Hospitalizations for Acute Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Thailand, 2008–2011

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Background. Few population-based estimates of the incidence of respiratory syncytial virus (RSV) infection in low- or middle-income countries are available. We describe the incidence and epidemiology of hospitalizations for RSV-associated acute lower respiratory tract infection (ALRI) detected by active population-based surveillance in 2 rural Thailand provinces during 2008–2011.

Methods. Patients hospitalized with ALRI were systematically sampled. Consenting patients provided nasopharyngeal swab specimens for RSV testing by real-time reverse-transcription polymerase chain reaction.

Results. Of 13 982 enrolled patients hospitalized with ALRI, 1137 (8.1%) were RSV positive. After adjustment for sampling and nonenrollment, the incidence of RSV-associated ALRI hospitalization was 85 cases per 100 000 persons/year. The highest rates occurred among children aged <5 years (981 cases per 100 000 persons/year) and <1 year (1543 cases per 100 000 persons/year). Rates were low among older children and young adults but high among persons aged >65 years (130 cases per 100 000 persons/year). Eight (0.7%) RSV-infected study patients died during hospitalization. Annual RSV hospitalizations peaked during July-October with almost no documented RSV hospitalizations during January–June.

Conclusions. Our findings demonstrate the substantial contribution of RSV to global ALRI burden, especially in children aged <5 years and the elderly, and underscore the urgent need for effective prevention measures.

Keywords. respiratory syncytial virus; acute lower respiratory infection; Thailand.

Acute lower respiratory tract infections (LRTIs), including pneumonia, remain a leading cause of childhood morbidity and mortality worldwide, with 156 million new episodes occurring annually [1–3], and cause approximately 1.6 million deaths among children aged <5 years each year [1, 3]. An estimated 30%–50% of acute LRTI episodes have a viral etiology, most commonly respiratory syncytial virus (RSV) [4]. Nair et al estimated that 33.8 million RSV-associated ALRI cases occurred among children aged <5 years in 2005 [1].

Although data on the incidence and epidemiology of RSV infection are limited from tropical and low- and middle-income countries, evidence is mounting that RSV contributes substantially to the severe ALRI burden, especially among young children [5, 6]. However, additional data are needed, especially among adults, to further detail the human health impact of RSV. Gathering more data on the seasonality and epidemiology of RSV infection is also important to guide prevention and control programs. We previously described RSV-associated ALRI hospitalizations in rural Thailand during 2003–2007 [5]. Here, we present updated data from
active population-based surveillance on the incidence, epidemiology, and clinical characteristics of ALRI hospitalizations due to RSV among all age groups from 2008 through 2011.

METHODS

Setting
The Thailand Ministry of Public Health, in collaboration with the International Emerging Infections Program of the Global Disease Detection Thailand Regional Center, has conducted active population-based surveillance for hospitalized cases of community-acquired ALRI in all 20 hospitals in 2 rural Thailand provinces since 2002 [5, 7–9]. Sa Kaeo and Nakhon Phanom provinces are located in eastern and northeastern Thailand, bordering Cambodia and Laos, respectively. These provinces had a combined population of approximately 1.3 million persons during 2010 [10]. We initiated a study in 2003 to determine pneumonia etiology, and the detailed methods and previous findings have been published [5, 6, 9].

Patient Selection
A case of ALRI was defined as evidence of both active infection (at least 1 of the following conditions: reported fever, reported chills, measured temperature of >38.2°C or <35°C, or an abnormal white blood cell count or differential) and lower respiratory tract disease (at least 1 of the following conditions: abnormal breath sounds, documented tachypnea, cough, sputum production, or dyspnea) in a hospitalized patient. Every other case patient with ALRI was systematically sampled for possible participation in an etiology study. Sampling was done chronologically on the basis of time of admission within each ward (eg, male ward, female ward, and pediatric ward). Chest radiographs, if obtained, were digitized and interpreted by a panel of 3 radiologists, using standard criteria as previously described [11]. Patients were considered to have radiographically confirmed pneumonia if 2 of 3 independent radiologists interpreted the chest radiograph as consistent with probable or definite pneumonia.

All adult participants and guardians of children aged <18 years provided written informed consent before study enrollment. A Centers for Disease Control and Prevention (CDC) institutional review board (protocol 3754) and the Ethical Review Committee of the Thailand Ministry of Public Health approved this study.

