Extreme weather conditions and dengue outbreak in Guangdong, China: spatial heterogeneity based on climate variability

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Competing interests: The authors declare they have no actual or potential competing financial interests.

Abstract

Background: Previous studies have shown associations between local weather factors and dengue incidence in tropical and subtropical regions. However, spatial variability in those associations remains unclear and evidence is scarce regarding the effects of weather extremes.

Objectives: We examined spatial variability in the effects of various weather conditions on the unprecedented dengue outbreak in Guangdong province of China in 2014 and explored how city characteristics modify weather-related risk.

Methods: A Bayesian spatial conditional autoregressive model was used to examine the overall and city-specific associations of dengue incidence with weather conditions including (1) average temperature, temperature variation, and average rainfall; and (2) weather extremes including numbers of days of extremely high temperature and high rainfall (both used 95th percentile as the cut-off). This model was run for cumulative dengue cases during five months from July to November (accounting for 99.8% of all dengue cases). A further analysis based on spatial variability was used to validate the modification effects by economic, demographic and environmental factors.

Results: We found a positive association of dengue incidence with average temperature in seven cities (relative risk (RR) range: 1.032 to 1.153), a positive association with average rainfall in seven cities (RR range: 1.237 to 1.974), and a negative association with temperature variation in four cities (RR range: 0.315 to 0.593). There was an overall positive association of dengue incidence with extremely high temperature (RR:1.054, 95% credible interval (CI): 1.016 to 1.094), without evidence of variation across cities, and an overall positive association of dengue with extremely high rainfall (RR:1.505, 95% CI: 1.096 to 2.080), with seven regions having stronger associations (RR range: 1.237 to 1.418). Greater effects of weather conditions appeared to occur in cities with higher economic level, lower green space coverage and lower elevation.

Conclusions: Spatially varied effects of weather conditions on dengue outbreaks necessitate area-specific dengue prevention and control measures. Extremes of temperature and rainfall have strong and positive associations with dengue outbreaks.

Keywords: Dengue outbreak; China; Spatial analysis; Extremely high temperature; Extremely high rainfall

Funding

This work was supported by the National Health and Medical Research Council (NHMRC) of Australia (project grant: APP 1138622).

1. Introduction

Dengue is a viral infection transmitted by female *Aedes* mosquitoes (WHO). Dengue virus is a mosquito-borne and single positive-stranded RNA virus consisting of four serotypes (DENV 1 to 4) that are members of the genus Flavivirus in the family Flaviviridae (Simmons et al. 2012). Annually, there are an estimated 100-400 million dengue infections worldwide and about half of the world's population is now at risk of infection (Bhatt et al. 2013; WHO). In the last decade, dengue outbreaks have frequently occurred in the Asia-Pacific region in tropical and subtropical climates such as the Philippines, Bangladesh, Vietnam and China (Bravo et al. 2014; Cheng et al. 2020b; Guo et al. 2017; Mone et al. 2019; Xu et al. 2017). Dengue outbreaks often led to a large number of cases, imposing great stress on local health systems and causing substantial economic burden (Shepard et al. 2016). Without effective prevention measures, dengue-related health and economic burden is expected to continue to increase in the context of global warming (Colón-González et al. 2018; Hales et al. 2002).

Dengue transmission is sensitive to environmental change. For instance, climatic factors such as temperature and rainfall can moderate many aspects of the biology of dengue transmission such as mosquito population dynamics and biting rate (Abdelrazec and Gumel 2017; Mordecai et al. 2017; Ndiaye et al. 2006; Xu et al. 2017; Zhu et al. 2019a). Associations between weather conditions and dengue incidence have been widely reported in previous studies, suggesting that rises in temperature, relative humidity, and rainfall are associated with increased dengue incidence (Li et al. 2018; Wu et al. 2018; Xu et al. 2017). Studies have also reported potential linkage of weather anomalies such as El Niño events, extremely hot days, and floods with dengue incidence (Cheng et al. 2020b; Ferreira 2014; Li et al. 2018). As climate change progresses, there will be more frequent and intensive weather extremes such as heatwaves, making it an urgent need to investigate the effects of extreme weather conditions on dengue incidence in many dengue-affected regions including China (Cheng et al. 2020b; Li et al. 2018).

Historically, the first dengue outbreak with serious consequences in China was in 1978, which occurred in Guangdong province, with 22,122 cases (16 fatalities) reported (Wu et al. 2010). Since then, Guangdong province and other regions of China have frequently suffered dengue epidemics or outbreaks and recorded a large number of cases almost every year. Guangdong province has become the epicentre of dengue outbreaks in China, accounting for most dengue cases on the mainland between 1990 and 2017 (Lai et al. 2015; Liu et al. 2018; Wu et al. 2010). In 2014, Guangdong province experienced its worst dengue outbreak, recording more than 40,000 dengue cases and exceeding in a single year the cumulative cases from 1990 to 2013 (Lai et al. 2015; Li et al. 2016). Potential reasons behind this unprecedented outbreak remain unclear. Available literature has revealed many key determinants of the dengue outbreak in 2014, such as socioeconomic and demographic factors, imported cases, urbanization, as well as local weather conditions (Li et al. 2016; Oidtman et al. 2019; Ren et al. 2017; Wu et al. 2018; Xu et al. 2017). However, the association between weather conditions and dengue incidence in China have been mostly examined through various statistical analyses restricted to a whole study area (e.g., a city or a province or a country) (Fan et al. 2014; Li et al. 2016; Liu et al. 2018; Xiang et al. 2017; Xiao et al. 2018; Xu et al. 2017). In practice, the effects of weather conditions are likely to vary across regions because regional differences such as sociodemographic factors, imported cases and the implementation of mosquito control measures could independently affect and interact with local weather conditions to affect dengue incidence (Cheng et al. 2017; Zhu et al. 2018). These interactions will consequently lead to a spatially heterogeneous response of dengue transmission capacity to weather conditions (Xu et al. 2019). Therefore, a better understanding of spatial variability in the impacts of weather conditions on dengue incidence would assist in developing an early warning system for dengue-affected areas that are particularly vulnerable to permissive weather conditions. Furthermore, although associations between weather variables and dengue incidence have been reported in many previous studies, evidence in China is still lacking concerning the effects of extreme weather conditions such as extremes of temperature and rainfall (Li et al. 2018). Abnormally high rainfall and high temperature are thought to have contributed to the Guangdong dengue outbreak in 2014 (Li et al. 2016; Shen et al. 2015), but this is yet to be tested.

