

Respiratory Syncytial Virus Hospitalizations Among American Indian and Alaska Native Infants and the General United States Infant Population

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ABSTRACT. *Objective.* To determine the burden of respiratory syncytial virus (RSV) disease among American Indian (AI) and Alaska Native (AN) infants, by examining RSV-associated hospitalizations.

Methods. Infant hospitalizations from 1997 through 2001 with RSV listed as a diagnosis were selected by using Indian Health Service/tribal hospital discharge data for AIs/ANs and National Hospital Discharge Survey data for the general US population.

Results. In 2000–2001, RSV disease was listed as a diagnosis for 14.4% of all AI/AN infant hospitalizations, with bronchiolitis attributable to RSV infection (12.2%) being among the top 5 listed diagnoses. The rate of RSV-specific hospitalizations was 34.4 hospitalizations per 1000 infants for AI/AN infants and 27.4 hospitalizations per 1000 births for the general US infant population. The hospitalization rates for AI/AN infants living in the Alaska and Southwest regions (70.9 and 48.2 hospitalizations per 1000 infants, respectively) were much higher than the overall rate for US infants.

Conclusions. RSV infection is one of the leading causes of hospitalization among all infants in the United States, and AI/AN infants living in the Southwest and Alaska regions are at especially high risk for hospitalizations associated with RSV infection. Development of vaccines, antiviral agents, and other strategies to prevent RSV disease could yield substantial public health benefits. *Pediatrics* 2004;114:e437–e444. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-0049; *infants, respiratory syncytial virus, RSV, respiratory disease, bronchiolitis, pneumonia, American Indian, Alaska Native, hospitalizations, epidemiology, United States.*

ABBREVIATIONS. RSV, respiratory syncytial virus; AI, American Indian; AN, Alaska Native; ICD-9-CM, *International Classification of*

Diseases, 9th Revision, Clinical Modification; IHS, Indian Health Service; NHDS, National Hospital Discharge Survey.

Respiratory syncytial virus (RSV) infection remains a major cause of lower respiratory tract disease among infants and children.^{1,2} Most RSV-related childhood hospitalizations occur among infants <6 months of age, and almost all children are infected with RSV by 2 years of age.^{2,3} One study estimated that between 73 000 and 126 000 RSV-associated hospitalizations per year occurred among US infants in 1994–1996.¹ Another study, using the newly introduced, RSV-specific diagnostic codes, estimated that ~96 000 RSV hospitalizations occurred annually in 1997–2000.⁴ That study also noted that bronchiolitis attributable to RSV was the leading cause of hospitalization among the general population of infants in the United States.

The availability of effective prophylaxis for some infants and young children and the promise of future vaccines make the identification of at-risk populations and the quantification of risk levels important for developing RSV prevention strategies. The risk of severe RSV-associated disease varies with age and is increased by the presence of comorbidities, such as underlying lung, cardiac, and immune-compromising conditions.^{2,5,6} Infants born prematurely are also at increased risk for RSV disease. In addition, previous studies suggested that American Indian (AI) and Alaska Native (AN) children and infants have higher rates of hospitalization associated with respiratory infections, compared with the general US population, with RSV being considered an important cause of these infections.^{7–14} One study reported that almost 75% of all infectious disease hospitalizations among AI/AN infants were associated with lower respiratory tract infections.¹³ It is estimated that 50% to 80% of infant hospitalizations for treatment of bronchiolitis and one-third of hospitalizations for treatment of pneumonia are RSV-related.^{1,6} RSV-specific *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnostic codes, which were introduced in October 1996, allow examination of hospitalizations associated with RSV disease among AI/AN and US infants. In this study, we describe the epidemiologic features of RSV-associated hospitalizations among AI/AN infants and evaluate the impact of these hospitalizations, in comparison with RSV-associated hospitalizations among the general population of infants in the United States.

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METHODS

Hospital discharge data from the Indian Health Service (IHS) Direct and Contract Health Service Inpatient Dataset for AI/AN infants (<1 year of age) and from the National Hospital Discharge Survey (NHDS) for the general US infant population^{15,16} were analyzed for calendar years 1997 through 2001. The Direct and Contract Health Service Inpatient Dataset is maintained by the IHS and consists of all patient discharge records obtained from IHS-operated and tribally operated hospitals and from hospitals that have contracted with the IHS or tribes to provide health care services to federally recognized AIs/ANs within the United States.⁸ The IHS California and Portland administrative areas were excluded from the hospitalization analysis because neither had any IHS-operated or tribally operated hospitals.¹⁷ In addition, California did not report contract health services inpatient data according to diagnoses, and Portland had limited contract health service funds for inpatient care.¹⁸ The NHDS is a representative sample of discharge records from short-stay, nonfederal, general and children's hospitals in the United States; it does not include hospitalizations in the IHS/tribal system.^{16,19} NHDS hospitalization records were weighted by using estimation procedures from the National Center for Health Statistics, to obtain national hospitalization estimates.^{16,19}

