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Joseph L. Servadio
Brown University School of Public Health

Samantha R. Rosenthal
Johnson & Wales University - Providence, Samantha.Rosenthal@jwu.edu

Lynn Carlson
Brown University

Cici Bauer
Brown University School of Public Health

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Climate patterns and mosquito-borne disease outbreaks in South and Southeast Asia

Joseph L. Servadio[a,b,*], Samantha R. Rosenthal[c], Lynn Carlson[d], Cici Bauer[a]

[a] Department of Biostatistics, Brown University School of Public Health, 121 South Main St., Providence, RI, USA
[b] Division of Environmental Health Sciences, University of Minnesota School of Public Health, 420 Delaware St. SE, Minneapolis, MN, USA
[c] Department of Epidemiology, Brown University School of Public Health, 121 South Main St., Providence, RI, USA
[d] Geological Sciences, Brown University, 85 Waterman St., Providence, RI, USA

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ABSTRACT

Background: Vector-borne infectious diseases, particularly mosquito-borne, pose a substantial threat to populations throughout South and Southeast Asia. Outbreaks have affected this region several times during the early years of the 21st century, notably through outbreaks of Chikungunya and Dengue. These diseases are believed to be highly prevalent at endemic levels in the region as well. With a changing global climate, the impacts of changes in ambient temperatures and precipitation levels on mosquito populations are important for understanding the effects on risk of mosquito-borne disease outbreaks. This study aims to make use of a large data set to determine how risk of mosquito-borne infectious disease outbreaks relates to the highest monthly average temperature and precipitation for each year in South and Southeast Asia.
Methods: Generalized additive models were used in a marked point process to fit nonlinear trends relating temperature and precipitation to outbreak risk, fitting splines for temperature and precipitation. Confounding factors for nation affluence, climate type, and ability to report outbreaks were also included.
Results: Parabolic trends for both temperature and precipitation were observed relating to outbreak risk. The trend for temperature, which was significant, showed that outbreak risk peaks near 33.5 °C as the highest monthly average temperature. Though not significant, a trend for precipitation was observed showing risk peaking when the highest monthly average precipitation is 650 mm.
Conclusions: Peak levels of temperature and precipitation were identified for outbreak risk. These findings support the notion of a poleward shift in the distribution of mosquitoes within this region rather than a poleward expansion in geographic range.

Introduction

Vector-borne infectious diseases infect over a billion people each year, contributing to over a million deaths globally [1]. Developing nations and low socioeconomic status groups are particularly vulnerable [1]. Recent resurgences in vector-borne diseases and concerns of global climate change have together prompted questions regarding their potential relationship [1,2]. The pathogens and parasites that cause these diseases as well as the insect vectors that transmit them exhibit sensitivity to levels of temperature and precipitation; these relationships are likely to be confounded by socioeconomic and geographic factors [3].

Among vector-borne outbreaks, mosquito-borne outbreaks occur with the highest frequency [4]. Common diseases transmitted by the *Aedes* or *Anopheles* genera include Chikungunya, malaria, and dengue [1–4]. As a result, infectious diseases transmitted by mosquitoes are of particular interest to researchers. Mosquitoes are known to breed in warm, wet regions, motivating interest in investigating their sensitivity to temperature and precipitation patterns.

Previous work has found that higher temperatures are associated with outbreaks, but the complex dynamics between the environment, vectors, and disease transmission warrant careful research [5–8]. In particular, ranges in temperature and extreme temperature effects may affect the ability of mosquitoes to effectively transmit disease pathogens [3]. Diurnal temperature ranges have been found to be more important than average temperatures when examining the development and transmission of malaria

* Corresponding author at: University of Minnesota School of Public Health, 420 Delaware St. SE, Rm 1225, Minneapolis, MN 55455, USA.
E-mail addresses: joseph_servadio@alumni.brown.edu (J.L. Servadio), samantha_rosenthal@brown.edu (S.R. Rosenthal), lynn_carlson@brown.edu (L. Carlson), cici_bauer@brown.edu (C. Bauer).

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parasites [9–11]. These findings indicate that patterns in climate besides average levels should be used to properly investigate the impact of climate change on mosquito-borne diseases. Similarly, extreme levels of precipitation have been indicated to be more useful than average precipitation. Events such as flooding or the drying of riverbeds has been demonstrated to bear a greater impact on the life cycles of the vectors and the incubation of the parasites [12]. Due to the various mechanisms by which climate and outbreak risk can interact, nonlinear trends are likely to exist [5,7]. These notions lead to interest in how maxima may relate to disease outbreaks.

