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Weather factors influencing the occurrence of dengue fever in Nakhon Si Thammarat, Thailand

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Abstract. This study explored the impact of weather variability on the transmission of dengue fever in Nakhon Si Thammarat, Thailand. Data on monthly-notified cases of dengue fever, over the period of January 1981 – June 2012 were collected from the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health. Weather data over the same period were obtained from the Thai Meteorological Department. Spearman correlation analysis and time-series adjusted Poisson regression analysis were performed to quantify the relationship between weather and the number of dengue cases. The results showed that maximum and minimum temperatures at a lag of zero months, the amount of rainfall, and relative humidity at a lag of two months were significant predictors of dengue incidence in Nakhon Si Thammarat. The time series Poisson regression model demonstrated goodness-of-fit with a correlation between observed and predicted number of dengue incidence rate of 91.82%. This model could be used to optimise dengue prevention by predicting trends in dengue incidence. Accurate predictions, for even a few months, provide an invaluable opportunity to mount a vector control intervention or to prepare for hospital demand in the community.

INTRODUCTION

Among the most significant anticipated health impacts of climate change is an increase in the incidence of mosquito-borne infectious diseases, including dengue fever (Shope, 1991; National Research Council, 2001). The occurrence of disease, like dengue fever is typical of the complex interaction between climate, environment, and man at the origin of epidemics (Guzmán & Kouri, 2002). Its main vector, *Aedes* (*Stegomyia*) *aegypti* (L.), develop in close proximity to human communities as it mainly bites humans and breeds preferentially in artificial water-holding containers such as discarded cans, bottles, plastic containers, and tires (WHO, 2008). No effective vaccine or chemotherapy is currently available for the prevention or treatment of dengue fever (Bruno *et al.*, 2011).

Since the first dengue epidemic outbreak in Thailand in 1958 (Halstead *et al.*, 1969), there has been an upward trend in the incidence of dengue, an acute and severe form of dengue virus infection. The Bureau of Epidemiology reports that there have been several regular outbreaks in Thailand. From January to June 2012, there were 9,178 dengue incidences in Thailand or 14.46 incidences per 100,000 population (Bureau of Epidemiology, 2012). The southern region had the highest incidence of dengue during this period, with 4,136 dengue incidences and a dengue incidence rate of 25.06 cases per 100,000 population (Bureau of Epidemiology, 2012). There were 314 incidences in Nakhon Si Thammarat province, or 20.58 dengue incidences per 100,000 population (Bureau of Epidemiology, 2012).

Environmental variables, such as temperature, humidity, rainfall, and wind speed affect the incidence of dengue, either through changes in the duration of mosquitoes and parasite life cycles or through their influences on human, vector, or parasite behaviour (Gubler *et al.*, 2001). Despite the sensitivity of dengue transmission to changes in environmental variables, and the fact that dengue is one of the biggest causes of worldwide mortality due to infectious diseases (WHO, 2008), there is still substantial debate as to the exact role that climate plays in driving dengue epidemics (Lindsay & Mackenzie, 1997; Patz *et al.*, 2000; Reiter, 2001).

Climate variables can increase the predictive power of dengue models (WHO, 2004). The relationship between climate and dengue has been assessed in multiple settings, using different statistical methods (Wu *et al.*, 2007; Luz *et al.*, 2008; Tipayamongkholgul *et al.*, 2009; Wongkoon *et al.*, 2011). Although changes in mean climatic conditions may drive long-term trends in incidence, temporal variability may be epidemiologically more relevant (McKenzie *et al.*, 2001), hence understanding the role of climatic heterogeneity constitutes a key modelling requirement. Regional studies are needed to explore the potential links between climatic variables and disease emergence (National Research Council, 2001). Time series analysis has a long history of application in econometrics (Hu *et al.*, 2004; 2006). Recently it has been used successfully in epidemiology to monitor and predict infectious diseases such as Ross River virus disease (Hu *et al.*, 2004; 2006), malaria and hepatitis A (Nobre *et al.*, 2001) and dengue fever (Silawan *et al.*, 2008; Gharbi *et al.*, 2011; Wongkoon *et al.*, 2011; 2012a, b). To predict dengue incidence related to weather factors and to provide policy implications for local health authorities and communities, we have studied time series Poisson regression model in Nakhon Si Thammarat, Thailand.

