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Evaluation of Early Aberration Reporting System for Dengue Outbreak Detection in Thailand

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Abstract

Thailand is one of the highest-burden countries for dengue infections in the South-East Asia Region of the World Health Organization. The 5-year median is normally used for outbreak detection; however, studies assessing the performance of this indicator against other detection methods are lacking. We, therefore, conducted a descriptive ecological study from a dataset comprised of patient visits to public hospitals for dengue treatment that were reported to the Ministry of Public Health. The aim was to evaluate the performance of an early aberration reporting system (EARS) in detecting dengue outbreaks, compared to using the 5-year median method. During 2003-2015, there were 1,014,201 patient visits and seven reported dengue outbreaks, with the largest occurring in 2013, and six seasonal peaks. The EARS was able to detect all seven dengue outbreaks and six seasonal peaks, including one outbreak that occurred in 2014 which was undetected by the 5-year median. However, EARS cannot provide information on trends, outbreak severity and issues noise signals. Our recommendation was to combine the EARS with the 5-year median method to reduce the number of false positive signals, or use the 5-year median method as a confirmatory tool.

Keywords: dengue, public health informatics, early disease detection, surveillance systems, disease notification, Thailand, EARS, 5-year median

Introduction

Dengue fever is a vector-borne disease caused by dengue virus. The virus is transmitted principally by *Aedes* mosquitoes, namely *A. aegypti* and *A. albopictus*, while both of which are commonly found in tropical regions. In 2012, dengue surpassed malaria as the most prominent vector-borne disease globally in terms of morbidity and cost of treatment.[1] The impact of dengue is the greatest in South-East Asia.[2] In 2015, 144,952 new dengue cases (223 per 100,000 population) were reported to the Ministry of Public Health (MOPH), including 147 deaths.[3] The burden of this disease in Thailand is one of the highest in the world.[4]

The World Health Organization formulated a dengue strategic plan in the South-East Asia Region, focusing on improving early detection and timely outbreak control efforts.[2] Most of the published papers focused on outbreak detection, yet only a few focused on detection of dengue outbreaks. Consequently, research on this topic was a high priority[5]. The MOPH currently uses the 5-year median as the threshold for outbreak detection. However, there were no studies assessing its performance against other detection methods.

The early aberration reporting system (EARS), developed by the US Centers for Disease Control and Prevention, was designed to detect early signals of upcoming outbreaks. The EARS has been used in several large public events such as the US Democratic National Convention in 2004, the Republican National Convention, the G8 Submit in Georgia 2004 and the 2004 Summer Olympics.[6] However, there are very few studies evaluating the implementation of EARS on vector-borne diseases, including early detection of dengue outbreaks[7,8].

This was the first study to examine the feasibility of implementing EARS and compare EARS against the current outbreak detection method (5-year median) in

Thailand. The objective was to compare the 5-year median method with the EARS for detecting dengue outbreaks in Thailand between 2003 and 2015.

Methods

Study Design

We conducted a descriptive ecological study based on secondary data obtained from the national (R506) surveillance system in the Bureau of Epidemiology, MOPH. The ecological unit was the weekly aggregation of dengue visits.

Study Population

The R506 national surveillance system captures health data from every public hospital in Thailand, which matches specific international classification of diseases (ICD)-10 codes and is compatible with disease prevention and epidemiological studies. The system is similar to the national electronic disease surveillance system of the United States Centers for Disease Control and Prevention. Data are submitted to provincial health offices on a weekly basis for validation and cleaning by local public health staff prior submission to the Bureau of Epidemiology. The target population was Thai patients using public hospitals with a diagnosis of any dengue condition.

Data Sources

A dataset of patients diagnosed with dengue (ICD-10 code A90 for dengue fever (DF), A91 for dengue hemorrhagic fever (DHF), and A99 for unspecified viral hemorrhagic fever) and visited a hospital during 2003 and 2015, which was created by the Bureau of Epidemiology. Approximately one million de-identified individual dengue records were obtained, containing data on individual visits for the following variables: gender, age, nationality, occupational status, location, hospital class, patient type, outcome, and time of diagnosis, visit and report.

Detection Methodologies

Five-year median

The 5-year median threshold was calculated from the weekly aggregated number of patient visits in the same week during the five years prior to the time point of interest. For example, the 5-year median for 52^{th} week in 2015 was calculated from the number of patient visits in 52^{th} weeks in 2014, 2013, 2012, 2011 and 2010.