Specimen Collection and Laboratory Testing
Nasopharyngeal swab specimens were collected from all participants, using polyester swabs (Puritan, Guilford, ME) from 2002 to June 2010 and flocked swabs (FLOQSwabs, Copan, Murrieta, CA) since July 2010. Nasopharyngeal specimens were inoculated in viral transport media, stored at 4°C–8°C for up to 24 hours before being frozen at −70°C, and transported weekly on dry ice to the Thailand National Institute of Health (NIH) for RSV testing using a sensitive real-time reverse transcription polymerase chain reaction (rRT-PCR) targeting conserved regions of the matrix gene as previously described [5, 12]. The Thailand NIH also tested for influenza A and B viruses, adenovirus, and human metapneumovirus by rRT-PCR described elsewhere [6]. Blood specimens were obtained for culture at clinician discretion, and cultures were processed using the BactT/Alert 3D system (bioMerieux) [13].

Data Analysis
Readmissions within 14 days after discharge from a previous hospitalization were not considered to be distinct from the previous hospital admission. Overall crude and age-specific incidence of RSV-associated ALRI hospitalizations for 2008–2011 were calculated using population estimates from Thailand’s National Economic and Social Development Board [10]. The board does not have population estimates by month for children aged <1 year, so we assumed an equal distribution of the population <12 months old. Incidence was calculated by dividing the total number of rRT-PCR–confirmed cases of RSV ALRI by the combined population of the 2 provinces. To account for cases missed because of the sampling frame and nonenrollment of eligible patients, we calculated adjusted incidence rates by assuming that the proportion positive for RSV was the same among hospitalized, enrolled patients with ALRI as that among hospitalized patients with acute LRTI who did not enroll within the same age group. The proportion of enrolled patients who were RSV positive was multiplied by the total number of eligible patients (ie, those hospitalized with ALRI), to serve as the numerator for the adjusted incidence. To calculate the incidence of RSV-associated ALRI hospitalizations involving chest radiography–confirmed pneumonia, the proportion of cases of chest radiography–confirmed pneumonia involving patients who tested positive for RSV was multiplied by the total number of cases of chest radiography–confirmed pneumonia; this adjusted number of cases of RSV-positive chest radiography–confirmed pneumonia served as the numerator for the adjusted incidence calculation. Confidence intervals (CIs) for adjusted incidence were calculated using the 95% CI for the proportion of RSV-positive cases, assuming a binomial distribution. Clinical and demographic characteristics were assessed for association with RSV positivity, using bivariate logistic regression. Adjusted odds ratios (aORs) were calculated using logistic regression models adjusted for sex and a categorical age group variable (ie, <5 years, 5–19 years, 20–49 years, 50–64 years, and ≥65 years). All analyses were conducted in SPSS, version 18 (SPSS).

RESULTS

From January 2008 through December 2011, 54 311 patients were hospitalized with acute LRTI in Sa Kaeo and Nakhon Phanom provinces (Table 1), of whom 13 982 (25.7%) were
Table 1. Incidence of Respiratory Syncytial Virus (RSV)–Associated Acute Lower Respiratory Tract Infection (ALRI) Hospitalizations, by Age Group—Sa Kaeo and Nakhon Phanom Provinces, Thailand, January 2008–December 2011