In this study, we used a Bayesian spatial analytical approach to examine the spatial variability in the effects of different weather conditions (particularly extreme weather) on dengue incidence. We further investigated if among-area differences in the effects of weather conditions can be predicted by regional characteristics such as economic, demographic and environmental factors, and imported cases. Ultimately, we wanted to identify the dengue-affected areas that were most vulnerable to weather conditions.

2. Methods

2.1. Study setting

This study was conducted in Guangdong, the largest province in southern China, with 88.7 million people residing in 21 cities (population density range: 179 to 2634 persons per km^2) in 2014 (http://tongji.cnki.net/kns55/navi/YearBook.aspx?id=N2016030128&floor=1). Guangdong features a subtropical climate with hot and humid summer, mild and dry winter, and abundant rainfall, providing the ideal climate for the development and population abundance of *Aedes* mosquitos (Guo et al. 2014; Lai et al. 2015; Xiao et al. 2016). Guangdong is also an economic, cultural and transport centre in China, as well as a hub for international travel and trade, in particular with the Asia-Pacific countries where dengue is endemic (Guo et al. 2014; Ooi 2015), and is therefore important in driving both the import and export of infected cases.

2.2. Data collection

Since 1989, dengue has been a statutorily notifiable infectious disease in China. All dengue cases were diagnosed according to the unified diagnostic criteria issued by the Chinese Ministry of Health (Lai et al. 2015). We obtained date of onset and place of onset of locally acquired and imported daily dengue cases in 2014 from Chinese Centre for Disease Control and Prevention. An imported case refers to a patient who had travelled to a dengue-affected foreign region and reported being bitten by mosquitoes within 15 days of the onset of illness; otherwise, a dengue case was regarded as a locally acquired case (Lai et al. 2015). In the present study, the study period of dengue cases was restricted to dengue peak months of July to November (Figure S1), contributing 99.8% of all cases recorded in 2014. The reason for this choice is because the monthly total number of dengue cases in those months (range: 249 to 22770 cases) exceeds the average monthly level (179 cases) in 2014. Also, the total number of dengue cases in July 2014 exceeds the average monthly level of 2017-2013 (249 cases versus 46 cases). Nevertheless, other study periods were also explored in later sensitivity analyses to test the spatial variability in the associations between weather conditions and dengue incidence.

Weather data on daily mean temperature and rainfall for the period 2013-2015 were collected from National Meteorological Information Centre (http://data.cma.cn/en). Weather data were available at 0.5°C × 0.5°C degrees grid spatial resolution, which covered the whole area of each city in Guangdong province. We averaged all values of temperature and rainfall within each city area, which were then used in later data analysis. To comprehensively assess the impact of weather conditions on dengue incidence, we considered two types of weather conditions including common weather conditions (i.e., one unit change in weather variables) and extreme weather conditions within the months of May to November allowing for potential delayed effects of weather conditions on dengue incidence (Xiao et al. 2018). The former was measured with average temperature (averaged daily temperature), average rainfall (averaged daily rainfall), and temperature variation (defined as the standard deviation of daily mean temperature) within the studied months in 2014. The latter included extremely high temperature and extremely high rainfall both measured as the number of days exceeding 95th percentile of their daily time-series distributions in 2013-2015.

We also obtained city-specific data on economic level, population density, Normalized Difference Vegetation Index (NDVI), and elevation in Guangdong in 2014. These variables were chosen because they have been previously reported to be strongly associated with dengue incidence (Qi et al. 2015; Zhu et al. 2018). There are also many other potential factors such as human movement and mosquito density that play a role in dengue transmission (Oidtman et al. 2019; Zhu et al. 2018), but such data were not available for our analysis. This study was approved by the University Human Research Ethics Committee of Queensland University of Technology (1800000058).

2.3. Data analysis

This study consisted of a two-stage data analyses. In the first stage, to examine the association between weather conditions and dengue incidence, we fitted a city-level spatial model because of reportedly high spatial correlation of dengue incidence across Guangdong province (Zhu et al. 2019b). Within study periods, the city-specific total number of dengue cases within July and November was the dependent variable, weather conditions within May to November were independent variables, and population size as an offset in the model. In line with our previous studies (Cheng et al. 2020a; Hu et al. 2015; Huang et al. 2017), we added in the model two additional area-specific effects, including spatially structured residual (to capture the spatial-correlation of dengue incidence) and spatially unstructured residual (to address the spatial variation in dengue incidence unexplained by terms included in the model). We applied a conditional autoregressive model (CAR) that is constructed as a function of its first-order neighbourhood to model the spatially structured residual; the spatially unstructured residual was modelled using exchangeability among all cities of Guangdong province (Cheng et al. 2020a; Huang et al. 2017). Both area-specific effects were assumed to follow Normal (0, $1/\sigma_v^2$), where $\log(1/\sigma_v^2) \sim$ logGamma (1, 0.0005). We chose this model given the lowest value of the deviance information criterion. The aim of this model was to estimate the overall association between weather conditions and dengue incidence for the whole Guangdong province, which can be described as Model 1:

$$y_i \sim Poisson\ (\rho_i E_i\ )$$

$$\log(\rho_i) = \alpha + \beta_1 \times \text{Average temperature}_i + \beta_2 \times \text{Temperature variation}_i + \beta_3 \times \text{Average rainfall}_i + \text{offset}\ (population_i) + \mu_i + \upsilon_i \quad (1)$$

Here, y_i is the observed total number of dengue cases in city i, with an assumption of Poisson distribution; E_i corresponded to expected dengue cases in city i; ρ_i represents the relative risk of dengue city i; α is the intercept; β_1, β_2, and β_3 are the coefficients for average temperature, temperature variation, average rainfall, which were used to derive the overall weather effect namely relative risk estimates via the equation $RR = \exp\ (\beta)$; offset $(population_i)$ refers to the population size of each city as an offset; μ_i and υ_i denote the spatially structured residual and spatially unstructured residual, respectively. In analysing extreme weather conditions, the items Average temperature and $Average$ rainfall were replaced by the number of days of extremely high temperature and rainfall.

Model 2 was developed to account for spatial variability in the effects of weather conditions. We modelled the city-specific associations with a random slope, which implies that the effects of weather conditions on dengue incidence are different for each city with an exchangeable structure (Blangiardo M 2015; Hondula and Barnett 2014). Cities with a positive slope and a 95% credible interval (CI) not including "0" were considered to have a statistically significant positive association, whereas a statistically significant negative association was noted for when a negative slope and its 95% CI did not include "0". This model took the form:

$$y_i \sim Poisson\ (\rho_i E_i\ )$$

$$\log(\rho_i) = \alpha + \beta_i \times weather\ conditions_i + \text{offset}\ (population_i) + \mu_i + \upsilon_i \quad (2)$$

where $weather\ conditions$ indicates the examined five weather variables (i.e., average temperature, average rainfall, temperature variation, number of days of extremely high temperature and rainfall) and β_i represents the coefficients in city i.