The continent of Asia has been identified as a particularly vulnerable region for mosquito-borne infectious diseases, particularly South and Southeast Asia [13]. In addition to its high vulnerability to mosquito-borne outbreaks, this region exhibits heterogeneity in socioeconomic factors that may confound this relationship as well as similarities in baseline climate [14–16].

Nations in South and Southeast Asia have experienced large outbreaks of mosquito-borne infectious diseases, commonly Chikungunya and dengue. Laos experienced large outbreaks of dengue in 2010 and 2013 [17]. Thailand experienced high incidences of dengue in 2001, 2002, and 2010. During these three years, the incidence was 50 percent higher than the average throughout the ten-year period [18]. Between 2000 and 2001, Laos experienced over 800,000 cases of dengue [18]. Chikungunya outbreaks were observed in India between 2005 and 2008, Sri Lanka in 2006, Malaysia in 2006 and 2008 [19], and Thailand between 2008 and 2009 [19,20]. Nearly all adults over the age of 45 in Thailand are seropositive for dengue, and approximately half are seropositive for Chikungunya [21]. Furthermore, Zika virus has been detected in humans in Cambodia in 2010 and in the Philippines in 2012, and in Indonesia in 2014 [22].

This study aims to investigate the relationships between maximum monthly temperature and precipitation and risk of mosquito-borne infectious disease outbreaks in South and Southeast Asia. Previous work has isolated specific diseases and small regions, without combining data for multiple diseases transmitted by an entire taxonomic family of vectors [5–12]. Combining multiple diseases would require the use of a comprehensive data source that provides adequate outbreak information. In the absence of a large database, past work has focused on data from prevalence estimates or textual records of first occurrence of pathogen emergence [14,23]. Such studies have suggested considering nonlinear trends [5,7], shown that increases in temperature are associated with increased risk of mosquito-borne diseases [6,8], and indicated that average temperatures are not ideal indicators [9–11].

This study attempts to combat this lack of big data solutions by using a large global database of infectious disease outbreaks. This database consists of records between 1980 and 2013, documenting over 12,000 outbreaks globally [4,14]. The data, combined with climate data for temperature and precipitation, were used in concert with covariates believed to confound the relationship between the climate variables and disease outbreak risk. The findings of this study not only add to the existing literature relating temperature and precipitation levels to risk of mosquito-borne diseases, but also demonstrate the use of large data sets to aggregate outbreak data by a common vector in a broader region.

Methods and materials

Outbreak data

The Global Infectious Disease and Epidemiology Online Network (GIDEON) compiles published reports of infectious disease outbreaks, recording information such as disease, transmission vector, country, year, and number of cases. GIDEON defines outbreaks when they are specified as such in source literature, when observed as a cluster or grouping of cases, or if citations of animal disease are specified [4]. The textual records of outbreaks were previously transformed with a bioinformatics pipeline into an accessible, published database containing records of outbreaks between 1980 and 2013 [14]. Mosquito-borne disease outbreak records occurring in South and Southeast Asia were selected for analysis. The nations included were: Bangladesh, Cambodia, India, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Thailand, and Vietnam. Fig. 1 displays the region of analysis as well as locations of all mosquito-borne outbreaks observed.

Each mosquito-borne disease outbreak record was manually reviewed and its specific location, i.e. city or town of a reported outbreak, was captured if reported. Latitude and longitude coordinate pairs were assigned to the outbreaks, representing the centroids of the reported outbreak locations.

Climate data

The University of East Anglia Climatic Research Unit (CRU) has compiled monthly climate data, including average temperature in degrees Celsius and precipitation in millimeters, from over 4000 weather stations worldwide [24]. Data were compiled into geographic grids of $0.5 \times 0.5^{\circ}$ of latitude and longitude. Cleaned data were available between 1970 and 2009. These grids provided the units for analysis.

Disease outbreaks were assigned to the grids containing the reported outbreak coordinates. Only CRU geographic grids associated with at least one disease outbreak between 1980 and 2009 were included in the analysis to ensure that grids where outbreaks cannot occur, including uninhabited regions, were excluded from analysis.

To conform to the yearly outbreak data, the monthly CRU data were transformed to yearly measurements by using the maximum of the 12 monthly averages to represent the maximum monthly average for each year. These maximum monthly averages were created for both temperature and precipitation. Each year is represented by the month with the highest mean temperature and with the highest mean precipitation.

