#### **ORIGINAL PAPER**



# Extreme weather events and dengue outbreaks in Guangzhou, China: a time-series quasi-binomial distributed lag non-linear model

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#### Abstract

Dengue transmission is climate-sensitive and permissive conditions regularly cause large outbreaks in Asia-Pacific area. As climate change progresses, extreme weather events such as heatwaves and unusually high rainfall are predicted more intense and frequent, but their impacts on dengue outbreaks remain unclear so far. This paper aimed to investigate the relationship between extreme weather events (i.e., heatwaves, extremely high rainfall and extremely high humidity) and dengue outbreaks in China. We obtained daily number of locally acquired dengue cases and weather factors for Guangzhou, China, for the period 2006–2015. The definition of dengue outbreaks was based on daily number of locally acquired cases above the threshold (i.e., mean + 2SD of daily distribution of dengue cases during peaking period). Heatwave was defined as  $\geq 2$  days with temperature  $\geq 95$ th percentile, and extreme rainfall and humidity defined as daily values  $\geq 95$ th percentile during 2006–2015. A generalized additive model was used to examine the associated with increased risk of dengue outbreaks, with a risk increase of 115–251% around 6 weeks after heatwaves, 173–258% around 6–13 weeks after extremely high rainfall, and 572–587% around 6–13 weeks after extremely high humidity. Each extreme weather event also had good capacity in predicting dengue outbreaks, with the model's sensitivity, specificity, accuracy, and area under the receiver operating characteristics curve all exceeding 86%. This study found that heatwaves, extremely high humidity could act as potential drivers of dengue outbreaks.

Keywords Dengue · Extreme weather · Heatwave · Extremely high rainfall · Extremely high humidity

### Introduction

About half of the world's population inhabit regions that experience dengue outbreaks, with those living in Asia-Pacific area at considerable risk (WHO (World Health Organization) n.d.; Bhatt et al. 2013). In the past few decades, a large number

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of dengue outbreaks have been documented (Guo et al. 2017), such as the 2013–2014 outbreak in Fiji with >25,000 cases reported, the 2014 outbreak in Guangzhou, China, and the 2015 outbreak in Taiwan, China, each with >40,000 cases reported (Kucharski et al. 2018; Wang et al. 2019; Zhao et al. 2016). Not only do dengue outbreaks incur substantial

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disease burden but also the associated economic costs are also extremely high (Bhatt et al. 2013; Stahl et al. 2013; Tran et al. 2018; Shepard et al. 2016). Identifying the underlying drivers or predictors of dengue outbreaks can aid in the development of early-warning systems and would help optimize the allocation of limited resources through targeted and focused interventions.

Being transmitted by mosquito vectors, dengue is a particularly climate-sensitive infectious disease (Morin et al. 2013; Xu et al. 2017). Climatic variables, i.e., mainly temperature, rainfall, and relative humidity, influence dengue viruses, human biology, mosquito vector ecology, and consequently the intensity and distribution of dengue (Morin et al. 2013; Banu et al. 2014; Xu et al. 2017). Many previous studies have demonstrated associations between climatic variables and dengue transmission. For example, non-linear temperature-dengue and humidity-dengue associations have been reported previously (Xiang et al. 2017; Wu et al. 2018). Some studies also reported potential associations of dengue incidence with extreme weather events such as drought, flood, typhoon, El Niño event, and extremely hot summer, but such investigation is still lacking and needed in Asia-Pacific area such as China and Vietnam, as evidenced by Li's systematic review and Cheng's research (Li et al. 2018; Cheng et al. 2020). Specifically, previous studies mainly examined the changes in dengue incidence associated with normal weather conditions such as increase or decrease in temperature, relative humidity, and rainfall, which failed to consider the additional stress of abnormal weather conditions such as heatwaves (i.e., several consecutive days of extremely high temperature) (Cheng et al. 2020; Li et al. 2018). Although studies have also examined some abnormal weather conditions such as El Niño event and extremely hot summer that last for a long time period (e.g., several months or the whole year) (Li et al. 2018), those abnormal weather conditions are different from heatwaves that describe a prolonged period (days to weeks) of extremely high temperature and may be a new risk factor of dengue outbreaks (Cheng et al. 2020).

