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

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

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32 **Abstract**

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

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

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

46 **Results:** We found a positive association of dengue incidence with average temperature in seven cities
47 (relative risk (RR) range: 1.032 to 1.153), a positive association with average rainfall in seven cities (RR
48 range: 1.237 to 1.974), and a negative association with temperature variation in four cities (RR range:
49 0.315 to 0.593). There was an overall positive association of dengue incidence with extremely high
50 temperature (RR:1.054, 95% credible interval (CI): 1.016 to 1.094), without evidence of variation across
51 cities, and an overall positive association of dengue with extremely high rainfall (RR:1.505, 95% CI:
52 1.096 to 2.080), with seven regions having stronger associations (RR range: 1.237 to 1.418). Greater
53 effects of weather conditions appeared to occur in cities with higher economic level, lower green space
54 coverage and lower elevation.

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

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

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67 **Funding**

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69 (project grant: APP 1138622).

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96 **1. Introduction**

97 Dengue is a viral infection transmitted by female *Aedes* mosquitoes (WHO). Dengue virus is a
98 mosquito-borne and single positive-stranded RNA virus consisting of four serotypes (DENV 1 to 4) that
99 are members of the genus *Flavivirus* in the family *Flaviviridae* (Simmons et al. 2012). Annually, there
100 are an estimated 100-400 million dengue infections worldwide and about half of the world's population
101 is now at risk of infection (Bhatt et al. 2013; WHO). In the last decade, dengue outbreaks have frequently
102 occurred in the Asia-Pacific region in tropical and subtropical climates such as the Philippines,
103 Bangladesh, Vietnam and China (Bravo et al. 2014; Cheng et al. 2020b; Guo et al. 2017; Mone et al.
104 2019; Xu et al. 2017). Dengue outbreaks often led to a large number of cases, imposing great stress on
105 local health systems and causing substantial economic burden (Shepard et al. 2016). Without effective
106 prevention measures, dengue-related health and economic burden is expected to continue to increase in
107 the context of global warming (Colón-González et al. 2018; Hales et al. 2002).

108 Dengue transmission is sensitive to environmental change. For instance, climatic factors such as
109 temperature and rainfall can moderate many aspects of the biology of dengue transmission such as
110 mosquito population dynamics and biting rate (Abdelrazec and Gumel 2017; Mordecai et al. 2017;
111 Ndiaye et al. 2006; Xu et al. 2017; Zhu et al. 2019a). Associations between weather conditions and
112 dengue incidence have been widely reported in previous studies, suggesting that rises in temperature,
113 relative humidity, and rainfall are associated with increased dengue incidence (Li et al. 2018; Wu et al.
114 2018; Xu et al. 2017). Studies have also reported potential linkage of weather anomalies such as El Niño
115 events, extremely hot days, and floods with dengue incidence (Cheng et al. 2020b; Ferreira 2014; Li et
116 al. 2018). As climate change progresses, there will be more frequent and intensive weather extremes such
117 as heatwaves, making it an urgent need to investigate the effects of extreme weather conditions on dengue
118 incidence in many dengue-affected regions including China (Cheng et al. 2020b; Li et al. 2018).

119 Historically, the first dengue outbreak with serious consequences in China was in 1978, which
120 occurred in Guangdong province, with 22,122 cases (16 fatalities) reported (Wu et al. 2010). Since then,
121 Guangdong province and other regions of China have frequently suffered dengue epidemics or outbreaks
122 and recorded a large number of cases almost every year. Guangdong province has become the epicentre
123 of dengue outbreaks in China, accounting for most dengue cases on the mainland between 1990 and 2017
124 (Lai et al. 2015; Liu et al. 2018; Wu et al. 2010). In 2014, Guangdong province experienced its worst
125 dengue outbreak, recording more than 40,000 dengue cases and exceeding in a single year the cumulative
126 cases from 1990 to 2013 (Lai et al. 2015; Li et al. 2016). Potential reasons behind this unprecedented
127 outbreak remain unclear. Available literature has revealed many key determinants of the dengue outbreak
128 in 2014, such as socioeconomic and demographic factors, imported cases, urbanization, as well as local
129 weather conditions (Li et al. 2016; Oidtman et al. 2019; Ren et al. 2017; Wu et al. 2018; Xu et al. 2017).
130 However, the association between weather conditions and dengue incidence in China have been mostly
131 examined through various statistical analyses restricted to a whole study area (e.g., a city or a province
132 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
133 al. 2017). In practice, the effects of weather conditions are likely to vary across regions because regional

134 differences such as sociodemographic factors, imported cases and the implementation of mosquito
135 control measures could independently affect and interact with local weather conditions to affect dengue
136 incidence (Cheng et al. 2017; Zhu et al. 2018). These interactions will consequently lead to a spatially
137 heterogeneous response of dengue transmission capacity to weather conditions (Xu et al. 2019).
138 Therefore, a better understanding of spatial variability in the impacts of weather conditions on dengue
139 incidence would assist in developing an early warning system for dengue-affected areas that are
140 particularly vulnerable to permissive weather conditions. Furthermore, although associations between
141 weather variables and dengue incidence have been reported in many previous studies, evidence in China
142 is still lacking concerning the effects of extreme weather conditions such as extremes of temperature and
143 rainfall (Li et al. 2018). Abnormally high rainfall and high temperature are thought to have contributed
144 to the Guangdong dengue outbreak in 2014 (Li et al. 2016; Shen et al. 2015), but this is yet to be tested.

