

For PNAS

Classification: Biological Sciences, Ecology

Climate variation drives dengue dynamics

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Abstract:

Dengue, a viral infection transmitted between people by mosquitoes, is today one of the most rapidly spreading diseases in the world. Here, we report the analyses covering 11 years (2005–2015) from the city of Guangzhou in southern China. Using the first eight years of data to develop an ecological-based model for the dengue system, we reliably predict the following three years of dengue dynamics – years with exceptionally extensive dengue outbreaks. We demonstrate that climate conditions, through the effects of rainfall and temperature on mosquito abundance and dengue transmission rate, play key roles in explaining the temporal dynamics of dengue incidence in the human population. Our study thus contributes to a better understanding of dengue dynamics and provides a predictive tool for preventive dengue-reduction strategies.

Keywords:

Dengue, Climate, Structural Equation Model, Zero-inflated Generalized Additive Models, Prediction

Significance Statement:

Dengue is a vector-borne infectious disease threatening human health on a global scale. Due to climate change, globalization and other factors, dengue has increasingly spread to new countries and over larger areas, from tropical to temperate zones. In this study, we found that climate has both direct effects on dengue incidence and indirect effects mediated by mosquito density, as mosquitoes are the vectors of dengue. The quantitative results derived from this study may be helpful towards advancing our understanding of how climate influences vector-borne diseases, and prove useful for the control and prevention of dengue fever.

Main Text:

Dengue is one of the most rapidly spreading diseases in the world (1), including within the Guangdong province of southern China (2). During the last 50 years, the incidence of dengue has increased 30-fold with increasing geographic expansion to new countries (1). **In 2010, an estimated 390 million dengue infections occurred, of which around 96 million showed symptoms (3).** Dengue outbreaks in China were previously thought to be imported and initiated by people travelling to China from dengue-endemic areas elsewhere (4); however, recent studies suggest that dengue may now be endemic to China as well (2). The epidemiological triangle of **both dengue fever and dengue hemorrhagic fever, which is the more serious form of dengue, includes hosts (humans), pathogens (one or more of five dengue virus serotypes) (5), and mosquito vectors (*Aedes albopictus* and *Aedes aegypti*) with their ecological interactions (6).** The dengue outbreaks are qualitatively known to be strongly influenced by temperature (7), **humidity, rainfall and socio-economic factors like urbanization (8).** However, a full understanding of the quantitative nature of such effects is largely lacking. With this paper we provide such a quantitative understanding of dengue dynamics.

In 2014, an extensive dengue outbreak hit China, with 47,127 dengue cases diagnosed, a new record since 1986 (9). Since the 1990s, dengue epidemics have gradually spread from Guangdong, Hainan and Guangxi provinces (9). We present here a time-series analysis of dengue dynamics, using dengue surveillance data for the years 2005–2015 from Guangzhou, the largest city in Guangdong and the city with the most dengue cases in China. We split the main analysis by using the first eight years to develop a model, and the three remaining years to test that model, as these latter years encompass exceptionally extensive dengue outbreaks.

Monthly human dengue incidence data (number of diagnosed cases) were obtained from the China National Notifiable Disease Surveillance System (10) (Fig. 1). Monthly surveillance data of *Ae. albopictus* density, the only dengue vector species in Guangzhou, were obtained from local Centers for Disease Control and Prevention (CDC) (11) (see Method part). We considered both indices of larval and adult densities. Temperature and precipitation data were obtained from the China Meteorological Data Sharing Service System (<http://cdc.cma.gov.cn>). We considered several alternative monthly temperature (°C) and precipitation indices in the subsequent analyses, including mean temperature, monthly average of daily minimum temperature, monthly average of daily maximum temperature, cumulative precipitation (mm), and number of days with rainfall.

We first explored the direct and indirect effects of temperature and precipitation on dengue outbreaks for all years from 2005–2015 using a Structural Equation Model (SEM) (12). The SEM results suggest significant direct, positive effects of temperature and precipitation on dengue incidence as well as indirect, positive effects of both variables through vector density (Fig. 2). Model diagnostics suggest that the

SEM was robust: the Normalized χ^2 -test (i.e. model χ^2 divided by the degrees of freedom) = 0.149, root mean square error of approximation < 0.001, and comparative fit index = 1 (12). However, due to the presence of many zeros in the data (zero-inflation), and the inability of the SEM to capture nonlinear effects, some caution in the interpretation of these results is needed. Nevertheless, this analysis serves as a good stepping stone for the full time-series model development using Generalized Additive Models (GAMs) (13) and zero-inflated GAMs (ZIGAMs) (14).

The generic model formulas for vector and dengue, respectively, are given by equations 1 and 2:

$$\text{Eq. 1: } \ln(V_t + 1) = a_0 + f_1(\ln(V_{t-1} + 1)) + f_2(T_{t-1}) + f_3(P_{t-1}) + \varepsilon_t$$

$$\text{Eq. 2: } D_t = I(b_0 + g_1(\ln(D_{t-1} + 1)) + g_2(V_{t-1}) + g_3(T_{t-1}) + g_4(P_{t-1})) \cdot \exp(b_1 + g_5(\ln(D_{t-1} + 1)) + g_6(V_{t-1}) + g_7(T_{t-1}) + g_8(P_{t-1}) + \delta_t)$$

Here, V_t and D_t indicate, respectively, monthly vector density and dengue incidence in month t . T_{t-1} and P_{t-1} indicate temperature and precipitation for month $t-1$. The parameters a_0 , b_0 and b_1 are intercepts. The functions $f_1, f_2, f_3, g_1, \dots$, and g_8 are either smooth (natural cubic splines) or linear functions. By optimizing model selection criteria that quantified the trade-off between model fit and parsimony (see Tables S1 and S2), the temperature, precipitation and vector indices to include in the models and the functional forms (linear or smooth) were chosen. Vector dynamics were analyzed with a GAM fitted on $\ln(V_t + 1)$ transformed data. The dengue data (but not the vector data) were zero-inflated (Fig. 1, Fig. S1). Hence, dengue incidence dynamics were analyzed with a ZIGAM that consisted of a binomial and a lognormal part. The function $I(\cdot)$ in Eq. 2 represents a Bernoulli variable that is either 0 (absent) or 1 (present), whose probability of success is given by the predictor expression enclosed within the parentheses, on the logit scale. The same predictor variables enter into the 2 sub-models of the ZIGAM, although with potentially different functional forms.

