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Impact of meteorological factors on the spatiotemporal patterns of dengue fever incidence

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ABSTRACT

Dengue fever is one of the most widespread vector-borne diseases and has caused more than 50 million infections annually over the world. For the purposes of disease prevention and climate change health impact assessment, it is crucial to understand the weather-disease associations for dengue fever. This study investigated the nonlinear delayed impact of meteorological conditions on the spatiotemporal variations of dengue fever in southern Taiwan during 1998–2011. We present a novel integration of a distributed lag nonlinear model and Markov random fields to assess the nonlinear lagged effects of weather variables on temporal dynamics of dengue fever and to account for the geographical heterogeneity. This study identified the most significant meteorological measures to dengue fever variations, i.e., weekly minimum temperature, and the weekly maximum 24-hour rainfall, by obtaining the relative risk (RR) with respect to disease counts and a continuous 20-week lagged time. Results show that RR increased as minimum temperature increased, especially for the lagged period 5–18 weeks, and also suggest that the time to high disease risks can be decreased. Once the occurrence of maximum 24-hour rainfall is >50 mm, an associated increased RR lasted for up to 15 weeks. A temporary one-month decrease in the RR of dengue fever is noted following the extreme rain. In addition, the elevated incidence risk is identified in highly populated areas. Our results highlight the high nonlinearity of temporal lagged effects and magnitudes of temperature and rainfall on dengue fever epidemics. The results can be a practical reference for the early warning of dengue fever.

1. Introduction

Dengue fever is one of the most significant and widespread vector-borne diseases that causes more than 50 million infections annually. Approximately 2.5 billion people in over 100 countries are at risk for developing this disease. It is especially prevalent in the tropical and subtropical regions of Southeast Asia and the Western Pacific (WHO, 2009). Dengue fever is transmitted by the mosquito vectors, e.g., *Aedes aegypti* and *Aedes albopictus*. However, unlike yellow fever or other mosquito-borne diseases, there is no vaccine available for dengue fever. Therefore, understanding the space–time characteristics of dengue fever epidemics and revealing the risk factors are essential to preventing the disease. Among them, meteorological factors have been evident in their importance to the space–time dynamics of dengue fever transmissions (Kuhn et al., 2005). To develop a disease early warning system (EWS), it is essential to understand the empirical relationships between meteorological factors and dengue fever (Descloux et al., 2012; Hii et al., 2009, 2012; Kuhn et al., 2005; Lowe et al., 2011a, 2013; Rubio-Palis et al., 2011; Yu et al., 2011). Especially, the selection of significant delayed temporal lags with respect to weather variables is important for the EWS development of dengue fever epidemics (Hii et al., 2012; Hurtado-Diaz et al., 2007; Luz et al., 2008; Wu et al., 2007). However, previous studies showed that the identified most significant temporal lags could vary significantly among locations (Arcari et al., 2007; Hurtado-Diaz et al., 2007). Some studies selected multiple temporal lags to demonstrate the delayed effects of meteorological variables on dengue fever (Wu et al., 2007; Yu et al., 2011). In addition, the longest lag time associated with either rainfall or temperature is generally identified as two months, as seen in studies of Taiwan and Indonesia (Arcari et al., 2007; Wu et al., 2007).

Identifying the temporal associations between meteorological variables and dengue fever incidences can encounter several challenges: 1) the collinear nature of weather variables and 2) the disease can interplay with various confounding factors. These characteristics add elements of uncertainty and increase the difficulty in understanding the underlying temporal effects of meteorological variables on dengue virus transmission and spread, especially in the cases that conventional regression approaches have been most widely used method for the

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analyses of empirical associations (Arcari et al., 2007; Hurtado-Diaz et al., 2007; Wu et al., 2007). In addition, the influences of meteorological factors on dengue fever transmission can depend upon not only the temporal lags but also their magnitudes. Alternatively, the distributed lag model (DLM) was developed to provide a systematic framework to analyze multiple time series and to quantify outcomes of interest resulting from contributing factors over a certain period of time (Braga et al., 2001). The DLM has been applied to assess the lag distribution of the disease outcomes under a variety of environmental exposures including air pollution (Fraga et al., 2011; Welty and Zeger, 2005), and weather factors (Braga et al., 2001, 2002; Ha et al., 2011; Teklehaimanot et al., 2004). An advanced DLM combining spatial functions was also applied in Asian dust storm research (Yu et al., 2012) and dengue fever studies (Lowe et al., 2011b, 2013), providing a broader scope to detect comprehensive spatiotemporal impacts of climate conditions on human health. Nonetheless, these DLM models dealt with risk factors along with each lag separately and did not consider the interaction between risk factors and lags. Recently the development of the distributed lag non-linear model (DLNM) relaxes the shape assumptions of the DLM and allows the consideration of the nonlinearity of both predictors and their associated delayed effects (Gasparrini et al., 2010). The DLNM has been applied to several time-series studies to assess the concurrent and deferred impacts of weather variables (temperature and rainfall) on mortality (Guo et al., 2012; Yang et al., 2012), malaria (Kim et al., 2012), and heart disease (Guo et al., 2013). To our knowledge, the DLNM has not been used in analyzing space–time data. Specifically, no spatial function was considered in its original development.

In this study, we propose a spatiotemporal quasi-Poisson model of dengue fever that is based on the DLNM approach. The proposed model is used to investigate the delayed effects of the selected averaged and extreme measures of weekly meteorological conditions and the incidence of dengue fever by relying on weekly-recorded cases of dengue fever from 1998 to 2011 in southern Taiwan. In addition, the