MATERIAL AND METHODS

Study area

Nakhon Si Thammarat, the second largest province in the south of Thailand, is located at 99°58' E longitude, and 08°28' N latitude, with an average elevation of 10 m. (Fig. 1). Nakhon Si Thammarat has a land area of 9,942 km^2, consisting of high plateaus and mountains in the west, which slope down towards the east and become a basin along the coastline of the Gulf of Thailand. The province has a population of about 1.52 million. The summer season in Nakhon Si Thammarat is from February to May. The rainy season starts in June and ends in January, with an annual rainfall of 4,201.6 mm. The annual mean temperature is about 27.2°C, with average maximum and minimum temperatures of 34.5 and 21.4°C, respectively.

Data collection

We obtained the computerised data set on monthly dengue cases in Nakhon Si Thammarat province for the period of January 1981 – June 2012 from the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health. Weather data over the same period were obtained from the Thai Meteorological Department (TMD). These consisted of minimum temperature (Tmin), maximum temperature (Tmax), relative humidity (RH), and the amount of rainfall (Rain).

Data analysis

We performed Spearman rank correlation tests to examine the relationship between monthly dengue incidence and weather variables with a lag of zero to two months. The monthly dengue incidence was modelled using a generalised estimating equations (GEE) approach, with a Poisson distribution. This model enabled both specification of an over-dispersion term and a first-order autoregressive structure that accounted for the autocorrelation of monthly numbers of dengue cases. A basic multivariate Poisson regression model can be written as:

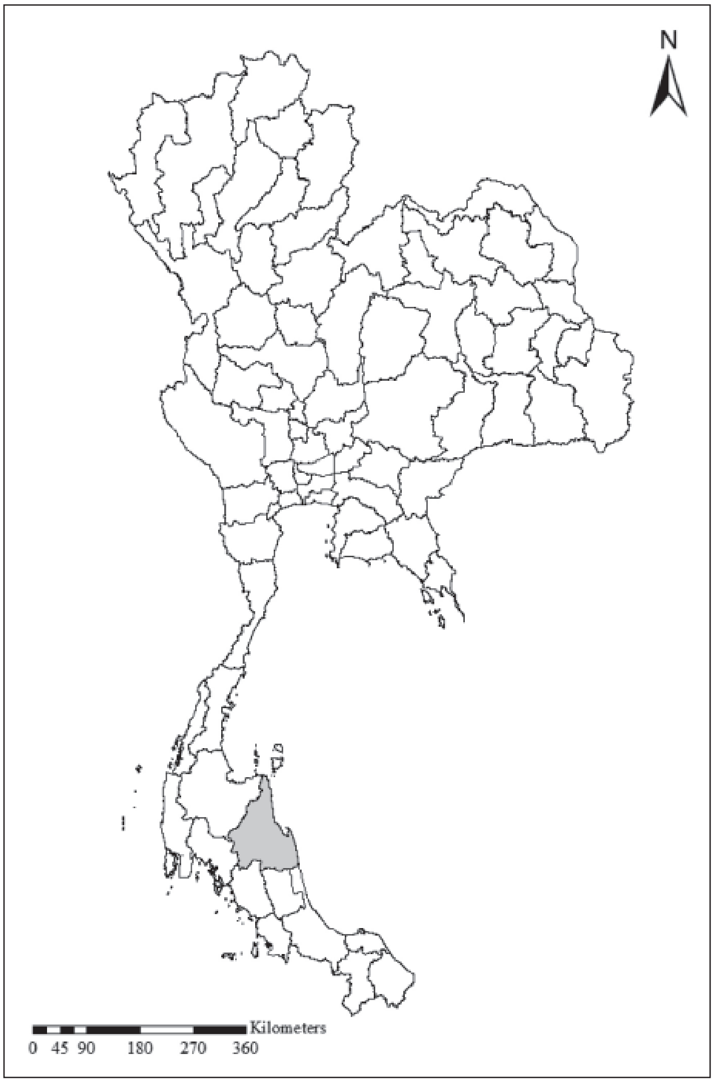

Figure 1. Study areas at Nakhon Si Thammarat, Thailand

$$\ln(Y) = \beta_0 + \beta_1 X_{Tmin} + \beta_2 X_{Tmax} + \beta_3 X_{RH} + \beta_4 X_{Rain} \quad \text{(Eq. 1)}$$