RSV-associated hospitalizations were defined by using the following ICD-9-CM diagnostic codes: RSV bronchiolitis (code 466.11), RSV pneumonia (code 480.1), and other RSV (code 079.6).²⁰ The RSV bronchiolitis and other RSV codes were introduced in October 1996. All infant hospital discharge records with an ICD-9-CM RSV diagnosis listed as any 1 of up to 6 diagnoses for AIs/ANs in the Direct and Contract Health Service Inpatient Dataset record^{8,15} and up to 7 diagnoses for those in the NHDS record¹⁶ were selected for the study. Hospital stays for newborns were excluded.

Hospital discharge records were examined for the period of 1997–2001. Results are presented for the recent study period of calendar years 2000 and 2001, unless otherwise specified. Because new RSV ICD-9-CM codes were introduced in October 1996, use of the study period of 2000–2001 also had the benefit of minimizing the effects of possible delays in the use of the newly introduced RSV codes in hospital discharge coding systems. For purposes of geographic analysis, the 5 IHS regions (IHS administrative areas) were as follows: East (Nashville area), Northern Plains (Aberdeen, Bemidji, and Billings areas), Alaska, Oklahoma, and Southwest (Albuquerque, Navajo, Phoenix, and Tucson areas).¹⁷ US regions were based on the standard census regions of Northeast, Midwest, South, and West. Hospitalizations were also examined according to month of discharge, outcome, and length of stay. Monthly estimates of US infant discharges were made by using only NHDS records sampled from hospitals that responded fully for that year.¹⁶ Race was not examined for the general infant US population, because race/ethnicity was missing from 23% of the NHDS infant RSV-associated discharge records in 2000–2001. Accompanying diagnoses for RSV-associated hospitalizations were also examined. It was not possible to identify multiple hospitalizations for individual patients, because unique

identifiers were not available for either AI/AN or US hospitalizations. The unit of analysis in this study was a hospitalization.

The annual infant hospitalization rates with 95% CIs were calculated as the number of hospitalizations per 1000 infants for AI/AN infants and per 1000 live births for US infants. AI/AN population denominators were determined for each year of the study by using the IHS fiscal year 2001 user population estimates (released March 2003) and adjusting retrospectively for annual changes in the IHS service population (released February 2002), excluding the IHS California and Portland areas.^{8,21} The user population includes all registered AI/AN patients who have received IHS-funded health care services at least once in the past 3 years.⁸ The service population is an estimate of AIs/ANs eligible for IHS-funded health care. Approximately 1.5 million AIs/ANs are eligible for medical care from the IHS, which operates and provides funds for a network of inpatient and ambulatory care facilities across the continental United States and Alaska.^{8,21,22} AI/AN infants in this study represent AI/AN infants who received direct or contract health care through IHS-operated or tribally operated facilities.⁸ The number of live births for US infants was obtained from the US natality data and was used to calculate hospitalization rates for infants in the general US population.²³ Annual and overall SEs of NHDS estimates for 95% CIs were calculated with SUDAAN software (Research Triangle Institute, Research Triangle Park, NC), to account for the stratified sampling techniques.^{16,24} Denominators were considered free from sampling error.¹⁶ For both the AI/AN and US infants, the populations for the <6-month-old age group and the 6- to 11-month-old age group were each estimated to be one-half of the total denominator used for infants. Comparisons of age group, gender, and region among AI/AN infants were made with risk ratios and 95% CIs.

RESULTS

Overall

In 1997–2001, 2841 AI/AN infant hospitalizations listed RSV disease as 1 of the discharge diagnoses; 1258 of these hospitalizations (44%) occurred in 2000–2001. We focused the analysis of RSV hospitalizations on the 2000–2001 study period. During this time, RSV disease was specifically listed on 14.4% of all AI/AN infant hospitalization records and on 13.6% (SE: 0.7%) of hospitalizations for the general infant US population. Twenty-nine percent of hospitalizations for AI/AN infants with lower respiratory tract infections had RSV disease listed as a diagnosis. RSV disease was listed as the first discharge diagnosis for 83.4% of the RSV-associated hospitalizations among AI/AN infants.