Results of ZIGAM analyses for the first eight years (2005–2012) suggested that dengue incidence was best predicted as positive smooth functions of dengue incidence in the previous month, adult mosquito density, monthly average of daily maximum temperature and number of days with rainfall (Fig. 3 and Table S2). We found that adult mosquito (i.e., vector) density was best predicted as linear effects of adult mosquito density in the previous month and number of days with rainfall (Table 1, Table S1).

We then used the selected GAM for climate effects on adult mosquito density (Table 1) and the selected ZIGAM for adult mosquito and climate effects on dengue (Fig. 3) to make one-month-ahead predictions for 2013–2015. **We found that the selected models were indeed able to predict the high peaks in dengue cases for these years (Fig. 4), although with broad prediction bands. The two highest mosquito peaks,**

in years 2007 and 2014, were not predictable from the model. The 2014 mosquito peak in Guangzhou has recently been associated with the seasonal distribution of precipitation, the daily temperature range and non-additive effects of temperature and precipitation (15), pointing to more complex species-environment relationships than accommodated by our model. As our focus was on prediction, we intendedly restricted model complexity to reduce the risk of overfitting.

Finally, we repeated model selection, using the whole dataset from 2005 to 2015 (Tables S1 and S2). The same variables were selected in these models and their estimated effects were similar, indicating that the same biological processes were driving the dynamics in the peak years from 2013 to 2015 as in the earlier period (Fig. 5, Table 1). No additional factors, e.g. related to dengue possibly becoming endemic **and potentially occurring earlier in the season** (2, 4), were thus needed to explain these peaks in dengue incidence.

This final ZIGAM of dengue dynamics shows that previous-month dengue incidence has positive effects on outbreak risk (i.e., on the probability of the incidence being larger than zero, Fig. 5A) and outbreak intensity (i.e., on $\ln(\text{incidence})$, given that incidence is larger than zero, Fig. 5E). Adult mosquito density mainly seems to affect outbreak intensity, but only after having reached a threshold of around 1–1.5 units on the mosquito index scale (monthly averaged *Ae. albopictus* captured per trap per night) (Fig. 5F). Temperature has significantly positive effects on both outbreak risk and intensity (Fig. 5C, G), with some indications of leveling off at high temperatures (Fig. 5G). Precipitation has a non-significant positive association with outbreak risk (Fig. 5D) and a significant, approximately linear, and positive association with outbreak intensity (Fig. 5H).

The positive association between temperature and dengue incidence in our study is similar to e.g. Taiwan (16, 17) which is at the same latitude as Guangzhou. Our findings show that this association is mainly related to direct effects of temperature on dengue transmission rate. Mechanisms for such direct effects include, for example, temperature effects on the biting rate of mosquitoes (18), incubation period of pathogens (19), and human exposure to mosquitoes (e.g., by influencing the time spent outdoors or with open windows). In contrast, GAM results show no significant **association of the temperature variables considered with** mosquito population dynamics. The temperature-mosquito association suggested by the SEM likely reflects the mosquitoes' seasonal cycle, with higher abundances in summer, as this model analyzes the total abundance rather than the change in abundance from one month to the next.

Our results show that precipitation influences dengue incidence both through direct effects on transmission rate (e.g., through effects on mosquito biting rate (18)), and indirect effects through mosquito population dynamics. Since *Ae. albopictus* breed in

small pools of water, rainfall could result in an increase of breeding sites (20). We found the number of days with rainfall to be a better predictor than the monthly cumulative precipitation, which suggests that the underlying mechanism may be related to the maintenance of humid conditions over time. These findings complement a recent study showing a positive association between interannual variability in dengue incidence and surface water area (21). Together, our studies show that changes in breeding area of *Ae. albopictus* are important drivers of dengue dynamics at both monthly and yearly time scales. However, while precipitation appears to be a key driver of the shorter-term changes (this study), urban landscape features, such as recently constructed artificial lakes in Guangzhou, appear to be key drivers of longer-term trends (21).

As in other dengue epidemic areas (11, 22, 23) we find a strong link between dengue incidence and density of *Aedes* mosquitoes, the vectors of dengue. These findings support the utility of vector population control **through, e.g., pesticides, *Wolbachia* bacteria-infection of mosquitoes or habitat measures**, for reducing the intensity of dengue outbreaks (24, 25). Interestingly, such control efforts may be the reason why mosquito density was lower in 2015 than we had predicted based on climate conditions, and why dengue incidence was lower than predicted for three months during the build-up phase of the outbreak that year.

Our study builds on previous research that link dengue and vector dynamics to climate variables (26, 27) and climate change (28), and extends these by quantifying relationships based on state-of-the-art statistical analysis of multi-year time-series. Our findings strongly suggest that climate conditions drive the outbreaks of dengue in Guangzhou. However, our modeling approaches have some limitations, such as the low number of years with very high dengue incidence during the study period (2013 and 2014). We did not consider potentially relevant local factors, such as population movements, the occurrence of household water tanks, vegetation cover, and distance to rivers or other water bodies. **Further, while our results point to climate factors associated with increased risk of dengue transmission and outbreaks, human activities and their impact on local ecology may be more important than climate factors in driving the long-term trends (29-31). Moreover, the role of climate is likely to vary among locations, and even over time in the same location (32).** However, the quantitative results derived from this study may be helpful towards advancing our understanding of how climate influences vector-borne diseases, and prove useful for the control and prevention of dengue fever.