Changes in the population dynamics of mosquitoes and the associated risk of dengue occurrence could happen after extreme weather events (Jia et al. 2019). Jia and Mordecai have identified systems whereby extreme weather events have detrimentally impacted mosquito populations resulting in reduced likelihood of arboviral transmission (Jia et al. 2019; Mordecai et al. 2017). However, there is evidence that transient extremely high temperatures were associated with mosquito abundance following a delay of a few weeks (Chaves et al. 2014). Similarly, outbreaks of other vector-borne disease such as West Nile fever have been observed to occur several weeks after heatwaves (Paz 2006; Semenza and Menne 2009). It appears that extreme weather events may delay vector-borne disease outbreaks but exacerbate their size (Anyamba et al. 2014). In the context of warming climate, extreme weather

events such as heatwaves and extremely high rainfall will become more frequent and intense (IPCC 2014; Meehl and Tebaldi 2004). It is thus necessary to disentangle the associations between extreme weather events and dengue outbreaks. Moreover, inconsistencies found among previous studies in their identified impacts of extreme weather events may stem from regional differences. This highlights the need to identify associations at a regional scale before any attempt to develop global models of projected dengue.

In the present study, we aimed to use daily data on locally acquired dengue cases and weather conditions in Guangzhou, China, to examine the associations of dengue outbreaks with three extreme weather events including heatwaves, extremely high rainfall, and extremely high humidity.

## Materials and methods

#### Study area

This study area is Guangzhou, which is the capital city of Guangdong Province and the largest city of Southeast China. In 2015, Guangzhou had a population of over 13.5 million and a population density of 1816 residents/km<sup>2</sup> (http://210.72.4.52/gzStat1/chaxun/ndsj.jsp). This metropolitan city features a subtropical climate and the warm and humid climate creates favorable conditions for the survival, growth, and breeding of mosquitoes such as *Aedes albopictus*, making Guangzhou a high-risk area for dengue epidemics (Xu et al. 2017). For example, in 2014, Guangzhou experienced its worst dengue outbreak on record, with >40,000 cases reported and the incidence rate exceeding the historical average by two orders of magnitude (Zhao et al. 2016; Oidtman et al. 2019).

#### Data collection

Dengue is a notifiable infectious disease in China. All dengue cases were diagnosed according to the National Diagnostic Criteria (WS216-2008) and then reported to the web-based National Notifiable Infectious Disease Reporting Information System within 24 h (Cheng et al. 2017). Based on the travel and mosquito biting history, dengue cases are categorized into imported and locally acquired cases. Imported cases refer to those who have travelled to dengue endemic regions and been bitten by mosquitoes less than 15 days before the symptom onset; otherwise, cases were defined as locally acquired (Cheng et al. 2017). In the present study, we collected daily number of locally acquired and imported dengue cases between January 1, 2006, and December 31, 2015, in Guangzhou from China Centre for Disease Control and Prevention. The detailed data collection has been

described elsewhere (Sang et al. 2015; Xiang et al. 2017; Wu et al. 2018).

Regarding weather data, we collected daily mean temperature and daily rainfall from the National Meteorological Information Center (http://www.cma.gov.cn/2011qxfw/ 2011qsjgx/). Initially, the weather data were stored in a gridded map file, with a spatial resolution of 0.5 °C\*0.5 °C (around 55 km\*55 km). We extracted and averaged the figures of two weather variables within the polygon of Guangzhou map, which were then used in later data analysis. Daily data on mean temperature, rainfall, and relative humidity from a ground monitoring station were also downloaded from the National Meteorological Information Center. This study was approved by University Human Research Ethics Committee of Queensland University of Technology (1800000058).