Country-level covariates

World Bank and Freedom House data were used to obtain country-level covariates that potentially confound the effect of climate on outbreak risk. These confounders may represent dynamics of mosquito-borne disease transmission or outbreak reporting. They are: population density (persons per square kilometer), gross domestic product (2013 US dollars), and press freedom (free, partially free, not free) [14–16,25]. Historical data were collected for the years 1980 through 2009.

Missing values for these covariates were singly imputed for all world nations using a Bayesian implementation of cubic B-splines. Worldwide nations were grouped based on geographic location and groupings in publications from the World Bank [16] and United Nations [26]. Within each group, Bayesian spline models were fit to impute missing values based on trends in nations with similar socioeconomic statuses. Details of the imputation can be found in the Supplementary materials. Imputation was desired rather than finding alternate data sources in order to maintain consistency of data sources.

Bands of latitude

Another potential source of confounding was the variability in typical climates found throughout the study region. Not all points in analysis are within the tropics, leading to differences in sea-

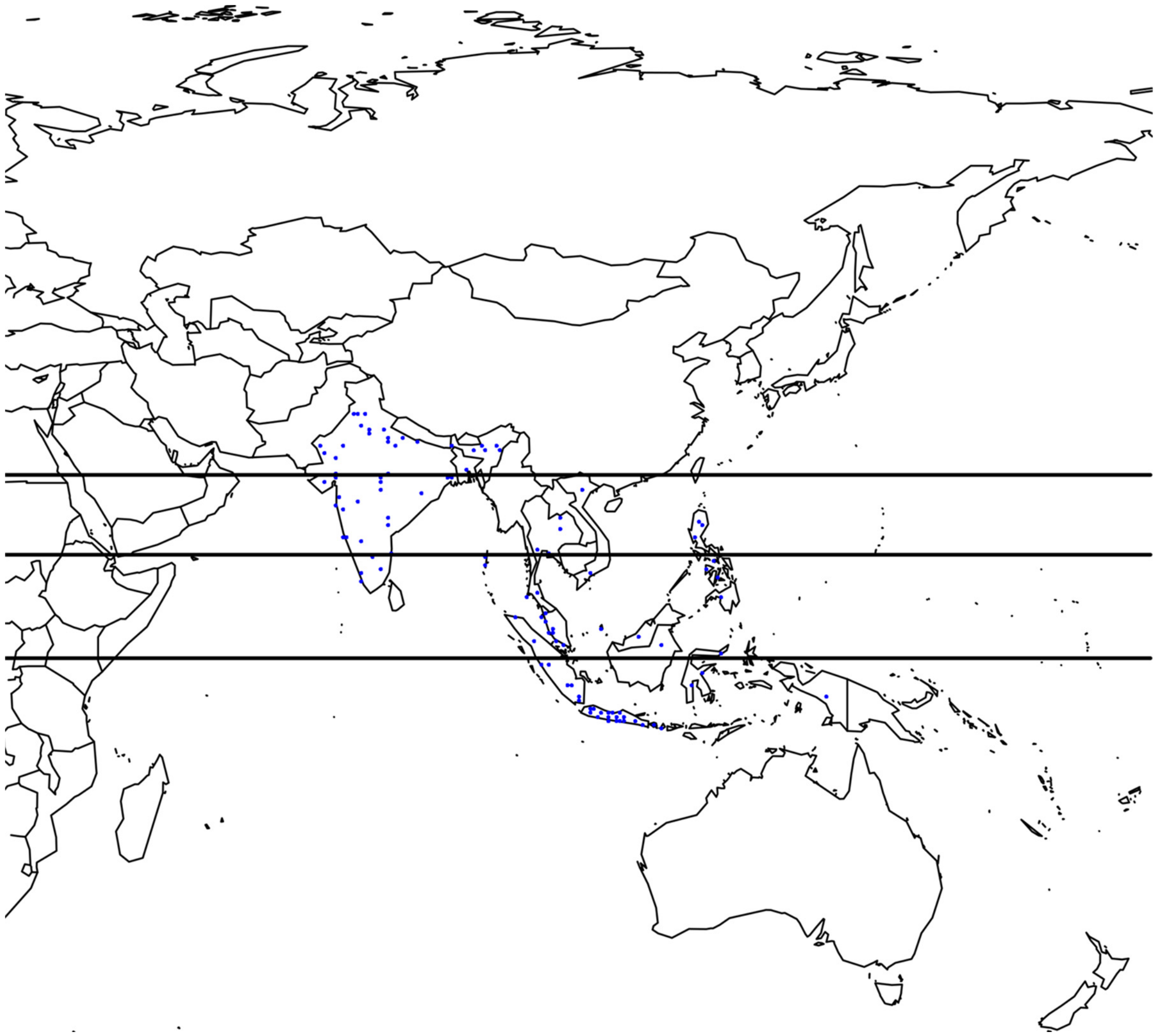

Fig. 1. Region of analysis and points with reported mosquito-borne disease outbreaks between 1980 and 2009. Latitude bands are shown that were used in analysis.