For 2000–2001, the average annual rate of RSV

TABLE 1. Hospitalizations Associated With RSV Among AI/AN Infants, 2000–2001

| Characteristic | RSV | | Acute Bronchiolitis Attributable to RSV Infection | |
|-----------------|--------------------------|---|---|---|
| | No. of Hospitalizations* | No. of Hospitalizations per 1000 Infants (95% CI) | No. of Hospitalizations* | No. of Hospitalizations per 1000 Infants (95% CI) |
| Gender | | | | |
| Male | 692 | 36.9 (34.3–39.7) | 586 | 31.2 (28.8–33.9) |
| Female | 566 | 31.7 (29.2–34.4) | 477 | 26.7 (24.4–29.2) |
| Age group | | | | |
| <6 mo | 815 | 44.5 (41.6–47.6) | 685 | 37.4 (34.7–40.3) |
| 6–11 mo | 443 | 24.2 (22.1–26.6) | 378 | 20.7 (18.7–22.8) |
| Region | | | | |
| Alaska | 322 | 70.9 (63.7–78.9) | 247 | 54.4 (48.1–61.5) |
| East | 37 | 38.3 (27.5–53.0) | 37 | 38.3 (27.5–53.0) |
| Northern Plains | 87 | 10.6 (8.5–13.1) | 49 | 6.0 (4.5–7.9) |
| Oklahoma | 71 | 9.4 (7.4–11.9) | 64 | 8.5 (6.6–10.9) |
| Southwest | 741 | 48.2 (44.9–51.8) | 666 | 43.4 (40.2–46.7) |
| Total | 1258 | 34.4 (32.5–36.3) | 1063 | 29.0 (27.3–30.8) |

* Number of any-listed RSV-associated hospitalizations for AI/AN infants who received IHS-funded health care (including health care from tribal facilities).

hospitalizations among AI/AN infants was 34.4 hospitalizations per 1000 infants (95% CI: 32.5–36.3 hospitalizations per 1000 infants) (Table 1). For most of these hospitalizations, RSV was the first-listed diagnosis (28.6 hospitalizations per 1000 infants; 95% CI: 27.0–30.4 hospitalizations per 1000 infants). The rates for the general US infant population were 27.4 hospitalizations per 1000 births (95% CI: 20.9–33.9 hospitalizations per 1000 births) (Table 2) and 25.3 hospitalizations per 1000 births (95% CI: 19.2–31.4 hospitalizations per 1000 births) for any-listed and first-listed RSV hospitalizations, respectively. Most RSV-associated hospitalizations were for treatment of RSV bronchiolitis. The RSV bronchiolitis hospitalization rates were 29.0 hospitalizations per 1000 infants (95% CI: 27.3–30.8 hospitalizations per 1000 infants) for AI/AN infants and 24.2 hospitalizations per 1000 births (95% CI: 18.1–30.3 hospitalizations per 1000 births) for the general population of US infants (Tables 1 and 2). The hospitalization rates for RSV pneumonia were 4.4 hospitalizations per 1000 infants (95% CI: 3.8–5.1 hospitalizations per 1000 infants) for AI/AN infants and 3.0 hospitalizations per 1000 births (95% CI: 1.4–4.6 hospitalizations per 1000 births) for US infants. RSV bronchiolitis was among the 5 most frequently any-listed and first-listed diagnoses for all infant hospitalizations (Table 3). Among first-listed diagnoses, RSV bronchiolitis was 1 of the top 3 diagnoses for all AI/AN infant hospitalizations. The most frequently any-listed diagnoses were acute bronchiolitis attributable to other infectious organisms (ICD-9-CM code 466.19), pneumonia, organism unspecified (code 486), unspecified otitis media (code 382.9), and volume depletion (code 276.5) (Table 3). RSV bronchiolitis was listed for 40.8% and 54.8% (SE: 2.3%) of the AI/AN and US infant bronchiolitis-associated hospitalizations (ICD-9-CM code 466.1), respectively. RSV bronchiolitis was the most frequently listed diagnosis for US infant hospitalizations.

Age, Gender, Region, and Seasonality

The median age at admission for RSV-associated hospitalizations was 4 months (quartiles: 2 and 7 months) among AI/AN infants and 3 months (quartiles: 1 and 5 months) among US infants for the

2-year study period (Fig 1). The rate of RSV hospitalization for infants <6 months of age was higher than that for infants 6 to 11 months of age (Tables 1 and 2). The greatest difference between rates for AI/AN infants and US infants was seen for the 6- to 11-month age group. The hospitalization rate was higher for AI/AN male infants than for AI/AN female infants, and the difference in rates according to age group was consistent for male and female infants.