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

151 **2. Methods**

152 **2.1. Study setting**

153 This study was conducted in Guangdong, the largest province in southern China, with 88.7 million
154 people residing in 21 cities (population density range: 179 to 2634 persons per km²) in 2014
155 (<http://tongji.cnki.net/kns55/navi/YearBook.aspx?id=N2016030128&floor=1>). Guangdong features a
156 subtropical climate with hot and humid summer, mild and dry winter, and abundant rainfall, providing
157 the ideal climate for the development and population abundance of *Aedes* mosquitos (Guo et al. 2014;
158 Lai et al. 2015; Xiao et al. 2016). Guangdong is also an economic, cultural and transport centre in China,
159 as well as a hub for international travel and trade, in particular with the Asia-Pacific countries where
160 dengue is endemic (Guo et al. 2014; Ooi 2015), and is therefore important in driving both the import and
161 export of infected cases.

162 **2.2. Data collection**

163 Since 1989, dengue has been a statutorily notifiable infectious disease in China. All dengue cases
164 were diagnosed according to the unified diagnostic criteria issued by the Chinese Ministry of Health (Lai
165 et al. 2015). We obtained date of onset and place of onset of locally acquired and imported daily dengue
166 cases in 2014 from Chinese Centre for Disease Control and Prevention. An imported case refers to a
167 patient who had travelled to a dengue-affected foreign region and reported being bitten by mosquitoes
168 within 15 days of the onset of illness; otherwise, a dengue case was regarded as a locally acquired case
169 (Lai et al. 2015). In the present study, the study period of dengue cases was restricted to dengue peak
170 months of July to November (Figure S1), contributing 99.8% of all cases recorded in 2014. The reason

171 for this choice is because the monthly total number of dengue cases in those months (range: 249 to 22770
172 cases) exceeds the average monthly level (179 cases) in 2014. Also, the total number of dengue cases in
173 July 2014 exceeds the average monthly level of 2017-2013 (249 cases versus 46 cases). Nevertheless,
174 other study periods were also explored in later sensitivity analyses to test the spatial variability in the
175 associations between weather conditions and dengue incidence.

176 Weather data on daily mean temperature and rainfall for the period 2013-2015 were collected from
177 National Meteorological Information Centre (<http://data.cma.cn/en>). Weather data were available at
178 $0.5^{\circ}\text{C} \times 0.5^{\circ}\text{C}$ degrees grid spatial resolution, which covered the whole area of each city in Guangdong
179 province. We averaged all values of temperature and rainfall within each city area, which were then used
180 in later data analysis. To comprehensively assess the impact of weather conditions on dengue incidence,
181 we considered two types of weather conditions including common weather conditions (i.e., one unit
182 change in weather variables) and extreme weather conditions within the months of May to November
183 allowing for potential delayed effects of weather conditions on dengue incidence (Xiao et al. 2018). The
184 former was measured with average temperature (averaged daily temperature), average rainfall (averaged
185 daily rainfall), and temperature variation (defined as the standard deviation of daily mean temperature)
186 within the studied months in 2014. The latter included extremely high temperature and extremely high
187 rainfall both measured as the number of days exceeding 95th percentile of their daily time-series
188 distributions in 2013-2015.

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

196 **2.3. Data analysis**

197 This study consisted of a two-stage data analyses. In the first stage, to examine the association
198 between weather conditions and dengue incidence, we fitted a city-level spatial model because of
199 reportedly high spatial correlation of dengue incidence across Guangdong province (Zhu et al. 2019b).
200 Within study periods, the city-specific total number of dengue cases within July and November was the
201 dependent variable, weather conditions within May to November were independent variables, and
202 population size as an offset in the model. In line with our previous studies (Cheng et al. 2020a; Hu et al.
203 2015; Huang et al. 2017), we added in the model two additional area-specific effects, including spatially
204 structured residual (to capture the spatial-correlation of dengue incidence) and spatially unstructured
205 residual (to address the spatial variation in dengue incidence unexplained by terms included in the model).
206 We applied a conditional autoregressive model (CAR) that is constructed as a function of its first-order
207 neighbourhood to model the spatially structured residual; the spatially unstructured residual was
208 modelled using exchangeability among all cities of Guangdong province (Cheng et al. 2020a; Huang et

209 [al. 2017](#)). Both area-specific effects were assumed to follow Normal $(0, 1/\sigma_v^2)$, where $\log(1/\sigma_v^2) \sim$
 210 $\log\text{Gamma}(1, 0.0005)$. We chose this model given the lowest value of the deviance information criterion.
 211 The aim of this model was to estimate the overall association between weather conditions and dengue
 212 incidence for the whole Guangdong province, which can be described as Model 1:

$$213 \quad y_i \sim \text{Poisson}(\rho_i E_i)$$

$$214 \quad \log(\rho_i) = \alpha + \beta_1 \times \text{Average temperature}_i + \beta_2 \times \text{Temperature variation}_i + \beta_3 \times \\ 215 \quad \text{Average rainfall}_i + \text{offset}(\text{population}_i) + \mu_i + \nu_i \quad (1)$$

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

224 Model 2 was developed to account for spatial variability in the effects of weather conditions. We
 225 modelled the city-specific associations with a random slope, which implies that the effects of weather
 226 conditions on dengue incidence are different for each city with an exchangeable structure ([Blangiardo M](#)
 227 [2015](#); [Hondula and Barnett 2014](#)). Cities with a positive slope and a 95% credible interval (CI) not
 228 including "0" were considered to have a statistically significant positive association, whereas a
 229 statistically significant negative association was noted for when a negative slope and its 95% CI did not
 230 include "0". This model took the form:

$$231 \quad y_i \sim \text{Poisson}(\rho_i E_i)$$

$$232 \quad \log(\rho_i) = \alpha + \beta_i \times \text{weather conditions}_i + \text{offset}(\text{population}_i) + \mu_i + \nu_i \quad (2)$$

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

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

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

252 $ER_j = |(RR_j - 1) * 100|$ (3) where ER is the excessive risk for weather variable j ;

253 $TER = \sum_{j=1}^n ER_j$ (4) where TER is the total excessive risk for common weather conditions ($n=3$),
254 extreme weather conditions ($n=2$), and all studied weather conditions ($n=5$).