# Definitions of dengue outbreaks and extreme weather events

To date, many methods have been used to define dengue outbreaks, without a universally accepted definition (Badurdeen et al. 2013; Brady et al. 2015). As motivated by previous work (Badurdeen et al. 2013; Brady et al. 2015), a dengue outbreak was defined here as daily number of locally acquired dengue cases above the threshold (mean + 2SD (standard deviation) of daily distribution of dengue cases during dengue incidence peak period, excluding the year 2014 that witnessed an unprecedented outbreak) (Sharmin et al. 2015). Dengue incidence peak period was between July and December, which accounted for >99% of total cases. This dengue outbreak definition has some advantages: (i) it is a simple and easy-to-understand approach from the statistical perspective; (ii) it can be easily used to inform the mass media and the public about the actual situation of dengue outbreaks such as the size of an outbreak in terms of duration and total number of dengue cases, which facilitates within-region and between-region comparisons; and (iii) it can serve to assess the cost-effectiveness of response mechanisms (Badurdeen et al. 2013; Brady et al. 2015). To be conservative, we also used the mean value of daily distribution of dengue cases as the threshold of dengue outbreaks in sensitivity analysis (Banu et al. 2014).

With respect to definitions for extreme weather events, we applied definitions of heatwaves, extremely high rainfall, and extremely high humidity as employed in previous studies (Zeng et al. 2014; Jia et al. 2019; Yan et al. 2019). Specifically, a heatwave was defined based on the combination of duration and intensity of high temperature:  $\geq 2$  days with temperatures  $\geq 95$ th percentile of daily distribution of temperature during the study period. This heatwave definition reflects how heat was experienced within each year of the study period while providing sufficient number of events to

detect the potential association with dengue outbreaks (Jia et al. 2019). Similar to previous studies (Yan et al. 2019; Cheng et al. 2014), we defined extremely high rainfall as rainfall  $\geq$ 95th percentile of its daily distribution, and extremely high humidity as humidity  $\geq$ 95th percentile of its daily distribution.

#### Statistical analysis

We performed a quasi-binomial generalized additive model within the framework of distributed lag non-linear model (DLNM) to investigate the associations between extreme weather events and dengue outbreaks. Compared with traditional generalized additive model and generalized linear model, DLNM has the advantage of simultaneously fitting the complex exposure-response and lag-response associations between environmental risk factors and health outcomes, as well as accounting for the autocorrelation of variables of exposure in the short term (Lowe et al. 2018; Gasparrini et al. 2015). DLNM has now been widely used in existing literature to examine temperature-dengue relationship and predict dengue incidence using climatic variables (Xiang et al. 2017; Lowe et al. 2018; Banu et al. 2014). In this study, we used DLNM by including extreme weather events as the binary independent variable ("1" for days with extreme weather events and "0" for days without extreme weather events) and dengue outbreaks as the binary dependent variable ("1" for outbreak days and "0" for non-outbreak days).

To eliminate the influence of potential confounders, we included in the model the long-term trend and seasonality by using "year" and "month" as the categorical variables, the day of week as a categorical variable, and a first-order autocorrelation structure (Sang et al. 2015; Xiang et al. 2017; Cheng et al. 2018). In fitting the associations between heatwaves and dengue outbreaks, we also controlled for daily rainfall and daily humidity, each using a natural cubic spline with three degrees of freedom. Similarly, daily temperature using a natural cubic spline with three degrees of freedom was considered in fitting the associations of dengue outbreaks with extremely high rainfall and extremely high humidity. We additionally in sensitivity analysis considered the influence of imported dengue cases to check the robustness of our findings. Considering the fact that relative humidity is confounded by air temperature, we also ran models with and without adjustment of relative humidity (mean temperature) for the association of dengue outbreaks with heatwaves (extremely high relative humidity). Additionally, we calculated the absolute humidity following the method in a recent study (Qi et al. 2020) and then examined the effect of extremely high absolute humidity on dengue outbreaks.