An outbreak is signaled when the number of dengue patient visits for any particular week exceeds the 5-year median. This approach is recognized by the Department of Disease Control and it is currently implemented as the default outbreak detection threshold in Thailand. The highest case number of each year that does not surpass the threshold or threshold is not available will be considered as "seasonal peak".

EARS Algorithms

The EARS consists of three components called C1, C2 and C3. C1 implements a moving average based on the previous seven days while C2 implements a moving average based on 7-day period three days prior to the baseline measurement (in other words a 2-day lag). C3 is calculated using a modified 3-day cumulative sum of C2. An outbreak is signaled at time t when either of C1 or C2 exceeds three or when C3 exceeds two. The components are given by the following formulas[9,10].

$$C_1(t) = \frac{Y(t) - \bar{Y}_1(t)}{S_1(t)}$$

$$C_2(t) = \frac{Y(t) - \bar{Y}_3(t)}{S_3(t)}$$

$$C_3(t) = \sum_{i=t}^{t-2} \max[0, C_2(i) - 1]$$

In the formulas above, Y(t) is the observed frequency count in period t, while S_i are the moving averages and standard deviations in period t for component n as defined below.

$$\bar{Y}_1(t) = \frac{1}{7}\sum_{i=t-1}^{t-7} Y(i) \quad \text{and} \quad S_1^2 = \frac{1}{6}\sum_{i=t-1}^{t-7}[Y(i) - \bar{Y}_1(i)]^2$$

$$\bar{Y}_3(t) = \frac{1}{7}\sum_{i=t-3}^{t-9} Y(i) \quad \text{and} \quad S_3^2 = \frac{1}{6}\sum_{i=t-3}^{t-9}[Y(i) - \bar{Y}_1(i)]^2$$

Data Analysis

Descriptive statistics were presented using frequencies, percentages, medians and interquartile ranges. Visualization was used in this study to compare the detection of surveillance algorithms and thresholds. All data analyses were conducted in R version 3.3.2[11].

The 5-year median was used as the gold standard for calculation of the sensitivity and specificity of the EARS. As the purpose of the EARS is to signal an alert before an outbreak occurs, we modified the sensitivity calculation using the number of outbreaks detected by the 5-year median that were preceded by any component of the EARS divided by the total number of outbreaks.

Specificity was defined as the number of weeks with no outbreak, according to the 5-year median method, divided by the number of weeks with no alert signal from any EARS component.

Results

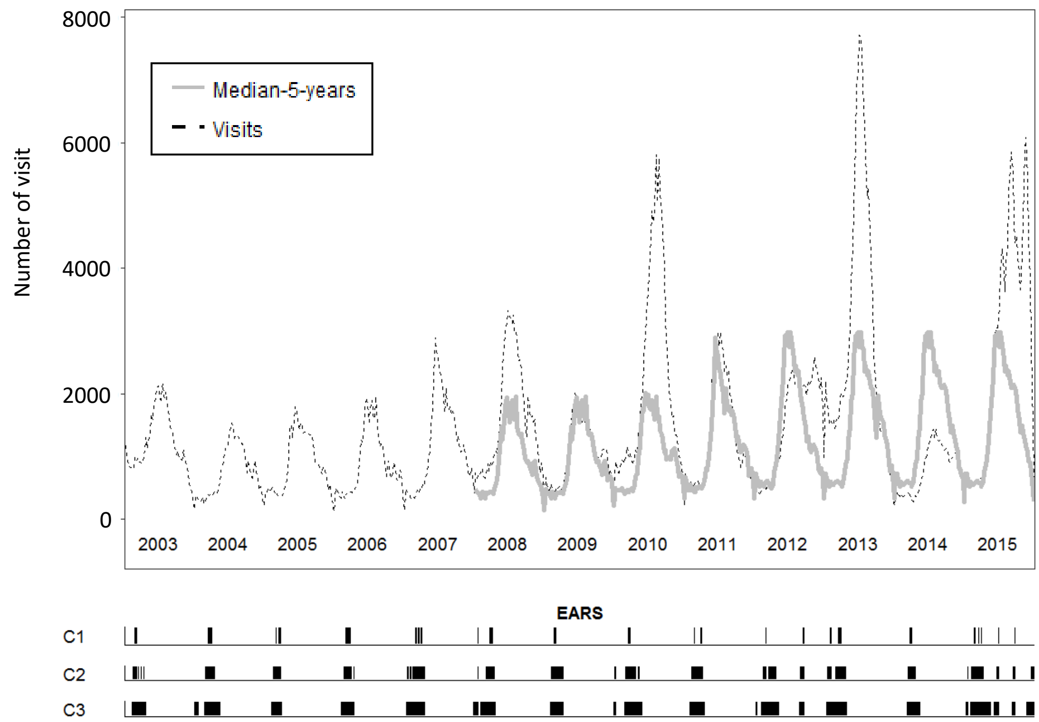
During 2003-2015, there were 1,014,201 patient visits to hospital with a diagnosis of either DF, DHF or dengue shock syndrome (DSS). During this time, there were 1,122 deaths recorded. There were 120 visits per 100,000 person-years. DF contributed the highest of the visits as 52.1% (528,291/1,014,201), followed by DHF as 46.2% (468,341/1,014,201) and DSS as 1.7% (17,569/1,014,201). Most patients were citizens of Thailand (97.9%) or Myanmar (1.3%). The median age was 15 years (Interquartile range 10-24 years), with a male to female ratio of 1.1:1. The age groups with the highest incidence were 5-12 years (28.6 per 100,000 person-years), followed by 13-18 years (25.3 per 100,000 person-years) and 26-45 years (18.8 per 100,000 person-year). Approximately half of the visits were by students (48.3%), followed by elementary workers (16.4%) and farmers (6.1%) (Table 1).