255 2.4. Sensitivity analysis

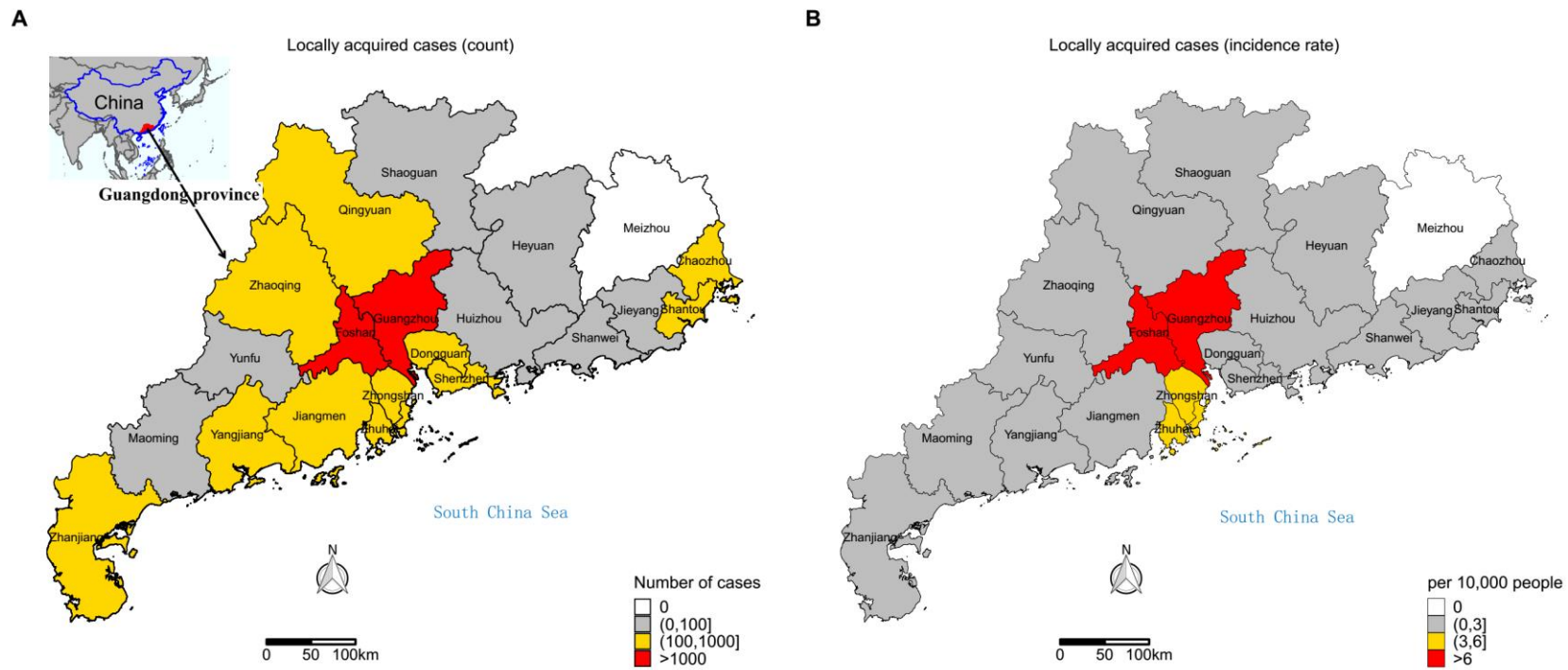
256 To check the robustness of our findings, we conducted several sensitivity analyses. First, we limited
257 the study period of dengue cases to the dengue peak months in each city instead of peak months for the
258 whole Guangdong province (Figure S2). Second, the measurement of various weather conditions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