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<tbody>
<tr>
<td>&lt;5 y</td>
<td>19 199</td>
<td>4839 (25.2)</td>
<td>802 (16.6)</td>
<td>420 (52.4)</td>
<td>327 (77.9)</td>
<td>3182 (2981–3383)</td>
<td>981 (919–1043)</td>
<td>287 (260–315)</td>
</tr>
<tr>
<td>&lt;12 mo overall</td>
<td>4883</td>
<td>1182 (24.2)</td>
<td>230 (19.5)</td>
<td>135 (58.7)</td>
<td>101 (74.8)</td>
<td>950 (840–1060)</td>
<td>1543 (1364–1722)</td>
<td>507 (421–593)</td>
</tr>
<tr>
<td>0–5 mo</td>
<td>1669</td>
<td>354 (21.2)</td>
<td>77 (21.8)</td>
<td>46 (59.7)</td>
<td>35 (76.1)</td>
<td>363 (291–435)</td>
<td>1195 (959–1431)</td>
<td>371 (265–478)</td>
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<tr>
<td>0–2 mo</td>
<td>728</td>
<td>119 (16.3)</td>
<td>36 (30.3)</td>
<td>23 (63.9)</td>
<td>20 (87.0)</td>
<td>220 (160–280)</td>
<td>1451 (1055–1846)</td>
<td>504 (331–677)</td>
</tr>
<tr>
<td>3–5 mo</td>
<td>941</td>
<td>235 (25.0)</td>
<td>41 (17.4)</td>
<td>23 (56.1)</td>
<td>15 (65.2)</td>
<td>164 (119–210)</td>
<td>1081 (781–1382)</td>
<td>293 (153–413)</td>
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<tr>
<td>6–11 mo</td>
<td>3214</td>
<td>828 (25.8)</td>
<td>153 (18.5)</td>
<td>89 (58.2)</td>
<td>66 (74.2)</td>
<td>594 (509–679)</td>
<td>1903 (1631–2175)</td>
<td>639 (505–773)</td>
</tr>
<tr>
<td>12–59 mo overall</td>
<td>14 316</td>
<td>3657 (25.5)</td>
<td>572 (15.6)</td>
<td>285 (49.8)</td>
<td>226 (79.3)</td>
<td>2239 (2071–2408)</td>
<td>852 (788–917)</td>
<td>237 (209–264)</td>
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<tr>
<td>12–23 mo</td>
<td>6131</td>
<td>1591 (26.8)</td>
<td>252 (15.8)</td>
<td>133 (52.8)</td>
<td>106 (79.7)</td>
<td>971 (861–1081)</td>
<td>1520 (1348–1692)</td>
<td>433 (360–506)</td>
</tr>
<tr>
<td>24–59 mo</td>
<td>8185</td>
<td>2066 (25.2)</td>
<td>320 (15.5)</td>
<td>152 (47.5)</td>
<td>120 (78.9)</td>
<td>1268 (1140–1395)</td>
<td>638 (574–702)</td>
<td>174 (147–202)</td>
</tr>
<tr>
<td>5–19 y</td>
<td>7220</td>
<td>1802 (25.0)</td>
<td>74 (4.1)</td>
<td>28 (37.8)</td>
<td>15 (53.6)</td>
<td>296 (230–363)</td>
<td>23 (18–29)</td>
<td>3 (2–5)</td>
</tr>
<tr>
<td>20–49 y</td>
<td>8490</td>
<td>2130 (25.1)</td>
<td>54 (2.5)</td>
<td>32 (59.3)</td>
<td>13 (25.0)</td>
<td>215 (158–272)</td>
<td>9 (6–11)</td>
<td>2 (1–3)</td>
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<tr>
<td>50–64 y</td>
<td>7292</td>
<td>1938 (26.5)</td>
<td>81 (4.2)</td>
<td>56 (69.1)</td>
<td>36 (64.3)</td>
<td>305 (240–370)</td>
<td>40 (32–49)</td>
<td>13 (9–18)</td>
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<tr>
<td>≥65 y</td>
<td>12 110</td>
<td>3275 (27.0)</td>
<td>126 (3.8)</td>
<td>86 (68.3)</td>
<td>39 (45.3)</td>
<td>466 (386–546)</td>
<td>130 (108–152)</td>
<td>31 (21–40)</td>
</tr>
<tr>
<td>Total</td>
<td>54 311</td>
<td>13 982 (25.7)</td>
<td>1137 (8.1)</td>
<td>622 (45.7)</td>
<td>430 (69.1)</td>
<td>4417 (3923–4663)</td>
<td>85 (60–90)</td>
<td>24 (22–26)</td>
</tr>
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Abbreviations: CI, confidence interval; CXR, chest radiography.

a To account for cases missed because of the sampling frame and nonenrollment of eligible patients, adjusted case numbers were calculated by assuming that the proportion positive for RSV among enrolled patients with ALRI was the same as among patients with ALRI who did not enroll. The value was calculated as the proportion of enrolled patients who were RSV positive times the total number of eligible patients (ie, those hospitalized with ALRI).

b Adjusted case numbers divided by population denominator × 100 000.

c Calculated as the proportion of CXR-confirmed pneumonia cases among patients testing positive for RSV, multiplied by the total number of CXR-confirmed pneumonia cases. This adjusted number of RSV-positive CXR-confirmed pneumonia cases served as the numerator for the adjusted incidence calculation.
enrolled and had nasopharyngeal swab specimens tested. Of those enrolled, 1137 (8.1%) were positive for RSV by rRT-PCR. The number of patients tested and the percentage positive for RSV varied by year. In 2008, 2969 patients were tested for RSV, and 285 (9.6%) were positive, compared with 129 positive (4.2%) of 3069 tested in 2009, 532 (12.7%) of 4191 in 2010, and 191 (5.1%) of 3753 in 2011. Among patients with ALRI who were enrolled and tested for RSV, 3.7% (522) required intubation, and 1.7% (247) died, compared with 6.8% (2757) and 3.7% (1503) who were not enrolled ($P < .0001$ for both). These differences persisted across age groups; the difference in the case-fatality proportion for enrolled versus nonenrolled patients with ALRI was less for patients aged <5 years (0.2% vs 0.4%) than for those aged ≥5 years (2.6% vs 5.6%).

