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An Evaluation of Influenza-like Illness (ILI) Epidemic Alert Thresholds in Two Provinces of Thailand, 2007-2010

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Abstract

Following introduction of influenza A (H1N1) pdm09 in Thailand during 2009, the national influenza-like illness (ILI) reporting system and short message alert signals was established by the Thailand Bureau of Epidemiology as a tool for early detection of influenza outbreaks. However, no specific threshold for determining the epidemic alert status existed. The objectives of this study were to determine baseline and epidemic alert thresholds of ILI proportions for different hospital sizes. The study was conducted in nine hospitals (three small, three medium and three large hospitals) in two provinces of Nakhon Ratchasima and Nakhon Si Thammarat. We reviewed hospital databases and collected data on ILI and all hospital visits during 2007-2010 from hospital databases. Then, we calculated mean, median and standard deviation (SD) of the weekly ILI proportions by hospital size over the 4-year period. We also used the Early Aberration Reporting System (EARS-X v2.8) to determine an aberration from baseline by calculating cumulative sum (CUSUM) by hospital types. We found that large hospitals had baseline ILI proportion lower than medium hospitals while baseline ILI proportion of medium hospitals was lower than that of small hospitals. The seasonality of the peak ILI proportions in 2009-2010 was different from pre-pandemic years of 2007-2008. Mean and median ILI proportions before the pandemic were lower than that of after the pandemic. Among individual hospitals, weekly ILI reporting was highly varied which prevented the use of CUSUM analyses. Aggregate reporting from several hospitals produced more reliable data for CUSUM analyses. No single signal in the EARS-X v2.8 software reliably predicted increased flu activity without signaling many false alerts. However, the combination of signals in the software reliably predicted the start of flu season with rare false alerts. We concluded that in Thailand, the baseline ILI proportion depended on hospital size. Due to variability in reporting from individual hospitals, we suggested choosing a method of epidemic alert threshold detection by level of health facilities using the CUSUM technique at the national level and median + 2 SD method at the hospital level.

Keywords: influenza-like illness (ILI), epidemic alert threshold, cumulative sum

Introduction

In April 2009, the first case of influenza A (H1N1) pdm09 was reported in the United States by US CDC.[1] This virus rapidly spread to other regions of the world and a pandemic was declared on 11 Jun 2009.[2] Thailand identified the first case of influenza A (H1N1) pdm09 in May 2009 from a patient who had a travel history to Mexico. Shortly after the first case was reported, there was a rapid spread of influenza A (H1N1) pdm09 throughout the country.[3]

At the beginning of the epidemic in Thailand, the influenza-like illness (ILI) reporting system was established in all provinces by the Bureau of Epidemiology (BOE) as a tool for early detection of influenza outbreaks.[3] Initially, provincial health offices gathered total number of ILI visits (in-patients and out-patients with ICD10 codes J00, J02.9, J06.9, J09, J10 and J11) and all-cause visits (in-patients and out-patients) from all hospitals every day. The data were reported daily to BOE to monitor trend of ILI and discover epidemic areas. Although this practice of daily reporting by all hospitals was continued throughout the first wave of the epidemic in Thailand, it required significant amount of time, resources and situation analytic capabilities that was difficult to sustain.

In January 2010, the ILI reporting system was revised and all registered hospitals began to electronically report number of ILI cases and total number of hospital visits to the ILI surveillance system website weekly (http://164.115.5.58/ili) where proportions of ILI cases and total out-patient visits were displayed for the whole country and also by districts.[4] The revised national system also added an alert system which delivered a short message (SMS) to executives, epidemiologists at hospitals and health departments in different levels when ILI proportion of all visits at a reporting facility reaches 5% and 10% (Figure 1).[2]