263 3. Results

264 3.1. Descriptive analysis of dengue cases and weather conditions

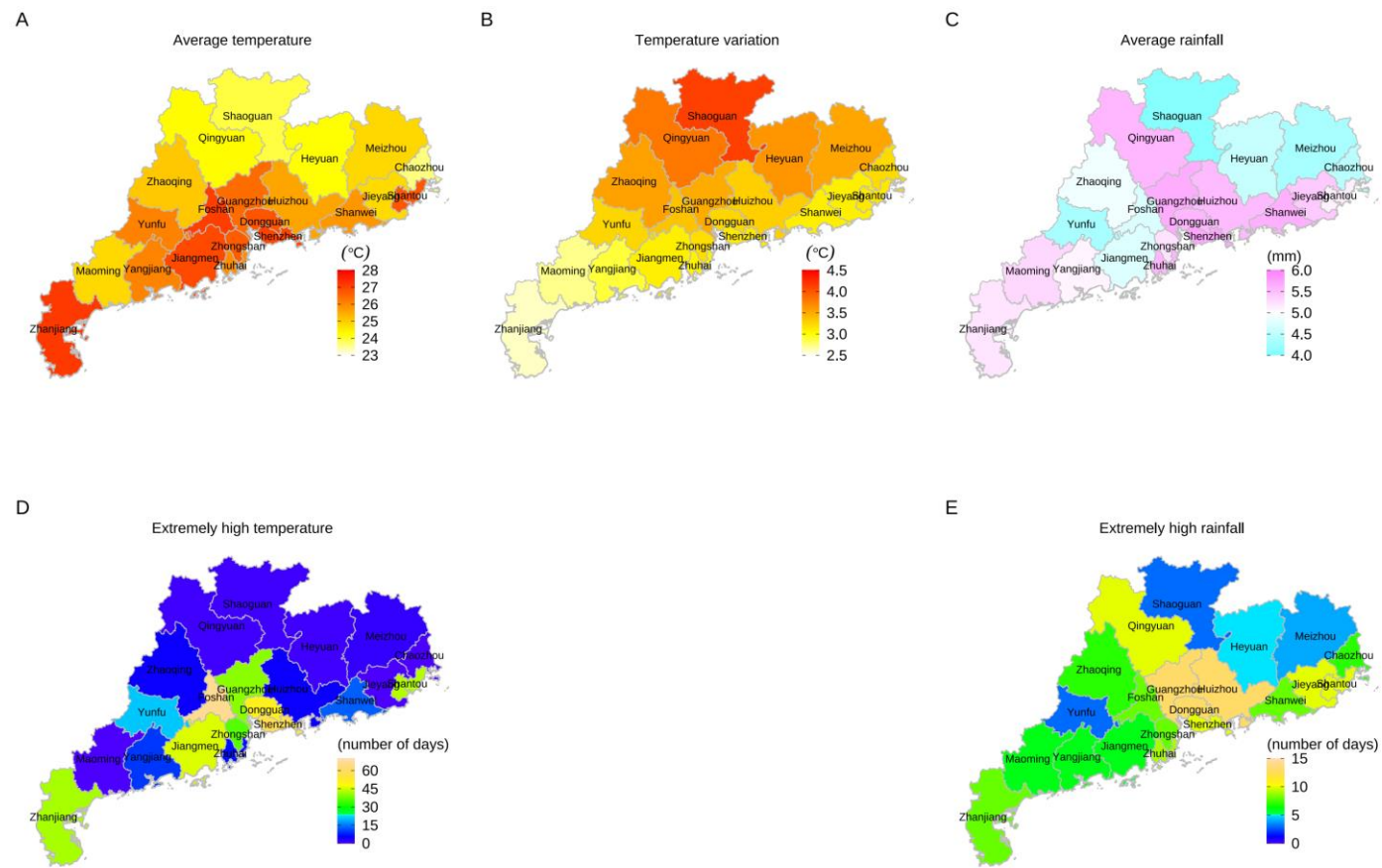
265 A total of 45,111 local dengue cases were recorded during the dengue peak months of May to
266 November in Guangdong province in 2014. The geographical distributions of dengue count and
267 incidence rate were shown in Figure 1. In general, Guangzhou and Foshan had the largest number of
268 dengue cases (>1,000) (Figure 1A) and the highest incidence rate (>6 per 10000 people) (Figure 1B).
269 Besides these, coastal cities such as Zhongshan and Zhuhai were also prone to dengue occurrence (Figure
270 1).

271 Figure 2 depicts the geographical distribution of five examined weather variables. Across 21 cities
272 of Guangdong province, the average temperature ranged between 23.6°C (Chaozhou) and 27.2°C
273 (Zhanjiang), temperature variation between 2.6°C (Zhanjiang) and 4.1°C (Shaoguan), rainfall between
274 4.0mm (Shaoguan) and 5.7mm (Shenzhen), number of days of extremely high temperature between 0
275 (Chaozhou, Jieyang, and Maoming) and 66 days (Foshan), and number of days of extremely high rainfall
276 between 3 (Shaoguan and Yunfu) and 13 days (Guangzhou, Huizhou, and Dongguan). There is a trend
277 that coastal cities have higher average temperature (Figure 2A), but lower temperature variation (Figure
278 2B). Cities in central Guangdong province tended to have higher rainfall (Figure 2C) and number of days
279 of extremely high temperature and rainfall (Figure 2D-2E).



280

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



282

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

284 **3.2. Association between weather conditions and dengue incidence**

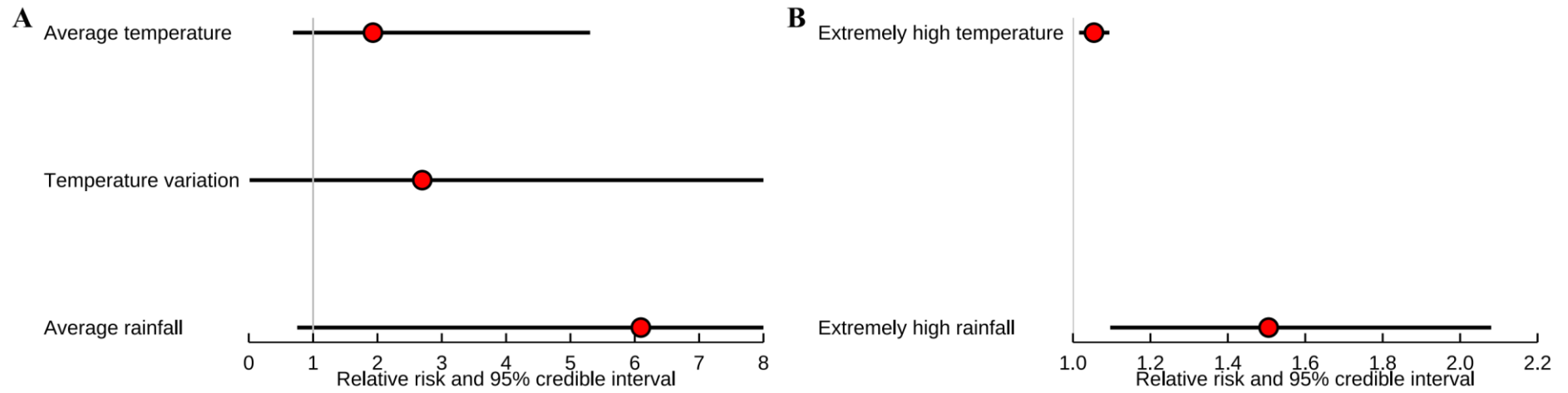
285 **Figure 3** shows the overall associations between weather conditions and dengue incidence for
286 Guangdong province as a whole. Average temperature, temperature variation, and average rainfall were
287 positively associated with dengue incidence, but the associations were not statistically significant (**Figure**
288 **3A**). By contrast, there were statistically significant positive associations with extremely high
289 temperature (RR:1.054, 95% CI: 1.016 to 1.094) and extremely high rainfall (RR: 1.505, 95% CI: 1.096
290 to 2.080) (**Figure 3B**).

