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Lessons learnt from a measles outbreak in Madang Province, Papua New Guinea, June 2014 – March 2015

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Objective: This study examined measles vaccine wastage during an outbreak response in Madang Province of Papua New Guinea from June 2014 to March 2015.

Methods: Vaccine wastage was defined as the number of doses received by a health centre minus the total number of doses administered during and returned following the outbreak vaccination campaign. Vaccine data were collected from the Provincial Health Information Office, the Provincial Vaccine Store register and clinic and health centre immunization registers for calculating the vaccine wastage. Interviews were conducted with all 48 health centres involved in the outbreak response using a structured questionnaire to explore the reasons for vaccine wastage.

Results: Of the 154 110 doses issued by Madang Province during the outbreak, a total of 85 236 (55%) doses were wasted. The wastage varied by district from 31% to 90%. The total cost of the vaccine wastage was estimated to be 589 810 Kina (US\$ 196 604). None of the health centres maintained vaccine stock registers. Most health centres indicated multiple failures in cold chain logistics. Almost 40% of health centres reported incorrectly diluting vaccines. The same percentage of health centres reported using incorrect injection techniques.

Discussion: Regular audits of cold chain logistics, staff training and improved processes for recording vaccine administration and wastage will decrease vaccine wastage during vaccine-preventable disease outbreaks and also benefit routine immunization activities.

A measles outbreak in Papua New Guinea affected all 22 provinces, spanned nine months from June 2014 to March 2015 and resulted in a reported total of 11 097 cases.¹ In Madang Province there were 5073 measles cases and 30 deaths recorded.¹ During 2009–2013, Madang Province had an average reported measles vaccination coverage of 38%.² A large-scale national vaccination campaign was implemented to bring the outbreak under control; in Madang Province, the campaign went from 1 June 2014 to 31 March 2015. During this campaign, 2.7 million doses of measles vaccine were supplied to all provinces by the National Expanded Program on Immunization (EPI) unit.

The World Health Organization (WHO) estimates that over 50% of vaccine doses administered during routine immunization programmes are wasted around the world.³ These high wastage rates are a key factor

driving up costs of the EPI. This paper reports on measles vaccine wastage and the reasons for this wastage during the 2014–2015 measles outbreak in Madang Province, Papua New Guinea.

METHODS

All 48 health centres (front-line health clinics that serve as the base for vaccination programmes, including mobile and outbreak clinics) in all six districts of Madang Province were included in this retrospective cross-sectional study of measles vaccine wastage during the outbreak. As there were no measles vaccines in any of the health centres before the vaccination campaign (due to an extended stock-out of measles vaccine), no vaccines were returned to the provincial office following the campaign, and the number of doses left in health centres after the campaign was assumed to be small. The start and end balances

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of the vaccine doses were not counted in calculating vaccine wastage rate. The vaccine wastage rate during the campaign was calculated using the following formula: $1 - (\text{number of doses administered} / \text{number of doses issued}) \times 100\%$. Data for the study were collected from the Provincial Health Information Office, the Provincial Vaccine Store register, clinic and health centre immunization registers and through interviews with 48 team leaders (one from each of the 48 health centres) who coordinated the vaccination response during the outbreak. Telephone interviews were conducted using a structured questionnaire that captured information on the knowledge, skills and techniques used in vaccine management. A retrospective review of vaccine practices during the outbreak was also conducted by discussions with the team leaders. All data were collected by the Provincial Disease Surveillance and Disaster Response Coordinator of Madang Province. The study period was from May to August 2015. All data were recorded, cleaned and analysed using Microsoft Excel.

RESULTS

Of the 154 110 doses issued by Madang Province during the outbreak response, a total of 85 236 (55%) doses were wasted. The wastage varied by district from 31% in Rai Coast to 90% in Middle Ramu (**Table 1**). The total cost of the vaccine wastage was estimated to be 589 810 Kina (US\$ 196 604).

Table 2 shows the results for the vaccine management interviews with the team leaders. None of the 48 health centres maintained vaccine stock registers. Most health centres indicated multiple failures in cold chain logistics. One third of health centres in the province did not have a functioning refrigerator. In Rai Coast district, 63% did not have functioning refrigerators. Less than half of health centres in the province had functional thermometers (44%), ice packs (42%) or cold boxes (44%); only 44% of staff in the health centres examined vaccine vial monitors before use. Although functioning thermometers were available in 44% of the health centres, none of the outbreak teams reported using a thermometer to monitor vaccine temperatures when working in the field. For health centres without vaccine cold boxes or vaccine carriers, the vaccines were stored in borrowed cold boxes or in the cartons used to deliver the vaccines. All reconstituted vaccines were discarded at the end of each session as per WHO guidelines.

Retrospective review of vaccine practices during the outbreak indicated that 40% of teams were incorrectly preparing the vaccines (diluting with 2.5 mL of diluent instead of 5 mL) (**Table 2**). This wastage was due to a change in the size of the diluent vials and health workers being unaware of this change. Forty per cent of the teams reported vaccinators who were incorrectly using syringes, resulting in the frequent locking of syringes and discarding of vaccine.

The health centres in Madang District reported the best overall results with regards to cold chain logistics, and they also reported below average vaccine wastage (36% wastage). The two districts with the highest levels of vaccine wastage (90% for Middle Ramu and 89% for Bogia) reported the highest number of health centres conducting small clinic sessions (63% for Middle Ramu and 50% for Bogia, respectively). Only half of the health centres in Middle Ramu reported having vaccine carriers, correctly diluting vaccine and using correct injection technique.

DISCUSSION

This study documented the number of vaccines wasted and explored the reasons for this wastage during a measles outbreak response in Madang Province, Papua New Guinea. The cost associated with vaccine wastage was almost US\$ 200 000. This estimated cost was for one antigen during one outbreak in one province. This review highlighted several areas that need to be addressed to reduce vaccine wastage during future outbreak response activities. Even though wastage during routine vaccination programmes was not evaluated in this study, efforts made to address outbreak-associated wastage will also benefit routine vaccination programmes. Investments made to reduce wastage will have significant benefits and are cost-saving in the long-term; for example, the cost to replace or repair refrigerators in all facilitates in Madang Province was estimated to be less than US\$ 70 000 (~35% the cost of the wasted vaccines).

India has set a routine vaccine wastage rate for most vaccines at 25%.⁴ This Indian policy encourages opening a multidose vial for a single beneficiary to avoid any missed opportunities. WHO recommends the following wastage rates for estimating vaccine needs for routine programmes: 50% wastage for 10–20 dose vials (lyophilized vaccines) and 10% wastage for 2–6

Table 1. Number of measles vaccine doses issued, wasted, percentage wasted and cost by districts in Madang Province, Papua New Guinea, June 2014 to March 2015

District	Number of doses issued	Number of doses administered	Number of doses wasted	Percentage of doses wasted	Cost of wastage (Kina)	Cost of wastage (US\$)
Middle Ramu	28 260	2743	25 517	90%	164 329	54 776
Bogia	23 400	5123	18 277	78%	134 447	44 816
Sumkar	18 350	4142	14 208	77%	117 710	39 237
Madang	50 480	32 202	18 278	36%	91 499	30 500
Usino Bundi	20 950	14 055	6895	33%	44 403	14 801
Rai Coast	19 020	13 209	5811	31%	37 422	12 474
Total	160 460	71 474	88 986	55%	589 810	196 604

1 Kina = 0.32 US\$

Table 2. Capacity for vaccine management by health centres (n = 48) in each district in Madang Province, Papua New Guinea, June 2014 to March 2015

Capacity	Middle Ramu (n = 8)	Bogia (n = 8)	Madang (n = 8)	Usino Bundi (n = 8)	Rai Coast (n = 8)	Sumkar (n = 8)	PROVINCE (n = 48)
Maintained vaccine stock register	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Functioning thermometer	4 (50%)	2 (25%)	5 (63%)	2 (25%)	3 (38%)	5 (63%)	21 (44%)
Ice packs for vaccine storage	2 (25%)	3 (38%)	5 (63%)	3 (38%)	2 (25%)	5 (63%)	20 (42%)
Maintained temperature chart	4 (50%)	2 (25%)	5 (63%)	2 (25%)	3 (38%)	5 (63%)	21 (44%)
Cold box for vaccine transport*	3 (38%)	3 (38%)	5 (63%)	3 (38%)	2 (25%)	5 (63%)	21 (44%)
Monitored vaccine vial monitors	3 (38%)	3 (38%)	5 (63%)	3 (38%)	2 (25%)	5 (63%)	21 (44%)
Functioning vaccine fridge	4 (50%)	6 (75%)	8 (100%)	5 (63%)	3 (38%)	6 (75%)	32 (67%)
Vaccine carriers**	4 (50%)	6 (75%)	8 (100%)	5 (63%)	3 (38%)	6 (75%)	32 (67%)
Correct dilution of vaccine	4 (50%)	5 (63%)	5 (63%)	5 (63%)	5 (63%)	5 (63%)	29 (60%)
Conducted small clinic sessions	5 (63%)	4 (50%)	2 (25%)	3 (38%)	3 (38%)	3 (38%)	20 (42%)
Correct injection techniques	4 (50%)	5 (63%)	5 (63%)	5 (63%)	5 (63%)	5 (63%)	29 (60%)

* Large cold box for vaccines: ~16 icepacks used to keep vaccines cool for up to 5–7 days

** Small cold box for vaccines: ~4 icepacks used to keep vaccines cool for 2–3 days

dose vials (lyophilized vaccines).⁵ Wastage of measles vaccine during outbreak campaigns and supplemental immunization activities (SIAs) is typically much less than during routine vaccination programmes because more children can get vaccinated in the same session. In Africa, most measles SIAs report wastage rates lower than 10%, and WHO suggests using a conservative 15% during SIA planning using 10-dose measles vaccines.^{6,7} In Papua New Guinea during the measles campaign, 10-dose vials of lyophilized measles vaccines were used along with 2.5 mL diluent vials; each dose should be diluted with 5 mL of diluent. The overall wastage of 55% in this study is much higher than the 15% WHO benchmark. The high wastage was primarily due to poor cold chain logistics and incorrect vaccine preparation and administration.

This study identified an urgent need for training and supervision of health-care workers prior to and during SIAs, especially when there are new immunization protocols being implemented. The change in volume of the diluent vials provided by the national office, from a 5 mL diluent vial to a 2.5 mL diluent vial, resulted in double strength vaccines being administered. Health-care workers were familiar with using 5 mL diluent vials and failed to realize the need for using two 2.5 mL vials per dose during the campaign. Almost 40% of health centres reported incorrectly diluting the vaccine during the outbreak response. There is also an urgent need for the national and/or provincial immunization programmes to review the vaccine logistics and procurement processes which led to incorrect diluent vials (2.5 mL instead of 5 mL) being bundled with the measles vaccine during this campaign. Clear instructions from the national/provincial levels on the use of the 2.5 mL vials were not adequately issued or conveyed to the field staff. Also, adequate training and supervision on the use of auto-disable syringes was not provided to field staff. Auto-disable syringes prevent the administration of vaccine if incorrect techniques are used. This safety feature results in high levels of wastage when poor injection techniques are employed. During the measles campaign, newly graduated health-care workers who had not used the auto-disable syringes were recruited. Training of staff on correct injection techniques should be provided on a

regular basis and especially when new staff are employed for SIA or routine vaccination programmes.

Poor documentation and communication resulted in the indiscriminate dissemination of vaccines to health centres and poorly planned clinics. Improper recording and reporting of vaccine stocks and not knowing the target population size during field clinics often resulted in a large number of vaccines being taken for small clinics. The absence of ice packs, thermometers and vaccine carriers resulted in high levels of wastage as leftover vaccines were discarded. Districts with more functional cold chains generally reported lower wastage. The exception was Sumkar district. It had one of the best cold chains but reported vaccine wastage of 77%. Further work is needed to explore in detail the factors contributing to the high wastage rate in this district.

Interventions undertaken during outbreaks like the one in this study are often accompanied by a great sense of urgency. This may lead to rushed interventions that are poorly planned and coordinated. Future training should incorporate aspects of managing mass vaccination campaigns during an outbreak response. Regular audits of cold chain and an assessment of surge capacity for mass vaccination campaigns should be incorporated into routine activities.

Since this study was conducted in a single province, the results cannot be generalized to the country as a whole. Madang Province is a mountainous province with challenging health centre access; it is also one of the poorest provinces in Papua New Guinea. The assumption that only a small number of vaccine doses remained in the health centres after the campaign may have led to an overestimation of the wastage rate. Other limitations of this study included the focus on team leaders rather than all staff involved in the vaccination programme and the absence of on-site inspections. Depending on the size of the vaccination teams, there may have been variations in practice between the vaccinators that were not adequately captured in this study. A future study on vaccine wastage may focus on routine vaccination and an assessment of individual health workers, including

on-site observations. A comprehensive training and audit plan that focuses on the routine vaccination programmes should be implemented. Systems should be developed to ensure the accurate documentation of routine vaccine administration and wastage at the provincial, district and health centre levels. This will assist not only in reducing wastage during routine programmes, but also in planning during outbreak response activities. Vaccine wastage report forms should be developed and routinely sent from the health centres to the District Health Office and from there to the Provincial Health Office. These vaccine wastage report forms should include reasons for wastage to guide ongoing efforts to reduce wastage.

An urgent and focused effort to strengthen the immunization programme in Madang Province would significantly reduce vaccine wastage and enhance the efficacy of both routine and outbreak response vaccination programmes. Efforts should focus on providing regular and pre-campaign training to vaccinators on correct technique, strengthening and monitoring cold chains and enhancing the documentation and evaluation of the immunization programme in the province. Enhanced documentation and improved supply management will prevent both stock-outs and excess wastage. Increasing efficiencies in the immunization programme by reducing wastage is critically important as the costs of routine and new vaccines continue to increase.

Conflict of interest

None.

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Sudden increase in human infection with avian influenza A(H7N9) virus in China, September–December 2016

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Since the first outbreak of avian influenza A(H7N9) virus in humans was identified in 2013, there have been five seasonal epidemics observed in China. An earlier start and a steep increase in the number of humans infected with H7N9 virus was observed between September and December 2016, raising great public concern in domestic and international societies. The epidemiological characteristics of the recently reported confirmed H7N9 cases were analysed. The results suggested that although more cases were reported recently, most cases in the fifth epidemic were still highly sporadically distributed without any epidemiology links; the main characteristics remained unchanged and the genetic characteristics of virus strains that were isolated in this epidemic remained similar to earlier epidemics. Interventions included live poultry market closures in several cities that reported more H7N9 cases recently.

The first three H7N9 cases were reported in China on 31 March 2013.¹ Four epidemics have been observed in China between February 2013 and September 2016. Studies have shown that the demographic, epidemiologic and virologic characteristics of H7N9 cases from these epidemics remained unchanged, while the epidemic curve illustrated a decline in the magnitude of outbreaks over time, particularly in the third and fourth seasons in 2015 and 2016.^{2,3} However, since September 2016, not only has the fifth outbreak started earlier than usual, but a steep increase in the number of humans infected with H7N9 virus has also been observed, causing domestic and international concern. On 9 January 2017, China notified the World Health Organization through the International Health Regulations mechanism of 106 cases.⁴ An analysis of recently reported human cases with H7N9 was conducted to describe the epidemiological characteristics of the current epidemic. As the epidemic is ongoing, China remains vigilant and is monitoring outbreaks closely.

METHODS

Surveillance system

The surveillance system and identification procedure for H7N9 infection has not changed in China since 2013.¹ A suspected H7N9 case in China is identified through the Chinese surveillance system for pneumonia of unknown etiology (PUE). In addition, suspected H7N9 cases with mild or moderate illness are identified from the Chinese sentinel surveillance system for influenza-like illness (ILI). The information from these systems are reported to the Internet-based National Notifiable Infectious Disease Report and Surveillance System (NNIDRSS). Each clinically diagnosed H7N9 case is confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR), conventional RT-PCR, virus isolation, or a four-fold rise in H7N9 antibody titres in serology using laboratory methods and procedures as previously described.⁵

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According to the national protocol of H7N9 disease control and prevention,⁶ once a suspected H7N9 case is identified in one jurisdiction, the local Center for Disease Control and Prevention (CDC) conducts a field investigation, defines and monitors the close contacts for seven days, enhances ILI and PUE surveillance in medical institutions that are secondary level and above for two weeks, and collects environmental samples from possible exposure locations and tests them for H7N9 virus. The method of identification and follow-up of close contacts has been described previously.¹

Data collection

The epidemics were defined according to the seasonality of the disease. For comparability with a prior report,² we defined the epidemic duration from 1 September to 31 August of the following year, with the exception of the first epidemic. The first epidemic started on 19 February 2013. This date corresponds to the illness onset date of the first H7N9 case. Therefore, 1 September 2016 marks the beginning of the fifth season.

In this study, the demographic information of recent H7N9 cases, including age, sex, location of residence and occupation, were obtained from the NNIDRSS. The field epidemiological investigation reports were collected from local CDCs as a supplementary source to determine clinical severity and time interval between date of illness onset and date of first visit to clinic, first hospitalization, diagnosis and receiving oseltamivir treatment. The Protocol for Diagnosis and Treatment for Human Infection with A(H7N9) Influenza Virus^{6,7} was followed to define a severe case as having any of the following: a chest X-ray indicative of multilobar lesions or a >50% increase in the size of the lesions within a 48 hour period; dyspnea or a respiratory rate of greater than 24 times per minute for adults; severe hypoxia defined as less than or equal to 92% oxygen saturation while receiving 3–5 litres of supplemental oxygen per minute; or shock, acute respiratory distress syndrome or multiple organ dysfunction syndrome. Field investigation reports were reviewed to collect information regarding control measures and interventions implemented by local governments.

Detailed exposure information was abstracted from the field investigation reports. To assess exposure to live

poultry markets (LPMs), we defined LPM as a market where live poultry is sold and could be touched. Individuals were considered to have a history of live poultry-related exposure in our analysis if they went to an LPM or bought poultry or other food in an LPM or touched poultry that was bought from an LPM within the past seven days. The definitions of other exposures, including direct and indirect contact with poultry, are previously described in a prior study conducted by China CDC.⁸

Data analysis

To describe the epidemic, maps illustrating the geographic distribution of cases at provincial level were generated. Using the date of illness onset of confirmed H7N9 cases, an epidemic curve was generated to illustrate five epidemics between 2013 and 2016. A separate epidemic curve was created specifically for the 2016 epidemic. The number of reported cases, affected provinces, counties and newly affected counties were compared among the second, third, fourth and fifth epidemics. We also described the demographic and epidemiological characteristics of confirmed cases in the fifth epidemic and compared them to the earlier epidemics. For the purpose of this analysis, Hong Kong SAR (China), Macao SAR (China) and Taiwan, China were not included.

