International Journal of Environmental Health Research
Vol. 21, No. 6, December 2011, 415–426

The influence of climate variables on dengue in Singapore

Edna Pinto[a], Micheline Coelho[a], Leuda Oliver[a] and Eduardo Massad[a,b]*

[a]*Department of Medicine, University of Sao Paulo, Sao Paulo, Brazil;* [b]*Department of Infectious Diseases, London School of Hygiene and Tropical Medicine, London, UK*

(*Received 10 December 2010; final version received 3 March 2011*)

In this work we correlated dengue cases with climatic variables for the city of Singapore. This was done through a Poisson Regression Model (PRM) that considers dengue cases as the dependent variable and the climatic variables (rainfall, maximum and minimum temperature and relative humidity) as independent variables. We also used Principal Components Analysis (PCA) to choose the variables that influence in the increase of the number of dengue cases in Singapore, where PC_1 (Principal component 1) is represented by temperature and rainfall and PC_2 (Principal component 2) is represented by relative humidity. We calculated the probability of occurrence of new cases of dengue and the relative risk of occurrence of dengue cases influenced by climatic variable. The months from July to September showed the highest probabilities of the occurrence of new cases of the disease throughout the year. This was based on an analysis of time series of maximum and minimum temperature. An interesting result was that for every 2–10°C of variation of the maximum temperature, there was an average increase of 22.2–184.6% in the number of dengue cases. For the minimum temperature, we observed that for the same variation, there was an average increase of 26.1–230.3% in the number of the dengue cases from April to August. The precipitation and the relative humidity, after analysis of correlation, were discarded in the use of Poisson Regression Model because they did not present good correlation with the dengue cases. Additionally, the relative risk of the occurrence of the cases of the disease under the influence of the variation of temperature was from 1.2–2.8 for maximum temperature and increased from 1.3–3.3 for minimum temperature. Therefore, the variable temperature (maximum and minimum) was the best predictor for the increased number of dengue cases in Singapore.

Keywords: dengue; Poisson Regression Model; Principal Component Analysis; temperature; relative risk

Introduction

Climate change is potentially the biggest global health threat in the 21st century (Costello et al. 2009). The World Health Organization (WHO) estimates attribute more than 150,000 deaths with 5 million DALY[1] due to diseases affected by changing climate in the last three decades (Patz et al. 2005).

It is expected that global temperature rise will increase the frequency of infectious vector-borne diseases like dengue, yellow fever and other viral diseases in the next decades (Husain and Chaudhary 2008). Temperature affects the rate of pathogen

*Corresponding author. Email: edmassad@usp.br

ISSN 0960-3123 print/ISSN 1369-1619 online

http://dx.doi.org/10.1080/09603123.2011.572279
http://www.tandfonline.com

maturation and replication in the mosquitoes, in the density of the vector in a particular area and increases the likelihood of infection (Costello et al. 2009).

The global prevalence of dengue has grown dramatically in recent decades. Currently it is estimated that some 2.5 billion people – two fifths of the world's population – are at risk from dengue (WHO 2010). About 100 countries of the Americas, Africa, Pacific Islands, Asia and the Mediterranean have the mosquito *Aedes aegypti* and it is estimated that 100 million people annually contracted dengue fever according to the World Health Organization (Ooi 2001; Dhang et al. 2005; Ooi et al. 2006; Halstead 2008; Ooi and Gubler 2008; WHO 2010). By 2080, about 6 billion people will be at risk of contracting dengue fever as a consequence of climate change, compared with 3.5 billion if the climate remained unchanged (Hales et al. 2002; Intergovernmental Panel on Climate Change [IPCC] 2007).

According to several epidemiological studies, the most relevant climatic variables are ambient temperature and precipitation, variables that influenced each stage of the life cycle of the vectors (Jetfen and Focks 1997; Halstead 2008; Smith and Gubler 2008; Câmara et al. 2009; Johansson et al. 2009).

Temperature, for example, imposes limits on the distribution of dengue in the world, since the *Aedes aegypti* rarely survives outside the region comprised by the parallel 45° N and 35° S, where the highest temperatures are registered (Câmara et al. 2009). The vector has a range of optimal conditions, both for temperature and rainfall, which influence mosquitoes' breeding, and for each phase of its life cycle (egg, pupae, larva and adult).