RSV hospitalization rates for AI/AN infants varied substantially between IHS regions (Table 1). Overall, AI/AN infants living in the Alaska and Southwest regions had the highest hospitalization rates, with the rate being highest for Alaska (Alaska versus Southwest region, risk ratio: 1.5; 95% CI: 1.3–1.7). In addition, the RSV hospitalization rates for the Alaska and Southwest regions were significantly higher than that for US infants (Tables 1 and 2). In Alaska, the RSV bronchiolitis and RSV pneumonia hospitalization rates were 54.4 hospitalizations per 1000 infants (95% CI: 48.1–61.5 hospitalizations per 1000 infants) and 15.6 hospitalizations per 1000 infants (95% CI: 12.3–19.8 hospitalizations per 1000 infants), respectively. These rates were greater than those for US infants (RSV bronchiolitis: 24.2 hospitalizations per 1000 births; 95% CI: 18.1–30.3 hospitalizations per 1000 births; RSV pneumonia: 3.0 hospitalizations per 1000 births; 95% CI: 1.4–4.6 hospitalizations per 1000 births). The Oklahoma region had the lowest RSV hospitalization rate of the IHS regions. In a comparison of the rates for infants <6 months of age, according to IHS region, with that for the general US population, both the Alaska and Southwest regions had significantly higher rates, whereas the rate for the East region was not significantly different and the rates for the Northern Plains and Oklahoma regions were significantly lower. Rates for the 6- to 11-month age group were significantly higher for the Alaska, East, and Southwest regions, the same for the Northern Plains region, and lower for the Oklahoma region, compared with that for the general US population.

RSV bronchiolitis was 1 of the 5 most frequently listed diagnoses among hospitalizations for all AI/AN infants living in the Alaska (fourth, 13.7%),

TABLE 2. Hospitalizations Associated With RSV Among US Infants, 2000–2001

| Characteristic | RSV | | Acute Bronchiolitis Attributable to RSV Infection | |
|----------------|-------------------------------|---|---|---|
| | No. of Hospitalizations (SE)* | No. of Hospitalizations per 1000 Live Births (95% CI) | No. of Hospitalizations (SE)* | No. of Hospitalizations per 1000 Live Births (95% CI) |
| Gender | | | | |
| Male | 125 113 (16 100) | 30.3 (22.7–37.9) | 111 681 (14 500) | 27.0 (20.1–33.9) |
| Female | 96 337 (12 500) | 24.4 (18.2–30.6) | 84 328 (11 800) | 21.3 (15.5–27.1) |
| Age group | | | | |
| <6 mo | 169 566 (21 100) | 41.9 (31.7–52.1) | 148 674 (19 700) | 36.8 (27.2–46.4) |
| 6–11 mo | 51 884 (6600) | 12.8 (9.6–16.0) | 47 335 (6400) | 11.7 (8.6–14.8) |
| Region | | | | |
| Northeast | 26 652 (12 200) | 19.4 (11.3–27.5) | 22 964 (5200) | 16.7 (9.3–24.1) |
| Midwest | 49 078 (16 800) | 27.5 (14.1–40.9) | 43 058 (12 000) | 24.1 (10.9–37.3) |
| South | 73 376 (15 900) | 24.7 (13.6–35.8) | 63 180 (15 000) | 21.3 (11.4–31.2) |
| West | 72 344 (26 700) | 37.0 (21.1–52.9) | 66 807 (15 500) | 34.1 (18.6–49.6) |
| Total | 221 450 | 27.4 (20.9–33.9) | 196 009 (25 700) | 24.2 (18.1–30.3) |

* Estimates of any-listed RSV-associated hospitalizations for the general US population of infants, derived from the NHDS data.

TABLE 3. Most Frequently Any-Listed and First-Listed Diagnoses for Hospitalizations Among AI/AN Infants (IHS/Tribal) and Among US Infants (NHDS), 2000–2001.

| Diagnosis (ICD-9-CM Code) | AI/AN Infants (<i>n</i> = 7796) | | | | General US Infant Population (<i>n</i> = 1 632 322) | | | |
|---|----------------------------------|---------|--------------|---------|--|--------------|--------------|--------------|
| | Any-Listed* | | First-Listed | | Any-Listed* | | First-Listed | |
| | Rank | Percent | Rank | Percent | Rank | Percent (SE) | Rank | Percent (SE) |
| Acute bronchiolitis, attributable to other infectious organisms (code 466.19) | 1 | 17.7 | 1 | 13.9 | 3 | 10.0 (0.6) | 2 | 8.4 (0.5) |
| Pneumonia (code 486) | 2 | 17.7 | 2 | 11.9 | 5 | 6.5 (0.5) | 3 | 4.3 (0.5) |
| Otitis media, organism unspecified (code 382.9) | 3 | 13.4 | | | 4 | 8.5 (0.5) | | |
| Volume depletion (code 276.5) | 4 | 13.4 | | | 2 | 11.2 (0.7) | 4 | 4.2 (0.6) |
| RSV bronchiolitis (code 466.11) | 5 | 12.2 | 3 | 10.6 | 1 | 12.0 (0.7) | 1 | 11.1 (0.6) |
| Unspecified fetal and neonatal jaundice (code 774.6) | | | 4 | 4.6 | | | 5 | 3.7 (0.5) |
| Other and unspecified noninfectious gastroenteritis and colitis (code 558.9) | | | 5 | 4.5 | | | | |