Ethics approval and consent to participate

All the case information was collected according to the regulations of the Law of Communicable Diseases Prevention and Control of the People's Republic of China as part of an emergency response; therefore, the study was exempt from obtaining ethics approval and participant consent.

RESULTS

As of 31 December 2016, a total of 889 confirmed H7N9 cases, including 361 deaths, were reported from 19 provinces in China since the first cases were reported in 2013. Nine provinces reported cases in all five epidemics (**Fig. 1a**). The H7N9 epidemics usually occurred within the winter–spring season except for the first epidemic in 2013. The outbreaks usually started in October, significantly increased in late December and then peaked in January of the next year (**Fig. 1b**).

Figure 1a. **Geographic distribution of human infection with H7N9 virus in China [excluding Hong Kong SAR (China), Macao SAR (China) and Taiwan, China], February 2013–December 2016**

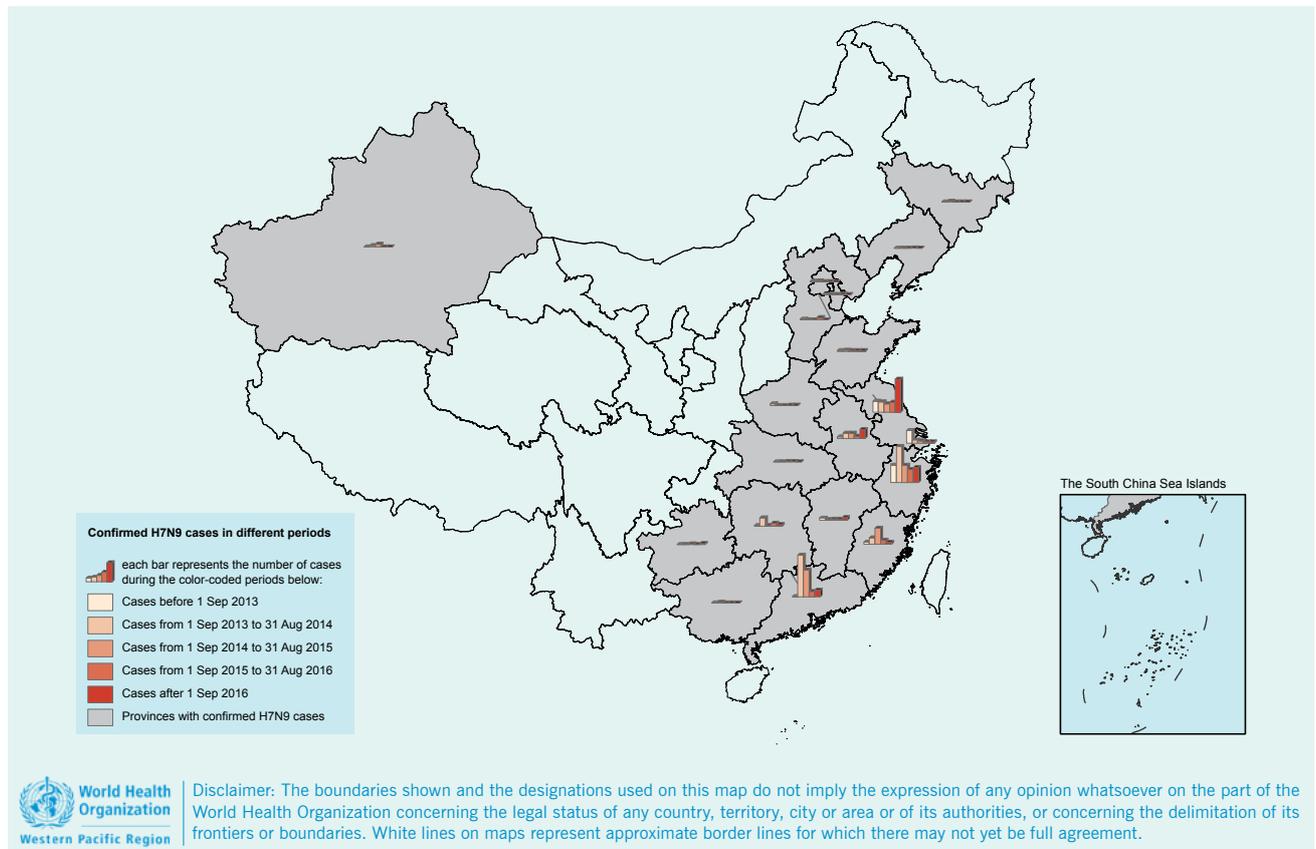
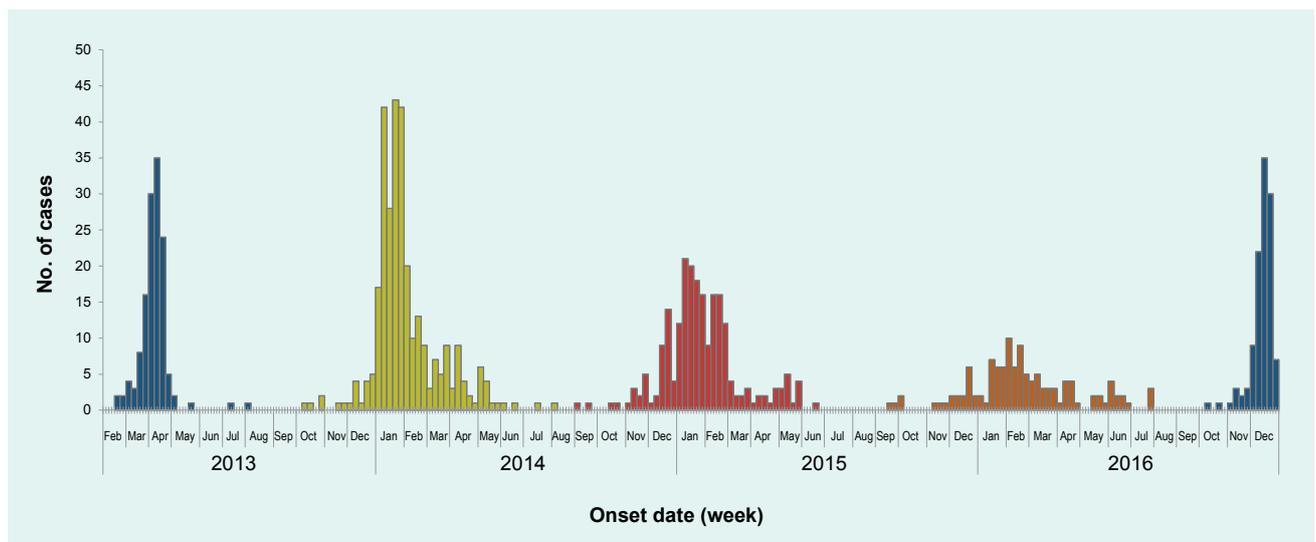


Figure 1b. **Epidemic curve of human infection with H7N9 virus in China [excluding Hong Kong SAR (China), Macao SAR (China) and Taiwan, China] by week, February 2013–December 2016**



However, since September 2016, not only has the fifth epidemic begun earlier than usual, but a steep increase in the number of humans infected with H7N9 virus has also been observed in early December. As of 31 December 2016, 114 confirmed cases, including 42 deaths, have been reported from seven provinces, affecting 75 counties (Fig. 1c).

The first case of the fifth epidemic had illness onset on 28 September 2016 in Zhejiang Province. In September, October and November 2016, a total of eight cases were reported in four provinces (Jiangsu, Zhejiang, Fujian, Guangdong), which is similar to the number of cases during the same period in prior epidemics. However, since 1 December 2016, the number of cases has substantially increased, with 106 cases reported in December 2016 alone (Fig. 1d). As of 31 December 2016, the number of reported cases in the fifth epidemic was 11.4, 2.7 and 6.1 times that observed in the corresponding periods in the second (10 cases), third (31 cases) and fourth (16 cases) epidemics, respectively.

In the fifth epidemic, the number of cases were higher and the cases were more widespread than the second, third and fourth epidemics (Table 1). The number of provinces affected by the H7N9 virus in the fifth epidemic increased from four provinces (Jiangsu, Zhejiang, Fujian and Guangdong) in September, October and November 2016, to seven provinces (Jiangsu, Zhejiang, Anhui, Guangdong, Fujian, Hunan, Shanghai) by 31 December 2016. In the fifth epidemic, the number of newly affected counties, where no case was reported in prior epidemics, was 23, while the number of newly affected counties in the second, third and fourth epidemics was 4, 13 and 0, respectively (Table 1).

Among the 114 cases reported to China CDC in the fifth epidemic, the median age was 55 years (range: 23–91); 68% were male (77/114); a quarter (29/114) were farmers, followed by retirees, persons who perform housework and persons who are unemployed. Of note, detailed clinical and exposure information within 10 days before illness onset was collected on 97 (85%) of the cases. All 97 cases developed pneumonia, and 87 (90%) of them had severe illness. Most (60/97, 62%) cases lived in urban areas, which remained similar to the earlier epidemics.² But in Zhejiang Province, most (16/21, 76%) cases lived in rural areas, which was higher than that in the prior epidemics (60%). Of the 97 cases with

detailed exposure history, 87 (90%) reported exposure to live poultry, including LPMs (72/87 cases, 83%) and backyard poultry (10/87 cases, 11%) and 5 (6%) were themselves poultry workers. The proportion of cases with history of exposure to LPMs was higher in the current epidemic period than the 2013–2016 period (83% vs 69%) (Table 2).

In the current epidemic, the median time intervals between illness onset and initial medical consultation, hospitalization, diagnosis and time to antiviral treatment initiation were 2, 4, 9, 5 days, respectively; these remained similar to the earlier epidemics. Only 5% (3/58) of cases received oseltamivir within 48 hours of symptom onset in the current epidemic.

Two clusters, each cluster including two cases, were identified through close contact identification and follow-up and were reported from Jiangsu and Anhui provinces. Limited human-to-human transmission could not be ruled out in these two clusters. In Jiangsu cluster, the index case was a 66-year-old man, who had illness onset on 25 November 2016 and went to a hospital for outpatient treatment on 26 and 27 November. He was admitted to the hospital on 28 November. He was diagnosed on 4 December and died on 12 December. He had no underlying medical conditions; he had visited a LPM to buy food every day within 10 days before his illness onset. He had no direct contact with live poultry in the market. He lived alone, but after his hospitalization, his 39-year-old daughter, who had taken care of her father in hospital and had close contact with her father without personal protection for three days (28–30 November), became the second confirmed case. The onset of her illness was on 6 December. She was admitted to the hospital on 8 December and diagnosed on 15 December. She had no underlying medical conditions and had no live poultry or LPM exposure before the illness onset, except taking care of her father.

In the Anhui cluster, the index case was a 66-year-old man who developed fever and cough on 16 December 2016, and was admitted to the nephrology ward in the hospital on 17 December because of his diabetic nephropathy and hypertension. His condition deteriorated and he was transferred from the nephrology ward to the intensive care unit on 19 December. He was diagnosed on 19 December and died on 20 December. He lived alone and had visited an LPM to buy food every day within 10

Figure 1c. **Geographic distribution of human infection with H7N9 virus in China [excluding Hong Kong SAR (China), Macao SAR (China) and Taiwan, China], September 2016–December 2016**

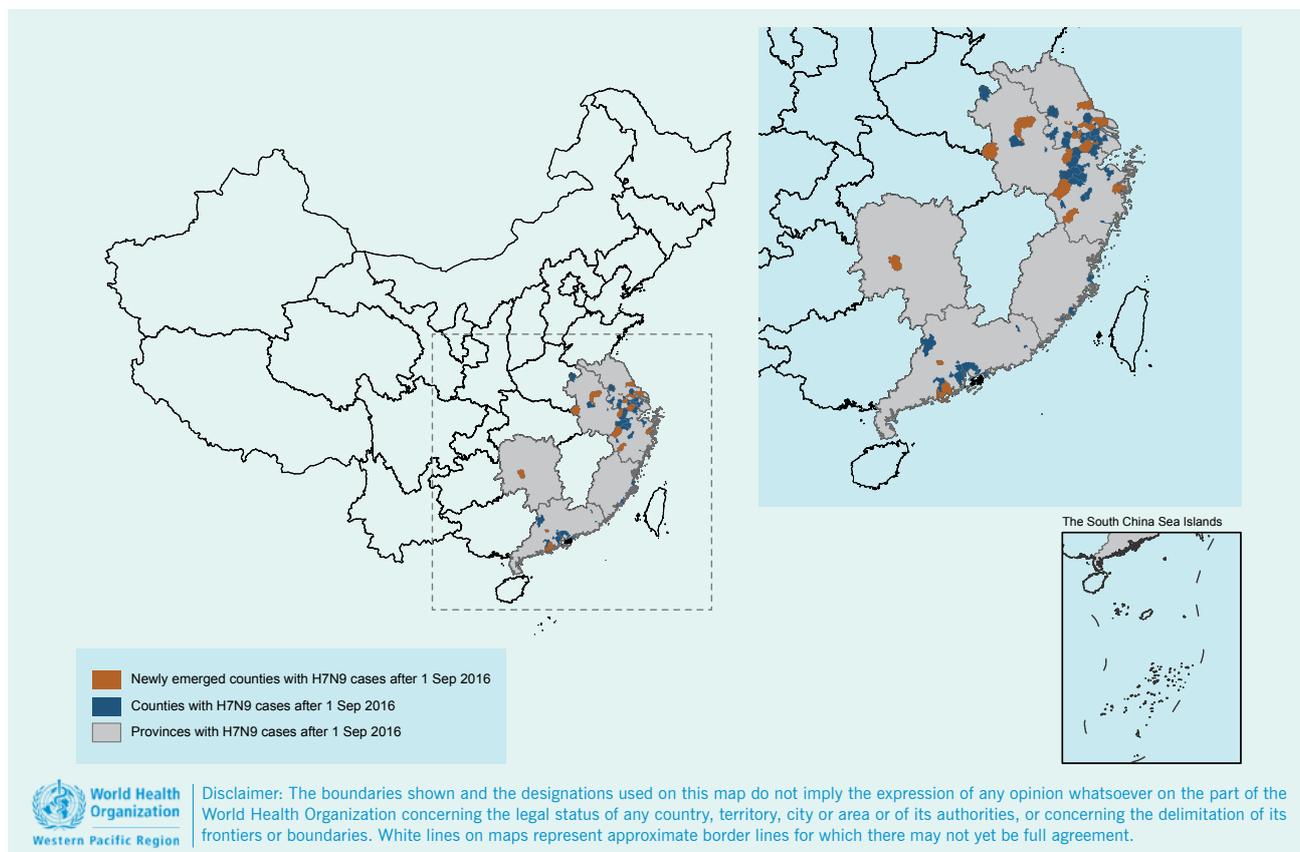
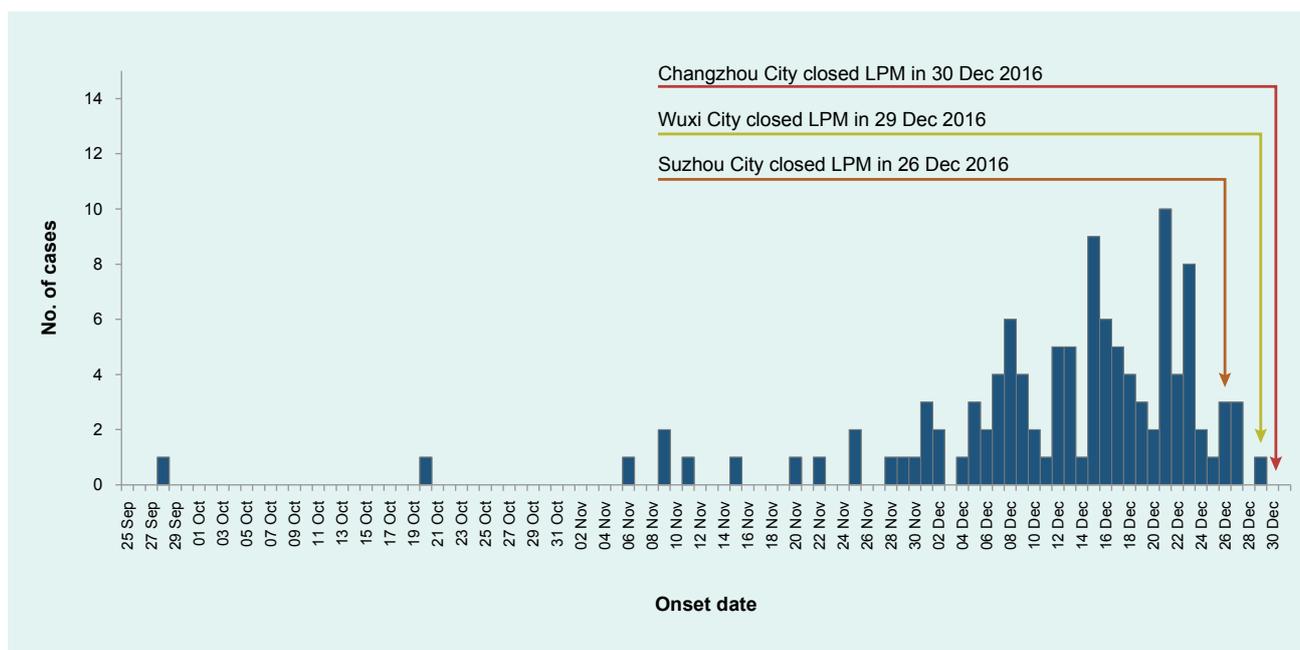


Figure 1d. **Epidemic curve of human infection with H7N9 virus in China [excluding Hong Kong SAR (China), Macao SAR (China) and Taiwan, China] by day, September 2016–December 2016**



days before his illness onset. He had no direct contact with live poultry in the market. The second case in this cluster was a 62-year-old man. He was admitted to the hospital for oedema. He and the index case stayed in the same room in the nephrology ward for approximately 20 hours. He had physical contact with the index case when assisting the index case to the bathroom. He had illness onset on 22 December and oseltamivir was given to him on the same day. He was diagnosed on 23 December. He had no history of exposure to live poultry or LPM before the illness onset.