To examine the delayed effects of extreme weather events on dengue outbreaks, we used a lag of up to 90 days in the model, which was determined based on the generalized crossvalidation scores and previous studies that suggest the maximum effects of temperature on dengue occurrence within 3 months (Banu et al. 2014; Lowe et al. 2018). The effects of extreme weather events were reported as relative risk (RR) and 95% confidence interval (CI) at three different time windows: (i) the first day with significantly increased risk of dengue outbreaks, (ii) the day with the maximum risk of dengue outbreaks, and (iii) the last day with significantly increased risk of dengue outbreaks.

In order to check the performance of the modelling strategy for each extreme weather event, we split the whole dataset into two parts: the dataset from 2006 to 2013 was used to develop the model, and the dataset from 2014 to 2015 was used to validate the model. The model's forecasting ability was measured with four indicators: sensitivity, specificity, accuracy, and area under the receiver operating characteristics (ROC) curve (AUC) (Banu et al. 2014; Lowe et al. 2018). Sensitivity, also known as the true positive rate, refers to the proportion (%) of true dengue outbreak events that were correctly predicted by the model (Lowe et al. 2018; Banu et al. 2014). Specificity, also known as the 1-false positive rate, represents the proportion of non-outbreak events that were correctly predicted by the model (Banu et al. 2014; Lowe et al. 2018). Accuracy is the ratio of correctly predicted events (i.e., outbreaks and non-outbreaks) with total events. The ROC curve is a graph of true positive rate against the false positive rate at various threshold settings and AUC is the area under the ROC curve (Lowe et al. 2018). AUC value ranges between 0 and 1, and a model with good predictive ability should have an AUC value close to 1.

#### Results

# Description of dengue outbreaks and extreme weather events

There were 39,690 locally acquired dengue cases during the study period. On average, there were 10.9 dengue cases per day, ranging between 0 and 1641 (Table 1). The averages of daily mean temperature, humidity, and rainfall were 21.8 °C (range: 0-31.7 °C), 74.9% (range: 25–100%), and 4.6 mm (range: 0-129.5 mm), respectively.

It was observed that dengue outbreaks occurred in three years (2006, 2013, and 2014), spanning a total of 215 (5.9%) days (Fig. 1). Heatwaves, extremely high rainfall, extremely high humidity, and extremely low humidity occurred almost every year, respectively totalling 160 (4.4%) days, 183 (5%) days, 220 (6%) days, and 189 (5.2%) days. Noticeably, there were gaps of several months ( $\geq$  3) between extremely low humidity days and dengue outbreaks; therefore, extremely low humidity events were dropped from further analysis, with focus being on the three remaining extreme weather events (i.e., heatwaves, extremely high rainfall, and extremely high humidity) for the remainder of the study.

# Associations between extreme weather events and dengue outbreaks

Table 2 shows the estimated effects (RR) of extreme weather events on dengue outbreaks. In general, each of the three extreme weather events examined was associated with increased risk of dengue outbreak. Specifically, the risk of dengue outbreaks began to increase 3 weeks after heatwaves, and 1 month after extremely high rainfall and extremely high humidity. The observed greatest dengue outbreak risk (RR) was between 2.15 and 3.51 about 1.5 months following heatwaves, between 2.73 and 3.58 about 1.5–3 months following extremely high rainfall, and between 6.72 and 6.87 about 1.5–3 months following extremely high humidity. Heatwave effects were found to disappear around 2 months later, whereas the effects of the other 2 events remained for approximately 3 months (Supplementary Fig. S1).

To exclude the influence of the unprecedented dengue outbreak in 2014, we repeated the above analysis for the period of 2006–2013 (Table 3). Associations between all three extreme weather events and dengue outbreaks were also observed, but the estimated effects were changed in few cases. For example, when accounting for extremely high rainfall and humidity, the associations between heatwaves and outbreaks were no longer significant. Further, the maximum increase in dengue outbreak risk was estimated around 1.5 months after extremely high rainfall (halving the delay identified when the 2014 outbreak data were included).

