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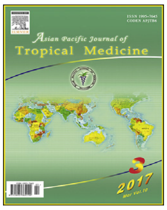

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Temporal patterns of dengue epidemics: The case of recent outbreaks in Kaohsiung

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ABSTRACT

Objective: To investigate whether major dengue outbreaks in the last two decades in Kaohsiung follow a precise temporal pattern.
Methods: Government daily lab-confirmed dengue case data from three major dengue outbreaks occurring during the last two decades in Kaohsiung in 2002, 2014 and 2015, is utilized to compute the corresponding weekly cumulative percentage of total case numbers. We divide each of the three time series data into two periods to examine the corresponding weekly cumulative percentages of case numbers for each period. Pearson's correlation coefficient was calculated to compare quantitatively the similarity between the temporal patterns of these three years.
Results: Three cutoff points produce the most interesting comparisons and the most different outcomes. Pearson's correlation coefficient indicates quantitative discrepancies in the similarity between temporal patterns of the three years when using different cutoff points.
Conclusions: Temporal patterns in 2002 and 2014 are comparatively more similar in early stage. The 2015 outbreak started late in the year, but ended more like the outbreak in 2014, both with record-breaking number of cases. The retrospective analysis shows that the temporal dynamics of dengue outbreaks in Kaohsiung can strongly vary from one year to another, making it difficult to identify any common predictor.

1. Introduction

Dengue fever is a mosquito-vectored viral disease, which thrives in tropical and sub-tropical climates. According to the last report released by World Health Organization [1], the last decades have seen an upsurge in both its incidence and its geographic expansion. Recent studies regarding its growing presence worldwide indicate that the number of infections per year is around 390 million [2], and that dengue is present in 128 countries, with 3.97 billion people at risk [3].

Taiwan is located in the tropical–subtropical region of the Northern Hemisphere, split near the middle of the island by the Tropic of Cancer, with *Aedes aegypti*, the main mosquito species causing dengue infection, manifesting mostly in the south [4]. Subsequently, the majority of dengue cases occurred in the southern tropical region, with Kaohsiung, and to a lesser degree Tainan, being the most affected. No outbreak had occurred on the main island of Taiwan since 1944 during World War II until 1987 [5] when martial law that was first implemented in Taiwan in 1949 was revoked, and traveling abroad was once again allowed. From 1998 to 2015, Kaohsiung registered 58.35% of the 77 569 cases reported in the entire country and was clearly a major focus of dengue virus activity in Taiwan [6]. Moreover, the number of reported dengue cases in southern Taiwan has increased abruptly and dramatically in the past two years (2014–2015). Figure 1 provides a comparison between reported cases in Taiwan and in Kaohsiung during the period 1998–2015 [7].

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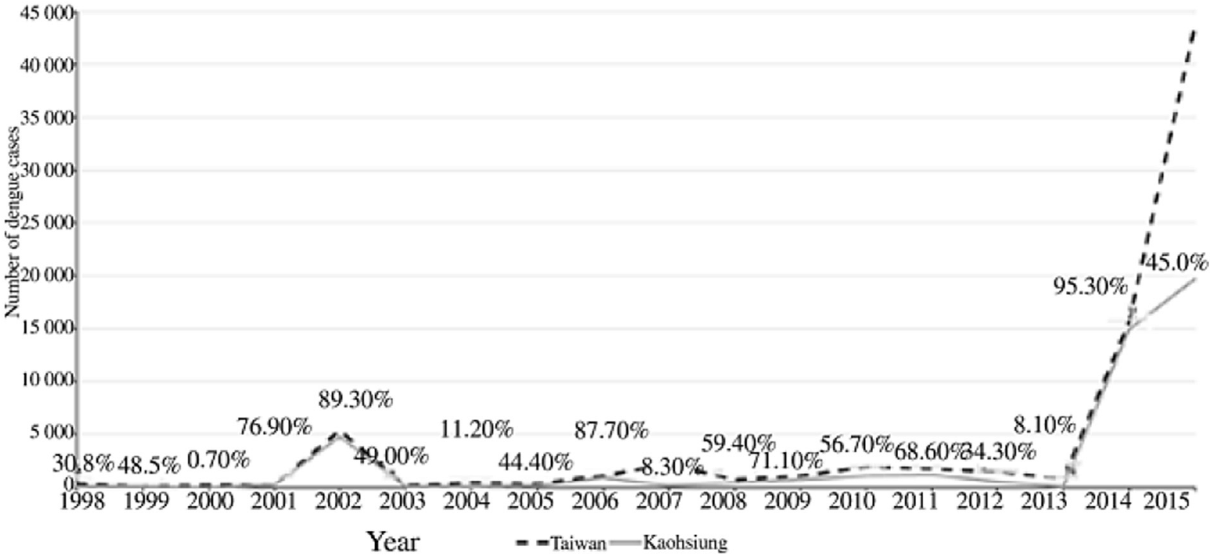