* More than 1 diagnosis may be listed on a record.

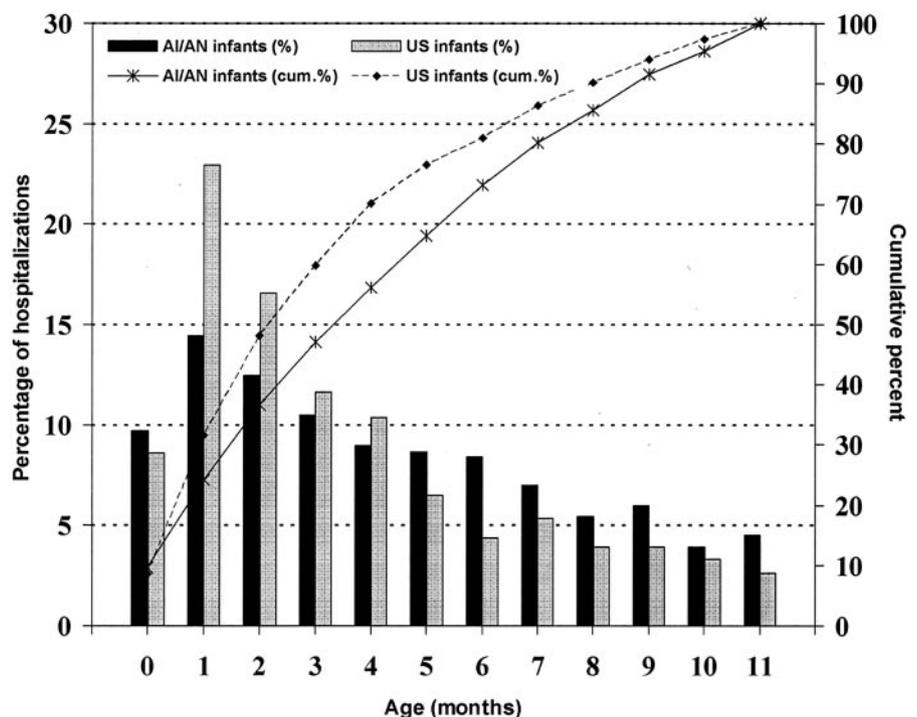


Fig 1. Percentage of RSV-specific hospitalizations among AI/AN infants (IHS/tribal) and US infants (NHDS) according to age, 2000–2001.

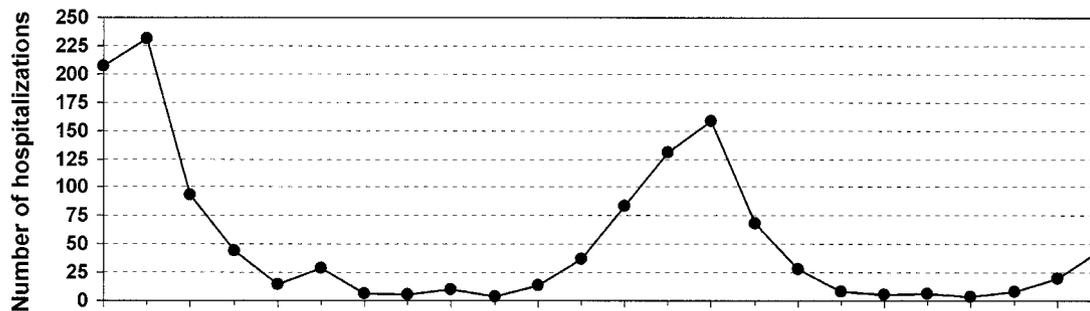
Southwest (fifth, 13.7%), and East (second, 28.9%) regions during the study period. It was also 1 of the 3 most frequently cited first-listed diagnoses for these regions. RSV bronchiolitis was the eighth and 12th most frequently listed diagnosis among infants living in the Oklahoma and Northern Plains regions, respectively. RSV-associated hospitalizations among AI/AN and US infants peaked in the winter months each year (Fig 2). Most (71.9%) RSV hospitalizations among AI/AN infants occurred in January through March; hospitalization rates were highest in January and February in 2000 and in February and March in 2001. Regionally, RSV hospitalizations peaked in January through March in the Southwest (82.2% of RSV

hospitalizations), Northern Plains (77.0%), and Oklahoma (88.7%) regions and in February through April in the Alaska region (54.3%). Hospitalization rates for US infants were highest in January and February.