291 **Figure 4** presents the spatial variability in the associations between weather conditions and dengue
292 incidence. We observed significant variability in the association with average temperature (**Figure 4A**);
293 seven cities have a statistically positive association (RR range: 1.032 to 1.153) and five cities have a
294 statistically negative association (RR range: 0.848 to 0.940). Association with temperature variation was
295 also found to vary spatially (**Figure 4B**); seven cities have a statistically positive association (RR range:
296 1.257 to 2.739) and four cities have a statistically negative association (RR range: 0.315 to 0.593).
297 Similarly, there were between-city variations in the association with average rainfall; seven cities have a
298 statistically positive association (RR range: 1.237 to 1.974) and five cities have a statistically negative
299 association (RR range: 0.373 to 0.835) (**Figure 4C**). After taking into account the impacts of average
300 temperature, temperature variation, and average rainfall, high spatial variability in the risk of dengue
301 occurrence was observed in the centre and east of Guangdong province, as indicated by spatially
302 unstructured residuals (**Figure S3**).

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

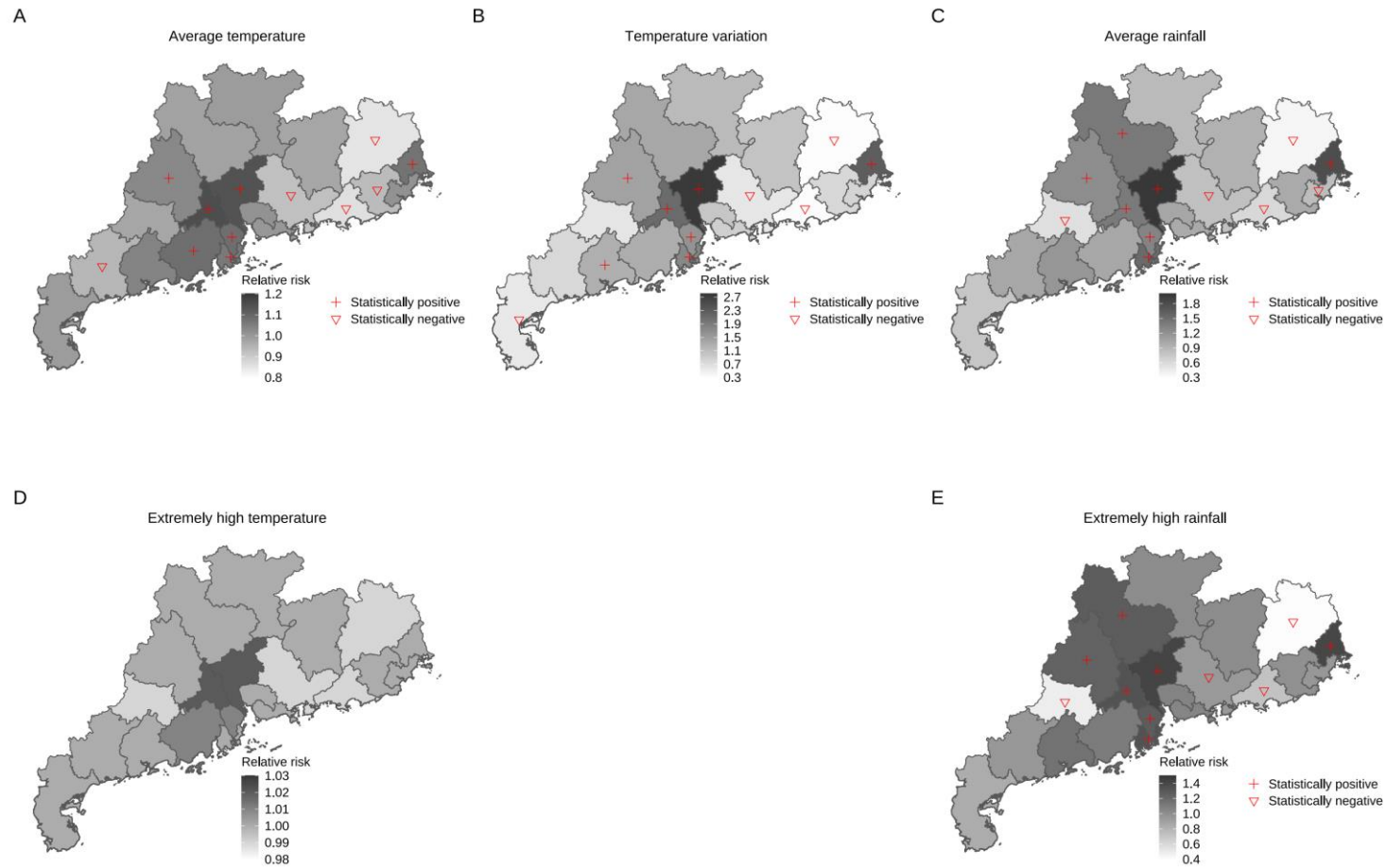
307 **3.3. Ranking of dengue-affected areas vulnerable to weather conditions**