The model that adjusted for first-order autocorrelation can be written as:

$$\ln(Y_t) = \beta_0 + \beta_1 \ln(Y_{t-1}) + \beta_2 X_{Tmin} + \beta_3 X_{Tmax} + \beta_4 X_{RH} + \beta_5 X_{Rain} \quad \text{(Eq. 2)}$$

Where X_{Tmin}, X_{Tmax}, X_{RH} and X_{Rain} stand for minimum temperature, maximum temperature, relative humidity and the amount of rainfall respectively.

In order to control for a potential long-term trends in the number of cases over the study period, a year variable was included in the regression model. In order to evaluate models, the data were split into two groups: training and validation groups. The data from January 1981 to December 2011 (the training group) were used to build the time series model. Then the forecasting accuracy of this model was verified using the data between January 2012 and June 2012 (the validation group) to evaluate the time series model.

Data analysis was performed using *Mathematica* software with a Time series package.

RESULTS

There were 69,443 reported dengue incidences in Nakhon Si Thammarat over the period from January 1981 to June 2012 (Fig. 2a). A seasonal pattern was apparent with most incidences occurring from June to November (Fig. 2a). Seasonal variations were characterised by the high rainfall from May to December (Fig. 2b) and high temperature from June to August (Fig. 2c). Relatively larger inter-annual variations were observed for the relative humidity. Two valleys in relative humidity corresponded to the two peaks of dengue incidences in 1990 and 1998 (Fig. 2d). There was a seasonal distribution of the disease, with most dengue incidences occurring in the wet season. Maximum and minimum temperatures at a lag of zero months, and the amount of rainfall and relative humidity at a lag of two months, were correlated with dengue incidences in Nakhon Si Thammarat (Table 1).

The dengue incidence rate in the current month was related to the incidence rate occurring in the previous month (Poisson regression Model: Incidence rate with lag 1, Table 2). Maximum and minimum temperatures at a lag of zero month, had a positive effect on dengue incidence (Poisson regression Model: Tmax and Tmin with lag 0, Table 2). The amount of rainfall and relative humidity at a lag of two months, had a positive and negative effect on dengue incidences, respectively (Poisson regression Model: rainfall and relative humidity with lag 2, Table 2).

The time series Poisson regression model was constructed with the data for the period of January 1981-December 2011 and predicted dengue incidences for the period of January 2012-June 2012 (Fig. 3). The model demonstrated goodness-of-fit with a correlation between the observed and predicted dengue incidences of 91.82% (Fig. 4). There was no significant auto-correlation between residuals at different lags in the Poisson time series regression model (Fig. 5). The graphic analysis shows that the residuals in the model appeared to fluctuate randomly around zero, with no obvious trend in variation as the predicted incidence values increased. The goodness-of-fit analyses reveals that the model fitted the data reasonably well (R^2 = 86.85%). The results appeared to be a good fit to the data.

DISCUSSION

Some global modelling studies on dengue fever cannot be used at the local level, where extensive model parameterisation is required to achieve a useful predictive model for preventive applications (Patz *et al.*, 2000). Climate change modelling studies on selected vector-borne diseases have found increases in the potential transmission of mosquito-borne diseases caused by anthropogenic warming and precipitation changes. Transmission factors thought to be temperature sensitive include mosquito density, feeding frequency, survival, and extrinsic incubation period (Patz *et al.*, 2000). This study represents another attempt to assess the temporal modelling for predicting dengue transmission in Nakhon Si Thammarat, Thailand. We used a time-series Poisson regression model based on generalised estimating equations (GEE) to examine the effect of climate variability on the incidence of dengue fever from January 1981 to June 2012. The results of this study suggest that an increase in the amount of rainfall and minimum/maximum temperatures, and a decrease in relative humidity were associated with an increase in dengue incidences in Nakhon Si Thammarat. All these weather variables were significant in the adjusted Poisson regression model. Relative humidity and the amount of rainfall play important roles in population dynamics of mosquitoes (Moore, 1985) and are likely to interact with temperature in their effects on population dynamics (Alto & Juliano, 2001). Similar findings have been reported for other vector-borne diseases. For example, rainfall, relative humidity, and temperature were found to be related to

