Annual circulation of influenza viruses causes substantial disease and death worldwide, disproportionately affecting young children and older adults (1,2). Globally, influenza causes ≈9.4 million hospitalizations each year (3) but remains an under-recognized contributor to hospitalizations in many countries (4). In 2014, the World Health Organization (WHO) published a manual to guide countries to estimate influenza disease burden using influenza surveillance data (5–10). Such estimates have been instrumental in demonstrating influenza as a common cause of hospitalization in tropical and low- and middle-income countries (11), including Southeast Asia countries (8,10,12), and have provided a platform for evaluating the cost-effectiveness of influenza vaccines. Country-specific burden estimates can inform decisions to invest resources in influenza prevention and control programs (4,13), whereas studies from other countries may not be sufficiently compelling among national leaders to guide policy or investments (14).

During the past 40 years, Vietnam has experienced rapid economic growth, shifting from a low-income to a lower middle-income classification (15). Correspondingly, government spending on national health programs has increased, including efforts to address public health threats from human and zoonotic influenza (14). Vietnam has had sustained influenza surveillance programs since 2006, generating data about influenza virus circulation through influenza-like illness (ILI) and severe acute respiratory infection (SARI) surveillance. In 2019, the Institute of Vaccines and Medical Biologicals successfully licensed the first locally manufactured seasonal influenza vaccine (16). To sustain Vietnam’s influenza prevention and control programs, information about the annual disease burden and value of averting costly hospitalizations is useful. Building on the established SARI sentinel surveillance, we conducted a hospital admission survey...
Influenza-Associated Hospitalizations, Vietnam

Methods

Vietnam’s 63 provinces are divided into the north, central, highlands, and south major health regions. The healthcare system includes both public and private hospitals, but public hospitals are most commonly used (17). In 2011, the Vietnam Ministry of Health began adopting electronic medical records (EMRs) in all public hospitals (18,19). For the HAS, we selected 1 province per region that had all public hospitals using EMRs, a nearby provincial-level hospital enrolled in SARI surveillance using trained surveillance officers, and no private hospitals routinely admitting acute respiratory infection (ARI) patients.

To estimate the influenza-associated respiratory hospitalization rate in Vietnam for comparison with other countries, we combined existing virologic data from SARI sentinel surveillance (20), EMR data, and a medical record review of a random set of ARI hospitalizations (5). Influenza burden data were interpreted in conjunction with influenza seasonality to inform vaccine formulation considerations for maximizing population benefit.

Data Sources

ARI Hospitalizations

We defined an ARI hospitalization as a hospitalization with an admission code from the International Classification of Diseases, 10th Revision (ICD-10), for either acute upper respiratory infection (J06) or codes to approximate SARI (influenza, J09–11; pneumonia, J12–18; or other acute lower respiratory infections, J20–J22) (5). An overnight stay was not required because of variability in thresholds for admission, cultural practice of taking the most severely ill patients home, minimum availability of precise admission and discharge times, and possible patient transfer. Using the EMR system, public hospitals provided a list of patients with an ARI admission code during 2014–2016 with the following data: admission and discharge ICD-10 codes; hospital admission and discharge dates; patient residential province, age, and sex; and outcome of hospitalization at discharge.

Medical Record Review to Identify SARI Proportion

From ARI hospitalizations for each hospital, a random selection of medical records was reviewed by health officers and clinical data collected to evaluate both the 2011 and 2014 WHO SARI case definitions. The 2011 definition was sudden onset of fever ≥38°C, with cough or sore throat, and with shortness of breath or difficulty breathing, and illness requiring hospitalization; the revised 2014 definition was temperature of ≥38°C or history of fever, cough of duration ≤10 days, and illness requiring hospitalization. We assumed that 50% of ARI hospitalizations would meet SARI case criteria and assigned 80 records per hospital to reach a sufficient sample size with a 5% margin of error.

Influenza Test Results from SARI Sentinel Surveillance

In 2011, Vietnam initiated SARI surveillance in sentinel hospitals representing the 4 major regions of Vietnam; 6–14 hospitals participated per year. Each week, sentinel hospitals reported the total number of SARI admissions. Surveillance staff collected nasopharyngeal and oropharyngeal swabs from 8 SARI patients per week (protocols varied by hospital and ward). Demographic and clinical information also were collected. The National Influenza Center conducted real-time reverse transcription PCR to detect influenza A (subtypes A(H1N1)pdm09, A/H3, A/H5, and A/H7) and B (20). Influenza virologic surveillance data were obtained from all SARI sentinel hospitals participating in surveillance during 2014–2016.

