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National spatial and temporal patterns of notified dengue cases, Colombia 2007–2010

Angela Cadavid Restrepo, Peter Baker and Archie C.A. Clements

School of Population Health, University of Queensland, Brisbane, Qld, Australia

Abstract

OBJECTIVES To explore the variation in the spatial distribution of notified dengue cases in Colombia from January 2007 to December 2010 and examine associations between the disease and selected environmental risk factors.

METHODS Data on the number of notified dengue cases in Colombia were obtained from the National Institute of Health (Instituto Nacional de Salud – INS) for the period 1 January 2007 through 31 December 2010. Data on environmental factors were collected from the Worldclim website. A Bayesian spatio-temporal conditional autoregressive model was used to quantify the relationship between monthly dengue cases and temperature, precipitation and elevation.

RESULTS Monthly dengue counts decreased by 18% (95% credible interval (CrI): 17–19%) in 2008 and increased by 30% (95% CrI: 28–31%) and 326% (95% CrI: 322–331%) in 2009 and 2010, respectively, compared to 2007. Additionally, there was a significant, nonlinear effect of monthly average precipitation.

CONCLUSIONS The results highlight the role of environmental risk factors in determining the spatial of dengue and show how these factors can be used to develop and refine preventive approaches for dengue in Colombia.

keywords spatial analysis, maps, Bayesian analysis, dengue, communicable diseases, Colombia

Introduction

Dengue is caused by flaviviruses and transmitted by *Aedes* mosquitoes, especially, Aedes *aegypti*, which has adapted to peri-domestic settings (Mandell *et al.* 2010). Therefore, dengue transmission occurs particularly in tropical urban centres with high population density. Over the past decades, the incidence of this infection has increased in many countries, and it is now considered a major international public health concern (Pan American Health Organization 2012). According to recent estimates, globally, there are 50–100 million infections every year, and approximately 500 000 of those cases are severe, in the form of dengue haemorrhagic fever (DHF)/ dengue shock syndrome (DSS) (WHO 2012). The mortality rate of severe dengue has been estimated at about 2.5% (WHO 2012).

In recent years, numbers of dengue and severe dengue cases have surpassed historic records in Central and South America (Pan American Health Organization 2012). The highest number of dengue cases that have been reported in the region was in 2010, when approximately 1.69 million dengue cases and 1185 deaths were registered by the Pan American Health Organization (PAHO). In Colombia, the number of notified severe dengue cases increased alarmingly from 5.2 cases per 100 000 population in 1990 to 18.1 cases per 100 000 population reported from 2006 to 2011 (Instituto Nacional de Salud 2012b). Based on these estimates, PAHO has reiterated the need of improving efforts to reduce dengue-associated morbidity and mortality (Pan American Health Organization 2012).

As there is no specific treatment, and an effective vaccine against dengue has not been developed, vector reduction is currently the main preventive measure used worldwide (WHO 2009). However, efforts to implement this strategy effectively have been limited in Colombia due to economic and sociopolitical constraints (Torres & Castro 2007). Furthermore, the lack of reliable epidemiological information does not allow estimation of the real impact of the disease in the country (Torres & Castro 2007).

The increased use of geographic information systems (GIS) has contributed to an improvement in the understanding of the epidemiology of dengue and has the potential to help overcome logistical and regional challenges (Eisen & Lozano-Fuentes 2009; Duncombe *et al.* 2012). GIS are being used to map and visualise disease patterns and changes over time (Duncombe *et al.* 2012). In addition, with the aid of GIS technologies and spatial statistical analysis, it is possible to identify local environmental and sociological factors that determine high-risk areas for dengue and analyse the relationships between these risk factors and the occurrence and distribution of the disease (Duncombe *et al.* 2012).

Using GIS and a Bayesian statistical framework, the present study describes the spatio-temporal patterns of notified dengue incidence in Colombia between 2007 and 2010. The aim was to identify dengue clusters in the country at the municipality level and also to visualise smoothed patterns of dengue risk. The study also aimed to determine whether local environmental factors such as temperature, precipitation and elevation are associated with the distribution and dynamics of the disease.