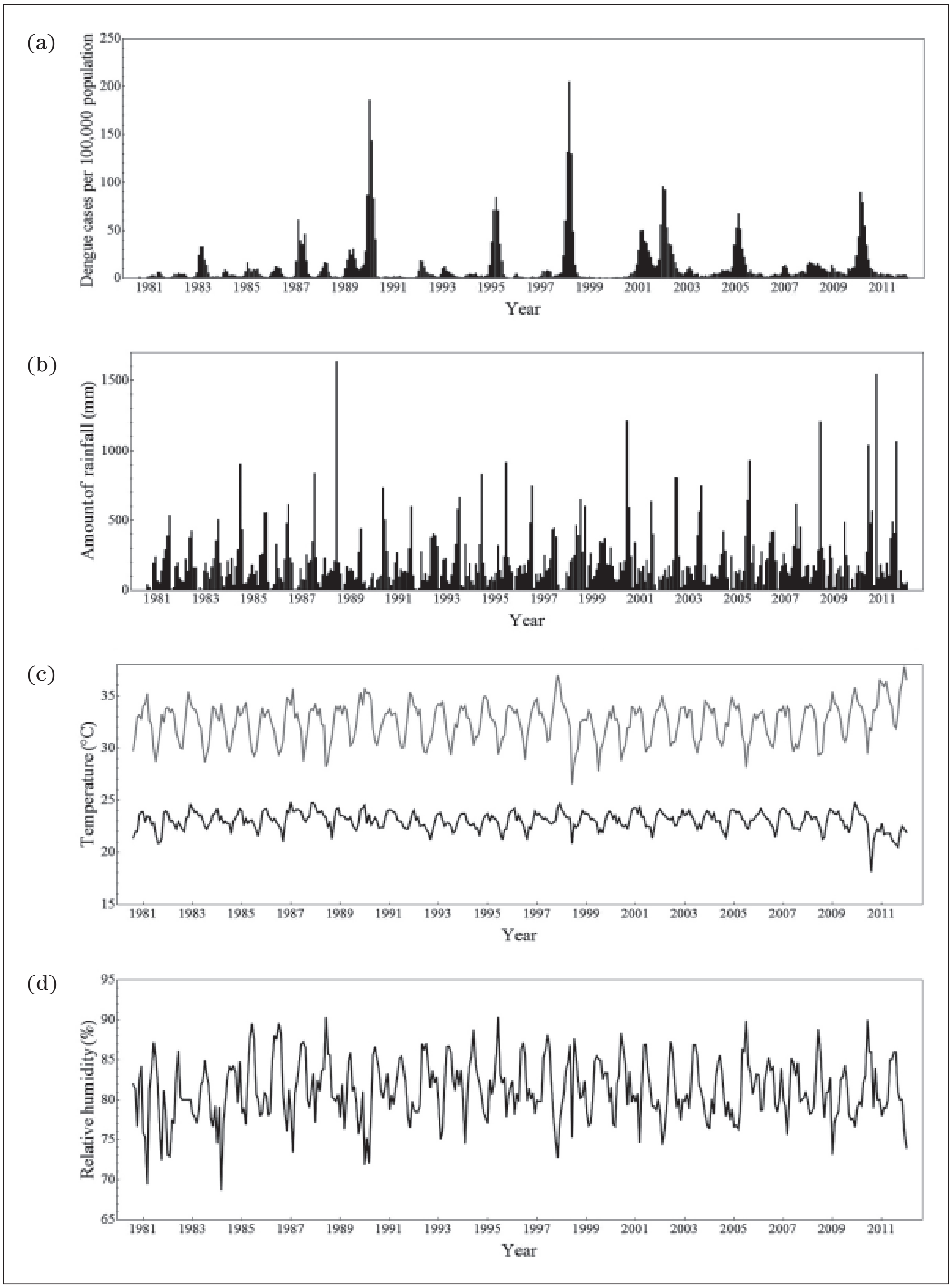

Figure 2. (a) Dengue incidences per 100,000 population, (b) the amount of rainfall (mm), (c) minimum (black line) and maximum (gray line) temperature (°C) and (d) Relative humidity (%) in Nakhon Si Thammarat, Thailand from January 1981 to June 2012

