Tropical Medicine and International Health doi:10.1111/j.1365-3156.2009.02277.x

VOLUME 14 NO 6 PP 628–638 JUNE 2009

Turning points, reproduction number, and impact of climatological events for multi-wave dengue outbreaks

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Summary

OBJECTIVES To study climatological and public health events which might have affected the 2007 two-wave dengue outbreak in Taiwan, an island with both tropical and subtropical regions, where the 2007 dengue incidence exceeded the combined total of the previous four years.

METHODS A multi-phase Richards model was fitted to weekly cumulative dengue data to pinpoint the turning points of the outbreak. We obtained the 'initial' reproduction numbers for the two waves of the outbreak. By means of correlation analysis we explored the possible impact of climatological events on the occurrence of turning points.

RESULTS Three turning points occurred around early August, late August/early September, and late October/early November. The 'initial' reproduction number for the first wave was R_i = 4.67 (95% CI: 0*–10.92), where 0* = max{0, lower bound}, and R_i = 3.93 (95% CI: 1.74–6.13) for the second wave. The highest correlation was between dengue incidence and two climatological variables: maximum temperature at a lag of 5 weeks (r = 0.66 and 0.71) and total precipitation at a lag of seven weeks (r = 0.53).

CONCLUSIONS The first two turning points were partially attributable to two typhoons around early to mid-August that brought a sharp drop in temperature and substantial rainfall. The drop in temperature first drove the dengue incidence down, then the rainfall drove it up at the beginning of fall. In recent years, Taiwan has witnessed increasingly frequent large summer dengue outbreaks that persisted into early winter, perhaps due to warmer autumns. This highlights the possible impact of global warming on the spread of infectious diseases.

keywords dengue, Taiwan, Richards model, turning point, intervention measure, reproduction number, climate change, global warming

Introduction

Dengue is an old disease which has become endemic in more than 100 countries in Africa, Latin America, and Asia. World Health Organization (2008) estimates that in the early 21st century, approximately 2.5 billion people, or two fifths of the world's population, are at risk from dengue (World Health Organization 2008).

Taiwan contains both tropical and subtropical regions, separated by the Tropic of Cancer. Regional dengue epidemics occur regularly in Taiwan in summer, typically to the south of Tropic of Cancer. In recent years there are signs of increasing frequency of large outbreaks totalling thousands, with two occurring in 2002 and in 2007. In 2002, epidemiological studies showed that most indigenous dengue cases can be traced to imported cases, mostly from southeast Asian countries (King *et al.* 2000; Lei *et al.* 2002). However, more recently the impact of imported index cases has fallen considerably, perhaps due to airport screening implemented in Taiwan in 2003 in the aftermath of SARS outbreak (Kuo *et al.* 2008), which led to a considerable proportion of dengue cases being detected at the border (Lai *et al.* 2008; TCDC 2008; Figure 1). In 2008 the dengue outbreak lasted into early 2009, albeit on a much smaller scale than that of 2007. Unusual warmer fall weather has also been observed in southern parts of Taiwan, with daily temperatures staying above the historical daily average temperature for every day of the month of October and through early November (Central Weather Bureau of Taiwan 2008), which perhaps highlights the possible impact of global warming on the spread of infectious diseases.

During the 2007 dengue outbreak, 2179 dengue cases were confirmed in Taiwan, which is more than the combined total of the previous four years, with Den-1 serotype being the main culprit, close to 90% (TCDC 2007). The outbreak was spatially centralized: 84.3% of all reported DF/DHF cases occurred in the metropolitan

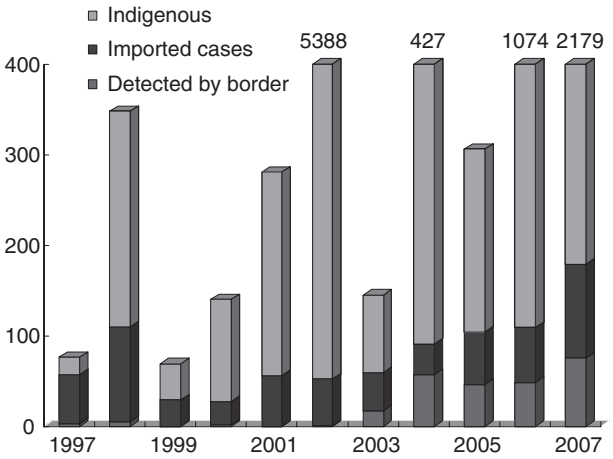

Figure 1 The 1997–2007 Numbers of DF/DHF cases detected by border screening (normal blocks), all imported cases (dark blocks), and indigenous cases (light blocks) in Taiwan. Source: Centers for Disease Control of Taiwan (2009), Kuo *et al.* (2008), Lai *et al.* (2008).

area of Tainan, including 1480 cases (67.9%) in Tainan City and 357 cases (16.4%) in surrounding Tainan County, in southern Taiwan just to the south of Tropic of Cancer (TCDC 2009). Of those 2179 cases, 2125 cases were reported starting in epidemiological-week (e-week) 23 on June 3–9 (TCDC 2008). The 2007 dengue incidence curve exhibits two peaks (Figure 2), a smaller one in August and a larger one in late October–early November. It is typical of a two-wave outbreak with multiple turning points, which was not evident during previous years' dengue outbreaks (see 2002–2007 weekly dengue incidence data, TCDC 2009).