During the fifth epidemic, as of 31 December 2016, a total of 33 H7N9 virus strains were isolated from 45 specimens collected from 40 confirmed cases in five provinces. All 33 viruses had completed full genetic analyses, and the genetic markers of mammalian adaptation and antiviral resistance of virus strains that were isolated in the fifth epidemics remained similar (Dr Yuelong Shu in China CDC, unpublished data) to earlier epidemics.⁹ The genetic sequences of these viruses will be shared with the international community through the usual channels.

DISCUSSION

Our analysis showed that the current epidemic corresponding to the fifth H7N9 epidemic started in September and experienced a steep increase in early December. This indicates that the fifth epidemic began earlier than the epidemics in 2013–2015 that started in October, significantly increased in late December and reached their peaks in January of the following year. In the fifth epidemic, the number of cases seemed to increase more rapidly than was observed in prior epidemics. There were newly affected counties in the fifth epidemic in comparison with the earlier epidemics, indicating a geographic spreading of the virus. Except on two clusters, the cases had no epidemiological link, indicating human infection with H7N9 virus in China was still sporadic. Regardless, the demographic characteristics of cases, such as age and sex distribution and exposure history in the fifth epidemic, were similar to those in earlier epidemics.^{2,3} Consistent with a prior report,¹⁰ elderly people, especially those with underlying medical conditions, remain the most vulnerable population.

Live poultry exposure, especially LPM exposure, remained the major risk factor of infection. Previous

studies determined that LPM exposure was associated with increased risk of infection with H7N9 virus.^{8,10} The proportion of cases with history of LPM exposure was higher than that in earlier epidemics, indicating that LPM exposure remained the major risk factor of infection in the fifth epidemic. Control measures at LPMs had been determined to be effective to control H7N9 outbreaks.¹¹ To control the epidemic, strict market management measures, such as market closures, had been implemented by the local governments of severely affected jurisdictions such as Suzhou (from 26 December 2016), Wuxi (from 29 December 2016) and Changzhou (from 30 December 2016) in Jiangsu Province,^{12–14} and Hefei (from 7 January 2017) in Anhui Province [Dr Jiabing Wu in Anhui CDC, personal communication]. While in Zhejiang and Guangdong provinces,^{15,16} live poultry trade has been permanently prohibited in the main urban areas in all prefectures, and all live poultry slaughtering processes must be centralized. As the traditional Chinese New Year is approaching, the consumption of poultry among the general population will be increasing, which will pose higher risk to residents, especially in the areas where LPMs have not been closed. It is highly likely that sporadic cases will continue to be reported. Whenever influenza viruses are circulating in poultry, sporadic infections or small clusters of human cases are possible, especially in people exposed to infected poultry or contaminated environments.

There were two clusters reported in the fifth epidemic from Jiangsu and Anhui provinces, and limited human-to-human transmission between two individuals cannot be ruled out. Although the genetic markers of mammalian adaptation and antiviral resistance of virus strains that were isolated in the fifth epidemic remained similar to earlier epidemics. Continued monitoring of the virus and outbreaks is important as the pandemic potential of H7N9 remains.

There were some possible reasons for the sudden increase of H7N9 cases in the fifth epidemic. One is increased environmental contamination by the H7N9 virus. Environmental contamination has been determined as an alert for the emergence of H7N9 cases.^{17,18} According to the routine environmental surveillance in affected provinces like Jiangsu, Zhejiang and Guangdong, the positive rate of environmental samples collected from LPMs or other live poultry-related environments increased in December 2016 and was higher compared to the

Table 1. Comparison of geographic distribution of human infection with H7N9 virus in the second, third, fourth and fifth epidemics*

	Sep–Dec 2016	Sep–Dec 2015	Sep–Dec 2014	Sep–Dec 2013
No. of reported cases	114	16	31	10
No. of affected provinces	7	4	8	2
No. of affected counties	75	16	24	6
No. of newly affected counties	23	0	13	4

* The epidemic duration is defined as 1 September to 31 August in the next year. The first epidemic started on 19 February 2013, the date of the first H7N9 case illness onset. For comparison, only data of cases reported from 1 September to 31 December in each epidemic were selected.

Table 2. Comparison of demographic and epidemiological characteristics of H7N9 virus infections reported by time period, 19 February 2013–31 December 2016

Characteristics	H7N9 infections reported during Sep–Dec 2016 (<i>n</i> = 114)	H7N9 infections reported during Feb 2013–Aug 2016 (<i>n</i> = 775) ²
Median age (range), years	55 (23–91yrs)	57 (9 mos–91yrs)
Male, <i>n</i> (%)	77 (68)	533 (69)
Male age group, <i>n</i> (%)		
0–14	0 (0)	21 (4)
15–29	1 (1)	27 (5)
30–44	11 (14)	84 (16)
45–59	31 (40)	159 (30)
60–74	23 (30)	163 (31)
> 75	11 (14)	79 (15)
Female age group, <i>n</i> (%)		
0–14	0 (0)	23 (10)
15–29	0 (0)	15 (6)
30–44	9 (24)	38 (16)
45–59	17 (46)	73 (30)
60–74	7 (19)	55 (23)
> 75	4 (11)	38 (16)
Living area, <i>n</i> (%)		
Cities and towns	60/97 (62)	438/775 (57)
Countryside and villages	37/97 (38)	337/775 (43)
Occupation, <i>n</i> (%)		
Farmer	29 (25)	210 (27)
Retiree	23 (20)	184 (24)
Person who does housework or is unemployed	22 (19)	91 (12)
Other occupations ^a	40 (35)	290 (37)
Live poultry-related exposure history, <i>n</i> (%)	87/97 (90)	659 (85)
Exposed to LPM or poultry from LPM	72/87 (83)	457 (69)
Exposed to household poultry raised in backyard or neighbour's backyard	10/87 (11)	163 (25)
Occupational exposure ^b	5/87 (6)	39 (6)
Severe illness, <i>n</i> (%)	87/97 (90)	506/592 (86)
Time interval, median days (IQR)		
From onset to first visit to clinic	2 (1–3)	1 (0–4)
From onset to first hospitalization	4 (2–5)	4 (3–7)
From onset to diagnosis	9 (6–10)	8 (6–11)
From onset to start oseltamivir treatment	5 (4–6)	6 (4–8)

^a Other occupations include workers, cadres (persons working in government or government-affiliated institutions), business service providers, children, students, etc.

^b Occupational exposure refers to a person who raises, transports, sells, slaughters live poultry or does other jobs related to live poultry for a living.

relative periods of the earlier years (Dr Changjun Bao in Jiangsu CDC, unpublished data; Dr Enfu Chen in Zhejiang CDC, unpublished data; and Dr Min Kang in Guangdong CDC, unpublished data). Another possible reason is that it is simply an early epidemic of influenza disease. There were early increases of ILI reports in the prior influenza seasons (ILI surveillance weekly report by China CDC): about two months earlier for the southern provinces and one month earlier for the northern provinces.

In response to the epidemic situation, a series of control measures and interventions have already been implemented by national authorities. Before the beginning of the fifth epidemic, to enhance surveillance of avian influenza disease, China CDC set a monthly risk assessment mechanism with provincial CDCs that has been ongoing since August 2016. China National Health and Family Planning Commission (NHFPC) organized a multidepartment official supervision to six provinces in November 2016. China NHFPC conducted joint supervision with Ministry of Agriculture and Ministry of Industry and Commerce to Zhejiang, Jiangsu and Anhui provinces where the number of reported cases at the early stage of the fifth epidemic was higher than other provinces at the end of December 2016. China NHFPC organized a multidepartment joint technical meeting including Ministry of Agriculture and Ministry of Industry and Commerce to discuss control measures. China NHFPC and China CDC strengthened risk communication with the general public through a hotline, a website, television and social chat applications such as WeChat (Tencent Holdings Limited). China CDC released a guideline to provincial CDCs to enhance H7N9 case detection and reporting, clinical management, nosocomial infection control, specimen collection and transportation, laboratory testing and virological analyses, field investigation and disease control in December 2016. The China Ministry of Agriculture issued a H7N9 virus elimination plan in 2014 to control infection and the spread of H7N9 virus among the poultry population, including control measures to decrease the exposure risk to residents during poultry raising, transportation and commercial trade.¹⁹

The study was unable to more thoroughly describe the fifth epidemic since the H7N9 outbreak is still

ongoing. It was not possible to calculate the mortality rate as some cases are still receiving medical treatment in hospital. All close contacts during field investigation may not have been traced. Some cases may have been missed because the H7N9 cases were mainly identified through the PUE surveillance system, while some mild cases were identified by the ILI surveillance system.²⁰ Viruses have been isolated from specimens collected from 35% (40/114) of confirmed cases as of 11 January 2017. The laboratory testing is ongoing.

In conclusion, this study described the sudden increase in cases that occurred earlier than in previous years and that were mainly urban and significantly associated with exposure at LPMs. Aside from two instances of possible human-to-human transmission between two individuals, cases remain sporadic in China.

Conflicts of interest

None.

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Enhanced surveillance for the Third United Nations Conference on Small Island Developing States, Apia, Samoa, September 2014

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The Ministry of Health in Samoa, in partnership with the Pacific Community, successfully implemented enhanced surveillance for the high-profile Third United Nations Conference on Small Island Developing States held concurrently with the popular local Teuila festival during a widespread chikungunya outbreak in September 2014.

Samoa's weekly syndromic surveillance system was expanded to 12 syndromes and 10 sentinel sites from four syndromes and seven sentinel sites; sites included the national hospital, four private health clinics and three national health service clinics. Daily situation reports were produced and were disseminated through PacNet (the email alert and communication tool of the Pacific Public Health Surveillance Network) together with daily prioritized line lists of syndrome activity to facilitate rapid response and investigation by the Samoan EpiNet team. Standard operating procedures for surveillance and response were introduced, together with a sustainability plan, including a monitoring and evaluation framework, to facilitate the transition of the mass gathering surveillance improvements to routine surveillance.

The enhanced surveillance performed well, providing vital disease early warning and health security assurance. A total of 2386 encounters and 708 syndrome cases were reported. Influenza-like illness was the most frequently seen syndrome (17%). No new infectious disease outbreaks were recorded. The experience emphasized: (1) the need for a long lead time to pilot the surveillance enhancements and to maximize their sustainability; (2) the importance of good communication between key stakeholders; and (3) having sufficient staff dedicated to both surveillance and response.

The Third United Nations Conference on Small Island Developing States (SIDS) was held in Apia, Samoa, from 1 to 4 September 2014. Attracting over 3000 delegates from more than 100 countries and territories,¹ this was the largest international event ever hosted by Samoa – a Pacific island nation of 187 820 people.² The SIDS conference occurred simultaneously with the annual Teuila festival, one of the Pacific region's largest cultural events.

Large gatherings present considerable public health disease risks,^{3,4} particularly where there is a large and diverse international population influx. This was demonstrated in Samoa, as the two events coincided with

outbreaks of chikungunya (CHIKV) locally⁵ and with the largest ever Ebola virus disease (EVD) outbreak in West Africa. While the EVD importation risk to Pacific island countries and areas was low,⁶ the stress on the Samoan health system to accommodate EVD cases in the event of any incidences would have been very high. The evolving CHIKV outbreak and ongoing dengue fever, measles and conjunctivitis outbreaks in neighbouring Pacific island countries and areas⁵ could have overwhelmed local health resources and disrupted the SIDS conference.

As part of meeting health security preparations for the SIDS conference, including International Health Regulations (2005) requirements for improving

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surveillance, the Samoan Ministry of Health (MoH) asked the Pacific Community (SPC) for technical support in planning, implementing and managing enhanced surveillance for the event. Enhanced surveillance is a practical response to elevated public health risks arising from “events attended by a sufficient number of people to strain the planning and response resources of a community state or nation”.⁷ As a foundation of disease prevention and control,⁸ surveillance provides early warning of potential disease outbreaks, allowing timely response and prioritized management of surge demands on health services. Mass gathering surveillance is commonly implemented in many countries for a range of sporting,^{4,5} religious and cultural festivals,^{3,9} and international political meetings,¹⁰ ranging in size from a few thousand people (8th Micronesian Games) to millions (Hajj pilgrimages).

SPC has accumulated considerable Pacific experience in implementing enhanced surveillance during mass gatherings, including the 2012 11th Festival of Pacific Arts, Solomon Islands; the 2013 Pacific Mini-games, Wallis and Futuna; and the 2014 8th Micronesian Games, Pohnpei State, Federated States of Micronesia. Here we describe the SIDS conference surveillance implemented by the Samoa MoH and SPC, highlighting lessons that may be helpful to public health planners in preparation for disease surveillance for mass gatherings.

Purpose of the mass gathering enhanced surveillance system

There were three primary purposes for the enhanced surveillance: (1) to provide a simple surveillance system for rapidly detecting and responding to disease episodes or outbreaks in a timely and effective manner; (2) to disseminate strategic epidemiological information throughout the Pacific region; and (3) to sustainably improve disease surveillance in Samoa beyond the mass gathering event.

Planning and implementation of the enhanced surveillance

SPC employs a three-stage process for enhanced surveillance (see **Fig. 1**) comprising preparation, operation and sustainability functions. Preparation should commence 12 months before the event and includes

assessing the surveillance system and disease risk and developing a work plan for enhanced surveillance. Surveillance operations of the second phase commences up to six months ahead of the event and includes pilot testing, training and implementing the enhanced surveillance system. The sustainability phase starts one week after the event and involves transition to the regular surveillance system and evaluation of the impact of the enhanced surveillance.

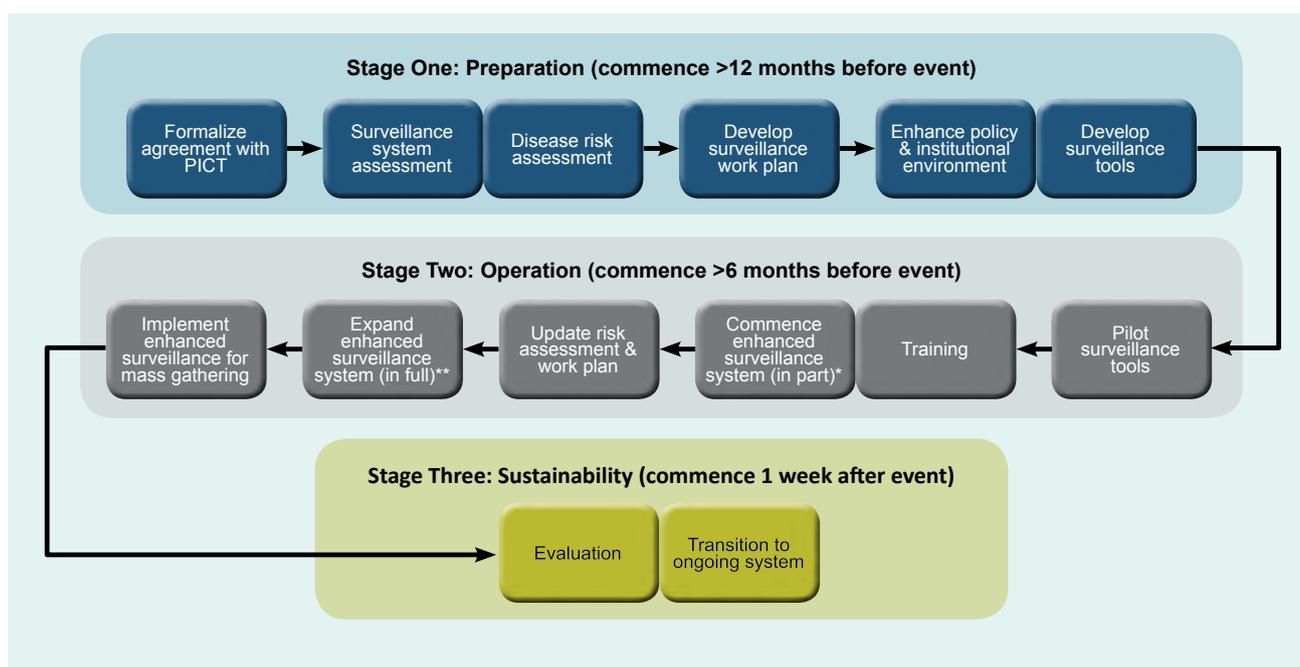
Stage 1 – Preparation: surveillance needs and disease risk assessment

The surveillance needs for the SIDS conference were determined by assessing: (1) the current scope and scale of the existing surveillance system; (2) the number and geographical diversity of SIDS conference delegates; and (3) the disease risks.

Four themes emerged from the health risk assessment: the current CHIKV outbreak, outbreaks of other infectious diseases in Pacific island countries and areas (dengue, measles), fear of EVD importation and the increased pressure on existing health services if an outbreak occurred. Based on the assessment and building on the existing syndromic surveillance system, the following modifications were made for the mass gathering surveillance:¹¹

- changing reporting frequency from weekly to daily;
- increasing the number of syndromes reported from seven to 12 (**Table 1**) covering a wide spectrum of disease priorities, including national and regional outbreaks, severe and notifiable diseases and food- and waterborne diseases;
- increasing the number of reporting sentinel sites in Apia from one to 10 to achieve greater population coverage;
- providing prioritized daily case reports of syndrome activity to facilitate rapid response and investigation; and
- introducing and adapting the Suite for Automated Global Electronic bioSurveillance Open ESSENCE (SAGES OE) surveillance system for data storage and analysis.