Hospital Stays and Other Characteristics

In 2000–2001, the median length of the hospital stay for RSV hospitalizations among AI/AN infants, as well as among US infants, was 3 days (quartiles: 2 and 4 days). The median length of stay for AI/AN infants was consistent with respect to age group and region. The median lengths of stay for RSV bronchiolitis and RSV pneumonia were 3 and 4 days, respectively. Eight percent of the AI/AN infant RSV hos-

A. AI/AN Infants



B. US Infants

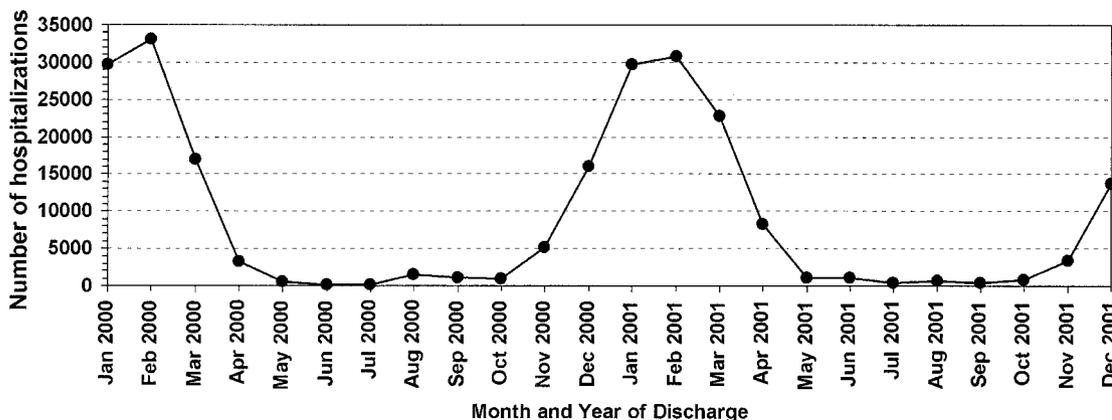


Fig 2. RSV-specific hospitalizations among AI/AN infants (IHS/tribal) (A) and US infants (NHDS) (B) according to month and year of discharge, 2000–2001.

pitalizations resulted in transfer to another facility. Transfers to another IHS or tribal facility and transfers to a non-IHS/nontribal facility could not be distinguished. No hospitalization deaths were reported for RSV hospitalizations among AI/AN infants, and the estimated number of deaths among US infants obtained from the NHDS was too small to be considered reliable.

During the study period, other diagnoses listed for at least 10% of the AI/AN infant RSV-associated hospitalizations were asphyxia (ICD-9-CM code 799.0; 18.5%), unspecified otitis media (code 382.9; 17.0%), and pneumonia (code 486; 13.6%). For US infants, only unspecified otitis media (17.6%; SE: 1.8%) was listed on at least 10% of the records for RSV-associated hospitalizations.

DISCUSSION

RSV accounts for substantial morbidity among infants; an estimated $\geq 100\ 000$ RSV hospitalizations occur annually among infants in the United States. Consistent with a previous study of US infant hospitalizations in 1997–2000,⁴ we found that RSV bronchiolitis continued to be the leading primary diagnosis for hospital discharges among US infants in 2000–2001. We also found that RSV bronchiolitis was among the 5 most frequently listed diagnoses for hospitalizations among AI/AN infants receiving IHS/tribal health care.

The RSV hospitalization rates for AI/AN infants living in the Alaska and Southwest regions were much higher than the rate for the general US infant

population. These regional disparities are consistent with previous studies, which found that AI/AN children and infants living in the Alaska and Southwest regions had higher rates of bronchiolitis, otitis media, and overall infectious disease hospitalizations, compared with AI/AN children living in other IHS regions.^{2,9,13,25} A high rate of RSV hospitalizations for AI/AN infants living in Alaska was also noted in a prospective patient-based study.¹¹

