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Expansion of the dengue transmission area in Brazil: the role of climate and cities

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Abstract

objectives To examine the spatial and temporal patterns of the recent expansion of dengue transmission area in Brazil (2001–2012) with the aim to identify pathways and constraints to dengue diffusion.

methods Synthetic indicators were calculated to characterise timing (year of first dengue outbreak), permanence (number of years with dengue outbreaks) and intensity (outbreak occurrence). The indicators were used to map dengue diffusion and compare cities within different climatic zones, with varying population densities.

results Currently, a large portion of the country comprises a dengue transmission area, but cities situated in the mesothermal zone, in the south, and remote areas, in the north, are relatively exempt. Diffusion waves are spread from metropolitan areas towards medium and small cities generating outbreaks in their influence region. However, long-term permanence of transmission depends on the existence of a favourable climate, abundant population and connectivity.

conclusions Large and warm cities sustain and spread dengue viruses, for which specific dengue control measures must be developed. The concentration of outbreaks along climate transition fringes indicates a boundary between two transmission regimes and raises awareness to the effects of ongoing climatic and socio-economic changes.

keywords disease diffusion, dengue epidemics, climate change, urban health

Introduction

Over the last decades, tropical countries have undergone uncontrolled dengue epidemics, which may expand beyond the supposed climatic and geopolitical boundaries. A combination of urbanisation, globalisation and lack of effective mosquito control has promoted the rapid spread of dengue (Gubler 2011). Dengue viruses are transmitted by *Aedes* mosquitoes, causing mainly subclinical infections of dengue fever (DF). However, the increasing incidence of dengue haemorrhagic fever (DHF), fatal complications and cases among children is of concern to the public health sector (Teixeira *et al.* 2009).

Latin America, South-East Asia and Central Africa are now considered as endemic regions, where large dengue outbreaks occur, affecting both large and small cities. Dengue diffusion is due to a complex process involving (i) the spread of *Aedes* mosquitoes and their adaptation to urban environments, (ii) population mobility that facilitates the circulation of the virus, and (iii) changes in climate that accelerate the transmission cycle. This is especially marked in cities where, due to urban heat island effects, ambient temperatures are warmer than in surrounding rural areas and rainfall regime alterations may favour the maintenance of mosquito breeding sites (Jetten & Focks 1997).

Large cities unite these components, providing favourable conditions for dengue transmission. Many studies have focussed on the internal heterogeneity of risk distribution within cities and their social inequalities, leading to controversial results (Flauzino *et al.* 2009). Result disparities may be a consequence of disregarding time–space relations of dengue epidemics. For instance, after large outbreaks, seroprevalence of dengue antibodies may reach up to 80% of the urban population (Teixeira *et al.* 2002), with herd immunity a major determinant for limiting the number of new infections (Siqueira-Junior *et al.* 2008). Therefore, the spatial distribution of dengue cases may differ considerably, depending on the immune status of the population when the study is carried out. Nevertheless, some of these studies have identified indicators such as demographic density, population mobility, mosquito infestation and sanitation conditions as important collective risk factors (Flauzino *et al.* 2009; Banu *et al.* 2011). Other studies concentrate on the interannual, seasonal and monthly variations in dengue and the impact of meteorological events preceding dengue outbreaks, to provide timely information for preventive actions (Lowe *et al.* 2011, 2013). Prolonged warm periods and accumulated precipitation arise as important precursors of large dengue epidemics (Banu *et al.* 2011).

Studies with wider geographical domains are still scarce in the dengue literature. Cummings *et al.* (2004) revealed rapid travelling waves of DHF emanating from Bangkok every 3 years and crossing Thailand. Chowell *et al.* (2011) distinguished different patterns of dengue diffusion in Peru among climatic zones, with local temperature identified as a strong regulator of dengue transmission persistence. The spread of dengue in Brazil has been associated with human mobility across the urban network, while remote rural regions have remained relatively protected (Catão & Guimarães 2011).

However, unlike contagious diseases, dengue epidemic diffusion is constrained by the environmental substrate in which the vector exists. In the case of dengue, geographical context plays a triple role of favouring places in which mosquitoes will reproduce; connecting vulnerable population groups; and promoting exposure to infected vectors (Randolph & Rogers 2010). Climate and environmental changes may exacerbate the present distribution of vectorborne diseases, as well as extend transmission to new niches and populations (Jetten & Focks 1997). Climate change affects populations in different ways and intensities according to the vulnerability of social groups, which is associated with their insertion in place and society. Spatial analyses offer important tools to measure and monitor health impacts on vulnerable populations under possible scenarios (Duncombe *et al.* 2012). Brazil presents a wide variety of temperature ranges and rainfall regimes. In addition, unequal urban infrastructure among cities and differential territory occupation patterns increase the complexity of dengue dynamics nationwide.