Fig. 1. SPC process map of the steps for the implementation of mass gathering surveillance



* Expand to all new sentinel sites; continue with weekly reporting; commence use of web-based data entry and analysis

** Change from weekly reporting to daily reporting

Table 1. SIDS conference enhanced surveillance syndromes and case definitions

Syndromes	Case definitions	Important diseases to consider
Acute fever and rash	Sudden onset of fever (>38 °C) AND acute non-blistering rash	Measles, dengue fever, rubella, meningitis, leptospirosis, chikungunya
Watery diarrhoea	3 or more watery stools in 24 hours	Cholera
Non-watery diarrhoea	3 or more loose stools in 24 hours	Viral or bacterial gastroenteritis, including food poisoning and ciguatera fish poisoning
Influenza-like illness	Sudden onset of fever (>38 °C) AND cough or sore throat	Influenza, other viral or bacterial respiratory infections
Prolonged fever	Any fever (>38 °C) lasting 3 or more days	Typhoid fever, dengue fever, leptospirosis, malaria
Chikungunya-like illness	Sudden onset of fever PLUS pain in multiple joints EITHER with or without rash	Chikungunya
Dengue-like illness	Fever for at least 2 days PLUS at least two of the following: nausea or vomiting, muscle or joint pain, severe headache or pain behind the eyes, rash, bleeding	Dengue fever, dengue haemorrhagic fever, dengue shock syndrome
Acute flaccid paralysis	Any cases of acute flaccid paralysis in a child <15 years old or Guillain-Barré syndrome or suspected polio in any age	Acute poliomyelitis
Neonatal tetanus	Any neonate with a normal ability to suck and cry during the first 2 days of life, and between 3 and 28 days of age cannot suck and cry normally and becomes stiff or has convulsions or both	Neonatal tetanus
Fever and jaundice	Any fever (>38 °C) AND jaundice	Hepatitis A
Acute fever and neurological symptoms	Sudden onset of fever with neurological symptoms, altered mental state, confusion, delirium, disorientation, seizure	Meningococcal meningitis, viral meningitis, other viral encephalitis (e.g. West Nile virus)
Foodborne diseases	Clustering of at least 2 cases having gastro-intestinal symptoms originating from same food outlet or catering site	Includes salmonella, staphylococcus, clostridium, campylobacter and rotavirus infections

Stage 2 – Operation: implementation of the enhanced surveillance

A two-day training course was held for the sentinel site focal points with refresher training occurring during daily data collection rounds. Training focused on:

- understanding the syndrome case definitions;
- accurate completion of the surveillance register; and
- specimen collection and referral of laboratory samples.

The surveillance was tested in the week preceding the SIDS conference and became operational on 26 August. The enhanced surveillance continued until 19 September, and the daily reporting ended on 6 September.

Data collection

A surveillance register system captured daily acute care encounters and syndrome cases. The surveillance registers were collected at each sentinel site each day and exchanged for new registers.

Surveillance tools, data analysis and generation of situation reports

SAGES OE is a freeware tool designed by Johns Hopkins University Applied Physics Laboratory (JHU-APL).¹² SAGES OE was adapted for the enhanced surveillance by JHU-APL and SPC and had successfully been used previously by SPC for mass gathering surveillance;¹³ however, technical challenges in locally hosting the system precluded the full use of SAGES OE at the SIDS conference, so a spreadsheet-based alternative was used to store the daily data and generate graphical output. This output was incorporated into daily situation reports (SitReps), providing descriptive summaries (including laboratory results) and narrative interpretation of daily syndrome and encounter activity.

Laboratory surveillance

A laboratory surveillance focal point was selected to link syndromic surveillance and laboratory surveillance at the national laboratory in the Tupua Tamasese Meaole Hospital (TTMH). The diagnostic process included off-

island sample referral protocols for confirmatory testing for epidemic-potential diseases.

Information exchange, investigation and response

The surveillance team provided early warning alerts for immediate response follow-up of any prioritized syndrome cases (such as acute fever and rash or bloody diarrhoea) that were found at the time of daily data collection. Additionally, daily case reports were given to the response team for follow-up investigation. SitReps were emailed to the MoH and the SIDS organizing stakeholders and were disseminated to regional public health professionals via the PacNet Pacific regional public health email network.

Stage 3 – Transition, sustainability, and monitoring and evaluation

A sustainability plan was generated to transition improvements from the mass gathering surveillance to the routine surveillance system to harness the considerable effort involved in implementing the enhanced surveillance. This included a monitoring and evaluation plan to benchmark surveillance performance for future assessment. The sustainability plan was discussed during a joint SPC and MoH debriefing session at the end of the mass gathering.

RESULTS

A total of 2386 encounters were seen at the 10 sentinel sites, from 26 August to 6 September 2014. Daily encounters at the sentinel sites ranged from 0 to 299. Seven hundred eight encounters (30%) presented with syndromes under surveillance (see **Table 2**). Three syndromes accounted for nearly 90% of all syndrome cases ($n = 631$) and more than a quarter of all encounters (26.4%): influenza-like illness – nearly 60% of syndrome cases ($n = 402$), acute fever and rash – 19% ($n = 134$) and chikungunya-like illness – 13% ($n = 95$). No acute flaccid paralysis, neonatal tetanus or foodborne diseases were reported. One case of dengue-like illness was investigated and tested positive by rapid test (NS1, Bio-Rad Laboratories, Marnes-la-Coquette, France), with evidence of acute (probable primary) dengue fever infection.¹³ Most syndrome cases were reported among Samoan nationals, and no importation of any infectious diseases among delegates and visitors were reported.

Table 2. Reports of syndrome cases by all points of care: 26 August to 6 September 2014

Syndrome	Number of syndrome cases	Syndrome cases as a percentage of all encounters	Syndrome cases as a percentage of all syndromes
Influenza-like illness	402	16.8	56.8
Acute fever and rash	134	5.6	18.9
Chikungunya-like illness	95	4.0	13.4
Watery diarrhoea	23	1.0	3.2
Prolonged fever	17	0.7	2.4
Non-watery diarrhoea	16	0.7	2.3
Dengue-like illness	15	0.6	2.1
Fever and neurological symptoms	4	0.2	0.6
Fever and jaundice	2	0.1	0.3
Acute flaccid paralysis	0	0	0
Neonatal tetanus	0	0	0
Foodborne disease outbreak	0	0	0
Total syndrome cases	708	29.7	100
Total acute encounters	2386		

DISCUSSION

No new infectious disease outbreaks were recorded for the SIDS conference, and the surveillance system performed well, providing important assurances for public health safety. The CHIKV outbreak was well managed and did not impact the conference. Increasing reporting frequency from weekly to daily, increasing the number of syndromes and the number of sentinel sites improved public awareness of the health risks to the local and international community. These measures together with sentinel clinicians' awareness and accurate identification of syndrome definitions improved surveillance sensitivity. This is shown with 30% of encounters as syndrome cases, compared to only 7%–10% of encounters recorded as syndrome cases in previous SPC-implemented mass gathering surveillance activities in the Pacific. (White P, Mercier A, Saketa S, Hoy D. Sustaining Enhanced Syndromic Surveillance in Pohnpei (FSM). Noumea: The Pacific Community (SPC), unpublished report. 2014), (Dr Sala Saketa, The Pacific Community (SPC), personal communication, 12 January 2014)

The benefits of enhanced surveillance can be sustained when the mass gathering surveillance experience is integrated into long-term surveillance

improvement plans rather than being treated as an isolated activity occurring only during a discrete time frame. Similarly, it is more likely that the extra effort involved in mass gathering enhanced surveillance will be implemented when the work involved is similar to the usual surveillance. The SIDS conference enhanced surveillance was implemented by building on the existing weekly surveillance, facilitating straightforward transition after the conference as well as enabling lessons learnt and benefits gained to be readily applied.

Lessons learnt from the SIDS conference enhanced surveillance experience identified important points for the future planning of mass gathering surveillance:

1. Early preparation is essential, avoiding the temptation to leave surveillance implementation to the 'last minute'. Planning for the enhanced surveillance should start at least 12 months before the event. The lead time is necessary to accommodate the preparatory activities in stage 1 and to ensure the operational tasks in stage 2 can be implemented satisfactorily.

Lead time enables planners to embed and pilot the enhanced surveillance, thereby avoiding disruption and time losses during the intense

period of surveillance operation and ensuring that newly implemented changes are understood. This was demonstrated at the SIDS conference, where insufficient time was allocated for testing the SAGES OE installation. These technical challenges did not adversely impact the surveillance because a functional substitute was straightforward to use, but this issue illustrated that greater time should have been planned for this activity. As not all increases in disease counts warrant investigation, lead time is also needed to generate and understand baselines arising from increasing the number of reporting sentinels. This frequently occurs where the increase in surveillance coverage results in apparent peaks and troughs in the data resulting from weekend and non-uniform daily operation of sentinel sites (particularly the variable operating times of general practitioners).

2. It is essential to run a pilot to test the surveillance system before it becomes operational to ensure that the system can perform as expected. Mass gathering surveillance is typified by a short period of intense activity to collect, collate and analyse data and generate meaningful interpretations on a daily basis. The SIDS conference surveillance data collection was time consuming as it relied on visiting each sentinel site daily. This was compounded by the number and locations of the sentinels that more than doubled for the enhanced surveillance from four to 10 and included the international airport 33 km from Apia. The pilot operation was valuable in highlighting the need to increase the number of data collection teams from two to three, to ensure the timely generation and dissemination of SitReps. While running three teams was more labour (and resource) intensive than running two teams, this approach ensured that the daily SitRep could be completed on time every day.

CONCLUSIONS

The enhanced surveillance for the SIDS conference was a large surveillance operation that provided important public health security assurance in support of a high-profile United Nations meeting simultaneously with an equally large local festival that both occurred concurrently with a widespread CHIKV outbreak. Sustainable benefits of the enhanced surveillance included fostering a closer working relationship between public health authorities, the TTMH laboratory and clinical services and improving surveillance activities.

Mass gathering surveillance typically involves a short period of intense activity that can be an extra burden on over-stretched public health resources. However, impacts on resources and staff can be minimized by building on and enhancing existing surveillance activities. This allows for the efficient commencement of enhanced surveillance and transition back to routine surveillance. This approach can result in improvements to public health systems in both capacity (training of staff) and capability (efficiency and quality improvements in the functioning of the surveillance system) that remain long after the mass gathering is over. The benefits from these improvements include better health security arising from the ongoing surveillance operations and indirect benefits from improvements to the epidemiological evidence base available to health planners that accrue through having better-trained surveillance staff, providing better-informed information, from improved data collection and surveillance coverage. Accordingly, mass gathering surveillance can stimulate improvements in public health surveillance that may not have otherwise occurred. The diligent work of the Samoan public health communicable disease surveillance team during the SIDS conference, and the experience they gained in enhanced surveillance, was applied during the mass gathering surveillance for 2015 Commonwealth Youth Games, which was also held in Apia, Samoa.

Conflicts of Interest

None.

Acknowledgements

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Establishing seasonal and alert influenza thresholds in Cambodia using the WHO method: implications for effective utilization of influenza surveillance in the tropics and subtropics

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Objective: To establish seasonal and alert thresholds and transmission intensity categories for influenza to provide timely triggers for preventive measures or upscaling control measures in Cambodia.

Methods: Using Cambodia's influenza-like illness (ILI) and laboratory-confirmed influenza surveillance data from 2009 to 2015, three parameters were assessed to monitor influenza activity: the proportion of ILI patients among all outpatients, proportion of ILI samples positive for influenza and the product of the two. With these parameters, four threshold levels (seasonal, moderate, high and alert) were established and transmission intensity was categorized based on a World Health Organization alignment method. Parameters were compared against their respective thresholds.

Results: Distinct seasonality was observed using the two parameters that incorporated laboratory data. Thresholds established using the composite parameter, combining syndromic and laboratory data, had the least number of false alarms in declaring season onset and were most useful in monitoring intensity. Unlike in temperate regions, the syndromic parameter was less useful in monitoring influenza activity or for setting thresholds.

Conclusion: Influenza thresholds based on appropriate parameters have the potential to provide timely triggers for public health measures in a tropical country where monitoring and assessing influenza activity has been challenging. Based on these findings, the Ministry of Health plans to raise general awareness regarding influenza among the medical community and the general public. Our findings have important implications for countries in the tropics/subtropics and in resource-limited settings, and categorized transmission intensity can be used to assess severity of potential pandemic influenza as well as seasonal influenza.

Influenza poses a substantial health and economic burden with high morbidity and mortality in temperate regions.^{1–4} The burden of influenza in the tropics and subtropics is not well understood, although growing evidence suggests that it is comparable to that of temperate regions.^{3–7} Furthermore, while yearly variations may occur, seasonality also appears to exist in most tropical and subtropical regions.^{8–11} Therefore, it is essential to analyse influenza surveillance data in a

practical and efficient manner to inform decision-making regarding influenza in the tropics and subtropics.

Recently, based on sentinel surveillance data from Cambodia's National Influenza Center established in 2006, distinct seasonality for influenza in Cambodia was demonstrated.^{12,13} Using the proportion of influenza-like illness (ILI) patient samples positive for influenza, the influenza season appeared to be between June and

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December, coinciding with the rainy season. However, such findings have not yet been fully used for routine public health practice. Establishing specific influenza thresholds at the national level for season onset and intensity levels could provide timely triggers for public health measures, such as awareness-raising for prevention, upscaling control measures and resource allocation. Various methods such as visual inspection, pre-set constant values and the moving epidemic method have been implemented in countries to signal season onset.^{8,14–16}

In the present study, a simple method proposed by the World Health Organization (WHO) was used to establish seasonal and alert influenza thresholds for Cambodia to better inform public health decision-making regarding influenza.¹⁷ The WHO method allows for monitoring intensity of not only seasonal influenza but also potential pandemics. A key lesson learnt from the 2009 pandemic was that WHO and most countries were not sufficiently prepared to assess the severity of a mild pandemic to inform timely risk management and communications. Following the International Health Regulations review committee recommendations, WHO is developing the Pandemic Influenza Severity Assessment (PISA) framework.¹⁸ To assess severity of a pandemic, comparison with historical data is important. Establishing influenza alert thresholds allows for the comparison of data during a pandemic relative to historical seasonal data. To our knowledge, this is one of the first documented assessments and applications of the WHO method for threshold setting in the tropics or subtropics.

METHODS

Influenza surveillance system in Cambodia

Cambodia's influenza surveillance system has two key components: (1) weekly syndromic ILI surveillance; and (2) laboratory testing of specimens collected from ILI patients for influenza virus, both of which come from sentinel sites. While there is also a surveillance system for severe acute respiratory illness (SARI), it was not included because only the past three years' data were available with too few SARI cases to establish thresholds.

There were eight sentinel sites in operation during the study period of week 1 of 2009 to week 25 of 2015,

including four health centres (HCs) in Battambang, Kampong Cham, Kampot and Mondul Kiri provinces; two paediatric hospitals in Phnom Penh and Siem Reap provinces; and two general hospitals in Svay Rieng and Takeo provinces. Not all sentinel sites provided data during the entire study period. The following contributed data during shorter periods: HCs in Kampot and Mondul Kiri provinces (since 2010), Svay Rieng Referral Hospital (since mid-2009) and Takeo Provincial Hospital (2009–2012). Thus, there were six to eight sentinel sites contributing data at a given time.

An ILI case was defined as a person presenting with sudden onset of fever (temperature >38 °C) and cough and/or sore throat in the absence of other diagnosis. Although the number of samples collected varied yearly due to minor protocol changes, approximately 5–10 nasopharyngeal swabs per site per week were collected from ILI patients. Collected specimens were laboratory tested for influenza virus at the National Institute of Public Health and/or Institut Pasteur in Cambodia, except for the site in Battambang province where the testing facility is in the province. Viral RNA was extracted using commercial extraction kits and amplified with reverse transcription polymerase chain reaction (RT-PCR) using standard protocols.^{12,13}

Data sources and parameters to monitor influenza activity

The following data were extracted from the sentinel surveillance system from four data sources: number of (1) new outpatients, (2) ILI patients, (3) specimens collected among ILI patients for laboratory testing, and (4) influenza positives among specimens collected. To establish thresholds, data from week 18 of 2010 to week 17 of 2014 were used, totalling 867 266 outpatients, 36 885 ILI patients, 9136 laboratory specimens from ILI patients and 1482 laboratory-confirmed influenza cases. Data before week 18 of 2010 were not used for threshold setting due to the 2009 pandemic. Three parameters were calculated for each week: (1) proportion of ILI patients among all outpatients (proportion ILI); (2) proportion of laboratory specimens from ILI patients positive for influenza (proportion positive); and (3) an ILI-influenza composite variable (composite), the product of proportion ILI and proportion positive proposed by Tay et al.¹⁹

Establishing seasonal and alert thresholds and categorizing transmission intensity

We adapted the WHO method described in the WHO Global Epidemiological Surveillance Standards for Influenza (WHO manual) to establish seasonal and alert thresholds for the three parameters described above, with some modifications (Fig. 1).¹⁷

First, to define different thresholds we drew weekly epidemic curves for the past 4–5 years (Fig. 1a). Next, the median week of peak occurrence was identified from these years (Fig. 1b). Then, respective peaks from previous years were aligned on the median week (Fig. 1c). An average epidemic curve, which captures a typical influenza season's temporal distribution and amplitude, was drawn by calculating an arithmetic mean over the years for each week (Fig. 1d).

Finally, four threshold levels were determined: (1) seasonal, (2) moderate, (3) high, and (4) alert (Fig. 1e). As the thresholds are context-specific, we explored a range of candidates, including those recommended in the WHO manual for seasonal and alert thresholds,¹⁷ those proposed by Tay et al¹⁹ and those proposed through key stakeholder discussions. Final selections were based on consensus among national and international experts for technical and practical reasons based on several meetings with in-depth discussions. To define season onset (seasonal threshold), the median value of all weeks during the study period¹⁷ was used since we assumed seasonality in influenza activity with approximately half of the year being in-season and the other half off-season. For the moderate threshold, which defines a mild season set between high and seasonal thresholds, we explored the mean and the median values of all weeks during the in-season weeks during the study period (i.e. all weeks above the seasonal threshold). For the high threshold, which defines a higher than average season, we compared the peak value of the average and median epidemic curves.^{17,19} Alert threshold defines extraordinarily severe seasons such as pandemics, and the upper 95% and 90% confidence interval (CI) and the 95th and 90th percentile of the peak values were explored.^{17,19} Based on these four threshold levels, intensity of influenza transmission was classified into five categories: (1) out of season, (2) low, (3) moderate, (4) high, and (5) extraordinary.

Assessment of thresholds

Data for the three parameters from week 1 of 2009 to week 25 of 2015 were plotted against the established thresholds. Influenza season was defined to start when the parameter increased above the seasonal threshold and to end when the parameter declined below the threshold. The number of times per year the seasonal threshold was crossed was used to assess the validity of the seasonal threshold; assuming one influenza season per year in Cambodia based on historic data,^{10,12,13} additional detected seasons were considered false alarms. We also compared results from two conventional rules to declare season onset: the first-week-declaration rule, where onset is declared on the first week the threshold is crossed and the two-consecutive-week-declaration rule, where onset is declared when the threshold is crossed for two consecutive weeks.¹⁹ As additional sensitivity analysis, thresholds were re-calculated including 2009/2010 data to assess the degree of the pandemic season's impact on the parameters and thresholds. The most recent data from week 18 of 2014 provided an opportunity to assess the proposed thresholds using data not included in establishing the thresholds, as would be the case in practice.