According to Donalísio and Glasser (2002), the variation of Relative Humidity and of rainfall, influence the longevity of *Aedes aegypti*, which can lead the infected female aedes to complete more than one cycle of the replication of the virus, thus becoming infective. This result agrees with that found by Andrade and Dantas (2004).

In Singapore, dengue is endemic with year-round transmission (Ministry of Health [MOH] of Singapore 2005). Sero-epidemiological surveys conducted in 1982–84, 1990–91, 1993 and 1998 indicated that dengue prevalence declined from 46% in 1982–84 to 29.4% in 1998 (Wilder-Smith et al. 2004). In spite of the great effort in *Aedes* control implemented in Singapore during the last decades, outbreaks had occurred with greater frequency and intensity with the largest outbreak reported in small dengue outbreaks until the large epidemic of 2004–2005.

The incidence of dengue increased from a baseline of 9.3 cases per 100,000 habitants in 1988 to 312.2 per 100,000 in 2005 (Burattini et al. 2008). All four dengue serotypes have been detected, with DEN-3 predominating in 1992, DEN-2 in 1998 and DEN-1 in 2004–2005 (Burattini et al. 2008).

Recently Burattini et al. (2008) proposed a mathematical model to assess the impact of environmental changes on dengue incidence by making the mosquitos carrying capacity as a state variable. This was based on the assumption that the increase in both the local average temperature observed in the previous 15 years, and the number of new construction sites providing breeding places for mosquitoes, were monotonically increasing functions of time. The model reproduced the actual number of cases with good accuracy, i.e., it reproduced qualitatively the real data and was used to propose control strategies to mitigate the epidemic in 2005.

As we show later in this paper, there was an observed trend of increase in temperature and dengue cases in Singapore in the period between 1989 and 2005 (National Environmental Agency [NEA] Singapore 2005), with a Pearson correlation coefficient between temperature and dengue estimated at 0.64 (Burattini et al. 2008).

In this work, we correlated the number of dengue cases with several climatic factors. This was performed through a Poisson Regression Model (PRM), considering the number of cases as the dependent variable and the climatic conditions of rainfall, maximum and minimum relative humidity and temperature as independent variables.

One of the objectives of the study was to estimate the effects of weather on the occurrence of dengue, the relative risk, and the increase of the probability of occurrence using Poisson Regression Model. Another objective was to use the model as a predictive PRM to monitor climate change and control the emergence of new outbreaks.

The studied region

Singapore is situated in Southeast Asia at approximately 137 km north of the equator near latitude 1.5° N and longitude 104° E. It is separated from Peninsular Malaysia by the Straits of Johor and from the Indonesian Islands by the Straits of Singapore. Its total land area (including smaller islands) is 641.4 km^2. The main island of Singapore, where almost all the country's residential commercial and industrial developments are located, covers an area of 580 km^2 and is about 42 km from west to east and 23 km from north to south.

Climatology of Singapore

The climate is characterized by high temperature and relative humidity and abundant rainfall. It can be divided into two main seasons: the Northeast Monsoon (December to early March) and the Southwest Monsoon (June to September), which are separated by two short periods of inter-monsoons: Pre-Southwest Monsoon (late March to May) and Pre-Northeast Monsoon (October to November).

Data

The study period consisted of a eight-year period from January 2000 to December 2007 with two different weekly date sets: meteorological and epidemiological. Epidemiological data, i.e., the number of dengue cases confirmed by the Ministry of Health Singapore (MOH 2008), were weekly averaged over the 416 weeks of the studied period. The meteorological variables are the maximum and minimum temperature (MaxTemp and MinTemp), the maximum and minimum relative humidity (MaxRH and MinRH) obtained from the Climate Diagnostic Center and National Oceanographic and Atmospheric Administration (CDC/NOAA 2008) and the rainfall obtained from the Tropical Rainfall Measuring Mission (TRMM 2008).

Regarding data analysis, the approach used was an ecological study of time series. This kind of study is characterized by the analysis of temporal trends of variables as well as by correlations between selected variables.

Methods

The Poisson Regression Model (PRM)

We applied a weekly lag structure on all the variables to know which of these meteorological variables can directly affect the number of dengue cases in the same weeks. Next, we constructed a correlation matrix with all the variables and their respective time lags. In this process it was possible to identify which time lags and variables were most representative in the correlation matrix.