 Table 1
 Descriptive statistics of daily weather conditions and dengue cases in Guangzhou, China, 2006–2015

Variables	Number of valid days	Minimum	5th percentile	Mean	Standard deviation	95th percentile	Maximum
Dengue cases	3652	0	0	10.9	85.7	12	1641
Mean temperature (°C)	3639	0	9.7	21.8	7.0	29.9	31.7
Relative humidity (%)	3652	25	51	74.9	12.6	92	100
Rainfall (mm)	3643	0	0	4.6	10.8	25.2	129.5



Fig. 1 Summary of the characteristics and daily distribution of dengue outbreaks and extreme weather events

#### Model's evaluation

Figure 2 shows the model's performance in predicting dengue outbreaks. For each extreme weather event, the proportion of dengue outbreaks that was correctly predicted was above 0.86 (sensitivity), correctly predicted non-outbreaks was above 0.99 (specificity), and correctly predicted both outbreaks and non-outbreaks was above 0.97 (accuracy). The estimated area under the ROC curve (AUC) was approximately 0.99 for each extreme weather event, indicating that the forecasting system performed excellently (note that a random-guess forecasting system, by definition, would yield an AUC score of 0.5) (Lowe et al. 2018).

#### **Results of sensitivity analyses**

To check the robustness of our findings, we used mean value as the alternative threshold to define dengue outbreaks. The

fitted associations between extreme weather events and dengue outbreaks remained stable (Supplementary Fig. S1), and the model's predicting ability was minorly changed (Supplementary Fig. S2). Meanwhile, the findings were not significantly altered before and after the adjustment of the influence of imported dengue cases (Supplementary Fig. S3). After using the ground monitored data on mean temperature and rainfall instead of gridded data, regression analyses also found adverse effects of heatwaves and extremely high rainfall on dengue outbreaks (Supplementary Fig. S4). Additionally, models returned comparable results before and after controlling for relative humidity (mean temperature) when fitting the association of dengue outbreaks with heatwaves (extremely high relative humidity) (Supplementary Figs. S5–S6). Using the absolute humidity as an alternative to relative humidity also found evidence of increased risk of dengue outbreaks associated with relatively high absolute humidity, with a seemingly smaller effect than relatively high relative humidity (Supplementary Fig. S7).

Table 2 Estimated effects of extreme weather events on dengue outbreaks in Guangzhou, China, 2006–2015

Variables	RR and 95% CI	Model's performance			
	Day of starting effects	Day of maximum effects	Day of ending effects	GCV value	$R^2$
Heatwaves	1.44 (1.03–2.01); lag 23	2.56 (1.56-4.20); lag 42	1.28 (1.01–1.62); lag 58	0.06	85.7%
Heatwaves + rainfall	1.65 (1.01-2.71); lag 26	3.51 (1.66-7.40); lag 41	1.71 (1.08-2.70); lag 53	0.05	87.4%
Heatwaves + humidity	1.75 (1.01-3.04); lag 38	2.15 (1.23-3.79); lag 47	1.50 (1.05-2.15); lag 60	0.05	87.0%
Extremely high rainfall	1.42 (1.06-1.89); lag 33	3.58 (1.99-6.45); lag 90	3.58 (1.99-6.45); lag 90	0.06	86.6%
Extremely high rainfall + temperature	1.34 (1.01-1.79); lag 31	2.73 (1.79-4.16); lag 47	2.68 (1.53-4.72); lag 90	0.06	86.8%
Extremely high humidity	1.60 (1.00-2.55); lag 35	6.87 (2.52-18.71); lag 90	6.87 (2.52-18.71); lag 90	0.05	87.8%
Extremely high humidity+ temperature	2.16 (1.12-4.17); lag 37	6.72 (1.98-22.81); lag49	4.17 (1.35–12.83); lag 90	0.04	89.4%