Ethics statement

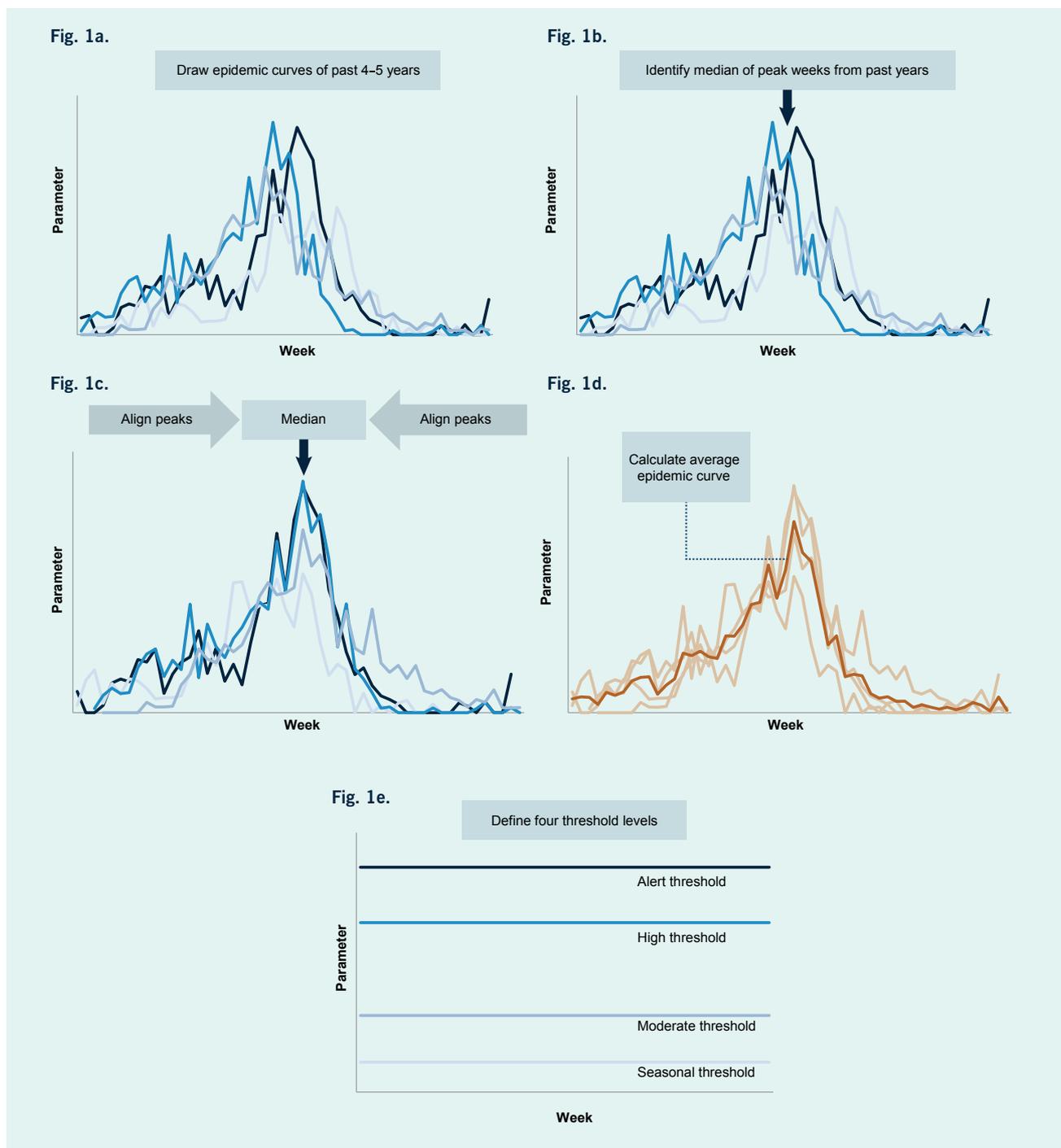
The ILI and influenza surveillance system is a public health activity organized by the Ministry of Health in Cambodia and has standing authorization from the National Ethics Committee, Cambodia. Data that could potentially identify individuals are not included.

RESULTS

Comparison of parameters to monitor influenza activities

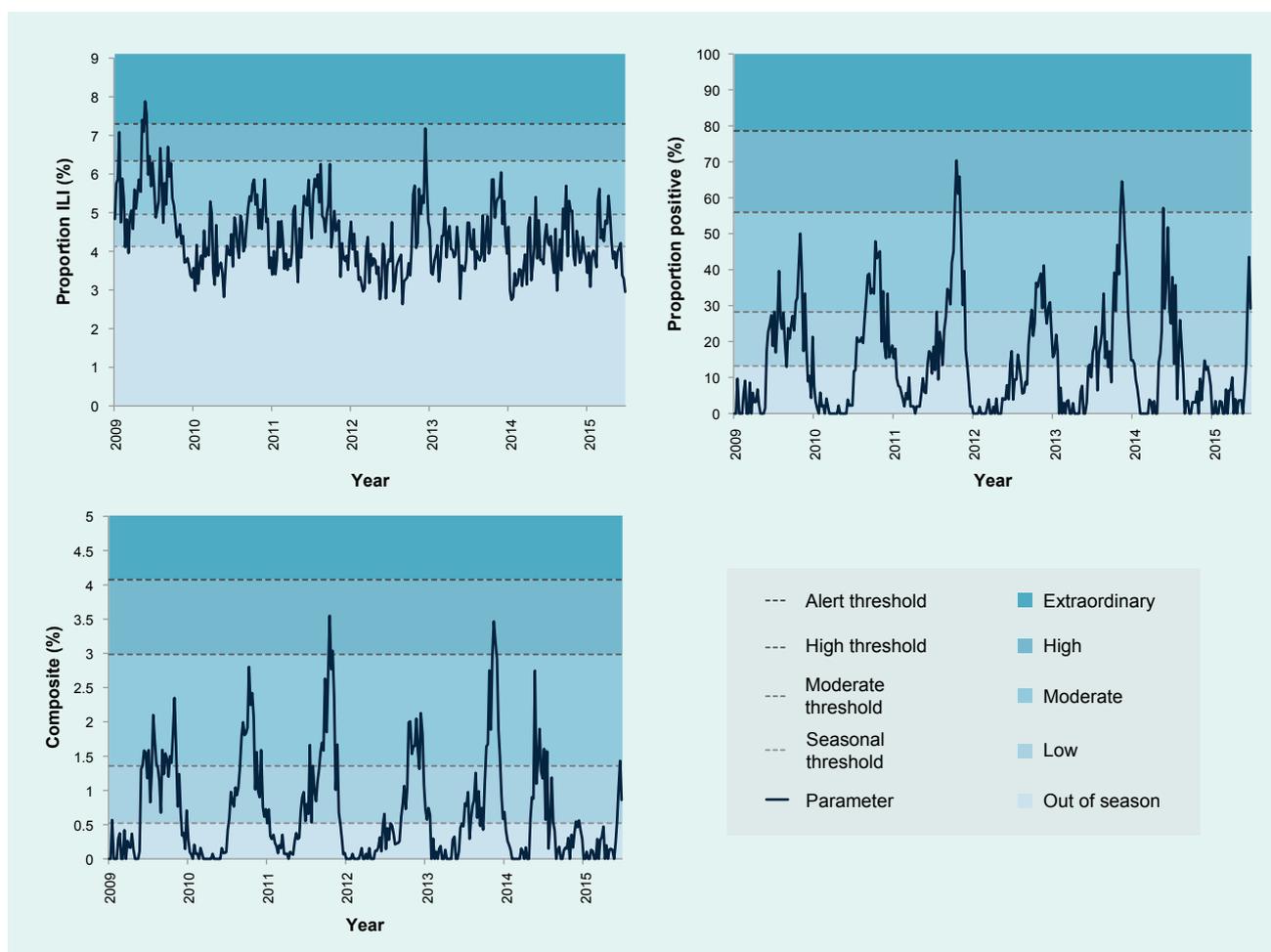
When 2009–2015 data were plotted for the three parameters, proportion ILI showed extensive weekly fluctuations with no clear seasonal pattern, but proportion positive and composite both exhibited clear seasonality, peaking between (1) October and December for the majority (5/6) of seasons (Fig. 2).

Fig. 1. Illustration of the WHO method to establish four levels of thresholds (adapted from WHO Global Epidemiological Surveillance Standards for Influenza) based on proportion of laboratory specimens from ILI patients positive for influenza (proportion positive) data from Cambodia, 2009 to 2015)



- A. Draw epidemic curves for previous 4 or 5 years with calendar week on x-axis and parameter on y-axis.
- B. Identify median of peak weeks from past years.
- C. Shift the data from previous years to the point where their respective peaks align on median of peak weeks identified in B.
- D. Calculate an average over the years for each week to create the average epidemic curve.
- E. Define thresholds levels.

Fig. 2. Surveillance data from 2009 to 2015 plotted against established thresholds and intensity categorization for three parameters: (1) proportion of ILI patients among all outpatients (proportion ILI), (2) proportion of laboratory specimens from ILI patients positive for influenza (proportion positive), and (3) the product of proportion ILI and proportion positive (composite)



Establishment and assessment of seasonal and alert thresholds and intensity categorization

Four threshold levels were established (Table 1), defining five categories of transmission intensity (Fig. 2). Each threshold was based on a different criterion process described below.

Seasonal threshold

While visual inspection indicated one season per year for most years based on the proportion positive and composite parameters (Fig. 2), with the first-week-declaration rule, the seasonal threshold was crossed multiple times for most years (Table 2). While multiple-season years were observed for all parameters, the frequency was greatest for the proportion ILI and least for the composite. The

two-consecutive-week-declaration rule reduced the frequency considerably regardless of parameter. Notably, all years were shown to have a single season using the composite.

Alert threshold

Exploring a range of CI and percentiles, the upper 90% CI of the average epidemic curve peak amplitude was adopted (Fig. 2) as suggested in the WHO manual¹⁷ and used previously in an Australian study.¹⁹ The upper 90% CI had consistently higher values than the 90th or 95th percentiles for proportion positive and composite (data not shown). The only time the alert threshold was crossed was during the 2009 pandemic year with proportion ILI (Table 3).

Table 1. Values of established thresholds for three parameters: (1) proportion of ILI patients among all outpatients (proportion ILI), (2) proportion of laboratory specimens from ILI patients positive for influenza (proportion positive), and (3) the product of proportion ILI and proportion positive (composite)

Threshold level	Proportion ILI (%)	Proportion positive (%)	Composite (%)
Seasonal	4.1	13.2	0.5
Moderate	5.0	28.2	1.4
High	6.3	56.0	3.0
Alert	7.3	78.6	4.1

Table 2. Number of seasons detected from 2009 to 2015 using the median value from all weeks as the seasonal threshold, with either the first-week-declaration rule or two-consecutive-week-declaration rule for the three parameters: proportion ILI, proportion positive and composite

Season*	Proportion ILI		Proportion positive		Composite	
	1 st week**	2 nd week***	1 st week**	2 nd week***	1 st week**	2 nd week***
2009/2010	5	2	3	1	2	1
2010/2011	7	3	1	1	1	1
2011/2012	6	2	4	1	1	1
2012/2013	7	2	3	3	3	1
2013/2014	9	4	6	1	6	1
2014/2015	10	5	3	1	4	1

* Starts on week 18 and ends on week 17 of the following year.

** Start or end of season declared on the first week threshold was crossed.

*** Start or end of season declared when threshold is crossed for two consecutive weeks.

High threshold

Peak amplitude of the average epidemic curve was adopted (Fig. 2) because average and median epidemic curves were found to be similar and sensitivity analysis including or excluding 2009/2010 data suggested that the average epidemic curve was more stable than the median when number of years used for threshold establishment was few (data not shown). Based on the proportion positive and composite, the 2009 pandemic year did not reach the high threshold (Table 3).

Moderate threshold

The mean rather than the median value was selected as it would better distribute the in-season weeks between the low and moderate levels (Fig. 2). Given the distribution of the data during the in-season period, the latter would set the threshold at a considerably low level, close to the seasonal threshold, and make the moderate threshold practically less useful.

Sensitivity analysis of thresholds with 2009 pandemic year data and application of thresholds to 2014–2015 data

Finally, we tested whether inclusion of data from the 2009 pandemic for threshold determination would affect thresholds for the three parameters. When 2009/2010 data were included, there was a considerable increase in threshold values with proportion ILI (Fig. 3). For the other two parameters, thresholds remained largely unaffected. The proposed thresholds performed similarly when applied to surveillance data from week 18 of 2014 that were not included in establishing the thresholds (Table 2 and Fig. 2).

DISCUSSION

In the present study based on the WHO method for establishing seasonal and alert influenza thresholds, we explored a range of thresholds for three readily available parameters and established practical influenza thresholds

Table 3. Duration of each intensity category* in weeks for influenza seasons from 2009 to 2015 for the three parameters: proportion ILI, proportion positive and composite

Season**	Out of season (weeks)	Low (weeks)	Moderate (weeks)	High (weeks)	Extraordinary (weeks)
Proportion ILI					
2009/2010	21	9	15	4	3
2010/2011	25	15	12	0	0
2011/2012	21	17	14	0	0
2012/2013	36	8	7	1	0
2013/2014	29	16	7	0	0
2014/2015	27	16	9	0	0
Proportion positive					
2009/2010	26	18	8	0	0
2010/2011	26	14	12	0	0
2011/2012	28	11	9	4	0
2012/2013	29	13	10	0	0
2013/2014	27	15	7	3	0
2014/2015	38	7	6	1	0
Composite					
2009/2010	25	14	13	0	0
2010/2011	25	16	11	0	0
2011/2012	25	15	10	2	0
2012/2013	33	10	9	0	0
2013/2014	28	14	8	2	0
2014/2015	38	9	5	0	0

* Intensity category is raised/lowered on the first week each threshold is crossed except for the seasonal threshold in which intensity is raised/lowered when the threshold is crossed for two consecutive weeks.

** Starts on week 18 and ends on week 17 of the following year.

for Cambodia. Based on consensus among national and international stakeholders, four thresholds were established to mark the start of the season and low, moderate, high and extraordinary levels of influenza activity.

When comparing the usefulness of the different parameters to monitor influenza activity, we found that the syndromic proportion ILI parameter lacked seasonality. However, proportion positive and composite, parameters that incorporate laboratory data, generally exhibited a single distinct season each year in Cambodia. Furthermore, the composite parameter using the two-consecutive-week rule to indicate season onset had no false signals during the study period.

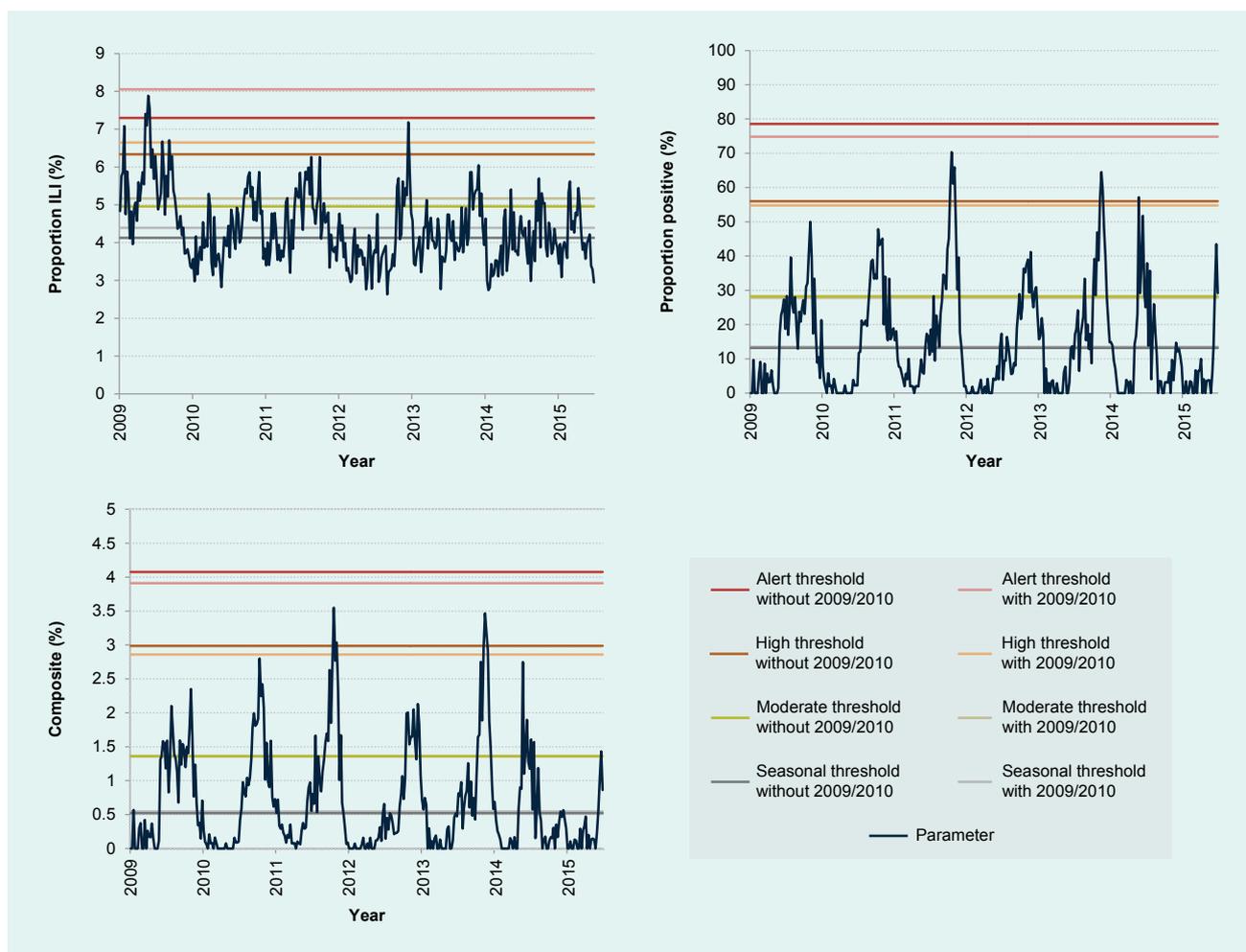
Sensitivity analysis of thresholds with inclusion of 2009 data showed that only the proportion ILI parameter was largely affected. The considerable increase in proportion ILI during the 2009 pandemic may have been due to greater awareness resulting in more patients seeking health care for ILI and/or more clinicians categorizing patients as ILI rather than a true increase in incidence.

