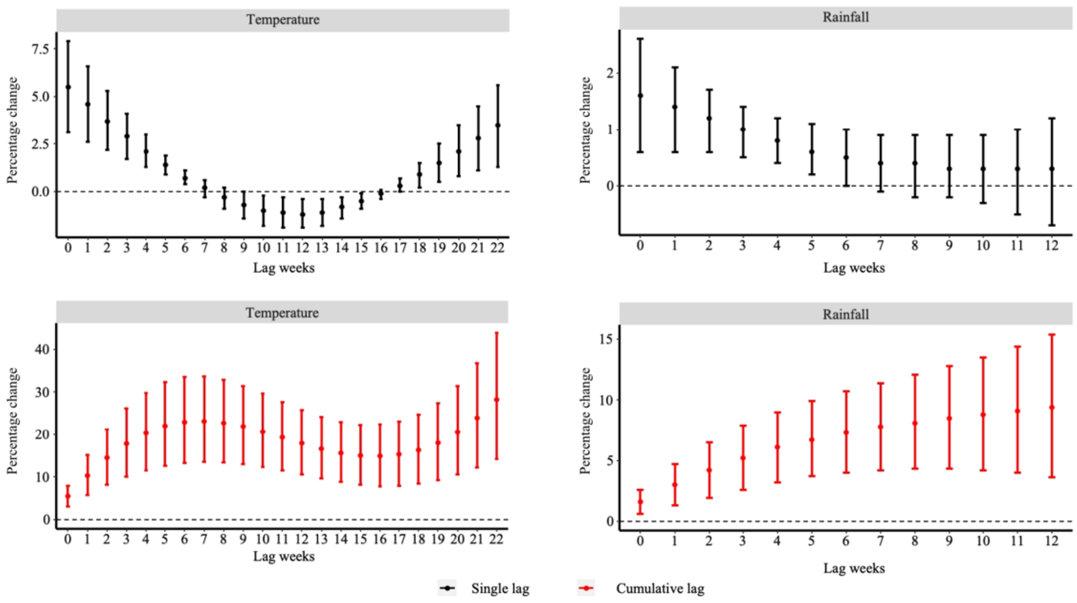


Fig 3 - Percent change (excess risk [ER]) of dengue cases for temperature and rainfall at various lags, Guangdong Province, PR China 2018-2019

Note: Risk estimates were expressed as excess risk (ER). Error bars denote 95% confidence intervals.

ER = (RR-1)×100

RR: relative risk

effects of temperature and rainfall occurred at lag 0-22 weeks and lag 0-12 weeks respectively, and the corresponding maximum percent changes was 28.3% (95% CI: 14.2-43.9%; lag 22 weeks) and 9.4% (95% CI: 3.6-15.4%; lag 12 weeks) respectively (Table 3).

**Influence of meteorological factors on the incidence of dengue**

With a weekly mean temperature of 22.8°C as a reference, the cumulative effect on the incidence of dengue was highest when the weekly mean temperature was 25.5°C (relative risk (RR) = 1.069; 95% CI): 0.998-1.147) (Fig 4). Using a mean rainfall of 5.1 mm as a reference, the cumulative effect on the incidence of dengue was highest when the average weekly rainfall was 9.0 mm (RR =1.623; 95% CI: 0.559-4.719) (Fig 4). The average rainfall percentile in the 85th week was approximately 9.0 mm, close to the 90th percentile, and could be considered a relatively large amount of rainfall. However, a protective effect was observed when rainfall was >20.0 mm.

**Delayed effects of meteorological factors on the incidence of dengue**

The effects of the persistence and lag of meteorological factors (weekly average temperature and weekly average rainfall) on the onset of dengue were analyzed when the cumulative effect was maximum (Fig 5). The analysis revealed that a weekly average temperature of 25.5°C had the greatest impact on the incidence of dengue of the week. The risk of dengue gradually decreased with time. A weekly average rainfall of 9.0 mm had the greatest impact on the incidence of dengue at week 3 and week 7. The risk then subsequently decreased, showing an inverted U-shape curve.

**Sensitivity analysis**

A sensitivity analysis indicated that adjusting seasonality had no significant effect on the main model after excluding the autocorrelation term.

## DISCUSSION

Dengue outbreaks have occurred in many areas worldwide in recent

Table 3

Percent changes in dengue incidence by temperature and rainfall lags, Guangdong, PR China January 2018 - December 2019