Table 1. Spearman Correlation coefficients between dengue incidence rate and weather factors at Nakhon Si Thammarat, Thailand

Weather factors	Spearman Correlation coefficient	Time Lag months
Minimum temperature (°C)	0.306*	0
Maximum temperature (°C)	0.237*	0
Monthly rainfall (mm)	0.203*	2
Relative humidity (%)	0.148*	2

* Significant at the 0.001 level (two-tailed)

Table 2. Estimated coefficients by adjusted Poisson regression Model between weather variables and dengue cases from January 1981 to June 2012 in Nakhon Si Thammarat, Thailand

Variables	β	S.E.	z-Statistic
Incidence rate (lag1)	0.865	0.021	40.706**
Minimum temperature (lag0)	0.228	0.422	5.403**
Maximum temperature (lag0)	0.098	0.019	5.159**
Monthly rainfall (lag2)	0.0003	0.0002	2.381*
Relative humidity (lag2)	-0.006	0.003	-2.270*
Year (lag1)	0.004	0.004	1.129
Constant	-15.618	6.976	-2.239*

β : coefficients, S.E.: standard error
*, ** Significant at the 0.05 and 0.001 level (two-tailed)

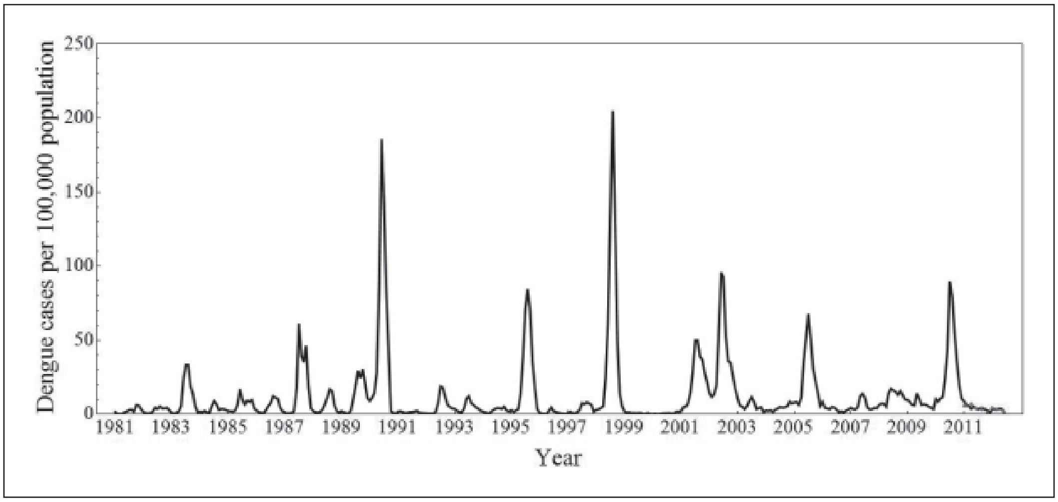

Figure 3. The actual monthly dengue cases per 100,000 population (black line) from 1981 to 2011 and the predicted monthly dengue cases per 100,000 population (red line) from January 2012 to June 2012 by the time series Poisson regression model in Nakhon Si Thammarat, Thailand

