Effects of climatic and social factors on dengue incidence in Mexican municipalities in the state of Veracruz

Grea Litai Moreno-Banda, PhD, MSc,[(1)] Horacio Riojas-Rodríguez, MD, MSc, PhD,[(1)]
Magali Hurtado-Díaz,MSc,[(1)] Rogelio Danis-Lozano, PhD, MSc,[(2)] Stephen Joel Rothenberg, PhD.[(1)]

Abstract

Objective. To assess links between the social variables and longer-term El Niño-Southern Oscillation (ENSO) related weather conditions as they relate to the week-to-week changes in dengue incidence at a regional level. **Materials and methods**. We collected data from 10 municipalities of the Olmeca region in México, over a 10 year period (January 1995 to December 2005). Negative binomial models with distributed lags were adjusted to look for associations between changes in the weekly incidence rate of dengue fever and climate variability. **Results**. Our results show that it takes approximately six weeks for sea surface temperatures (SST -34) to affect dengue incidence adjusted by weather and social variables. **Conclusion.** Such models could be used as early as two months in advance to provide information to decision makers about potential epidemics. Elucidating the effect of climatic variability and social variables, could assist in the development of accurate early warning systems for epidemics like dengue, Chikungunya and Zika.

Keywords: dengue; disease vectors; El Nino-southern oscillation; climate; time series studies

Resumen

Objetivo. Evaluar los vínculos entre las variables sociales y las condiciones climáticas de largo plazo relacionadas con El Niño-oscilación del sur (ENOS) y con los cambios semanales en la incidencia del dengue a nivel regional. **Material y métodos**. Los datos fueron recolectados en diez municipios de la región Olmeca, México, durante un periodo de 10 años (enero de 1995 a diciembre de 2005). Se ajustaron modelos binomial negativo con rezagos distribuidos para evaluar las asociaciones entre los cambios en la tasa de incidencia semanal de dengue y la variabilidad climática. **Resultados.** Se requieren aproximadamente seis semanas para observar un efecto del incremento de la temperatura de la superficie marina (TSM -34) sobre la incidencia de dengue, ajustando por variables de tiempo y variables sociales. **Conclusiones.** Estos modelos se pueden usar con dos meses de antelación para proveer de información a tomadores de decisión sobre potenciales epidemias. Elucidar el efecto de la variabilidad climática en conjunto con las variables sociales puede favorecer el desarrollo de los sistemas de alerta temprana ante epidemias como dengue, Chikungunya y Zika.

Palabras clave: dengue; vectores de enfermedades; El Niño oscilación del sur; clima; estudios de series de temporales

(1) Instituto Nacional de Salud Pública. Cuernavaca, México.
(2) Instituto Nacional de Salud Pública. Tapachula, México.

World Health Organization recognizes dengue fever (DF) as the fastest spreading tropical disease across the world, with approximately three billion people at risk of contracting dengue virus.[1] Different studies estimated more than 400 million cases of classic dengue and 500 thousand cases of dengue hemorrhagic fever registered, with mortality reaching 5% in the latter.[2,3]

Local climate and the El Niño-Southern Oscillation (ENSO) play a key role in the ecology and biology of mosquito vectors and the viruses they transmit, and consequently have a strong influence on the risk of dengue transmission.[4-19]

Precipitation changes may create larger or new habitats for mosquito larva, increasing vector populations.[7,20-23] Ambient temperatures influence rates of mosquito larval development,[24,25] adult biting activity,[26] [27] the gonotrophic cycle,[28] and reduction of the extrinsic incubation period.[29]

ENSO has an influence on the global climate system, especially over the tropics, through inter-annual variations in atmospheric circulation, temperature and precipitation at different distant locations, which is termed teleconnection.[20,30] These are the theoretical causal mechanisms linking ENSO with dengue in certain geographical regions.

It is generally understood that dengue is a climate-sensitive disease. However there are serious knowledge gaps in understanding the complex relationship between these teleconnections, weather, social factors and DF. This gap has continued to date and the factors that determine whether epidemic transmissions will occur are complex.

There is evidence that increase in air temperature, sea surface temperatures (SST), rainfall and ENSO have been associated with increased DF in some regions.[5,6,15,31,32] Dengue transmission in warm and humid regions of México has been shown to be a strongly associated with ENSO and weather variables.[8,9,12,14] Less is known about the relation with cultural and social factors (social backwardness, the lack of water access and the use of uncovered water tanks not using mosquitoes nets, the lack of health services and health education), which also play an important role in the prevalence of the disease.[9,33,34] Also unplanned urbanization and inadequate resources for vector control are factors that promote transmission and are characteristic of poor countries. In México, Hurtado and colleagues found[14] that these dengue control activities increased only after a rise in dengue cases. Reiter and colleagues[35] studied dengue transmission on the Mexico-USA border and found higher rates in the Mexican city compared to the American one. Also, Brunkard and colleagues[36] made a cross-sectional serosurvey in Brownsville, Texas, and its cross-border neighbor Matamoros, Mexico. Their results show that low income across both cities was the dominant risk factor for dengue infection, highlighting the importance of identifying and assessing the effects of social factors in analyses of inter-annual variability.

In 2005, the Mexican national rate of classic dengue morbidity was 16.3 per 100 000 inhabitants, however, in the state of Veracruz the rate was 53.5 per 100 000 inhabitants.[37] The occurrence of epidemic classical dengue, hemorrhagic dengue and dengue shock syndrome in the Americas make this vector borne disease an important public health concern.

Study objectives

The aim of this study was to assess linkages between weekly incidence rate of dengue and climate variability adjusted by weather and social variables. We analyzed a larger geographical area compared to studies that focused on small areas by including data from 10 municipalities of the Olmeca region in Veracruz State and only considered sero-confirmed weekly dengue cases.

Materials and methods

Data

We used a negative binomial model (NBM) to evaluate the role of climatic and social variables on dengue incidence over a ten year period (1995-2005) using dengue cases, registered weekly by the health jurisdiction in ten municipalities with complete epidemiological and climatic data of the Olmeca region in the Veracruz state, during the 10 year study period.[12,14,38,39]

The Olmeca region is located in Veracruz State. It is the region with the highest surface area with 17 603.25 km^2 and consists of 25 municipalities. According to the 2010 census, the region had a population of 1 194 392 inhabitants (15.69% of the total population of the State). The Olmeca region lacks basic services: 30.6% of homes lack water utilities, 20.69% lack sewage facilities, and 52.26% of households suffer from overcrowding.[40]

We compiled daily weather data for maximum temperature, minimum temperature and rainfall, from the most representative (in terms of geographical location, altitude, temperature and rainfall) meteorological stations in the region operated by the National Meteorological Service.[41]

Weekly records for sea surface temperature (SST-34) for the 3.4 Niño region (5S-5N, 170W-120W) were obtained from openly available databases of the National Oceanic and Atmospheric Administration[42] of the United States Government.

The Unified Epidemiological Surveillance System (SUIVE) of the Health Ministry of the State of Veracruz[43] provided weekly epidemiological information on dengue cases from 1995 to 2005. We calculated weekly maximum temperature (maxT), minimum temperature (minT) and total accumulated weekly rainfall (r) corresponding with weekly epidemiological dengue reporting. All dengue case reports were serologically confirmed by the state lab (*Laboratorio Estatal de Salud Pública*) in Veracruz, Veracruz, México.