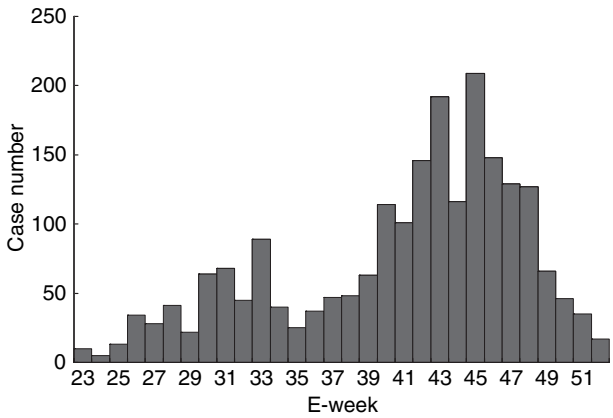

Figure 2 Daily confirmed dengue (DF/DHF) case data by onset date for Taiwan, e-weeks 23–52, 2007. Source: TCDC.

Recently, Hsieh and Cheng (2006) used the SARS case data of Greater Toronto area (GTA) to demonstrate that the Richards model, a simple logistic-type epidemic model, can be used to study the turning points and basic reproduction number of a two-wave epidemic outbreak. Hsieh (2008) reviewed the Richards model and its application to all major SARS-infected regions in 2003, namely Beijing, Hong Kong, Taiwan, Singapore, and GTA; Hsieh and Ma (2009) modelled the 2005 Singapore dengue outbreak using it. In this study we used the Richards model to pinpoint the turning points of the outbreak, in order to explore the underlying causes for this rare occurrence.

Materials and methods

Data

The data used for this study is the e-weekly distribution of Taiwan DF/DHF cases by onset date starting from e-week 23 to e-week 52 of 2007 taken from the weekly incidence data on the Centers for Disease Control of Taiwan (TCDC) website (2009) in Figure 2. The weekly data then were converted into a cumulative case curve by e-weeks in Figure 3. E-week 23, starting on June 3, was clearly the beginning of summer outbreak since two dengue cases had occurred this week, the first in more than 10 weeks.

Richards model

Richards (1959) proposed the following model to study the growth of biological populations:

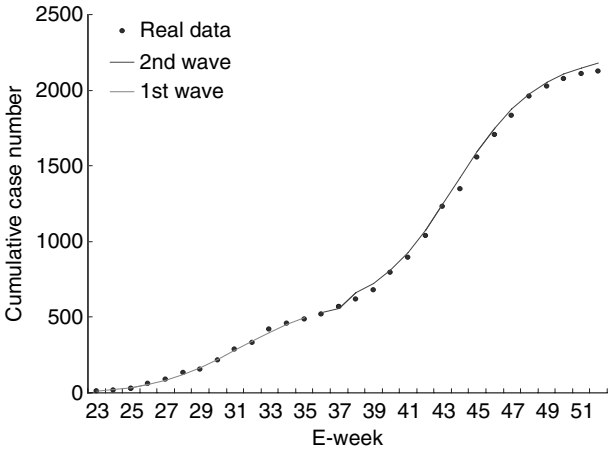

Figure 3 Predicted Richards model for the first wave (e-weeks 23–35 in thin line) and second wave (e-weeks 35–52 in thick line) compared with real data (dots).

$$I'(t) = rI(t)\left[1 - \left(\frac{I}{K}\right)^a\right].$$

Here the prime "' denote the time rate of change and the time unit is in e-weeks. As a model for the growth of an epidemic outbreak, *I(t)* is the cumulative number of notification cases at time t (in week), K is the maximum case number over a single wave of outbreak, r is the per capita growth rate of the infected population, and a is the exponent of deviation. The explicit solution of Richards model is well-known to be of the form $I(t) = K[1 + e^{-r(t-t_m)}]^{1/a}$. Here the parameter t_m is related to the turning point t_i of the epidemic (or the inflection point of the cumulative case curve) by the simple formula $t_m = t_i + (\ln a)/r$, where ln denotes the natural logarithm function (Hsieh *et al.* 2004; Hsieh & Cheng 2006; Hsieh 2008).

Unlike the more commonly used Susceptible-Infective-Removal (SIR) model with several compartments which are used to describe the transmission dynamics of an infectious disease, the Richards model considers only the cumulative infected population size with saturation in growth as the outbreak progresses, possibly caused by implementation of control measures or other factors such as climate change. The basic premise of the Richards model is that the incidence curve of a single wave of infections consists of a single peak of high incidence, resulting in an S-shaped epidemic curve and a single turning point of the outbreak. The turning point, defined as the point in time at which the rate of accumulation changes from increasing to decreasing, or vice versa, can be easily pinpointed by locating the inflection point of the cumulative case curve, i.e. the moment at which the trajectory begins to decline. This quantity has obvious epidemiologic importance, indicating either the beginning (i.e. moment of acceleration after deceleration) or end (i.e. moment of deceleration after acceleration) of a wave of infections.