In fact, influenza A(H1N1)pdm09 virus accounted for only one-third of all influenza subtypes detected in Cambodia during the pandemic (data not shown). These findings further confirmed the robustness of parameters and thresholds that incorporate laboratory information.

The composite variable appeared particularly useful, likely due to higher specificity for a true increase in influenza cases by accounting for both syndromic activity and laboratory positivity; for instance, it accounts for situations where there is high proportion ILI but low proportion positive as in the 2009 pandemic. Similarly, when there is high proportion positive but low proportion ILI, the composite approach would be more conservative than using proportion positive alone and would reduce false positive declarations. Additionally, in settings where the number of samples for laboratory testing is limited or small resulting in high fluctuations in proportion positive, accounting for syndromic data may be useful.

Finally, the five categories of intensity proposed here can be applied to both seasonal influenza and potential

Figure 3. Sensitivity analysis of established thresholds for the three parameters including or excluding 2009 pandemic year data



pandemic influenza within the PISA framework.¹⁸ The composite approach may be especially useful for pandemic influenza assessment by accounting for a potential increase in awareness, health-care access and/or reporting. As Cambodia is one of several countries affected by human infections with avian influenza, its pandemic preparedness is especially important both domestically and globally.²⁰

Our study has several limitations. First, the assessment was limited to approximately five to 10 laboratory samples per site per week, and reporting varied between six and eight sentinel sites during the study period. Nevertheless, the quantity and distribution of the data were sufficient to describe seasonality and establish thresholds. Next, the sentinel surveillance system covers public hospitals and health centres but not private clinics, and therefore may not be representative of the

overall Cambodian population. A special study such as a health-care utilization survey is an important next step to better understand the burden of influenza nationwide. Finally, data from paediatric and non-paediatric sites were combined to establish thresholds due to sample size limitations, although paediatric sites generally had higher values for proportion positive. However, the yearly trends were similar between the two site types (data not presented). Regardless, to assess influenza activity, thresholds should be interpreted with other information such as subtypes and other parameters.

Our findings have practical public health significance. Once parameters, thresholds and categorizations are determined, it is possible to implement specific public health actions,²¹ such as risk communication that could be triggered from crossing a threshold. In Cambodia, knowledge regarding influenza

is still scarce among health workers and the general public and information regarding seasonality is just emerging. Therefore, as a first step based on these findings, the Ministry of Health plans to raise awareness among the medical community and the public regarding (1) general knowledge of influenza and its seasonality, (2) preventive measures such as respiratory and hand hygiene, and (3) prevention of antimicrobial misuse. We consider channels such as press releases, the Internet, posters and the National Respiratory Disease and Influenza Bulletin to convey these messages. In the long term, the seasonal threshold will be helpful for vaccination timing;^{10,11,21} continuous re-evaluation of vaccination timing will be necessary as the timing of season onset has been observed to vary in the tropics.

Although one country's experience cannot be generalized, our findings provide novel insights with global implications, specifically for countries in the tropics and subtropics. First, ILI syndromic surveillance may not be an appropriate parameter for influenza activity in the tropics and subtropics. This contrasts to what is known for ILI data that are routinely used in temperate regions such as Europe, the United States of America and Australia as a proxy to monitor influenza activity.^{14-16,19} Lack of apparent ILI seasonality could be unique in the tropics and subtropics with various pathogens circulating year-round that cause acute respiratory illnesses.^{8-11,21-32} Instead, use of proportion positive and composite approaches may be suggested given recent studies with laboratory information indicating that most countries, including non-temperate countries, exhibit distinct seasonal patterns.^{8-11,21-32} Our findings regarding the usefulness of the composite variable agree with those from a temperate region in Australia¹⁹ and highlight the importance of using multiple sources of information to guide assessment. Considering similar surveillance systems in Cambodia and those in other tropical and subtropical countries,²¹⁻²⁸ our approach may be adapted to fit each country's context. For Cambodia, eight sentinel sites with approximately 35 samples per week nationwide were enough to describe influenza activity. Furthermore, there are several key observations in influenza activity that are unique to the tropics and subtropics:^{9-11,27,29} (1) annual timing of season onset and peak vary considerably, (2) season onset appears more gradual, and (3) magnitude of influenza season is not as distinct from off-season. These were also observed in the present study (Fig. 2). Such characteristics make it especially meaningful to set explicit thresholds based on

appropriate parameters to support routine public health communications and allocate resources effectively and efficiently.²¹ In addition to the leadership of respective ministries of health, global efforts by WHO, the Centers for Disease Control and Prevention and other organizations have supported the establishment of national influenza surveillance systems in many resource-limited countries in non-temperate climates.^{10,11,21-34} We believe it is time to maximize utilization of influenza surveillance data for routine actions for domestic and global public health assessment and response.

In summary, distinct seasonality of influenza activity in Cambodia was observed using two parameters that incorporate laboratory information, allowing for the establishment of thresholds and transmission intensity categories. The composite variable that accounts for syndromic and laboratory data was the most specific in declaring season onset and the most useful in monitoring intensity. This categorization can assess not only seasonal influenza but also potential pandemic influenza, contributing to the country's pandemic preparedness. These findings have important implications for countries in the tropics, subtropics and in resource-limited settings.

Conflicts of interest

None declared. None of the authors have any affiliations with or financial involvement in any organization or entity with any actual or potential financial, political, or personal interest in the subject matter or materials of the research discussed in the manuscript.

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Is population ageing cancelling out progress made in tuberculosis control in Hong Kong SAR (China)? Age-adjusted analysis of case notification data, 1990–2015

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For most countries and areas in the World Health Organization (WHO) Western Pacific Region, the decline of tuberculosis (TB) epidemics and the ageing of the population occurred simultaneously in the past decades. According to latest reports, people aged 60 years and over accounted for 13% of the population in 2010 in the Region, and the number will grow faster due to longer life expectancy and declining fertility.¹

The impact of population ageing on TB epidemiology is complex and may vary between and within countries. In some high- and middle-income settings, like Hong Kong SAR (China), the TB notification rate had declined slowly after a rapid downward trend.² Consistent high TB prevalence and incidence in older people is one potential reason and is increasingly becoming an important public health challenge.³

In Hong Kong SAR, one study demonstrated the TB rate decreased in those under 60, remained unchanged in those between 60 and 69 and increased in those more than 70 years of age from 1989 to 1998.⁴ Tackling the challenge of an ageing population appears to be a key step for TB elimination. This report analyses surveillance data of TB notifications in Hong Kong SAR from 1990 to 2015 and discusses the impact of population ageing on achieving the WHO End TB Strategy targets.⁵

METHODS

TB has been a statutory notifiable disease in Hong Kong SAR since 1939.³ Based on TB notification systems, the information of registered TB patients is collated and compiled in annual reports of the Tuberculosis and Chest Service, Department of Health, Hong Kong SAR.² We extracted the number of all forms of TB notifications by age and sex between 1990 and 2015. The number of the corresponding population was extracted from online publications of population estimates released by Census and Statistics Department, Hong Kong SAR.⁶

Descriptive analysis of TB rates from 1990 to 2015 was conducted. The age-specific TB rates by sex were analysed to compare the trends in each age group. In addition to crude TB rates, age-adjusted rates from 1991 to 2015 were calculated by using the population in 1990 as reference. The annual rate of reduction in TB notification was determined by fitting an exponential linear regression model for crude and age-adjusted TB rates respectively from 1998 to 2015. Then each fitted model was extrapolated up to the year 2035 to estimate and examine future TB rates in line with the End TB Strategy target (90% reduction in incidence by 2035 compared to 2015 level). All analyses were conducted by the statistical software environment R version 3.3.1 (R Core Team, Vienna, Austria, 2016).

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RESULTS

The proportion of older people (people aged 65 years and over) in the population increased from 8.5% in 1990 to 15.3% in 2015, while the proportion of older TB patients increased from 21% in 1990 to around 40% in 2004 and subsequent years.

An overall downward trend of TB rates was observed in all age and sex groups after 2000 (Fig. 1a). The rates in older people were significantly higher than younger groups in both males and females. The rate in males was not obviously different from the rate in females in people under 35. However, the rate in males increased faster than that of females after age 35. In females, the rates between 15 and 34 years of age were conversely higher than those between 35 and 54 years of age.

The annual decline was an average of 3.9% per year in crude TB rates (3.7% in males and 3.9% in females); the decline was 5.4% per year in age-adjusted TB rates (5.7% in males and 4.9% in females) from 1998 to 2015 (Fig. 1b). Extrapolating this trend, the crude and age-adjusted rates were expected to reach 28.0 and 15.0 per 100 000 in 2035, which would result in a total reduction of 54.5% and 66.2% compared to the rates in 2015.

DISCUSSION

The results demonstrate Hong Kong SAR age-specific TB rates in recent years. Along with implementation of the DOTS strategy, TB associated with progressive primary infection or exogenous reinfection had been well reduced in the community.³ However, the diseases developing from endogenous reactivation were less affected.³ Previous studies in Hong Kong SAR elaborated on the transition from high TB risk to far lower risk in young adults and TB rate increases with age in all birth cohorts after 1978.^{7,8} Accordingly, the proportion of TB reactivation was estimated to increase from 46% to 70% between 1968 and 2008,⁹ and almost to 100% by 2000 for the 65–74 years age group.¹⁰ Older people are more likely to be infected in their earlier adult years and reactivate TB due to decreased immunocompetency. This may explain consistently higher rates in older people and the increasing TB trend with age in Hong Kong SAR.

The rates in males are obviously higher, probably due to more exposure and high-risk factors for progression such as comorbidity, smoking or alcohol abuse.¹¹ Higher rates among young to middle-aged women have also been observed in industrialized countries during the mid-twentieth century and in China in the past decades. Potential reasons, such as stress of pregnancy or immigration of female workers, warrant further studies.¹¹

Overall, the impact of population ageing on TB rates seems substantial in Hong Kong SAR. When ageing progresses together with a decline in TB rates, the former would partially cancel out the progress by slowing down the reduction of TB rates as observed in Japan after the 1980s.¹² In Hong Kong SAR, the epidemiologic transition may take several decades in line with the demographic changes. Towards the End TB Strategy targets, although the decline of TB rates can be positively accredited, an additional 12% reduction would be lost exclusively ascribed to population ageing. In addition, the extrapolation should also consider the quality of current TB data, population estimated, declined annual risk of infection and a smaller proportion of infected migrants in subsequent birth cohorts.^{7,8}

Therefore, a more targeted response is needed to move towards the End TB Strategy targets. Considering the limitation of existing tools for diagnosis and treatment, preventing reactivation from higher prevalence of latent TB infection in older people will remain a major challenge. Enhanced surveillance together with age-sensitive analysis particularly focusing on older people is critical to accurately monitor the situation under demographic changes, including migration, that are happening in Hong Kong SAR and other parts of Asia.

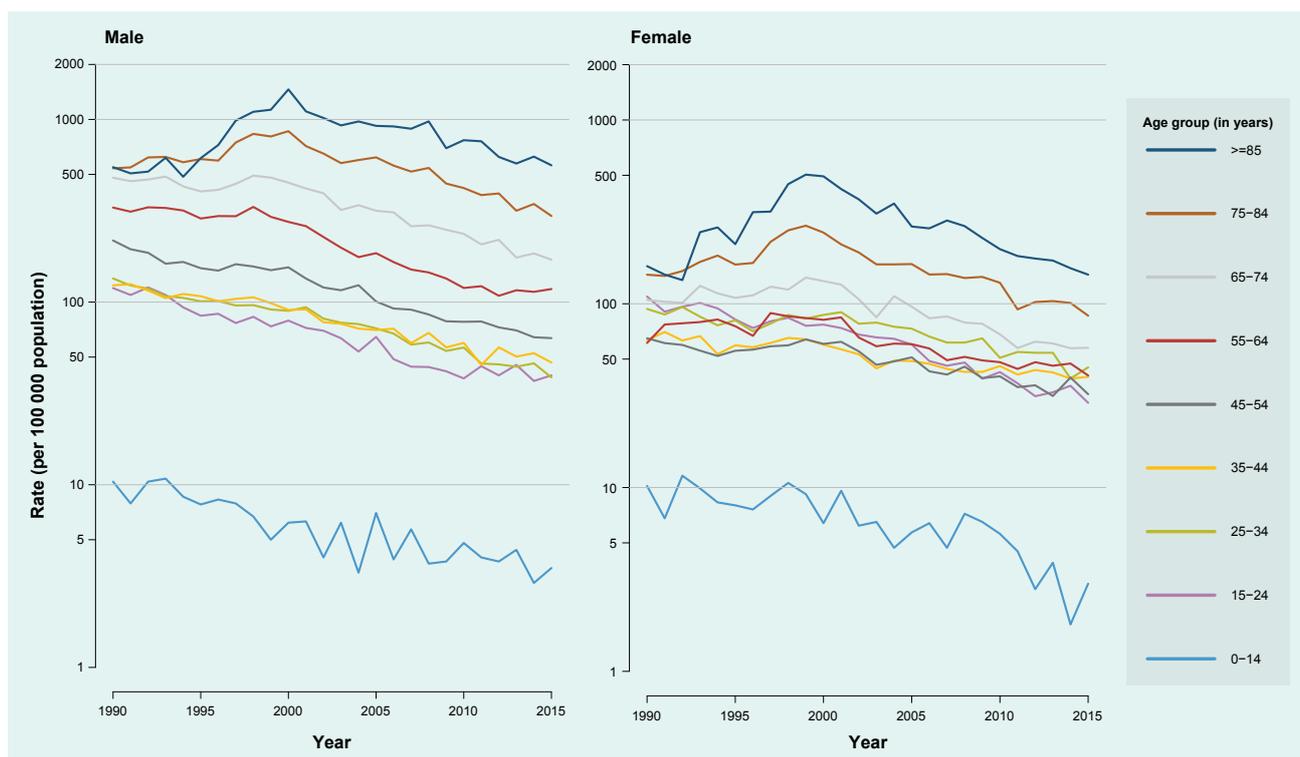
Conflicts of interest

None declared.

Funding

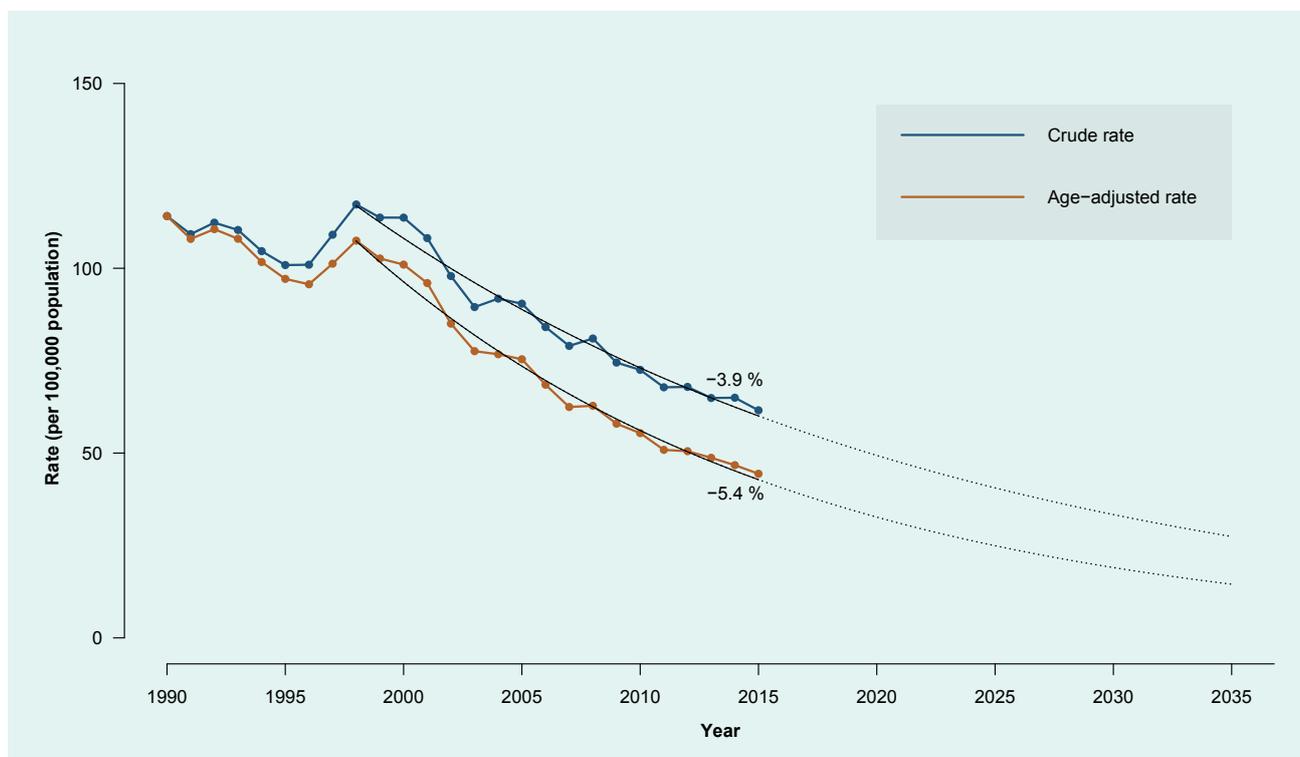
This project is supported by the Health and Medical Research Fund, Food and Health Bureau, Hong Kong SAR (China).

Figure 1a. Tuberculosis notification rate by age and sex, Hong Kong SAR (China), 1990–2015*#



* Data in 2015 are provisional.
All forms of tuberculosis were included in the analysis.

Figure 1b. Crude and age-adjusted tuberculosis notification rates, Hong Kong SAR (China), 1990–2015*#



* Data in 2015 are provisional.
All forms of tuberculosis were included in the analysis.

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Exposure to H1 genotype measles virus at an international airport in Japan on 31 July 2016 results in a measles outbreak

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In March 2015, the Measles Regional Verification Commission for the World Health Organization Western Pacific Region verified that Japan had achieved measles elimination¹ based on the verification criteria.² Only 35 confirmed measles cases were reported in 2015, and for 2016, measles activity was low until July ($n = 16$, as of 3 August). However, the number of reported measles cases surged in the middle of August 2016. Several cases were considered sporadic cases without a known source of infection or imported cases because they initially seemed to be unrelated. However, through vigilant daily monitoring of national surveillance data by surveillance officers at the national level, including fellows of the Field Epidemiology Training Program at the National Institute of Infectious Diseases, and their close communication with local public health staff, five cases were found to have been present at a large international airport on the same day as a possible index case was found.