Aedes aegypti re-infestation was unveiled in Brazil in 1979, and the first dengue mass transmission was reported in 1986. Nowadays, all four dengue virus serotypes circulate in the country. More than three decades since its re-emergence, Brazil became the country that produces the most dengue cases in the world (Teixeira *et al.* 2009). Thus, it is somehow surprising that the whole Brazilian territory is not completely overrun by the epidemic. This work aims to investigate the pathways by which dengue epidemics have been diffused in the country in recent years (2001–2012), based on two underlying categories: population and climate. Conversely, by explaining diffusion, the constraints of dengue transmission area expansion are revealed, which can provide guidance for targeting preventive actions.

Methodology

Data were obtained from the Notifiable Diseases Information System (SINAN), organised by the Brazilian Ministry of Health and freely available via the Health Information Department (DATASUS). All DF confirmed cases were considered in the analysis, from 2001 to 2012, and were summarised by year and city of residence. Cases were confirmed by clinical and epidemiological evidence, with epidemiological investigations carried out by local health surveillance teams. Approximately 30% of dengue cases were also laboratory-confirmed (Siqueira-Junior *et al.* 2005).

In this study, rather than calculating standard incidence rates, alternative epidemic metrics were calculated to quantify the timing, permanence and intensity of dengue epidemics. These indices can help health surveillance services to identify risk areas and time periods (Galli & Chiaravalloti Neto 2008), as disease incidence figures based on notifications can be considerably underestimated, especially during low endemicity periods, due to the differential operation of health services (Teixeira *et al.* 2002). However, during outbreaks, the number of cases can be even overestimated. Dengue outbreaks often provoke social upheaval (Madoff *et al.* 2011) and attract media attention (França *et al.* 2004). As stated by specialists gathered in workshops of the Brazilian Observatory of Climate and Health, 'there is no way to hide an epidemic' (Observatory of Climate & Health 2011). The proposed indices try to capture the presence and timing of an excess of notified cases, or outbreaks.

In this article, 'intensity' was measured by the occurrence of outbreaks, 'permanence' was assessed by the number of years with high incidence, and 'timing' was assessed by identifying the first year of high incidence, as a proxy of onset of local dengue transmission. The proposed indicators were used to map dengue diffusion and compare cities within different climate zones with varying population densities.

For each of the 5506 cities, the first year during which the incidence rate exceeded 300 cases per 100 000 inhabitants (YD300, i.e. timing) was identified. This threshold is commonly used by the National Dengue Control Programme in Brazil to characterise periods of intensive transmission (Lowe *et al.* 2013). Similarly, the number of years presenting incidence rates greater than 300 cases per 100 000 inhabitants was counted (NYD300, i.e. permanence). These indicators were used to create diffusion maps, according to Haggett (2000). A third indicator was calculated to detect outbreaks that occurred by city and year (OTBy, i.e. intensity, where y is the year from 2001 to 2012). The number of cases per year was compared with the mean plus two standard deviations of the time series. This statistical approach is traditionally employed by epidemiological surveillance services to detect outbreaks using a control chart (Buczak *et al.* 2012). An outbreak was then considered if the observed number of cases exceeds this limit, assuming a Poisson distribution.

Cities were categorised into climate zones obtained from the Brazilian Institute of Geography and Statistics (IBGE): mesothermal, with mean minimum temperature between 10 and 15 °C; subwarm, with mean minimum temperatures between 15 and 18 °C; and warm, with mean minimum temperature above 18 °C. Cities were also classified according to their size, considering the logarithm of urban population and the proportion of the population living in cities, according to the 2010 demographic census. As dengue in Brazil is predominantly an urban epidemic (Taiul 2002), only urban populations of municipalities were considered at risk.

All indicators were geocoded and mapped using the coordinates of each urban centre. This position was used to create maps and assign information derived from other information layers, such as climate and roads, in a geographic information system (GIS). These indicators were interpolated using ordinary kriging, to produce a smoothed surface of probabilities in space. The shape of this surface was obtained using cross sections available in Vertical Mapper (Mapinfo version 9, Pitney Bowes Software, Stamford, CT, USA).