sons throughout the region. Latitude bands were constructed such that points within and outside the tropics were separated and that bands contained similar numbers of points. The bands created spanned from 9° South to the equator, from the equator to 13° North, between 13° North and 23° North, and between 23° North and 31° North. The extreme boundaries, 9° South and 31° North, represent the extreme observed latitudes. The northernmost band contains all points above the Tropic of Cancer. The latitude bands are shown in Fig. 1.

Statistical analysis

A marked point process generalized additive model with a logit link was used to analyze the data. To preserve statistical power, missing covariate data were first imputed as described in Section "Country-level Covariates".

Analyses were performed using R version 3.2.0 [27]. A generalized additive model (GAM) with P-splines for temperature and precipitation evaluated nonlinear relationships between the probability of mosquito-borne disease outbreak occurrence and maximum temperature and precipitation [28]. Spline models were selected over linear models as the former provide greater flexibility, allowing nonlinear trends to be fit.

One model was fit, including both splines for temperature and precipitation. Also included in the model were the confounders described in Section "Country-level Covariates", the latitude bands described in Section "Bands of Latitude", and the year of observation. The model was constructed using the R package 'mgcv' (Mixed GAM Computation Vehicle) 1.11 [29]. The response variable was an indicator for the occurrence of an outbreak in each grid in each year. Because it was uncommon to observe multiple outbreaks in the same CRU grid in one year, single and multiple outbreaks in a grid in a year were collapsed. Of the point-years used in analysis, approximately six percent had occurrence of an outbreak. To account for the large number of zero values, this response variable was specified to be quasi-binomial rather than binomial.

Splines were generated using the 'ps' smoother option in the 'mgcv' package. Four inner knots spanning the study time period were used for both splines; the number of knots was chosen to allow flexibility while avoiding over-fitting. To assess sensitivity to knot choices, models with three, five, and six inner knots were tested and showed minor variations in the shape of the relationship. F statistics testing a zero effect of each smoother term were used to determine the significance of the relationships between outbreak risk and the maximum temperature and precipitation.

Results

Between 1980 and 2009, 105 unique points contained at least one outbreak. Of the point-years that contained an outbreak, 167

Table 1
Mosquito-borne infectious disease, principal vector, agents, and number of observed outbreaks in study region between 1980 and 2009.

Disease	Principal vector	Agent	Number of outbreaks
Chikungunya	*Aedes* spp. mosquito	Chikungunya virus	103
Dengue	*Aedes* spp. mosquito	Dengue virus	64
Malaria	*Anopheles* spp. mosquito	*Plasmodium* spp.	35
West Nile Fever	Mosquito	West Nile virus	1

Table 2
Descriptive statistics for maximum temperature and maximum precipitation between 1980 and 2009.

	Maximum temperature	Maximum precipitation
Min	23.00	5.90
5%	24.50	168.19
10%	26.00	221.16
25%	27.40	313.75
50%	28.70	406.05
75%	31.60	529.93
90%	33.90	678.03
95%	34.60	803.56
Max	37.10	1417.00
Mean	29.38	435.20
Sd	2.97	191.89