Population Data

A national census survey was conducted in 2009 with annual population projections (21). To calculate population-based rates of ARI and SARI, we used 2014–2016 provincial and national population projections for 4 age groups: <5 years, 5–49 years, 50–64 years, and ≥65 years. Evaluation of 14 demographic, health, and healthcare characteristics in each province within the 4 regions demonstrated that provinces selected for the HAS were representative and could be combined for a national estimate of ARI and SARI rates in Vietnam (Appendix, https://wwwnc.cdc.gov/EID/article/27/10/20-4765-App1.pdf).

Data Analysis

ARI and SARI Hospitalizations

We reviewed the reported ARI hospitalizations and excluded patients with non-ARI ICD-10 codes and those residing outside of the province. Eight hospitals in 2014 and 7 in 2015 reported zero or near-zero ARI hospitalizations during the introduction of the EMR system. To compensate for underreporting, we used the individual hospital’s 2016 ARI counts to estimate the expected number of hospitalizations in 2014 and
2015. We further adjusted for patients with missing age information by using the distribution of patients with known ages (Appendix Figure 1). We assessed the percentage of ARI hospitalizations meeting the SARI case definition by province, hospital, year, age group, and ICD-10 code.

### Estimating the Rate of Influenza-Associated Hospitalizations

We estimated the influenza-attributable proportion of ARI and SARI hospitalizations by using 2014–2016 SARI sentinel surveillance data. We calculated influenza-associated ARI and SARI hospitalization rates by multiplying the age- and month-specific number of hospitalizations and percentage of SARI surveillance patients positive for influenza, then dividing by the age-specific census population estimates for each province. We summed the monthly rate estimates to calculate the annual age-adjusted rates. We calculated the 95% uncertainty intervals (UI) for estimated rates by using 1,000 Monte Carlo simulation iterations, assuming a Poisson distribution for the number of hospitalizations and a binomial distribution for the proportion of SARI patients positive for influenza. We used the same method to calculate influenza-associated SARI hospitalization rates, but first we multiplied ARI hospitalization totals by the percentage of ARI hospitalizations meeting SARI criteria to obtain the age- and month-specific number of influenza-associated SARI hospitalizations. The 95% UIs assumed a binomial distribution for the proportion meeting the SARI case definition. We extrapolated the number of influenza-associated ARI and SARI hospitalizations by multiplying age-specific influenza rates by the provincial census population.

To estimate national rates, we summed age- and month-specific provincial counts of all-cause ARI and SARI and influenza-associated ARI and SARI across the provinces, and then divided the sum by the total population of the 4 provinces. We obtained the 95% UIs by calculating the upper and lower 2.5% percentiles from the distribution of provincial rate estimates.

We used χ² tests of proportions to assess statistical differences and calculate 95% CIs by using the observed data when appropriate. We performed all analyses using SAS 9.4 (SAS Institute, https://www.sas.com).

This activity was reviewed by the US Centers for Disease Control and Prevention and the ethics committee and scientific committee of the National Institute of Hygiene and Epidemiology (Hanoi, Vietnam). The data are considered nonresearch; therefore, Institutional Review Board review was not required.

### Results

#### Reported ARI Hospitalizations

The provinces identified for the HAS included Quang Ninh (14 hospitals) in the north region, Khanh Hoa (10 hospitals) in the central region, Dak Lak (15 hospitals) in the highlands region, and Dong Thap (12 hospitals) in the south region (Figure 1). During January 2014–December 2016, a total of 220,217 ARI hospitalizations were reported, excluding 2,781 patients living outside of the province and 4,960 patients who did not have qualifying ARI ICD-10 codes. We identified 8 hospitals with clear underreporting during EMR implementation in 2014 and 2015 and imputed the expected number of ARI hospitalizations by using the 2016 percentage distribution of patient counts across hospitals, giving an overall estimated 4.1% underreporting of ARI hospitalizations and an adjusted total of 229,144 ARI hospitalizations included in analysis.

Among patients with known age, 61% were <5 years, 15% were 5–49 years, 7.4% were 50–64 years, and 17% were ≥65 years (Table 1). The median length of hospitalization was 6 days (interquartile range 4–6 days). Among 180,316 ARI hospitalizations with a known discharge disposition, 482 (0.3%) patients died and 4,376 (2.4%) were sent home as too severely ill to be cured.