The prevalence of RSV among study patients hospitalized with ALRI varied by age group, with the highest prevalence among those aged <5 years (Table 1); 230 (19.5%) of 1182 infants aged <1 year were RSV positive, as were 572 (15.6%) of 3657 children aged 1–4 years. The RSV prevalence was lower among older children and adults and was high among those aged ≥65 years. Of 1137 RSV-positive patients, 622 (54.7%) underwent chest radiography and had the radiograph evaluated by radiologists; of these, 430 (69.1%) had radiograph findings interpreted as consistent with pneumonia. Among patients who underwent chest radiography, the proportion of RSV-positive ALRI case patients with chest radiography–confirmed pneumonia was higher among those aged <5 years (77.9%) 53.6 than among those aged ≥5 years (25%–69%) years (25%–64%). If we assume that all patients who did not undergo chest radiography did not have radiographic evidence of pneumonia, the percentage of all RSV-positive ALRI case patients with chest radiography–confirmed pneumonia was higher among those aged <5 years (77.9%) 53.6% than among those aged ≥5 years (25%–69%) years (25%–64%). If we assume that all patients who did not undergo chest radiography did not have radiographic evidence of pneumonia, the percentage of all RSV-positive ALRI case patients with chest radiography–confirmed pneumonia would be 40.8% among children aged <5 years, 20.3% among those aged 5–19 years, 24.1% among those aged 20–49 years, 44.4% among those aged 50–64 years, and 31% among those aged ≥65 years.

Incidence of RSV-Associated ALRI Hospitalizations

After adjustment for the sampling frame and nonenrollment of patients with eligible cases, the incidence of RSV-associated ALRI hospitalization was 85 cases per 100,000 persons/year. Rates were high among children aged <5 years (981 cases per 100,000 persons/year), especially infants aged <12 months (1543 cases per 100,000 persons/year). The highest rates occurred among children aged 6–11 months, at 1903 cases per 100,000 persons/year. Rates were relatively low among older children and young adults, higher among persons aged 50–64 years, and peaked again among persons aged ≥65 years (130 cases per 100,000 persons/year).

Age group–specific rates of RSV-positive chest radiography-confirmed pneumonia followed similar trends as the rates of all RSV-positive ALRI hospitalizations. Rates were highest among children aged 6–11 months, lower among persons aged 5–49 years, and slightly higher among older adults. Rates of RSV-associated ALRI hospitalizations varied by year, with the highest rates occurring during 2008 and 2010 among almost all age groups (Figure 1). Age group trends in incidence rate were similar across 2008–2010, but in 2011 the highest rate occurred among those aged 0–2 months.

Factors Associated With RSV-Associated ALRI Hospitalization

Among participants hospitalized with ALRI and tested for RSV, RSV positivity was not significantly associated with sex but was strongly associated with age of <5 years (Table 2); 70% of RSV-positive ALRI cases involved patients aged <5 years, compared with 31% of RSV-negative cases (aOR, 7.7 [95% CI, 5.8–10.2]). RSV positivity was also significantly associated with older age (50–64 years and ≥65 years) (aOR, 1.7 [95% CI, 1.2–2.4] and 1.5 [95% CI, 1.1–2.1]), respectively, compared with the reference age group of 20–49 years. Among RSV-infected participants, coinfections with influenza A virus (6.8%), influenza B virus (1.2%), adenovirus (1.9%), and human metapneumovirus (2.8% [of 181 tested]) occurred and were less common than among RSV-uninfected participants.