Methods

The protocol for this study was reviewed and approved by the Ethics Committee of the School of Population Health, University of Queensland.

Country context

Colombia is located in the Northwest of South America between latitudes 12°26′46″ North and 4°12′30″ South, and between longitudes 60°50′54″ East and 79°02′33″ West. It is an equatorial country that shares borders with Panama, Venezuela, Brazil, Peru and Ecuador. The national territory, including an island region in the territorial waters of the Caribbean, is divided into 32 departments, which are subsequently subdivided into municipalities and non-municipality areas called corregimientos. According to recent estimates, the Colombian population is 46 728 468 people (Departamento Administrativo Nacional de Estadistica - DANE 2012).

The geographic composition of Colombia includes five natural regions: the Andean highlands, the Pacific and the Caribbean lowlands, the Amazon and the Orinoquía. Geographic differences between these regions influence the variation in temperature and precipitation across the country. In general, the weather is relatively uniform thorough the year. The main seasons in Colombia include two wet seasons, extending from April to May and from October to November, and two dry seasons, extending from December to January and from July to August. The average annual rainfall varies greatly from less than 400 mm in the Guajira peninsula to more than 11 000 mm in the Pacific lowlands (Instituto de Hidrología Meteorología y Estudios Ambientales - IDEAM 2012).

In this study, municipalities (1104) and corregimientos (20, covering a large area in the south of the country) were the spatial unit of analysis.

Dengue data collection

Data on reported dengue cases in Colombia from January 1 2007 to December 31 2010 were obtained from the National Institute of Health (Instituto Nacional de Salud - INS). Dengue is a notifiable disease in the country by law, and all diagnosed cases of dengue must be reported to the INS via the National Public Health Surveillance System (Subsistema de Información en Salud Pública – SIVIGILA). The weekly number of probable and confirmed dengue cases is collected from municipalities and non-municipality areas by the INS to be analysed and archived by the dengue surveillance and control unit (Instituto Nacional de Salud 2012a).

Both probable and confirmed dengue cases were included in this study. The case definition used by the INS met the case definition recommended by the WHO (Servicio de Salud en Colombia 2000; Instituto Nacional de Salud 2012b). Probable dengue fever is a clinical diagnosis reported by physicians when acute illness is present with at least two of the following symptoms: headache, severe retro-orbital pain, myalgia, arthralgia, haemorrhagic manifestations (petechiae, epistaxis, metrorrhagia and gingivorrhagia), rash and leukopenia. A confirmed case of dengue is notified when the diagnosis is supported by laboratory tests (positive results for virus isolation and identification, detection of viral RNA using the RT-PCR technique and detection of antidengue antibodies) (WHO 2009). All laboratory methods for establishing the diagnosis of dengue are available in Colombia. However, most diagnoses are confirmed when there is an increase of four times or more in specific IgG antibody titres, or a positive IgM antibody test on a late-acute or convalescent phase, and also when a dengue case occurs in close contact with another confirmed dengue case (Instituto Nacional de Salud 2012b).

Variable selection

The independent variables considered for the analysis were as follows: temperature, precipitation and elevation. Data on these environmental factors were downloaded from the WorldClim – Global Climate Data website (Worldclim 2012). ESRI grids (i.e. raster surfaces) including elevation and monthly mean temperature and precipitation were available globally at the resolution of 1 km (approximately 30 arc-seconds) grid. Administrative boundary maps were downloaded from the DIVA-GIS website (DIVA-GIS 2012). Administrative boundaries have changed in Colombia over time; while dengue data were obtained from the 1124 municipalities and corregimientos, the administrative boundary map downloaded from the website only included 1065 administrative areas. To conduct the analysis, dengue data from those 59 municipalities and corregimientos that were created by splitting old municipalities were reconciled to match the boundary map, giving a final number of 1065 spatial units.