Finally, a Poisson Regression Model was proposed, considering the number of dengue cases as dependent variable and rainfall, maximum and minimum relative humidity and temperature as independent variables. The univariate Poisson Regression Model (PRM) was based on the following model (Coelho-Zanotti 2007; Coelho-Zanotti et al. 2010):

$$Log\,\lambda(t) = \alpha + \sum_{l} \beta * (X) \tag{1}$$

where, $\lambda(t)$ is the dependent variable, X represents the range of the independent variables and α and β are estimated coefficients.

Next, we applied the estimated coefficients to calculate the increase in the number of dengue cases (INDC), the relative risk (RR) with the confidence interval (CI) and the probability (Prob) using the following equations:

$$INDC = \left[\left(\exp^{(\beta * X)}\right) - 1\right] * 100 \tag{2}$$

where the *INDC* is in percentage (%).

$$RR = \exp^{(\beta * X)} \tag{3}$$

$$CI_{95\%} = \exp\left[\beta \pm 1.96 * \mathrm{se}(\beta)\right] \tag{4}$$

where $se(\beta)$ is the Standard Error of β.

$$Prob = \frac{1}{1 + e^{-(\alpha + \beta * X)}} \tag{5}$$

where the *Prob* is in percentage (%). All analyses were carried out with R-Plus and SPSS 15 software and we set all significant levels at 5%.

Principal Components Analysis (PCA)

The Principal Component Analysis used Factorial Analysis (FA), a statistical technique designed to interpret the structure of a series of multivariate data from their respective variance-covariance matrix. This technique can use, among others, the method of Principal Components Analysis (PCA). PCA transforms a set of original variables into a smaller set of linear combinations that better explain the greater part of the variance of the original series of data. The purpose of PCA is to determine the factors (or Principal components [PCs]) underlying the data, in order to determine the amount of the total variance that can be explained by the fewest of these factors (Wilks 1995). The calculations of FA and PCA were carried out with SPSS 15 software.

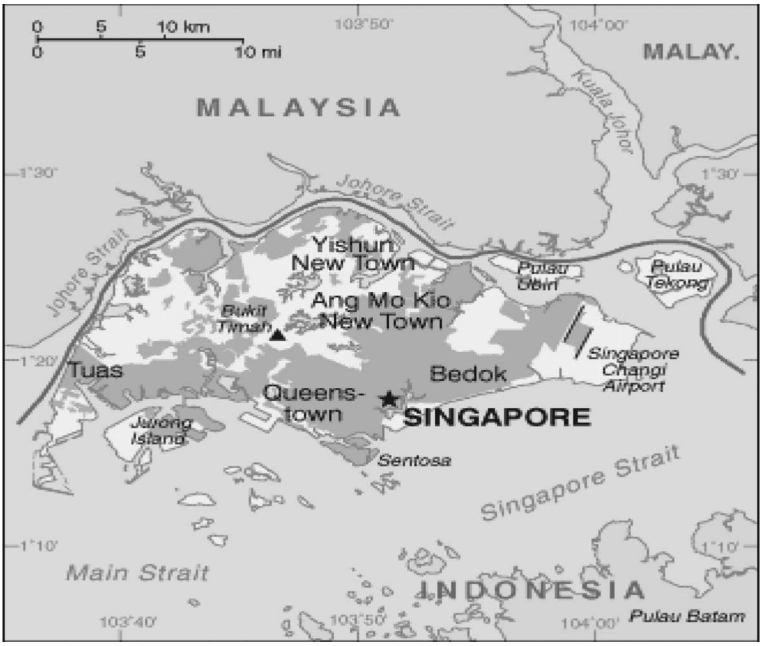

Figure 1. The total area of the Singapore region localized in Southeast Asia (NEA) National Environmental Agency, Singapore, http://www.dengue.gov.sg.

Results

Time series of the variables

It should be noted that the increase in the disease shows a pronounced seasonality, with peaks from May to September. The highest total incidence of dengue cases occurred in the years 2004 (9,059 cases), 2005 (13,874 cases) and 2007 (8,664 cases). In the period between 2000 and 2007, the maximum rainfall volume recorded was 2,816 mm (in December 2006); the average maximum and minimum temperature was of 29.7°C (in May 2005) and 24.7°C (in January 2007). The maximum and minimum relative humidity in the period was 100% (in December 2006) and 83.5% (in August 2004). Figure 2 shows the time series of the variables.

Figure 3 shows the total monthly averaged number of confirmed dengue cases in the period between 2000 and 2007. The period of highest incidence of disease are the months of June, July, August and September with a peak in July (6,564 cases) and September (7,343 cases).