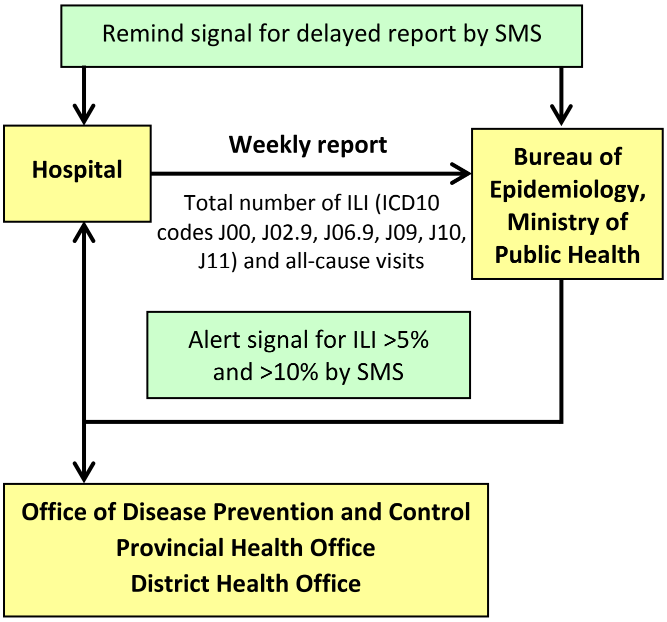


Figure 1. Data flow of influenza-like illness (ILI) reporting system in Thailand

For the alert system with SMS, the 5% and 10% were selected based on the literature reviews.[4] Not only the utility of these alerts was to assess influenza activities on level of warning and control implementation, but the alert system was used for triaging to separate ILI patients from other patients in the hospital, enlist more health care workers, open a temporary ILI clinic and ILI ward, order and store drugs and laboratory equipment such as influenza rapid tests, personal protective equipment (PPE) including face masks, gloves and alcohol gel, and prepare teams for outbreak investigation.[5]

The objectives of this study were to determine the baseline ILI proportions in 2007-2010 using data from nine hospitals in two provinces and to determine hospital-type-specific epidemic alert thresholds for ILI outbreak alerts from seasonal and pandemic data using two methods: median + 2 standard deviations (SD)[6] and a one-sided positive cumulative sum aberration detection method.[7]

Methods

We conducted the study in Nakhon Ratchasima and Nakhon Si Thammarat Provinces of Thailand where high number of influenza A (H1N1) pdm09 cases were reported in 2010 compared to other provinces. In each province, we reviewed a list of all registered hospitals in the ILI reporting system and divided them into three categories based on number of beds: small (30 beds), medium (60-90 beds) and large (120 or more beds). Then, we selected hospitals from each category by simple random sampling. We selected two hospitals in each category for Nakhon Ratchasima Province and one hospital in each category for the Nakhon Si Thammarat Province. In total, our study was conducted in nine hospitals (three small, three medium and three large hospitals) in two provinces.

We reviewed and collected data on out-patient ILI cases and all out-patient visits during 2007-2010 from hospital databases. We calculated weekly ILI proportions in 2007-2010 to understand trends of ILI proportions by hospital size. We also calculated mean, median and SD of weekly ILI proportions in 2007-2010, and before and after the epidemic peak in 2009 for each category to estimate baseline and epidemic alert thresholds. The epidemic peak was occurred during week 26 of 2009.

We used the Early Aberration Reporting System (EARS-X v2.8, US CDC) to determine an aberration of baseline by calculating one-sided positive cumulative sum (CUSUM). EARS uses three limited baseline aberration detection methods called C1-MILD, C2-MEDIUM and C3-ULTRA.[7] As data were tabulated weekly; our time unit for analysis was one week. C1-MILD has the lowest sensitivity, and mean and SD for C1-MILD were obtained from previous data for seven weeks in the closest proximity to the current value, week (t-7) through week (t-1). C2-MEDIUM, used a 7-week baseline period based on week (t-9) through week (t-3). C3-ULTRA used the same baseline period as C2-MEDIUM, but the threshold was based on a 3-week average run length of the one-sided positive CUSUM (Figure 2).[7]