After adjustment for age and sex, RSV-positive patients with ALRI were more likely than RSV-negative patients with ALRI to have a temperature ≥38°C, reported fever, cough, sputum production, dyspnea, rhonchi, and rales on lung examination (Table 2). Wheezing was common among all hospitalized ALRI patients and did not differ significantly by RSV positivity for children aged <5 years. Among patients aged ≥5 years, wheezing was more common among those with RSV infection. Chest radiography–confirmed pneumonia was more common among RSV-positive patients than among RSV-negative patients (aOR, 1.49 [95% CI, 1.30–1.69]). Among RSV-infected patients aged ≥50 years with ALRI, the prevalence of cancer (2.4%), liver disease (1.4%), renal disease (2.4%), cerebrovascular disease (1.0%), and heart disease (20%) was not meaningfully different from that among RSV-negative patients with ALRI. However, in this same group, chronic obstructive lung disease or another chronic lung condition (based on discharge diagnosis) was more common among RSV-positive patients (34.3%) than among RSV-negative patients (29.7%; aOR, 1.28 [95% CI, 0.95–1.71]). Eight RSV-infected patients (0.7%) died during hospitalization: 1 was aged 3 years, 2 were aged 50–64 years, and 5 were aged ≥65 years. Intubation and death were less common among RSV-positive patients than among RSV-negative patients, but after adjustment for age and sex the association was not statistically significant.

Among 290 RSV-positive patients (25.5%) with blood cultures performed, 5.2% (15) were positive for a likely bacterial pathogen, which was lower than the proportion of RSV-negative patients with a positive blood culture (335 [6.7%] of 4984); 237 blood cultures overall (4.5%) grew presumed contaminants. The most common bacterial pathogens isolated among RSV-
positive patients were *Burkholderia pseudomallei* (3 patients), *Staphylococcus aureus* (2), and *Escherichia coli* (2).

**RSV Seasonality**
Seasonal peaks in RSV cases occurred most years during July–October (Figure 2), except during 2009, when the peak occurred during September–December and cases continued through March 2010. There were almost no RSV-associated hospitalizations detected during January–June in most years. The highest percentage of cases of ALRI involving RSV-positive patients occurred during September or October each year. Larger peaks of RSV positivity among ALRI cases occurred during 2008 (9.6%) and 2010 (12.7%), alternating with smaller peaks during 2009 (8.8%) and 2011 (5.1%).

**DISCUSSION**

We documented the substantial incidence of RSV-associated ALRI hospitalizations in rural Thailand and confirmed the particularly high burden among children aged <5 years. As in previous studies [1, 3, 5], we found that RSV infection was strongly associated with younger age and that incidence was highest among patients aged <5 years. We estimated that nearly 1 in 100 children aged <5 years and 2 in 100 children aged 6–11 months were hospitalized with RSV-associated ALRI annually. We also found that RSV is an important cause of ALRI hospitalizations among older adults and that 7 of 8 deaths occurred among patients aged ≥50 years.

Our findings confirm and update those of a previous study from the same 2 provinces in Thailand conducted during September 2003–December 2007 [5]. Compared with the previous study, we found 1.5–2-fold higher rates of RSV-associated ALRI hospitalizations overall (85 vs 46 cases per 100 000 persons/year) and by age group (among ages <5 years, 981 vs 507 per 100 000 persons/year). These differences are likely due to a change in enrollment criteria rather than a representation of true increases. Before 2008, only patients with clinician-ordered chest radiographs were eligible for enrollment, so previous estimates did not capture RSV-associated hospitalizations among patients without chest radiographs. We believe that the current estimates better represent the true incidence and burden of RSV-associated hospitalizations. Rates of chest radiography–confirmed pneumonia, which should not have been affected by the changed eligibility criteria, were very similar in the current and previous studies, which supports the validity of these estimates.