Table 1 shows the descriptive statistics of the data used in this study. Data are presented monthly. In addition, the variables were transformed from weekly to monthly data, in order to compose the table in the same time scale.

The Poisson Regression Model

The lag structure was determined by varying from 0–40 weeks between the dependent and the independet variables. Next, we constructed a correlation matrix with all the variables and their respective time lags. In this process it was possible to identify which time lags and which variables were most representative in the correlation matrix. The most significant lags found were 0–16 weeks.

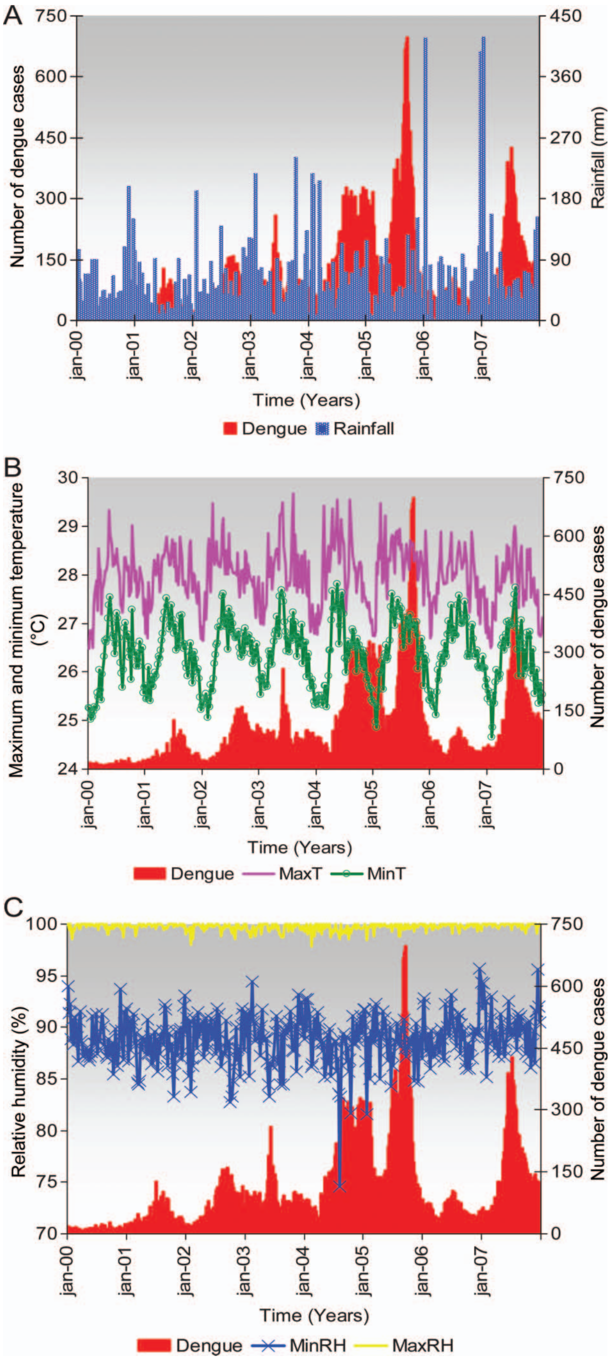

Figure 2. The time series of the weekly accumulated number of dengue cases (red bars): (a) with the weekly accumulated of rainfall (blue bars); (b) with the weekly average of the maximum (rose line) and minimum (green line) temperature and (c) with the weekly average of the maximum (yellow line) and minimum (blue line) relative humidity in the period from 2000–2007.

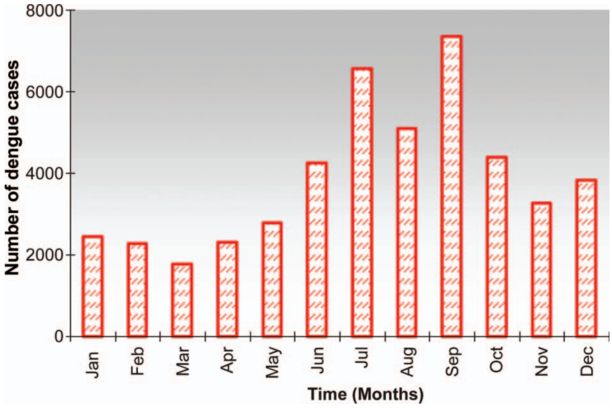

Figure 3. Monthly average of the total number cases of the disease in the period from 2000–2007.