Spatial datasets were imported into the Quantum GIS software package, version 1.8.0, 'Lisboa' (Quantum GIS Development Team 2012) and linked spatially to the boundary map. Spatial mean values of temperature, precipitation and elevation were calculated in the GIS for each municipality to define parameters in subsequent statistical models.

Data analysis

Initially, a descriptive analysis of notified dengue cases was performed. Crude standardised morbidity ratios (SMRs) for each administrative area for the 4-year period were calculated by dividing the observed number of cases by the expected number of cases (calculated using the overall incidence rate for the whole country over the whole study period, multiplied by the population of each municipality).

Univariate Poisson regression models were implemented using the R software, version 2.15.2 (R Development Core Team 2012). Collinearity was assessed among predictors using Spearman correlation analyses. If a pair of variables had a correlation coefficient >0.9, the variable with the highest value of the AIC in the univariate model was excluded. Nonlinear associations between predictors and the number of dengue counts were modelled using quadratic terms.

Separate Poisson regression models were constructed in a Bayesian framework using the WinBUGS software, version 1.4.3 (MRC Biostatistics Unit 2008). The first model (Model I), assumed that spatial autocorrelation was not present in the relative risk of dengue. This model was developed including time in years (modelled as a categorical variable), temperature, precipitation and a quadratic term for precipitation as explanatory variables, and an unstructured random effect for municipalities; the second model (Model II) included the same explanatory variables and a spatially structured random effect; the final model (Model III), a convolution model, contained all of the components of the preceding two models.

This last model assumed that the observed counts of dengue, Y, for the ith municipality ($i = 1 \ldots 1065$) in the jth month (January 2007–December 2010) followed a Poisson distribution with mean (μ_{ij}), that is,

$$Y_{ij} \sim \mathrm{Poisson}(\mu_{ij})$$

$$\log(\mu_{ij}) = \log(\mathrm{E}_i) + \theta_{ij}$$

$$\begin{aligned}\theta_{ij} = \alpha + \beta_1\mathrm{year\_2008}_j + \beta_2\mathrm{year\_2009}_j + \beta_3\mathrm{year\_2010}_j \\ + \beta_4\mathrm{Temp}_{ij} + \beta_5\mathrm{Precip}_{ij} + \beta_6(\mathrm{Precipi}_{ij})^2 + \mathrm{u}_i + \mathrm{s}_i\end{aligned}$$

where E_i is the expected number of cases in municipality i (acting as an offset to control for population size) and θ_{ij} is the mean log relative risk (RR); α is the intercept, and $\beta 1$, $\beta 2$, $\beta 3$, $\beta 4$, $\beta 5$ and $\beta 6$ the coefficients for years 2008, 2009 and 2010 (with a reference category of 2007), and also for temperature, precipitation and a quadratic term for precipitation, respectively; u_i is the unstructured random effect with mean zero and variance σu2, and s_i is the spatially structured random effect with mean zero and variance σs2.

A conditional autoregressive (CAR) prior structure was used to model the spatially structured random effect (Besag *et al.* 1991). In this model, spatial relationships between municipalities were determined using an adjacency weights matrix. If two municipalities shared a border, the weight = 1 and if they did not, the weight = 0. A flat prior distribution was specified for the intercept, whereas a normal prior distribution was used for the coefficients (normal priors with a mean = 0 and a precision = 1 × 10–4). The priors for the precision of unstructured and spatially structured random effects were specified using non-informative gamma distributions with shape and scale parameters equal to 0.01.

An initial burn-in of 1000 iterations was run, and these iterations were discarded. Subsequent blocks of 20 000 iterations were run and examined for convergence. Convergence was assessed by visual inspection of posterior density and history plots, and occurred at approximately 100 000 iterations for each model. Ten thousand values from the posterior distributions of each model parameters were stored and summarised for the analysis (posterior mean and 95% credible intervals). The deviance information criterion (DIC) was calculated for model selection, where lower DIC indicates a better model fit. In all analyses, an α-level of 0.05 was adopted to indicate statistical significance (as indicated by 95% credible intervals (95% CrI) for relative risks (RR) that excluded 1).