Few previous studies have estimated the RSV incidence in low- or middle-income settings with known population denominators. RSV-associated ALRI hospitalization rates among children aged <5 years in our study (981 cases per 100 000 persons/year) exceeded those reported in a 2009 study in Kenya (293 cases per 100 000 persons/year) [14]. However, the Kenya study included only children with severe or very severe pneumonia, making direct comparison with findings from our study difficult. Moreover, hospitalization rates in the Kenya study decreased with distance from hospital, suggesting that the true rates of disease warranting hospitalization were much higher. In an analysis of community-based studies from Indonesia, Mozambique, Nigeria, and South Africa [15], rates of RSV-associated LRI among children aged <5 years exceeded those in our study, but rates of RSV-associated severe LRI, which may be more comparable to hospitalized cases, were...
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ALRI (n = 54 311)</th>
<th>RSV-Positive ALRI (n = 1137)</th>
<th>RSV-Negative ALRI (n = 12 845)</th>
<th>Crude ORa (95% CI)</th>
<th>Adjusted ORb (95% CI)</th>
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<td>Age, y</td>
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<td>Age group</td>
<td></td>
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<tr>
<td>&lt;5 y</td>
<td>19 199 (35.4)</td>
<td>802 (70.5)</td>
<td>4037 (21.4)</td>
<td>7.64 (5.77–10.11)</td>
<td>7.70 (5.82–10.20)</td>
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<td>5–19 y</td>
<td>7220 (13.3)</td>
<td>74 (6.5)</td>
<td>1728 (13.5)</td>
<td>1.65 (1.15–2.35)</td>
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<tr>
<td>20–49 y</td>
<td>8492 (15.6)</td>
<td>54 (4.8)</td>
<td>2076 (16.2)</td>
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<td>Reference</td>
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<td>≥50 y</td>
<td>7292 (13.4)</td>
<td>81 (7.1)</td>
<td>1855 (14.4)</td>
<td>1.68 (1.18–2.38)</td>
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<tr>
<td>Male sex</td>
<td>12 108 (22.3)</td>
<td>126 (11.1)</td>
<td>3149 (24.5)</td>
<td>1.54 (1.11–2.13)</td>
<td>1.54 (1.11–2.13)</td>
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<td>Province</td>
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<tr>
<td>Sa Kaeo</td>
<td>22 749 (41.9)</td>
<td>459 (40.4)</td>
<td>5248 (40.9)</td>
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<td>Reference</td>
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<td>Nakhon Phanom</td>
<td>31 562 (58.1)</td>
<td>678 (59.6)</td>
<td>7597 (59.1)</td>
<td>1.02 (0.90–1.16)</td>
<td>0.93 (0.82–1.06)</td>
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<td>Clinical sign/symptom</td>
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<tr>
<td>Temperature ≥38°C</td>
<td>23 006 (42.4)</td>
<td>608 (53.5)</td>
<td>5663 (44.1)</td>
<td>1.46 (1.29–1.65)</td>
<td>1.22 (1.07–1.38)</td>
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<tr>
<td>Fever by report</td>
<td>45 818 (84.4)</td>
<td>1076 (94.6)</td>
<td>11 278 (87.8)</td>
<td>2.45 (1.88–3.19)</td>
<td>1.59 (1.21–2.09)</td>
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<tr>
<td>Cough</td>
<td>48 120 (88.6)</td>
<td>1120 (98.5)</td>
<td>12 018 (93.6)</td>
<td>4.53 (2.79–7.36)</td>
<td>2.50 (1.53–4.08)</td>
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<td>Sputum production</td>
<td>27 024 (49.8)</td>
<td>761 (66.9)</td>
<td>7131 (55.5)</td>
<td>1.62 (1.42–1.84)</td>
<td>1.53 (1.34–1.74)</td>
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<tr>
<td>Dyspnea</td>
<td>30 618 (56.4)</td>
<td>844 (74.2)</td>
<td>7403 (57.6)</td>
<td>2.12 (1.85–2.43)</td>
<td>1.70 (1.47–1.96)</td>
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<td>Rhonchi</td>
<td>11 893 (21.9)</td>
<td>501 (44.1)</td>
<td>2930 (22.8)</td>
<td>2.67 (2.36–3.02)</td>
<td>1.73 (1.51–1.97)</td>
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<td>Wheezing</td>
<td>15 409 (28.4)</td>
<td>404 (35.5)</td>
<td>3793 (29.5)</td>
<td>1.32 (1.16–1.49)</td>
<td>1.13 (0.99–1.29)</td>
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<td>Age &lt;6 mo</td>
<td>344 (20.6)</td>
<td>15 (19.5)</td>
<td>69 (24.9)</td>
<td>0.73 (0.39–1.36)</td>
<td>0.73 (0.39–1.37)</td>
</tr>
<tr>
<td>Age 6–11 mo</td>
<td>981 (30.5)</td>
<td>59 (38.6)</td>
<td>231 (34.2)</td>
<td>1.21 (0.84–1.73)</td>
<td>1.19 (0.83–1.71)</td>
</tr>
<tr>
<td>Age 1–4 y</td>
<td>5055 (35.3)</td>
<td>203 (35.5)</td>
<td>1137 (36.9)</td>
<td>0.94 (0.78–1.14)</td>
<td>0.95 (0.79–1.14)</td>
</tr>
<tr>
<td>Age ≥5 y</td>
<td>9029 (25.7)</td>
<td>127 (37.9)</td>
<td>2356 (26.8)</td>
<td>1.67 (1.33–2.10)</td>
<td>1.69 (1.35–2.11)</td>
</tr>
<tr>
<td>Rales</td>
<td>14 331 (26.4)</td>
<td>492 (43.3)</td>
<td>3764 (29.3)</td>
<td>1.84 (1.63–2.08)</td>
<td>1.72 (1.51–1.96)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>30 250 (55.7)</td>
<td>564 (49.6)</td>
<td>7500 (58.4)</td>
<td>0.70 (0.62–0.79)</td>
<td>0.70 (0.62–0.79)</td>
</tr>
<tr>
<td>Other viruses detected</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Influenza A virus</td>
<td>77 (6.8)</td>
<td>1254 (9.8)</td>
<td>0.67 (0.53–0.85)</td>
<td>0.83 (0.65–1.06)</td>
<td></td>
</tr>
<tr>
<td>Influenza B virus</td>
<td>14 (1.2)</td>
<td>461 (3.6)</td>
<td>0.34 (0.20–0.57)</td>
<td>0.36 (0.21–0.61)</td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>21 (1.9)</td>
<td>292 (2.3)</td>
<td>0.81 (0.52–1.27)</td>
<td>0.52 (0.33–0.81)</td>
<td></td>
</tr>
<tr>
<td>HMPV</td>
<td>5/181 (2.8)d</td>
<td>146/1731 (8.4)d</td>
<td>0.31 (0.13–0.76)</td>
<td>0.20 (0.08–0.51)</td>
<td></td>
</tr>
<tr>
<td>CXR finding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Performed</td>
<td>31 612 (58.2)</td>
<td>768 (67.5)</td>
<td>8241 (64.2)</td>
<td>1.16 (1.02–1.32)</td>
<td>1.40 (1.22–1.59)</td>
</tr>
<tr>
<td>Interpretation completed (among CXRs performed)</td>
<td>21 968 (69.5)</td>
<td>622 (81.0)</td>
<td>6851 (83.1)</td>
<td>1.16 (1.02–1.31)</td>
<td>1.37 (1.21–1.56)</td>
</tr>
<tr>
<td>CXR-confirmed pneumonia (among CXRs interpreted)</td>
<td>12 636 (57.5)</td>
<td>430 (69.1)</td>
<td>3953 (57.7)</td>
<td>1.37 (1.21–1.55)</td>
<td>1.49 (1.30–1.69)</td>
</tr>
<tr>
<td>Clinical course and outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>3279 (6.0)</td>
<td>16 (1.4)</td>
<td>506 (3.9)</td>
<td>0.35 (0.21–0.58)</td>
<td>0.64 (0.38–1.07)</td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>18 706 (34.4)</td>
<td>410 (36.1)</td>
<td>4431 (34.5)</td>
<td>1.07 (0.94–1.22)</td>
<td>1.33 (1.17–1.52)</td>
</tr>
<tr>
<td>Hospitalization duration, d</td>
<td>3 (2–5)</td>
<td>4 (3–5)</td>
<td>3 (2–5)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Death</td>
<td>1750 (3.2)</td>
<td>8 (0.7)</td>
<td>239 (1.9)</td>
<td>0.37 (0.18–0.76)</td>
<td>0.79 (0.38–1.61)</td>
</tr>
</tbody>
</table>