Table 1. Descriptive statistics of the variables.

Variables	Average	Median	Minimum	Maximum	Std. Deviation	CV
Rainfall (mm)	44.2	32.4	0.0	417.8	51.3	116.2
MaxTemp (°C)	28.0	28.0	26.5	29.7	0.6	2.2
MinTemp (°C)	26.4	26.4	24.7	27.8	0.6	2.4
MaxRH (%)	99.7	99.9	97.9	100.0	0.4	0.4
MinRH (%)	88.8	89.0	74.6	95.7	2.3	2.6
Dengue cases	111.4	75.5	3.0	697.0	111.8	100.3

The variables that were best correlated with statistical significance were the maximum and minimum temperature and so the modeling was performed with only these variables. Table 2 shows the correlation matrix with the Pearson's correlations for maximum and minimum temperatures and their significance level. The Kolmogorov-Smirnov adherence test to a normal distribution, showed values of 8.0 and 9.2 to maximum and minimum temperature, respectively. With the parameters estimated by the PRM we calculated the increase of the disease, the relative risk increase influenced by the maximum and minimum temperatures, and the probability of occurrence of new dengue cases in Singapore.

Increase in the number of dengue cases

In Table 3, the coefficients α and β estimated by the model and used to calculate the INDC, RR, CI and Prob with a range from 2–10°C of variation in the maximum and minimum temperatures are presented.

The coefficients α and β were then applied in Equation 2 to calculate the INDC (Table 4). For every 2–10°C of variation of the maximum and minimum temperature there was an average increase of 22.2–184.6% in the number of dengue cases. For the minimum temperature, we observed that for same variation, there was an average increase of 26.1–230.3% in the number of the dengue cases from April to August.

Table 2. Pearson's Correlation between number of dengue cases and meteorological variables (maximum and minimum temperature) and the statistical significance levels.

Variables' lags	r (p <0.005)	Variables' lags	r (p <0.005)
MaxTemp lag 0	0.140	MinTemp lag 0	0.188
MaxTemp lag 1	0.162	MinTemp lag 1	0.215
MaxTemp lag 2	0.173	MinTemp lag 2	0.241
MaxTemp lag 3	0.188	MinTemp lag 3	0.257
MaxTemp lag 4	0.177	MinTemp lag 4	0.265
MaxTemp lag 5	0.185	MinTemp lag 5	0.284
MaxTemp lag 6	0.183	MinTemp lag 6	0.287
MaxTemp lag 7	0.194	MinTemp lag 7	0.294
MaxTemp lag 8	0.217	MinTemp lag 8	0.298
MaxTemp lag 9	0.210	MinTemp lag 9	0.291
MaxTemp lag 10	0.220	MinTemp lag 10	0.291
MaxTemp lag 11	0.240	MinTemp lag 11	0.287
MaxTemp lag 12	0.234	MinTemp lag 12	0.275
MaxTemp lag 13	0.238	MinTemp lag 13	0.259
MaxTemp lag 14	0.233	MinTemp lag 14	0.234
MaxTemp lag 15	0.223	MinTemp lag 15	0.207
MaxTemp lag 16	0.206	MinTemp lag 16	0175

Table 3. The coefficients α and β estimated by the PRM to maximum and minimum temperatures.

Variables	α	β
MaxTemp	2.043	0.094
MinTemp	1.136	0.109

Table 4. Variation in the range of maximum and minimum temperature at which they cause an increase in the numbers of dengue cases.

			Increase of the numbers of dengue cases (%)				
Variables		Months	Δ2 (°C)	Δ4 (°C)	Δ6 (°C)	Δ8 (°C)	Δ10 (°C)
Temperature	**Maximum**	April	30.5	70.2	122.0	189.6	277.9
		May	18.5	40.5	66.5	97.5	134.4
		June	16.0	35.2	58.0	85.3	118.0
		July	21.1	47.2	79.3	119.1	168.4
		August	24.8	56.9	98.5	152.9	224.1
		Average	22.2	50.0	84.9	128.9	184.6
	Minimum	April	22.0	49.0	82.1	122.9	173.2
		May	23.7	53.0	89.3	134.2	189.8
		July	23.1	52.1	89.0	136.0	196.2
		August	35.8	84.5	150.5	240.3	362.2
		Average	26.1	59.6	102.7	158.4	230.3

The RR was calculated to determine how the occurrence of dengue cases was related to the influence of maximum and minimum temperatures. However, if there were a variation in the maximum temperature of 2–10°C, the increased risk of occurrence of the disease would be from 1.2–2.8 with a $C/_{95}$ 1.13: 1.09. For minimum temperature, in the same interval, the increase would be from 1.3–3.3 with a CI_{95} 1.15: 1.10 (Figure 4).