The Quantum GIS software was used to create choropleth maps of crude SMRs for the 1065 administrative areas of Colombia for the period 2007–2010. Maps of the spatial distribution of posterior means of the unstructured and structured random effects obtained from the three models were also constructed.

Results

A total of 304 984 dengue cases were notified in Colombia from 1 January 2007 to 31 December 2010. Except for a slight decrease in the number of cases in 2008, the occurrence of dengue fever followed an upward trend and experienced a dramatic increase in 2010, when the number of dengue cases reported was 177 658. This number accounts for 58.3% of the total reported cases in Colombia during the entire period (Table 1).

The number of monthly dengue cases reported by administrative area in Colombia from 2007 to 2010 ranged from 0 to 3647, with a mean of 5.9. The mean monthly temperature during the same period was 11.8 °C, the mean monthly precipitation was 79.8 mm, and the mean elevation of the administrative areas was 1266.7 m (Table 2).

In general, there were no clear seasonal patterns observed in the occurrence of dengue fever in Colombia during the 4-year period. The monthly number of reported dengue cases displayed three years of relatively stable numbers of notifications followed by a large peak in 2010 (Figure 1).

Table 1 Numbers of reported dengue cases in Colombia by year from 2007 to 2010

Reported dengue cases				
Year	Frequency	Per cent of total dengue cases in the period (%)	Cumulative frequency	Cumulative per cent (%)
2007	40 376	13.2	40 376	13.2
2008	33 484	11	73 860	24.2
2009	53 466	17.5	127 326	41.7
2010	177 658	58.3	304 984	100
Total cases	304 984	100	–	–

Table 2 Descriptive statistics for number of reported dengue fever cases, temperature, precipitation and elevation by municipality in Colombia from 1 January 2007 to 31 December 2010

Variable	Mean	Standard deviation	Minimum	Maximum
Dengue cases	5.9	50	0	3647
Temperature (°C)	11.8	168.1	4.8	30
Precipitation (mm)	79.8	1749.3	0	880.3
Elevation (m)	1266.7	2063.8	4.32	3831.4

The map of standardised morbidity ratios (SMR) for dengue by municipality during the period 2007–2010 shows a significant spatial variability in the incidence of notified dengue cases across the country (Figure 2). A general pattern observed in the map is the high SMR in those municipalities located in the eastern and central part of the country and the low SMR in the south, north and west of Colombia (the Amazon, the Pacific and the Caribbean regions).

The analysis of correlations between explanatory variables revealed that temperature and elevation were highly correlated ($\rho = -0.95$, $P < 0.001$). Because elevation had a higher AIC than temperature in the univariate analysis, the covariate elevation was not included in the final multivariate model. All other pairs of variables had a correlation (Spearman's rho) of <0.4.

Spatio-temporal model

Based on DIC values, the analyses show that Model III, containing the unstructured and the spatially structured random effect, had the best fit among all the models examined (Table 3). In Model III, there was an estimated decrease of 18% in dengue counts (95% CrI: 17–19%) in 2008 and an increase of 30% (95%CrI: 28–31%) and 326% (95%CrI: 322–331%) in 2009 and 2010, respectively, compared to 2007. The quadratic term for precipitation was significant, indicating that the association between this variable and the outcome was nonlinear. Based on the 95% CrI, the association between temperature and dengue counts was not significant. The variance of the unstructured random effect in this model was 0.35 (95% CrI: 0.18–0.66), and the variance of the spatially structured random effect was 6.25 (95% CrI: 4.76–7.70),

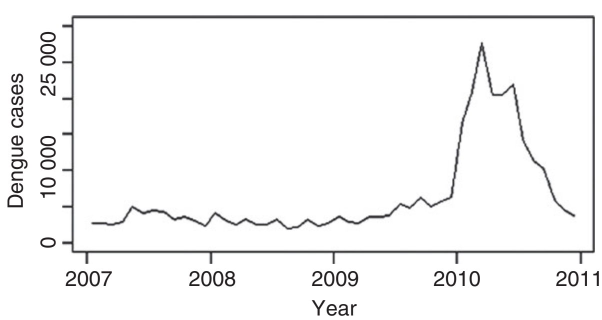


Figure 1 Number of notified dengue cases by year (2007–2010) in Colombia for the period 1 January 2007 to 31 December 2010.