At this stage, regional characteristics including economic and demographic factors, imported cases, NDVI, and elevation were not included in the model. This is because there were strong correlations between regional characteristics and weather variables (the highest Spearman coefficients were 0.55 for Per Capital GRP, -0.63 for imported cases, -0.67 for NDVI and 0.54 for elevation). Meanwhile, the model without the inclusion of regional characteristics would allow us to further check if effects of weather conditions could be influenced by local characteristics. Similar methods have been used to examine spatially varied effects of environmental risk factors on human health (He et al. 2020; Hondula and Barnett 2014; Sera et al. 2019; Xiao et al. 2017). Following these studies, we did a univariate linear regression to explore potential modification effects of weather conditions by city characteristics.

In the second stage, we attempted to rank all cities from the most affected city to the least affected city by the overall effects of studied weather conditions. On the basis of risk estimates (RR) for each weather condition derived from first stage analyses, we calculated city-specific excessive risk based on the equation (3), which indicates the percentage increase in the risk of dengue associated with changes of either a rise or a drop in weather variables. We then summed the excessive risk estimates for all studied weather conditions (equation 4), and the area most vulnerable to the overall effects of weather conditions had the highest excessive risk and vice versa.

$ER_j = |(RR_j - 1) * 100|$ (3) where ER is the excessive risk for weather variable j;

$\text{TER} = \sum_{j=1}^{n} ER_j$ (4) where TER is the total excessive risk for common weather conditions (n=3), extreme weather conditions (n=2), and all studied weather conditions (n=5).

2.4. Sensitivity analysis

To check the robustness of our findings, we conducted several sensitivity analyses. First, we limited the study period of dengue cases to the dengue peak months in each city instead of peak months for the whole Guangdong province (Figure S2). Second, the measurement of various weather conditions was restricted to dengue peak months for the whole Guangdong province and in each city. Third, imported cases in each city were incorporated in spatial regression model to check if space-varied effects of weather conditions still existed. All data analyses were carried out in R software (version: 3.6.3) with packages "INLA" and "stats".

3. Results

3.1. Descriptive analysis of dengue cases and weather conditions

A total of 45,111 local dengue cases were recorded during the dengue peak months of May to November in Guangdong province in 2014. The geographical distributions of dengue count and incidence rate were shown in Figure 1. In general, Guangzhou and Foshan had the largest number of dengue cases (>1,000) (Figure 1A) and the highest incidence rate (>6 per 10000 people) (Figure 1B). Besides these, coastal cities such as Zhongshan and Zhuhai were also prone to dengue occurrence (Figure 1).

Figure 2 depicts the geographical distribution of five examined weather variables. Across 21 cities of Guangdong province, the average temperature ranged between 23.6°C (Chaozhou) and 27.2°C (Zhanjiang), temperature variation between 2.6°C (Zhanjiang) and 4.1°C (Shaoguan), rainfall between 4.0mm (Shaoguan) and 5.7mm (Shenzhen), number of days of extremely high temperature between 0 (Chaozhou, Jieyang, and Maoming) and 66 days (Foshan), and number of days of extremely high rainfall between 3 (Shaoguan and Yunfu) and 13 days (Guangzhou, Huizhou, and Dongguan). There is a trend that coastal cities have higher average temperature (Figure 2A), but lower temperature variation (Figure 2B). Cities in central Guangdong province tended to have higher rainfall (Figure 2C) and number of days of extremely high temperature and rainfall (Figure 2D-2E).

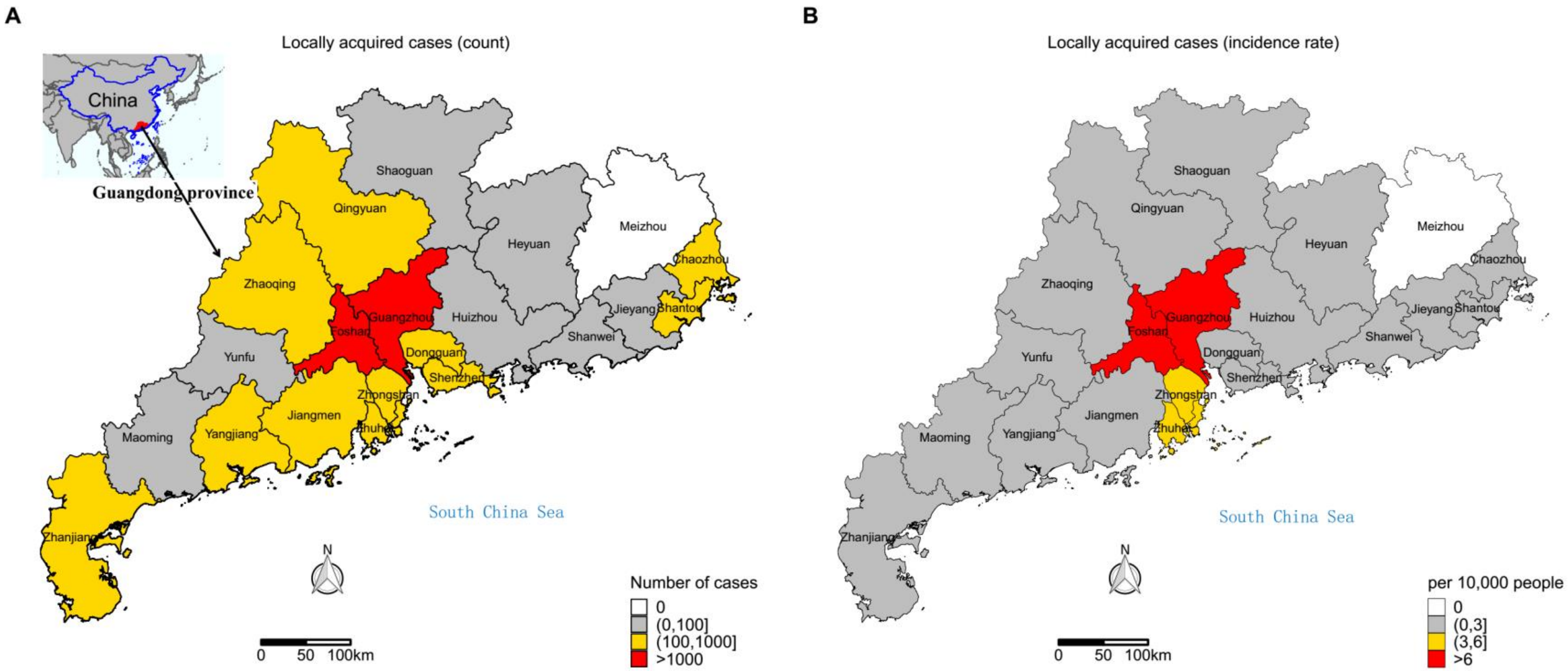

Figure 1: Geographical distribution of dengue counts and incidence rate in Guangdong province of China in 2014.