Recent measles situation in Japan

Measles became a case-based notifiable disease in 2008. The case definition for measles used in national surveillance is based on clinical symptoms and laboratory tests. The diagnosis of measles is confirmed by laboratory test results, including a positive result for measles-specific immunoglobulin M (IgM) titre, significant increase in measles-specific immunoglobulin G (IgG) titre using paired serum, the detection of measles

virus (MV) by reverse transcription polymerase chain reaction (RT-PCR) or isolation of MV in cell culture. MV detection, isolation and genotyping are performed mainly at designated local governmental (i.e. municipal or prefectural) public health institutions within each local government area. The number of reported measles cases in Japan has declined markedly from 11 013 in 2008 to 35 in 2015.³ The D5 genotype strain of MV, which was endemic in Japan, has not been detected since May 2010; however, limited local transmission following importation of MV has been observed, as in 2014.⁴

Common exposure to H1 genotype MV at an international airport

In 2016, although measles activity remained at the lowest level since 2008, the number of reported measles cases surged in epidemiological week 33.⁵ Surveillance officers and Field Epidemiology Training Program fellows noted five measles cases (**Table 1**, cases 1–5) with close onset dates reported from different prefectures that seemingly did not have any common exposure history. Case 1 was a ground crew member at Kansai International Airport (KIX) in Osaka Prefecture, the third largest international airport in Japan, handling about 64 000 passengers per day.⁶ This patient had no recent history of overseas travel. Case 5 had travelled domestically before the onset of measles. The other three (cases 2–4) had travelled to Indonesia, the Republic of Korea and Viet Nam; they were initially suspected to have become infected with MV at their

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Table 1. **Cases with H1 genotype measles virus likely acquired at Kansai International Airport, July–August 2016**

Case	Age group	Sex	Vaccination history	Travel history (destination and period)	Onset date (fever or rash)	Reporting prefecture	Reported date at KIX*
1	20–24 years	F	Unknown	None	9 Aug	A	31 Jul
2	15–19 years	M	None	Indonesia, 31 Jul–5 Aug	9 Aug	B	31 Jul
3	25–29 years	M	Unknown	Viet Nam, 31 Jul–6 Aug	10 Aug	C	31 Jul
4	30–34 years	M	None	Republic of Korea, 31 Jul–2 Aug	10 Aug	D	31 Jul
5	40–49 years	M	None	Domestic travel, 31 Jul–3 Aug	10 Aug	E	31 Jul

* KIX = Kansai International Airport

destination. However, MV was confirmed in all cases by RT–PCR and determined to be the H1 genotype strain, the predominant genotype reported from China and parts of South-Eastern Asia over the past three years.⁷

Because the genotype H1 strain is not endemic in Indonesia, Japan or the Republic of Korea, we obtained epidemiological information from local health authorities at each reporting prefecture to clarify travel itineraries, including domestic transit, of the five cases. We found that these five cases had spent time on the same floor of KIX on 31 July 2016. Sequence analysis revealed high nucleotide sequence homology between the H1 genotype MV strains detected in the five cases. Based on these findings, we concluded that KIX was the likely place of exposure.

Alert to the general public

The National Institute of Infectious Diseases (NIID) and the Ministry of Health, Labour and Welfare of Japan announced an increase in the number of measles cases in late August 2016 to remind the general public to get vaccinated and to raise physicians' awareness (i.e. to consider measles when examining patients with fever, rash, and travel history and/or epidemiological information such as contact with people displaying measles-like symptoms during the incubation period). In addition, information about the cases suspected to have been exposed to H1 genotype MV on 31 July 2016 at KIX were posted on NIID's website to inform the general

public and health-care providers of the risk of exposure to MV at KIX.

Possible source of the H1 genotype MV at KIX

In late August, person A (sex not disclosed) reported information that provided insight into the source of exposure at KIX. MV infection was confirmed in person A by measles-specific IgM. Person A reported having contact before measles onset with person B, who had returned from China to Japan on 20 July 2016 and developed measles-like symptoms on 26 July. Person B (sex not disclosed), who had visited KIX on 31 July, consulted physicians and was diagnosed with the common cold and/or drug eruption before measles-specific IgM was confirmed. Given that person B returned from China during the measles incubation period and visited KIX while symptomatic on 31 July, this person was considered to be the possible source of MV for all five cases, even though the confirmation of genotype H1 strain was not obtained from the case.

Additional cases due to transmission at KIX

Following further investigations, the Osaka Prefecture local government reported on 31 August an additional 16 laboratory-confirmed cases, all of whom shared a single office at KIX with case 1 (Table 1), a ground crew member. The outbreak investigation in this office was conducted and its findings will be reported elsewhere.

DISCUSSION

This cluster reminds us that an international airport is a potential hotspot for measles and may act as a mixing place for travellers from measles-endemic countries and any unvaccinated non-immune persons, as reported previously.^{8–10} As of 7 December 2016,⁵ no additional cases related to this KIX cluster have been reported, and the numbers of both suspected and confirmed cases have been declining. However, authorities should remain vigilant about the risk of importation of MV from endemic countries. High-quality surveillance and high vaccination coverage must be continued for Japan to preserve measles elimination status.

Conflicts of interest

None.

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Epidemiological and virological characteristics of seasonal influenza in the Western Pacific Region of the World Health Organization, 2011–2015

Members of the WHO Western Pacific Region Global Influenza Surveillance and Response System[°]

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Seasonal influenza is an acute viral infection that causes annual epidemics. The World Health Organization (WHO) estimates that the global disease burden of seasonal influenza is approximately one billion cases annually resulting in up to 500 000 deaths.¹ Epidemics are well defined as seasonal in northern and southern temperate climates with annual epidemics occurring in late winter or early spring.² In contrast, seasonal patterns in tropical and subtropical regions are less clear and tend to show more consistent levels of transmission year-round.^{3,4}

The Western Pacific Region (WPR) of WHO comprises 37 diverse countries and areas with temperate and tropical climates inhabited by approximately 1.8 billion people in 2016.⁵ Therefore, influenza is consistently circulating in variable locations in the Region. Collection and analysis of influenza surveillance data in WPR is particularly important due to evidence that novel influenza may emerge from persistent influenza reservoirs in the tropics and then spread to temperate regions.⁴ A more comprehensive understanding of virological characteristics of influenza in this Region will contribute to improved predictions of emerging global influenza trends. For example, there is evidence that between 2002 and 2007 influenza viruses originating in several tropical WPR nations seeded seasonal A(H3N2) epidemics in temperate zones.⁶

The Global Influenza Surveillance and Response System (GISRS) is a WHO network that monitors global impact of influenza and evaluates potential pandemic risk of emerging strains.⁷ GISRS also provides recommendations regarding viral strains in seasonal influenza vaccines, laboratory diagnostics and antiviral

susceptibility. GISRS comprises 143 National Influenza Centres (NICs), six WHO collaborating centres (CCs), four Essential Regulatory Laboratories and other ad hoc laboratories. The WHO WPR has 21 NICs, three WHO CCs and two Essential Regulatory Laboratories. The NICs process thousands of specimens yearly of which a subset is sent to WHO CCs.⁸ FluNet is a global platform that allows NICs and other GISRS-affiliated laboratories to upload virological information regarding number of specimens tested and resulting type, subtype and lineage.⁹ It has been used in WPR since 1996. FluID, currently in a pilot phase, is a platform for sharing country epidemiological data that includes influenza-like illness (ILI) consultations by age group, total number of outpatients and total number of surveillance sites.¹⁰

Embedding influenza surveillance strategies within the Asia Pacific Strategy for Emerging Diseases (APSED) framework has supported significant advances in WPR influenza capacity.¹¹ Advances include improved surveillance systems, increased laboratory capacity and greater rates of reporting to FluNet.¹² An evaluation of the Region between 2006 and 2010 indicated increased sample submission and reporting through regional systems, particularly in response to the 2009 A(H1N1) pandemic.¹² In light of continued efforts to enhance influenza surveillance in the Region, this review provides an updated description of regional influenza surveillance systems focused on the epidemiological and virological characteristics of seasonal influenza. This review updates the results from the previous 2012 review,¹² considers how recommendations regarding surveillance strategy improvements have been implemented in the Region and discusses suggested future steps.

[°] Members of the WHO Western Pacific Region Global Influenza Surveillance and Response System are provided in the Acknowledgements.

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METHODS

Data collection

Influenza surveillance data for 2011 to 2015 were collected from the 15 countries and areas with NICs in the WPR: Australia, Cambodia, China (including Hong Kong SAR), Fiji, Japan, the Lao People's Democratic Republic, Malaysia, Mongolia, New Caledonia (France), New Zealand, Papua New Guinea, the Philippines, the Republic of Korea, Singapore and Viet Nam.

Virological surveillance data included number of specimens collected, tested and influenza positive subtypes and lineages. These data were extracted from FluNet and confirmed by NIC focal points.

Descriptive and epidemiological data were collected from NICs via questionnaires developed in Microsoft Excel®. Questionnaires of descriptive surveillance system data and epidemiological data were collected from December 2015 through August 2016. The data collected included descriptive surveillance system information such as ILI case definitions and the numbers and descriptions of active surveillance sites as of 31 December 2015. Epidemiological data, including number of ILI cases by age group and geographic location of surveillance sites, were collected.

Data analysis

Country-specific information on ILI surveillance systems, site numbers and case definitions were extracted from submitted questionnaires and compiled.

Virological and epidemiological data reported by epidemiologic week were combined into data per month. Data were graphed and grouped into four regions according to location and similarities in influenza patterns and to allow comparison with previously reported trends.¹² The groups were: (A) Northern temperate (Mongolia and the Republic of Korea); (B) China (including Hong Kong SAR); (C) Tropical (Cambodia, the Lao People's Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam); and (D) Southern (Australia, Fiji, New Caledonia (France), New Zealand and Papua New Guinea). When data were available, per cent ILI consultations were determined by taking monthly ILI consultations divided by total monthly consultations. Proportions for each

group were calculated by adding ILI consultations or positive cases and dividing by total consultations or total specimens tested, respectively. Per cent positive data and total positive samples were also analysed by subtype and lineage, that is, A(H1), A(H3), A(other) and influenza B by year. Positive specimens from Japan were included in regional number of influenza positive cases.

RESULTS

Surveillance systems

All 15 countries and areas reported data to FluNet during the reporting period. All countries and areas had ILI surveillance systems with variations in ILI case definition, type of surveillance systems and number of reporting sites (**Table 1**). At the time of reporting, Mongolia used the 2014 WHO case definition of acute respiratory infection with measured fever of ≥ 38 °C and cough with onset within the last 10 days.¹³ Hong Kong SAR, Malaysia, Papua New Guinea, the Philippines and Viet Nam used the previous WHO ILI case definition of sudden onset of fever of >38 °C and cough or sore throat in the absence of other diagnosis.¹³ The others reported case definitions that required additional respiratory symptoms or a modified time frame of symptom onset. Minor case definition differences were reported among various ILI surveillance sites within Australia, Cambodia, Hong Kong SAR and New Zealand.

For ILI patients that met the country case definition, the method for selecting cases for specimen collection varied among countries. Most commonly a set number of cases per week were selected for testing. All countries and areas also used various laboratory testing methodologies for influenza and subtype confirmation, including rapid test, reverse transcription polymerase chain reaction (RT-PCR), serology and virus culture.

Virological and epidemiological characteristics

The number of reported specimens tested for influenza between 2011 and 2015 tripled (**Table 2**), with over two million specimens reported to FluNet from WPR. Of positive specimens reported to FluNet from WPR, over 70% of the specimens were from China followed by Japan (11%) and Australia (5%). During this time period, 13% ($n = 293\ 501$) of processed specimens from countries and areas that submitted data on number of specimens

Table 1. Outpatient surveillance systems and case definitions, 2011–2015

Country	Surveillance system	ILI case definition
Australia	242 GPs and 69 EDs	Fever (≥ 38 °C), cough and fatigue (some within four days of presentation)
	Community online data collection and national call centre network	Cough and fever
Cambodia	7 hospitals	Sudden onset of fever ≥ 38 °C axillary within 5 days of presentation and fever at time of presentation, cough and/or sore throat in absence of other diagnosis
	3 health facilities	Sudden onset of fever ≥ 38 °C axillary and fever at time of presentation, cough and/or sore throat in absence of other diagnosis
China	562 hospitals and 408 network laboratories	Sudden onset of fever of >38 °C and cough or sore throat
China, Hong Kong SAR	17 EDs	Cases with clinical diagnosis related to influenza, upper respiratory tract infection, fever, cough, sore throat or pneumonia
	64 outpatient clinics, about 50 GPs, 30 TCM clinics	Prior WHO definition*
Fiji	5 sentinel sites	Sudden onset of fever of >38 °C plus cough and/or sore throat
Japan	Approximately 5000 sentinel health facilities (approximately 3000 paediatric and 2000 internal medicine health-care facility sites)	1) All of the following: sudden onset, high fever, upper respiratory tract inflammation, general malaise or other systemic symptoms. OR: 2) confirmation based on rapid diagnostic kit (regardless of symptoms).
Lao People's Democratic Republic	8 hospitals	Acute respiratory infection with fever of ≥ 38 °C and cough, with onset within last 7 days
Malaysia	239 sentinel outpatient sites	Prior WHO definition*
Mongolia	115 sentinel sites	2014 WHO definition**
New Zealand	Approximately 200 GPs	An acute respiratory tract infection with abrupt onset of at least two of the following: fever, chills, headache and myalgia
	Call centre network	One of 18 symptoms
Papua New Guinea	2 hospitals	Prior WHO definition*
Philippines	18 sites	Prior WHO definition*
Republic of Korea	200 sentinel clinics	Sudden onset of fever of >38 °C and cough or sore throat
Singapore	18 polyclinics, 99 GPs	An acute respiratory infection with measured fever of ≥ 38 °C and cough or sore throat; with onset within the last 10 days
Viet Nam		
Hanoi	15 sentinel hospitals	Prior WHO definition*
Ho Chi Minh City	5 sentinel hospitals	Prior WHO definition*

*Prior WHO definition: a person with sudden onset of fever of >38 °C and cough or sore throat in the absence of other diagnosis

**2014 WHO definition: acute respiratory infection with measured fever of ≥ 38 °C and cough; with onset within the last 10 days

ED: emergency department; GP: general practitioner; TCM: traditional Chinese medicine

Note: no data provided for New Caledonia (France)

tested were positive for influenza virus, with a yearly variation from 9% to 17% positive.

Epidemiologic data were provided by 12 countries and areas. Fiji, New Caledonia, New Zealand and Papua New Guinea provided total number of weekly ILI consultations. Hong Kong SAR provided weekly ILI consultation rates per 1000 consultations by type of surveillance system (for example, general practitioners or traditional Chinese medicine practitioners). Australia, Cambodia, China, the Lao People's Democratic Republic, Malaysia, Mongolia, Singapore and Viet Nam provided data on number of ILI cases and total consultations.

Between 2011 and 2015, peaks in per cent ILI were generally consistent with per cent positive trends, particularly in the northern temperate and southern zones (Fig. 1). In Mongolia and the Republic of Korea, per cent ILI and per cent positive followed a northern temperate trend with yearly seasonal peaks occurring in the winter between January and March (Panel A, Fig. 1). Japan also exhibited the temperate northern hemisphere seasonality with distinct peaks in number of positive specimens seen at the beginning of each year (January or February). China (including Hong Kong SAR) demonstrated a bimodal influenza season with peak influenza activity between January and March consistent with the northern

Table 2. Specimens tested and specimens positive for influenza by type/subtype/lineage in Western Pacific Region countries, 2011–2015

	2011*	2012**	2013**	2014**	2015***
Number of specimens tested	217 975	339 229	456 918	583 004	652 124
Number of influenza positive specimens	24 382 (11.2%)	58 430 (17.2%)	42 251 (9.2%)	86 884 (14.9%)	81 554 (12.5%)
Seasonal influenza-positive specimens by type/subtype/lineage					
Influenza A total	14 994	31 617	33 921	63 301	55 471
A(H1)	10 487	963	15 855	22 909	4598
A(H3)	3460	28 542	17 064	38 519	50 588
A(other)	1039	2101	975	1862	1710
Influenza B total	9387	26 813	8309	23 556	26 136
B(Victoria)	728	8911	451	704	1368
B(Yamagata)	468	3837	1867	8641	16 593
B(lineage not determined)	8191	14 065	5991	14 211	8476

Note: total number of influenza positive specimens includes seasonal and non-seasonal influenza subtypes while influenza positive specimens by type/subtype/lineage includes only seasonal influenza

* 2011: Data from Australia, Cambodia, China, Fiji, the Lao People's Democratic Republic, Mongolia, Malaysia, New Caledonia (France), New Zealand, the Philippines, the Republic of Korea, Singapore and Viet Nam

** 2012–2014: Data from 2011 countries plus Hong Kong SAR

*** 2015: Data from 2012–2014 countries plus Papua New Guinea

temperate season and secondary peaks occurring in June or July in some years (Panel B, Fig. 1). Seasonal trends were less evident for countries in the tropical region with occasional peaks several times a year. In 2014–2015, a peak around July appears to correspond with the secondary peak seen in China (including Hong Kong SAR) (Panels B and C, Fig. 1). The southern zone showed evidence of seasonal influenza transmission with highest levels of positive specimens and per cent ILI consultations reported between July and September each year (Panel D, Fig. 1).