Methods

Dengue incidence data

Daily records of human dengue cases from 2005 to 2015 were obtained from the China National Notifiable Disease Surveillance System. **All human dengue cases were diagnosed according to the diagnostic criteria for Dengue Fever (WS216–2008) enacted by Chinese Ministry of Health (11, 33).** The information of individual dengue cases included whether they were local or imported (local cases were defined as dengue cases where infection most likely occurred due to local transmission as there was no documentation of travel to dengue-endemic foreign regions; imported cases were those where infection most likely occurred outside of China). Human dengue incidence data were aggregated per month (denoted as D_t) and matched to monthly surveillance data of adult mosquito population density.

Vector density data

We considered both the adult mosquito density (denoted as V_t^a) and the larval density (denoted as V_t^l). Adult mosquitoes (*Aedes albopictus*) were sampled by light traps. Larval density was measured by the *Breteau index*, which is defined as the number of positive containers per 100 houses inspected (34). Both adult density and larval density combined the information on mosquito density sampled in residential area households (> 50 households sampled per month), parks, construction sites and other urban areas.

Climate variables in the models

We considered several different monthly temperature and precipitation variables for model selection. The temperature variables (°C) included average temperature (denoted as T_{t-1}^a), average of daily lowest temperature (denoted as T_{t-1}^l) and average of daily highest temperature (denoted as T_{t-1}^h). Precipitation variables included accumulated precipitation (mm, denoted as P_{t-1}), and number of days with rainfall (days, denoted as P_{t-1}^d). We modeled the effects of climate variables on dengue incidence with $t = 1$ month time lag in order to be consistent with the survival time of *Ae. albopictus* under field conditions: 50% of the population has been found to survive ≥ 10 days and 5% to survive ≥ 40 days; the time for *Aedes albopictus* transmission of dengue may be less than 40 days (35, 36).

Statistical modeling

Structural Equation Modeling: rational, model construction and selection

Structural Equation Modeling (SEM) estimates the structural correlation among the variables (37, 38). SEM was used to analyze the structural linear correlation (as shown in Fig. 2) between temperature (average maximum temperature), precipitation (number of days with rainfall), vector density (monthly averaged mosquitoes captured per trap per night) and dengue incidence (ln transformed). The effects of temperature and precipitation on dengue were divided into direct effects and effects mediated by vector density. At the same time, the correlation between the variables of temperature and precipitation was assessed in the model. A dummy variable YEAR2014 (year

2014 = 1, other years = 0) was added into the SEM model as a control variable, because the large outbreak of dengue in year 2014 (39) otherwise hindered convergence and adding the dummy control variable was preferred from model selection.

Generalized Additive Model of vector dynamics

The ‘mgcv’ package (version 1.7-29) of R was used for Generalized Additive Model (GAM) analyses (40). Because the different temperature and precipitation variables were strongly correlated, we considered all combinations of the alternative temperature, precipitation and vector density variables (but no more than one variable for each factor in the model). To account for density-dependence we included $\ln(1 + \text{density})$ in the previous month as a predictor variable in the model. We also compared linear and nonlinear model formulations, by letting the covariate effects in *Eq. 1* to either be linear or smooth (natural cubic splines with a maximum of three degrees of freedom). As selection criterion we used the generalized cross validation criterion (GCV). A model with lower GCV has more predictive power and was hence selected (Table S1). To evaluate an additional conservative criterion, we used genuine cross validation. Specifically, we removed one “test” year at a time, fitted the model on the remaining dataset, made predictions for the test year, repeated this for all years, and calculated log-scale root-mean-square prediction error (i.e., the square root of the sum of squared differences $\ln(\text{observed density} + 1) - \ln(\text{predicted density} + 1)$). Deviance residuals from the final models were checked for temporal autocorrelation using autocorrelation and partial autocorrelation functions.

ZIGAM of dengue dynamics

Histograms of dengue incidence clearly showed zero inflation problems (Fig. S1). The ‘COZIGAM’ package (version 2.0-4) of R was used for Constrained and Unconstrained Zero-Inflated Generalized Additive Models (14). The constrained (CoZIGAM) and the unconstrained (UnZIGAM) models differ in that CoZIGAM constrains the fitted values of the binomial part of the model to be proportional to the fitted values of the lognormal part (on the linear scales of the predictors). As model selection criterion we used an approximation of the log of the marginal likelihood (logE), which is related to the Bayesian Information Criterion. Models with higher logE are preferred. As response variable, only the incidence of locally infected dengue cases was considered. For the autoregressive term, $\ln(1 + \text{incidence})$ in the previous month, both local and imported dengue cases were considered.

The maximum degrees of freedom for the smooth terms was set to three in the model selection. By inspecting the model providing the highest logE for the first eight years (Table S2), we found that the effect of average maximum temperature was not biologically interpretable (Fig. S2). Most likely this reflects overfitting, and hence we modified the model by reducing the maximum degrees of freedom for this term to two. This rendered an interpretable temperature effect (Fig. 3). The logE of this model (-60.515) remained a better fit than those of other candidate models from Table S2.

Hence, this model was used for predictions.

Predictions of dengue incidence for 2013 to 2015

The selected vector and dengue models based on data from 2005 to 2012 were used to calculate one-month-ahead predictions for 2013 to 2015. Predictions of mosquito density and dengue incidence for month t were calculated based on observed temperature, precipitation, dengue incidence and mosquito density in month $t-1$. The predicted mosquito density for month t was used as input in the prediction of dengue for month t .