We obtained municipal population and population density (number of inhabitants per km² surface) data from the National Institute of Statistics and Geography (INEGI) for 1990, 1995, 2000 and 2005.[44-47] Information about the index of social backwardness and marginality was obtained from the National Council of Evaluation of Social Development Policy[48] and from the National Population Council,[49,50] which incorporates indicators of education, access to health services, basic services, quality and housing space, and assets at home from the same years. We used a polynomial regression to interpolate the weekly population and social variables (homes with dirt floor and population density) of the study area during the period of analysis to take into account historical population and social variable trends based on data from 1995 to 2005, from the every five year points given by the national census of the region.

Statistical analysis

The first step of the analysis examined temporal trends and seasonal variations of dengue cases, social variables (backwardness index, illiteracy, crowded housing, homes without electricity and homes with dirt floor), weather variables (maxT, minT, r) and the climate variable (SST-34), interpolated to each week in each of the 10 municipalities analyzed. For each municipality we used a model with minT and r as weather variables, SST-34 as climate variable, homes with dirt floor, population density and municipal population as social variables for each Municipality.

In a second step, we determined a lack of temporal trend (Dickey Fuller unit root test)[51] and we diagnosed serial correlation of Pearson residuals with autocorrelation and partial autocorrelation functions. We empirically reduced serial correlation by addition of lagged autoregressive Pearson residual terms to the series until the portmanteau Q statistic[52] indicated no significant auto or partial autocorrelation in the adjusted series.

One of the assumptions of ordinary least square regression models, that the multiple observations of the dependent variable be independent of one another, is usually violated in time series.[53] Knowledge of such correlation structures allowed us to determine an unbiased estimation.[54]

In a third step, we took into account different model assumptions and used penalized smoothing splines to seasonally adjust the model[55,56] fitting the spline function to the original series of dengue cases. We used restricted polynomial distributed lag models to verify the influence of exposure of climate and weather variables over previous weeks on incidence of dengue, avoiding multi-collinearity or correlated covariates[57] with orthogonal third-degree polynomials with up to 20 weeks of lag from SST-34 and 6 weeks of lag from minT and r, allowing weekly Incidence Rate Ratio (IRR) of dengue to be influenced by SST-34, minT and r over previous weeks. A distributed-lag model is a dynamical model in which the effect of a regressor x on y occurs over time rather than all at once.[58] The most common application of the polynomial distributed lag is restricting the lag coefficients to lie on a polynomial function. This imposes smoothness on the coefficients, but allows for considerable flexibility in the shapes of the lag distributions that it permits.[58]

Negative binomial models (NBM) were better than Poisson models for all localities analyzed as indicated by the significant over-dispersion statistic and by the Akaike Information Criterion. All the models were adjusted by social variables (homes with dirt floor and population density).

Finally, the predicted population size weekly series was added to each model to adjust dengue cases for changes in population over the period. Statistical calculations were done using Stata 14 (Stata Corporation, San Antonio, TX, USA).

Ethics

This is a study of secondary data, the names of individuals with confirmed cases were randomly assigned to a numerical identifier to allow anonymity of cases in the region. The ethics committee of the *Instituto Nacional de Salud Pública* (National Public Health Institute) approved the conduct of this research.

Results

We assigned a representative meteorological station to each municipality using criteria of nearest geographic location, altimetry, temperature and precipitation (figure 1).
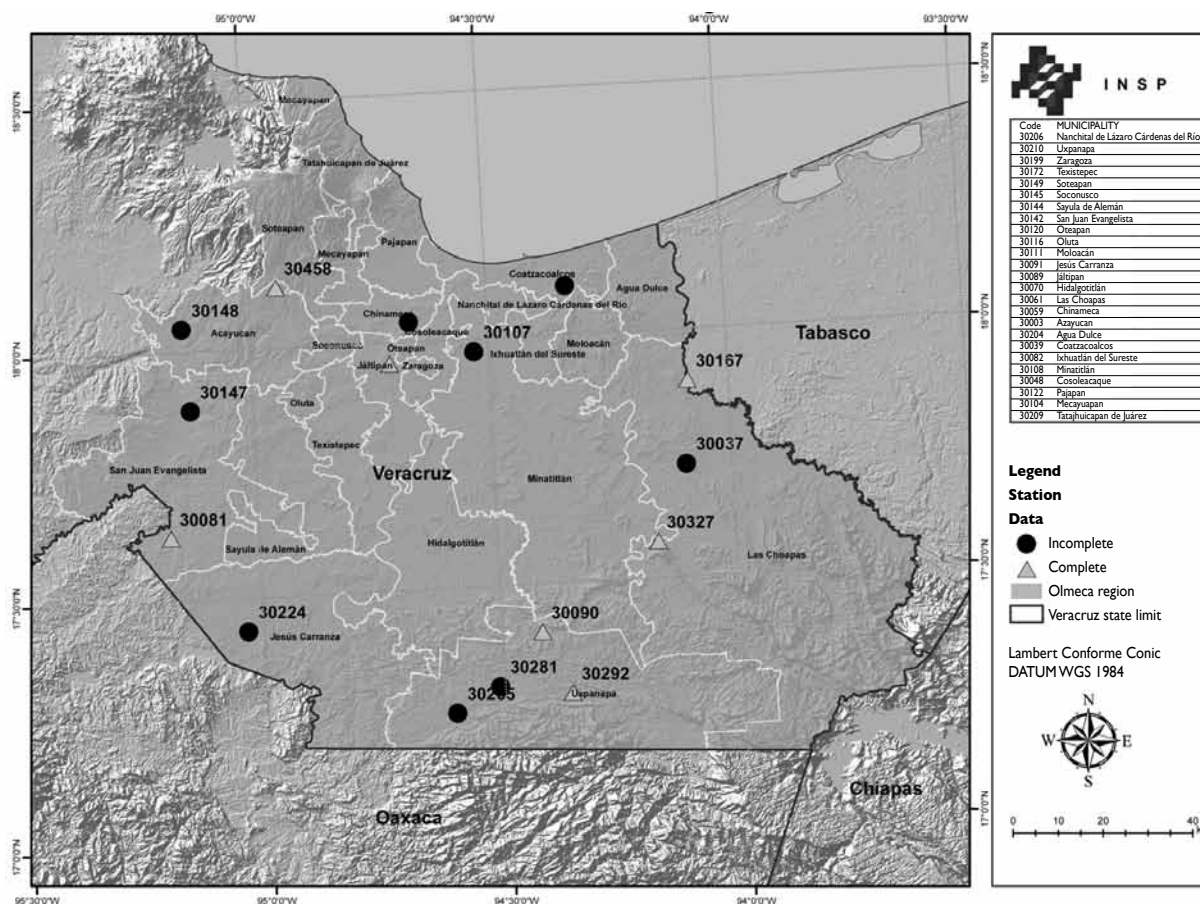
Figure 1. Location of weather stations in the Olmeca Region. Mexico

Climatic characteristics

The average maximum temperature recorded at stations for the municipalities located in the mountains was 30.4 to 33.6°C, with temperatures up to 43.1°C in municipalities at lower altitudes (<500 meters above sea level). Minimum temperature ranged from 9.8 to 14.2°C in all the municipalities. The highest cumulative weekly precipitation was found in the coastal municipalities and lowest in the central part of the study area (figure 2).

The highest SST-34 was recorded during the periods 1997–1998 and 2002–2003.

Dengue morbidity rates

Dengue has been present in the Olmeca region from at least 1995 to 2005 (table I). The municipalities of Mecayapan and Coatzacoalcos showed the highest rates of dengue fever (above 200 cases per 100 000 inhabitants). However in the municipality of Jesús Carranza there has been a considerable decrease in the rate of dengue over the study time period (figures 3a-3c).