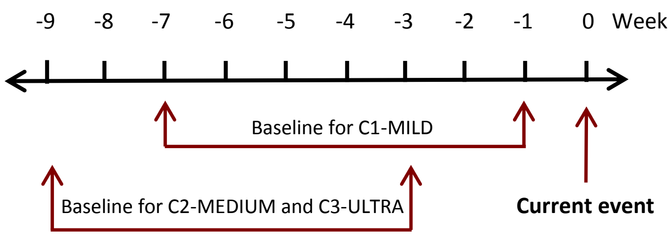


Figure 2. Baseline periods for 3 methods of cumulative sum calculation

Table 1. Mean, median and standard deviation (SD) of baseline ILI proportions in 2007-2010, and before pandemic and after epidemic peak in 2009-2010 by hospital size in Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand

Hospital size	2007 – 2010			Before pandemic (week 1 of 2007 to week 25 of 2009)			After pandemic (week 26 of 2009 to week 52 of 2010)		
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
Large	3.5	3.2	1.5	3.3	3.2	1.1	3.8	3.3	1.9
Medium	6.3	5.8	2.7	5.9	5.7	2.2	7.0	6.4	2.9
Small	9.1	8.7	3.6	8.7	8.4	2.7	9.9	9.2	3.8

For C1 and C2, the method was based on CUSUM, but the threshold reduced to the mean + 3 SD. For C3, the method was also based on CUSUM and calculated by summing the positive differences of the current value from the mean for three weeks and comparing the CUSUM to the baseline period to determine its significance.[7] If the calculated value was more than two, a C3 warning was produced.

Results

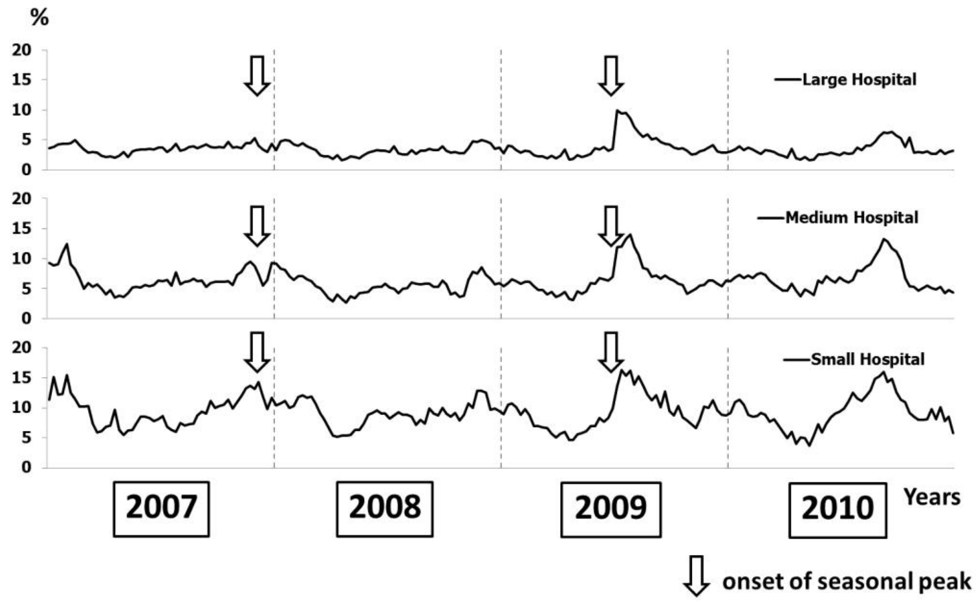
The results showed that large hospitals had baseline ILI proportion lower than medium hospitals and baseline ILI proportion of medium hospitals was lower than that of small hospitals. Mean and median ILI proportions before the pandemic were lower than those of after the pandemic in all hospital sizes (Table 1).

We used median + 2 SD for epidemic alert thresholds in small, medium and large hospital categories and compared total number of signals per hospital in each category during 2007-2010 (Table 2). The median was chosen over the mean because there was less variability in the median values before and after the pandemic. This reduced the number of signals per year in each hospital category.

