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# **National burden of influenza-associated hospitalizations in Cambodia, 2015 and 2016**

## **Supplementary appendix**

### **Appendix I. Severe Acute Respiratory Infection (SARI) sentinel surveillance sites**

SARI sentinel sites were Svay Rieng Provincial Hospital (located in Svay Rieng province, south-eastern Cambodia, near the Vietnam border), Angkor Hospital for Children (located in Siem Reap province, north-western Cambodia), and Kampong Cham Provincial Hospital (located in Kampong Cham province, central lowlands of Cambodia). Two of the public healthcare facilities (HCFs) were public general hospitals (Svay Rieng, a 168-bed facility, and Kampong Cham, with 265 beds) serving a predominantly rural population and one was an 85-bed paediatric hospital located in a township (Siem Reap). Selected sentinel sites provided a climatically and demographically representative sample of hospitalisations in Cambodia. Our analysis used surveillance data for 2015 for Svay Rieng Provincial Hospital, and surveillance data for 2016 for the two other sites. Field work was conducted in Svay Rieng in 2016 with the aim of operationalising methods recommended by the World Health Organization to estimate influenza burden.<sup>1</sup> Field work for the remaining sites was conducted a year later incorporating lessons learned the previous year.

## **Appendix II. Case definitions and laboratory methods**

All sentinel sites used the same SARI case definition. Clinical examination of cases was conducted by hospital clinicians and recorded with demographic information on a standardised case report form.

### **Influenza case definition**

An influenza case was defined as laboratory confirmation of influenza infection through detection of influenza A or B ribonucleic acid (RNA) in a person with SARI.

### **Laboratory methods**

All hospitalised patients meeting the SARI case definition were eligible to have nasopharyngeal swabs collected soon after admission using previously described protocols.<sup>2</sup> Specimens from children under five years of age were collected with parental consent. Each week, swabs were transported in viral transport media to the National Public Health Laboratory in Phnom Penh for testing. Viral RNA was extracted from specimens using the QIAamp Viral RNA Isolation Kit (QIAGEN, Valencia, CA, USA) and amplified using a multiplex real time reverse transcription polymerase chain reaction (real time RT PCR) targeting seasonal influenza A and B viruses as previously described.<sup>3</sup> All influenza-positive specimens and 10% of negative specimens were forwarded to the Virology Unit at Institut Pasteur du Cambodge in Phnom Penh for confirmation, using real time RT PCR as previously described.<sup>2</sup>

## **Appendix III. Staff survey methodology and results**

### **Staff survey methodology**

We administered structured, face-to-face questionnaires to all clinical staff responsible for enrolling SARI patients at two sentinel sites (five in Siem Reap: three physicians and two nurses; and 19 in Kampong Cham: six physicians and 13 nurses). Questionnaires were designed to gain insight into the enablers, benefits and challenges of SARI surveillance, the mechanisms for case identification, specimen collection and patient management at each site. Interviews were conducted in English with the assistance of one translator at the Siem Reap site, and in Khmer at the Kampong Cham site. Qualitative content analysis was applied to interview responses as previously described.<sup>4</sup> The two main themes explored by the questionnaire were perceptions regarding participation in SARI surveillance and the technical aspects of SARI surveillance. Text from all interviews was abstracted into several codes within three categories: enablers, benefits and challenges of participating in SARI surveillance.

### **Staff survey results**

Content analysis of the qualitative interviews administered to 24 staff at the Siem Reap and Kampong Cham sentinel sites are shown in Table 1.

The main benefits cited from participating in SARI surveillance were the opportunity for professional development through increased understanding of the importance of SARI, acquiring technical skills in swabbing patients and gaining confidence educating patient contacts about SARI.

In terms of the technical aspects of SARI surveillance, respondents reported strict adherence to the SARI case definition when determining whom to swab and that it was expected that swabbing would assist in differential diagnoses. However, flexibility in swabbing practices was mentioned, meaning that swabs were also sometimes collected from patients with suspected influenza or atypical SARI presentation. Clinicians reported that their decision to swab a patient was influenced by their awareness of surveillance reports indicating increased community-acquired influenza. Some respondents reported avoiding taking specimens from patients under three months of age and young children.

Analysis of responses discussing the impact that participating in SARI surveillance had on clinical patient management showed mixed results. Some respondents reported no change in use of antivirals while some reported a change although it was not clear if this represented an increase or a decrease in use. A physician stated, 'Here we don't use antivirals much. We only use them when we suspect avian flu.' Some reported that diagnosing SARI became easier and one reported a reduction in use of antibiotics as a result of participation in SARI surveillance.