When there is more than one wave of infections, as in the cases of the 2003 SARS outbreaks in Singapore and Greater Toronto area (GTA) in Canada, a variation of the S-shaped Richards model was proposed (Hsieh & Cheng 2006) which makes a distinction between two types of turning points. Other than the inflection point of the initial S curve which signifies the first turning point ending the initial exponential growth, there is a second type of turning point in a multi-wave epidemic curve where the growth rate of the number of cumulative cases begin to increase again, signifying the beginning of the next wave. For a multi-phase Richards model, multiple phases, one for each of the S-shaped segments, result from the multiple waves of infection during this outbreak. Moreover, distinct waves are distinguished by the turning points (or inflection points), denoting acceleration after deceleration at the end of each S-shaped segment, which are also the local minima of the corresponding incidence curve. For an n-phase epidemic outbreak, $n - 1$ local minima separate the n phases. For example, the SARS incidence curves for GTA and Singapore contain two peaks (local maximum or turning point of the first type) and one valley (local minimum or turning point of second type) (Hsieh & Cheng 2006; Hsieh 2008). A detailed multistage Richards model procedure is described in the Appendix (also see Hsieh & Cheng 2006).

By considering successive S-shaped segments of the epidemic curve separately, one can estimate the maximum case number, K, and locate the turning points, thus providing an estimate for the cumulative number of cases during each phase of the outbreak. The cumulative case data in Figure 3 are then fitted to the cumulative case function $I(t)$ in the Richards model with the initial time $t_0 = 0$ being e-week 23 and the initial case number $S_0 = S(0) = 2$, the number of new cases in that week. The data fit can be performed easily and efficiently using any standard software with a least-squares approximation tool, e.g. SAS, MATLAB, etc.

Results

Fitting the above cumulative DF/DHF case data to the previously described multistage Richards model procedure, the parameter estimates of the two waves were obtained (Table 1), with the corresponding theoretical epidemic curve (Figure 3). Table 1 gives the estimation results for the turning points t_i, growth rate r, and maximum case number (or the cumulated case number) K for each wave of the outbreak in bold, where K is also the estimate for the cumulated case numbers at the end of each wave. Note that the true cumulated case numbers for the first wave during e-weeks 23–35 and the second wave during e-weeks 35–52 are 484 and 1706, respectively, both of which are well within the 95% CI of our estimates of K for each wave.

From the estimation results using the data of the first wave occurring during e-weeks 23–35 (third and fourth rows in bold), we observe that $t_i = 8.13$ implies that the first turning point had occurred 8.13 weeks after the initial e-week 23, or around the 32nd e-week (23 + 8.13 = 31.13), or between 5 and 11 August. During this period the outbreak started to ease, reversing the initial exponential growth. However, the divergent estimates for t_i using increasing number of weeks of case data indicate that a second turning point probably had occurred around e-weeks 35–36 (August 26–September 8), when the weekly number of new cases started to increase again. Finally, using the data of e-weeks 36–52 (last row in bold) yields

Table 1 Estimation results of the model parameters for the first wave during e-week 23–35 and the second wave during e-week 35–52. Note that the maximum case number is rounded off to integer

Time Period (e-week)	Turning point t_i (95% CI)	Growth rate r (95% CI)	Max case number K (95% CI)
23–33	2.05 (0*, 110973.11)	0.149 (0*, 16.157)	230 (0*, 7982)
23–34	9.80 (0*, 131.71)	0.171 (0*, 0.497)	1042 (0*, 2590)
23–35 (first wave)	8.13 (5.01, 11.25)	0.449 (0.096, 0.802)	577 (432, 723)
23–36 (first wave)	8.14 (5.42, 10.85)	0.439 (0.194, 0.684)	582 (494, 670)
23–37	8.19 (3.11, 13.27)	0.332 (0.162, 0.501)	643 (543, 744)
23–38	8.30 (0*, 22.55)	0.243 (0.113, 0.372)	731 (582,871)
36–45	9.25 (16.68, 159.18)	0.170 (0*, 0.542)	2931.4 (0*, 8634)
36–49	7.62 (4.64, 10.59)	0.322 (0.229, 0.416)	1838.9 (1662, 2015)
36–52 (second wave)	7.63 (6.36, 8.90)	0.400 (0.336, 0.463)	1713 (1665, 1760)

*Max(0, lower bound).

t_i = 7.73, or that the third turning point had occurred around e-week 44 (36 + 7.63 = 43.63) or around October 28–November 3.