In addition, we also found that seasonality of peak ILI proportions in 2009-2010 (September to October) was different from pre-pandemic years of 2007-2008 (December to January) (Figure 3).

Table 2. Number of signal over median + 2 SD in each hospital category, Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand, 2007-2010

Hospital size	Number of signal over median + 2 SD				
	2007	2008	2009	2010	Total
Large	2	0	6	2	10
Medium	2	0	6	4	12
Small	3	0	5	3	11



Note: Data not available for one medium hospital in 2007-2008 and one small hospital for two months in 2007

Figure 3. Trend of weekly ILI proportions in each hospital category, Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand, 2007-2010

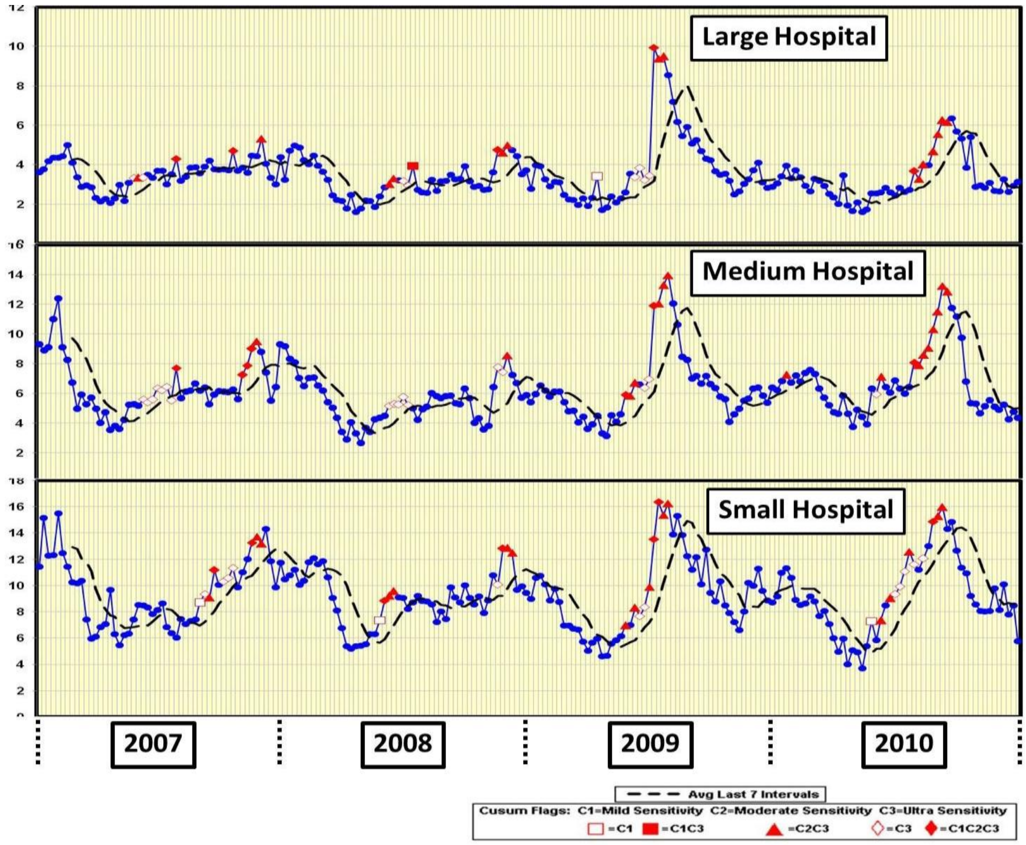


Figure 4. Aberration from baseline ILI proportions in each hospital category by EARS-X v2.8, Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand, 2007-2010

Table 3. Number of single and combination signal in each hospital category in Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand, 2007-2010

Hospital size	Number of signal				
	C1	C3	C1C3	C2C3	C1C2C3
Large	1	8	1	14	5
Medium	0	17	0	16	7
Small	3	12	0	17	7