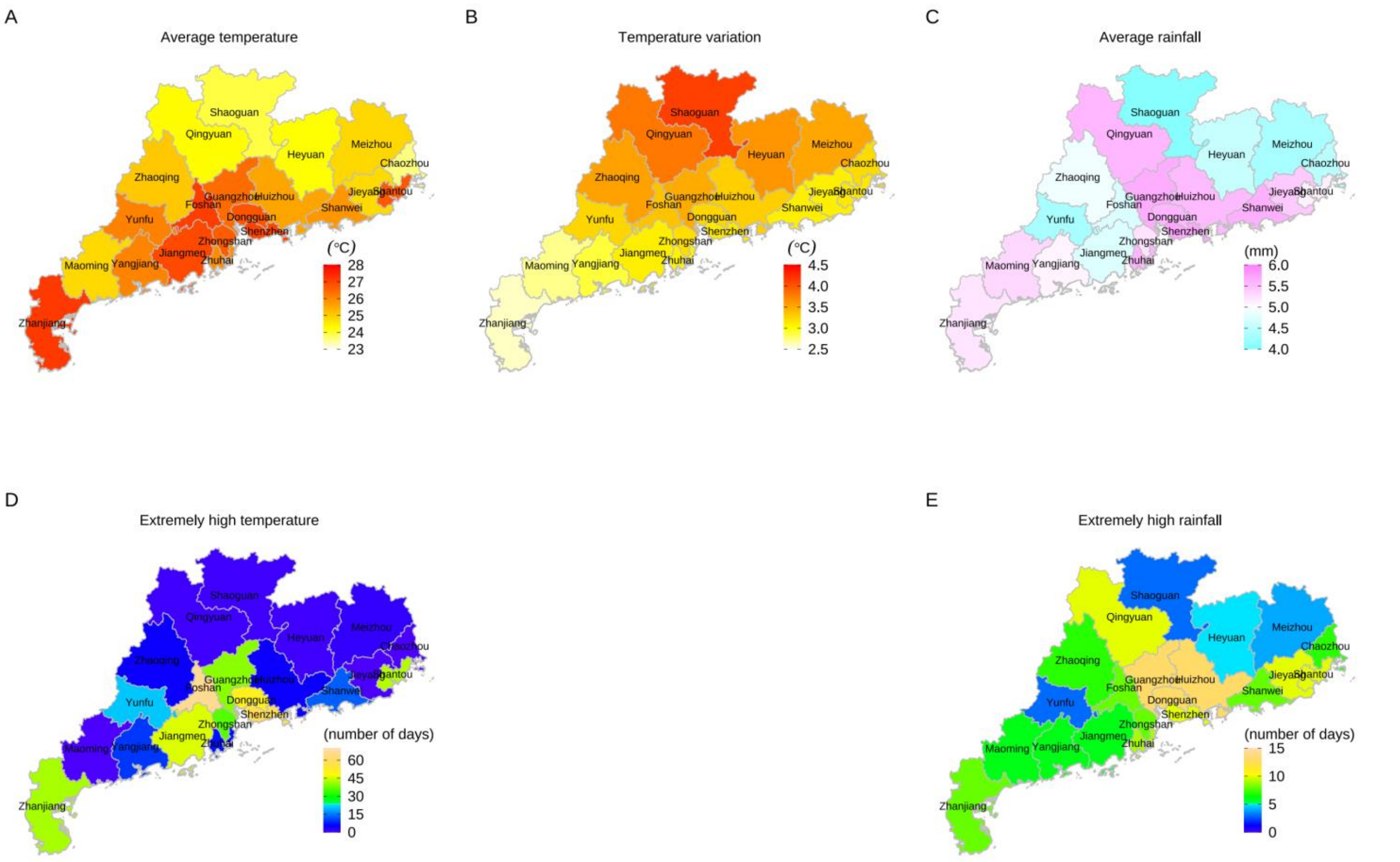

Figure 2: Geographical distribution of weather conditions in Guangdong province of China in 2014.

3.2. Association between weather conditions and dengue incidence

Figure 3 shows the overall associations between weather conditions and dengue incidence for Guangdong province as a whole. Average temperature, temperature variation, and average rainfall were positively associated with dengue incidence, but the associations were not statistically significant (Figure 3A). By contrast, there were statistically significant positive associations with extremely high temperature (RR:1.054, 95% CI: 1.016 to 1.094) and extremely high rainfall (RR: 1.505, 95% CI: 1.096 to 2.080) (Figure 3B).

Figure 4 presents the spatial variability in the associations between weather conditions and dengue incidence. We observed significant variability in the association with average temperature (Figure 4A); seven cities have a statistically positive association (RR range: 1.032 to 1.153) and five cities have a statistically negative association (RR range: 0.848 to 0.940). Association with temperature variation was also found to vary spatially (Figure 4B); seven cities have a statistically positive association (RR range: 1.257 to 2.739) and four cities have a statistically negative association (RR range: 0.315 to 0.593). Similarly, there were between-city variations in the association with average rainfall; seven cities have a statistically positive association (RR range: 1.237 to 1.974) and five cities have a statistically negative association (RR range: 0.373 to 0.835) (Figure 4C). After taking into account the impacts of average temperature, temperature variation, and average rainfall, high spatial variability in the risk of dengue occurrence was observed in the centre and east of Guangdong province, as indicated by spatially unstructured residuals (Figure S3).

We did not find evidence of spatial variability in the association with extremely high temperature (Figure 4D). However, the association with extremely high rainfall varied across cities (Figure 4E), with seven cities having statistically positive association (RR range: 1.237 to 1.418) and four cities having a statistically negative association (RR range: 0.411 to 0.938).