The end of the second wave in Taiwan, with downturn occurring during October 28–November 3, may be in part attributable to large-scale TCDC dengue intervention measures before and during October 20–25 when over 15 000 athletes and staff participated in the National Games held in Tainan City and Tainan County, where more than 90% of all reported DF/DHF cases had occurred (TCDC 2009). Noting that our dengue data is by onset day and the intrinsic dengue incubation period within human, or the time from being bitten to onset of symptoms, averages from 4 to 7 days (US CDC 2008), the delay from infection to onset is nearly one week. The measures, which included having a task force with a commander and 41 disease controllers living onsite and administering dengue fever prevention tasks and monitoring the health of staff and athletes, were modeled after the epidemic monitoring system used at 2000 Sydney Olympics (Wu *et al.* 2008) and could have contributed to the downward turning point which occurred one week later.

However, the occurrence of the first wave, with a downturn around 5–11 August and an upturn around August 26–September 8, requires further study. We found no significant public health events that seem to match these dates. By applying regression analysis to weekly case DF/DHF notification data from the 2005 Singapore dengue outbreak stratified by the 'carpet-combing' vector control exercises implemented by the Singapore government at that time, Ang *et al.* (2007) concluded that the contribution of the time component was deemed to be greater than that of the carpet-combing operations in the reduction of dengue notifications. In a recent modelling study fitting Richards model to 2005 Singapore dengue outbreak, Hsieh and Ma (2009) found that the turning point for the outbreak had most likely occurred before large-scale intervention measures were implemented. Therefore, these two earlier turning points in August/September were likely affected by natural causes. Hence we shall explore how climatological changes might have played a role in these turning points occurring.

We focused on the reported climate data, or more specifically the daily average temperature and precipitation data, which can be obtained through the Central Weather Bureau (CWB) of Taiwan website. As an illustration, the climate data for Tainan area in August 2007 (taken from CWB of Taiwan 2008) are given in Figure 4 together with the weekly DF/DHF data of that month for Taiwan, of which most had occurred in Tainan.

Some dengue studies (Chowell & Sanchez 2006; Wu *et al.* 2007) using monthly incidence and climate data have observed that dengue incidence to be correlated with temperature and precipitation/humidity, albeit often with lags of 1–3 months. Therefore we investigated the association between two climatological variables, namely,

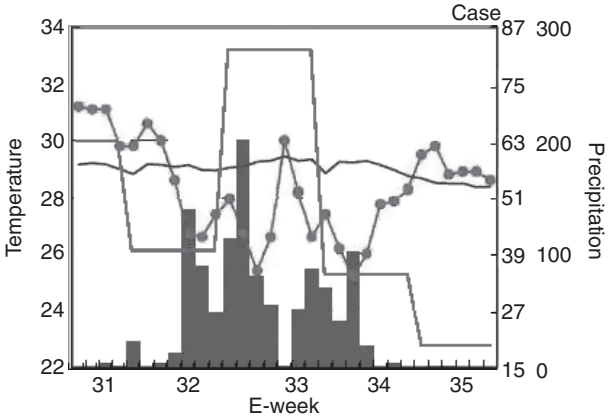

Figure 4 Weekly DF/DHF data (in dots), daily average temperature (in piecewise straight line), historical average daily temperature (in curved line), and daily precipitation (in blocks) In Taiwan during August 2007. Source: Taiwan CWB.

temperature (in centigrade) and precipitation (mm), and weekly dengue incidence. Moreover, to avoid spurious regression which could possibly result in biased and inconsistent estimator, we needed to determinate if the relevant time series are stationary. A stationary time series means that its statistical characteristics do not change in time. Time series of case numbers and climatological variables, temperature and precipitation were suitably transformed to achieve stationarity.

$$\nabla \mathrm{Case}_t = \ln\left(\frac{\mathrm{Case}_t}{\mathrm{Case}_{t-1}}\right) = \ln(\mathrm{Case}_t) - \ln(\mathrm{Case}_{t-1})$$

$$\mathrm{LogCase}_t = \ln(\mathrm{Case}_t)$$

$$\mathrm{CaseRate}_t = \frac{\mathrm{Case}_t}{\mathrm{Case}_{t-1}}$$

$$\nabla \text{Max. Temp}_t = \text{Max. Temp}_t - \text{Max. Temp}_{t-1}$$

$$\nabla \text{Min. Temp}_t = \text{Min. Temp}_t - \text{Min. Temp}_{t-1}$$

$$\nabla \text{Mean Temp}_t = \text{Mean Temp}_t - \text{Mean Temp}_{t-1}$$

$$\nabla \text{Max. Precipitation}_t = \text{Max. Precipitation}_t - \text{Max. Precipitation}_{t-1} \nabla \text{Total Precipitation}_t = \text{Total Precipitation}_t - \text{Total Precipitation}_{t-1}$$

Here ∇Y indicates that 'change' or 'increment' between periods $t-1$ and t. The test results indicate that, for time series of the first wave during week 23–35, ∇Case, CaseRate, ∇Mean Temp, ∇Max. Temp, ∇Min. Temp, ∇Max. Precipitation, and ∇Total Precipitation are stationary. Discussions on stationarity test and details of the tests carried out are given in the Appendix. Note that seasonal time series need to have trend and seasonality removed before computing correlations between disease incidence and climatological variables (Bowie & Prothero 1981). However, we did not consider removing seasonality since our focus is on a very short time period, namely the summer/fall outbreak, which does not constitute one complete season (year).