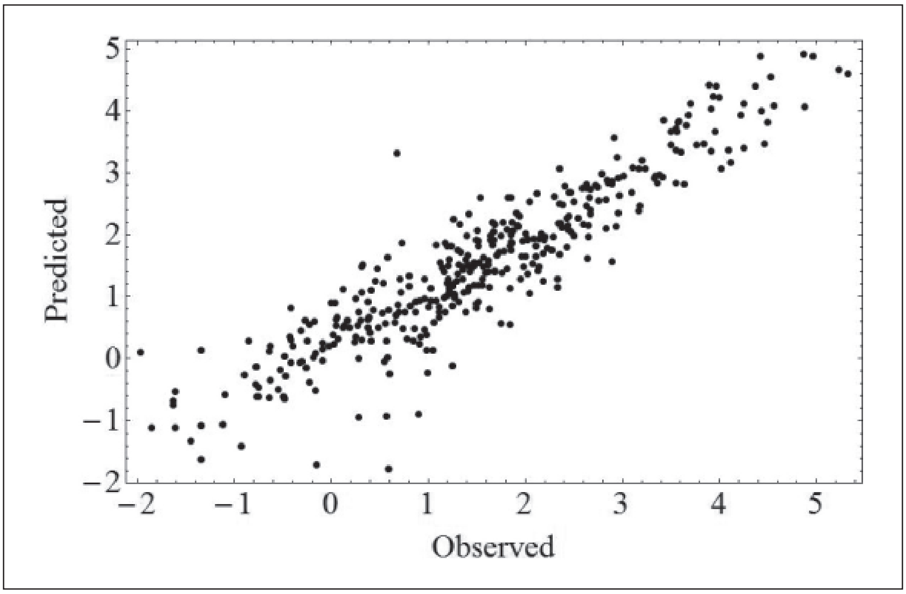

Figure 4. The correlation between the observed and predicted dengue incidences from January 1981 to June 2012 in Nakhon Si Thammarat, Thailand

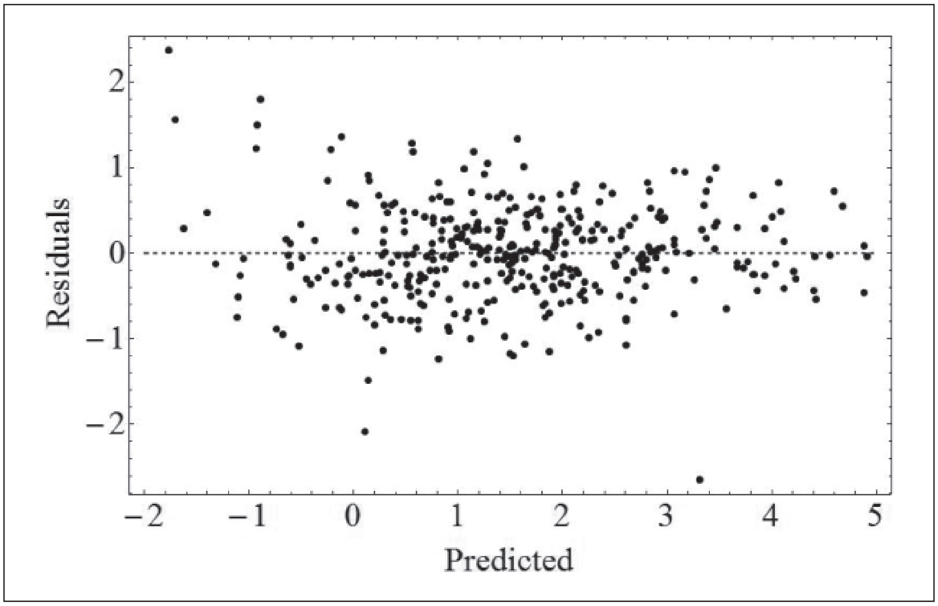

Figure 5. Scatter plot of residuals at different lags in the time series Poisson regression model

epidemics of malaria in Pakistan (Lindsay & Mackenzie, 1997) and Ross River Virus (RRV) in Australia (Hu *et al.*, 2004).