Figure 1. Temporal pattern of dengue cases in Taiwan and in Kaohsiung alone.

The aim of this paper is to investigate the temporal pattern of three major outbreaks that had occurred in Kaohsiung in the last two decades, namely in 2002, 2014 and 2015, by comparing their respective behavior at different periods of the year. In a previous study [8], it is shown that the 2007 2-wave dengue outbreak in Tainan was correlated to two typhoons with heavy rainfalls that came in less than two weeks in early August. More precisely, the drop in temperature had led to a decrease in reported cases immediately after the typhoons, with a subsequent upturn of cases after several weeks due to maturation of mosquitos bred in excess water reservoir in the aftermath of heavy rainfall that started a second and even larger wave of infections.

Our purpose is to investigate whether these major outbreaks follow a precise temporal pattern, or whether these outbreaks can be easily affected by some exogenous factors, i.e., climatologic and other events that lead to the disease outbreak suddenly altering its course (also see, e.g., [9–11]). In order to highlight any temporal discrepancies between the outbreaks, our analysis will focus on their corresponding weekly cumulative percentage of total case number at any given time.

2. Materials and methods

2.1. Data

Daily confirmed dengue case data reported in Kaohsiung is publicly available at the Taiwan Government Open Data Platform website [12]. The dataset covers dengue cases reported since 1998 at district level and, for the last years, at the smaller administrative “li” level. We choose major outbreaks that had occurred in 2002, 2014 and 2015 for this study (Figure 2). For simplicity's sake, we aggregate the daily data into epidemiological-week data, i.e., week starting on Sundays. Moreover, we organized the data for each year beginning in week 8 around mid-February, to avoid any residue effect from the previous year's outbreak, and ending in week 52.

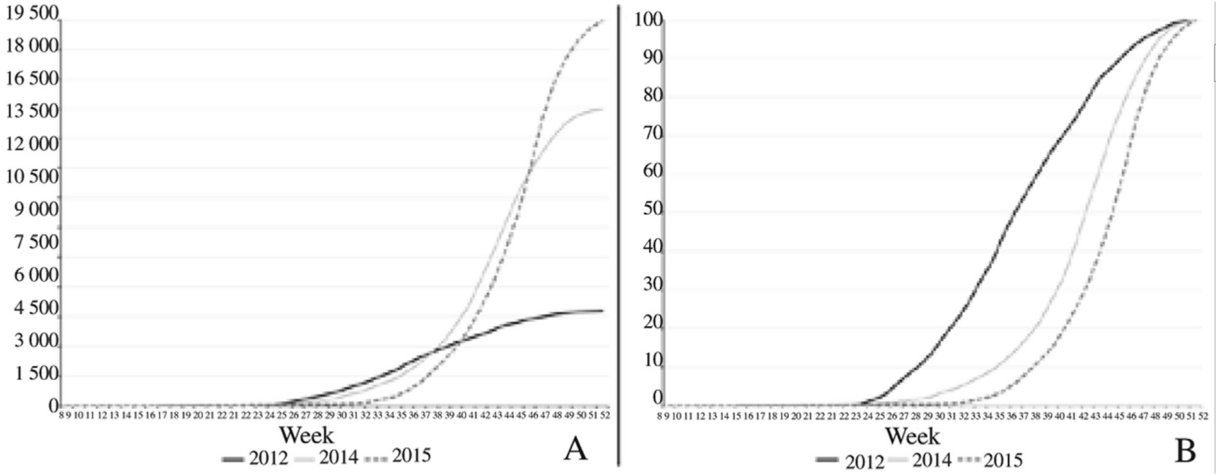

Figure 2. Dengue cases reported in Kaohsiung during the outbreaks occurred in 2002, 2014, and 2015. (A) the week cumulative number of cases; (B) the cumulative percentages of the week number of cases registered at the end of each epidemic.