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



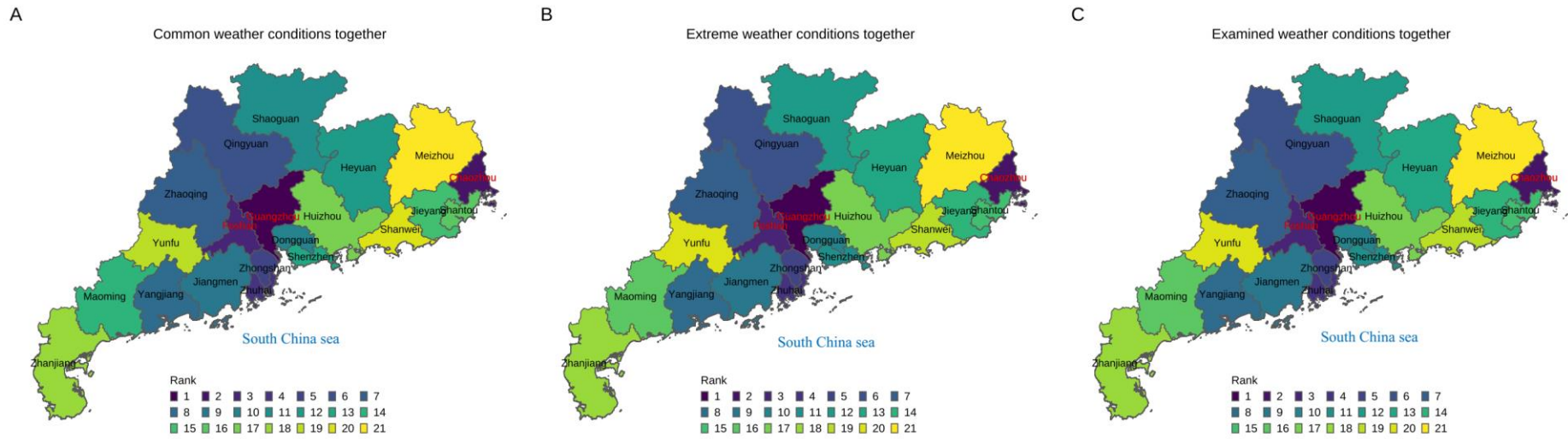
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 316 **Figure 3:** Estimated overall associations of dengue incidence with weather conditions in Guangdong province as a whole.
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326 **Figure 4:** Estimated associations of dengue incidence with weather conditions for each city in Guangdong province.



327

328 **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
 329 city.

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334 **3.4. Modification effects of city characteristics**

335 We then explored if the observed spatial variability in the association between weather conditions and
336 dengue incidence could be partly explained by city characteristics (Figure 6). Of five variables tested,
337 four variables (i.e., NDVI, elevation, Per Capital GRP, imported cases – but, not population density)
338 were statistically significantly associated with the spatial variability in weather-related dengue incidence.
339 We estimated that one unit decrease in NDVI index was associated with 0.35% and 0.04% decrease in
340 the slope for the association of dengue with average temperature and extremely high temperature (Figure
341 6A). Similarly, there was a negative association between elevation and effects of weather conditions
342 (Figure 6B), with slope decreases of <0.01% for the average temperature-dengue association, 0.01% for
343 the average rainfall-dengue association, <0.01% for the extremely high rainfall-dengue association. By
344 contrast, Per Capital GRP and imported cases were statistically positive associated with the effects of
345 weather conditions (Figure 6C-6D). Specifically, slopes for the associations of dengue with all examined
346 weather conditions increased by <0.01% associated with 1 unit increase in Per Capital GRP. The slope
347 for the association between extremely high temperature and dengue incidence rose by <0.01% per 1
348 imported case increase.