3.3. Ranking of dengue-affected areas vulnerable to weather conditions

Our model-derived ranking of dengue-affected areas vulnerable to weather conditions is presented in Figure 5. Guangzhou, Chaozhou, and Foshan were found to be the most vulnerable to weather conditions, regardless of the effects from common or extreme weather conditions (Figures 5A-5C). Central and coastal cities such as Zhongshan, Zhuhai, Qingyuan, and Yangjiang also ranked quite high in their vulnerability to weather conditions. By contrast, there were also some cities that appeared to be marginally or negligibly affected by weather conditions including Meizhou, Yunfu, Shangwei, Huizhou, and Zhangjiang.

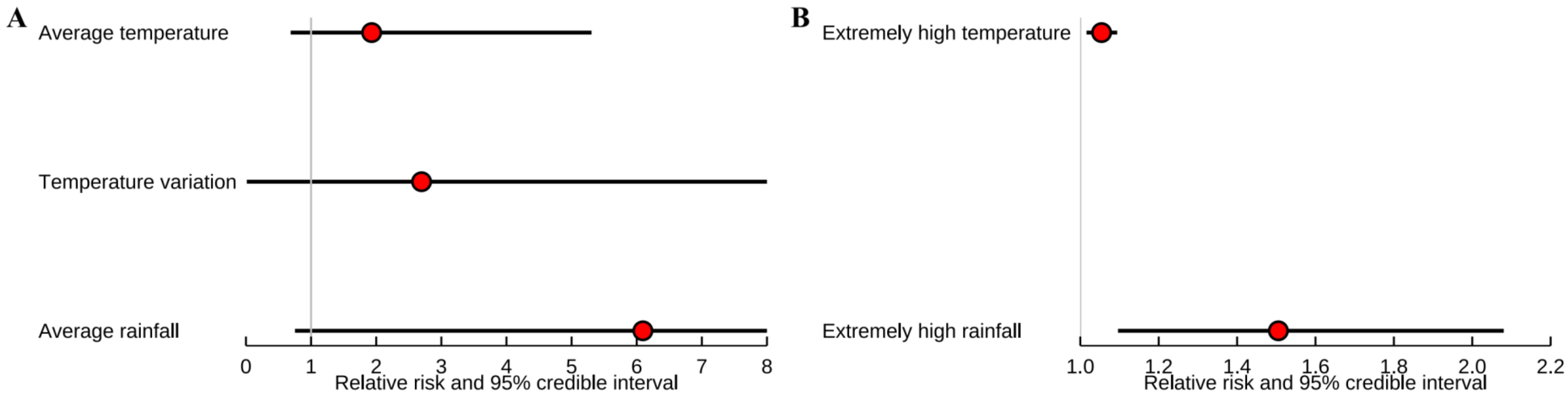

Figure 3: Estimated overall associations of dengue incidence with weather conditions in Guangdong province as a whole.

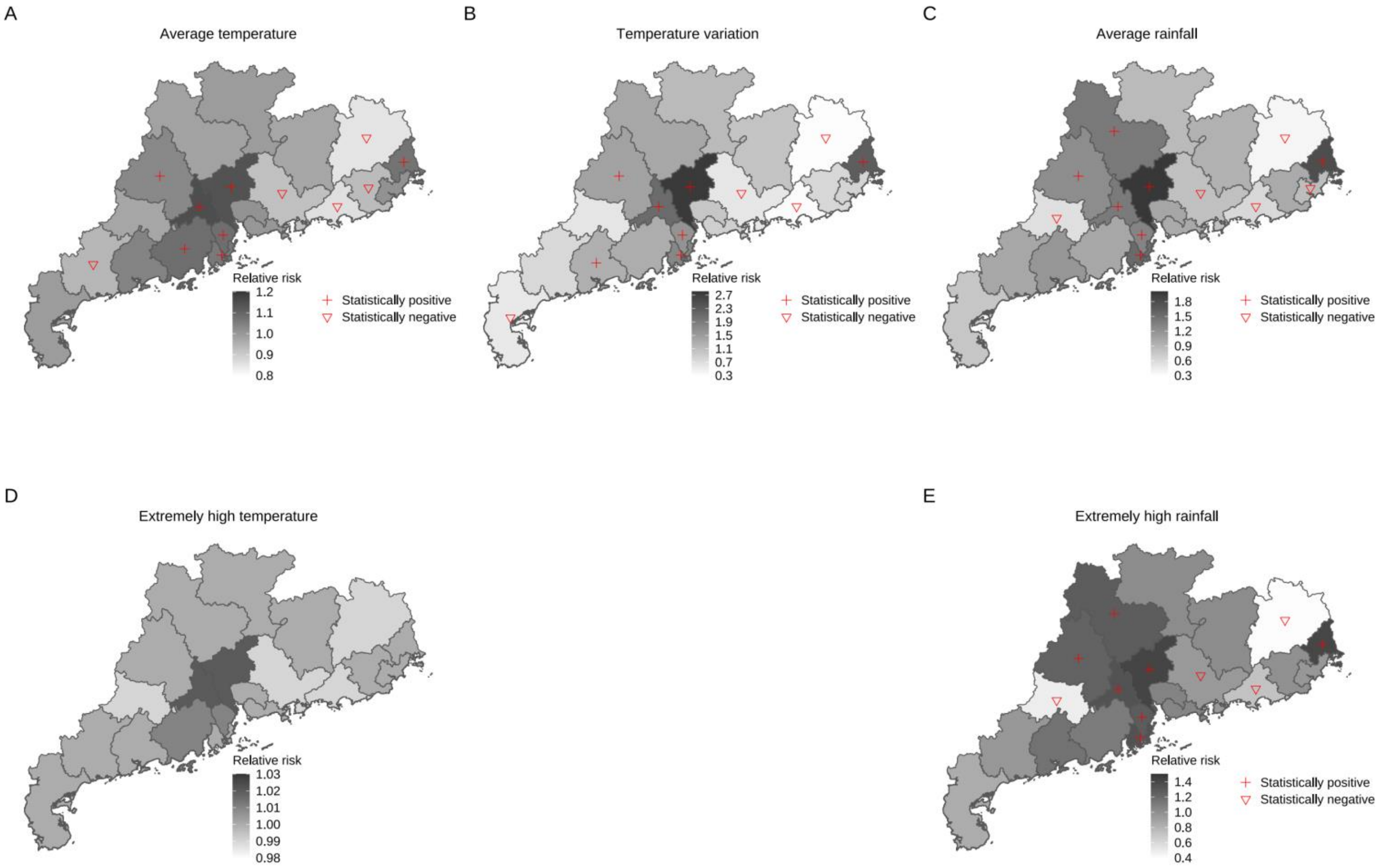

Figure 4: Estimated associations of dengue incidence with weather conditions for each city in Guangdong province.