Heatwave is defined as  $\geq 2$  days with temperature  $\geq 95$ th percentile

Extremely high rainfall is defined as rainfall ≥95th percentile

Extremely high humidity is defined as humidity ≥95th percentile

Lower GCV value means better model's performance

Higher  $R^2$  value means better model's performance

GCV, generalized cross-validation;  $R^2$ , R square; RR, relative risk; CI, confidence interval

Table 3	Estimated	effects o	f extreme	weather	events or	1 dengue	outbreaks	in Guar	1gzhou,	China,	2006-	-2013
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Variables	RR and 95% CI	Model's performance			
	Day of starting effects	Day of maximum effects	Day of ending effects	GCV value	$R^2$
Heatwaves	1.91 (1.02–3.59); lag 36	2.39 (1.20-4.79); lag 44	1.42 (1.01–1.99); lag 55	0.05	75.7%
Heatwaves + rainfall	NA	NA	NA	0.04	79.1%
Heatwaves + humidity	NA	NA	NA	0.04	78.8%
Extremely high rainfall	1.95 (1.09-3.50); lag 27	16.40 (4.67-57.56); lag 45	1.61 (1.06-2.44); lag 69	0.03	83.4%
Extremely high rainfall + temperature	2.25 (1.06-4.80); lag 28	23.55 (6.02–92.20); lag 45	1.68 (1.01-2.78); lag 68	0.03	84.3%
Extremely high humidity	1.84 (1.04-3.26); lag 35	6.55 (1.80-23.87); lag 90	6.55 (1.80-23.87); lag 90	0.04	79.8%
Extreme high humidity + temperature	2.07 (1.03-4.15); lag 35	14.28 (2.16–94.38); lag 49	5.09 (1.23–20.97); lag 90	0.04	86.8%

Heatwave is defined as  $\geq 2$  days with temperature  $\geq 95$ th percentile

Extremely high rainfall is defined as rainfall ≥95th percentile

Extremely high humidity is defined as humidity ≥95th percentile

Lower GCV value means better model's performance

Higher  $R^2$  value means better model' performance

GCV, generalized cross-validation;  $R^2$ , R square; RR, relative risk; CI, confidence interval; NA, adverse effects of extreme climate events were not observed

### Discussion

Because of global warming observations over recent decades, impacts of extreme weather events such as heatwaves and extreme rainfall on human health have attracted increasing attention (Cheng et al. 2014; Cheng et al. 2019). However, the associations between extreme weather events and outbreaks of vector-borne disease such as dengue remain unclear due to qualitatively different impacts reported among the relatively few studies on this topic. Using daily data on locally acquired dengue cases and weather in Guangzhou, China, this study found evidence of associations of dengue outbreaks with several extreme weather events including heatwaves, extremely high rainfall, and extremely high relative humidity. In addition, the occurrence of dengue outbreaks was well predicted by each of these extreme weather event types. These findings contribute important new insights into the impacts of climate change on dengue transmission that should be exploitable in developing more temporally targeted control and prevention measures.

Prompted by the very large outbreak in 2014, the associations between weather conditions and dengue incidence in Guangzhou have been investigated in many previous studies. Several of these studies consistently report that common weather conditions such as rises in temperature, rainfall, and humidity were associated with increases in the number of dengue cases (Shen et al. 2015; Xiang et al. 2017; Wu et al. 2018). Our findings build on these previous studies by highlighting the distinct roles that extreme weather events have on dengue outbreaks.