Several factors could contribute to the high rates of RSV hospitalization among AI/AN children living in the Alaska and Southwest regions. Most of the AIs/ANs living in these regions reside in remote villages or on rural reservations. The distance traveled by some patients in these regions to reach health care facilities may predispose some physicians to use a lower threshold for hospital admission for treatment of illnesses such as RSV infections. Alternatively, the need to travel long distances to reach health care facilities may prevent parents from seeking medical care for their infant until an illness becomes severe enough to require hospitalization. High levels of household crowding and a lack of sanitation facilities have been reported for some rural villages in Alaska and some tribes in the Southwest, and limited access to medical facilities in Alaska has been described.^{26–28} In addition, exposure to smoke from wood-burning stoves (common in both regions) was associated with increased risk of hospitalization attributable to lower respiratory illness among Navajo children <2 years of age.^{29,30} The high RSV hospitalization rates for the 2 regions suggest that AI/AN

infants living in these regions are at high risk for RSV disease. Additional studies of RSV illness, including cost-benefit analyses for RSV prophylaxis, should be considered for infants living in these regions.

In contrast to the high RSV disease hospitalization rates for the Alaska and Southwest regions, the rate for the Oklahoma region was the lowest among the IHS regions and was lower than the rate for the general US infant population. Lower hospitalization rates associated with infectious diseases among AIs/ANs living in the Oklahoma region were reported in other studies.^{9,13,25,31} The reasons for the lower rates are not clear but could include a higher socioeconomic status among AIs/ANs living in the Oklahoma region, relative to AIs/ANs living in other IHS regions, with associated improvements in infant health. For example, AIs/ANs living in the Oklahoma region have a higher percentage of college graduates (11.4%), a lower birth rate (22.4%), and a lower infant mortality rate (7.5%), compared with AIs/ANs living in other IHS regions.¹⁷ It is also possible that some AIs/ANs living in urban areas within the Oklahoma region may receive some health care services outside the IHS/tribal system, because they may have health insurance and better access to private health care providers.

For both AI/AN and US infants, RSV-associated hospitalization rates were higher for infants <6 months of age than for infants 6 to 11 months of age. It is interesting to note that the hospitalization rate for AI/AN infants <6 months of age was similar to that for US infants, whereas the rate for AI/AN infants 6 to 11 months of age was higher than that for US infants. The RSV hospitalization rate decreased more rapidly with age among infants in the general US population, compared with AI/AN infants. As infants grow, the influence of prenatal, neonatal, and maternal risk factors decreases and environmental or other risk factors may have more prominent effects on the risk of RSV infection. Additional study is needed to determine how external risk factors for RSV infection (eg, household crowding, indoor smoke exposure, and socioeconomic status) contributed to this rate difference among 6- to 11-month-old infants.

The higher rate of RSV-associated hospitalizations among AI/AN infants, compared with the general US population of infants, suggests that AI/AN infants are among high-risk groups that might benefit from RSV prevention strategies. Some interventions that might prevent RSV-associated disease include encouraging breastfeeding, decreasing household crowding, decreasing indoor smoke exposure, and maximizing use of RSV-specific monoclonal antibody among at-risk infants. Breastfeeding has been shown consistently to be protective against respiratory tract infections among both AI/AN and non-AI/AN infants.^{26,32–36} Exposure to environmental tobacco smoke has been associated with increased risk of respiratory tract infections, and programs to eliminate maternal smoking could reduce RSV morbidity among infants.^{37–40} Because RSV is the most common cause of bronchiolitis and pneumonia in infancy,^{41–43} the development of a vaccine for RSV and implemen-

tation of other interventions should substantially benefit the health of AI/AN infants.^{44–48}

There are limitations associated with the use of ICD-9-CM codes to estimate RSV hospitalizations. In general, discharge diagnoses may be incomplete or miscoded, and diagnostic criteria may vary regionally. It is likely that most RSV-specific coded diagnoses are based not on RSV laboratory diagnostic findings but instead on clinical criteria. In some cases, the diagnoses among US infants may be guided by insurance reimbursement levels associated with diagnostic codes.⁴ In addition, it is likely that the diagnoses for some RSV-infected patients are coded as unspecified bronchiolitis or pneumonia. Limited data from a hospital in Alaska suggest that relying on RSV-specific diagnoses identifies a substantial proportion of laboratory-confirmed RSV hospitalizations. In that hospital, approximately one-half of the infants admitted in 2000–2001 were tested for RSV, 89% of the infants with a RSV ICD-9-CM code on their discharge records had confirmed positive RSV test results, and 80% of all hospitalized infants who tested RSV-positive had a RSV ICD-9-CM code on their discharge records (G. Varney, unpublished data). Data from additional sites are needed to better gauge the sensitivity and specificity of the use of the RSV ICD-9-CM codes. Lack of RSV testing in some IHS/tribal facilities might have contributed to our observation that unspecified bronchiolitis, and not RSV bronchiolitis, was the leading diagnosis among AI/AN infants.