Uncertainty estimation

Prediction bands were calculated using bootstrap, as follows: For vector dynamics, we used a wild bootstrap approach (41). The residuals from the model for the reduced dataset (2005–2012) were first rescaled to have the same variance as estimated by the model. We did this by multiplying the residuals with the square root of the scale factor estimated from the model divided by the variance of the residuals. Ten thousand bootstrap datasets of the same size as the original reduced dataset were generated by adding to the fitted values their corresponding (rescaled) residuals, with the sign of the residuals randomly flipped. Specifically, each residual was multiplied by a random variable that equaled 1 or -1 with equal probability, before being added back to the fitted values. A bootstrap distribution for vector density predictions was generated by refitting the vector model on each bootstrap dataset and using these refitted models to make predictions for the whole period (2005–2015).

For dengue dynamics we generated 10,000 bootstrap datasets in a two-step approach. In the first step, we sampled with replacement the rescaled residuals from the lognormal part of the ZIGAM and added them back to the fitted values. In the second step, each data point was multiplied by 0 or 1, with probability p being the fitted value from the binomial part of the ZIGAM. We then refitted the ZIGAM with the bootstrap data. Finally, we used these refitted ZIGAMs and the bootstrap time-series of mosquito density to generate a bootstrap distribution of dengue incidence for the whole period.

The 0.025 [0.05] and 0.975 [0.95] quantiles from this distribution delineate the 95 % [90 %] prediction limits.

Acknowledgments:

We thank Sari C. Cunningham for improving the English of this manuscript. This research was supported by the National Basic Research Program of China (973 Program) (Grant No. 2012CB955504); the National Natural Science Foundation of China (NSFC) (Grant No. 81273139); State Key Laboratory for Infectious Disease Prevention and Control Independent Fund (2014SKLID106) and the Centre for Ecological and Evolutionary Synthesis (CEES) of the University of Oslo. Authors declare no conflict of interests.

Author Contributions:

N.C.S., Q.L. and J.X. designed the study. N.C.S., L.X., and L.C.S. did most of the writing of the paper. L.X., L.C.S. K.S.C. and J.Z. performed the analysis. J.Y., S.S., M.W., Z.Y., Z.Y., T.J., L.L., Y.Y., X.L. and H.L. contributed to data provision, data processing, and interpretation. All authors discussed and commented on the manuscript.

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42. Supplementary Materials including Tables S1 - S2, Figs. S1 - S2, Ref. 33 - 42.

Table 1. Final model for adult mosquito density. Model coefficients \pm standard errors. All terms are statistically significant at $p < 0.01$.

Model formula	Deviance explained
Using the first eight years of data 2005–2012	
$\ln(V_t^a + 1) = -0.040 + 0.58[s.e. 0.072] \ln(V_{t-1}^a + 1) + 0.021[s.e. 0.0041] P_{t-1}^d + \varepsilon_t$	64.4%
Using the whole dataset 2005–2015	
$\ln(V_t^a + 1) = -0.048 + 0.64[s.e. 0.057] \ln(V_{t-1}^a + 1) + 0.019[s.e. 0.0032] P_{t-1}^d + \varepsilon_t$	67.0%

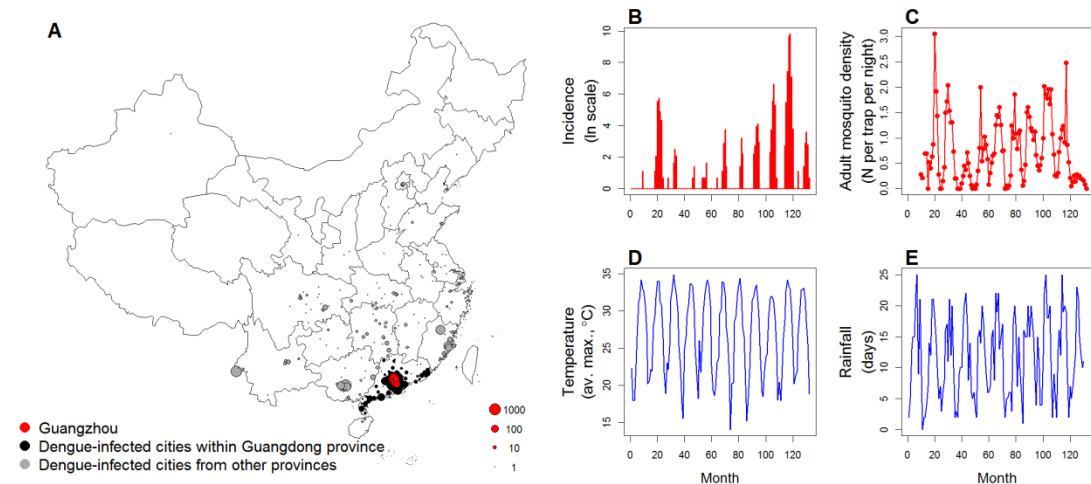


Fig. 1. Spatiotemporal dynamics of dengue in mainland China from the beginning of 2005 to the end of 2015. **A.** Geographical distribution of dengue incidence in China. Radiuses of circles indicate incidence of dengue. Red circles represent dengue in Guangzhou, black circles other cities in Guangdong province, and grey circles other provinces. **B.** Monthly time series of dengue incidence in Guangzhou. **C.** Monthly time series of adult population density of the dengue vector *Ae. albopictus*. **D.** Monthly time series of average maximum temperature in Guangzhou. **E.** Monthly time series of number of days with rainfall in Guangzhou.