Incidence Relative Risk (IRR) of weekly dengue cases

Analyzing the risk of dengue through NBM with distributed lags of minT, r and SST-34 as explicative variables adjusted by population density, population and homes with dirt floor, we found that all the municipalities showed increased dengue cases per 1°C increase in SST-34 with different distributed lags (between 0 to 6 weeks lag) (table II). However, only three municipalities had a significant increase: Acayucan shows an accumulated IRR of 1.89 (CI95%: 1.347, 2.670) over a 2 to 6 week lag; Mecayapan shows an accumulated IRR of 2.34
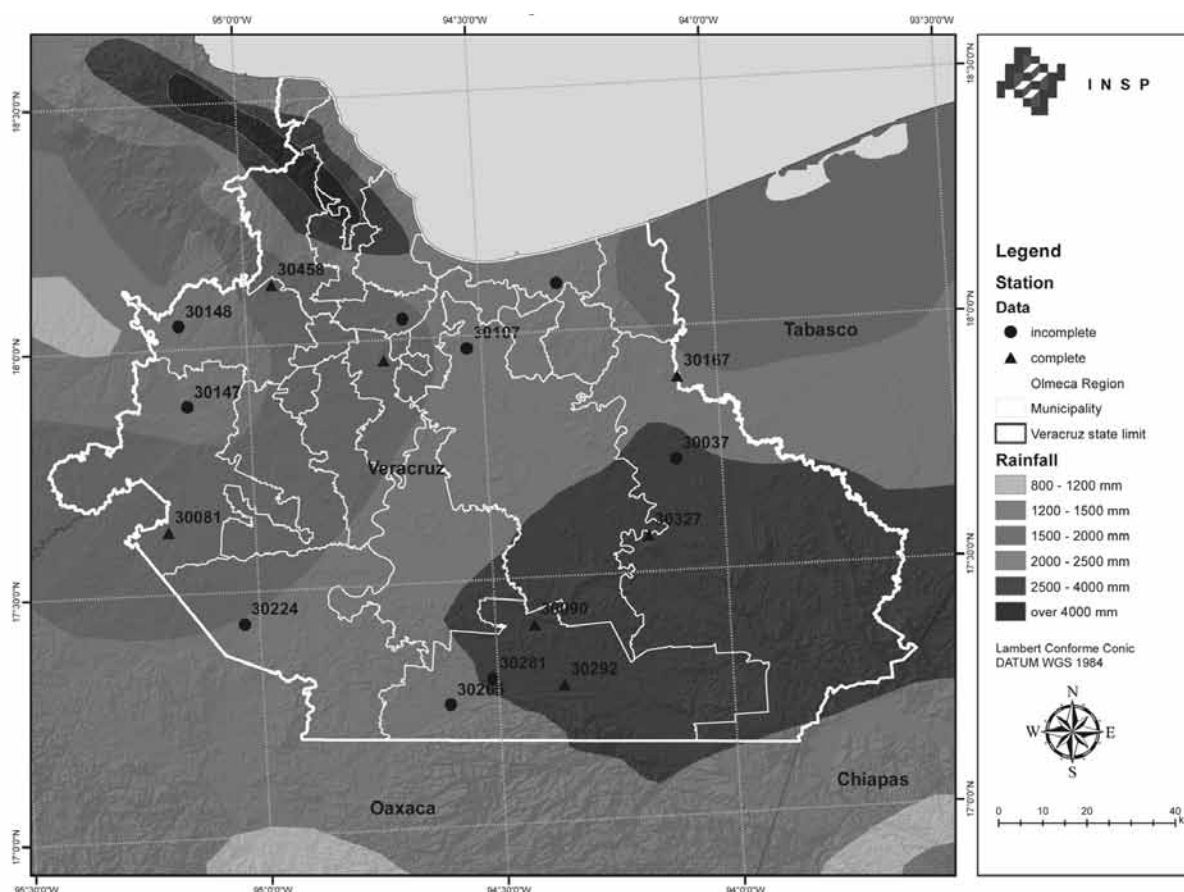
FIGURE 2. ANNUAL RAINFALL IN THE OLMECA REGION. MEXICO

Table I

TOTAL POPULATION AT THE BEGINNING AND END OF THE STUDY AND ACCUMULATED DENGUE CASES IN MUNICIPALITIES OF THE OLMECA REGION, 1995-2005. MEXICO

Municipality	Population 1995	Population 2005	Accumulated dengue cases
Acayucan	77 760	81 136	1 101
Coatzacoalcos	259 096	286 000	3 387
Cosoleacaque	64 796	107 710	297
Chinameca	13 912	14 200	52
Las Choapas	69 408	75 355	427
Jesús Carranza	23 845	28 936	136
Mecayapan	12 382	22 764	104
Minatitlán	139 584	202 965	1 477
Nanchital	26 665	27 256	707
Soteapan	26 967	29 314	70

(CI95%:1.310, 4.195) over a 3 to 6 week lag and Soteapan an accumulated IRR of 1.64 (CI95%: 1.149, 2.353) over a 2 to 3 week lag. All the models were adjusted by weather and social variables. Time series were plotted for SST-34 and dengue incidence to observe their behavior and patterns of seasonal and inter-annual variability (figure 4).

An increase in dengue cases for each 1% increase in homes with dirt floor was found in eight of the ten municipalities analyzed. Only three municipalities had a significant increase: Coatzacoalcos (IRR: 3.389, CI95%: 1.390, 8.260); Mecayapan (IRR: 1.199, CI95%: 1.022, 1.408) and Soteapan (IRR: 1.068, CI95%: 1.022, 1.225).