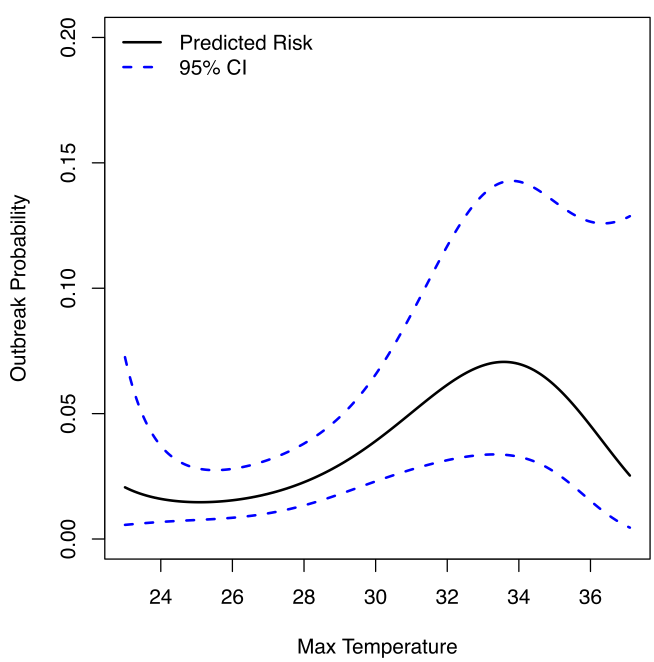

Fig. 2. Maximum average monthly temperature and probability of a mosquito-borne disease outbreak.

contained a single outbreak, and 18 contained two outbreaks, including instances where the same disease was reported twice in a point during a year. Table 1 shows the diseases observed in the region. The maximum temperature and precipitation data did not contain anomalous observations. Table 2 shows descriptive statistics for these data.

Temperature

A nonlinear relationship was observed between maximum temperature and outbreak probability. Fig. 2 shows the fitted relationship, which is parabolic peaking at temperatures near 33.5 °C. At temperatures above or below this value, outbreak risk is lower.

The mgcv package calculates F statistics to test spline terms for a zero effect. The temperature spline term was found to be significantly different from a zero effect ($p = 0.0085$).

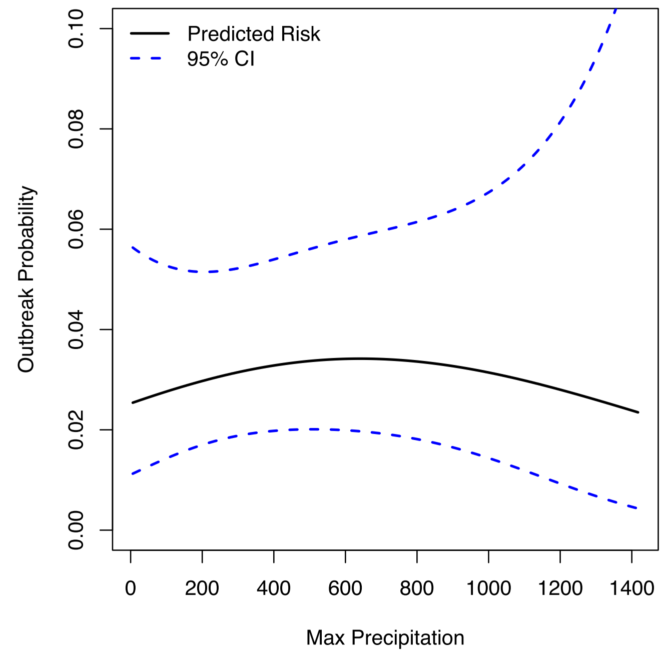

Fig. 3. Maximum average monthly precipitation and probability of a mosquito-borne disease outbreak.

Precipitation

The relationship between maximum precipitation and outbreak probability, shown graphically in Fig. 3, is also parabolic. The maximum estimated outbreak risk occurs near 650 mm of precipitation, with decreases in outbreak risk as precipitation deviates from these values. This spline term was not found to be significant ($p = 0.7871$).

Discussion

Summary of findings

This study aimed to investigate relationships between climate patterns and risk of mosquito-borne disease outbreaks using a large historical database. Prior studies that used mean climatic values or focused on small geographic regions, one vector, or one disease, have highlighted the need for expanded spatiotemporal analysis [6,30,31]. The existence of online disease outbreak reporting and computational feasibility with large data sets permit exploration of large-scale associations between climate and mosquito-borne disease outbreaks.

The finding of a statistically significant parabolic association between maximum average monthly temperature and mosquito-borne disease outbreak risk adds to the literature regarding the complicated interaction of temperature and disease: while warming at lower temperatures may increase vector and pathogen proliferation, warming at higher temperatures may decrease vector-borne disease outbreaks [5,7].