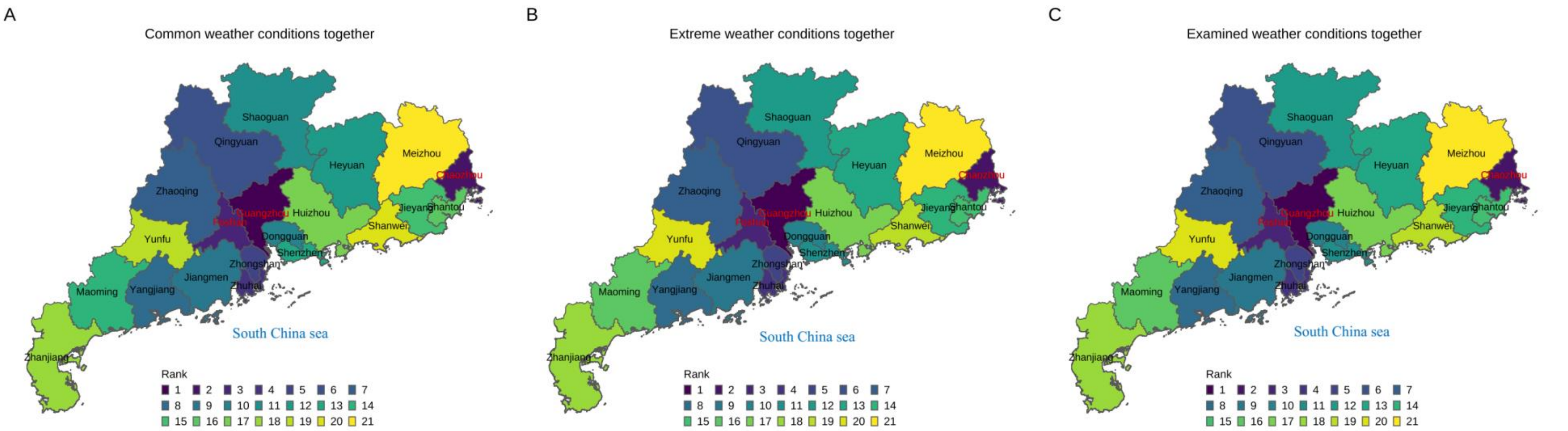

Figure 5: Ranking of cities vulnerable to effects of weather conditions on dengue incidence. Rank 1 represent the most vulnerable city and rank 21 represents the least vulnerable city.

3.4. Modification effects of city characteristics

We then explored if the observed spatial variability in the association between weather conditions and dengue incidence could be partly explained by city characteristics (Figure 6). Of five variables tested, four variables (i.e., NDVI, elevation, Per Capital GRP, imported cases – but, not population density) were statistically significantly associated with the spatial variability in weather-related dengue incidence. We estimated that one unit decrease in NDVI index was associated with 0.35% and 0.04% decrease in the slope for the association of dengue with average temperature and extremely high temperature (Figure 6A). Similarly, there was a negative association between elevation and effects of weather conditions (Figure 6B), with slope decreases of <0.01% for the average temperature-dengue association, 0.01% for the average rainfall-dengue association, <0.01% for the extremely high rainfall-dengue association. By contrast, Per Capital GRP and imported cases were statistically positive associated with the effects of weather conditions (Figure 6C-6D). Specifically, slopes for the associations of dengue with all examined weather conditions increased by <0.01% associated with 1 unit increase in Per Capital GRP. The slope for the association between extremely high temperature and dengue incidence rose by <0.01% per 1 imported case increase.

3.5. Results of sensitivity analyses

Our sensitivity analyses also revealed evidence of spatial variability in the association of dengue incidence for all examined weather variables, except for extremely high temperature (Figures S4-S6). Meanwhile, similar rankings of dengue-affected cities' vulnerability to weather conditions were also noted (Figures S7-S9).