349 **3.5. Results of sensitivity analyses**

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

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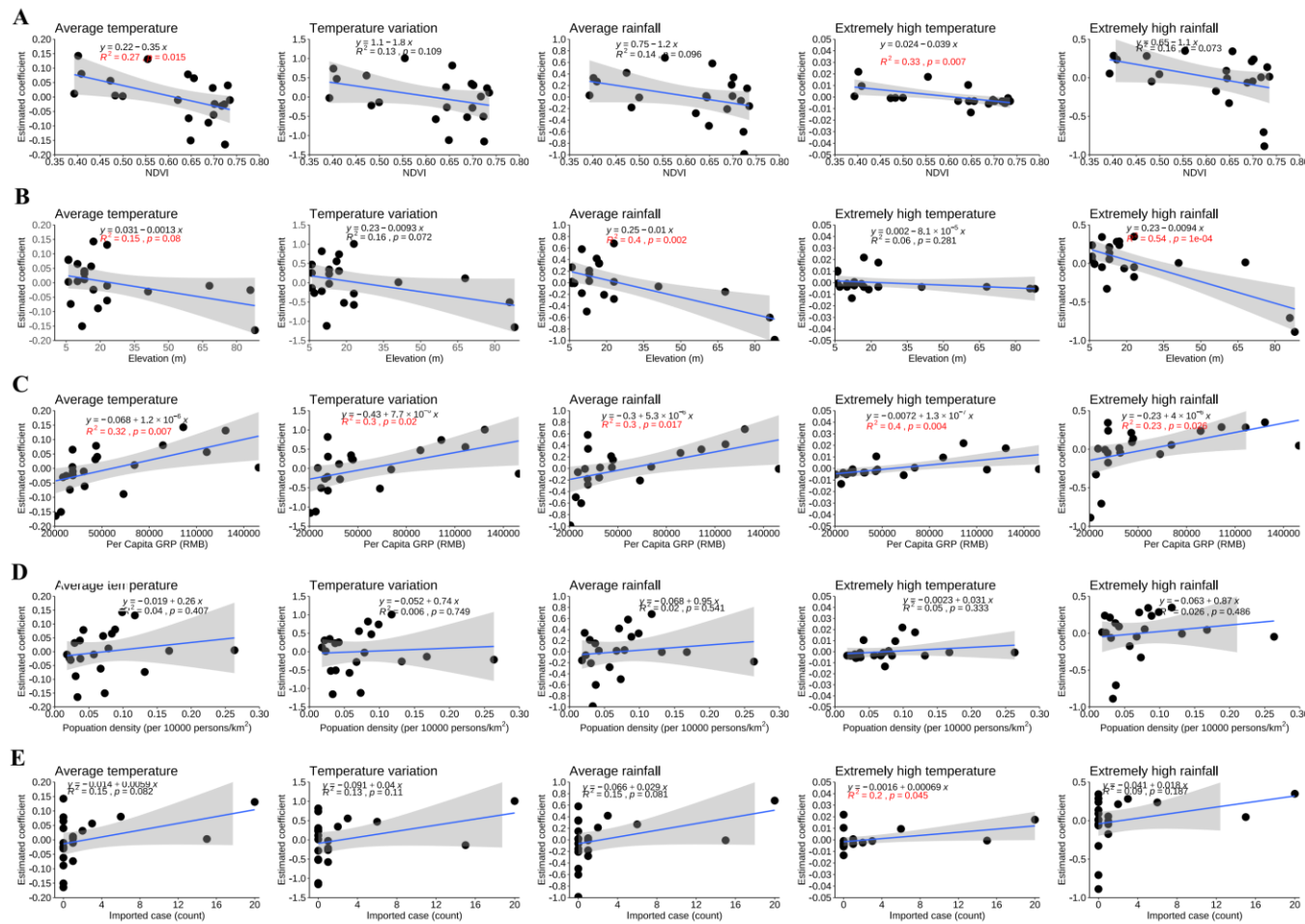
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367 **Figure 6:** Modification effects of city characteristics on the association between weather condition and dengue incidence. y-axis is the estimated city-specific slopes of
 368 associations between weather conditions and dengue incidence; x-axis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

370 **4. Discussion**

371 The most serious dengue outbreak on record in Guangdong province of China in 2014 resulted in over
372 40,000 cases but the underlying reasons for this dengue outbreak remain largely unknown. This study
373 sought to provide an answer to this puzzle from the perspective of weather effects, which are critical for
374 dengue virus and the vectors' (mosquitoes) population dynamics (Abdelrazec and Gumel 2017; Mordecai
375 et al. 2017; Ndiaye et al. 2006; Xu et al. 2017; Zhu et al. 2019a). By examining the spatially
376 heterogeneous effects of local weather conditions, our data analyses yielded four major findings: (1)
377 Extreme weather conditions including extremely high temperature and rainfall were associated with
378 higher dengue incidence for Guangdong province as a whole; (2) Associations of dengue incidence with
379 weather conditions (i.e., average temperature, temperature variation, average rainfall, and extremely high
380 rainfall) varied spatially between the cities of Guangdong province, with both statistically positive and
381 negative associations observed in different cities; (3) Dengue-affected cities with relatively higher
382 vulnerability to weather conditions are the central and coastal cities such as Guangzhou, Chaozhou,
383 Foshan, Zhuhai, and Qingyuan; (4) Cities with higher economic level, lower green space coverage and
384 lower elevation appeared to be at higher risk of weather-related vulnerability to dengue incidence. These
385 findings emphasise continued investigation into the effects of weather extremes and help policymakers
386 target areas particularly vulnerable to weather conditions that promote dengue occurrence. In addition,
387 the method presented here could be applied to other locations with health data available at finer spatial
388 resolution.

389 Prior research has found that typical weather conditions such as rises or drops in temperature,
390 relative humidity, rainfall have impacts on dengue transmission (Abdelrazec and Gumel 2017; Mordecai
391 et al. 2017; Ndiaye et al. 2006), as well as dengue incidence (Fan et al. 2014; Li et al. 2018; Li et al.
392 2016; Xiang et al. 2017; Xiao et al. 2018; Xu et al. 2017). As an important supplement to this literature,
393 our analyses further revealed that extreme weather conditions, including extremely high temperature and
394 rainfall, could act as an important driver or predictor of dengue occurrence. There is evidence in Asia
395 suggesting hot weather can force delayed mosquito outbreaks (Chaves et al. 2014), which could possibly
396 contribute to later dengue outbreaks. For example, our recent study found prolonged hot weather (i.e.,
397 heatwaves) precipitated dengue outbreaks (Cheng et al. 2020b). Likewise, outbreaks of some other
398 vector-borne diseases such as West Nile fever have been observed after heatwaves (Paz 2006; Semenza
399 and Menne 2009). Besides, spatial variability in association with extremely high temperature was not
400 observed, which possibly suggests that all cities of Guangdong province could be affected by extremely
401 high temperature. In the context of global warming, there will be more frequent and more intensive
402 weather extremes such as heatwaves and rainfall (IPCC ; Meehl and Tebaldi 2004). Therefore,
403 accounting for the role of extreme weather conditions would be beneficial to improve state-of-the-art,
404 region-specific early warning systems for preventing dengue outbreaks.