A hierarchical model was formulated to assess the relative contribution of climate and population to dengue transmission sustainability, that is, permanence (*NYD300).* A Binomial model (Equation 1) was assumed for each city (i, i = 1, …, 5506), where y_i is the number of years in which dengue incidence exceeded the epidemic threshold of 300 cases per 100,000 inhabitants (i.e. NYD300), p_i is the unknown underlying probability of dengue incidence exceeding the epidemic threshold and n_i is the number of years ($n_i = 12$). A logistic regression was applied to model the unknown probability, with climate zone (w_i) and the logarithm of urban population (x_i) as categorical and continuous explanatory variables, respectively. Cities in the mesothermal climate class were assigned a value of 1; subwarm, value 2; and warm, value 3. Note that the mesothermal zone (level 1) was set as the reference level, such that its effect was aliased in the model intercept α. To allow for overdispersion, an unstructured (exchangeable) random effect (θ_i) was included to introduce an extra source of variability (a latent effect) into the model, to capture the impact of unobserved heterogeneity and unknown confounding factors (see Lowe *et al.* 2011 for details).

$$y_i \sim \mathrm{Binomial}(p_i, n_i)$$

$$\mathrm{logit}(p_i) = \alpha + \beta_j w_i + \gamma x_i + \theta_i \quad (1)$$

Model parameters were estimated within a Bayesian framework using Markov Chain Monte Carlo (MCMC) and were considered to be statistically significant if their 95% credible interval did not contain zero. The Bayesian approach accounts for parameter uncertainty by assigning prior distributions to the parameters (Gilks *et al.* 1996). A Gaussian distribution with zero mean was assigned to the exchangeable random effects $\theta_i \sim N(0, \sigma_\theta^2)$ with a diffuse gamma hyperprior assigned to the precision (hyperparameter), that is, the reciprocal of the variance $\tau_\theta = 1/\sigma_\theta^2$ (see Clayton and Kaldor 1987).

Results

Figure 1 shows the diffusion of dengue transmission in Brazil. According to the map, dengue has been expanding its transmission area across almost the entire Brazilian territory, consolidating as hyperendemic along the east coast and the central regions. Some of the diffusion axes depicted from the figure correspond to important roads connecting large cities. A wide diffusion occurred before 2002 and between 2005 and 2009 corresponding to an overall nationwide increase in dengue incidence.

However, the southernmost region of Brazil was not reached by the epidemics, with the exception of the north-west corner in Paraná state. Likewise, other regions have been preserved from epidemics, such as portions of the Amazon in the north. Large cities present high dengue incidence since the beginning of dengue re-emergence, such as Rio de Janeiro, Salvador, Recife, Fortaleza and Belem along the coast, as well as Campo Grande, Cuiabá, Goiania, Belo Horizonte, Manaus and Boa Vista in the inner country regions. However, this is not the case for capitals in the south (Curitiba, Florianópolis and Porto Alegre), where few dengue cases have been registered, most of them imported from endemic regions. It is important to highlight that due to the spatial analysis assumptions, based on the spatial smoothing among neighbouring point values, some episodical and isolated increases in dengue cases do not appear in the map. This is the case of the southern state capitals and medium cities in the interior, where recent and localised outbreaks have occurred.