#### Estimated SARI Hospitalizations

Of 3,626 medical record reviews from ARI hospitalizations, 61% met the SARI case definition, whereas 27% did not have documented fever, 8% did not have cough, and 4% had neither. SARI accounted for 75% of ARI hospitalizations among children <5 years of age, compared with patients 5–49 years of age (59%), 50–64 years of age (38%), and ≥65 years of age (34%) (p<0.001) (Table 1). The ICD-10 codes most commonly listed for patients with illness meeting SARI criteria were acute bronchiolitis (J21 [72%]) and acute upper respiratory tract infection (J06 [71%]) among codes reported for ≥10 patients. Influenza codes were reported infrequently, and significantly less frequently among patients with illness meeting the SARI criteria (37%) compared with other diagnoses (p<0.001) (Table 1).

#### Influenza Detection

The SARI sentinel surveillance collected specimens from 6,647 patients. Influenza detection varied significantly by age (p<0.001), and was less frequent among children <5 years of age (13% [95% CI 12%–14%]) and patients ≥65 years of age (16% [95% CI 14%–18%])
compared with patients 5–49 years of age (23% [95%
CI 21%–24%]) and patients 50–64 years of age (23%
[95% CI 20%–25%]). The age-weighted proportion of
samples testing positive for influenza was 22% (95%
CI 21%–23%), varying by year (20% in 2014, 18% in
2015, and 23% in 2016). Influenza detections did not
vary substantially by region (Appendix Figure 2);
therefore, we combined data to allow stratification by
age and month.

Across all years, ≈74.4% of influenza detections
occurred during March–July (Figure 2). Influenza A
viruses predominated in 2014 and 2015; subtype H1N1
made up 44% of viruses detected in 2014 and subtype
H3N2 65% of viruses detected in 2015. In 2016, influ-
enza viruses cocirculated; 36% were A(H1N1), 28%
A(H3N2), and 35% B, but H1N1 and B co-circulated
during March–June, whereas most H3N2 detections
occurred during June–November (Figure 2).

Rates of Influenza-Associated ARI and
SARI Hospitalizations

Provincial Rates of Influenza-Associated ARI and
SARI Hospitalizations
During 2014–2016, the mean annual influenza-assoc-
iated ARI hospitalization rates ranged by province
from 183 (95% UI 159–206) to 284 (95% UI 256–312)
per 100,000 population (Table 2). The provincial in-
fluenza-associated ARI hospitalization rates were
lower in 2014, when influenza viruses were primarily
detected during January–June, compared with 2016,
when influenza was detected throughout the year
and all 3 viruses circulated.

National Rates of ARI Hospitalizations and Influenza-
Associated ARI Hospitalizations
Across the 4 provinces, the mean annual ARI
hospitalization rate was 1,263 (95% UI 1,248–
1,278)/100,000 population and the influenza-assoc-
iated ARI hospitalization rate was 218 (95% UI
197–238)/100,000 population (Table 3). The age-ad-
justed rate of influenza-associated ARI was higher
in 2016 (295 [95% UI 273–318]/100,000 population)
compared with 2014 (142 [95% UI 128–157]/100,000
population). After extrapolating provincial rates to
Vietnam’s population of ≈93 million during 2014–
2016, we estimated that 129,019 influenza-associat-
ed ARI hospitalizations occurred in 2014, 195,795
in 2015, and 273,357 in 2016. Using the extrapolated
counts, we found that the mean influenza-associ-
ted ARI hospitalizations during April–September,
when Southern Hemisphere influenza vaccines
typically are available, was 116,324 compared with
69,493 during October–March, when Northern
Hemisphere influenza vaccines typically are avail-
able (Appendix Figure 3).