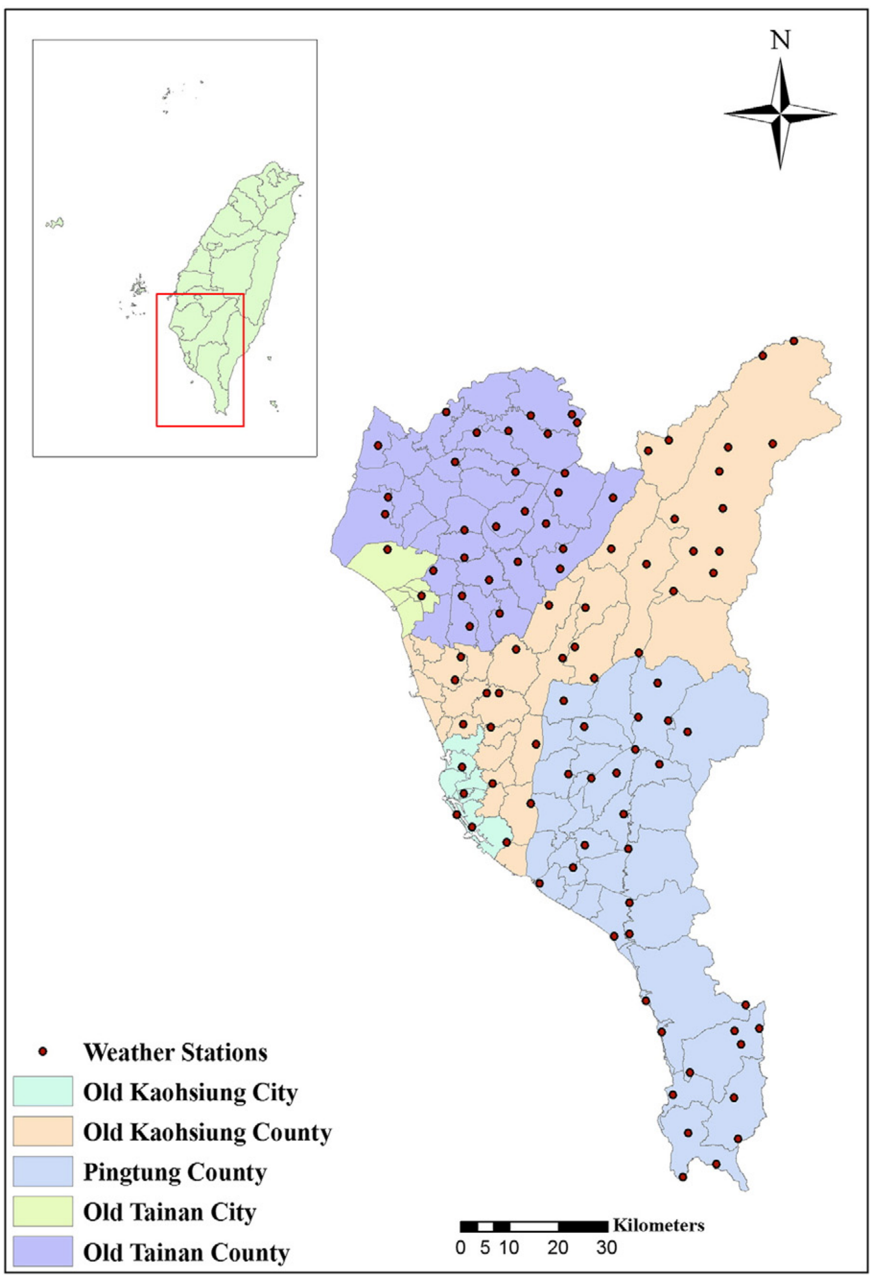

Fig. 1. Map of the study area, which includes 107 districts in southern Taiwan, and the location of automatic observation stations and weather stations.

proposed model considers the heterogeneity of dengue fever incidence across the study area.

2. Materials and methods

2.1. Study area and data

Dengue fever epidemics of various magnitudes have plagued in southern Taiwan annually for decades, i.e. Tainan, Kaohsiung, and Pingtung, as shown in Fig. 1. The number of dengue fever cases in these areas accounted for over 94% of the total number of cases in Taiwan over the last decade. This study investigated the weekly cases of dengue fever that were recorded in 107 districts in southern Taiwan from 1998 to 2011 (Fig. 2). The average number of annual dengue fever cases is 1006 (total population is about 5.5 million) during the study period. In the dengue dataset, about 2% of the total reported DF cases were considered as imported cases and no significant distributional patterns of imported cases across space and time were present. In general, a strong seasonal pattern is shown in temporal variations of dengue fever cases, with an increasing average number of cases occurring during the summer and fall seasons and a decreasing average number of cases occurring during the spring and winter seasons. The serotypes of dengue outbreaks were different from year to year, and closely associated with those imported from neighboring countries (Chang et al., 2012). All of the epidemiological data was obtained from the Taiwan Center of Disease Control Surveillance Database. Weekly meteorological data in every district came from the Central Weather Bureau and the Water Resource Agency's weather monitoring stations. Among them, the temporal variations of averaged temperature and rainfalls over the study area are also shown in Fig. 2, in which a clear