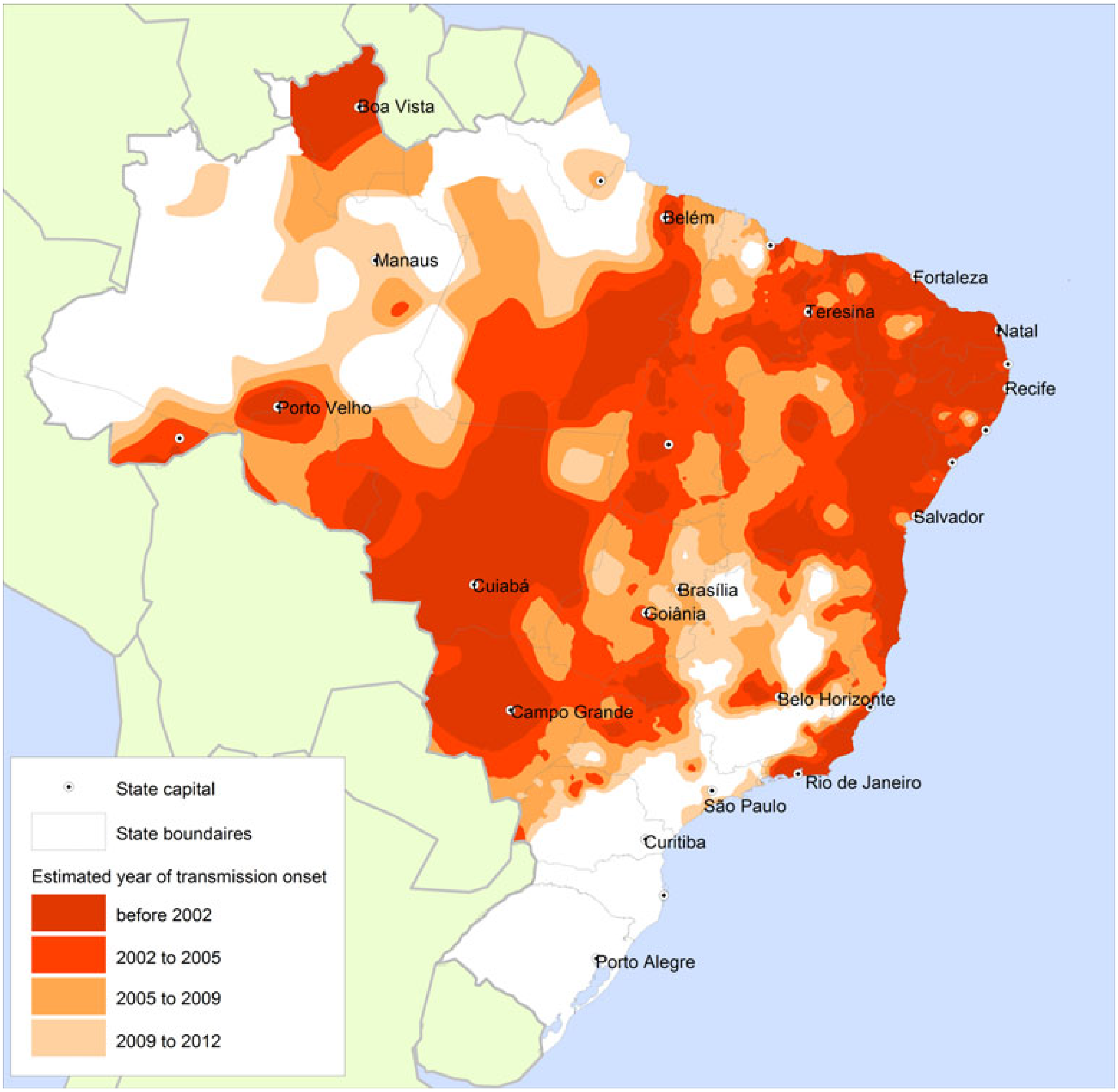

Figure 1 Expansion of dengue transmission area in Brazil. The intervals of colours correspond to the spatial mean (kriging) of the first year of high incidence rate (more than 300 cases per 100 000 inhabitants) from 2001 to 2012.

The estimated current transmission area is shown in Figure 2, considering the last period (until 2012 as shown in Figure 1) as the present transmission area. The identified outbreaks are overlaid to this area. A general agreement is observed between the southern limits of the transmission area and the dominance of mesothermal climate, beyond which outbreaks are rarely observed.

Outbreaks were observed in 2028 of 5506 Brazilian cities, mostly in medium and large cities (more than 50 000 inhabitants) in warm zones. Conversely, cities located in the mesothermal zone, even with a large population, rarely registered outbreaks during the study period.

Outbreaks are clustered in the north-east region and surprisingly in the south, along the fringe of the transmission area. In the central portion of the country, dengue outbreak occurrence is more dispersed. This double pattern of outbreak distribution may reveal the existence of