National Rates of Influenza-Associated SARI
We estimated age-adjusted influenza-associated SARI
dates per 100,000 population of 87 in 2014, 134 in 2015,
and 180 in 2016. The mean age-adjusted annual rate
was 134 (95% UI 119–149)/100,000 population. Chil-
dren <5 years of age had the highest rates of influen-
za-associated SARI (1,123 [95% UI 946–1,301]/100,000
population), followed by adults aged ≥65 years (207
[95% UI 186–227]/100,000 population).
Discussion

Using HAS methodology in 4 of Vietnam’s provinces during 2014–2016, we estimated influenza virus infections were associated with 123,000–200,000 respiratory hospitalizations each year and demonstrated influenza as a common cause of hospitalization in young children and older adults. We estimated the influenza-associated hospitalization rate using both an expanded set of ICD-10 codes to define our ARI case definition (218/100,000 population) and a medical chart review to establish rates with the commonly used SARI case definition (134/100,000 population). Among age groups specifically recommended by WHO for vaccination (22), we estimated higher rates of hospitalization among children <5 years of age (ARI, 1,508/100,000 population; SARI, 1,123/100,000 population) and adults ≥65 years of age (ARI, 600/100,000 population; SARI, 207/100,000 population). We also found in any year that 74% of influenza detections were identified during March–July, when Southern Hemisphere influenza vaccines typically are available.

In Vietnam, influenza viruses were detected among 18%–23% of SARI patients, a finding that is consistent with assessments of influenza detection among SARI patients conducted in New Zealand and Hong Kong (23,24) but higher than those reported in systematic reviews that focus specifically on acute lower respiratory tract infections (2,3). Our influenza-associated SARI hospitalization rates were similar to those found in a study in the Philippines that used comparable methods (25) and other studies in Bhutan, Korea, Thailand, and China that reported a comparable percentage of cases positive for influenza (10,26–28). Our estimates among children <5 years of age (1,123/100,000 population) were 5–35 times higher than the other age groups, potentially reflecting differences in healthcare utilization. The government of Vietnam pays all medical costs for children <5 years of age, thus removing important barriers to healthcare access. Conversely, among adults ≥65 years of age, our estimated influenza-associated SARI hospitalization rate (207/100,000) was

Table 1. Percentages of ARI hospitalizations that met SARI case criteria from medical chart review, by age group, qualifying admission code, and province, Vietnam, 2014–2016*

<table>
<thead>
<tr>
<th>Category</th>
<th>Overall</th>
<th>Medical record reviewed</th>
<th>Met SARI criteria†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, y§</td>
<td>All ARI hospitalizations‡</td>
<td>220,217 (100)</td>
<td>3,626 (100)</td>
</tr>
<tr>
<td>&lt;5</td>
<td>132,076 (61.0)</td>
<td>1,934 (53.4)</td>
<td>1,443 (74.6)</td>
</tr>
<tr>
<td>5–49</td>
<td>32,112 (14.8)</td>
<td>716 (19.8)</td>
<td>421 (58.8)</td>
</tr>
<tr>
<td>50–64</td>
<td>16,030 (7.4)</td>
<td>324 (8.9)</td>
<td>123 (38.0)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>36,329 (16.8)</td>
<td>647 (17.8)</td>
<td>217 (33.5)</td>
</tr>
</tbody>
</table>

Table 1. Percentages of ARI hospitalizations that met SARI case criteria from medical chart review, by age group, qualifying admission code, and province, Vietnam, 2014–2016*