2.2. Cumulative percentage and Pearson's correlation coefficient

For each of the three years under investigation, we first use the weekly data to calculate the cumulative percentage of the total number of dengue cases reported over the entire year. The cumulative percentage curve is commonly used in plant disease epidemiology, to represent the temporal evolution of an epidemic, by plotting against time the percentage of diseased hosts per space unit [13,14] or the disease severity, i.e. the proportion of the plant affected by disease [15]. It is also used to quantify disease resistance, through the calculation of the AUDPC (area under the disease-progress curve) [16], to predict yield losses [17] and to compare the effectiveness of different treatments [14].

For comparison, we then split the resulting time series data in two parts: the first containing the data recorded from week 8 to week *n* of the year, $(ndc_{y,8}, \cdots, ndc_{y,n})$, where the subscript *y* is the year and *ndc* stands for "number of dengue cases"; the second containing the data recorded from week *n+1* to week 52 $(ndc_{y,n+1}, \cdots, ndc_{y,52})$. We shall call week *n* the "cutoff point" for this division of time series data. We therefore computed the total number of cases for each subset, i.e. $tot_{y,1} = \sum_{i=8}^{n} ndc_{y,i}$ and $tot_{y,2} = \sum_{i=n+1}^{52} ndc_{y,i}$, and the corresponding weekly cumulative percentage:

$$for\ j \le n,\ \ p_{y,j} = 100 \cdot \left(\sum_{i=8}^{j} ndc_{y,i} \right) \Big/ tot_{y,1};$$

$$for\ j > n,\ \ p_{y,j} = 100 \cdot \left(\sum_{i=n+1}^{j} ndc_{y,i} \right) \Big/ tot_{y,2}.$$

The entire procedure is repeated varying the cutoff point (i.e. week *n*) and examining its consequences on the temporal patterns of the cumulative percentages. For a closer examination, we compute the Pearson's correlation coefficient between each pair of the time series data, in order to compare quantitatively the similarity between the temporal patterns of these three years.

3. Results

We first examine the temporal patterns of the three major outbreaks of dengue cases that occurred in Kaohsiung in the last two decades, i.e. in 2002, 2014, and 2015 (Figure 2), where the weekly cumulative case curves exhibit classical sigmoidal shape for each outbreak (Figure 2A), despite the difference in magnitude. However, the week cumulative percentage of the number of cases (Figure 2B) indicates that the 2002 outbreak is markedly different when compared to the other two years. To further our comparison of the three outbreaks, we calculate the Pearson's correlation coefficient between each pair of the three years' time series data. The result is given in Table 1.

Table 1

Pearson's correlation coefficient (r) between 2002, 2014 and 2015 data. Each coefficient is calculated from the weekly cumulative percentage of the number of cases.

r	2002	2014	2015
2002	1.000		
2014	0.934	1.000	
2015	0.870	0.984	1.000

Next, we divide each of the three time series data into two periods using the same cutoff point, and examine the corresponding weekly cumulative percentages of case numbers before and after the cutoff point. Three cutoff points produce the most interesting comparisons and the most different outcomes, namely week 26, week 32 and week 40. For the temporal pattern of the cumulative percentages up to week 26 (Figure 3 and Table 2), it can be observed that the behavior of the 2015 outbreak is quite distinct from the other two years. We further calculate the corresponding Pearson's correlation coefficients as shown in Table 3.

Another cutoff point of interest is week 32 (Figure 4 and Table 2), where the temporal behavior of 2015 data starts to align with the 2002 and 2014 curves after week 29. Moreover, the corresponding Pearson's correlation coefficients are given in Table 3. Finally, we compute the weekly cumulative percentages of the number of cases reported up to and after week 40 for each year (Figure 5 and Table 2). The corresponding Pearson's correlation coefficients are again computed in Table 3.