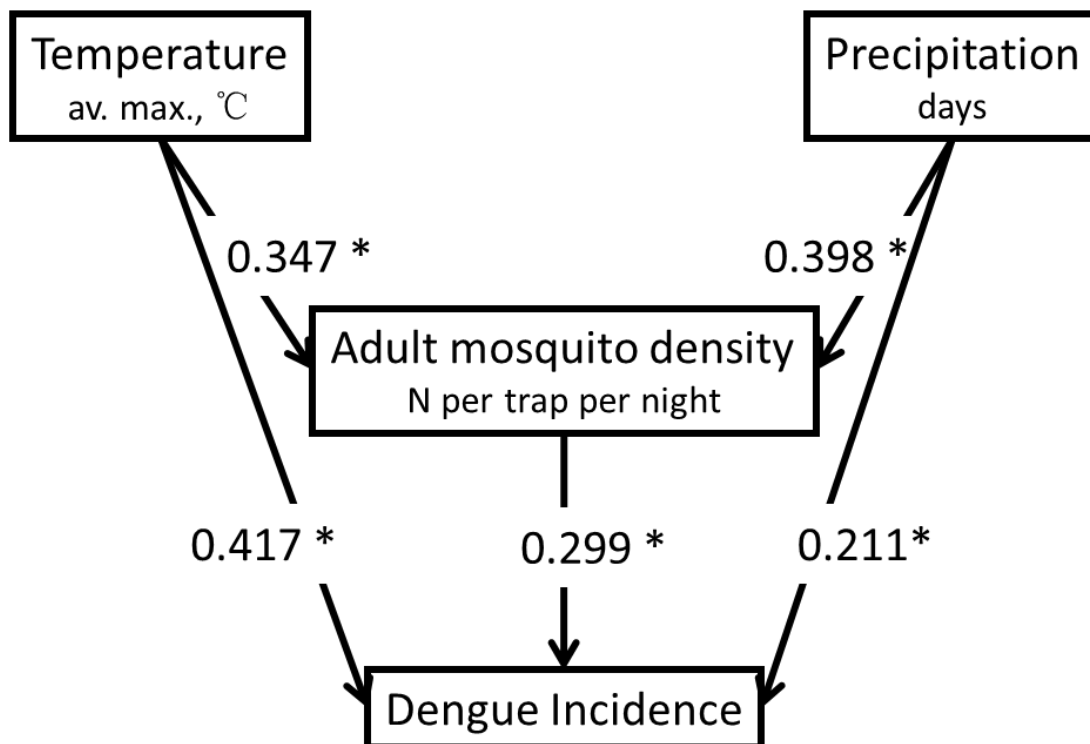


Fig. 2. Structural Equation Model analysis revealed direct and indirect climate effects on dengue incidence in Guangzhou from 2005 to 2015. Arrows with numbers indicate ecological effects and standardized coefficients. Temperature and precipitation are correlated (correlation coefficient = 0.39). Asterisks indicate statistically significant pathways ($p < 0.05$).

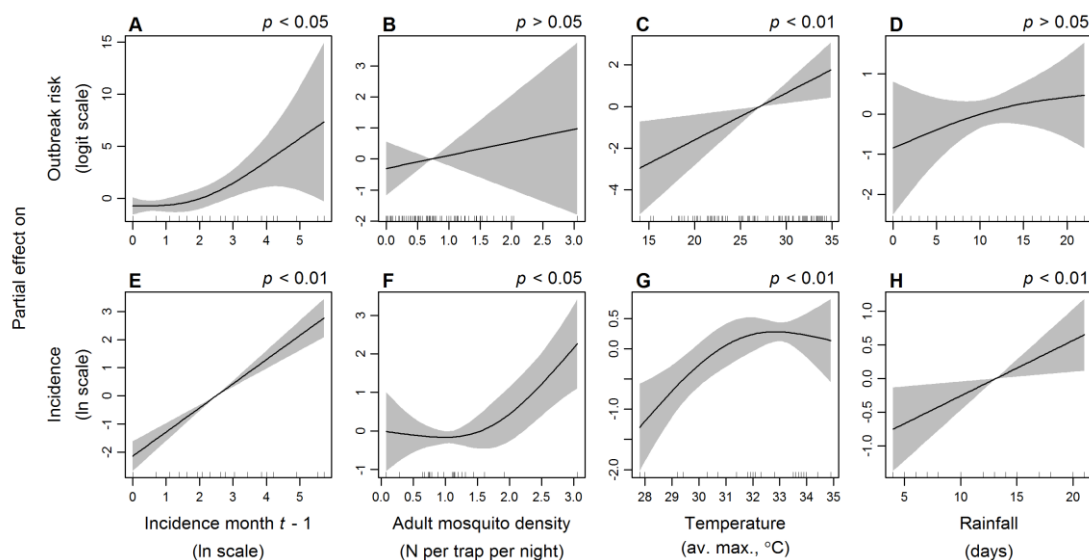


Fig. 3. Analysis of potentially nonlinear influences on dengue incidence in Guangzhou based on data from years 2005–2012, i.e., excluding the 3 last years of data. To account for zero-inflation, a separate binomial sub-model quantifies predictor effects on outbreak risk (logit scale probability of incidence > 0 , upper row) and a log-normal sub-model quantifies predictor effects on outbreak intensity when an outbreak occurs ($\ln(\text{incidence})$, lower row).