<table>
<thead>
<tr>
<th>Diagnosis, ICD-10 code</th>
<th>Overall</th>
<th>Medical record reviewed</th>
<th>Met SARI criteria†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute upper respiratory infections, J06</td>
<td>37,957 (17.2)</td>
<td>459 (12.7)</td>
<td>325 (70.8)</td>
</tr>
<tr>
<td>Influenza</td>
<td>4,278 (1.9)</td>
<td>82 (2.3)</td>
<td>30 (36.6)</td>
</tr>
<tr>
<td>Influenza caused by other identified influenza virus, J10</td>
<td>963 (0.4)</td>
<td>36 (1.0)</td>
<td>9 (25.0)</td>
</tr>
<tr>
<td>Influenza caused by unidentified influenza virus, J11</td>
<td>3,315 (1.5)</td>
<td>46 (1.3)</td>
<td>21 (45.7)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>117,890 (53.5)</td>
<td>1,946 (53.7)</td>
<td>271 (13.9)</td>
</tr>
<tr>
<td>Viral pneumonia, not elsewhere classified, J12</td>
<td>470 (0.2)</td>
<td>10 (0.3)</td>
<td>7 (70.0)</td>
</tr>
<tr>
<td>Pneumonia caused by Streptococcus pneumoniae, J13</td>
<td>82 (0)</td>
<td>9 (0.2)</td>
<td>7 (77.8)</td>
</tr>
<tr>
<td>Pneumonia caused by Hemophilus influenzae, J14</td>
<td>51 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Bacterial pneumonia, not elsewhere classified, J15</td>
<td>22,252 (10.1)</td>
<td>399 (11.0)</td>
<td>257 (64.4)</td>
</tr>
<tr>
<td>Pneumonia caused by other infectious organisms, J16</td>
<td>10,629 (4.8)</td>
<td>40 (1.1)</td>
<td>28 (70.0)</td>
</tr>
<tr>
<td>Pneumonia in diseases classified elsewhere, J17</td>
<td>65 (0)</td>
<td>3 (0.1)</td>
<td>3 (100.0)</td>
</tr>
<tr>
<td>Pneumonia, unspecified organism, J18</td>
<td>84,341 (38.3)</td>
<td>1,485 (41.0)</td>
<td>970 (65.3)</td>
</tr>
<tr>
<td>Other acute lower respiratory infections¶</td>
<td>60,092 (27.3)</td>
<td>1,139 (31.4)</td>
<td>578 (50.7)</td>
</tr>
<tr>
<td>Acute bronchitis, J20</td>
<td>55,492 (25.2)</td>
<td>1,096 (30.2)</td>
<td>547 (49.9)</td>
</tr>
<tr>
<td>Acute bronchiolitis, J21</td>
<td>4,563 (2.1)</td>
<td>43 (1.2)</td>
<td>31 (72.1)</td>
</tr>
<tr>
<td>Unspecified acute lower respiratory infection, J22</td>
<td>37 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*ARI, acute respiratory infection; ICD-10, International Classification of Diseases, 10th Revision; SARI, severe acute respiratory infection.
†Percentages show the overall proportion of patients in the listed category (column percentage).
‡Percentages show the proportion of patients with illness meeting SARI case criteria (row percentage), defined as temperature of ≥38°C or history of fever, cough of duration <10 d, and illness requiring hospitalization; all proportions varied substantially within categories.
§Age data were missing for 3,670 ARI and 5 patients with medical record review.
¶Admission ICD codes J14 and J22 were not identified among reviewed patient records; J09 was not identified among any patients.

In Vietnam, influenza viruses were detected among 18%–23% of SARI patients, a finding that is consistent with assessments of influenza detection among SARI patients conducted in New Zealand and Hong Kong (23,24) but higher than those reported in systematic reviews that focus specifically on acute lower respiratory tract infections (2,3). Our influenza-associated SARI hospitalization rates were similar to those found in a study in the Philippines that used comparable methods (25) and other studies in Bhutan, Korea, Thailand, and China that reported a comparable percentage of cases positive for influenza (10,26–28). Our estimates among children <5 years of age (1,123/100,000 population) were 5–35 times higher than the other age groups, potentially reflecting differences in healthcare utilization. The government of Vietnam pays all medical costs for children <5 years of age, thus removing important barriers to healthcare access. Conversely, among adults ≥65 years of age, our estimated influenza-associated SARI hospitalization rate (207/100,000) was
lower than those reported from the United States and Hong Kong (29,30).

Influenza burden estimates specific to Vietnam support local decision making and targeted risk communications for subpopulations at higher risk for influenza-associated complications and clinicians for targeted use of treatment and nonpharmaceutical interventions. In supporting decision-making for governmental leaders, burden estimates can provide evidence to sustain influenza surveillance programs and investments in pandemic planning, influenza treatment, and vaccination programs. The government of Vietnam has supported influenza virus surveillance and supported the development of the first licensed, locally produced influenza vaccine. Vaccination remains the best way to prevent influenza (29), and establishing a strong seasonal vaccine program may also be useful in providing the necessary infrastructure required for pandemic vaccines in the event of an emergent influenza virus or other pandemic respiratory viruses, such as severe acute respiratory syndrome coronavirus 2 (31). Burden estimates also can help in understanding the potential impact of a possible future vaccination program.