Discussion

Several of the municipalities in the study show sufficient rainfall all year to create year-round breeding sites.
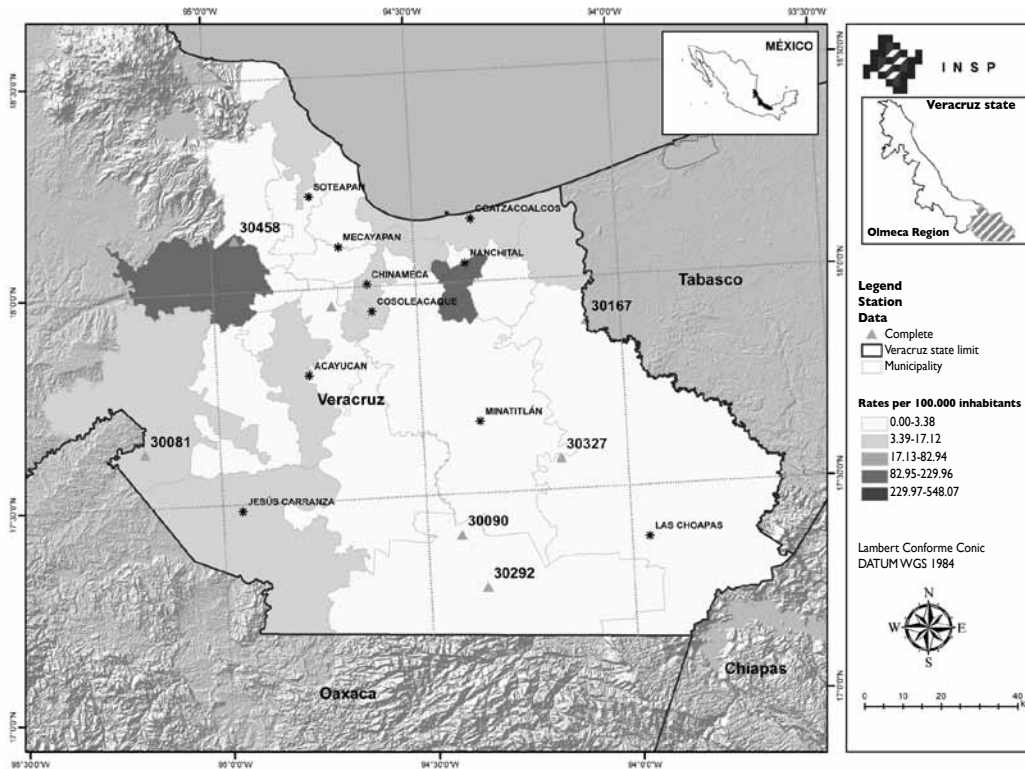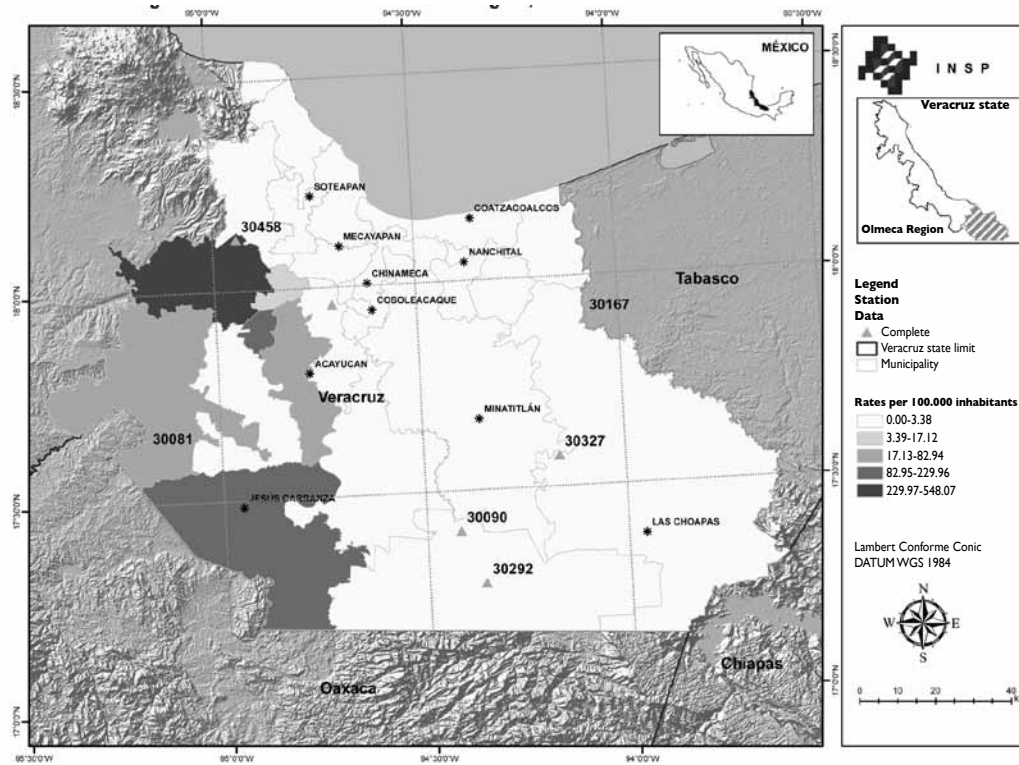
Figures 3a-3b. Dengue incidence rate in the Olmeca Region during 1995 and 2000. Mexico
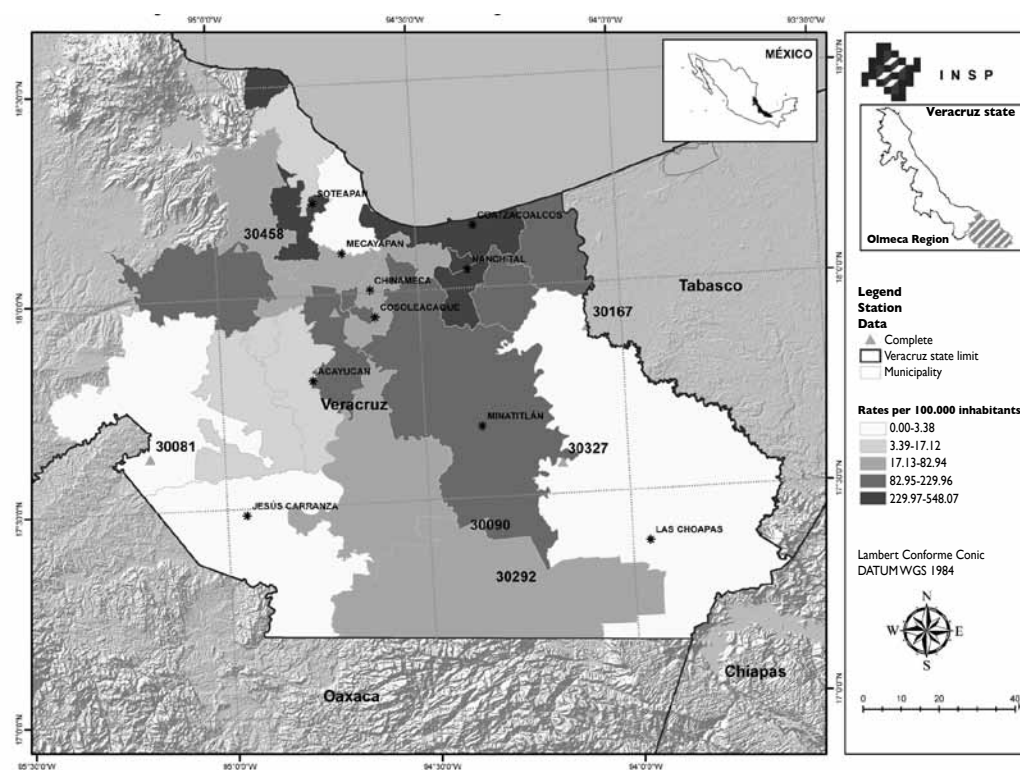
FIGURES 3C. DENGUE INCIDENCE RATE IN THE OLMECA REGION DURING 2005. MEXICO

Table II

INCIDENCE RATE RATIO OF WEEKLY DENGUE CASES IN TEN MUNICIPALITIES OF THE OLMECA REGION USING WEEKLY LAGS OF CLIMATE AND WEATHER, ALONG WITH SOCIAL FACTORS, 1995-2005. MEXICO