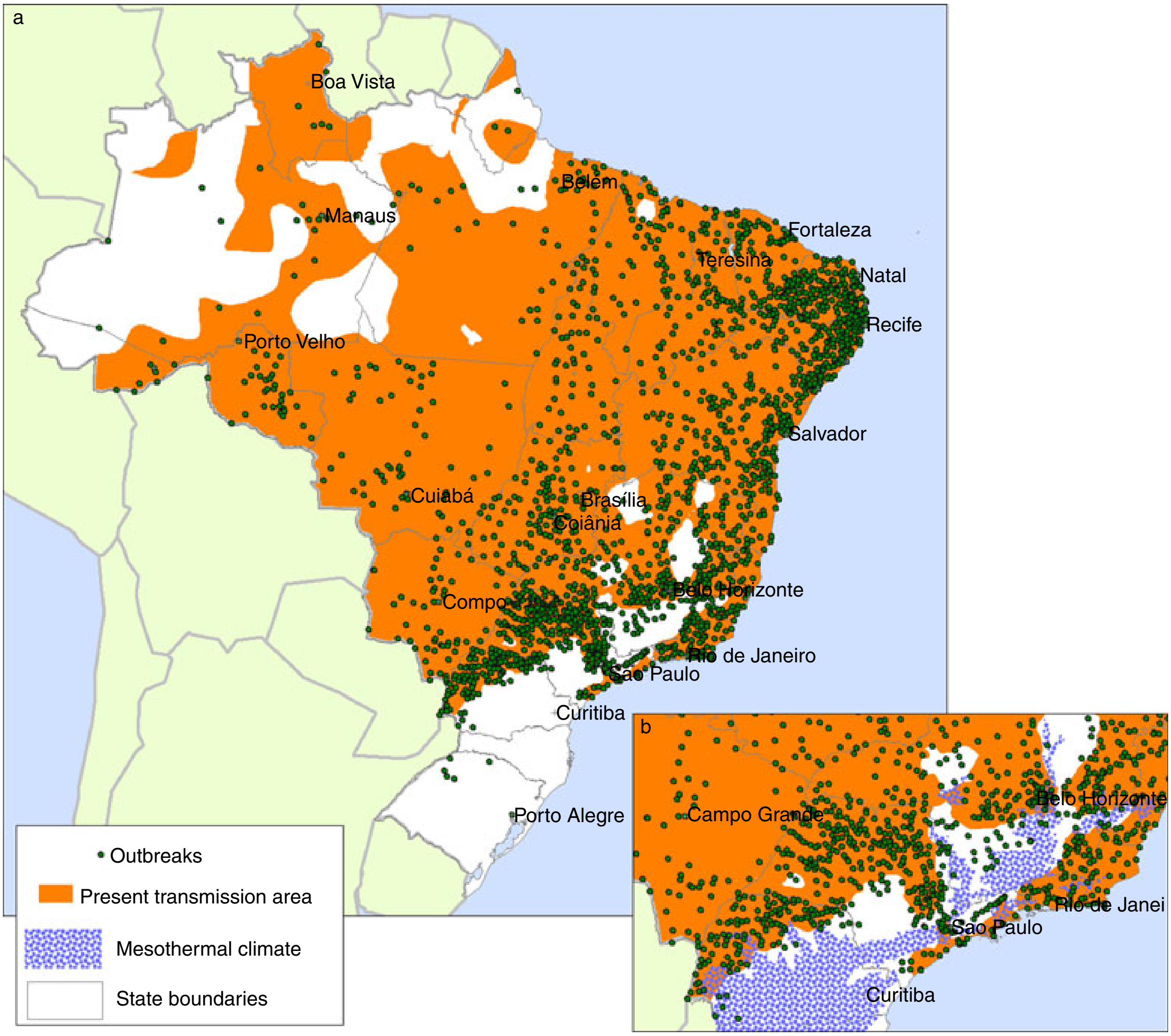

Figure 2 Estimated dengue transmission area and location of dengue outbreaks in Brazil between 2001 and 2012. Outbreaks were considered as an excess of cases with respect to the recent history (significantly higher than the historic mean plus two standard deviations according to a Poisson test). (a) Dengue transmission area as in 2012 and outbreaks in Brazil between 2001 and 2012. (b) Dengue transmission and mesothermal climate zone (in blue).

two regimes of spatial diffusion: (i) areas where outbreaks precede a sustainable transmission, constituting epidemiological events that inaugurate a permanent circulation of virus, and (ii) other areas where outbreaks are sporadic and transmission is discontinued. Outbreaks mark the arrival of dengue viruses in places where the vector is already present. However, establishment and spread are necessary for permanent transmission (Randolph & Rogers 2010). The differential epidemic permanence (establishment) is thus related to the city location. Within the mesothermal zone, outbreaks were identified in only 57 of 1133 cities.

Table 1 shows the posterior mean and credible intervals of the parameters estimated from the hierarchical model, relating dengue transmission permanence (*NYD300*) to climate zone and urban population size, while accounting for unobserved confounding factors. Results show that population size has a positive and statistically significant association with dengue transmission permanence. Cities located in the warm climate zone

Table 1 Posterior means and 95% credible intervals (CI, obtained from the 2.5% and 97.5% quantiles of the marginal posterior distribution) for the model intercept, parameters associated with the explanatory variables climate zone (categorical variable) and log population (continuous variable), and the variance of the exchangeable random. Note that climate zone level 1 (mesothermal zone) is incorporated into the model intercept. Level 2 (subwarm) and 3 (warm) parameter estimates express the difference from level 1

Parameter		Posterior mean (95% CI)
Intercept	α	−7.719 (−8.087, −7.252)
Climate zone (difference from mesothermal zone)		
Subwarm	β_2	3.043 (2.793, 3.313)
Warm	β_3	4.072 (3.833, 4.328)
Log population	γ	0.469 (0.384, 0.539)
Random effect variance	σ_θ^2	0.852 (0.778, 0.942)

increase the risk of dengue transmission permanence above that of cities located in the subwarm zone, and in turn, cities in the subwarm zone have an increased likelihood of dengue transmission permanence than those located in the mesothermal zone. The posterior mean variance for the unstructured random effects, σ_θ^2, was also statistically significant, highlighting the contribution of this latent effect in capturing within area variation of each city, *i*, compared with the map as a whole.

A likelihood ratio test statistic R_{LR}^2 was calculated as a goodness-of-fit measure, by comparing the fitted model (Equation 1) to a null model (with only the model intercept). The model was found to have $R_{\mathrm{LR}}^2 = 83\%$. Note that $0 \leq R_{\mathrm{LR}}^2 \leq 1$, with $R_{\mathrm{LR}}^2 = 1$ corresponding to a perfect fit and $R_{\mathrm{LR}}^2 \geq 0$ for any reasonable specified model (see Stewart-Ibarra & Lowe 2013). Therefore, this model explains a considerable proportion of the variance in dengue transmission permanence.