### Table 2. Provincial estimates of influenza-associated ARI and SARI hospitalizations and rates for all ages, Vietnam, 2014–2016*

<table>
<thead>
<tr>
<th>Year and province</th>
<th>ARI Hospitalizations</th>
<th>Estimated SARI Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (95% UI)</td>
<td>No. (95% UI)</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
<td>Influenza-associated rate</td>
</tr>
<tr>
<td>Dak Lak</td>
<td>20,746</td>
<td>1,017 (1,091–1,122)</td>
</tr>
<tr>
<td>Dong Thap</td>
<td>22,582</td>
<td>1,314 (1,297–1,330)</td>
</tr>
<tr>
<td>Khanh Hoa</td>
<td>20,433</td>
<td>1,665 (1,645–1,686)</td>
</tr>
<tr>
<td>Quang Ninh</td>
<td>12,620</td>
<td>1,030 (1,011–1,046)</td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dak Lak</td>
<td>18,592</td>
<td>1,004 (988–1,021)</td>
</tr>
<tr>
<td>Dong Thap</td>
<td>22,188</td>
<td>1,299 (1,281–1,319)</td>
</tr>
<tr>
<td>Khanh Hoa</td>
<td>18,788</td>
<td>1,546 (1,523–1,570)</td>
</tr>
<tr>
<td>Quang Ninh</td>
<td>11,171</td>
<td>921 (902–938)</td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dak Lak</td>
<td>19,605</td>
<td>1,046 (1,030–1,061)</td>
</tr>
<tr>
<td>Dong Thap</td>
<td>20,655</td>
<td>1,202 (1,185–1,219)</td>
</tr>
<tr>
<td>Khanh Hoa</td>
<td>20,919</td>
<td>1,705 (1,682–1,728)</td>
</tr>
<tr>
<td>Quang Ninh</td>
<td>11,216</td>
<td>915 (893–935)</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dak Lak</td>
<td>24,041</td>
<td>1,266 (1,249–1,283)</td>
</tr>
<tr>
<td>Dong Thap</td>
<td>24,903</td>
<td>1,440 (1,422–1,459)</td>
</tr>
<tr>
<td>Khanh Hoa</td>
<td>21,593</td>
<td>1,743 (1720–1768)</td>
</tr>
<tr>
<td>Quang Ninh</td>
<td>15,473</td>
<td>1,251 (1227–1273)</td>
</tr>
</tbody>
</table>

*Rates are given per 100,000 population and age-adjusted. Rates were calculated regionally using reported ARI hospitalizations multiplied by the percentage of patients meeting the SARI criteria upon medical chart review. Regional hospitalization counts were multiplied by the national percentage of specimens testing influenza-positive from SARI sentinel surveillance, adjusted by age and month, and then divided by the combined population of the regions. ARI, acute respiratory infection; SARI, severe acute respiratory infection; UI, uncertainty interval.
The seasonal distribution of influenza detections suggested circulation in Vietnam occurred primarily during January–July. We demonstrated that 75% of influenza detections were observed during March–July, which was consistent when evaluating all available years of SARI sentinel surveillance data, including data published previously from 2011–2014 (20). Nguyen et al. demonstrated variable timing of peaks for influenza A and B viruses; 76% of influenza A viruses were detected in May–October, and little pattern was observed for influenza B viruses (32). Our findings are similar to those in neighboring Thailand (27) and Cambodia (33), suggesting that most influenza circulation occurs during the rainyest months (April–August) (34) and that a Southern Hemisphere vaccine formulation is appropriate for use in Vietnam.

To align our work with existing literature and evaluate the broad potential burden of influenza, we studied influenza in patients with illness meeting...
the SARI and ARI case definitions. Previous studies have demonstrated that the SARI case definition is less sensitive and more specific (35), ensuring more efficient use of resources for virologic surveillance; however, the actual influenza hospitalization burden may be underestimated. A more sensitive case definition is needed to encompass the entirety of influenza disease burden. Furthermore, a recent review of influenza-associated hospitalization rates underscored the effect of heterogeneity in methods and case definitions on burden estimates (36). A strength of our study is the use of a medical chart review to identify SARI in ≈60% of hospitalized patients with ARI, which is consistent with a previous study evaluating the sensitivity of administrative codes to identify SARI (37) and enabled us to provide burden estimates that may contribute to pooled estimates in studies using different case definitions. Additional research is needed to understand the relationship between diagnostic codes indicative of ARI, the SARI case definition, and influenza detection.