The monthly probabilities of occurrence of new cases of dengue were calculated using Equation 5. During the months of May to September the chances of new cases further increased in July (85–95%) and September (84–94%). However, regardless of climatic variables, there was a probability of 79% of new cases that can be attributed to other causes, such as sanitation, water accumulated in containers, potted plants, gardens badly treated, among others.

The months from April to September showed the highest probabilities of the occurrence of dengue, although the incidence values were very high in the spring and summer seasons too. We found that the probability increased slightly from 82% (in October) to 91% (in December). This latter period represents the beginning of the rainy season (Figure 5).

Principal Components Analysis (PCA)

The need for a second analysis was to attempt to corroborate through a second statistical method the influences of meteorological variables on the number of

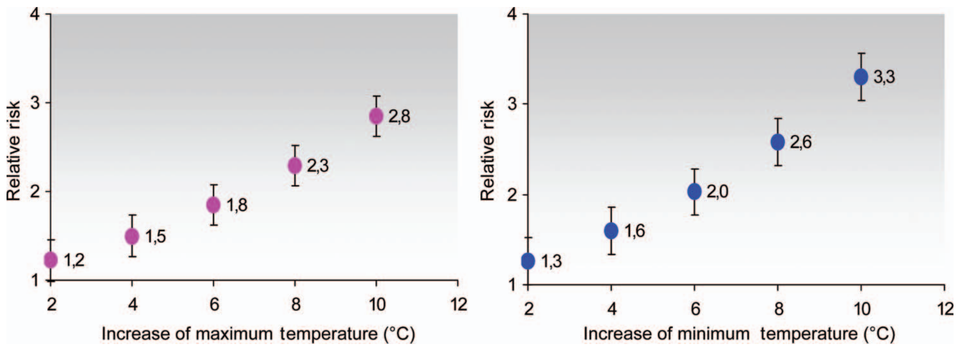

Figure 4. The increase in the risk of ocorrence of dengue cases with the influence of the (a) maximum and (b) minimum temperature.

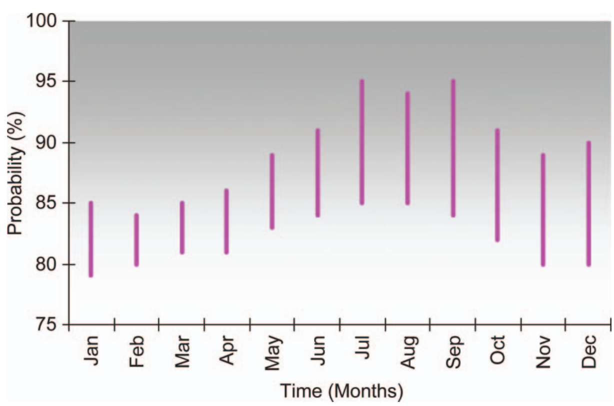

Figure 5. Monthly probability of occurrence of new dengue cases in the period from 2000–2007.

dengue cases in Singapore. PCA was used to confirm that the meteorological variables influence the number of dengue cases in Singapore. The model with the scores of the PCA was in accordance with the PRM, where PC_1 was represented by temperatures and rainfall and PC_2 was represented by relative humidity. The variable precipitation was discarded for not having a significant correlation with the variable dengue. Varimax rotation[2] was used. Table 5 shows the factor analysis of the meteorological variables rainfall, MaxTemp, MinTemp, MaxRH and MinRH, the factors being considered PC_1 and PC_2 that together explain 67.8% of variance of data, being satisfied with the explanation of the procedure (Wilks 1995).

The PC_1 explains 45.4% of the variance, and the rainfall was negatively associated with the temperatures. The PC_2 explaining 22.4% of the variance in this case was the relative humidity. Temperatures have the largest share, followed by relative humidity. The sum of PC1+PC2 should represent 70% of the original set of data used in a study with such an approach.

Discussion

Our results reflect the climatic characteristics of Singapore; more rainy in December to March and less rainy in June to September, a typically tropical climate. However, we must remember that it rains throughout the year and temperatures are also high throughout the year. The analysis of cases of dengue and climate variables showed a positive correlation between the disease and the maximum and minimum temperatures. The PRM model was able to predict with acceptable error the increase in the number of cases of Dengue based on this climatic variable.