Subsequently we analysed the correlation between the weekly dengue case data (∇Case and CaseRate) of the first wave (e-week 23–35) and the above-mentioned five climatological variables. The correlation coefficient is a useful measure of linear strength between two random variables. The correlation coefficient plots are given in Figure 5. We would like to check whether ∇Case (Case Rate) and ∇Max. Temp are independent. Figure 5 shows the most significant at Lag 5. We employ a distributed lag model (DLM) to describe the relationship of weekly dengue case and five climatological variables, respectively. The detailed procedure of DLM model is provided in the Appendix and the results are given in Table A3 on the most significant lags as suggested by correlation coefficient plots. In summary, we found that both ∇Case and CaseRate are most correlated with the changes in maximum temperature ($r = 0.66$ with P-value = 0.0194 and 0.71 with P-value = 0.0102, respectively) at a lag of 5 weeks. Moreover, both ∇Case and CaseRate have high correlation with the changes in average temperature ($r = 0.56$ and 0.46, respectively) at a lag of 6 weeks, and with the changes in minimum temperature at a lag of 3 weeks. In Figure 5b, increment of the total precipitation has highest correlation with ∇Case and CaseRate at a lag of 7 weeks ($r = 0.53$ and 0.53, respectively), while increment of the maximum precipitation has highest correlation with ∇Case and CaseRate at a lag of 7 weeks ($r = 0.50$ and 0.42, respectively).

Conclusions and discussion

To ascertain the role of climatological factors, we first note that all variables, including DF/DHF case number, are transformed to take into account of the changes from one time period (week in our case) to the next. Combining all our results in Figure 5, the change in dengue case number appears to be most closely correlated with change in temperature at lags of 3–6 weeks, while the changes in precipitation seems to be most correlated with change in dengue case number at a lag of 7 weeks.

There were two climatological events of importance in Taiwan during August: during August 9–13 (around e-week 32) typhoon Wutip brought massive rainfall (>315 mm during the week) and substantial drop in temperature (from average temperature of almost 31 °C on August 6 down to a little over 26 °C on August 9) in Tainan area, and typhoon Sepat brought more of the same, but to a lesser degree, during August 17–21 around e-week 33 (Figure 4). Again taking into account of the delay from infection to onset of symptoms of nearly one week, a lag of 3–6 weeks for correlation between temperature and dengue incidence data, recorded by onset date of symptoms, implies a lag of about 2–5 weeks for dengue infections. Hence the drop in temperature during e-weeks 32–33 due to the two typhoons contributed to low dengue infections during e-week 34–38 (and low incidence by onset during e-weeks 35–38).

Similarly, a lag of 7 weeks for correlation between precipitation brought by the typhoons during e-weeks 32–33 and dengue incidence by onset implies a lag of about 6 weeks for correlation with dengue infections, leading to increasing dengue incidence by infection during e-weeks 38–39, and by onset during e-weeks 39–40, when substantial increase in dengue incidence set in (Figure 4). Therefore, the 2007 dengue outbreak in Taiwan was unique in two aspects: first, the occurrence of an additional wave during August, which was caused by a sharp drop in