The first limitation of our study is that we were only able to perform the HAS in 4 of Vietnam’s 63 provinces. Although our comparison of provincial characteristics demonstrated minimal variation within each region from the HAS referent provinces, we could not account for many characteristics that might lead to differences in influenza hospitalization rates, such as healthcare-seeking behaviors. Second, the EMR transition was delayed in some hospitals during 2014 and 2015, resulting in underestimation of the number of respiratory hospitalizations recorded. We imputed an expected number of hospitalizations for hospitals with known delays and increased the total ARI hospitalization accordingly, but other hospitals may have had unidentified implementation challenges that were not captured. Third, in accordance with reporting procedures in Vietnam, only the primary reason for a hospitalization was listed in the EMR for each patient (37). Although this practice serves to indicate the primary reason for a hospitalization, patients with other conditions in conjunction with a respiratory illness may be missed (38). Fourth, participation in SARI surveillance was not continuous for all hospitals, potentially underrepresenting the central and highlands regions and resulting in insufficient sample size to calculate both age- and region-specific influenza detection percentage positives. However, we identified minimal variability in region-specific influenza circulation and thus stratified analyses by age only (Appendix).

Our results highlight the burden of influenza-associated hospitalizations in Vietnam during 2014–2016 and underscore the value of country-specific disease burden studies. As Vietnam undertakes the production of influenza vaccine locally, influenza prevention and control investments and well-timed public health interventions such as vaccination campaigns and empiric antiviral use during epidemics may be supported through burden estimates like ours. Systematic testing of SARI patients can be used to identify the prevalent influenza subtypes and strains that inform vaccine strain selection for in-country influenza vaccines being produced. Our methods largely used existing hospitalization and surveillance data, which will be helpful to efforts to replicate or update the results. These and future efforts to better quantify influenza disease burden can be used with vaccine effectiveness and coverage data to estimate potential averted illnesses with vaccination, inform cost-effectiveness analyses, and direct communications to vulnerable populations.

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References


Influenza-Associated Hospitalizations, Vietnam


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EID SPOTLIGHT TOPIC

MERS is an illness caused by a virus called Middle East Respiratory Syndrome Coronavirus (MERS-CoV). MERS affects the respiratory system. Severe acute respiratory illness with symptoms of fever, cough, and shortness of breath develop in most patients. Health officials first reported the disease in Saudi Arabia in September 2012. Through retrospective investigations, health officials later identified that the first known cases of MERS occurred in Jordan in April 2012. MERS-CoV has spread from people with the virus to others through close contact, such as caring for or living with an infected person.

http://wwwnc.cdc.gov/eid/page/mers-spotlight

Appendix

Methods for Estimating the Rate of Influenza-Associated Hospitalizations

The influenza-attributable proportion of ARI and SARI hospitalizations was estimated using 2014–2016 SARI sentinel surveillance data. Influenza-associated ARI and SARI hospitalization rates were calculated by multiplying the number of hospitalizations and percent of SARI surveillance patients positive for influenza by age and month, then dividing by census population estimates for each province. The monthly rate estimates were summed to calculate the annual age-adjusted rates as given by the formula:

\[ I_a = \sum I_{am} = \frac{H_{am} F_{am}}{P_a T_{am}} \]

where \( I_a \) is the age-specific annual rate of influenza-associated ARI hospitalizations; \( H_{am} \) is the age- and month-specific number of hospitalizations; \( F_{am} \) is the age- and month-specific number of SARI patients testing positive for influenza; \( T_{am} \) is the total number of SARI patients tested for influenza; \( P_a \) is the age-specific census population. We calculated the 95% uncertainty intervals (UI) for estimated rates using 1,000 Monte Carlo simulation iterations, assuming a Poisson distribution for the number of hospitalizations and a binomial distribution for the proportion of SARI patients positive for influenza. The same method was used to calculate influenza-associated SARI hospitalization rates, but ARI hospitalization totals were first multiplied by the percent of ARI meeting SARI criteria, given by \( S_a \), to obtain the age- and month-specific number of influenza-associated SARI hospitalizations as given by the adjusted formula:

\[ I_a = \sum I_{am} = \frac{H_{am} S_a F_{am}}{P_a T_{am}} \]
The 95% UIs assumed a binomial distribution for the proportion meeting the SARI case definition. We extrapolated the number of influenza-associated ARI and SARI hospitalizations by multiplying age-specific influenza rates by the provincial census population.

To estimate national rates, age- and month-specific provincial counts of all-cause ARI and SARI and influenza-associated ARI and SARI were each summed across the provinces, and then divided by the total population of the four provinces. The 95% UIs were obtained by calculating the upper and lower 2.5% percentiles from the distribution of provincial rate estimates.