| Lag (weeks) | Temperature | | Rainfall | |
|---|---|---|---|---|
| | Single lag* | Cumulative lag* | Single lag* | Cumulative lag* |
| lag 0 | 5.5 (3.1-7.9) | 5.5 (3.1-7.9) | 1.6 (0.6-2.6) | 1.6 (0.6-2.6) |
| lag 1 | 4.6 (2.6-6.6) | 10.3 (5.8–15.1) | 1.4 (0.6-2.1) | 3.0 (1.3-4.7) |
| lag 2 | 3.7 (2.2-5.3) | 14.5 (8.1-21.2) | 1.2 (0.6-1.7) | 4.2 (1.9-6.5) |
| lag 3 | 2.9 (1.7-4.1) | 17.8 (10.0-26.1) | 1.0 (0-1.4) | 5.2 (2.6-7.9) |
| lag 4 | 2.1 (1.3-3.0) | 20.3 (11.5-29.8) | 0.8 (0.4-1.2) | 6.1 (3.2-9.0) |
| lag 5 | 1.4 (0.9-1.9) | 22.0 (12.6-32.3) | 0.6 (0.2-1.1) | 6.7 (3.7-9.9) |
| lag 6 | 0.7 (0.4-1.1) | 22.9 (13.2-33.5) | 0.5 (0-1) | 7.3 (4.0-10.7) |
| lag 7 | 0.2 (-0.3-0.6) | 23.1 (13.5-33.6) | 0.4 (-0.1-0.9) | 7.8 (4.2-11.4) |
| lag 8 | -0.3 (-0.9-0.2) | 22.7 (13.4-32.9) | 0.4 (-0.2-0.9) | 8.1 (4.3-12.1) |
| lag 9 | -0.7 (-0.14-0) | 21.9 (13.0-31.4) | 0.3 (-0.2-0.9) | 8.5 (4.3-12.8) |
| lag 10 | -1 (-1.8-0.2) | 20.6 (12.3-29.6) | 0.3 (-0.3-0.9) | 8.8 (4.2-13.5) |
| lag 11 | -1.1 (-1.9-0.3) | 19.3 (11.5-27.6) | 0.3 (-0.5-1.0) | 9.1 (4.0-14.4) |
| lag 12 | -1.2 (-1.9-0.4) | 17.9 (10.6-25.7) | 0.3 (-0.7-1.2) | 9.4 (3.6-15.4) |
| lag 13 | -1.1 (-1.8-0.4) | 16.6 (9.6-24.1) | N/D | N/D |
| lag 14 | -0.8 (-1.4-0.3) | 15.6 (8.8-22.9) | N/D | N/D |

Table 3 (cont)

| Lag (weeks) | Temperature | | Rainfall | |
| --- | --- | --- | --- | --- |
| | Single lag* | Cumulative lag* | Single lag* | Cumulative lag* |
| lag 15 | -0.5 (-0.9-0.1) | 15,0 (8.2-22.3) | N/D | N/D |
| lag 16 | -0.1 (-0.4-0.1) | 14.9 (7.8-22.4) | N/D | N/D |
| lag 17 | 0.3 (0-0.7) | 15.3 (7.9-23.1) | N/D | N/D |
| lag 18 | 0.9 (0.2-1.5) | 16.3 (8.4-24.7) | N/D | N/D |
| lag 19 | 1.5 (0.5-2.5) | 18.0 (9.3-27.4) | N/D | N/D |
| lag 20 | 2.1 (0.8-3.5) | 20.5 (10.6-31.3) | N/D | N/D |
| lag 21 | 2.8 (1.1-4.5) | 23.9 (12.2-36.7) | N/D | N/D |
| lag 22 | 3.5 (1.3-5.6) | 28.3 (14.2-43.9) | N/D | N/D |

*% excess risk (95% confidence interval)

N/D: no data

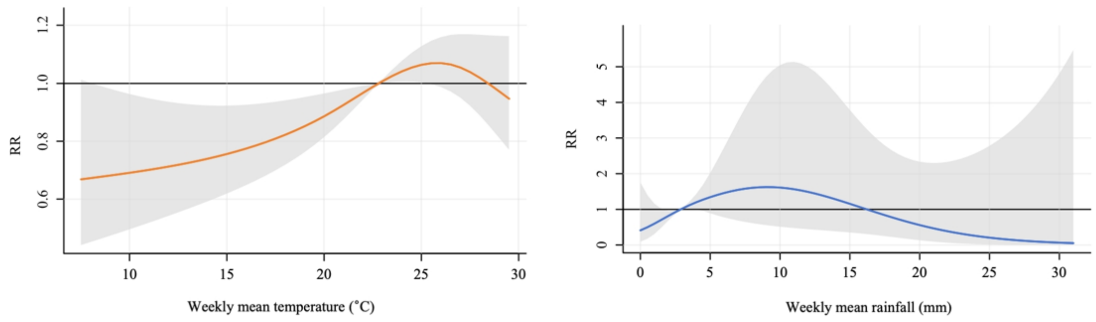


Fig 4 - Influence of meteorological factors on the incidence of dengue fever, Guangdong Province, PR China 2018-2019

Note: The solid line represents the estimated spline curve, and the shaded region indicates the 95% confidence interval.