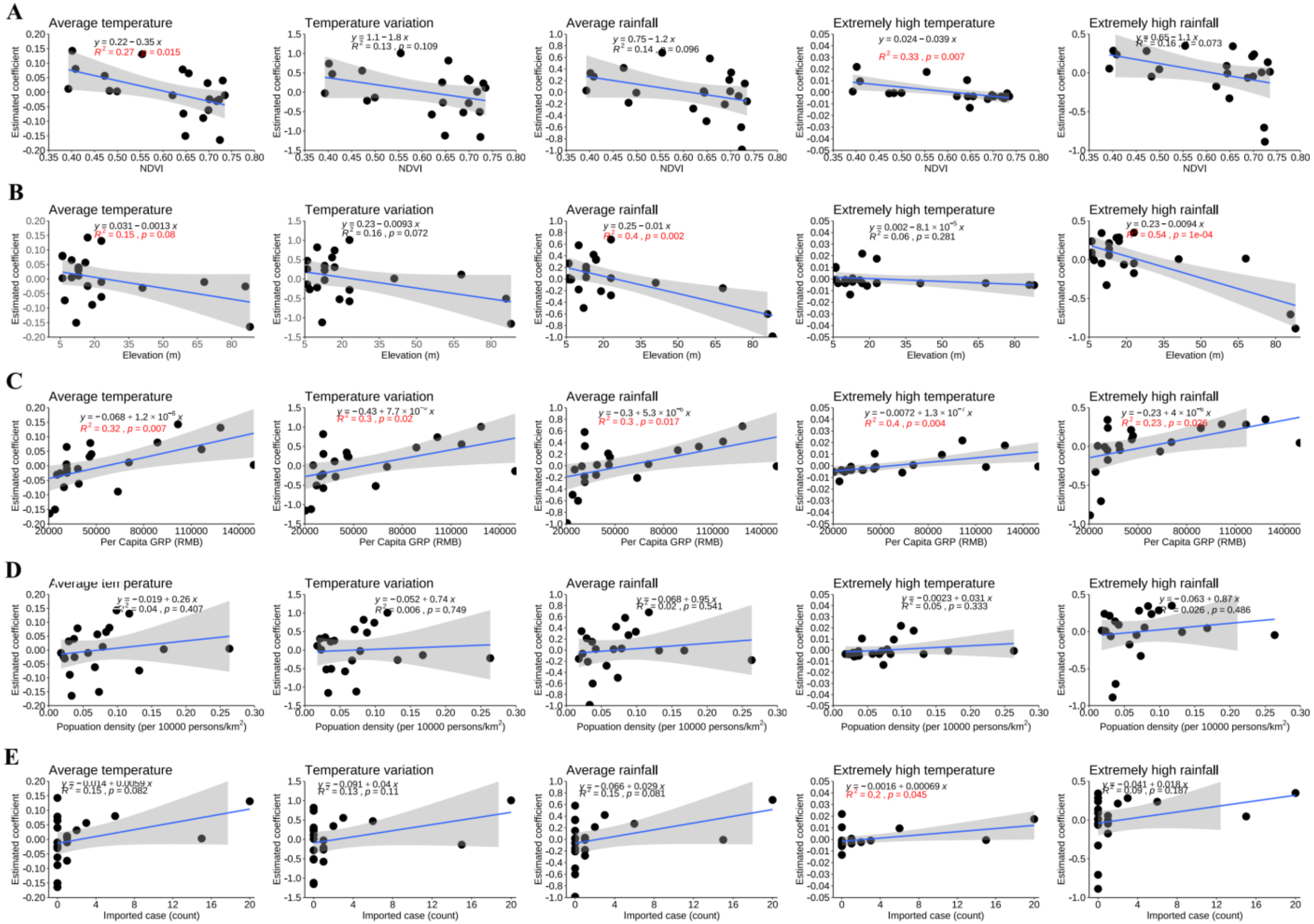

Figure 6: Modification effects of city characteristics on the association between weather condition and dengue incidence. y-axis is the estimated city-specific slopes of associations between weather conditions and dengue incidence; x-axis is the city characteristics; a negative x-y-axis relationship indicates smaller slope associated with increases in city characteristics and vice versa.

4. Discussion

The most serious dengue outbreak on record in Guangdong province of China in 2014 resulted in over 40,000 cases but the underlying reasons for this dengue outbreak remain largely unknown. This study sought to provide an answer to this puzzle from the perspective of weather effects, which are critical for dengue virus and the vectors' (mosquitoes) population dynamics (Abdelrazec and Gumel 2017; Mordecai et al. 2017; Ndiaye et al. 2006; Xu et al. 2017; Zhu et al. 2019a). By examining the spatially heterogeneous effects of local weather conditions, our data analyses yielded four major findings: (1) Extreme weather conditions including extremely high temperature and rainfall were associated with higher dengue incidence for Guangdong province as a whole; (2) Associations of dengue incidence with weather conditions (i.e., average temperature, temperature variation, average rainfall, and extremely high rainfall) varied spatially between the cities of Guangdong province, with both statistically positive and negative associations observed in different cities; (3) Dengue-affected cities with relatively higher vulnerability to weather conditions are the central and coastal cities such as Guangzhou, Chaozhou, Foshan, Zhuhai, and Qingyuan; (4) Cities with higher economic level, lower green space coverage and lower elevation appeared to be at higher risk of weather-related vulnerability to dengue incidence. These findings emphasise continued investigation into the effects of weather extremes and help policymakers target areas particularly vulnerable to weather conditions that promote dengue occurrence. In addition, the method presented here could be applied to other locations with health data available at finer spatial resolution.

Prior research has found that typical weather conditions such as rises or drops in temperature, relative humidity, rainfall have impacts on dengue transmission (Abdelrazec and Gumel 2017; Mordecai et al. 2017; Ndiaye et al. 2006), as well as dengue incidence (Fan et al. 2014; Li et al. 2018; Li et al. 2016; Xiang et al. 2017; Xiao et al. 2018; Xu et al. 2017). As an important supplement to this literature, our analyses further revealed that extreme weather conditions, including extremely high temperature and rainfall, could act as an important driver or predictor of dengue occurrence. There is evidence in Asia suggesting hot weather can force delayed mosquito outbreaks (Chaves et al. 2014), which could possibly contribute to later dengue outbreaks. For example, our recent study found prolonged hot weather (i.e., heatwaves) precipitated dengue outbreaks (Cheng et al. 2020b). Likewise, outbreaks of some other vector-borne diseases such as West Nile fever have been observed after heatwaves (Paz 2006; Semenza and Menne 2009). Besides, spatial variability in association with extremely high temperature was not observed, which possibly suggests that all cities of Guangdong province could be affected by extremely high temperature. In the context of global warming, there will be more frequent and more intensive weather extremes such as heatwaves and rainfall (IPCC ; Meehl and Tebaldi 2004). Therefore, accounting for the role of extreme weather conditions would be beneficial to improve state-of-the-art, region-specific early warning systems for preventing dengue outbreaks.

Our finding that the association of dengue incidence with weather variables varied geographically adds evidence to the existing literature in China documenting an overall positive association with temperature and rainfall within a city or a larger geographical area as a whole (Fan et al. 2014; Xiao et al. 2018; Xu et al. 2017). However, positive statistically significant associations with weather variables were found only in some cities of Guangdong province such as Guangzhou, Foshan, Zhongshan and Zhuhai. Moreover, these cities are mainly located in the Pearl River Delta area, with many characteristics that favour dengue transmission such as higher population density, higher numbers of imported dengue cases, higher values in average temperature, average rainfall, and extremely high temperature. This finding partly explains why the Pearl River Delta area is the primary cluster of dengue cases (or higher risk of dengue occurrence), as documented in previous studies (Fan et al. 2014; Liu et al. 2018; Zhu et al. 2019b).

Importantly, we also observed a negative statistically significant association of dengue incidence with weather conditions in some cities of Guangdong province. This is probably a reflection of the negative impact of other factors such as low human mobility, less frequent domestic and international trade and travel on dengue incidence (which reduce the likelihood of dengue transmission) that outweighs the positive impact of suitable weather conditions (which favour of dengue transmission). Another possible reason is that these cities had lower mosquito population densities. These hypotheses need to be tested in future analyses.

Consistent with available reports on the impact of temperature variation on dengue incidence (Liu et al. 2017; Sharmin et al. 2015), we observed both positive and negative statistically significant associations with temperature variation. Positive statistically significant associations with temperature variation were evident in seven cities of Guangdong province (Figure 4B); these cities are almost the same with cities having positive associations with temperature and rainfall (Figure 4A, 4C, 4E), probably mirroring the effects of these two weather variables. However, four cities of in Guangdong province saw a negative statistically significant association. This seemingly paradoxical result may suggest the interplay (synergistic and antagonistic effects) between temperature variation and other factors (e.g., mean temperature and rainfall) in influencing dengue transmission (Carrington et al. 2013; Lambrechts et al. 2011). Consequently, negative and positive impacts of temperature variation on dengue incidence could present across regions. Therefore, additional consideration of the influence of temperature variation would assist in improving mosquito and dengue surveillance systems for a region.