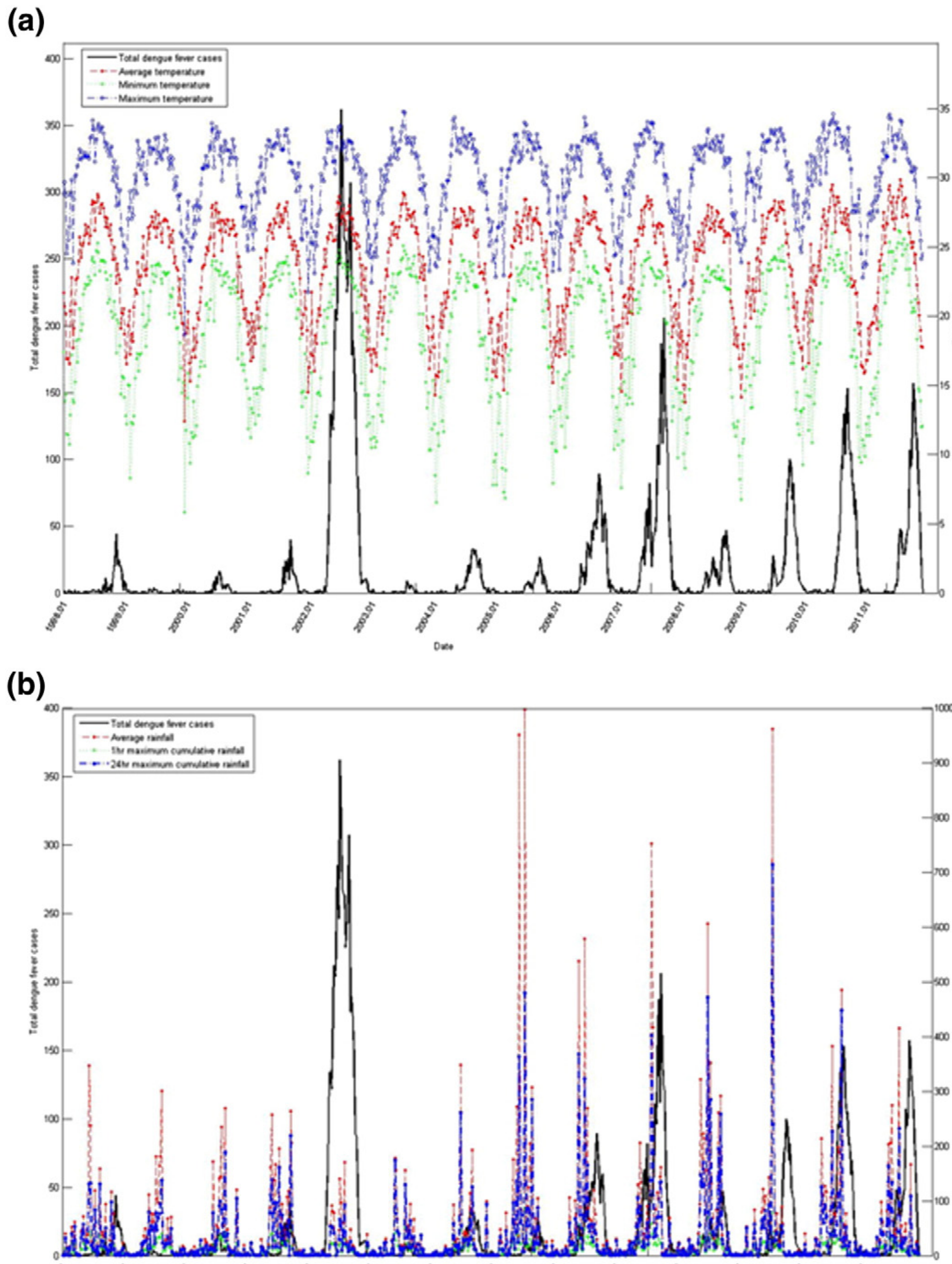

Fig. 2. Trend plot of (a) weekly total dengue fever cases and temperature measures, and (b) weekly total dengue fever cases and rainfall measures.

seasonality in both temperature and rainfalls can be observed. To characterize the spatial variation of weather variables, an inverse distance weighting method was used to estimate weekly meteorological measurements for every district, i.e., estimations at the centroids of the centroid of the districts (Fotheringham et al., 2000), based upon the comprehensive spatial coverage of the rain gauges in the study area as shown in Fig. 1. The selected weekly meteorological variables at each district are estimated, including the averaged temperature, the maximum temperature, the minimum temperature, the total rainfall, the maximum 24-h rainfall, and the maximum 1-h rainfall.

2.2. Distributed lag nonlinear model (DLNM)

We developed a DLNM model in order to simultaneously assess the nonlinear temporal lagged effects of meteorological factors and the geographical heterogeneity on the spatiotemporal distribution of dengue fever incidences. Assume that Y_{dt}, represents the number of weekly dengue fever cases at calendar time (week) $t \in (1, 2, \ldots, 53)$ in district $d \in (1, 2, \ldots, 107)$, and follows a Poisson distribution by $Y_{dt} \mid \mu_{dt} \sim POI(\mu_{dt})$, where μ_{dt} is the expected value of Y_{dt}. Hence, a DLNM was established based upon a geoadditive structure with quasi-Poisson family by:

$$\log(\mu_{dt}) = \alpha + \boldsymbol{\beta} \times (\text{Year}) + f(\text{Time}) + f(\text{TP}, \text{lag} = 20) + f(RF, \text{lag} = 20) + f_{\text{spac}}(d) + \text{offset} \quad (1)$$

where α is the intercept, and the 1×14 vector $\boldsymbol{\beta}$ represents the coefficients of the dummy variable Year. The time smoother f(Time) with respect to the week is a cubic spline for controlling temporal autocorrelations. The effect of meteorological variation is investigated via two cross-basis functions f(TP, lag) and f(RF, lag) in order to describe the association among the space of temperature (TP)/rainfall (RF) with the maximum temporal lag of 20 weeks. The choice of 20 weeks is based upon the potential delayed periods of meteorological effects of previous studies (Chen et al., 2010; Wu et al., 2007; Yu et al., 2011). Note that each rainfall variable was log-transformed before being fit into the model. The spatial function $f_{spac}(d)$ adopts Markov random fields for adjusting spatial autocorrelations and describing geographic heterogeneity (Kindermann and Snell, 1980). The geographical heterogeneity $f_{spac}(d)$ denotes the spatial variations of dengue fever cases which cannot be explained by meteorological variables. The Markov random field of $f_{spac}(d)$ is achieved by a conditional autoregressive prior with a normal distribution with a mean of $\sum_{d' \in \Omega} \varphi_{d'}/N_d$ and a variance of σ_d^2/N_d. The neighborhood set as Ω contains all the adjacent districts, which have overlapped boundaries designated as 'd'. The spatial effect of an adjacent district 'd' is denoted by $\varphi_{d'}$, and N_d is the number of adjacent districts nearby district 'd'. In other words, the spatial function is a function of districts, which accounts for the logarithm of relative risks across the districts within the study area and considers the spatial autocorrelation of incidence under Markov random fields framework. The estimation of spatial function under the generalized additive structure was based upon the Markov Chain Monte Carlo algorithm (Musio et al., 2010). The offset is the logarithm of the district-level population averaged from the annual census data from 1998 to 2011 (Department of Household Registration, 2012). The averaged data is used due to the limited change of population sizes of every district over the study area during the study period.

In order to choose the best combination of f(TP, lag = 20) and f(RF, lag = 20) from the six climatic factors, a cross-basis function selection was implemented in order to choose the best degrees of freedom (df) from 3 to 7 in the two natural cubic splines for predictors and lags, respectively. The optimal df for the cross-basis functions of temperature and rainfall as shown in Eq. (1) were determined by the smallest quasi-AIC (QAIC), respectively. In order to compare models to determine the most suitable temperature and rainfall cross-basis functions in the final model, the smallest QAIC criteria are further used for the model selection process. In this step, we only considered models with only one temperature factor and one rainfall factor to prevent concurvity issues among the different measures of a meteorological factor. The explanation level of each component on dengue fever in the DLNM was also evaluated by adding the following terms in order: f(Time), Year,