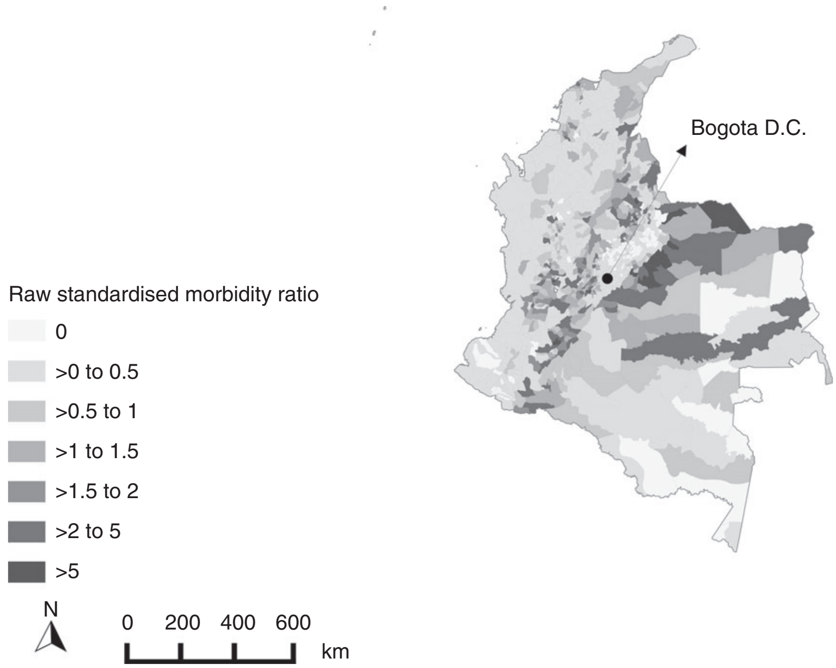


Figure 2 Raw standardised morbidity ratios for dengue by municipalities in Colombia for the period 1 January 2007 to 31 December 2010.

indicating that after accounting for precipitation and temperature, most of the residual area-level variation was spatially structured.

The map of the posterior means of spatially structured random effects demonstrates evidence of clustering after accounting for the covariates (Figure 3). There was a higher dengue risk occurring at the central and eastern parts of Colombia, and a lower risk occurring at southern and north-western areas. As expected, the map of the posterior means of unstructured random effects, which represented the effects of unmeasured risk factors that are spatially random, did not show a geographic pattern.

Discussion

The results of the present study are consistent with reports of recent upward trends in the number of dengue fever cases throughout the tropics and particularly in Latin America (San Martín *et al.* 2010). The increasing incidence of dengue fever in Colombia observed in this study, especially in the year 2010, was also experienced by many other Latin American countries, including Brazil, Venezuela, Mexico, Puerto Rico and Honduras (San Martín *et al.* 2010).

The findings also concur with other studies conducted in multiple different settings where environmental variables were also identified as important predictors of dengue infection (Chakravarti & Kumaria 2005; Hii *et al.* 2009; Wu *et al.* 2009; Hu *et al.* 2012). The current study found that precipitation was associated with dengue incidence. Because long-term average monthly values of this variable were analysed, this association may be partially explained by the variability of this predictor across the regions of Colombia. The nonlinear relationship between precipitation and dengue incidence observed in this study suggests that the number of dengue counts may have increased progressively due to the creation of rain-filled breeding sites, whereas the decrease in dengue incidence at high levels of precipitation could have been the result of the washout of such breeding sites.