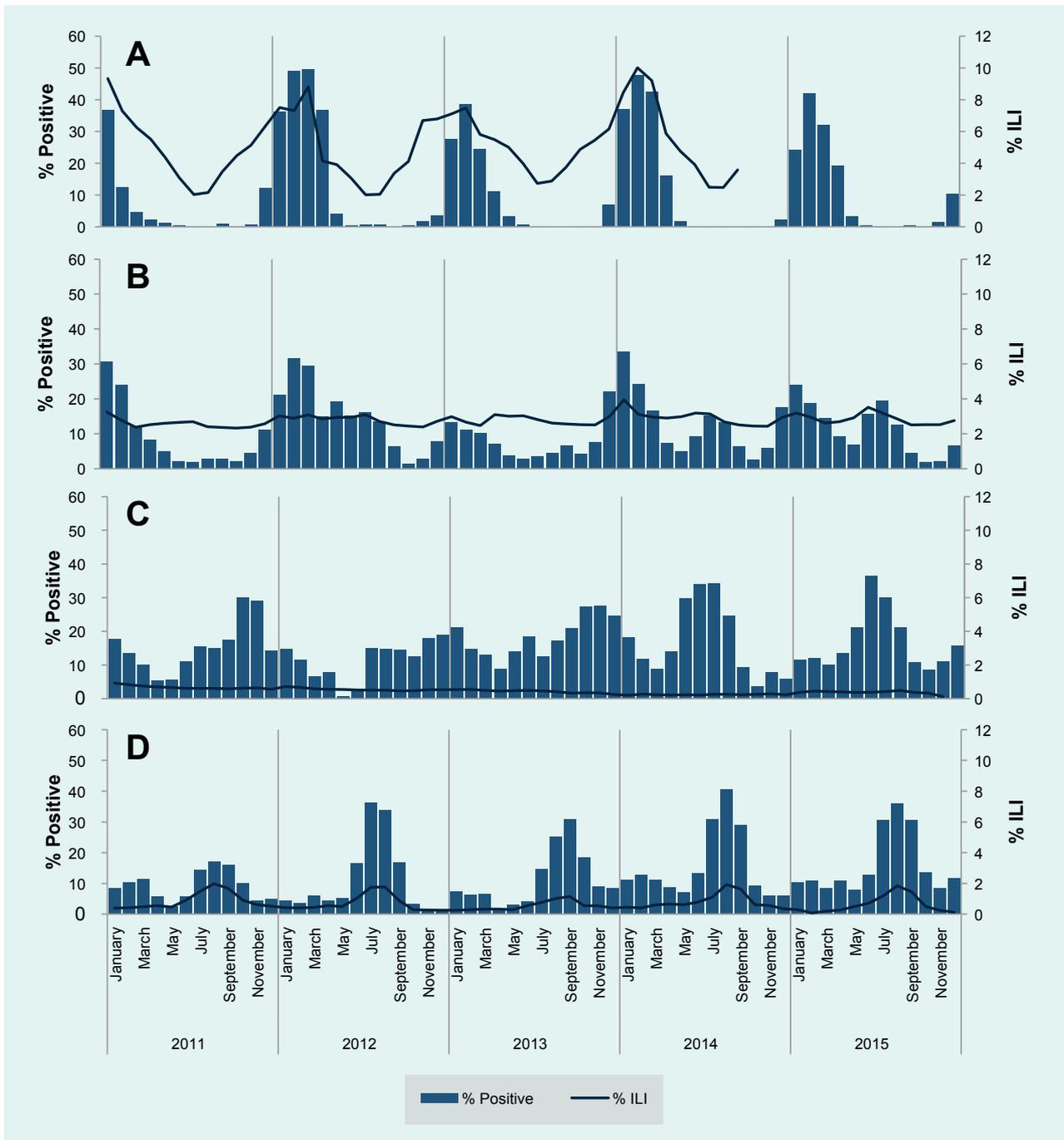
Influenza A was the predominant influenza type reported across all five years, for the entire WPR and by zone (Table 2 and Fig. 2). In 2011, influenza virus A(H1) predominantly circulated during the first half of the year followed by B (lineage not determined) later in the year (Table 2 and Fig. 2). In 2012, influenza B continued to circulate into the beginning of 2012 until influenza A(H3) began to predominate for the remainder of the year. From 2012 to 2015, the subtype A(H3) accounted for the largest proportion of the total influenza samples – ranging from 40% to 62%. From 2012 to 2015, A(H3) was the most frequently reported influenza subtype while secondary influenza subtypes and lineages varied during this time.

DISCUSSION

All countries and areas with NICs in WPR exhibited expected seasonal influenza prevalence and trends from 2011 to 2015. Advances in surveillance systems and laboratory capacity have been well documented over the past 10 years. There was a 10-fold increase in the number of ILI specimens tested between 2006 and 2015, driven predominately by increases in data submissions from China (including Hong Kong SAR).¹² This increase was likely due in part to increased awareness of the importance of specimen collection and submission following the A(H1N1) 2009 pandemic.¹² These data improve regional understanding of circulating viral subtype seasonal trends despite variations in laboratory and surveillance systems, case definitions and number of surveillance sites.

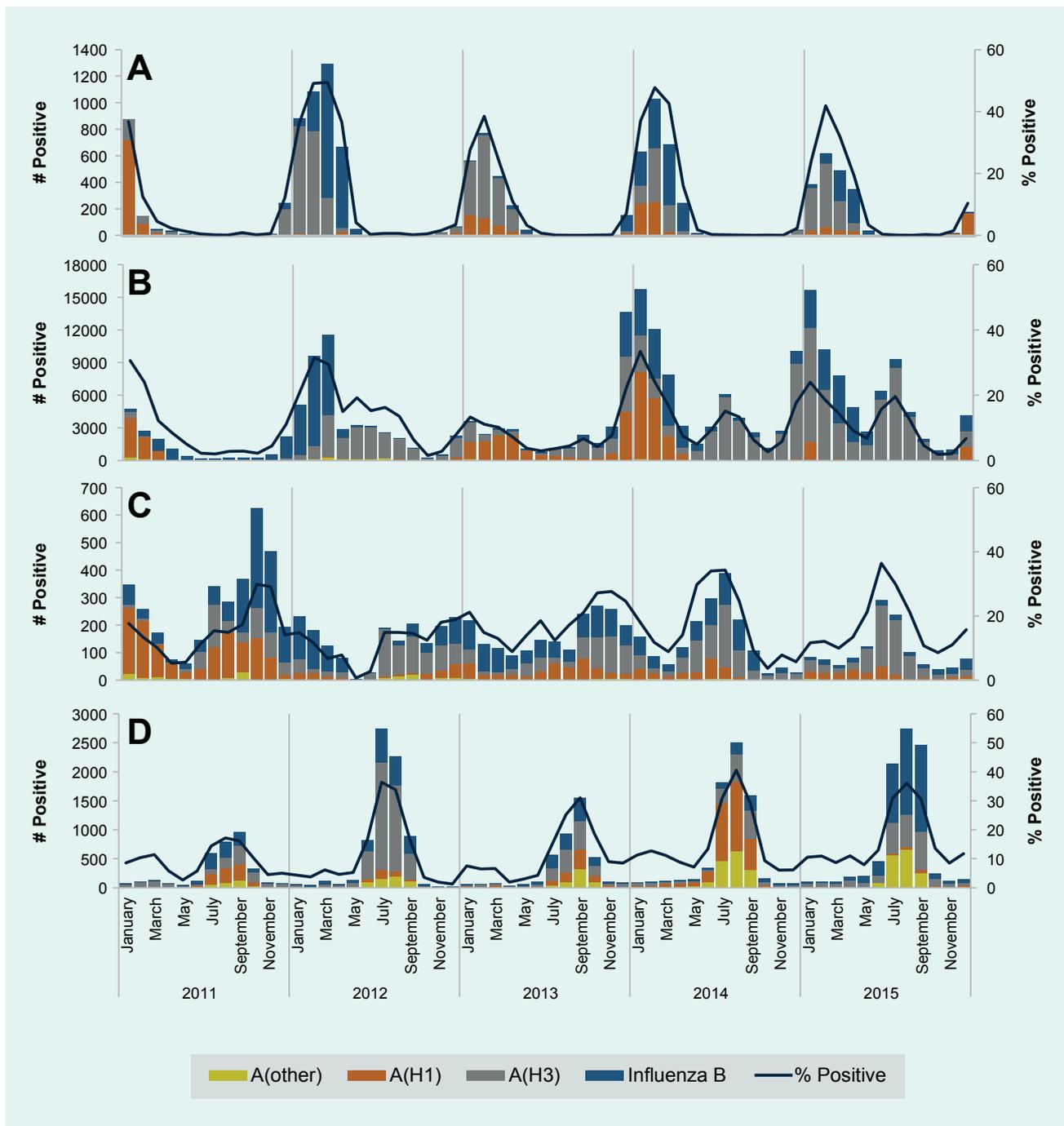
All 15 countries and areas surveyed have sentinel influenza surveillance systems in place. Since the last regional overview, ILI case definitions and number of surveillance sites have changed within many countries included in this review (see Table 3). The previous regional overview (2006–2010) reported that eight countries and areas used the WHO case definition.¹² In 2014, the official WHO case definition for ILI changed from sudden onset of fever of >38 °C and cough or sore throat to a

Fig. 1. Proportion of specimens positive for influenza virus and proportion of consultations meeting influenza-like-illness (ILI) case definition by subregion within the Western Pacific Region, 2011–2015



Panel A: Northern temperate (% positive from Mongolia and the Republic of Korea and % ILI from Mongolia (2011–2014)); **Panel B:** China and Hong Kong SAR (% positive from China and Hong Kong SAR and % ILI from China); **Panel C:** Tropics (% positive from Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam and % ILI from Cambodia (2011–October 2015), the Lao People’s Democratic Republic (2011–September 2015), Malaysia (2011–November 2015), Singapore (2011–2015) and Viet Nam (January–November 2015)); **Panel D:** Southern zone (% positive from Australia, Fiji, New Caledonia (France), New Zealand, Papua New Guinea and % ILI from Australia)

Fig. 2. Number of influenza viruses by type/subtype and proportion of specimens positive for influenza virus in Western Pacific Region, 2011–2015



Panel A: Northern temperate (Mongolia and Republic of Korea); **Panel B:** China and Hong Kong SAR; **Panel C:** Tropics (Cambodia, Lao People's Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam); **Panel D:** Southern zone (Australia, Fiji, New Caledonia (France), New Zealand, and Papua New Guinea)

Table 3. ILI case definitions and surveillance systems in the Western Pacific Region, 2006–2010 compared to 2011–2015

Year	Country	Surveillance system	ILI case definition
2006–2010	Australia	Approximately 25 GP clinics 69 EDs	Fever (≥ 38 °C), cough and fatigue Fever (≥ 38 °C) or feverish plus at least one of the following symptoms: cough or sore throat
		Community online data collection	Cough and fever
2011–2015		242 GPs and 69 EDs	Fever (≥ 38 °C), cough and fatigue (some within four days of presentation)
		Community online data collection and national call centre network	Cough and fever
2006–2010	Cambodia	8 hospitals	Sudden onset of fever of >38 °C and cough or sore throat within 5 days
2011–2015		7 outpatient department hospitals	Sudden onset of fever ≥ 38 °C axillary within 5 days of presentation and fever at time of presentation, cough and/or sore throat in absence of other diagnosis
		3 health facilities	Sudden onset of fever ≥ 38 °C axillary and fever at time of presentation, cough and/or sore throat in absence of other diagnosis
2006–2010	China	2010: 556 sentinel hospitals and 411 network laboratories	Sudden onset of fever of >38 °C and cough or sore throat
2011–2015		562 hospitals and 408 network laboratories	As above
2006–2010	Hong KongSAR	114 public and private outpatient clinics	Prior WHO definition*
2011–2015		17 EDs	Cases with clinical diagnosis related to influenza, upper respiratory tract infection, fever, cough, sore throat or pneumonia
		64 outpatient clinics, 50 GPs, 30 TCM clinics	Prior WHO definition*
2006–2010	Fiji	13 sentinel hospitals	Prior WHO definition*
2011–2015		5 sentinel sites	Sudden onset of fever of >38 °C plus cough and/or sore throat
2006–2010	Japan	3000 paediatric and 2000 internal medicine sites	Sudden onset of fever of >38 °C, upper respiratory infection and feeling tired
2011–2015		Approximately 5000 sentinel health facilities (approximately 3000 paediatric and 2000 internal medicine health care facility sites)	1) All of the following: sudden onset, high fever, upper respiratory tract inflammation, general malaise or other systemic symptoms, OR: 2) confirmation based on rapid diagnostic kit (regardless of symptoms).
2006–2010	Lao People's Democratic Republic	8 hospitals	Prior WHO definition*
2011–2015		8 hospitals	Acute respiratory infection with fever of ≥ 38 °C and cough, with onset within last 7 days
2006–2010	Malaysia	Approximately 600 government health clinics	Prior WHO definition*
2011–2015		239 sentinel outpatient sites	Prior WHO definition*
2006–2010	Mongolia	37 hospitals and 121 health centres	Prior WHO definition*
2011–2015		115 sentinel sites	New WHO definition**
2006–2010	New Caledonia (France)	2 hospitals and 7 health centres	Sudden onset of fever ≥ 38 °C (or shiver if temperature not available) and cough (or sore throat)
2006–2010	New Zealand	Approximately 101 sentinel GPs operating May–September	An acute respiratory tract infection with abrupt onset of at least two of the following: fever, chills, headache and myalgia
2011–2015		Approximately 200 GPs	As above
		Call centre network	One of 18 symptoms
2011–2015	Papua New Guinea	2 hospitals	Prior WHO definition*
2006–2010	Philippines	59 health centres and hospitals	Fever of >38 °C and cough or sore throat. For children ≤ 3 years, fever of >38 °C and cough, sore throat or runny nose
		18 sites	Prior WHO definition*
2006–2010	Republic of Korea	Approximately 800 sentinel sites	Sudden onset of fever of >38 °C and cough or sore throat
2011–2015		200 sentinel clinics (since 2013)	Sudden onset of fever of >38 °C and cough or sore throat
2006–2010	Singapore	18 government clinics, 98 GP clinics	Prior WHO definition*
2011–2015		18 polyclinics, 99 GPs	An acute respiratory infection with measured fever of ≥ 38 °C and cough or sore throat; with onset within the last 10 days
2006–2010	Viet Nam		
	Hanoi	15 sentinel hospitals	Prior WHO definition*
	Ho Chi Minh City	5 sentinel hospitals	Prior WHO definition*
2011–2015	Hanoi	15 sentinel hospitals	Prior WHO definition*
	Ho Chi Minh City	5 sentinel hospitals	Prior WHO definition*

* Prior WHO definition: a person with sudden onset of fever of >38 °C and cough or sore throat in the absence of other diagnosis

**New WHO definition: acute respiratory infection with measured fever of >38 °C and cough; with onset within the last 10 days

ED: emergency department; GP: general practitioner; TCM: traditional Chinese medicine

Note: no data provided for New Caledonia (France) 2011–2015

new case definition that removed sore throat from the definition and required symptom onset within 10 days of presentation.¹³ In 2015, one country used the 2014 WHO case definition, five countries and areas reported the use of the previous WHO case definition, and the other countries reported use of alternatives (see [Table 1](#)). As changes in case definition have been shown to impact the sensitivity and positive predictive value of ILI sentinel surveillance, this should be taken into consideration when interpreting these results.¹³

The proportion of outpatient visits for ILI followed expected trends in the northern temperate zone, China (including Hong Kong SAR) and the southern zone, with peak consultations occurring during the same months as peak per cent positive specimens ([Fig. 1](#)). Per cent ILI in the tropical zone was low and consistent throughout the year. Seasonal trends in circulating virus identified predictable temperate zone peaks and consistent tropical circulation similar to the previous regional overview.¹² However, in 2014 and 2015, both China (including Hong Kong SAR) and the tropics appear to exhibit more distinct seasonal patterns with a bimodal distribution in China (including Hong Kong SAR) and occasional sharp peaks in the tropics (Panels B and C, [Fig. 2](#)).

Improvements in tropical indicator-based surveillance for ILI over recent years indicate that more definitive determination of tropical seasonality may be possible in the near future. For example, in the American tropics a recent study has shown that 13 out of 16 countries in that region experience peak influenza transmission between April and September with smaller secondary epidemics.¹⁴ The observed peaks were not as distinct as those found in temperate regions; however, initial patterns of predictable seasonality emerged. This evidence of influenza seasonality illustrates the importance of strong outpatient indicator-based surveillance systems and reporting for determining seasonality which may impact vaccine policy.

The 2012 report recommended advancement of the following three areas of influenza surveillance: (a) improving virological testing capacity, (b) improving communication through regional and global networks, and (c) defining regional burden of disease.¹² Advances were documented in all three areas. Virological testing

capacity continues to be strengthened. The number of reported virological tests conducted on influenza specimens has steadily increased from 65 103 specimens in 2006 to 307 584 in 2010¹² and 652 124 in 2015; some countries showed slight decreases in the amount of data submitted as they continue to optimize their surveillance systems. Although the increase in number of samples over time does not necessarily constitute system improvement, consistent specimen submission does indicate both improved capacity and continued viability of the system itself. Evidence from the WHO external quality assessment programme shows an increase in the number of laboratories in the Region participating in the programme and consistently good results from participating laboratories (personal communication). Continued efforts placed on quality laboratory testing will ensure an accurate understanding of influenza in the Region.

Communication in the Region and globally continues to improve with increased reporting by NICs to FluNet. Other platforms such as the biweekly influenza situation updates published by the WHO Western Pacific Regional Office and periodic journal articles illustrate how communication and collaboration within the Region is prioritized. Using data visualization technologies, an online regional influenza dashboard is under way to integrate laboratory and epidemiological data in near real-time and provide a more complete picture of regional influenza activity. Finally, significant progress in regional risk communication capacity in response to recent emerging events (for example influenza A(H7N9) in China, 2013 and Zika, 2016) also benefits influenza surveillance and response efforts.¹⁵

Influenza surveillance in the Region continues to advance, and efforts to determine burden of disease are ongoing. WHO guidelines recommend assessing burden from acute lower respiratory infection and/or severe acute respiratory infection surveillance.¹⁶ Several WPR countries, including Cambodia, the Lao People's Democratic Republic, Mongolia and Viet Nam, have begun burden of disease estimates including sentinel site catchment population determination. These estimates will contribute to national, regional and global burden estimates and may support consideration of vaccination in high-risk populations.

Conclusions and way forward

Successful collaborative efforts between 2011 and 2015 continue to outline influenza epidemiological and virological characteristics in WPR and improve data to support ongoing public health action. A geographically wide range of influenza circulation patterns, covered by an extensive outpatient surveillance network, indicated temperate and tropical trends similar to those reported previously. Moving forward, WPR countries and areas are encouraged to focus on continued virus sharing through global networks while strengthening event-based surveillance, risk assessment and decision-making capacities. In addition, prioritization of high-quality, representative surveillance data of both outpatient and hospitalized respiratory disease will allow, respectively, improved appreciation of seasonality and economic burden of disease estimates. Finally, such estimates will support national influenza vaccination policies in high-risk groups. Advances in these areas will allow the Region to remain vigilant in the face of the continued, unpredictable influenza threat and further support the critical use of influenza vaccines in vulnerable populations.

Conflicts of interest

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