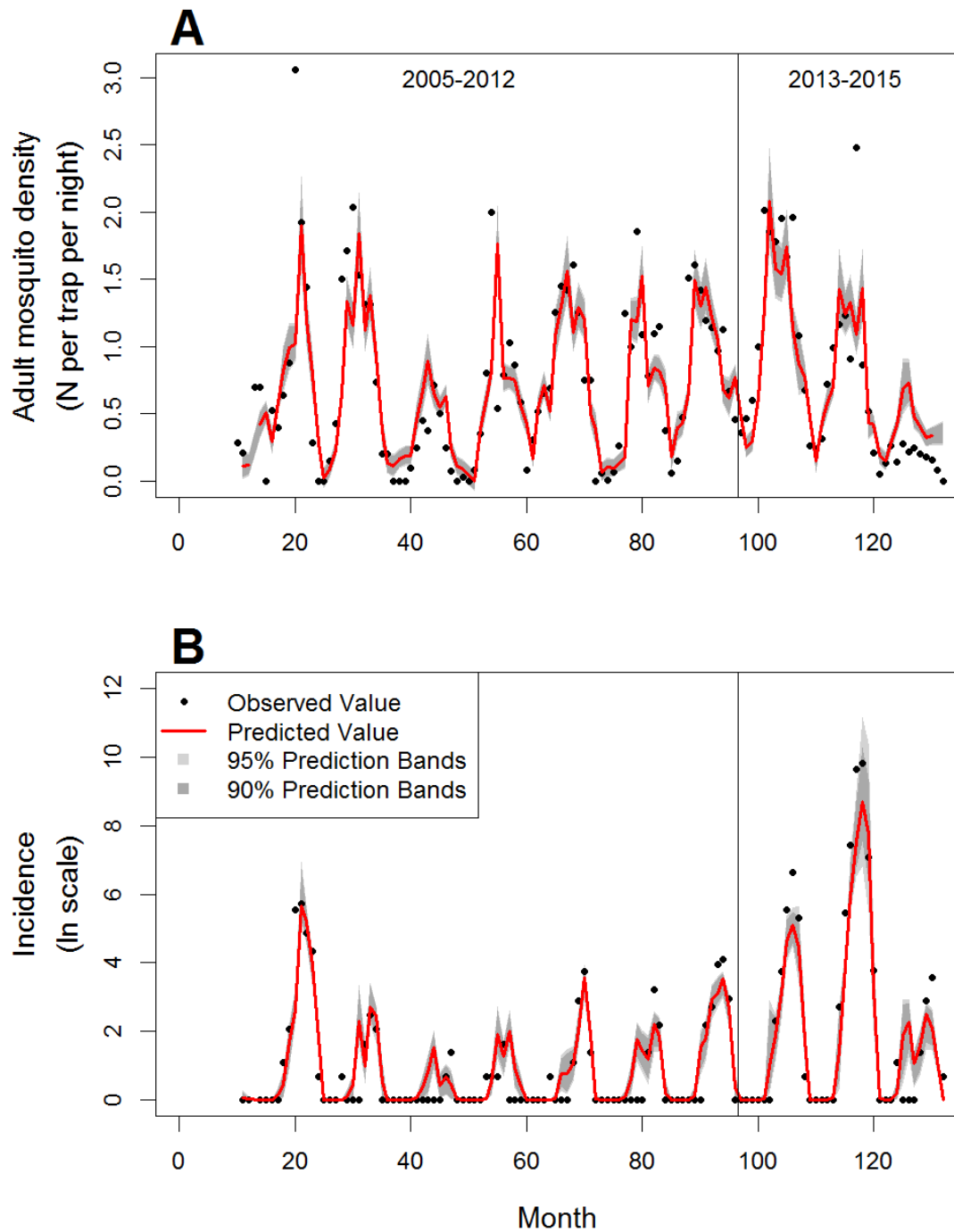


Fig. 4. Observations and one-month-ahead predictions. **A.** Adult mosquito density. **B.** Dengue incidence. The vertical lines separate the years 2005–2012 from the years 2013–2015 over which out-of-sample predictions were made.

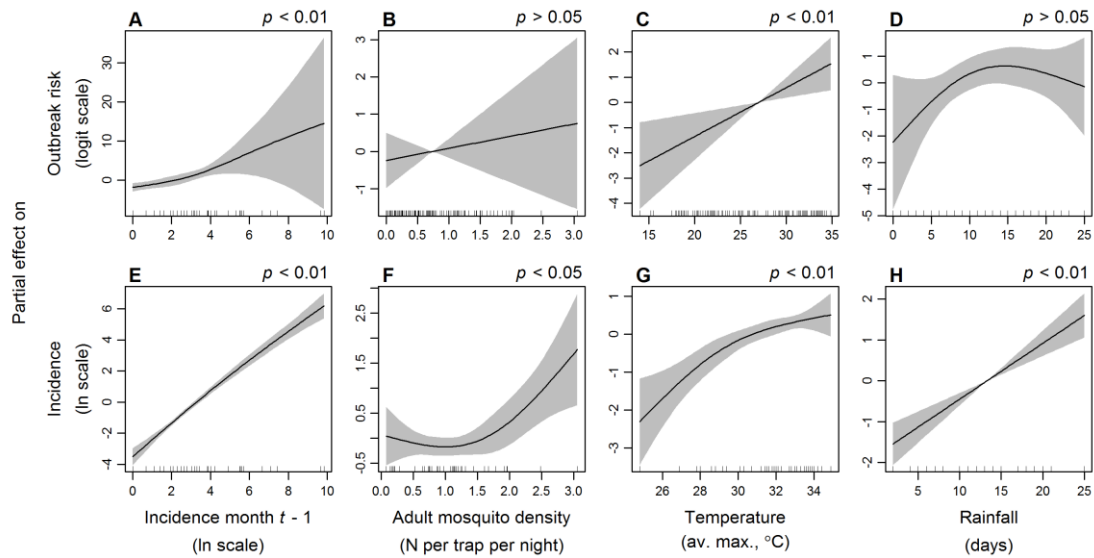


Fig. 5. Analysis of potentially nonlinear influences on dengue incidence in Guangzhou based on data from all years 2005–2015. To account for zero-inflation, a separate binomial sub-model quantifies predictor effects on outbreak risk (logit scale probability of incidence > 0 , upper row) and a log-normal sub-model quantifies predictor effects on outbreak intensity when an outbreak occurs ($\ln(\text{incidence})$, lower row).

Supporting information

Climate variation drives dengue dynamics

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Table S1. The model selection results for adult mosquito density. The top five models were selected based on minimizing the GCV criteria. We also list genuine CV calculated by leaving one year out at a time.