| Municipality	Minimum Temperature (°C)			Rainfall mm			Sea surface Temperature (3-4 Region) (°C)			Dirt Floor (%)		Population density Inhab/km2	
	Lag	IRR	CI 95%	Lag	IRR	CI95%	Lag	IRR	CI95%	IRR	CI95%	IRR	CI95%
Acayucan	0-2	0.962	0.814-1.137	4-6	1.098*	1.017, 1.185	2-6	1.896*	1.347, 2.670	1.071	0.952, 1.204	1.678*	1.093, 2.577
Coatzacoalcos	0-2	1.003	0.893, 1.126	0-2	1.007	0.952, 1.050	0-5	1.048	0.760, 1.444	3.389*	1.390, 8.260	1.061*	1.019, 1.104
Cosoleacaque	4-6	0.815*	0.701, 0.948	0-2	0.911	0.896, 1.104	2-6	1.320	0.855, 1.039	0.965	0.870, 1.070	0.997	0.987, 1.006
Chinameca	3	1.072*	1.006, 1.195	1	0.938*	0.884, 0.995	2-6	1.870	0.778, 4.492	1.016	0.912, 1.131	0.185	0.027, 1.262
Las Choapas	0-2	0.782	0.661, 0.924	3-6	1.165*	1.046, 1.298	2-6	1.538	0.842, 2.809	1.157	0.920, 1.454	0.219	0.047, 1.019
Jesús Carranza	3-6	1.389*	1.022, 1.888	0	1.078*	1.006, 1.154	2-6	1.152	0.641, 2.070	1.136	0.691, 1.867	0.219	0.036, 1.313
Mecayapan	1-2	1.999*	1.344, 2.974	4-6	1.094	0.981, 1.220	3-6	2.344*	1.310, 4.195	1.199*	1.022, 1.408	1.111*	1.011, 1.222
Minatitlán	4-6	0.857*	0.744, 0.987	0-2	1.035	0.944, 1.060	2-6	1.139	0.800, 1.622	0.943	0.865, 1.029	0.937*	0.902, 0.974
Nanchital	1-2	1.047	0.870, 1.260	0-2	1.011	0.935, 1.069	2-3	1.031	0.864, 1.231	1.351	0.313, 5.832	0.896*	0.805, 0.998
Soteapan	1-2	1.604*	1.090, 2.361	1-4	1.372*	1.189, 1.584	2-3	1.644*	1.149, 2.353	1.068*	1.022, 1.115	4.328*	1.614, 11.604

* p < 0.05

Lag= number of distributed week-lag
Note: All the models were adjusted by population
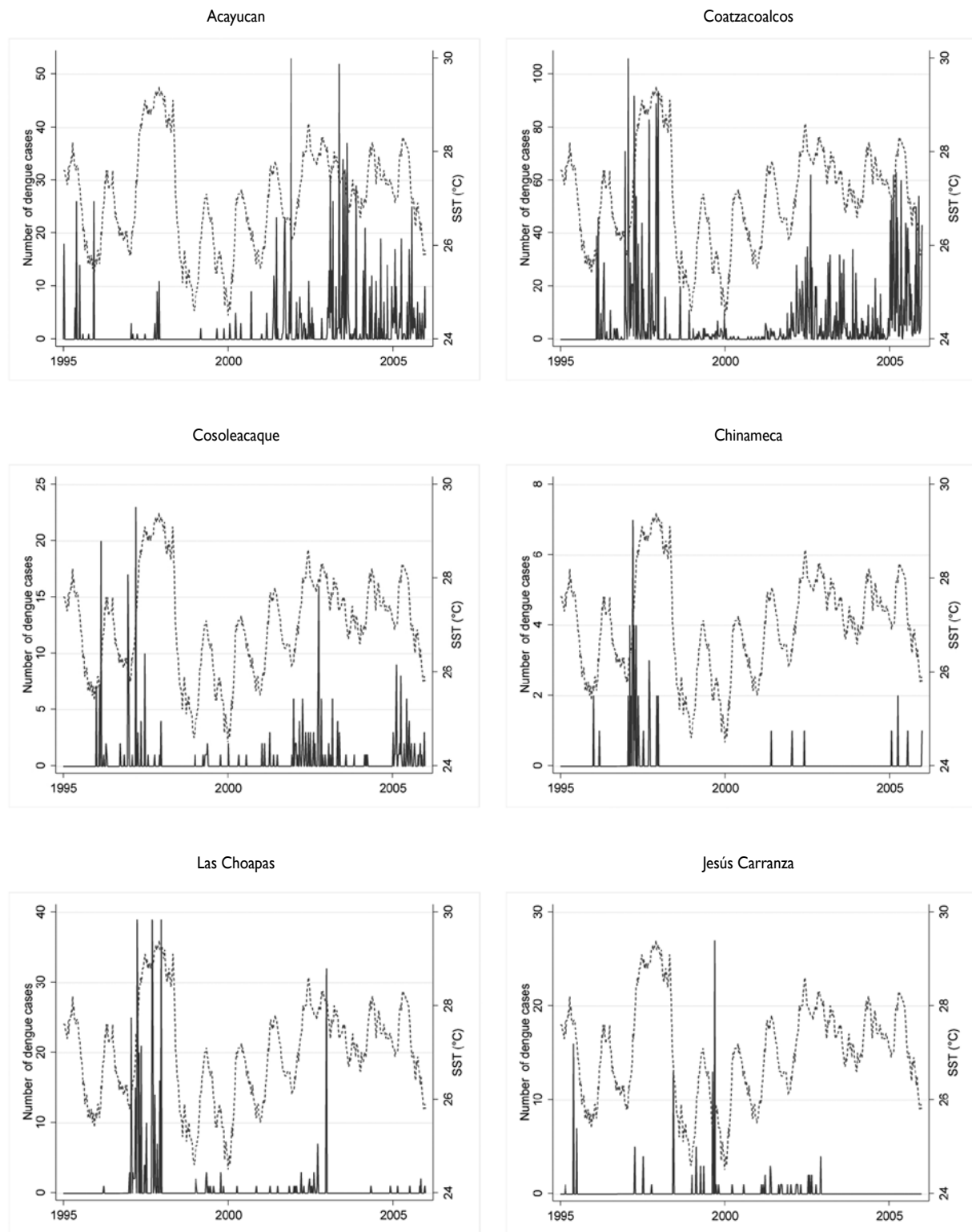
FIGURE 4. TIME SERIES OF DENGUE CONFIRMED CASES IN TEN MUNICIPALITIES OF THE OLMECA REGION AND PLOTS OF SEA SURFACE TEMPERATURE ANOMALIES (°C), REGION 3-4, DURING THE PERIOD 1995 TO 2005. MEXICO

(continues…)

(continuation)