In the present study, we observed the associations of dengue outbreaks with three extreme weather events including heatwaves, extremely high rainfall, and extremely high humidity. Direct comparison with previous literature in China is difficult because such investigations are not common. Nevertheless, there are some plausible mechanisms for our



Fig. 2 The evaluation of model's predictivity, reported as sensitivity, specificity, accuracy, and AUC. AUC, area under the receiver operating characteristics curve

observations. In an environment of extremely high temperatures, the mosquito development and biting rate, fecundity, and life span will be suppressed or reduced (Mordecai et al. 2017). Similarly, Jia et al. found mosquito abundance to plummet shortly after extremely high temperatures (Jia et al. 2019), and Morin et al. identified high rainfall and humidity negatively impacting mosquito breeding sites (Morin et al. 2013). Our findings do not refute these previous studies but actually, to a certain extent, corroborate them. Supplementary Figure S1 shows dengue outbreak risk did not increase (and, in some cases decreased) during and immediately following extreme weather events. Noticeably, few weeks or months after extreme weather events, weather conditions will return to normal but mosquito outbreaks, i.e., sudden extraordinary increases in mosquito abundance, could happen. For example, Chaves et al. noted extraordinary increases in mosquito abundance a couple of months after extreme weather events in Thailand, proposing that this is a compensatory (or, perhaps even over-compensatory) mechanism or population persistence (Chaves et al. 2014). Over-compensatory density dependence in Aedes aegypti populations is relatively well established (Legros et al. 2009), and the resilience of this species to downward perturbations (either natural or through anthropogenic control) has been demonstrated in mathematical models (Yakob and Bonsall 2008). Consequently, the risk of dengue outbreaks will increase after extreme weather events, as supported by previous observations that outbreaks of vector-borne disease (e.g., West Nile fever) took place after heatwaves (Paz 2006; Semenza and Menne 2009).

We also observed the greatest dengue outbreak risk around 1.5 months after heatwaves, and around 1.5–3 months after extremely high rainfall and extremely high humidity. Similarly, previous studies have reported long-delayed effects of normal weather conditions on dengue incidence (Xiang et al. 2017; Wu et al. 2018; Lowe et al. 2018). Our recent study in Hanoi, Vietnam, also showed evidence of an association between heatwaves and delayed dengue outbreaks (Cheng et al. 2020). The delayed effects may be a reflection of the duration of both positive and negative effects of weather conditions on dengue transmission, as well as the build-up phase of dengue epidemics or outbreaks. The crucial time-windows identified in the present study allow sufficient time for local health authorities to make early preparations to prevent or reduce impending dengue outbreaks.

Extreme weather events have different characteristics in terms of onset time, duration, and intensity, which play a pivotal role in influencing human health and likewise the risk of dengue outbreaks through their complex effects on mosquito population dynamics (Jia et al. 2019; Tong et al. 2015; Tong et al. 2014). For instance, longer-lasting heatwaves were found to have greater effects in suppressing the mosquito's population growth (Jia et al. 2019). However, the present study only collected 10-year time-series data and dengue

outbreaks occurred only in three years, which limited our ability to further examine how the associations between extreme weather events and dengue outbreaks were changed by the characteristics of extreme weather events. Considering the fact that climate change will bring about more intense and more frequent heatwaves and extreme high rainfall (IPCC (Intergovernmental Panel on Climate Change). Climate Change 2014; Meehl and Tebaldi 2004), more research into the impacts of different characteristics of extreme weather events on dengue outbreaks is needed.

Many regions of the world have witnessed dengue outbreaks in recent years (Kucharski et al. 2018; Wang et al. 2019; Zhao et al. 2016). An effective early warning system for dengue epidemics or outbreaks relies heavily on reliable and accurate detection ahead of time. In previous literature, many advanced statistical and mathematical models have been developed to forecast the dengue occurrence, which have important implications for early detection and prevention of dengue outbreaks (Lowe et al. 2018; Li et al. 2019; Guo et al. 2019). Our study adds to these by providing evidence for extreme weather events having positive as well as negative associations with dengue outbreak risk in China. Furthermore, we found good capacity for each extreme weather event in predicting dengue outbreaks. These findings possibly imply that extreme weather events can be used to improve future dengue prediction. In the context of climate change, more frequent or serious dengue outbreaks likely hit susceptive regions such as Asia and America in the absence of effective countermeasures (WHO (World Health Organization) n.d.; Watts et al. 2018). If our findings are reproducible in other regions, it is necessary to incorporate extreme weather events such as heatwaves in the development of a state-of-the-art predictive framework for dengue outbreaks. Nevertheless, this study only explored whether or not dengue outbreaks can be affected by extreme weather events. Further research is thus needed to investigate the impacts of extreme weather events on different magnitudes of dengue outbreaks (e.g., large- and small-scale outbreaks), which will provide important evidence for the health authority.