mm: millimeter; RR: relative risk; °C: Degree Celsius

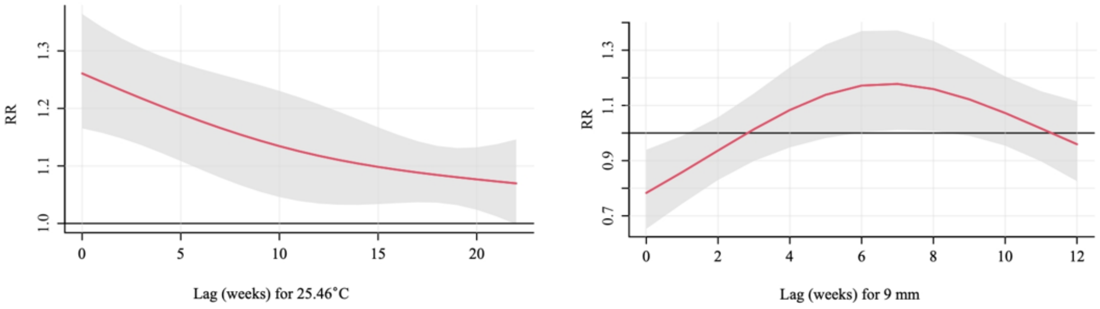


Fig 5 - Delayed effects of meteorological factors on the incidence of dengue, Guangdong Province, PR China 2018-2019

Note: The solid line represents the estimated spline curve, and the shaded region indicates the 95% confidence interval.

mm: millimeter; RR: relative risk; °C: Degree Celsius years (Kucharski *et al*, 2018). For example, in 2014, Guangzhou Province experienced the worst recorded dengue outbreak in the country, with more than 40,000 cases reported and a prevalence two orders of magnitude higher than the historical average (Zhao *et al*, 2016; Oidtman *et al*, 2019). Over the years, the incidence of dengue in Guangdong Province has attained a leading position in China; thus, the province is a key area for the implementation of dengue prevention and control measures.

A recent systematic review of climate change and dengue in China highlighted the lack of evidence on the impact of high temperatures on dengue prevalence (Li *et al*, 2018). Using DLNM analysis (Gasparrini *et al*, 2010) of various weather parameters gathered in Guangdong Province from 2018 to 2019, we found that the risk of dengue infection increased as the weekly average temperature increased. In addition, the association of weekly average rainfall and dengue incidence showed an inverted U-shape relationship, with moderate rainfall being associated with the highest risk of dengue infection whereas excessive rainfall has a protective effect. Weather data were collected from all ground monitoring stations ($n$ = 86) in the entire Guangdong Province, thereby reducing errors in temperature and rainfall measurements.

Our finding of an increasing risk of dengue infection with increasing temperature is consistent with previous studies (Johansson *et al*, 2009; Lu *et al*, 2009; Wu *et al*, 2018; Kakarla *et al*, 2019; Xu *et al*, 2019). Higher temperatures accelerate the replication of dengue virus in Aedes mosquitoes while shortening the incubation period (Naish *et al*, 2014), thus increasing the rate of transmission of dengue virus and the number of dengue cases. We observed a long-term delayed effect in the association between temperature and dengue incidence, consistent with findings on the association between severe dengue cases and temperature reported by Xiang *et al* (2017). This delayed effect may reflect the duration of both positive and negative effects of weather conditions on dengue transmission, as well as the accumulation phase of dengue epidemics or outbreaks. The critical time window we identified will give local health authorities adequate time to make early preparations to prevent or reduce imminent dengue outbreaks.

A positive correlation has been reported between dengue prevalence and rainfall (Wongkoon *et al*, 2013). However, we found an inverted U-shape relationship between rainfall and dengue, with moderate rainfall causing the highest dengue risk and excessive rainfall having a protective effect. A possible explanation is that heavy rain washes away mosquito breeding sites, together with mosquito eggs and larvae (Seidahmed and Eltahir, 2016). However, Coalson *et al* (2021) noted that the prevalence of dengue infection decreased for less than a month after a flood event, followed by an increase in dengue cases 1-4 months later. Similarly, Morin *et al* (2013) reported that high rainfall and humidity have a negative impact on mosquito breeding grounds. Given that mosquitoes can live from 2 weeks to a month, maximum rainfall may be an important parameter in determining whether the mosquito's life cycle is maintained.

Our study has several strengths: (i) The disease and meteorological data used in the study were updated to 2019, allowing us to better analyze the relationship between meteorological factors and dengue incidence in Guangdong Province; and (ii) The distributed lag nonlinear model (DLNM) considered the nonlinear and delayed effects of temperature and rainfall on dengue incidence. However, this study also has several limitations: (i) Entomological data on dengue vectors were lacking, preventing us from studying how vector distribution affected the relationship between meteorological factors and dengue incidence; (ii) There were no data on diagnostic methods, virus serotype, patient's age, or dengue severity; therefore, there was some discrepancy between the number of dengue cases included in our study and the actual number of cases.

However, the difference in the number of disease cases was evenly distributed in time and did not cause significant fluctuations in the study results; and (iii) Our findings suggest that excessive rainfall may reduce the number of vectors; however, the mechanisms by which rainfall affects mosquito population dynamics remain unclear.

In conclusion, we show that the risk of dengue incidence in Guangdong Province was seasonal and influenced by meteorological factors, in particular temperature and rainfall. The cumulative incidence risk of dengue fever was highest when the average temperature and rainfall was 25.5°C and 9.0 mm respectively, with a significant lag effect, which decreased with extreme rainfall. Our findings should be of assistance in the development of more timely control and prevention measures against dengue outbreaks in Guangdong Province.

## CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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