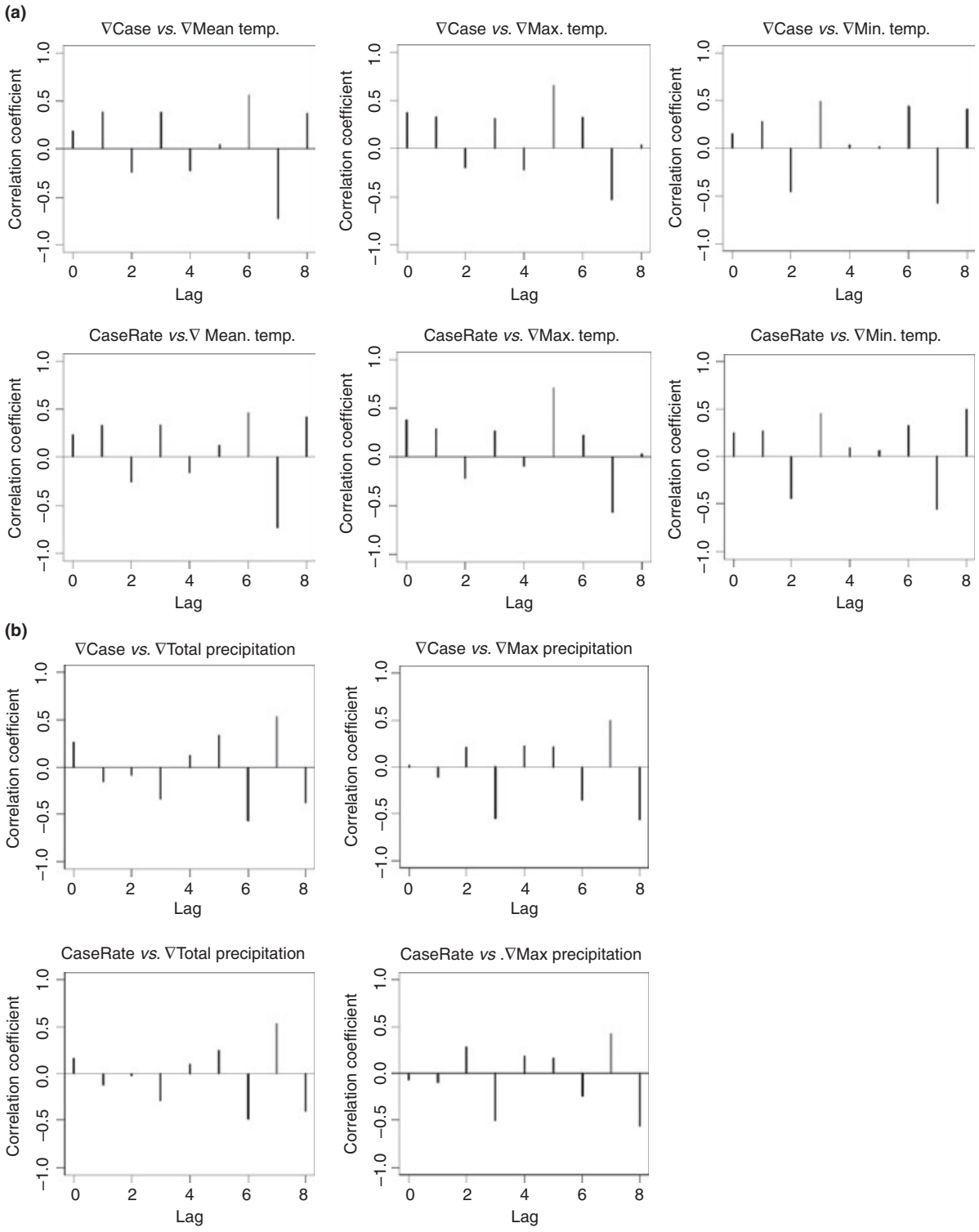

Figure 5 (a) Cross-correlation between ∇Case and CaseRate with temperature for e-weeks 23–35. (b) Cross-correlation between ∇Case and CaseRate with precipitation for e-weeks 23–35.

dengue incidence due to the drastic drop in temperature caused by two typhoons which came in quickly succession during e-weeks 32–33, resulting in low dengue incidence 3–6 weeks later during e-weeks 35–39; second, the atypically large number of confirmed dengue cases, which our results indicate was driven by the unusually large rainfall brought by the two typhoons, leading to sharp increase in dengue incidence 7 weeks later, around e-weeks 39–40. In short, both uncommon phenomena have the same root in climatological events, namely, two typhoons that came in short succession, which highlights the important role climate change plays in the spread of infectious diseases. We note that there are, of course, other possible courses for this phenomenon, e.g., the natural inter-epidemic cycle of dengue cases, which one could explore further in future work.

Finally, the Richards model is also useful in computing the 'initial' reproduction number of a dengue outbreak. The computation of well-known basic reproduction number R_0, the expected number of hosts who would be infected after one generation of the parasite by a single infectious person who had been introduced into an immunologically naïve population, was defined by Hsieh *et al.* (2004). However, since many of the regions with dengue outbreaks are endemic with dengue for several decades, the populations considered are far from 'immunologically naïve'. Indeed, some studies have shown that some of these populations were less than 60% susceptible to some subtypes of dengue (Wilder-Smith *et al.* 2004; Egger *et al.* 2008). Therefore, the estimates of reproduction number obtained from dengue outbreak data are at best the 'initial' basic reproduction, or the expected number of hosts who would be infected after one generation of the parasite by a single infectious person who had been introduced into an endemic population at the beginning of an outbreak (Hsieh & Ma 2009).

In short, the initial reproduction number $R_i = \exp(rT)$ where T is the generation time of the disease, the average interval from infection of one individual to when their contacts are infected (Hsieh *et al.* 2004; Hsieh 2008; Hsieh & Ma 2009 for application to SARS and dengue). 'r' is the per capita intrinsic growth rate in Richards model, the estimate of which is given in Table 1. For the first wave, we used the estimated value of $r = 0.449$ (95% CI: 0.096–0.802), which is the convergent estimate for r obtained by using the case data of week 23–35. For the second wave, we used the estimated value for $r = 0.408$ (95% CI: 0.347–0.469).

For the generation time of vector-host disease transmission, MacDonald had argued (see Bailey 1982 or Diekmann *et al.* 1990 for a discussion) that one should consider the average number of cases in the host population arising from one case in the host population via vector cases. Massad *et al.* (2001) had used a mean extrinsic incubation period of about 14 days, ranging from 10 to 16 days from Halstead (1990), and the duration of viremia of 5 days with range of 3–8 days for dengue. Together with the intrinsic dengue incubation period of 4–7 days, we arrive at the estimated generation time of 24 days, ranging from 16–34 days (also see Hsieh & Ma 2009).