Table 4. Number of C1C2C3 signal in each hospital category in Nakhon Ratchasima Province and Nakhon Si Thammarat Province, Thailand, 2007-2010

Hospital size	Number of C1C2C3 signal			
	2007	2008	2009	2010
Large	2	1	1	1
Medium	4	0	2	1
Small	2	2	2	1

Using EARS-X v2.8 software, we determined aberrations from baseline ILI proportions in each hospital size category (Figure 4). The results showed there were many C1, C2 and C3 alert signals, making any single CUSUM technique challenging to implement. However, combinations of signals (C2C3 or C1C2C3) appeared to signal the start of flu season and there were not many alerts in non-peak periods over the four years studied (Tables 3 and 4).

Discussion

We used two methods to determine epidemic thresholds among different sized hospitals in Thailand: median + 2 SD and the cumulative sum aberration detection method, using data from nine hospitals in two provinces.[6,8] There were fewer alert signals when we used the C1C2C3 combined cumulative sum aberration detection method in each hospital category compared with median + 2 SD in each category. There were only 1-2 signals per year using the C1C2C3 combined CUSUM technique and these tended to correspond to the onset of seasonal peaks in ILI proportions. Mean and median ILI proportions were varied substantially by hospital sizes, indicating that a single standard might not be appropriate for all hospitals. The difference in ILI proportions by hospital sizes might be attributed to the fact that large hospitals in Thailand have more patients and serve as referral centers, receiving severely ill patients from all district hospitals in the province.[9] Therefore, they have higher in-patient to out-patient ratios than medium and small hospitals. However, adjusting the differences of in-patient and out-patient volume did not completely eliminate the difference noted between hospitals of different sizes. This suggested that there might be inherent care-seeking differences in communities served by small versus larger hospitals and also reflected the fact that larger hospitals might have more non-respiratory admissions due to sub-specialty services.

When ILI proportion increased more than the epidemic alert threshold determined by either method, it did not mean that there was an influenza epidemic in the area because this system was only syndromic surveillance.[10] Combining laboratory data from sentinel sites to this syndromic surveillance would improve influenza epidemic detection and help to reduce non-influenza alerts.[10] Non-influenza alerts are still useful to individual hospitals to institute infection control practices. However, oseltamivir should be administrated to the outbreaks with significant alerts in the areas where influenza viruses are known to be circulating.[5] However, the simple method of epidemic threshold for alert system with SMS (3% of ILI proportion in large hospitals, 6% for medium and 10% for small) might reflect hospital size than the selected 5% and 10% alert threshold at the national level.

The second method using the EARS-X program for aberration detection could be applied to all different sized hospitals uniformly since aberrations were determined from historical data. However, week-to-week biases in consistency and quality of reporting at the level of the individual hospital may produce signals frequently that are of little clinical significance. Therefore, this method appeared to be more suitable for aggregate reporting at the regional or national level.

Public Health Actions and Recommendations

We suggested choosing a method of epidemic threshold detection by level of health system. The EARS-X v2.8 program using the CUSUM technique (C2C3 or C1C2C3 signals) to determine the aberration of ILI baseline would be a potentially useful tool at the sub-national level, especially if combined with laboratory data confirming influenza circulation. For each hospital, we suggested the simple methods such as median + 2 SD to determine epidemic threshold.[6,11] However, inconsistent reporting may reduce the utility of any method and alerts may not be useful if there are substantial issues with reporting and data quality.

Limitations

Our study had several limitations. First, we selected a small number of health facilities because data had to be collected at the level of the health facility before the ILI surveillance system was initiated in 2009. In addition, some hospitals did not use computerized record systems until 2009. Thus, data were limited for two hospitals as mentioned previously. Finally, the current system did not incorporate laboratory confirmation of influenza virus circulation in the province. Adding this information would be useful to help clinicians rationally use oseltamivir in hospitalized patients with severe respiratory illnesses.[5]

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