A recent systematic review on climate change and dengue in China highlights that evidence is lacking regarding the effects of heatwaves on dengue (Li et al. 2018). In the present study, weather data were collected from gridded maps of temperature and rainfall covering the whole study region, rather than from one or several ground monitoring stations (Sharmin et al. 2015; Xiang et al. 2017; Wu et al. 2018), which to some extent reduced the measurement error of temperature exposure. We found increased risk of dengue outbreaks associated with heatwaves, extremely high rainfall, and extremely high relative humidity, which may shed new light on early detection and prevention of dengue outbreaks. Additionally, these extreme weather events are strongly correlated with the dengue outbreaks, implying the necessity of incorporating extreme weather events into forecasting models, especially in view of the warming climate of the twenty-first century (IPCC (Intergovernmental Panel on Climate Change). Climate Change 2014).

Some limitations of this study should be acknowledged. First, in addition to the weather data included in the present study, many other time variant factors such as changes in mosquito density, population movements and habits, and vector control measures also play an important role in affecting dengue transmission (Li et al. 2019). Cautions are thus needed when interpreting the findings of this study. Second, during the 10-year study period in Guangzhou only three years saw dengue outbreaks, which results from the use of a strict dengue heatwave definition (cases > mean + 2SD (standard deviation) of daily distribution of dengue cases) and likely reduces the statistical power of examining the associations of dengue outbreaks with extreme weather events. However, our findings were robust to sensitivity analyses using a looser dengue heatwave definition (cases > mean of daily distribution of dengue cases). Meanwhile, our recent study in another subtropical Asia-Pacific region (i.e., Hanoi, Vietnam) also revealed significant heatwave-dengue outbreak association (Cheng et al. 2020). Nevertheless, similar research is urgently needed to testify the associations between extreme weather events and dengue outbreaks in other dengue-prone Asia-Pacific countries. Third, as with many previous studies (Sharmin et al. 2015; Xiang et al. 2017; Wu et al. 2018), the study design does not allow us to ascertain the casual associations of dengue outbreaks with extreme weather events. In view of more intense and more frequent extreme weather events resulting from climate change (Sun et al. 2014; IPCC (Intergovernmental Panel on Climate Change). Climate Change 2014; Meehl and Tebaldi 2004), future investigations are urgently needed to study how extreme weather events lead to the formation of dengue outbreaks (Jia et al. 2019). Fourth, relative humidity has been found to have a significant effect on dengue outbreaks in the present study. But relative humidity is a moisture variable that can be confounded by air temperature. There was a weak correlation between relative humidity and mean temperature (Spearman's correlation  $(\rho)$  was 0.11 and the collinearity was not a big concern). Further, sensitivity analysis with and without the adjustment of relative humidity or mean temperature in the model generated similar results. However, we found relatively high relative humidity seemed to have a greater effect on dengue outbreaks than did relatively high absolute humidity. Future research needs to check how the effect of relative humidity on dengue outbreaks will be changed after using other moisture variables such as absolute humidity and specific humidity (Davis et al. 2016).

### Conclusion

This study suggests that extreme weather events including heatwaves, extremely high rainfall, and extremely high relative humidity may increase the risk of dengue outbreaks. These extreme weather events also showed high accuracy in predicting dengue outbreaks. Considering extreme weather events may help to develop an effective early warning system of dengue outbreaks, especially in the context of global warming.

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#### Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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