To illustrate the spatial pattern of dengue outbreaks, longitudinal sections were created along approximately 500 km of important roads connecting state capitals to smaller cities (Figure 3). The value of '*z*' was obtained by interpolating outbreak density along these axes for the years 2008, 2010 and 2012. As previously described, outbreak is a dichotomic variable (*OTBy*) and its spatial smoothing represents the probability to find an outbreak in a given area, *i*.

The first cross section starts in Recife, located along the coast of the north-east region, and extends towards the west, where medium and small cities are connected by a road network. The inner and final stretch of this

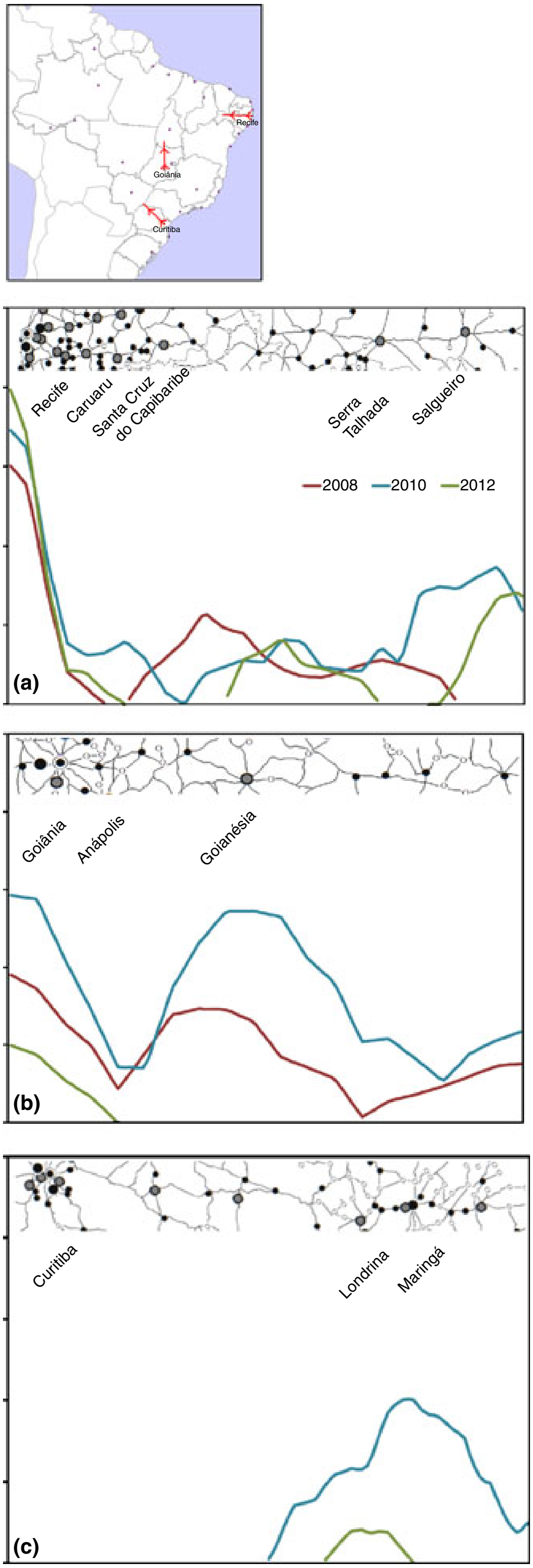

Figure 3 Cross sections of outbreak probabilities along roads starting in (a) Recife, (b) Goiania and (c) Curitiba. *Z* values represent the spatial smoothed density of outbreak occurrence.

transect crosses a semi-arid zone, where precipitation is markedly seasonal but temperature is warm and uniform. The second cross section begins in Goiania, in the central Brazilian plateau and extends northwards to the Amazonian biome. The third cross section starts in Curitiba in the south and extends towards the north-west, crossing two climatic domains throughout a dense road system connecting medium and large cities.

In Recife, outbreaks are observed throughout all years, while outbreaks occur periodically along the inner stretch. The first wave (2008) reaches cities near the Recife metropolitan region and in 2010 and 2012, the outbreaks are displaced to farther regions. During all these years, outbreaks were registered along this transect, moving to different cities. Along the transect from Goiania, moving outbreak waves are also observed in 2008 and 2010, when outbreaks were also more intense in the capital and its surroundings. However, in 2012, no outbreaks were verified in the northern stretch and their intensity diminishes in the Goiania metropolitan region. Conversely, in the case of Curitiba, no outbreaks were detected in the metropolitan region. Westwards, outbreaks were absent in 2008, then emerged in 2010 in the farther and warmer stretch and diminished in intensity in 2012.