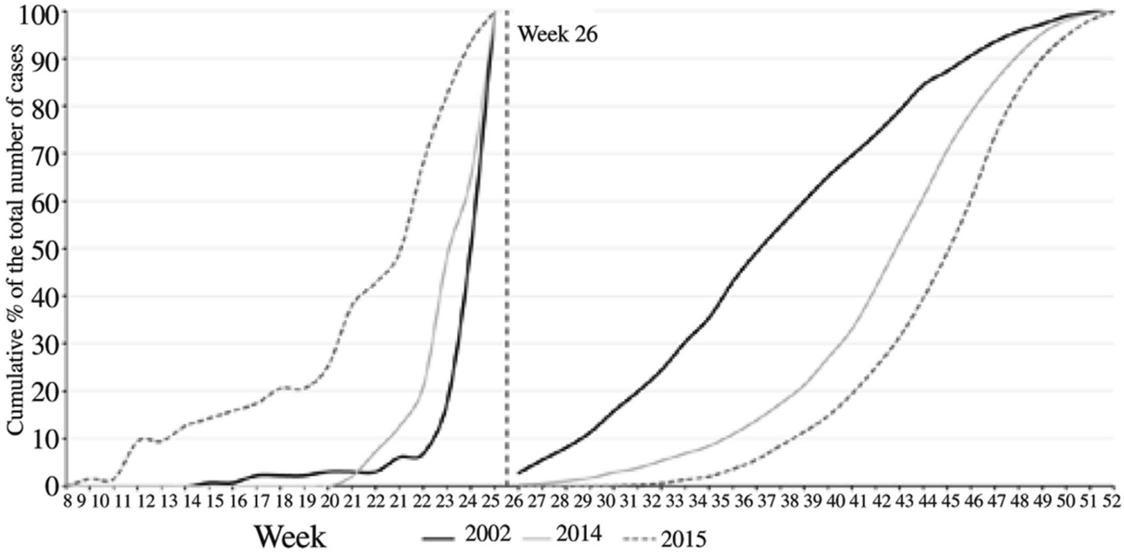

Figure 3. Cumulative percentage of the total number of dengue cases reported from the beginning of the epidemic to week 26 (on the left), and from week 27 to the end of the epidemic (on the right).

Table 2

Yearly case number of week 8–52 and number of cases at 3 time cutoff points.

Year	Case number (Week 8–52)	Cutoff point 1 (*n*, %)		Cutoff point 2 (*n*, %)		Cutoff point 3 (*n*, %)	
		Week 8–26	Week 27–52	Week 8–32	Week 33–52	Week 8–40	Week 41–52
2002	4799	130 (2.71)	4669 (97.29)	1061 (22.11)	3738 (77.89)	3177 (66.20)	1622 (33.80)
2014	14970	95 (0.63)	14875 (99.37)	670 (4.48)	14300 (95.52)	4128 (27.58)	10842 (72.42)
2015	19452	63 (0.32)	19389 (99.68)	132 (0.68)	19320 (99.32)	2937 (15.10)	16515 (84.90)

Table 3

Pearson's correlation coefficients (r) between 2002, 2014 and 2015 data at 3 time cutoff points.

Year	Time cutoff point 1						Time cutoff point 2						Time cutoff point 3					
	Week 8–26			Week 27–52			Week 8–32			Week 33–52			Week 8–40			Week 41–52		
	2002	2014	2015	2002	2014	2015	2002	2014	2015	2002	2014	2015	2002	2014	2015	2002	2014	2015
2002	1.000			1.000			1.000			1.000			1.000			1.000		
2014	0.955	1.000		0.934	1.000		0.994	1.000		0.956	1.000		0.971	1.000		0.998	1.000	
2015	0.778	0.895	1.000	0.873	0.984	1.000	0.888	0.898	1.000	0.908	0.984	1.000	0.892	0.973	1.000	0.975	0.984	1.000