Model formula	GCV	CV leaving one year out
Using the first eight years of data 2005–2012		
Linear Model		
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 P_{t-1}^d + \varepsilon_t$	0.046	0.218*
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^a + a_3 P_{t-1}^d + \varepsilon_t$	0.047	0.226
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^l + a_3 P_{t-1}^d + \varepsilon_t$	0.047	0.227
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^h + a_3 P_{t-1}^d + \varepsilon_t$	0.047	0.226
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^l + \varepsilon_t$	0.058	0.248
Nonlinear Model		
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(P_{t-1}^d) + \varepsilon_t$	0.046	0.223
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^a) + f_3(P_{t-1}^d) + \varepsilon_t$	0.046	0.234
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^h) + f_3(P_{t-1}^d) + \varepsilon_t$	0.046	0.233
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^l) + f_3(P_{t-1}^d) + \varepsilon_t$	0.046	0.234
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(P_{t-1}) + \varepsilon_t$	0.056	0.238
Using the whole dataset 2005–2015		
Linear Model		
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 P_{t-1}^d + \varepsilon_t$	0.043	0.210*
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^l + a_3 P_{t-1}^d + \varepsilon_t$	0.043	0.214
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^a + a_3 P_{t-1}^d + \varepsilon_t$	0.043	0.214
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 T_{t-1}^h + a_3 P_{t-1}^d + \varepsilon_t$	0.043	0.214
$\ln(V_t^a + 1) = a_0 + a_1 \ln(V_{t-1}^a + 1) + a_2 P_{t-1} + \varepsilon_t$	0.052	0.231
Nonlinear Model		
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(P_{t-1}^d) + \varepsilon_t$	0.042	0.213
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^h) + f_3(P_{t-1}^d) + \varepsilon_t$	0.043	0.219
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^l) + f_3(P_{t-1}^d) + \varepsilon_t$	0.043	0.218
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(T_{t-1}^a) + f_3(P_{t-1}^d) + \varepsilon_t$	0.043	0.219
$\ln(V_t^a + 1) = a_0 + f_1(\ln(V_{t-1}^a + 1)) + f_2(P_{t-1}) + \varepsilon_t$	0.048	0.224

* The model used for predictions, which is also the model formulation selected by using the whole dataset.

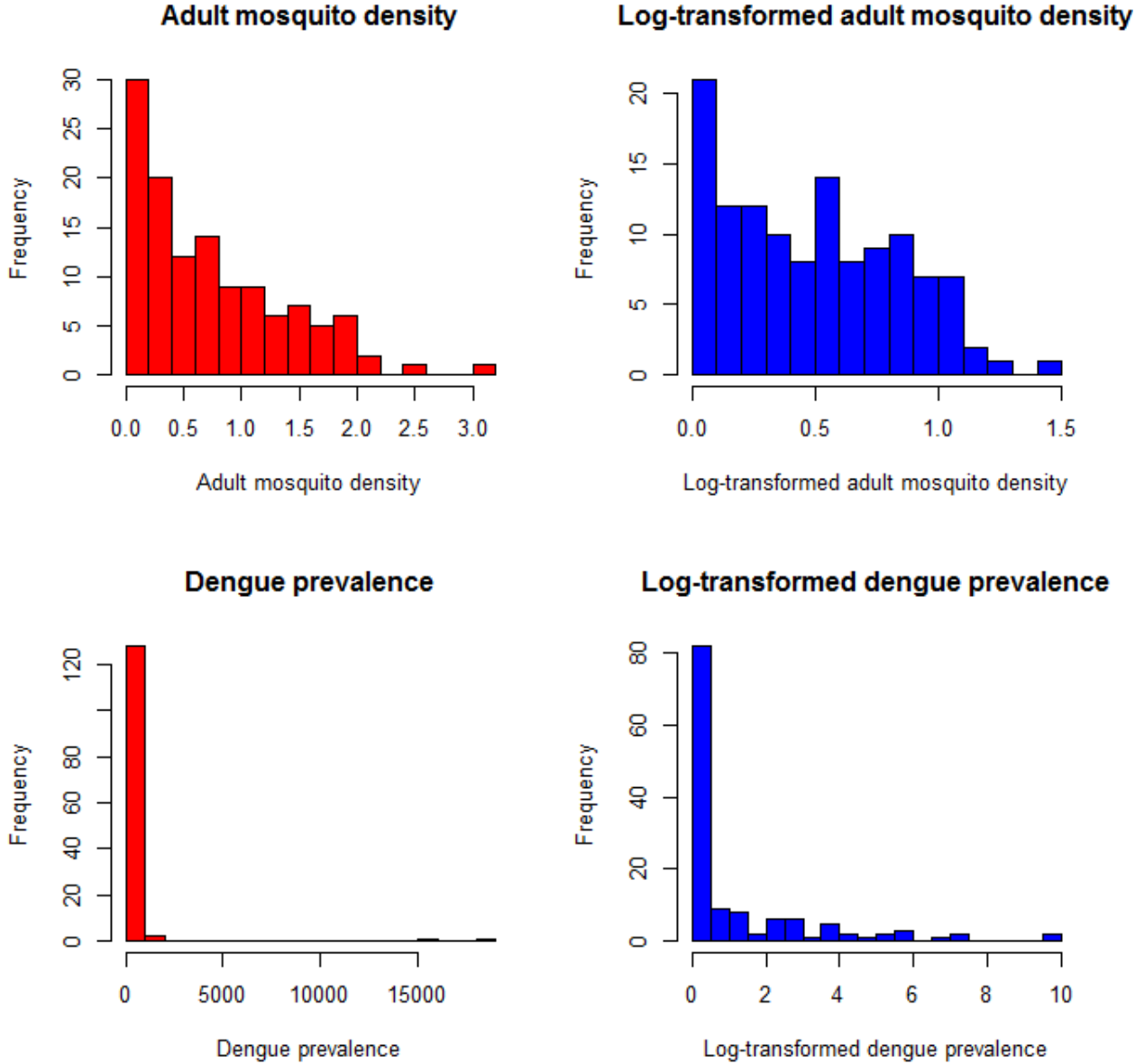
Table S2. Model selection results (log of marginal likelihood, logE) for dengue incidence. Models with higher logE are preferred. Unconstrained ZIGAMs (UnZIGAM) consistently give higher logE than constrained ZIGAMs (CoZIGAM).