Discussion and conclusions

Dengue epidemics are still diffusing in Brazil, such that outbreaks may or may not inaugurate a permanent and sustainable transmission cycle. Population and goods mobility corridors are important diffusion axes by which virus and vectors are dispersed. Diffusion waves were more intense between 2005 and 2009. Before the mid-1990s, dengue was typically limited to large cities (Siqueira-Junior *et al.* 2005). The epidemic spread was particularly observed in the state of Bahia between 1995 and 1998, starting from its capital Salvador, crossing humid but also dry climate zones through the major roads (Melo *et al.* 2010).

Despite the dispersed spatial pattern of outbreaks, the sustainability of dengue transmission is strictly related to climate. Cities located in the mesothermal climate zone present a lower probability of outbreak occurrence, with less favourable conditions for permanent transmission, even in the presence of the vector. The region of Curitiba illustrates the role of temperature regime in the fluctuation of dengue transmission cycles. In recent years, three epidemic waves produced numerous dengue cases, spreading rapidly due to the absence of previous population immunity. However, in Curitiba, very few cases were notified. The city, as well as the central plateau and coastal mountains, is dominated by mesothermal climate, where the vector is virtually absent and autochthonous cases are rare (Duque *et al.* 2010).

On the other hand, rainfall regime does not appear to represent an important constraint for dengue transmission. The decreasing humidity gradient, as well as the predominance of long dry seasons, does not hamper the occurrence of outbreaks and sustainable dengue transmission in the semi-arid region in the north-east. In this case, drought is thought to play a double role of restricting natural mosquito breeding sites, but stimulating local population to store water in improvised tanks (Caprara *et al.* 2009; Pilger *et al.* 2011).

It is worth noting the concentration of dengue outbreaks along the fringe of the mesothermal climatic zone. This spatial pattern may represent a tension between two dengue transmission regimes: one in which dengue transmission is permanent, the vector is abundant and a large portion of the population is immune to several dengue serotypes; and the other where transmission is discontinuous and the population is susceptible. The intermittent arrival of dengue viruses and the invasion of the *Aedes* mosquito along this fringe may produce outbreaks among susceptible populations. The climate and ecological transition zones, such as ecotones, may amplify the frequency and severity of disease transmission by exporting the vector to new environments (Magori & Drake 2013) and exposing susceptible population groups to new pathogens (Despommier *et al.* 2006), as observed for malaria and yellow fever.

In this sense, epidemic pulses are materialised by a peak (in time) and an extent of transmission (in space) by which new areas are reached. As the time evolution of incidence curves are asymmetric, it is expected that epidemic propagation waves in space present fast and skewed fronts and an asymptotic decreasing tail (Hanert *et al.* 2011).

The outbreak waves comprise expansion periods, but also retractions. Outbreak waves oscillate along major circulation routes, emanating from large and warm cities. This process was verified in South-East Asia, where rapid epidemic waves cross countries driven by human mobility (Cummings *et al.* 2004). However, in this study, we observed that in determinate conditions waves ceased and transmission was interrupted, likely due to the scarcity of population, weak human mobility among cities and unfavourable climatic conditions. In this sense, isolation may act as a protective barrier for small cities (Teurlai *et al.* 2012). Remote areas in the Brazilian Amazon remain protected from large dengue epidemics, as depicted from the diffusion map (Figure 1), possibly due to the long distances, high costs and operational difficulties imposed on human mobility (Barcellos *et al.* 2010).

The exploratory model presented in this study indicated that large and warm cities presented a high probability of long-term dengue transmission. The association between population size and dengue transmission sustainability reveals that large and connected cities may play an important role in epidemic maintenance (Haggett 2000), as well as diffusion epicentres towards their influence region due to several combined factors.

First, demographic density is a key variable that promotes efficient interactions between vectors and susceptible populations, thus affecting the basic reproduction number (R_0). Large cities configure a viable landscape for human interactions and mosquito reproduction (Stoddard *et al.* 2013).

Second, large cities are areas where vast numbers of people circulate, promoting virus dispersal. Tourism, specialised services and commerce stimulate human displacements from inner regions and international travel to metropolises. It is not a coincidence that Rio de Janeiro was the city of arrival and spread of all dengue virus types.

Third, large cities often have a high concentration of immigration and demographic growth, permitting the re-establishment of susceptible populations. The recent trend of increasing incidence among children in Recife demonstrates the renewal of susceptible groups, even in a hyperendemic city (Rodriguez-Barraquer *et al.* 2011).

Lastly, large cities have become heat islands, which results in warmer nights and winter periods. The reduction in temperature variability in inner city areas may create favourable microclimates for mosquito reproduction (Mendonça 2006).