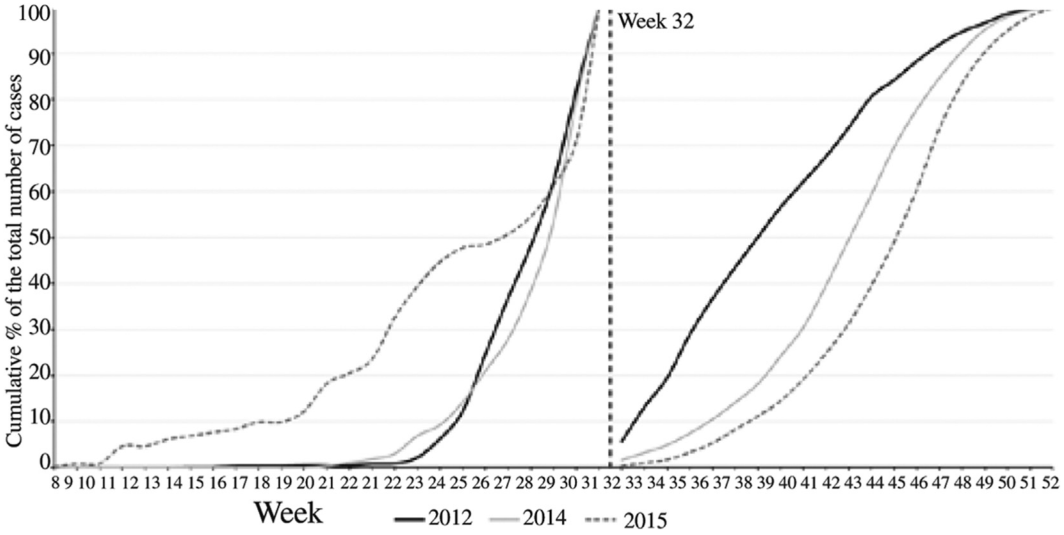

Figure 4. Cumulative percentage of the total number of dengue cases reported from the beginning of the epidemic to week 32 (on the left), and from week 33 to the end of the epidemic (on the right).

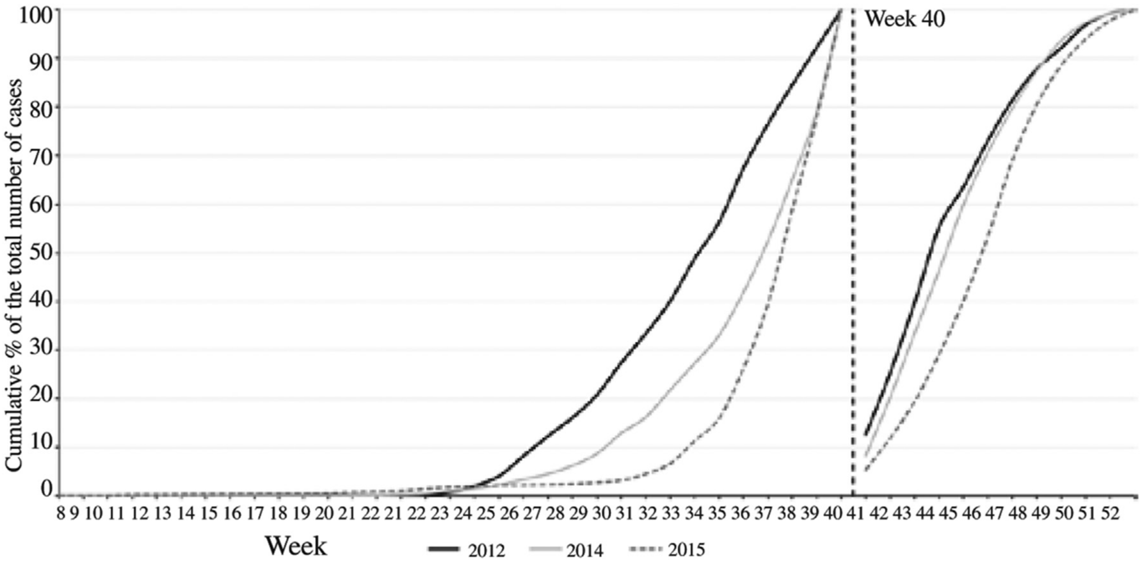

Figure 5. Cumulative percentage of the total number of dengue cases reported from the beginning of the epidemic to week 40 (on the left), and from week 41 to the end of the epidemic (on the right).

4. Discussion

While the weekly cumulative case curves for all three major outbreaks exhibit classical sigmoidal shape (Figure 2A), the sigmoid profile of the 2002 data is comparatively less obvious, partly due to the scaling of the y-axis. Moreover, considering the week cumulative percentage of the total number of cases (Figure 2B), it is evident that the 2002 outbreak had a markedly early start. That year, for example, the 25% of the cases occurred approximately two months earlier than that of 2014 and 2015. Nonetheless, the disease spread in 2002 was noticeably slower from the end of September to the end of November when, on the contrary, the increase in weekly cumulative percentage was very high in both 2014 and 2015.

Such discrepancies, however, compensate for each other, as demonstrated by calculating the Pearson's correlation coefficients (Table 1). The degree of linear association between the three datasets is actually quite close, leading us to conclude that the overall temporal patterns of the outbreaks reported in Kaohsiung in 2002, 2014 and 2015 differ only slightly, even though their outcomes in terms of number of people infected are quite dissimilar, as shown in Figure 2A.