Through PCA, we observed that the greatest weight was for the temperature variable, followed by precipitation. Therefore, the PCA analysis corroborates the results of the PRM model, showing that the variable that most influenced the increase in the number of dengue cases is the same temperature (Wilks 1995).

In addition, our results are consistent, in the sense that minimum temperature ranging on average between 25°C and 27°C through the year, facilitating precipitation and the cycle of life of the mosquito, which in turn results in the spreading of the disease. Temperature explains a great portion of the variance because in Singapore rain is a consequence of increased temperatures inducing convection and precipitation in the period of the Southeast Monsoon (April to September).

It is important to note that, in a recent publication, Wilder-Smith et al. (2010) did not obtain any significant association between temperature and dengue cases. However, those authors applied a different statistical model to the data, namely the Autoregressive Integrated Moving Average (ARIMA) model, which is a time-series

Table 5. Factor analysis with Varimax rotation and commonalities (h^2) concerning the meteorological variables.

Variables	PC_1	PC_2	h^2
Rainfall	−0.634	0.159	0.427
MaxTemp	0.895	0.219	0.849
MinTemp	0.733	0.490	0.777
MaxRH	−0.208	0.796	0.677
MinRH	−0.697	0.415	0.658
Eigenvalues	2.269	1.120	Total
% of variance	45.384	22.402	67.786 ≈ 70%

analysis and not a multivariate model as the Poisson Regression model applied in this paper.

Finally, the dengue epidemic and its increase can be monitored by this methodology, because it shows how and when there is an increase in the number of cases of the disease. Therefore, for too much rain in the northeast monsoon (December to early March), there is an expected increase in disease, because excess water will interfere with the life cycle of the mosquito, allowing it to ''wash out'' the mosquitoes.

However, during hot, dry weather in the southeast monsoon (June to September), mosquitoes are in a perfect environment for their entire life cycle, thus generating a high incidence of dengue in the city of Singapore. Therefore, this work represents an important step in understanding the disease and to find a way to help in the designing of a control strategy for reducing the number of dengue cases.

Thus, we conclude that the variable temperature (maximum and minimum) is the best predictor for the number of dengue cases in the city of Singapore. PCA is a very good alternative when working with many variables of different units because we consider the use of the scores given to each of these variables. The results obtained with this technique were compared with the results of PRM and were very satisfactory.

If we know beforehand the change or increase in weather variable, we can use the PRM model to estimate how much the increase in the value of those variables influences the number of cases of the disease. This suggests that results of the model PRM can be optimized with more variables that provide the best forecast for the number of cases.

Acknowledgements

This work was partially supported by CNPq, CAPES, FAPESP and LIM01/HCFMUSP.

Notes

1. DALY, ''The Disability-Adjusted Life Year'', is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death (Murray and Lopez 1996).
2. Varimax rotation is used to simplify factors by maximizing the variance of the weights (weights of the new factors were divided by the square roots of their commonalities). This process of rotating the initial factor aims to create a clearer separation between the factors.

References

Andrade IS, Dantas RT. 2004. Estudo da Influência de Elementos Meteorológicos nos Casos de Cólera, Dengue e Meningite na Cidade de Campina Grande, Anais CBMET, Edição XIII, Fortaleza.

Burattini MN, Chen M, Chow A, Coutinho FAB, Goh KT, Lopez LF, Ma S, Massad E. 2008. Modelling the control strategies against dengue in Singapore. Epidemiol Infect. 136(3):309–319.

Câmara FP, Gomes AF, Santos GT, Câmara DCP. 2009. Clima E Epidemias de Dengue no Estado do Rio de Janeiro. Rev da Sociedade Brasileira Med Trop. 42(2):137–140.

Climate Diagnostic Center/National Oceanographic and Atmospheric Administration (CDC/NOAA). 2008. Accessed 19 July 2008 from the website: http://www.cdc.noaa.gov/.

Coelho-Zanotti MSS. 2007. Uma Análise Estatística com Vistas a Previsibilidade de Interações por Doenças Respiratórias em Função de Condições Meteorológicas na Cidade de São Paulo. Tese de Doutorado em Meteorologia no Instituto de Astronomia, Geofísica e Ciências Atmosférica da USP/São Paulo, 178 f.