In Latin America and the Caribbean region, interannual changes in precipitation and temperature are strongly influenced by variations in the Pacific sea surface temperatures as part of the El Niño Southern Oscillation (ENSO) phenomenon (Grimm *et al.* 2000). These climate fluctuations have been partially related to the cyclic nature of dengue outbreaks (Patz *et al.* 2005; Fuller *et al.* 2009; Johansson *et al.* 2009; Hu *et al.* 2010). The current study did not analyse a sufficiently long time series to investigate the effects of ENSO, and future research should investigate the role of ENSO in driving dengue in Colombia. The incorporation of GIS technologies and statistical analysis in dengue surveillance activities may offer an opportunity for enhancing early warning systems and implementing prevention strategies, especially before outbreaks. Knowledge of the role of ENSO would greatly facilitate these objectives.

The current study also found significant variation in the spatial distribution of dengue incidence in Colombia.

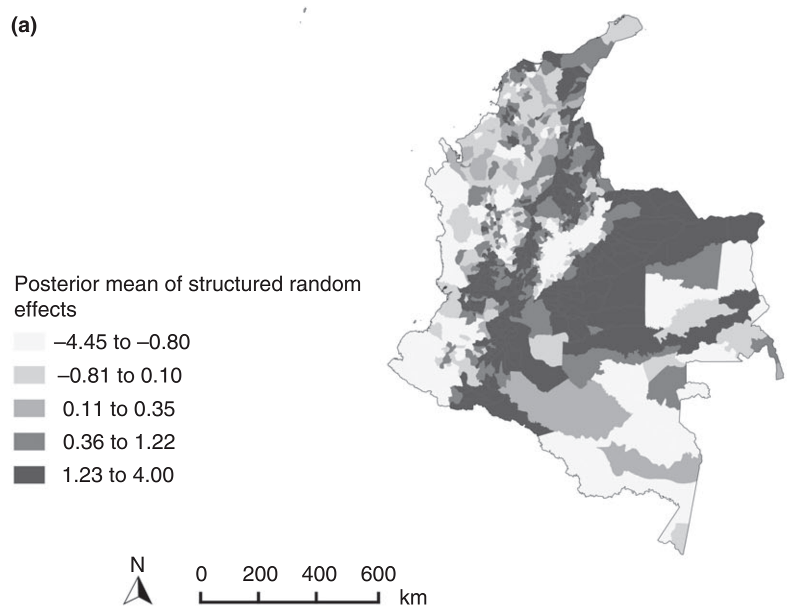
Table 3 Regression coefficients, RRs and 95% CrI from Bayesian spatial and non-spatial models for dengue fever cases in Colombia from 1 January 2007 to 31 December 2010*