Examining the temporal pattern of the dengue infections reported up to and after week 26 (Figure 3), it can be observed that the early behavior of the 2015 weekly cumulative percentage curve is quite distinct from the others. The early number of reported cases in 2015 is clearly less than the numbers observed during the same period in 2002 and 2014, respectively (Table 2). Moreover, in early 2015, the disease spread follows a faster and more erratic course, while both in 2002 and in 2014 a sudden increase is clearly visible between weeks 20 and 23. On the other hand, the temporal behavior of the outbreak from week 27 to week 52 is very similar for all three years to the one which can be observed from week 8 to week 52 (Figure 2B). The corresponding Pearson's correlation coefficients calculated after week 26 are similar to those presented in Table 1, but up to week 26 the correlation coefficients between 2015 and 2014, and especially between 2015 and 2002, are markedly lower (0.984 *vs.* 0.895 and 0.870 *vs.* 0.778, respectively).

Another cutoff point of interest is the cases of dengue fever recorded up to and after week 32 (Figure 4). The temporal behavior of 2015 data is still erratic up to week 29, after which it starts to align with the 2002 and 2014 curves. In 2015, the amount of infections has doubled, from week 26 to week 32, but the number of cases is still substantially lower than those registered during the same periods in 2002 and 2014, due to massive increases in case numbers reported in 2002 and 2014 from week 26 to week 32 (Table 2). However, there is no noticeable difference in temporal patterns after week 32 with respect to the entire period (Figure 2B). Moreover, the linear association degree has actually increased, except for the correlation between 2014 and 2015 (Tables 1 and 3).

Moving the cutoff point to be week 40 strongly affects the shape of the curves, as displayed in Figure 5. For the period of week 8–40, the temporal pattern of the 2015 outbreak is more exponential-like, and more similar to both 2002 and 2014. From week 35 to week 40, it has the steepest increase among the three outbreaks. At the same time, the cumulative number of people infected by week 40 does not vary substantially from one year to another, even though the value relative to 2015 accounts for only 15% of the total (Table 2). Furthermore, it can be seen that after the cutoff point, the three curves almost superimposed, indicating no significant difference of behavior between them. Consequently, all the correlation coefficients calculated after the cutoff point are greater than 0.97, while those referred to the first period (week 40 and before) are slightly lower, but still greater than 0.89 (Table 3).

To summarize, by considering the weekly cumulative percentage of total case number, the overall temporal patterns of the major dengue outbreaks in these three years are similar (Figure 2 and Table 1), most likely driven by the impact of yearly variations in climate on mosquito population, despite of the disparate numbers of reported cases. By dividing the time series data into two periods, we are able to elucidate the differing early and latter patterns of the outbreaks. In the period up to June (week 26), the early temporal increase of cumulative percentage of cases in 2015 is comparatively faster than those of 2002 and 2014 (Figure 3), even though the actual case number is much smaller. This pattern continues until the beginning of August (week 32 – Figure 4), while at the beginning of October (week 40), 2015 becomes more similar to 2014, but more distinct from 2002 outbreak (Figure 5). Therefore, the 2015 outbreak, with the most cases reported in history in Kaohsiung, started very late in the season, but ended more like 2014, which already had a record-breaking number of cases by October. On the other hand, the temporal patterns of 2002 and 2014 are comparatively more similar at least before week 32