This parabolic association is consistent with previous findings concerning the life cycles of mosquitoes. Increasing lower temperatures has been suggested to lead to increases in mosquito populations, and increasing higher temperatures has been suggested to lead to population decreases [32–35]. This has been studied in *Aedes albopictus*, a known dengue vector. When temperatures become too high, the length of the mosquitoes' life cycle shortens, potentially to where it is too short to fully incubate dengue fever [32]. This has also been reported in *Aedes aegypti* [33]. This common malaria, dengue, and Chikungunya vector was found to have maximum development rate at temperatures between 28 and 32 °C and showed inhibited development above this range. These disruptions are seen at egg, larval, and adult stages [34]. Additionally, very few or even no mosquitoes survive long enough to incubate malaria at temperatures under 18 °C or over 34 °C, and no mosquitoes were able to develop into adulthood at these temperatures [34,35]. The mosquitoes' responses to both high and low temperatures support the notion of a parabolic trend. Temperatures may also impact parasites and pathogens, such as malaria parasites, which cannot develop at temperatures above 39 °C [33].

The results from these studies align with the result of the current study, suggesting that there exist temperature ranges that are too high for effective transmission of mosquito-borne diseases, whether through the inability of the mosquitoes to incubate the diseases or through an inability for the parasites or pathogens to develop within the mosquitoes. Other studies on this topic do not consider these high temperatures, considering narrower temperature ranges and linear associations [36–38]. Such studies have found significant associations between higher temperatures and dengue prevalence when only considering temperatures under 34 °C [36] and faster incubation of dengue at 30° compared to 26 or 28° [37].

The lack of significant trends for precipitation prompts questions regarding the ability of maximum precipitation to explain mosquito-borne outbreak risk. Previous work attributes precipitation levels sustained among several months to outbreak risk [35] rather than precipitation in one month. It is also possible that decreased precipitation does not necessarily lead to decreases in outbreak risk. In Indonesia in 1997, a drought allowed *Anopheles punctualus* to breed along the edges of rivers that were previously inhospitable. This drought was associated with a malaria epidemic [33]. During times of decreased rainfall, human activities such as more diligent water collection can increase standing water available to mosquitoes, providing breeding grounds [38,39]. Increased precipitation may also inhibit transmission of these diseases, as heavy rainfall may destroy breeding areas for mosquitoes and kill larvae [38]. Other work on the topic has shown that linear associations between precipitation and disease risk show inconsistencies, even when examining the same country [40]. It is likely that relationships between precipitation and mosquito-borne disease outbreak risk are not characterized well by yearly trends.

These findings support previous claims that climate change can lead to shifts in geographic regions affected by vector-borne outbreaks rather than simple expansion [7,32]. It was previously believed that rising global temperatures would lead to poleward expansions of the vectors' habitats. Others argued that the expansion would also be accompanied by fewer outbreaks in regions that become inhospitable for vectors and reservoirs [7]. These findings support the latter claim, suggesting that higher maximum monthly temperatures may lead to fewer outbreaks of mosquito-borne diseases.

Limitations

Data on mosquito-borne outbreaks originated from aggregated published reports and may be subject to reporting biases, motivating the use of the confounding covariates. Some diseases classified as mosquito-borne may be also transmitted directly, as indicated in Table 1. Differences in outbreak severity (e.g. mortality, severity of infection, or number of cases) were not incorporated. Outbreak data were reported with the year of occurrence, requiring analysis at low temporal resolution.

The months in which the maxima occurred were not considered. These months may not be important to mosquitoes' life cycles, making their values less directly relevant. Rather than using the highest monthly average, measurements from specific months may be advantageous. Selecting specific months may also control for human behavior, as season changes affect time spent outdoors and susceptible to mosquito bites [33]. Using data with a finer temporal resolution may prove advantageous. Studies using monthly data investigated lagged effects of temperature and precipitation [38].

Conclusions

Utilizing a large, structured database of reported mosquito-borne disease outbreaks from 1980 to 2009, this study found a significant parabolic association between maximum average monthly temperature and mosquito-borne disease outbreak risk in South and Southeast Asia. Climate change will continue to impact the resurgence and reemergence of vector-borne diseases in concert with a multitude of epidemiological, ecological and socioeconomic factors. These results support the theories of a shift, rather than an expansion, in the world regions most susceptible to mosquito-borne disease outbreaks. Analyzing large historical data is essential to understanding how climate change and other variables contribute to future outbreaks. While much previous work relies on localized analyses and conclusions, aggregating diseases and regions allows global conclusions to be drawn, increasing their impact.

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Competing interests

None declared.

Ethical approval

Not required.

Author contributions

JLS and CB designed the study. LC acquired data, geocoded outbreak locations, and cleaned climate data. JLS, SRR, and CB developed the analytic plan and conducted data analysis. JLS, SRR, and CB prepared the manuscript for publication.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jiph.2017.12.006.

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