405 Our finding that the association of dengue incidence with weather variables varied geographically
406 adds evidence to the existing literature in China documenting an overall positive association with
407 temperature and rainfall within a city or a larger geographical area as a whole (Fan et al. 2014; Xiao et

408 [al. 2018; Xu et al. 2017](#)). However, positive statistically significant associations with weather variables
409 were found only in some cities of Guangdong province such as Guangzhou, Foshan, Zhongshan and
410 Zhuhai. Moreover, these cities are mainly located in the Pearl River Delta area, with many characteristics
411 that favour dengue transmission such as higher population density, higher numbers of imported dengue
412 cases, higher values in average temperature, average rainfall, and extremely high temperature. This
413 finding partly explains why the Pearl River Delta area is the primary cluster of dengue cases (or higher
414 risk of dengue occurrence), as documented in previous studies ([Fan et al. 2014; Liu et al. 2018; Zhu et](#)
415 [al. 2019b](#)).

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

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

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

443 Population vulnerability to dengue infection within a region requires the presence of multiple factors,
444 not only suitable weather conditions but also many other factors involving vector, socioeconomic,
445 demographic, behavioural, environmental characteristics and health systems. These factors are pivotal

446 for determining the changes in population exposure and susceptibility to dengue infection. Our findings
447 suggested that increases in the NDVI and elevation weaken the association between weather variables
448 and dengue incidence, but an opposite modification effect was shown for economic level and imported
449 cases. Previous reports in China revealed a trend of lower dengue incidence in areas with higher
450 vegetation greenness and elevation (Huang et al. 2018; Liu et al. 2018). In Guangdong province, cities
451 with higher NDVI and elevation tend to have lower average temperature and larger temperature variation
452 that have negative impacts on dengue transmission (Lambrechts et al. 2011; Mordecai et al. 2017). By
453 contrast, higher economic level is highly associated with higher degree of urbanization (e.g., more
454 crowded environment, higher human mobility, heat island effect, complex drainage network, and more
455 frequent travel with other regions) that may increase the likelihood of dengue infection and amplify the
456 effects of weather conditions on dengue incidence (Li et al. 2018; Wu et al. 2009). The number of
457 imported cases has been reported as an important predictor of locally acquired cases and a trigger of local
458 dengue outbreak in China (Jing et al. 2018; Peng et al. 2012; Wang et al. 2020). Therefore, the presence
459 of more imported cases and suitable weather conditions could synergistically affect dengue incidence
460 within a region (Jing et al. 2018). To improve the adaptive capacity of a community, it is necessary to
461 have a better city development plan and effective surveillance and management of dengue cases imported
462 from foreign areas.

463 To date, it still remains an unanswered question about why an unprecedented outbreak of dengue
464 fever occurred in 2014 in Guangzhou, China. Nevertheless, researchers in past years have been
465 conducting studies to understand the driving force for this record-high dengue outbreak. Existing
466 evidence points to a number of factors contributing to the 2014 dengue outbreak. For example, the
467 imported cases, climate variables (e.g., temperature and rainfall), human movement, socioeconomic and
468 demographic levels and delayed mosquito control have been suggested to drive the dengue outbreak in
469 2014 (Li et al. 2016; Zhu et al. 2018; Ren et al. 2017). As a climate-sensitive disease, dengue fever has
470 been increasingly reported to be affected by weather conditions including temperature and rainfall (Li et
471 al. 2018; Xu et al. 2017). The present study found extreme weather conditions including extremely high
472 temperature and rainfall were associated with higher dengue incidence, echoing to findings of previous
473 studies (Cheng et al. 2017; Cheng et al. 2020b; Wu et al. 2018). Some researchers also found the dengue
474 incidence could be well predicted using weather variables (Sang et al. 2015; Xu et al. 2017). It is
475 reasonable to believe that weather conditions make a partial contribution to the outbreak of dengue in
476 2014. However, a comparison with other non-weather factors should be made in future research to
477 understand the importance of different determinants of dengue occurrence.

478 Our findings may have some implications for the prevention of dengue outbreaks. There are
479 increasing studies in support of an association of dengue occurrence or outbreaks with weather extremes
480 such as extremely high rainfall and heatwaves (Wu et al. 2018; Cheng et al. 2020b). In the present study,
481 we also found evidence that extremely high temperature and rainfall increased the risk of dengue
482 incidence. This finding implies that extreme weather events is a risk factor of dengue occurrence and
483 incorporating such information into the climate-based dengue projection model would improve the

484 prediction accuracy, especially in the context of climate change that is projected to lead to more frequent
485 and intensive weather extremes (IPCC; Meehl and Tebaldi 2004). Besides, we also found spatial
486 variation in city's vulnerability to weather conditions. Among all cities of Guangdong province, some
487 central and coastal cities such as Guangzhou, Chaozhou, Foshan, Zhongshan, Zhuhai, Qingyuan, and
488 Yangjiang were most vulnerable. So, weather conditions in these cities should be closely monitored in
489 early warning system and used in conjunction with dengue control measures in order to minimize weather
490 effects on local dengue incidence.

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

511 **5. Conclusions**

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

517

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