Simplified model formula (see Eq. 2 for full formulation)	2005–2012		2005–2015	
	CoZIGAM	ZIGAM	CoZIGAM	ZIGAM
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^h) + g_4(P_{t-1}^d) + \varepsilon_t$	-137.4	-54.9*	-134.1	-92.0*
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^h) + g_4(P_{t-1}) + \varepsilon_t$	-105.0	-62.3	-129.7	-100.4
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^h) + \varepsilon_t$	-82.9	-63.7	-127.4	-115.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^a) + g_4(P_{t-1}^d) + \varepsilon_t$	-80.5	-63.8	-140.1	-94.2
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^l) + g_4(P_{t-1}^d) + \varepsilon_t$	-80.2	-64.4	-136.9	-95.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^a) + g_4(P_{t-1}) + \varepsilon_t$	-80.6	-65.2	-128.3	-109.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^l) + g_4(P_{t-1}) + \varepsilon_t$	-80.3	-65.7	-127.7	-100.9
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^a) + \varepsilon_t$	-79.7	-66.3	-126.6	-113.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(T_{t-1}^l) + \varepsilon_t$	-79.4	-67.2	-125.8	-116.3
$D_t = b_0 + g_1(D_{t-1}) + g_2(T_{t-1}^a) + g_3(P_{t-1}^d) + \varepsilon_t$	-86.1	-68.1	-128.8	-97.7
$D_t = b_0 + g_1(D_{t-1}) + g_2(T_{t-1}^l) + g_3(P_{t-1}^d) + \varepsilon_t$	-85.0	-68.3	-137.9	-98.35
$D_t = b_0 + g_1(D_{t-1}) + g_2(T_{t-1}^h) + g_3(P_{t-1}) + \varepsilon_t$	-105.1	-69.1	-136.2	-103.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(T_{t-1}^l) + g_3(P_{t-1}) + \varepsilon_t$	-104.3	-69.7	-132.3	-103.4
$D_t = b_0 + g_1(D_{t-1}) + g_2(T_{t-1}^a) + g_3(P_{t-1}) + \varepsilon_t$	-104.7	-69.8	-133.7	-103.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(P_{t-1}^d) + \varepsilon_t$	-91.4	-70.0	-145.1	-114.6
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + g_3(P_{t-1}) + \varepsilon_t$	-88.2	-72.6	-139.4	-110.8
$D_t = b_0 + g_1(D_{t-1}) + g_2(V_t^a) + \varepsilon_t$	-92.0	-74.6	-150.7	-117.5
$D_t = b_0 + g_1(D_{t-1}) + g_2(P_{t-1}^d) + \varepsilon_t$	-95.7	-76.2	-162.5	-119.1
$D_t = b_0 + g_1(D_{t-1}) + g_2(P_{t-1}) + \varepsilon_t$	-98.9	-80.1	-149.9	-125.7
$D_t = b_0 + g_1(D_{t-1}) + \varepsilon_t$	-107.1	-85.7	--	-133.5

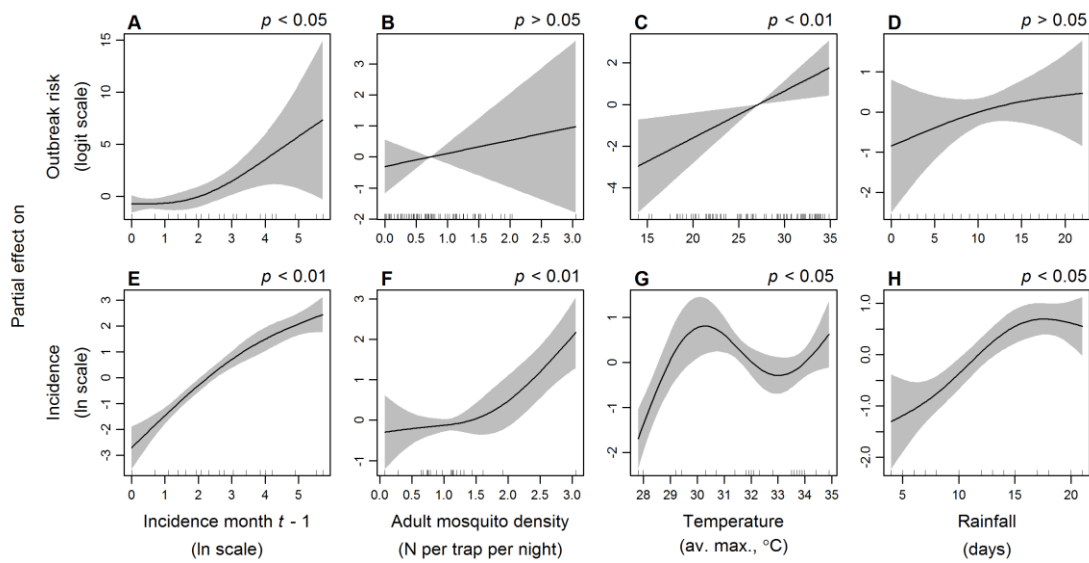
-- Model did not converge.

*The model used for predictions, which is also the model formulation selected by using the whole dataset.

Fig. S1. Test of zero-inflation. Histogram plots of monthly mosquito density and dengue incidence data.



- 1 **Fig. S2.** The initially selected ZIGAM of dengue incidence based on data from 2005
- 2 to 2012. The effect of average maximum temperature in panel G is likely over fitted.



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