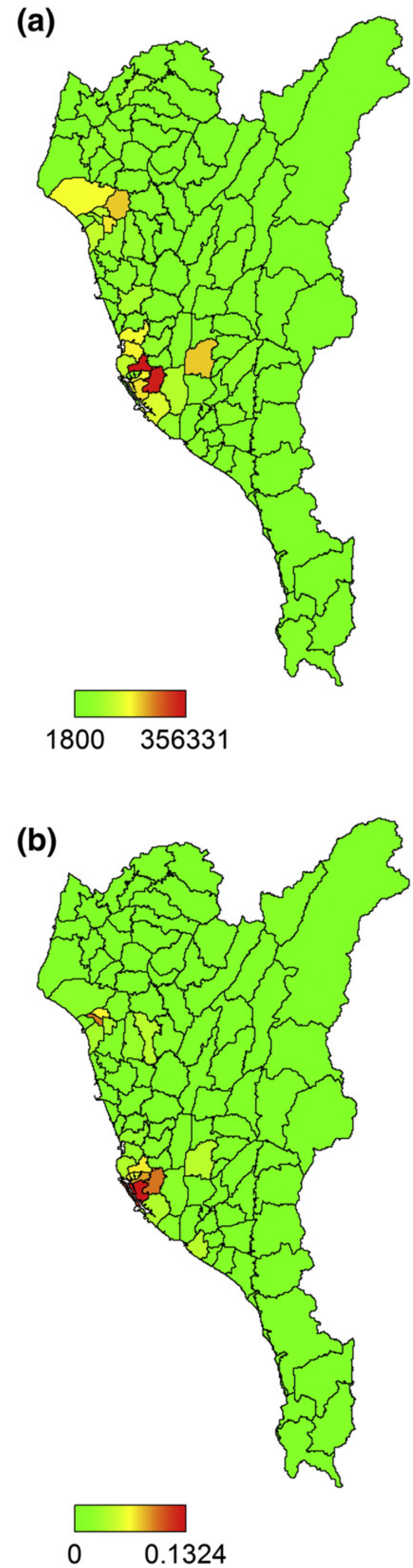

Fig. 3. Spatial distribution of (a) average population and (b) crude weekly dengue fever incidence rate in southern Taiwan, 1998–2011.

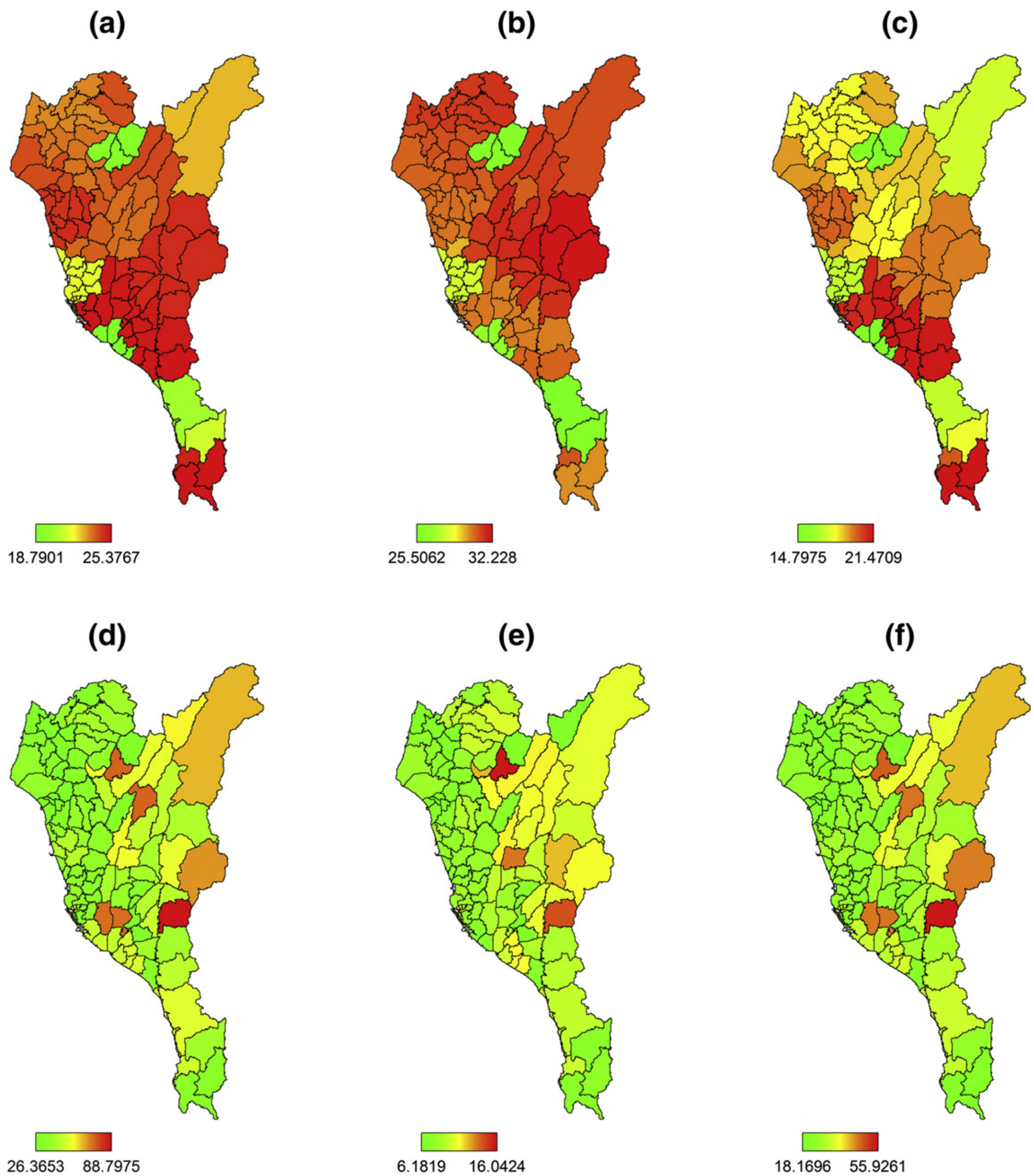

Fig. 4. Spatial distribution of weekly mean for (a) averaged temperature, (b) maximum temperature, (c) minimum temperature, (d) average rainfall, (e) maximum 24-h rainfall, and (f) 1-h maximum rainfall in southern Taiwan, 1998–2011.

f(RF, lag = 20), f(TP, lag = 20), and $f_{spac}(d)$. Sensitivity analyses were performed by changing the maximum lags from 20 weeks to 10 and 24 weeks in the cross-basis functions of both temperature and rainfall variables in the final model, as well as the consideration of spatial function in the DLNM model. Data analysis was conducted in the R version 2.14.1 (R Development Core Team, 2011) and SAS V9.3 (SAS Institute Inc., Cary). Statistical significance was determined by the 95% confidence interval (CI).

3. Results

Fig. 3 depicts the population and the crude rate of weekly dengue fever cases across the 107 districts in southern Taiwan. Among them, fifteen districts had zero dengue fever case during the 14 years of our study. In those districts with dengue fever cases, the crude rate ranged from 0.0004 to 0.1324 cases per 10,000 persons. Fig. 4 visualizes the spatial distribution of the weekly mean of district-level weather

Table 1
Model selection by the ordered quasi-Akaike information criterion (QAIC).