Mecayapan

Minatitlán

Nanchital

Soteapan
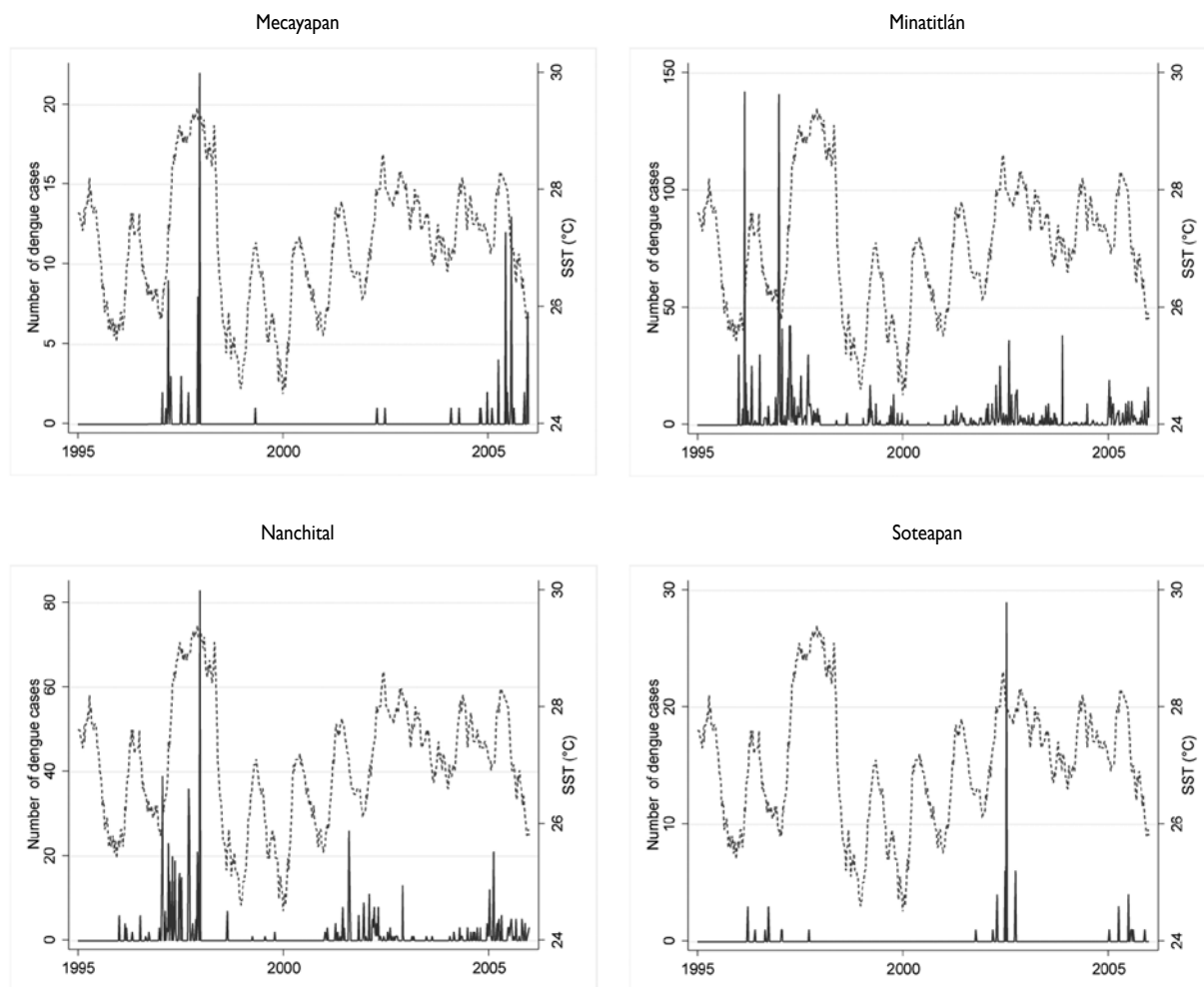
However dengue incidence is higher in municipalities with more population.

This finding corroborates previous studies in other world regions. For example, the strong association between weather variables and dengue found in Barbados at a lags of 6 to 16 weeks for vapor pressure and minimum and maximum temperature,[58] the highest correlation with total rainfall a lag of seven weeks in Taiwan,[59] and the strong positive association with absolute humidity in Thailand.[33]

Dengue incidence is sensitive to both periodic fluctuations and sustained changes in global and local climates, because vector biology and viral replication are dependent on temperature and moisture.[3] Nonetheless, the already published associations between dengue incidence and weather variables were more or less strong, depending in the approach of analysis and the study areas.

In México, Colón-González and colleagues[9] used multiple linear regression models to examine the associations between changes in the climate variability and dengue incidence in the warm and humid Mexican region. They demonstrated that dengue incidence was associated with the strength of El-Niño and the minimum temperature, especially during the cool and dry seasons.

Time series modeling approaches have been extensively applied in assessing the impact of climate variables on dengue incidence. For example Brunkard and colleagues[12] use an auto-regressive model to evaluate the role of climatic factors on dengue incidence in one Mexican border city and found that weather and climatic factors together play a small but significant role in dengue transmission in that Mexican city. Hurtado-Díaz and colleagues[14] used time-series analysis with auto-regressive models to examine the impact of SST-34

on probable cases of dengue in two municipalities of Veracruz State. They suggested that increases in SST (with 16 and 20 week-lag), temperature and rainfall were followed by increased dengue cases. In these examples, they do not include factors that impact dengue transmission like social and demographic changes, economic status, human behavior and education.

Our study differs from previous efforts in Mexico because we used a binomial negative regression model appropriate to the count nature of dengue cases. We also used distributed lags that allowed us to find differential lag effects following SST-34 that were statistically associated with increased dengue incidence. All models were adjusted for the distributed-lag effects of minimum temperature and rainfall and by social variables (homes with dirt floor, population density and total population).

In addition, we modeled weekly incidence aggregates instead of monthly. The temporal resolution of our models is higher than that used in other dengue studies, which is typically based on monthly data. This is very important because outbreaks of dengue occur quickly, and weekly data are more appropriate than monthly data, allowing faster capture fluctuations in the variable of interest.

In México, there are multiple factors that are associated with dengue, including uncontrolled urbanization with steadily increased human population and lack of adequate public services.[48-50] We know that high levels of urbanization increase the risk of dengue.[60-61]

Also an inadequate water supply and sewage and solid waste disposal services increase the likelihood of water stagnation and offer potential breeding sites for the vector.[7]

The effectiveness of vector control, under-reporting of cases and immunity to the circulating serotypes,[9] suggest feasible prediction on a municipal level, using statistical models that include weather, climate and social variables. The selection of the localities in the study and the lack of information about the circulating serotypes are limitations of this study. We need to incorporate longer time series and other important human related factors such as unplanned urbanization and dengue-infected human movement in modeling studies to determine the vulnerability of each municipality.[6,15]

Climatic factors do not, however, act in isolation, and social variables including population density, population growth, human movement and environmental changes have had far more to do with the global resurgence in dengue witnessed over recent decades than any direct effects of climate.[9,53,62-64] The influences of climatic and non-climatic determinants on current and future dengue transmission are very difficult to disentangle.[65]

In contrast to the results found by Brunkard and colleagues[12] and Hurtado-Díaz and colleagues[14] our analysis suggest that it takes environmental conditions approximately 6 weeks for SST-34, rainfall and minimum temperature, adjusted by homes with dirt floor, population density and municipal population to affect dengue incidence. That means the model may be used as early as approximately two months in advance to provide valuable information to decision makers about future epidemics.

However, we believe that the model can be used to report on vector control programs at national level, including preventive measures (taking special precautions to avoid being bitten by mosquitoes, keeping windows unscreened and doors closed, keeping window and door screens repaired, getting rid of areas where mosquitoes breed, such as standing water in flower pots, containers, birdbaths, discarded tires, etc.) and planning medical services based on the information of climatic variability, weather and social variables, for those who may be affected during future dengue outbreaks. Dengue, like all vector borne-diseases, is sensitive to climatic conditions which affect virus replication, vector development and survival, and therefore help define the geographical and seasonal limits that can support dengue-virus transmission.[9,14,16,35,36,59,66-70]

Conclusions

The challenge in refining models of dengue transmission to maximize their utility in predicting the location, magnitude and timing of future dengue epidemics or multiannual peaks in endemic cycles is to use data at appropriate spatial and temporal scales so that relevant ecological, social and demographic variables that operate at a local or regional scale can be adequately incorporated into the models.

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

References

1. World Health Organization. Dengue factsheet, 2015. Geneva: WHO, 2015 [accessed: May 1, 2015]. Available at: http://www.who.int/mediacentre/factsheets/fs117/en/
2. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, *et al.* The global distribution and burden of dengue. Nature 2013;496(7446):504-507. http://doi.to/k4n
3. Thai KTD, Anders KL. The role of climate variability and change in the transmission dynamics and geographic distribution of dengue. Exp Biol Med 2011;236:(8)944-954. http://doi.org/btmmcc
4. Ortiz PL, Rivero A, Linares Y, Pérez A, Vázquez JR. Spatial models for prediction and early warning of Aedes aegypti proliferation from data in climate change and variability in Cuba. MEDICC Review 2015;17(2):20-28.