For all these reasons, large and warm cities 'spawn' dengue viruses and permit the spread to neighbouring and connected surroundings (Gubler 2004).

In contrast to contagious diseases, dengue epidemics require an environmental substrate on which the vector will reproduce. The map of *Aedes aegypti* distribution released by SVS/MS (Braga & Valle 2007) is relatively analogous to the present dengue transmission area, as projected in this work. However, vector infestation distribution is wider than the transmission area and the number of infested cities is continuously increasing in the country, while dengue incidence presents oscillations in the number of cases and the number of cities reporting autochthonous cases (Teixeira *et al.* 2009). *Aedes* aegypti infestation was assessed in São Paulo state, showing a rapid dispersion among contiguous cities. Infestation was considered as irreversible, as elimination was only observed in few cities and for short periods (Glasser & Gomes 2000). Vector presence is thus a necessary but not a sufficient condition for sustainable transmission.

Among the limitations of this study, it is worth noting the difficulties to identify the autochthony of cases and to confirm diagnostics by laboratory tests. These factors reinforce the importance of using synthetic and precautious indicators to assess transmission timing and permanence. Working with elevated incidence rate periods and places centres the attention on outbreaks, which are more accurately registered than single and isolated cases, and avoids the bias of differential capacity of health services. Also, dengue strain type identification is not available for all notified cases, but is available for a sample of state populations. It is known that in central states, all serotypes are circulating, which may explain the repeated occurrence of outbreaks in cities at the core of the transmission area (Figure 2). The introduction of new strains may cause rapid variations in time (outbreaks) and generate new epidemic waves, but is not likely to produce an expansion of the transmission area, which is constrained by the abundance of vector and demographic dynamics. In fact, incidence has been oscillating during recent years, but the number of cities presenting cases and vector infestation tends to stabilise (Barreto & Teixeira 2008).

The exploratory model employed in this study estimates the relative contribution of climate and population size to dengue transmission permanence, while accounting for unobserved heterogeneity and unknown confounding factors via the inclusion of unstructured random effects. However, this does not allow for explicit spatial dependence between cities, arising through similar dengue transmission patterns, for example, in neighbouring densely populated urban areas as opposed to sparsely populated cities. Conditional intrinsic Gaussian autoregressive (CAR) models are often employed to account for spatial dependency in disease mapping (Besag *et al.* 1991). When undertaking CAR modelling of area data, it is necessary to define an adjacency matrix that characterises the neighbourhood structure of the data being analysed (Earnest *et al.* 2007). However, in certain situations, the selection of a suitable structural form is not trivial. Typical approaches include defining neighbours according to the distances between centroids or assuming that each area is dependent only on areas that share a common boundary. However, municipalities in the Amazon region share boundaries but the cities are very far apart, so dengue is less likely to spread, whereas small cities in central and southern regions are very close to each other and diffusion is facilitated in this case. In Brazil, certain cities may be more closely related, in terms of dengue transmission, to remote areas connected by air or road transport links, rather than neighbouring or nearby municipalities. A neighbourhood matrix based on the hierarchical structure of urban centres defined on the basis of the flow of goods, services and people via air and road transport links will be explored as this research develops.

Classifying climate into three fixed categories provides an overall picture of the role of temperature in sustaining dengue transmission. However, dynamic models may be useful in further studies, for example, considering annual, seasonal and intraseasonal variations of separate meteorological variables (Lowe *et al.* 2011, 2013).

Final remarks and recommendations

Health surveillance activities, such as vector control, target geographical areas rather than individuals or populations, due to the absence of a vaccine and the ineffectiveness of human mobility restrictions. This work may contribute to the improvement of health surveillance systems, by identifying warm and large cities as centres of sustainable dengue virus circulation. It would be more effective to target these diffusion centres to hamper or reduce the intensity of epidemic waves.

In this study, temporal and spatial patterns of dengue diffusion were identified. Peaks in dengue incidence correspond to a spread of dengue viruses in areas where the vector already exists. These pulses may reach distant cities, where susceptible populations could be infected. The concentration of dengue outbreaks along climate zone fringes highlights the future risk under the perspective of climate change, for example, prolonged warm seasons and increased rainfall in southern Brazil (Marengo 2007). Equally, special attention should be targeted at small and remote cities, which may undergo severe outbreaks in the coming years if this isolation is broken. The construction of roads towards remote areas of the Amazon is a threat for these populations (Barcellos *et al.* 2010).

The maps produced in this study are preliminary. They will soon be changed by climatic and socio-economic moving boundaries. However, these alterations are not random. These processes are determined by ongoing climate variability and socio-demographic changes. Understanding these environmental and societal determinants is essential for developing strategies for dengue control.

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