Model/variable	Coefficient, posterior mean (95% CrI)	RRs, posterior mean (95% CrI)
Model I		
α (Intercept)	−2.10 (−2.22 to −1.92)	–
Time (year)		
2008	−0.20 (−0.21 to −0.18)	0.82 (0.81 to 0.83)
2009	0.26 (0.25 to 0.27)	1.30 (1.28 to 1.31)
2010	1.45 (1.44 to 1.46)	4.26 (4.22 to 4.31)
Temperature (°C)	3×10^{-3} (-3×10^{-5} to 6^{-4})	1 (0.99 to 1)
Precipitation (100 mm)	0.06 (0.05 to 0.06)	1.06 (1.05 to 1.06)
Precipitation squared (100 mm)	0.003 (0.002 to 0.004)	1.003 (1.003 to 1.004)
Heterogeneity		–
Unstructured	3.57 (3.2 to 4)	
DIC	336 886	
Model II		
α (Intercept)	−2.14 (−2.18 to −2.11)	–
Time (year)		
2008	−0.20 (−0.21 to −0.18)	0.82 (0.81 to 0.83)
2009	0.26 (0.25 to 0.27)	1.30 (1.28 to 1.31)
2010	1.45 (1.44 to 1.46)	4.26 (4.21 to 4.31)
Temperature (°C)	3×10^{-4} (-4×10^{-5} to 6×10^{-4})	1 (0.99 to 1)
Precipitation (100 mm)	0.06 (0.05 to 0.06)	1.06 (1.05 to 1.07)
Precipitation squared (100 mm)	0.003 (0.002 to 0.003)	1.003 (1.003 to 1.004)
Heterogeneity		–
Structured	8.33 (7.7 to 9.1)	
DIC	337 052	
Model III		
α (Intercept)	−2.14 (−2.18 to −2.10)	–
Time (year)		
2008	−0.20 (−0.21 to −0.18)	0.82 (0.81 to 0.83)
2009	0.26 (0.25 to 0.27)	1.30 (1.28 to 1.31)
2010	1.45 (1.44 to 1.46)	4.26 (4.22 to 4.31)
Temperature (°C)	3×10^{-4} (-6×10^{-5} to 5×10^{-4})	1 (0.99 to 1)
Precipitation (100 mm)	0.06 (0.05 to 0.06)	1.06 (1.05 to 1.06)
Precipitation squared (100 mm)	0.003 (0.003 to 0.004)	1.003 (1.003 to 1.004)
Heterogeneity		–
Unstructured	0.35 (0.18 to 0.66)	
Structured	6.25 (4.76 to 7.70)	
DIC	336 797	

*RRs, relative risks; 95% CrI, 95% credible interval.

This spatial variability may have been partially driven by the environmental factors examined in this study, but significant residual spatial variation was also found, indicating that potentially important, unmeasured factors partly drive the spatio-temporal dynamics of dengue in Colombia. Further research should be carried out to identify these factors, some potential examples of which are described in the next two paragraphs.

Dengue fever risk was spatially clustered in the eastern and central parts of Colombia. This area covers the Andes Mountains and the natural region of the Orinoquia, also called the Eastern plains. The Orinoquia region is located on the border with Venezuela, a country that is also recognised for the high incidence of DHF (San Martín *et al.* 2010). These regions are affected directly by the ongoing armed conflict in Colombia, with high levels of forced migration, and poor access to education in some areas (Viloria de la Hoz 2009). Colombia has a high index of displacement of people due to the sociopolitical situation of the country (Internal Displacement Monitoring Centre 2012). The constant movement of people between affected and unaffected areas may be contributing to the spread of dengue in recent decades and to unplanned urbanisation in highly populated areas, which typically provide ideal habitats for the anthropogenic *Aedes* vectors of dengue.