For the first wave (e-weeks 23–37), we obtain $R_i = 4.67$ with 95% CI range of (0*, 10.92), where 0* = max{0, lower bound}. For the second wave (e-weeks 36–52), we obtain $R_i = 3.93$ with 95% CI range of (1.74, 6.13). Note that the lower estimate of the initial reproduction number

Table 2 Comparison of reproduction numbers for dengue

Source	R_0 (95% CI range)	Region/date
Hsieh and Ma (2009)	2.23 (1.47, 3.00)	Singapore 2005
This work	3.93–4.67 (0*, 10.92)	Taiwan 2007
Koopman *et al.* (1991)	1.33–2.40	70 locations in Mexico 1986
Marques *et al.* (1994)	1.6–2.4	Sao Paolo 1990–91
Khoa *et al.* (2005)	1.25–1.75	Southern Vietnam
Chowell *et al.* (2007)†	method 1: 3.09 (2.34, 3.84) method 2: 2.0 (1.75, 2.23)	Colima, Mexico 2002
Chowell *et al.* (2008)	1.76 (IQR‡ 0.83–4.46)	Peru 1994–2006
Luz *et al.* (2003)	0.66–22.4 (high), 0.03–14.4 (low)	Rio de Janeiro
Favier *et al.* (2006)	2.0 (Fortaleza) to 103 (Brasilia)	Fortaleza 2003, Brasilia 2001
Ferguson *et al.* (1999)	4–8 (multi-strain)	Rayong, Thailand, early 1980
Massad *et al.* (2008)	1.9	Singapore 2002

*Max{0, lower bound}.
†Mean reproduction number R_p.
‡Inter-quartile ranges.

R_i for the second wave might be attributable to government intervention measures implemented before the second wave began. For dengue, there has been a wide range of estimates of R_0; a list of some past related results is given in Table 2. We observe that our estimate of R_i for Taiwan is significantly higher than most estimates in the literature, including the 2005 estimate for Singapore dengue using the same method (Hsieh 2008). Due to low dengue endemicity in Taiwan, our high estimate for R_i might in fact comparatively better reflect the actual basic reproduction number for dengue. We also note that multiple dengue serotypes must play a role in the accuracy of estimate for R_i, although over 90% of the 2007 virus samples serotyped in Taiwan are of DEN-1, thus negating the effect of multi-strain in our estimated R_i. It is interesting to note that Ferguson *et al.* (1999), which used a multi-strain dengue model, obtained estimates for R_0 which are closest to our estimate.

We have used a fixed generation length in our computation of R_i. However, the shape of the generation interval distribution often affects the resulting reproductive number (Chowell *et al.* 2007; Wallinga & Lipsitch 2007). Our formula used in this paper would yield upper bounds on the reproduction number which perhaps in part also contributes to the significantly higher estimates obtained compared to previous studies. Statistically rigorous methods using realistic assumptions about the intrinsic and extrinsic incubation periods and infectious period in humans have been proposed (Chowell *et al.* 2008) but are beyond the scope of this study.

Acknowledgement

YHH is supported by grant (97-2314-B-039-013-MY3) from National Science Council of Taiwan. The authors would like to thank the referees for their constructive and insightful comments which significantly improved this paper.

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Appendix

The multistage Richards model procedure

The multistage Richards model procedure requires the following five steps:

1. Fit the Richards model to cumulative cases on successive days by using a standard least-square routine. For single-phase outbreaks, parameter estimate for t_i will converge as the trajectory approaches the maximum case number over the course of the outbreak K, as demonstrated in the Taiwan, Beijing, and Hong Kong SARS outbreaks.
2. If estimated parameter t_i remains convergent until no more new cases are detected, the outbreak has only one phase. However, if the estimate begins to diverge from the heretofore convergent value, one knows that a turning point denoting the start of a second phase has occurred.
3. Locate the turning point, $t_{\min}$, separating two S-shaped phases of the epidemic as the local minimum of the weekly incidence curve given in Figure 1.
4. Fit the Richards model to the cumulative case curve again, but starting from $t_{\min} + 1$, the day after the start of second phase. The estimated parameter t_i will again converge as the curve approaches the maximum case number K for the second phase.
5. Repeat steps 2–4 in the event more phases occur until the outbreak ends.