Five-year Median

There were seven dengue outbreaks and six seasonal peaks (2003-2007 and 2014) signaled in the study period based on the 5-year median. Most of the outbreaks exhibited a seasonal pattern with emergence (May) and subsidence (August), occurring at approximately the same period each year. The outbreak with the highest number of patient visits occurred in 2013 and the seasonal peak occurred in 2014 (Figure 1).

Table 1. Demographic characteristic of dengue patients who visited public hospitals under the Ministry of Public Health, Thailand, 2003-2015

Characteristic	Number of visit	Percent
Nationality (n=1,014,201)		
Thailand	99,2528	97.9
Myanmar	13,320	1.3
Others	8,353	0.8
Gender (n=1,000,914)		
Male	516,921	51.6
Female	483,993	48.4
Occupation (n=1,000,864)		
Student	489,746	48.9
Elementary service worker	164,430	16.4
Farmer	61,994	6.2
Unemployed	25,081	2.5
Merchant	16,386	1.6
Others	243,227	24.4
Age group (year) (n=1,000,706)		
0-4	50,196	5.0
5-12	283,197	28.3
13-18	266,846	26.7
19-25	153,129	15.3
26-45	182,211	18.2
46-60	47,558	4.7
>60	17,569	1.8



Solid black bars represent alert signals from C1, C2 and C3. As the 5-year median method requires five years of historical data, the threshold was available only after 2008 while the EARS needs only the previous 7-10 days, and was therefore readily available since 2003. EARS signals appear before every outbreak and disappear after visit numbers start to rise.

Figure 1. Comparison between algorithms of early aberration reporting system (EARS) and moving-5-year median of dengue infection, Thailand, 2003-2015

Table 2 Positive predictive value, sensitivity and specificity of early aberration reporting system (EARS) compared to the five-year median of dengue infection, Thailand, 2003-2015

Method	Total signal	Total number of week	Sensitivity[1] (n=7)	Specificity[2]
C1	23	291	100%	97.6% (122/125)
C2	80	291	100%	86.4% (108/125)
C3	122	291	100%	79.2% (99/125)

[1] As the purpose of the EARS is to provide an early warning, not an outbreak threshold, the sensitivity was calculated based on whether the signals appeared before the seven outbreaks defined by median-5-years.

[2] In contrary to the sensitivity, the specific was calculated using "week" unit. The nominator was the non-outbreak week without EARS signal and the denominator was the total non-outbreak week.

EARS

In 291 weeks during the study period, EARS C3 issued the highest number of signals at 122 while C2 issued 80 signals and C1 issued 23 signals. As the EARS detected every outbreak and seasonal peak by sending early warning signal, the sensitivity of all three EARS components was 100.0% (7/7 outbreaks). There were 125 weeks with no EARS signal. C1 had the highest specificity of 97.6% (122/125 weeks) while C3 had the lowest with a rate of 79.2% (99/125).

The three EARS components were able to detect every outbreak during 2008-2015, including the outbreak in 2014 which was a seasonal peak and did not classify as an outbreak by the 5-year median method. C3 often provided the first early signal, followed by C2 and C1. The durations of all three signals, from the first signal to the peak of the outbreak, were similar. When approaching the outbreak peak, all three EARS algorithms signaled an outbreak in the period, leading up to the peak with C3 often providing the first signal. However, after the peak, the signals disappeared altogether. From figure 1 and table 2, C3 issued more signals than C2 while C2 issued more signals than C1. C3 often overlapped with C2 while C2 overlapped with C1. In other words, C1 seemed to retain the EARS early warning capacity while issuing the lowest number of signals. All three EARS components were able to signal a seasonal peak during 2003-2007 while the 5-year median threshold was not available due to lack of historical data.