Data are no. (%) of patients or median value (interquartile range), unless otherwise indicated.

Abbreviation: CI, confidence interval; CXR, chest radiography; OR, odds ratio; rRT-PCR, real-time reverse-transcription polymerase chain reaction.

a For the comparison of RSV-positive to RSV-negative patients with ALRI.

b Adjusted for age group and sex. The adjusted OR for age group was adjusted only for sex, whereas the adjusted OR for sex was adjusted only for age group.

c Age-specific tachypnea: ≥50 breaths/min if aged <12 months; ≥40 breaths/min if aged 1–4 years; ≥24 breaths/min if aged 5–9 years; ≥22 breaths/min if aged 10–14 years; and ≥20 breaths/min if aged ≥15 years.

d Data are proportion (%) of patients tested because human metapneumovirus (HMPV) testing was only performed during January–September 2008 and July–December 2011 (1912 individuals were tested).

P = .47, by the Kruskal-Wallis test.
similar to the Thailand rates. In a comprehensive analysis and review by Nair et al [1], region-specific rates of RSV-associated severe ALRI varied widely, with 3–50 cases per 1000 children/year among children aged <5 years and 6–96 cases per 1000 children/year among those <1 year, but were generally consistent with the rates of RSV-associated hospitalization we describe for Thailand. Annual RSV hospitalization rates in the United States were lower than the rates we found in Thailand among children aged <5 years overall (300 vs 981 cases per 100 000 persons/year) but slightly higher for children aged <6 months (1700 vs 1195 cases per 100 000 persons/year) [16].