Model #	Temperature + rainfall[a]	QAIC[b]	ΔQAIC
1	Mintemp + Maxcrain	887.54	–
2	Mintemp + Maxrain	898.01	10.47
3	Mintemp + Avgrain	941.07	53.53
7	Avgtemp + Maxcrain	903.07	15.53
8	Avgtemp + Maxrain	911.28	23.74
9	Avgtemp + Avgrain	952.79	65.25
4	Maxtemp + Maxcrain	978.33	90.79
5	Maxtemp + Maxrain	985.15	97.61
6	Maxtemp + Avgrain	1031.74	144.2

[a] Maxtemp = maximum temperature; Mintemp = minimum temperature; Avgtemp = average temperature; Maxcrain = maximum 24-h rainfall; Maxrain = maximum 1-h rainfall; Avgrain = average rainfall.

[b] QAIC = −2 × (log-likelihood function) + 2 × (the number of parameters) × (overdispersion coefficient).

conditions, where temperature displayed a more explicit spatial pattern than rainfall. A greater average of three temperature measurements distributed in middle southern Taiwan and three counties in the bottom of Pingtung, see Fig. 4a–c, while a greater rainfall average more likely appeared in districts located in mountain areas of southern Taiwan, see Fig. 4d–f. Table 1 shows nine models in the final model selection process. The model with the two cross-basis functions for minimum temperature and maximum 24-h rainfall was selected as the best model with the smallest QAIC = 887.54.

Fig. 5(a) shows a 3-D graph of the RR as it relates to minimum temperature and lags. In order to better reveal the effect of minimum temperature changes on the incidence of dengue fever, an overall mean of minimum temperature 18.82 °C was defined as a reference. The plot suggests that at greater minimum temperatures and more lagged weeks, a higher incidence of dengue fever was noted in southern Taiwan. The plot in Fig. 5(b) is the contour representation of the 3-D graph for more clearly identifying the change of RR with the variation of minimum temperature and lag increase. The RR of dengue fever elevated as minimum temperature increased, and reached the greatest RR = 2.10 (95% CI = 2.03, 2.17) when the minimum temperature climbed to 29 °C at lagged week 13. Fig. 5(c) displays how the RR varied with changes in the log of maximum 24-h rainfall at different lags. These comparisons use a reference maximum 24-h rainfall at 6.62 mm. The 3-D plot presents the apex of RR for dengue fever and occurs when the maximum 24-h rainfall exceeded 150 mm ($=e^5$) at lagged weeks 10 to 15. Fig. 5(d) clearly depicts that a RR greater than 2 was from lagged weeks 11 to 17 when maximum 24-h rainfall was over 400 mm ($=e^6$). The RR gradually increased with greater maximum 24-h rainfall after lagged week 4, and eventually reaches the maximum value of 3.98 (95% CI = 3.47, 4.57) when there is extreme rainfall at lagged week 15.

In Fig. 6, the graphs on the left display the changes in the RR of dengue fever by minimum temperatures at specific lagged weeks (0, 4, 8 and 15), and the graphs on the left display the changes in RR for dengue fever at different lagged weeks at specific minimum temperatures (20 °C, 23 °C, 26 °C, and 29 °C). Among the right plots, the minimum temperatures at 20 °C had no significant association with the incidence of dengue fever. The RR gradually increased as the minimum temperature is higher than 20 °C, particularly in lagged weeks 5 to 18. Among the left plots, it is also more explicit that the RR elevated greatly along with the increase of minimum temperature as shown at lagged weeks 8 and 15. Fig. 7 shows the RR of dengue fever by maximum 24-h rainfalls at specific

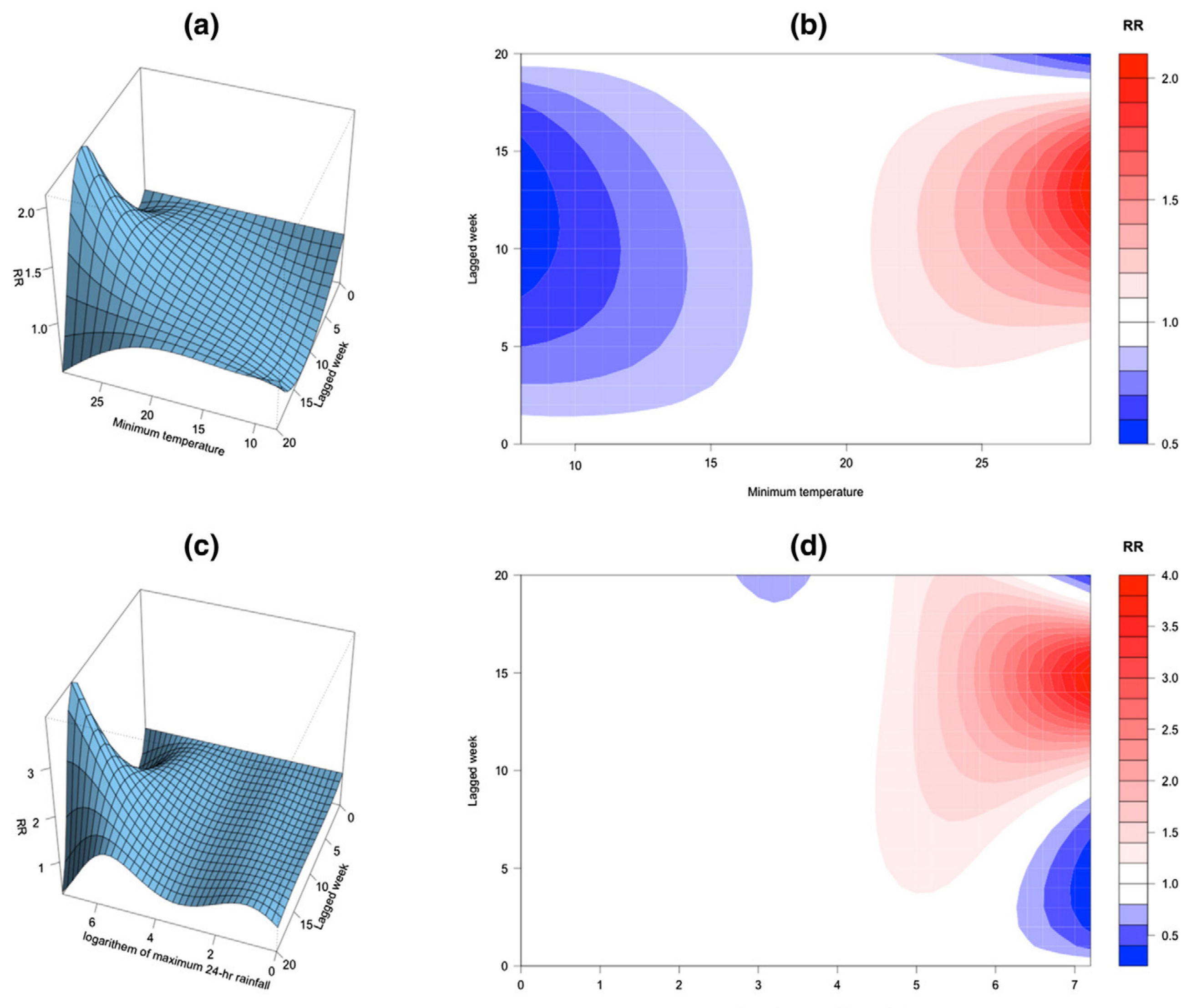

Fig. 5. 3D graphs and corresponding contour plots showing the relative risk of dengue fever incidence at lagged weeks along with minimum temperature (a & b) and the logarithm of 24-h maximum cumulative rainfall (c & d).