Discussion

Dengue outbreaks occur every year in Thailand, and thus, detection methods that can provide information on the timing and severity of any impending outbreak is important. This was the first national study to evaluate the EARS for dengue outbreak detection in Thailand.

The 5-year median threshold method has been used in Thailand for several years for detecting dengue outbreaks. It is easy to comprehend and calculate, and based on our results, could detect all, except one with the seasonal peak in 2014. However, at the beginning of each dengue outbreak, the number of patient visits will increase rapidly and the current 5-year median detection method cannot detect any outbreak early enough to allow preparation for control measures to be implemented. In effect, it can only be used as a confirmatory indicator, not as early warning system for an impending outbreak. Although emergence of a dengue outbreak can be anticipated during the rainy season, having an early warning system is very important for public health as it allows more time to prepare for the upcoming outbreaks or unanticipated second peaks in MOPH.

The EARS, while able to signal all the outbreaks beforehand, was able to detect the upcoming second peak during 2012, 2013 and 2015 outbreaks as well. Normally, the EARS stopped issuing signals after a peak, except during the outbreaks in 2012, 2013 and 2015, and continued to issue signals after the peak. These alerts were followed by a second peak. This finding was consistent with a recent study in China which found that the EARS was able to provide an early signal predicting an upcoming outbreak as well as its peak[12].

EARS also successfully detected every seasonal peak during 2003-2007. These outbreaks could not be confirmed by the 5-year median method since the method requires five years of historical data for the threshold calculation. EARS proved to retain warning performance even without historical data. Implementation of EARS, therefore, might prove to be of great benefit as a signal for upcoming dengue outbreaks and seasonal peaks, encouraging the Thai MOPH to initiate timelier dengue control measures.

However, there are some drawbacks of the EARS. Firstly, it does not provide any information on the severity of an outbreak. Secondly, many alerts are signaled before an outbreak actually occurs, a situation which can make interpretation difficult.

Recommendations

Even though the EARS provides potentially invaluable information, it can cause confusion among decision makers whether they should take actions since there could be also noise signals. Many of the EARS algorithms on influenza and influenza-like illnesses exist challenges[13]. This can result in putting more burden on local health workers as MOPH depends on them to validate and respond to noise signals[14]. We recommended that the EARS should be used for early warning purpose in combination with the 5-year median method as a confirmatory indicator in MOPH.

This study was conducted using weekly dengue information from Thailand, a tropical country in South-East Asia. Application of the EARS to other countries should take into consideration of differences in the data reporting systems, dengue outbreak characteristics and available public health infrastructures. We would like to encourage other public health authorities and researchers from tropical countries to review and evaluate these innovative early detection methods to continuously improve their public health surveillance and control programs.

Limitations

Our data sources were collected merely from the public hospitals. Private hospitals and clinics in Thailand are not required to submit health data to MOPH. However, as the capacity of private hospitals in Thailand is much lower than that of the public hospitals, they would have contributed a small proportion of the cases.

The number of dengue patient visits was used, not the number of illness episodes, as the numerator for calculating the incidence rate due to lack of computational resources. However, the data were validated and deduplicated from local and regional health offices. Thus, the use of patient visits should be acceptable for estimation of incidence rates.

Conclusion

In summary, implementing the EARS is valuable in detecting dengue outbreaks. However, there is no one-fit-all solution for early outbreak detection of dengue. The 5-year median method is simple to calculate and widely used, yet it does not provide an early warning mechanism and therefore, can only serve as a confirmatory indicator. The EARS algorithms were able to detect every outbreak during 2008-2015, including the seasonal peak in 2014. However, the EARS does not provide information on trends and outbreak severity and issues noise signal. To reduce the number of noises, we suggested MOPH to rely mainly on C1 as we did not observe any information gained in adding C2 or C3, or any combination, to C1. Another possible approach was to combine C1 with the 5-year median method to reduce the number of false signals or use the 5-year median method as a severity and confirmatory indicator only. As this study was specific for climate and the reporting system in Thailand, implementing our recommendations in other countries might need to consider the specific contexts of local public health surveillance systems and epidemiological risk factors of dengue outbreaks in the areas. However, there are several other early detection methods available and other countries are encouraged to explore the specific dengue data and epidemiological situations in order to improve the public health surveillance systems.

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