To achieve stationarity

A stationary time series means that its statistical characteristics do not change in time. Classical regression model was devised to deal with relationships between stationary variables, which is not appropriate to apply to non-stationary series. More precisely, if we have two independent non-stationary series, then we may find evidence of a relationship when in reality none exists (i.e. spurious regression problem). Therefore, we employ augmented Dickey-Fuller (ADF) test (Said & Dickey 1984) to verify if the random variables satisfy the stationary series. Three equations are used to test if the series process has non-stationary character:

1. Without drift and trend terms:
$$\Delta Y_t = \rho Y_{t-1} + \sum_{i=1}^{k} \gamma_i \Delta Y_{t-i} + \varepsilon_t$$
2. Including drift term without trend term:
$$\Delta Y_t = \alpha + \rho Y_{t-1} + \sum_{i=1}^{k} \gamma_i \Delta Y_{t-i} + \varepsilon_t$$
3. Both drift and trend terms:
$$\Delta Y_t = \alpha + \beta t + \rho Y_{t-1} + \sum_{i=1}^{k} \gamma_i \Delta Y_{t-i} + \varepsilon_t$$

The null hypothesis is non-stationary or unit root, i.e. H_0:$\gamma_1 = \cdots = \gamma_k = 0$. The series $\{Y_t\}$ has unit root if we cannot reject the hypothesis. The ADF statistics given in Tables A1 and A2, are negative numbers. The more negative it is, more assuredly we can reject the hypothesis that there is a unit root at some level of confidence. For time series of e-weeks 23–35, unit root tests for ∇Case, CaseRate, ∇Mean Temp, ∇Max. Temp, ∇Min. Temp, ∇Max. Precipitation, and ∇Total Precipitation are rejected at 1% significant level, and hence we conclude that they are stationary. Being stationary means that the models can be used outside the range of data for which they were estimated.

Distributed lag model

It is important to know whether the weekly dengue case data is related to lagged values of climatological variables.

Table A1 ADF tests for a unit root on case, log-case, and log-case rate changes, where *P*-value is in parentheses

Variable	Case	∇Case	LogCase	CaseRate
Type 1	−0.913 (0.301)	−4.186 (0.001)	−0.028 (0.654)	−1.400 (0.141)
Type 2	−2.202 (0.215)	−4.219 (0.010)	−1.843 (0.344)	−3.913 (0.016)
Type 3	−2.434 (0.347)	−5.544 (0.006)	−1.710 (0.683)	−4.992 (0.012)

The lower *P*-value indicates the null hypothesis of non-stationary can be rejected.

Table A2 ADF tests for a unit root on the changes in climatological variables, temperature and precipitation, where *P*-value is in parentheses

Variable	∇Mean Temp.	∇Max. Temp.	∇Min. Temp.	∇Max. precipitation	∇Total.precipitation
Type 1	−7.971 (<0.001)	−5.345 (<0.001)	−1.374 (0.152)	−4.750 (<0.001)	−5.267 (<0.001)
Type 2	−8.127 (<0.001)	−5.605 (<0.001)	−4.351 (0.003)	−4.646 (0.001)	−5.251 (<0.001)
Type 3	−8.725 (<0.001)	−5.231 (<0.001)	−5.747 (0.001)	−4.429 (0.010)	−5.133 (0.002)

The lower *P*-value indicates the null hypothesis of non-stationary can be rejected.

Table A3 Results of linear regression analysis for e-weeks 23–35

∇Y	∇X	Lag	β_1	*P*-value	*r*
∇Case	∇Mean Temp.	6	0.3046	0.0588	0.5590
CaseRate	∇Mean Temp.	6	0.3355	0.1274	0.4653
∇Case	∇Max. Temp.	5	0.8471	0.0194	0.6605
CaseRate	∇Max. Temp.	5	1.1985	0.0102	0.7063
∇Case	∇Min. Temp.	3	0.1763	0.1086	0.4867
CaseRate	∇Min. Temp.	3	0.2148	0.1441	0.4480
∇Case	∇Total Precipitation	7	0.0046	0.0743	0.5332
CaseRate	∇Total Precipitation	7	0.0061	0.0758	0.5308
∇Case	∇Max. Precipitation	7	0.0061	0.0998	0.4975
CaseRate	∇Max. Precipitation	7	0.0068	0.1753	0.4189

We employ a distributed lag model (DLM) to describe the weekly dengue case data. A DLM is a regression model that includes current and lagged values of one or more explanatory variables. This model allows us to determine what the effects are of a change in a case numbers. DLMs have recently been used in environmental epidemiology for quantifying the cumulative effects of weather and air pollution on mortality and morbidity. A distributed lag model (DLM) with r lags of other variable is stated as follows:

$$\nabla Y_t = \beta_0 + \beta_1 \nabla X_{t-1} + \cdots + \beta_r \nabla X_{t-r} + \varepsilon_t.$$

Our model can be further simplified as follows:

$$\nabla Y_t = \beta_0 + \beta_1 \nabla X_{t-\text{lag}} + \varepsilon_t,$$

where the intercept $\beta_0$and the slope β_1 are unknown coefficients and ϵ_t is a random error component. The lag value is chosen by inspecting the Figure 5. Using e-weeks 23–35 observations, a linear regression analysis was performed (Table A3). The sample coefficient of correlation is denoted by '*r*'. The correlation quantifies the strength of the linear relationship between ∇Y (the weekly dengue case data) and ∇X (climatological variable). It's of interest to assess the possibility of lagged effects of these climatological variables on dengue incidence.