Coelho-Zanotti MSS, Gonçalves FLT, Latorre MRDO. 2010. Statistical analysis aiming at predicting respiratory tract disease hospital admissions from environmental variables in the city of São Paulo. J Environ Public Health. Vol. 2010, Article ID 209270, 11 pages (DOI: 10.1155/2010/209270).

Costello A, Abbas M, Allen A, Ball S, Bellamy R, Friel S, Grace N, Johnson A, Kett M, Lee M, Levy C, Maslin M, McCoy D, McGuire B, Montgomery H, Napier D, Pagel C, Patel J, Oliveira JAP, Redclift N, Rees H, Rogger D, Scott J, Stephenson J, Twigg J, Wolff J, Patterson C. 2009. managing the health effects of climate change. Lancet. 373:1693–1733.

Donalísio MR, Glasser CM. 2002. Vigilância entomológica e controle de vetores do dengue. Rev Bras Epidemiol. 5:259–272.

Dhang CC, Benjamin S, Saranum MM, Fook CY, Lim LH, Ahmad NW, Azirun MS. 2005. Dengue vector surveillance in urban residential and settlement areas in Selangor, Malaysia. Trop Biomed. 22(1):39–43.

Hales S, de Wet N, Maindonald J, Woodward A. 2002. Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. Lancet. 360:830–834.

Halstead SB. 2008. Dengue virus-mosquito interactions. Ann Rev Entomol. 53:273–291.

Husain T, Chaudhary JR. 2008. Human helath risk assessment due to global warming – a case study of the Gulf countries. Int J Environ Res Public Health. 5:204–212.

Intergovernmental Panel on Climate Change (IPCC). 2007. Impacts, adaptations and vulnerability. In: Parry ML, Canziani OF, Palutikof JP, van der Linden PJ, editors. Contribution of working group II to the 4th assessment report of the IPCC. Cambridge: Cambridge University Press.

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

Johansson MA, Dominici F, Glass EG. 2009. Local and global effects of climate on dengue transmission in Puerto Rico. PLOS Neglected Trop Dis. 3(2):e382.

Ministry of Health of Singapore (MOH). 2005. Final report of the expert panel on dengue. Accessed 21 September 2005 from the website: http://www.moh.gov.sg/cmaweb/attachments/topic/3625c5ae51QU/ Final_Reportdengue_7_Oct_05.pdf. Accessed 16 July 2008 from the MOH website: http://www.moh.gov.sg/mohcorp/default.aspx.

Murray CJL, Lopez AD. 1996. The global burden of disease. Geneva: World Health Organization and the World Bank.

National Environmental Agency (NEA), Ministry of Environment and Water Resources of Singapore. 2005. NEA's key operation strategies in dengue control. Accessed 8 September 2005 from the website:http://app2.nea.gov.sg/localclimate_ClimatologyOfSingapore. aspx.

Ooi EE, Gubler DJ. 2008. Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. Caderno de Saúde Pública, Rio de Janeiro. 25(Supp1S):115–124.

Ooi EE, Goh KT, Gubler DJ. 2006. Dengue prevention and 35 years of vector control in Singapore. Emerg Infect Dis. 12:6.

Ooi EE. 2001. Changing pattern of dengue transmission in Singapore. Dengue Bull. vol. 25.

Patz JA, Lendrum DC, Holloway T, Foley JA. 2005. Impact of regional climate change on human health. Nature. 438:310–317.

Smith AW, Gubler DJ. 2008. Geographic expansion of dengue: the impact of international travel. Méd Clin N Am. 92:1377–1390.

Tropical Rainfall Measuring Mission (TRMM). 2008. Accessed 19 July 2008 from the website:http://disc2.nascom.nasa.gov/Giovanni/tovas/TRMMV6.3B42.shtml.

Wilder-Smith A, Earnest A, Tan SB, Ooi EE, Gubler DJ. 2010. Lack of association of dengue activity with dengue. Epidemiol Infect. 138:962–967.

Wilder-Smith A, Foo W, Earnest A, Sremulanathan S, Paton N. 2004. Seroepidemiology of dengue in the adult population of Singapore. Trop Med Int Health. 9:305.

Wilks DS. 1995. Statistical methods in the atmospheric sciences: an introduction. San Diego: Academic Press. p. 467.

World Health Organization (WHO). 2010. Dengue and dengue haemorrhagic fever. Fact sheet No. 117. Accessed 2 August 2010 from the website:http://www.who.int/mediacentre/factsheets/fs117/en/, 2005.