Rainfall is an important element in the transmission of dengue infection because of its effect on the breeding and larval development of mosquitoes (Hurtado-Diaz *et al.*, 2007). All mosquitoes have aquatic larval and pupal stages and therefore require water for breeding (Lindsay & Mackenzie, 1997). Rainfall has shown to be positively associated with dengue incidences in many countries such as Brazil (Luz *et al.*, 2008), Taiwan (Wu *et al.*, 2007), and Thailand (Wongkoon *et al.*, 2011). In this study, the amount of rainfall was positively associated with the incidence of dengue fever in Nakhon Si Thammarat over the study period, with two-month lagged effect. The lagged effect of rainfall on the incidence of dengue infection is very important because such delays are consistent with the development of mosquitoes, the external period of incubation of dengue within mosquitoes, and the incubation period of the virus in the host (Hu *et al.*, 2004). *Aedes aegypti* reared under laboratory conditions can live for an extraordinarily long time; some live for as long as 225 days (Schoof, 1967). In nature, however, females survive 15 days on average with a maximum of 42 days (Schoof, 1967). Some stochastic models choose 45 days to be the maximum period of survival with a survival rate in the range of (0.8-0.95) or a lower survival rate of (0.87-0.91) with no maximum lifespan (Barbazan *et al.*, 2010). In addition, rainfall also increases the range of the natural habitats suitable for mosquito breeding and can facilitate dengue transmission (Hurtado-Diaz *et al.*, 2007).

Our results showed that minimum and maximum temperatures at a lag of zero months, are positively associated with dengue incidence in the study area. This finding is in general agreement with other studies (Hurtado-Diaz *et al.*, 2007; Wu *et al.*, 2007) in which minimum temperature is reported to be a precipitating factor for dengue transmission. Increased temperatures directly affect the spread of vector-borne diseases by expanding the geographic range of the vector (Bangs *et al.*, 2006). Higher ambient temperatures enhance virus replication and shorten the extrinsic incubation period (EIP) in the vector (Watts *et al.*, 1987). Mosquito survival is temperature dependent. Higher temperature yields shorter developmental time for the first cohort, higher average adult mortality, higher eclosion rates (Alto & Juliano, 2001), shorter persistence of free water and lower relative humidity (Rueda *et al.*, 1990). Temperature also influences biting rates, gonotrophic cycle lengths, and vector size (Schoof, 1967; Rueda *et al.*, 1990), most likely due to an increase in the metabolism of the adult mosquito and the replication speed of the virus (Westbrook *et al.*, 2009). An increase in temperature in Thailand resulted in a significant increase in blood feeding (Scott *et al.*, 2000). *Aedes aegypti* 's range of activity is also temperature dependent as normal flight is not seen below 21.1°C. Flight is possible but limited and clumsy below this range. Very little activity is observed and no flight occurs at 10°C (Schoof, 1967). Reduction in flight and activity potentially affects mosquito survival (Schoof, 1967), thereby increasing vectorial efficiency (Bangs *et al.*, 2006) and risk of an epidemic (Schoof, 1967).

Our results show that relative humidity contributes to dengue transmission as its inclusion in the predictive model for dengue incidence provided a better fit. Relative humidity is an important environmental parameter with respect to the survival of mosquitoes, dispersal distance, mating, feeding behaviour, oviposition of vector species and survival of mosquito eggs and adults (Tong & Hu, 2001; Lu *et al.*, 2009). Newly laid eggs are subject to desiccation and the adults to moisture related reductions in survival throughout their lifetimes (Lu *et al.*, 2009). Under conditions of optimal humidity, mosquitoes tend to survive for a longer period, which allows them to disperse further and to have a greater opportunity to participate in transmission cycles (Lindsay & Mackenzie, 1997). Humidity also affects the rate of water evaporation at breeding sites. Our results support Tipayamongkholgul *et al.*'s (2009) study in Thailand, which states that relative humidity at a lag of 2 months, was negatively associated with dengue incidence in the model. This relationship might occur because the decrease in relative humidity can reduce the flow of water in streams and thus produce stagnant pools, often high in organic matter, which make perfect breeding sites for a number of mosquito species (Tong & Hu, 2001).

The time series Poisson regression model indicates that the number of dengue cases in a month can be estimated from the number of dengue incidences occurring in the previous month. The model could be used to optimise dengue prevention by providing estimates on dengue incidence trends using local weather data. Early warning, based on forecasts from the model, can help improve vector control, personal protection, and provide an invaluable opportunity to prepare for hospital demand. Extensions of this model can also be envisioned for monitoring and predicting other infectious diseases in other geographic areas. Weather variables that predict the occurrence of dengue fever are likely to be best suited for forecasting the distribution of the disease. However, the transmission of dengue is very complicated, and detailed ecological and epidemiological studies are still needed to assess the true local risk of an epidemic.

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