Age-specific incidence is important for targeting future prevention and control strategies. Our large sample size allowed incidence estimates in finer age strata than those presented in some previous studies [5, 6], although the estimates in age groups with small numbers of patients had wide CIs. We found that the incidence of ALRI hospitalizations involving RSV-positive patients was highest among children aged <12 months and that the incidence among children aged 6–11 months exceeded that among children aged <6 months. Finding the highest rates among children aged 6–11 months was consistent across most years in Thailand but differed from previous studies that found higher rates of RSV-associated hospitalization among those aged <6 months [1, 14, 16]. This difference may be attributable to higher rates of hospitalization among children aged 6–11 months in Thailand, compared with rates in other settings, rather than higher rates of infection. Hospital access in Thailand is good, even in rural areas [17, 18], and physicians tend to have a relatively low threshold for hospitalization. Hospital access and clinician thresholds for hospital admission may vary less across settings for infants aged <6 months than for older infants and children, for whom good hospital access and lower admission thresholds in Thailand may have led to relatively higher RSV-associated hospitalization rates. Furthermore, our case definition required evidence of acute infection, such as fever, which may not be present in RSV infection, particularly among younger infants [19, 20] and elderly persons [21]. Our study was not designed to assess factors that could have influenced age-specific differences in the risk of acquiring RSV or developing disease severe enough to require hospitalization, such as host immunity, maternal antibodies, airway physiology, or breast feeding.

The incidence of RSV infection varied considerably by year but showed very consistent seasonality, which supports the importance of seasonally timed interventions, such as hospital infection control measures (eg, cohorting) [22]. The predictable timing of annual RSV infection peaks in Thailand, as in temperate regions, also supports the feasibility of prevention measures that would require annual administration, including future vaccines. However, currently available prevention measures, such as palivizumab therapy for high-risk infants, involve complex delivery schedules [23] and are prohibitively expensive for low- to middle-income countries.

Our study was strengthened by the systematic selection of patients hospitalized with ALRI through a long-standing ALRI surveillance system in all hospitals in 2 different provinces. This design reduces selection bias and improves the generalizability of our findings to other parts of Thailand. The study also has limitations. RSV testing was limited to rRT-PCR of nasopharyngeal specimens, which may have missed cases and underestimated incidence. We did not perform serologic testing, which, in previous studies, has increased case detection by 25%–35% [24], or viral culture. In addition, our incidence estimates relied on statistical adjustments that assumed that enrolled and nonenrolled patients had an identical prevalence of RSV infection. Patients admitted during nights and weekends were underrepresented in our sample and may have differed from patients admitted during weekdays in terms of demographic characteristics, disease severity, and RSV infection prevalence. Furthermore, because of challenges enrolling patients with severe disease, we know that the frequency of intubation and death among RSV-infected patients was likely

Figure 2. Respiratory syncytial virus (RSV)–associated acute lower respiratory tract infection (ALRI) hospitalizations, by month and year of admission—Sa Kaeo and Nakhon Phanom provinces, Thailand, January 2008 through December 2011.
underestimated. Our study was limited to hospitalized patients
and did not account for the substantial outpatient burden of
RSV disease. Previous healthcare utilization surveys in these 2
provinces found that 96% of patients with probable pneumonia
sought care outside the home, including at hospitals (58%–80% of
patients), private clinics, or healthcare centers [17, 18], sug-
gestig that we did not miss many cases sick enough to warrant
hospitalization. Finally, we did not have data on RSV group because
the assay used does not discriminate between RSV types A and
B; previous work in these sites found that RSV types A and B
circulated during annual peaks and that RSV type B was asso-
ciated with wheezing and older age [5].

Our findings provide evidence of the substantial contribu-
tion of RSV to the global burden of ALRI, especially among
infants <1 year of age, and underscore the urgent need for effec-
tive prevention measures. The incidence of RSV-associated
ALRI hospitalizations among elderly individuals in Thailand is
also substantial, and prevention and control measures are also
needed for this vulnerable age group. Measures of the economic
impact of RSV disease are needed to further quantify its overall
burden, especially in middle-income countries where these data
are lacking.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential
Conflicts of Interest. Conflicts that the editors consider relevant to the
content of the manuscript have been disclosed.

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