5. Banu S, Guo Y, Hu W, Dale P, Mackenzie JS, Mengersen K, *et al.* Impacts of El Niño Southern Oscillation and Indian Ocean Dipole on dengue incidence in Bangladesh. Nature 2014;5:1-9. http://doi.org/bqzx

6. Naish S, Dale P, Mackenzie JS, McBride J, Mengersen K, Tong S. Climate change and dengue: a critical and systematic review of quantitative modelling approaches. BMC Infect Dis 2014;14:167. http://doi.org/bqzz

7. Stewart-Ibarra AM, Lowe R. Climate and non-climate drivers of dengue epidemics in southern coastal Ecuador. Am J Trop Med Hyg 2013;88(5):971-981. http://doi.org/bqz2

8. Cólon-González FJ, Fezzi C, Lake IR, Hunter PR. The effects of weather and climate change on dengue. PLos Negl Trop Dis 2013;7(11):e2503-10. http://doi.org/bqz3

9. Colón-González FJ, Lake IR, Bentham G. Climate variability and dengue fever in warm and humid Mexico. Am J Trop Med Hyg 2011;84(5):757-763. http://doi.org/ddnz5z

10. Fuller DO, Troyo A, Beier JC. El Niño Southern Oscillation and vegetation dynamics as predictors of dengue fever cases in Costa Rica. Environ Res Lett 2009;4:140111-140118. http://doi.org/c8szwq

11. Johansson MA, Dominici F, Glass GE. Local and global effects of climate on dengue transmission in Puerto Rico. PLoS Negl Trop Dis 2009;3(2):e382. http://doi.org/fdw6n8

12. Brunkard JM, Cifuentes E, Rothenberg SJ. Assessing the roles of temperature, precipitation, and ENSO in dengue re-emergence on Texas-Mexico border region. Salud Publica Mex 2008;50(3):227-234. http://doi.org/d84jtt

13. Zell R, Krumbholz A, Wutzler P. Impact of global warming on viral diseases: what is the evidence? Curr Opin Biotechnol 2008;19(6):652-660. http://doi.org/c8ntg6

14. Hurtado-Díaz M, Riojas-Rodríguez H, Rothenberg SJ, Gomez-Dantés H, Cifuentes-García E. Impact of climate variability on the incidence of dengue in Mexico. Trop Med Int Health 2007;12(11):1327-1337. http://doi.org/dm7c6x

15. Ortiz Bultó PL, Pérez A, Rivero A, León N, Díaz M, Pérez A. Assessment of human health and vulnerability to climate variability and change in Cuba. Environ Health Perspect 2006; 114(12):1942-1949. http://doi.org/fft8w4

16. Reiter P. Climate change and mosquito-borne disease. Environ Health Perspect 2001; 109 Supp1: 141-161. http://doi.org/fwwx99

17. Jetten TH, Focks DA. Potential changes in the distribution of dengue transmission under climate warming. Am J Trop Med Hyg 1997;57(3):285-297.

18. Shope R. Global climate change and infectious diseases. Environ Health Perspect 1991;96:171-174. http://doi.org/dr3cb5

19. Patz JA, Epstein PR, Burke TA, Balbus JM. Global climate change and emerging infectious diseases. JAMA 1996;275(3):217-223. http://doi.org/d5hbc8

20. Anyamba A, Linthicum KJ, Small JL, Collins KM, Tucker CJ, Pak EW, *et al.* Climate teleconnections and recent patterns of human and animal disease outbreaks. PLoS Negl Trop Dis 2012;6(1):e1465. http://doi.org/fxqs73

21. Barrera R, Amador M, Clark GG. Use of the pupal survey technique for measuring Aedes aegypti (Diptera: Culicidae) productivity in Puerto Rico. Am J Trop Med Hyg 2006;74(2): 290-302.

22. Montgomery BL, Ritchie SA. Roof gutters: a key container for *Aedes aegypti* and *Ochlerotatus notoscriptus* (Diptera:Culicidae) in Australia. Am J Trop Med Hyg 2002;67(3): 244-246.

23. Moore CB, Cline BL, Ruiz-Tiben E, Lee D, Romney-Joseph H, Rivera-Correa E. Aedes aegypti in Puerto Rico: environmental determinants of larval abundance and relation to dengue virus transmission. Am J Trop Med Hyg 1978;27(6):1225-1231.

24. Mohammed A, Chadee DD. Effects of different temperature regimens on the development of Aedes aegypti (L.) (Diptera: Culicidae) mosquitoes. Acta Trop 2011;119(1):38-43. http://doi.org/cprr53

25. Tun-Lin W, Burkot TR, Kay BH. Effects of temperature and larval diet on development rates and survival of the dengue vector Aedes aegypti in north Queensland, Australia. Med Vet Entomol 2000;14(1):31-37. http://doi.org/fm5h96

26. Rueda LM, Patel KJ, Axtell RC, Stinner RE. Temperature-dependent development and survival rates of Culex quinquefasciatus and Aedes aegypti (Diptera: Culicidae). J Med Entomol 1990;27(5):892-898. http://doi.org/bqz4

27. Yasuno M, Tonn RJ. A study of biting habits of *Aedes aegypti* in Bangkok, Thailand. Bull World Health Organ 1970;43(2):319-325.

28. Delatte H, Gimonneau G, Triboire A, Fontenille D. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of Aedes albopictus, vector of chikungunya and dengue in the Indian Ocean. J Med Entomol 2009;46(1):33-41. http://doi.org/d37r2z

29. Watts DM, Burke DS, Harrison BA, Whitmire RE, Nisalak A. Effect of temperature on the vector efficiency of Aedes aegypti for dengue 2 virus. Am J Trop Med Hyg 1987;36(1):143-152.

30. Poveda G, Rojas W, Quiñones ML, Vélez ID, Mantilla RI, Ruiz D, *et al.* Coupling between annual and ENSO timescales in the malaria–climate association in Colombia. Environ Health Perspect 2001;109(5):489-493. http://doi.org/d8mhrz

31. Ferreria MC. Geographical distribution of the association between El Niño South Oscillation and dengue fever in the Americas: a continental analysis using geographical information system-based techniques. Geospatial Health 2014;9(1):141-151. http://doi.org/bqz5

32. Earnest A, Tan SB, Wilder-Smith A. Meteorological factors and El Niño Southern Oscillation are independently associated with dengue infections. Epidemiol Infect 2012;140(7):1244-1251. http://doi.org/d86htx

33. Nagao Y, Thavara U, Chitnumsup P, Tawatsin A, Chansang C, Campbell-Lendrum D. Climatic and social risk factors for Aedes infestation in rural Thailand. Trop Med Int Health 2003;8(7):650-659. http://doi.org/d4tbbs

34. Mondini A, Chiaravalloti-Neto F. Socioeconomic variables and dengue transmission. Rev Saúde Publica 2007;41(6):923-930. http://doi.org/ctn8gn

35. Reiter P, Lathrop S, Bunning M, Biggerstaff B, Singer D, Tiwari T, *et al.* Texas lifestyle limits transmission of dengue virus. Emerg Infect Dis 2003;9(1):86-89. http://doi.org/bqz6

36. Brunkard JM, Robles-López JL, Ramírez J, Cifuentes E, Rothenberg SJ, Hunsperger EA, *et al.* Dengue fever seroprevalence and risk factors, Texas-Mexico border, 2004. Emerg Infect Dis 2007;13(10):1477-1483. http://doi.org/bk8b