#### **Appendix IV. Estimated catchment populations of sentinel surveillance sites**

In each hospital admission survey (HAS), we collected data on a proxy measure for SARI hospitalisations in non-sentinel healthcare facilities identified in the catchment area of each site. The overall proportion of patients admitted due to SARI at SARI sentinel sites out of the total SARI proxy admissions at all HCF in the catchment area was 52% for Svay Rieng Provincial Hospital, 18% for Angkor Hospital for Children (Siem Reap) and 21% for Kampong Cham Provincial Hospital. The age-specific proportion of patients admitted to each sentinel site and their estimated catchment populations are shown in Table 2.

**Table 1** Summary of interview responses regarding enablers, challenges and technical aspects of severe acute respiratory illness (SARI) surveillance among SARI surveillance staff, May and July 2017, Siem Reap and Kampong Cham sites, Cambodia,.

<b>‘From a user perspective, what are the enablers, benefits and challenges of SARI surveillance at your facility?’</b>		
Perceptions regarding participation in SARI surveillance system		
Enablers	Benefits	Challenges
Very acceptable/acceptable workload	Opportunity for professional development	Obtaining parental consent for specimen collection in children
Sharing surveillance tasks among staff	SARI epidemiology knowledge acquisition	Difficulty swabbing distressed children
Sharing responsibility in SARI diagnosis	Gain technical skills in swabbing patients	Incomplete/unclear medical history
Case definition is a useful guide	Increased confidence educating patient contacts about SARI	Delays in obtaining laboratory results, exacerbated by lack of weekend specimen processing
Flexible swabbing practices (swab collected if requested by senior staff and if SARI was suspected even if case does not fit case definition)		SARI more difficult to identify in neonates
Infants (1 month - 2 years) easier to identify in high season		Lack of knowledge on swab collection technique, swabbing kit stock outs, lack of access to training
Useful when internal influenza activity reports are available		Poor reporting feedback of SARI activity
Cooperation among staff		Fear of reprimand if unable to obtain consent to swab

Table 1 Cont.

<b>What are the mechanisms for case identification, swabbing and patient management at sentinel sites?</b>	
Technical aspects of SARI surveillance	
Swabbing practices (who, when, why)	Change in clinical patient management
Mostly patients with classical SARI symptoms (as per case definition)	No change in antiviral use
Infants (< 3months) and young children sometimes avoided due to lack of parental consent or difficulties swabbing	Reduction in antibiotic use
Sometimes patients with unusual presentation (SARI suspicion)	SARI became easier to diagnose
Increases in reported community-acquired influenza prompts to swab	
When seeking differential diagnosis	

Notes:

Nine physicians and 15 nurses were interviewed.

Items are listed in no particular order.

**Table 2** Estimated catchment population by age group for three SARI sentinel healthcare facilities in Cambodia, 1 January – 31 December 2015 (Svay Rieng), and 1 January 1 – 31 December 2016 (Siem Reap and Kampong Cham).

Age Group (years)	Svay Rieng				Siem Reap				Kampong Cham			
	Influenza-associated SARI cases†	Population*	Proportion of patients admitted to SRPH	Estimated catchment population for SRPH	Influenza-associated SARI cases†	Population*	Proportion of patients admitted to AHC	Estimated catchment population for AHC	Influenza-associated SARI cases†	Population*	Proportion of patients admitted to KCPH	Estimated catchment population for KCPH
	A	B	C	D = B x C	A	B	C	D = B x C	A	B	C	D = B x C
<1	0	9,010	0.56	5,046	47	39,206	0.35	13,722	38	30,812	0.25	7,698
1 - 4	2	32,872	0.41	13,478	41	142,108	0.14	19,812	53	116,560	0.14	15,771
5 - 15	2	87,162	0.49	42,709	9	329,531	0.83	27,386	47	303,245	0.07	24,069
16 - 24	1	101,926	0.52	53,002	NA				11	330,044	0.20	65,720
25 - 49	3	145,348	0.57	82,848					28	458,514	0.27	125,564
50 - 64	4	53,433	0.58	30,991					28	164,949	0.38	62,329
≥65	5	23,048	0.60	13,829					37	84,554	0.40	33,660
Total	17	452,799	0.52	241,902	97	510,845	0.18	60,920	242	1,488,678	0.21	334,812

**Notes:**

AHC: Angkor Hospital for Children; KCPH: Kampong Cham Provincial Hospital; SRPH: Svay Rieng Provincial Hospital

†Influenza-associated SARI cases were adjusted by applying the age-specific percent positive for influenza for each month (proportion of positive specimens from total number of specimens tested) to the corresponding SARI case count for each month.

\*Population data was obtained from the Ministry of Health Management Information System.

## References

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