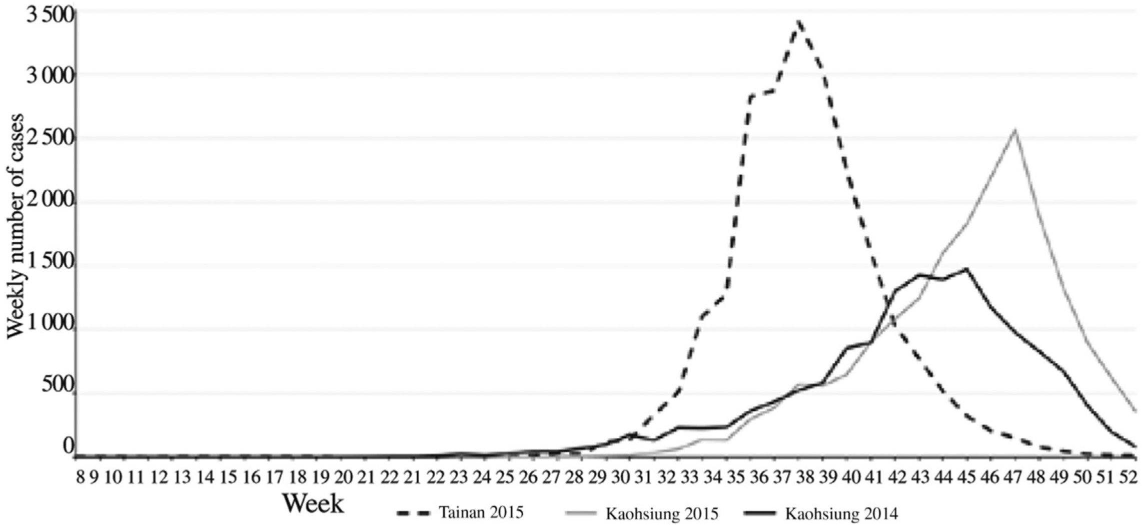

Figure 6. Weekly number of dengue cases reported in Tainin (2015) and Kaohsiung (2014 and 2015).

(Table 3), even though the magnitude of outbreaks in 2014 and 2015 are much more in agreement.

Hsieh & Chen [18] propose that the large number of cases recorded in 2002 was probably due to the drier and warmer weather conditions registered that year. Kan *et al.* [19] also suggest that the introduction of dengue virus serotype 2 (DENV-2) and a failure to contain the spreading by the local environment protection agency and the local health department were the main factors contributing to the large number of reported cases. With regard to the 2014 outbreak, Wang *et al.* [20,21] propose among possible factors the underground pipeline gas explosions that occurred in Qianzhen and Lingya districts on July 31, combined with a subsequent period of high temperatures and heavy rainfall. The results of our analysis, however, seem to exclude that the gas explosion played a key role at least in the magnitude of subsequent outbreak, since an exponential increase of cases was already well observable by the end of June, i.e. one month before the event.

The exceptional number of cases reported in 2015 in Kaohsiung is related to an earlier and even more massive dengue outbreak occurred that year in Tainan (Figure 6). In September alone, almost 13 000 new cases (i.e. more than half of the total case number) were already reported in Tainan and, by the end of the month, the cumulative case number reached around 75% of the total. By the same time in Kaohsiung, 3 841 cases were reported (or less than 20% of the total case number), clearly indicating that the outbreak in Kaohsiung was lagging behind that of Tainan. Given the proximity and high mobility of the two municipalities, it is reasonable to suppose that the contacts between the two populations are very frequent. Consequently, once the number of people infected in Tainan becomes significant, the probability of transmission to people in Kaohsiung increases accordingly.

We note that one important factor for the large number of laboratory confirmed cases being reported in Taiwan in 2015 was due to a change in diagnostic policy during the ongoing outbreak in Tainan in September 17 in week 37 (and continued through the later Kaohsiung outbreak), when considerably more SN1 antigen tests were performed. The antigen tests allowed rapid confirmation of a large number of cases shortly after the onset of illness symptoms [22]. However, this change in testing procedure in week 37 does not seem to have much impact on the temporal pattern of the cumulative percentages of 2015 in Kaohsiung (Figures 3–5).

The analysis of the temporal pattern of three major dengue outbreaks in Kaohsiung in the last two decades highlights that their temporal patterns are only partially comparable, as it does not seem possible to identify clearly a common pattern in the outbreaks under consideration. The retrospective analysis based on different time periods shows that the temporal dynamics of dengue outbreaks in Kaohsiung can strongly vary from one year to another, making it difficult to identify any common predictor. Our study highlights the difficulty in prediction of disease outbreak, especially for vector-borne diseases such as dengue where sudden change in climate or environment could lead to an unpredictable turn of event. With the additional consideration of a high proportion of asymptomatic cases, active syndromic surveillance of clinical cases remains the most important means to prevention and control of dengue.

Conflict of interest statement

We declare that we have no conflicts of interest.

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References

[1] World Health Organization. WHO TDR – World Health Organization special programme for research and training in tropical diseases. Dengue: guidelines for diagnosis, treatment, prevention and control, Geneva: WHO; 2009.

[2] Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013; **496**(7446): 504-507.