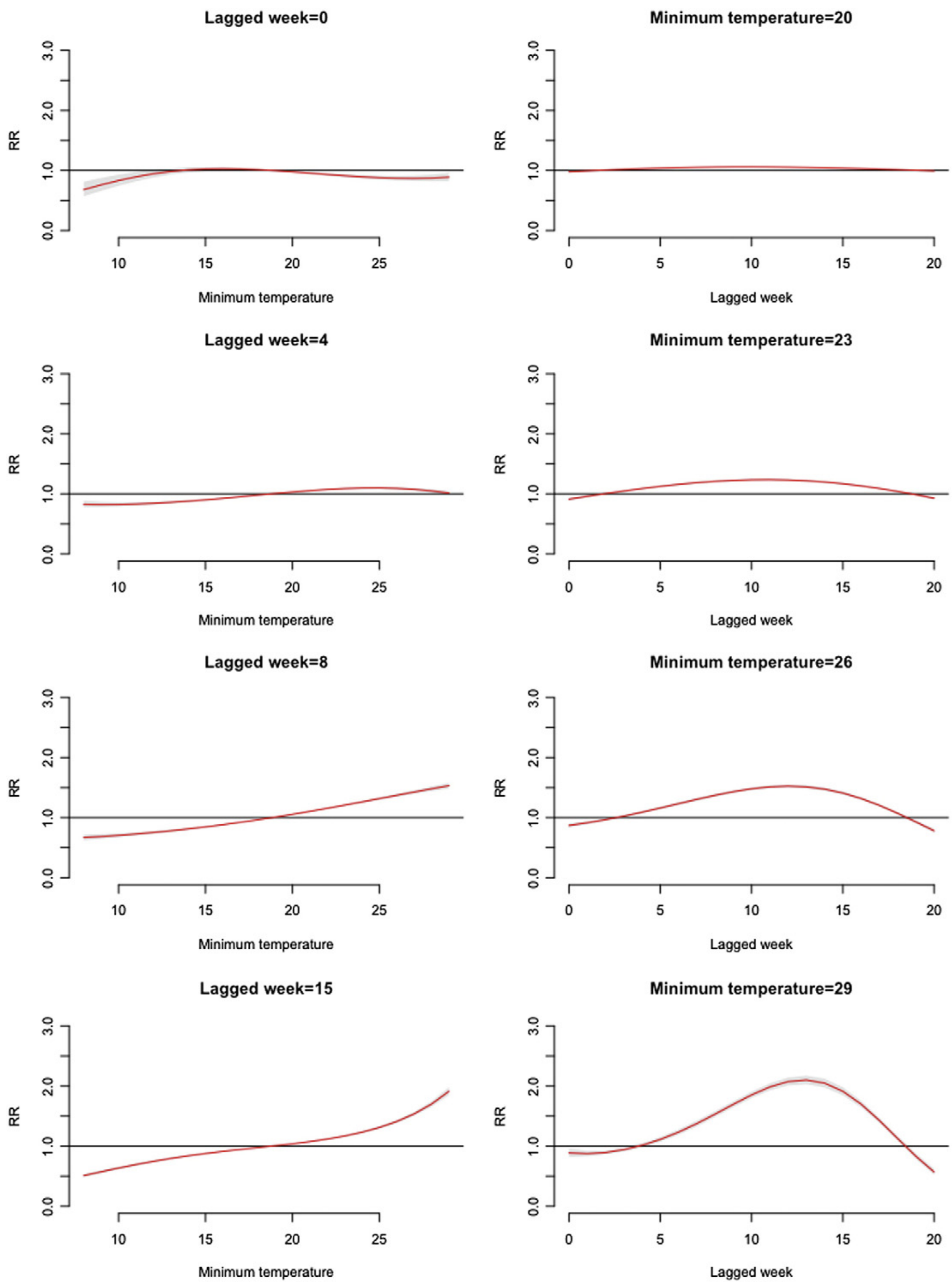

Fig. 6. Relative risk of dengue fever associated with minimum temperatures at selected lagged weeks (left), and lagged weeks with respect to selected minimum temperatures (right).

lagged weeks (0, 4, 8 and 15) on the left and by lagged weeks at specific maximum 24-h rainfalls (50 mm, 100 mm, 200 mm, and 330 mm) on the right. Results show that when rainfall was less than 50 mm, all RRs were around 1 in all lagged weeks. Nonetheless, RRs were significantly greater than 1 for all lagged weeks when the maximum 24-h rainfall is higher than 44.70 mm and lower than 330 mm. Notice that the occurrence of extreme rainfall at 330 mm can decrease the RR for approximately four weeks.

The estimated spatial function was drawn in Fig. 8, displaying the geographical distribution of dengue fever in terms of log(RR) across the study area, in which the reference level is the overall average incidence rate. Districts with a greater log(RR) for dengue fever are located in the Kaohsiung city and Tainan city areas. Eventually, all linear and nonlinear predictors were able to explain 54.5% variation of dengue fever, where the spatial function explained the greatest proportion by 24.9%, the year indicators explained 13.4%, the cross-basis function of minimum temperature explained 8.6%, the time smoother explained 5.6%, and the cross-basis function of maximum 24-h rainfall explained the least proportion by 2.0%. Sensitivity analyses show that the lagged effect estimation for rainfall and temperature was robust with respect