Supplemental Evaluation of Vietnam's Provincial Characteristics Between HAS and Other Provinces

Comparison of provincial characteristics to identify variability between individual provinces and HAS representative provinces within the major health regions of Vietnam.

Objective

To develop a multiplier that adjusts influenza-associated hospitalization rates based on a health statistical score for each province in Vietnam.

Methods

Using data provided in the Health Statistics Yearbook 2015 (Vietnam Ministry of Health’s Government Statistics Office, https://thongke.gov.vn/data-and-statistics/2019/10/statistical-yearbook-of-vietnam-2015-2), we evaluated 14 demographic, health and healthcare characteristics potentially associated with variation in hospitalization risks in each province. Each characteristic was calculated as both a percentage and as a normalized value. Two scores were calculated: the average of the percentages and the average of the normalized values. The multiplier for each province was then calculated by dividing the score for each province in a region by the corresponding score for the HAS province in that region (Appendix Table). The range and distribution of average scores and multipliers for each region were summarized.

Covariates

Calculated as percentages and normalized as (value-min/max-min):

% Urban
Physicians per population
Birth rate
Death rate
Under 5 mortality
Literacy
Employment
Income per capita
Health budget
Beds per 100 residents
Nutrition scores: wasting, stunting, underweight
HIV rate

Findings

The average scores varied by a total of only 6 percentage points (average score range = 15.6 – 21.2%). The resulting multiplier therefore ranges from 0.8 – 1.2. The only HAS province that did not have an average score in the middle of the region’s range was Quang Ninh; the score was on the high end of the range at 25%, but still within a small score range of 18 – 27% (Appendix Figure 4, 5).

Conclusion

Evaluation by region of 14 demographic, health and healthcare characteristics in each province demonstrated that the provinces in which the HAS was conducted were reasonably representative.

**Appendix Table.** Multiplier calculation for an example province from each region

<table>
<thead>
<tr>
<th>Region</th>
<th>Example province</th>
<th>Multiplier calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red River</td>
<td>Hanoi</td>
<td>Average score Hanoi/ Average score Quang Ninh</td>
</tr>
<tr>
<td>Northern Mountain</td>
<td>Lao Cai</td>
<td>Average score Lao Cai/Average score Quang Ninh</td>
</tr>
<tr>
<td>North Central</td>
<td>Ha Tinh</td>
<td>Average score Ha Tinh/Average score Khanh Hoa</td>
</tr>
<tr>
<td>Central Highlands</td>
<td>Gia Lai</td>
<td>Average score Gia Lai/Average score Dak Lak</td>
</tr>
<tr>
<td>Mekong River</td>
<td>Ca Mau</td>
<td>Average score Ca Mau/Average score Dong Thap</td>
</tr>
<tr>
<td>Southeast</td>
<td>Ho Chi Min City</td>
<td>Average score HCMC/Average score Dong Thap</td>
</tr>
</tbody>
</table>
Appendix Figure 1. Comparison of acute respiratory infection hospitalization counts adjusted for hospitals with incomplete electronic medical record implementation in 2014 and 2015. The expected number of ARI hospitalizations for 8 hospitals with clear under-reporting in 2014 and 2015 were calculated using the 2016 percent distribution of counts. The adjusted count reflects a 4.1% adjusted total of 229,144 ARI hospitalizations included in analysis.
Appendix Figure 2. Comparison of seasonal influenza detection by three major regions of Vietnam, 2014–2016. Central Coast and Central Highland regions were combined due to insufficient data. The weekly percent positive for each region was smoothed using a 3-week moving average of observed data.

Appendix Figure 3. Cumulative counts of influenza-associated ARI for the 6-month periods following Southern (April to September) and Northern (October to March) Hemisphere influenza vaccination timing 2014–2016 in Vietnam.
Appendix Figure 4. Health statistical scores calculated from normalized province-level health indicators for each major health region of Vietnam. Inset boxes illustrate the health statistical score of the HAS province representing the region. Abbreviations: Quang Ninh, QN; Khanh Hoa, KH; Dak Lak, DL; Dong Thap, DT. Average scores were calculated from normalized values of 14 different demographic, health and healthcare characteristics potentially associated with variation in hospitalization risks in each province.
Appendix Figure 5. Demonstration of minimal variation in the range and distribution of average health statistical scores for each major health region of Vietnam. Multiplier values were calculated by dividing the score for each province in a region by the corresponding score for the HAS province in that region.