[3] Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis* 2012; **6**(8): e1760.

[4] Chang SF, Huang JH, Shu PY. Characteristics of dengue epidemics in Taiwan. *J Formos Med Assoc* 2012; **111**(6): 297-299.

[5] Ko YC. [Epidemiology of dengue fever in Taiwan]. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1989; **5**: 1-11. In Chinese.

[6] Lin CH, Schiøler KL, Jepsen MR, Ho CK, Li SH, Konradsen F. Dengue outbreaks in high-income area, Kaohsiung city, Taiwan, 2003–2009. *Emerg Infect Dis* 2012; **18**(10): 1603-1611.

[7] Taiwan CDC, TNIDSS – Taiwan Centers for Disease Control, Taiwan National Infectious Disease Statistics System. Title of the article [Online] Available at: http://nidss.cdc.gov.tw/en/ [Accessed on April, 2016].

[8] Hsieh YH, Chen CW. Turning points, reproduction number, and impact of climatological events on multi-wave dengue outbreaks. *Trop Med Int Health* 2009; **14**(6): 628-638.

[9] Wiwanitkit V. Correspondence-malaria and dengue infection after Tsunami in southern Thailand. *Trop Doct* 2007; **37**(3): 194.

[10] Caceres JLH, Kumma BD, Wright G. An attempt of early prediction and later assessment of the cholera outbreak in Haiti. *Electron J Biomed* 2010; **1**: 87-90.

[11] Hsieh YH, de Arazoza H, Lounes R. Temporal patterns and regional variability of 2001–2002 multi-wave DENV-3 epidemic in havana city: did hurricane michelle contribute to its severity? *Trop Med Int Health* 2013; **18**(7): 830-838.

[12] TGODP – Taiwan Government Open Data Platform. *Daily confirmed dengue case statistic*. Taipei: Taiwan Government; 1998. [Online]. Available at: http://data.gov.tw/node/21025 [Accessed on April, 2016]

[13] Oliva J, Boberg JB, Hopkins AJ, Stenlid J, Gonthier P, Nicolotti G. Concepts of epidemiology of forest diseases. In: Gonthier P, Nicolotti G, editors. *Infectious forest diseases*. Oxfordshire: CABI; 2013, p. 1-28.

[14] Gilligan CA. Comparison of disease progress curves. *New Phytol* 1990; **115**: 223-242.

[15] Bowen KL. Plant disease epidemiology. In: Trigiano RN, Windham MT, Windham AS, editors. *Plant pathology: concepts & laboratory exercises*. Boca Raton: CRC Press; 2003, p. 277-290.

[16] Jeger MJ, Viljanen-Rollinson SLH. The use of the area under the disease-progress curve (AUDPC) to assess quantitative disease resistance in crop cultivars. *Theor Appl Genet* 2001; **102**: 32-40.

[17] Madden LV, Hughes G, Irwin ME. Coupling disease-progress-curve and time-of-infection functions for predicting yield loss of crops. *Phytopathology* 2000; **90**(8): 788-800.

[18] Hsieh CJ, Chen MJ. Epidemiological trends of dengue infection in Taiwan. *EU J Health* 2013; **2013**: 5. ISSN 2052-5249.

[19] Kan CC, Lee PF, Wen TH, Chao DY, Wu MH, Lin NH, et al. Two clustering diffusion patterns identified from the 2001–2003 dengue epidemic, Kaohsiung, Taiwan. *Am J Trop Med Hyg* 2008; **79**(3): 344-352.

[20] Wang SF, Chang K, Lu RW, Wang WH, Chen YH, Chen M, et al. Large Dengue virus type 1 outbreak in Taiwan. *Emerg Microbes Infect* 2015; **4**(8): e46.

[21] Wang SF, Wang WH, Chang K, Chen YH, Tseng SP, Yen CH, et al. Severe dengue fever outbreak in Taiwan. *Am J Trop Med Hyg* 2016; **94**(1): 193-197.

[22] Taiwan Centers for Disease Control (TCDC). Medical care advisory committee and government-funded NS1 antigen test to launch on September 17 to ensure health of the public [Online]. Available at: http://www.cdc.gov.tw/english/info.aspx?treeid=BC2D4E89B154059B&nowtreeid=EE0A2987CFBA3222&tid=D1F370B0F6CFEFBB [Accessed on 14th July 2016].