In addition to cities in Pearl River Delta area, other cities in central and coastal cities of Guangdong province were also found to be particularly sensitive to weather conditions, including common and extreme weather conditions (Figure 5). The key areas for developing dengue prevention and control measures should not be confined to the widely investigated Pearl River Delta area (e.g., Guangzhou and Foshan). Other cities such as Chaozhou and Zhuhai also require an early detection and warning system in response to potential dengue outbreaks. This finding can help inform dengue mitigation programs such as mosquito control measures, and optimise the allocation of limited resources to carry out targeted and focused interventions.

Population vulnerability to dengue infection within a region requires the presence of multiple factors, not only suitable weather conditions but also many other factors involving vector, socioeconomic, demographic, behavioural, environmental characteristics and health systems. These factors are pivotal for determining the changes in population exposure and susceptibility to dengue infection. Our findings suggested that increases in the NDVI and elevation weaken the association between weather variables and dengue incidence, but an opposite modification effect was shown for economic level and imported cases. Previous reports in China revealed a trend of lower dengue incidence in areas with higher vegetation greenness and elevation (Huang et al. 2018; Liu et al. 2018). In Guangdong province, cities with higher NDVI and elevation tend to have lower average temperature and larger temperature variation that have negative impacts on dengue transmission (Lambrechts et al. 2011; Mordecai et al. 2017). By contrast, higher economic level is highly associated with higher degree of urbanization (e.g., more crowded environment, higher human mobility, heat island effect, complex drainage network, and more frequent travel with other regions) that may increase the likelihood of dengue infection and amplify the effects of weather conditions on dengue incidence (Li et al. 2018; Wu et al. 2009). The number of imported cases has been reported as an important predictor of locally acquired cases and a trigger of local dengue outbreak in China (Jing et al. 2018; Peng et al. 2012; Wang et al. 2020). Therefore, the presence of more imported cases and suitable weather conditions could synergistically affect dengue incidence within a region (Jing et al. 2018). To improve the adaptive capacity of a community, it is necessary to have a better city development plan and effective surveillance and management of dengue cases imported from foreign areas.

To date, it still remains an unanswered question about why an unprecedented outbreak of dengue fever occurred in 2014 in Guangzhou, China. Nevertheless, researchers in past years have been conducting studies to understand the driving force for this record-high dengue outbreak. Existing evidence points to a number of factors contributing to the 2014 dengue outbreak. For example, the imported cases, climate variables (e.g., temperature and rainfall), human movement, socioeconomic and demographic levels and delayed mosquito control have been suggested to drive the dengue outbreak in 2014 (Li et al. 2016; Zhu et al. 2018; Ren et al. 2017). As a climate-sensitive disease, dengue fever has been increasingly reported to be affected by weather conditions including temperature and rainfall (Li et al. 2018; Xu et al. 2017). The present study found extreme weather conditions including extremely high temperature and rainfall were associated with higher dengue incidence, echoing to findings of previous studies (Cheng et al. 2017; Cheng et al. 2020b; Wu et al. 2018). Some researchers also found the dengue incidence could be well predicted using weather variables (Sang et al. 2015; Xu et al. 2017). It is reasonable to believe that weather conditions make a partial contribution to the outbreak of dengue in 2014. However, a comparison with other non-weather factors should be made in future research to understand the importance of different determinants of dengue occurrence.

Our findings may have some implications for the prevention of dengue outbreaks. There are increasing studies in support of an association of dengue occurrence or outbreaks with weather extremes such as extremely high rainfall and heatwaves (Wu et al. 2018; Cheng et al. 2020b). In the present study, we also found evidence that extremely high temperature and rainfall increased the risk of dengue incidence. This finding implies that extreme weather events is a risk factor of dengue occurrence and incorporating such information into the climate-based dengue projection model would improve the prediction accuracy, especially in the context of climate change that is projected to lead to more frequent and intensive weather extremes (IPCC; Meehl and Tebaldi 2004). Besides, we also found spatial variation in city's vulnerability to weather conditions. Among all cities of Guangdong province, some central and coastal cities such as Guangzhou, Chaozhou, Foshan, Zhongshan, Zhuhai, Qingyuan, and Yangjiang were most vulnerable. So, weather conditions in these cities should be closely monitored in early warning system and used in conjunction with dengue control measures in order to minimize weather effects on local dengue incidence.

It should be acknowledged that this study has several limitations. First, we performed spatial regression analyses based on dengue and weather data aggregated at a relatively coarse spatial scale (i.e., at city level) and temporal level (e.g., within several months). Because it is difficult to determine the best spatial and temporal resolution for spatial analysis, our findings need to be verified using data at finer spatial scale (e.g., county and district) and temporal level (e.g., monthly and weekly level). Second, due to the nature of ecological study design, our findings cannot prove the causal association between examined weather variables and dengue incidence, which merits further mechanistic investigation. Third, this study explored potential reasons for spatially heterogeneous dengue incidence only from the influence of weather. Many other factors such as mosquito density, mosquito control measures, and human mobility, believed to play a key role in dengue transmission, are likely to contribute to spatial variability in dengue incidence. Fourth, this study only investigated the 2014 dengue outbreak in Guangdong province of China. It would therefore be useful to conduct a similar analysis in other regions to assess the generalizability of the spatial heterogeneities identified in this study. Fifth, due to the issue of data availability, we were unable to consider the influence of mosquito dynamics in fitting the association of dengue incidence with weather conditions. In addition, dengue control measures were not incorporated into the regression model because such data for each city was not available for the present study. Because dengue control measures such as larval breeding site destruction, killing adult mosquitoes, public health education and community involvement have been confirmed to be effective in reducing the number of dengue cases (Lin et al. 2016), regression models would return more precise results of the effects of weather conditions on dengue incidence once these additional factors were included.

5. Conclusions

In conclusion, this study identifies that weather conditions appear to have played an important role in shaping the dengue outbreak in Guangdong province of China in 2014, with spatially varied effects of weather on dengue incidence. Dengue mitigation measures should target central and coastal areas such as Guangzhou, Chaozhou, and Foshan as these are particularly vulnerable to weather conditions. The importance of accounting for weather extremes is also demonstrated.

Acknowledgments: The authors would like to thank China Centre for Disease Control and Prevention and National Meteorological Information Center for providing data set for this study.

Conflict of interest: The authors declare no conflict of interest.

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