37. Dirección General de Epidemiología (DGE) 2014. Anuarios de morbilidad 1995 al 2005. Sistema Único de Información para la Vigilancia Epidemiológica/SSA (SUIVE). DGE, 2014 [accessed Feb 10, 2015]. Available at: http://www.epidemiologia.salud.gob.mx/dgae/infoepid/inicio_anuarios.html

38. Bhatnagar S, Lai V, Gupta SD, Gupta OP. Forecasting incidence of dengue in Rajasthan using time series analyses. Indian J Public Health 2012;56(4):281-285. http://doi.org/bqz7

39. Tong S, Hu W. Climate variation and incidence of Ross River Virus in Cairns, Australia: A Time-series analysis. Environ Health Perspect 2001;109(12):1271-1273. http://doi.org/cdd9h4

40. Instituto Nacional de Estadística y Geografía (INEGI) 2011. Data base. Censo de Población y Vivienda 2010. INEGI, 2011 [accessed: Sep 21, 2013]. Available at: http://www.censo2010.org.mx/

41. Servicio Meteorológico Nacional (SMN) 2006. Data base. Estaciones Meteorológicas y Estación Sinóptica Meteorológica Automáticas 1995 al 2005 [accessed Feb 5, 2006]. Available at: http://smn.cna.gob.mx/es/climatologia and http://smn.cna.gob.mx/es/emas

42. National Oceanic and Atmospheric Administration (NOAA) 2009. Data base. Global temperatures well above average; slightly above-average for U.S. NOAA, 2009 [accessed Dec 3, 2009]. Available at: http://www.noaanews.noaa.gov/stories2009/20091208_globalstats.html

43. Dirección General Adjunta de Epidemiología (DGE) 2005 [accessed Jul 22, 2013]. Available at: http://www.epidemiologia.salud.gob.mx/dgae

44. Instituto Nacional de Estadística y Geografía (INEGI) 2006. Data base. II Conteo de Población y Vivienda 2005. Veracruz, Ver. INEGI, 2006 [accessed Sep 21, 2013]. Available at: http://www.inegi.org.mx/

45. Instituto Nacional de Estadística y Geografía (INEGI) 2001. Data base. XII Censo General de Población y Vivienda, 2000. Veracruz, Ver. INEGI, 2001 [accessed Sep 21, 2013]. http://www.inegi.org.mx/

46. Instituto Nacional de Estadística y Geografía (INEGI) 1996. Data base. I Conteo de Población y Vivienda 1995. Veracruz, Ver. INEGI, 1996 [accessed Sep 21, 2013]. Available at: http://www.inegi.org.mx/

47. Instituto Nacional de Estadística y Geografía (INEGI) 1992. Data base. XI Censo General de Población y Vivienda, 1990. Veracruz, Ver. INEGI, 1992 [accessed Sep 21, 2013]. Available at: http://www.inegi.org.mx/

48. Consejo Nacional de Evaluación de la Política de Desarrollo Social (CONEVAL) 2006. Data base. Índice de rezago social 2005 a nivel municipal y por localidad. CONEVAL, 2006 [accessed May 14, 2015]. Available at: http://www.coneval.org.mx/Medicion/IRS/Paginas/Indice-de-rezago-social-2005.aspx

49. Consejo Nacional de Población (Conapo) 2015. Data base. Índice de marginación por entidad federativa 1990-2015. Conapo, 2015 [accessed May 15, 2016]. Available at: http://www.conapo.gob.mx/es/CONAPO/Datos_Abiertos_del_Indice_de_Marginacion

50. Consejo Nacional de Población (Conapo) 2015. Data base. Índice de marginación por municipio 1990-2015. Conapo, 2015 [accessed May 15, 2016]. Available at: http://www.conapo.gob.mx/es/CONAPO/Datos_Abiertos_del_Indice_de_Marginacion

51. Said S, Dickey D. Testing for unit roots in autoregressive-moving average models of unknown order. Biometrika 1984;71(3):599-607. http://doi.org/fjngds

52. Newton HJ. A time series analysis laboratory. Pacific Grove. California: Wads-worth & Brooks / Cole Publishing Company, 1996.

53. Hales S, Weinstein P, Souares Y, Woodward A. El Nino and the dynamics of vector borne disease transmission. Environ Health Perspect 1999;107(2):99-102.

54. Uriel E. Análisis de series temporales. 2ª Edición. Madrid: Modelos ARIMA Paraninfo, 1992.

55. Durbán M. An introduction to smoothing with penalties: P-splines. Boletín de Estadística e Investigación Operativa 2009;25(3):195-205.

56. Royston P, Sauerbrei W. Multivariable modeling with cubic regression splines: A principled approach. Stata Journal 2007;7(1):45-70.

57. Dear K, Ranmuthugala G, Kjellström T, Skinner C, Hanigan I. Effects of temperature and ozone on daily mortality during the August 2003 heat wave in France. Archives of environmental & occupational health 2010;60(4):205-212. http://doi.org/bt6g3h

58. Romer D. Advanced Macroeconomics. 4th ed. New York: McGraw-Hill, 2012.

59. Depradine CA, Lovell EH. Climatological variables and the incidence of dengue fever in Barbados. Int J Environ Res 2004;14(6):429-441. http://doi.org/ft6qkr

60. Hsieh YH, Chen SWS. Turning points, reproduction number, and impact of climatological events on multi-wave dengue outbreaks. Trop Med Int Health 2009;14(6):628-638. http://doi.org/dh8bt6

61. Gómez-Dantés H. Elementos económicos y políticos que impactan en el control del dengue en México. Salud Publica Mex 2007;49:117-119.

62. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature 2008;451(7181):990-994. http://doi.org/cbxh9h

63. Hopp MJ, Foley JA. Worldwide fluctuations in dengue fever cases related to climate variability. Climate Research 2003;25(1):85-94. http://doi.org/bt6vsm

64. IPCC, Climate Change 2014: Impacts, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. New York, NY, USA. Cambridge, United Kingdom: Cambridge University Press, 2014:1132.

65. Morin CW, Comrie AC, Ernst KC. Climate and dengue transmission: evidence and implications. Environ Health Perspect 2013;121(11-12):1264-1272. http://doi.org/bqz8

66. Lu L, Lin H, Tian L, Yang W, Sun J, Liu Q. Time series analysis of dengue fever and weather in Guangzhou, China. BMC Publ Health 2009;9:395. http://doi.org/c3m9x4

67. Wu PC, Guo HR, Lung SC, Lin CY, Su HJ. Weather as an effective predictor for occurrence of dengue fever in Taiwan. Acta Trop 2007;103:(1)50-57. http://doi.org/fhtjh6

68. Cazelles B, Chavez M, McMichael AJ, Hales S. Nonstationary influence of El Nino on the synchronous dengue epidemics in Thailand. PLoS Med 2005;2(4):e106. http://doi.org/ftw9z8

69. Patz JA, McGeehin MA, Bernard SM, Ebi KL, Epstein PR, Grambsch A, et al. The potential health impacts of climate variability and change for the U.S.: Executive summary of the report of the Health Sector of the U.S. National Assessment. Environ Health Perspect 2000;108(4):367-376. http://doi.org/bshqhp

70. Bai L, Morton LC, Liu Q. Climate change and mosquito-borne diseases in China: a review. Global Health 2013;9:10. http://doi.org/bqz9