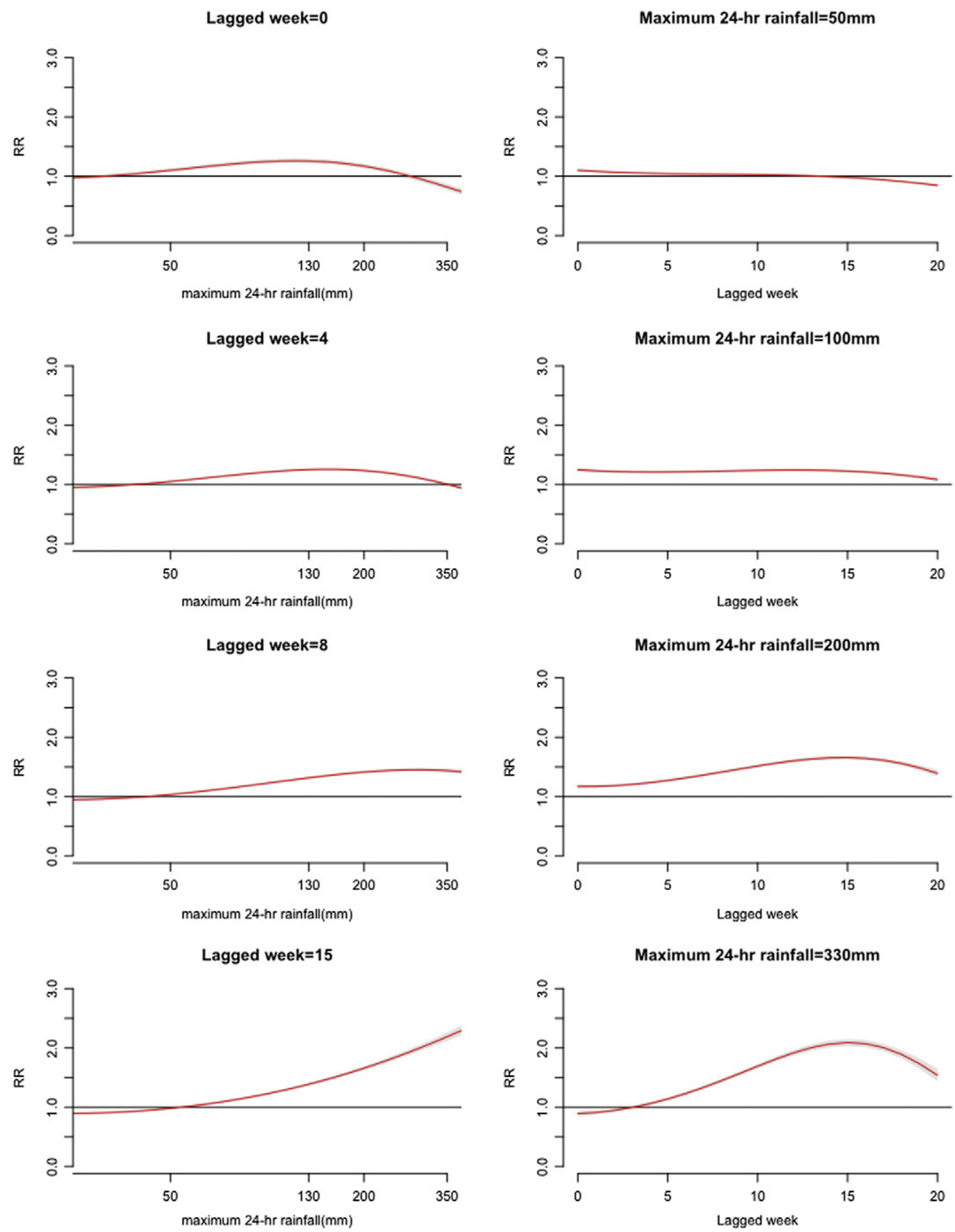

Fig. 7. Relative risk of dengue fever associated with 24-h maximum cumulative rainfalls at selected lagged weeks (left), and lagged weeks with respect to selected maximum 24-h rainfalls (right).

to varying maximum lags and the use of spatial function. It implies that the DLNM in this study can adequately capture the main effects of temperature and rainfall on dengue fever incidence.

4. Discussion

This study identifies that the minimum temperature and extreme daily rainfall are the most significant dengue weather-based risk factors in south Taiwan. Furthermore, the impact of these factors on dengue fever is revealed in terms of the two-dimensional RR maps with respect to their magnitude and lagged time. This analysis was achieved by the first-time application of the integration of the Markov random fields and DLNM framework in the dengue fever modeling. The space–time lagged associations identified in this study can be useful for the prediction or projection of dengue fever cases in the coming weeks and therefore our results can serve as the valuable reference for the implementation of early warning systems for governmental agencies.

Temperature has been identified as the most important weather variable affecting a dengue fever epidemic (Cummings et al., 2004; Herrera-Martinez and Rodriguez-Morales, 2010; Hii et al., 2009; Karim et al., 2012; Richardson et al., 2011). Though previous studies mostly used average temperature to characterize the temperature effect in dengue fever modeling (Chen and Hsieh, 2012; Chen et al., 2010; Tsai et al., 2012; Wu et al., 2007), some investigators noted that the weekly minimum temperature is more closely associated with dengue fever vector development (Padmanabha et al., 2012; Tun-Lin et al., 2000). We substantiate that the weekly ambient minimum temperature is the most proper temperature measure for projecting the magnitude of dengue fever outbreaks in the study area. We found that the increase of weekly minimum temperature can elevate the dengue fever RR,

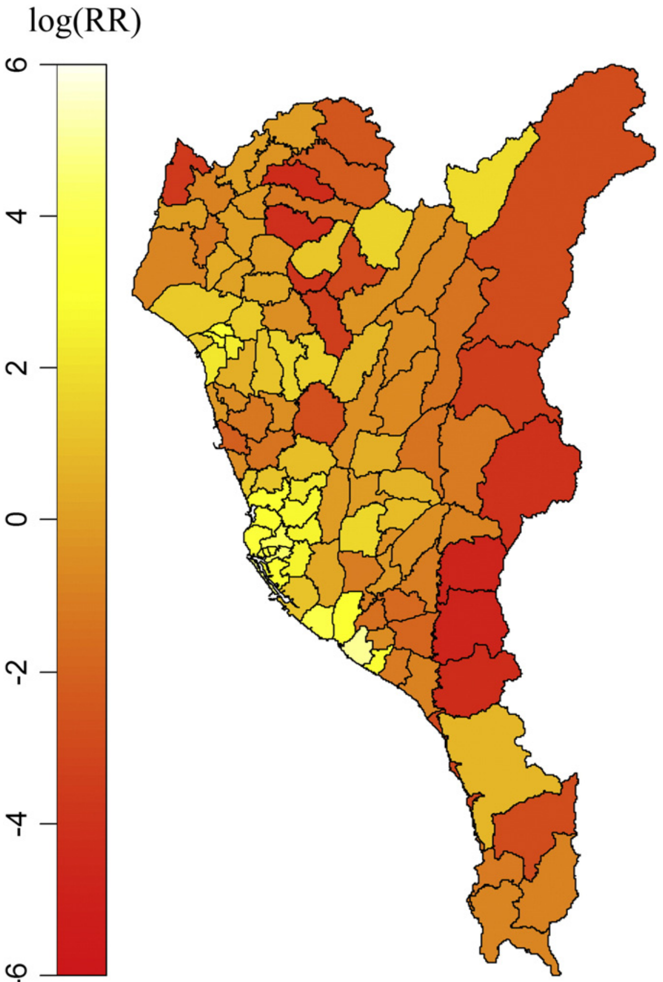

Fig. 8. Map of the logarithm of relative rates of the incidence of dengue fever in southern Taiwan.