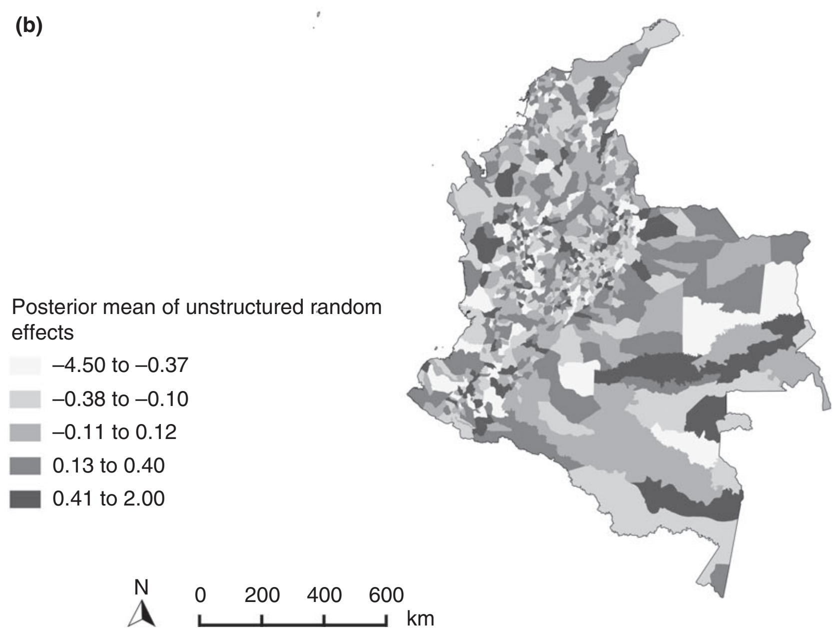


Figure 3 Spatial distribution of the posterior means of random effects for dengue in Colombia in Model III. (a) Spatially structured random effects (b) unstructured random effects.

According to previous studies, the Pacific and the Amazon regions have suitable environmental and epidemiological characteristics for dengue transmission (Hayes *et al.* 1996; Singh *et al.* 2005; Rosa-Freitas *et al.* 2006). However, relatively few dengue cases were notified from these areas during the 4-year period. These findings could indicate that part of the observed residual variation in dengue incidence is due to differences in reporting between the regions of Colombia. Although SIVIGILA is a national public health surveillance system widely available in the country, the quality and completeness of the data may be partially influenced by inequalities in the access to health care. The General System of Social Security in Health in Colombia consists of two main health insurance categories, the contributive and the subsidised schemes. The contributive scheme covers the population formally employed, while the subsidised scheme covers people who cannot afford to pay insurance fees. In general, access to health care services is more limited for those insured by the subsidised scheme. According to national estimates from 2010, the majority of the population in the Caribbean, the Amazon and the Pacific regions were covered by the subsidised scheme (Departamento Administrativo Nacional de Estadistica - DANE 2011. If variable quality of reporting is confirmed, better monitoring of dengue surveillance is likely to be required to achieve a more accurate assessment of the distribution of dengue in Colombia.

The use of GIS technologies and spatial statistical analysis for the study of the spatio-temporal dynamics of reported dengue cases provides relevant information to monitor trends in dengue occurrence and environmental and social risk factors. Therefore, these technologies may be used to enhance early warning systems by ensuring an early detection of human infection and an appropriate and rapid response.

In South America, GIS have been used most widely in Brazil to explore and understand the local dynamics of dengue and to target community-based control programs (Siquiera *et al.* 2004; Almeida *et al.* 2007)). However, outside of Brazil, there have been few investigations of the spatio-temporal dynamics of dengue in Latin America, and the only country in which the disease burden has been subject to spatial investigation at the national level is Peru (Chowell *et al.* 2008, 2011). Colombia has a high burden of dengue (ranked third among countries in Latin America for numbers of cases (Bhatt *et al.* 2013)), and this research is the first attempt to analyse the national spatial and temporal patterns of reported dengue cases at the township level and the association with local environmental factors. These findings provide a basis for future research that would help improve local dengue surveillance and control programs.

The main limitations of this study include that it relied on passive surveillance of clinical dengue cases, which overlooks the relative contribution of asymptomatic dengue fever cases and is likely to be affected by under-reporting and, potentially, misreporting due to a lack of laboratory capacity to correctly diagnose the disease. While dengue fever is a notifiable disease in the country by law, further work needs to be carried out to evaluate and improve dengue surveillance in Colombia.

Conclusion

There was interannual variability in the number of notified dengue cases in Colombia during the study period. This study suggests that dengue is spatially clustered in areas located in the eastern and central part of the country. In all models examined, precipitation was an important predictor of dengue transmission. These results give some indication of the potential impact that environmental factors might have on the high incidence of dengue in the country. Evidence on the local risk factors and the spatial and temporal aspects of dengue in Colombia may contribute to enhancing preventive and control efforts by providing valuable information to improve early warning systems and to allocate resources effectively.

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Corresponding Author Angela Cadavid Restrepo, Level 1, Public Health Building, School of Population Health, University of Queensland, Herston Road, QLD 4006, Australia. Tel.: +61-44-9559402; E-mail: a.cadavidrestrepo@uq.edu.au