especially when the lag is over 4 weeks (see Figs. 5–6). The contour plot in Fig. 5 shows that a higher minimum temperature decreased the lag period of a dengue fever outbreak, suggesting that higher temperatures may account for increasing rate of onset of the disease. Considering the exponential RR increase as soon as the weekly minimum temperature is higher than its overall average, i.e., 18.82 °C, at certain lags, for the purposes of disease control, the minimum temperature of 20 °C can be suggested as a criterion for the preparation of the relatively larger disease outbreak. This finding can be supported by the entomological evidences including the idea that the favorable temperature range for dengue fever transmission spans between 15 °C to 35 °C (Padmanabha et al., 2012; Wu et al., 2007). As shown in Fig. 2(b), temperatures in our study areas are generally favorable to the life cycle of *A. aegypti*, with the fact that dengue fever outbreaks occur annually in these regions. Temperature variations within 15–35 °C can directly or indirectly affect the dengue fever vector by affecting its life cycle, growth efficiency, blood feeding frequency, extrinsic incubation period, reproduction and mortality rates, and population dynamics (Chan and Johansson, 2012; Lindsay and Birley, 1996; Padmanabha et al., 2012; Tun-Lin et al., 2000; Yang et al., 2009a,b). For example, an increase in temperature within this range may increase the development and oviposition rates and shorten the extrinsic incubation period of the vectors significantly with different rate changes at different temperature levels (Chan and Johansson, 2012). In the case of the mortality and reproduction rates of disease vectors, non-monotonic curves were identified across varying temperature levels (Tun-Lin et al., 2000; Yang et al., 2009b). It implies that the magnitude and lagged time of dengue fever can highly depend upon the temperature levels as shown in the empirical results of this study. Some previous empirical relationships also present the significant delayed periods between temperature and dengue fever incidences in south Taiwan. The identified temporal lags can range from one month (Tsai et al., 2012) to 2–3 months (Chen et al., 2010; Wu et al., 2007; Yu et al., 2011). In addition, a mathematical model showed the optimal average temperature for dengue fever transmission in the study area is about 28 °C (Chen and Hsieh, 2012).

Rainfall is usually also considered as an important risk factor for dengue fever, though it can also depend upon the human activities about water storage and management. This study identifies the multi-aspect relationship among rainfall intensities, temporal lags and dengue risks. Moreover, the RR for dengue fever increases as soon as the weekly maximum 24-h rainfall exceeds approximately 50 mm. The increased risk for dengue fever can be seen from the onset of the rainfall and can last for at least three months. With extreme rainfalls, a rainfall of 330 mm of water or more, a dengue fever epidemic may be temporarily mitigated for 1 month. Our result is consistent with a previous empirical analysis for extreme rainfalls performed in the same study that the events of daily rainfall ≥130 mm can elevate dengue fever incidence with the temporal lag about 70 days (Chen et al., 2012). Our results further show the nonlinear associations between rainfalls and dengue fever. Generally speaking, increased rainfalls generally provide more favorable environments for mosquitoes and their larvae, and extremely heavy rainfalls can potentially have an adverse impact on the dengue fever vectors' habitats (Lifson, 1996; Reiter, 2001; Smith et al., 2004). As for the fact of the reduction of dengue fever under extreme rainfall conditions, some studies suggested that the extreme events can commonly associate with flooding that can cause the elimination of mosquito habitats and the decrease the overall mosquito population (Wu et al., 2007; Yu et al., 2011). The influence of rainfalls on dengue fever can depend upon not only on the rainfall intensity and magnitude, but also on human activities, including water usages, storage patterns, and development of drainage systems. For example, a well-designed water drainage system can effectively reduce the occurrence of flooding events; however, the drainage systems are only effective for overland flow reduction and cannot reduce soil moisture or storage, both of which have more of an impact on mosquito habitats. In general, the drainage systems for the metropolitan areas in Taiwan, including old Kaohsiung city and old Tainan city in the study area, have the capacity to effectively drain water at a maximum 24-h rainfall level of 350 mm, which is also the cutoff level for governmental agencies to issue flood warnings (DGPA, 2011). This design capacity is closely related to the rainfall threshold for the temporary disease risk reduction in our results. The occurrence of the extreme 24-hour rainfalls usually results from the visits of typhoon which can occur 3–4 times annually.

The spatial heterogeneity not explained by the meteorological variables is shown in Fig. 8, and can be more associated with non-climatic variable, e.g., land use patterns, geographical distribution of vector abundance, and interactions between human and vector populations (Gubler and Clark, 1995; Lo Re and Gluckman, 2003; Wilson, 1995). In general, the higher risk areas are located in the higher urbanized areas, i.e. Kaohsiung and Tainan cities. It has been shown that the urbanized level is a highly influential factor to elevate the risk of dengue fever incidence in Taiwan (Wu et al., 2009), i.e., the locations with higher population density and socioeconomic status can be associated with higher dengue fever incidence. This can result from the fact that *A. aegypti* is the primary vector responsible to the dengue fever epidemics in Taiwan though both *A. aegypti* and *A. albopictus* coexist in Taiwan (Chang et al., 2012; Tuan et al., 2009). Studies have found that urban areas are generally preferable habitats for *A. aegypti* (Hiscox et al., 2013; Tsuda et al., 2006). Fig. 8 also shows its high correspondence with the geographical distribution of a mosquito abundance survey (Tuan et al., 2009), in which water-holding containers, such as water bucket, were identified as important sources for mosquito breeding in southern Taiwan. In addition, some other non-climatic factors, like immunity of human population, serotypes of dengue virus, and imported cases, can also be important confounders for the spatial and temporal dynamics of dengue fever (Anderson and Rico-Hesse, 2006; Hay et al., 2000; Shang et al., 2010). Research claimed that these factors can possibly be more important than meteorological factors to temporal dynamics of the dengue fever dynamics (Hay et al., 2000). Some other limitations of this study can present in our empirical associations because of the under-reporting issue of dengue fever as discussed in some previous studies (Cuong et al., 2013). In this study, we focused the nonlinear effects of meteorological variables to dengue fever dynamics and proposed some meteorological-based indicators as the reference for the purposes of disease early warning; however, for the more comprehensive knowledge of spatiotemporal patterns of dengue dynamics in Taiwan, further investigations of non-meteorological variables can be required to supplement the findings of this study and will be included in our future study.

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