We also note some limitations associated with IHS/tribal hospital discharge data. AI/AN infants eligible for IHS/tribal services could have received medical care outside the IHS/tribal system, resulting in underestimation of RSV-associated hospitalization rates for AI/AN infants. AIs/ANs are likely to seek IHS/tribal medical care, however, because prepaid health care is provided to eligible AIs/ANs.^{8,21,49} In addition, the hospital fatality rate for AI/AN infants in our study might have been underestimated, because AI/AN infants with severe RSV disease might have been transferred to non-IHS/tribal facilities, resulting in the loss of eventual outcomes for the infants' hospitalizations. With respect to disease severity, there was not enough clinical information available in the hospitalization data for assessment of the severity of RSV disease in our study. However, with the use of length of stay as a gross indicator of disease severity, the median length of stay for RSV-associated hospitalizations did not differ between AI/AN infants and the general US infant population. Because only basic demographic and diagnostic data are primarily available in hospital discharge datasets, additional studies focusing on more-detailed epidemiologic factors associated with the regional variations in RSV hospitalization rates would be useful. The AI/AN infants in this study received IHS-funded health care and might not be representative of all AI/AN infants in the United States.

This study suggests that estimates of RSV hospitalizations based on the application to hospital discharge data of RSV-associated bronchiolitis and pneumonia rates determined in prospective studies

are reasonable. It also highlights the importance of RSV as a cause of hospitalization. RSV is the leading discharge diagnosis for the general population of US infants and is among the top 5 discharge diagnoses for AI/AN infants. This study shows that the increase in RSV-associated discharge diagnoses that was noted in earlier studies^{1,4} has continued, and it shows high rates of RSV-associated disease among AI/AN infants. The findings highlight the substantial public health benefit that efforts to prevent RSV disease could have for high-risk populations, such as AI/AN infants, and for the general population of US infants.

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REFERENCES

- Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980–1996. *JAMA*. 1999;282:1440–1446
- Shay DK, Holman RC, Rosevelt GE, Clarke MJ, Anderson LJ. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979–1997. *J Infect Dis*. 2001;183:16–22
- Glezen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. *Am J Dis Child*. 1986;140:543–546
- Leader S, Kohlhas K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. *J Pediatr*. 2003;143(suppl):S127–S132
- Boyce TG, Mellen BG, Mitchel EF, Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in Medicaid. *J Pediatr*. 2000;137:865–870
- Hall CB. Respiratory syncytial virus. In: Feigin RD, Cherry JD, eds. *Textbook of Pediatric Infectious Diseases*. 4th ed. Philadelphia, PA: WB Saunders; 1998:2084–2111
- Young TK. *The Health of Native Americans*. New York, NY: Oxford University Press; 1994
- Indian Health Service. *Trends in Indian Health: 1998–99*. Rockville, MD: Indian Health Service; 2002
- Lowther SA, Shay DK, Holman RC, Clarke MJ, Kaufman SF, Anderson LJ. Bronchiolitis-associated hospitalizations among American Indian and Alaska Native children. *Pediatr Infect Dis J*. 2000;19:11–17
- Singleton RJ, Petersen KM, Berner JE, et al. Hospitalizations for respiratory syncytial virus infection in Alaska Native children. *Pediatr Infect Dis J*. 1995;14:26–30
- Karron RA, Singleton RJ, Bulkow L, et al. Severe respiratory syncytial virus disease in Alaska Native children. *J Infect Dis*. 1999;180:41–49
- Bockova J, O'Brien KL, Oski J, et al. Respiratory syncytial virus infection in Navajo and White Mountain Apache children. *Pediatrics*. 2002;110(2). Available at: www.pediatrics.org/cgi/content/full/110/2/e20
- Holman RC, Curns AT, Cheek JE, Singleton RJ, Anderson LJ, Pinner RW. Infectious disease hospitalizations among American Indian and Alaska Native infants. *Pediatrics*. 2003;111(2). Available at: www.pediatrics.org/cgi/content/full/111/2/e176
- Centers for Disease Control and Prevention. Bronchiolitis-associated outpatient visits and hospitalizations among American Indian and Alaska Native children: United States, 1990–2000. *MMWR Morb Mortal Wkly Rep*. 2003;52:707–710
- Indian Health Service. *Inpatient/CHS Inpatient Data Fiscal Years 1980–2002: National Patient Information Reporting System*. Albuquerque, NM: Indian Health Service; 2003
- National Center for Health Statistics. *National Hospital Discharge Survey: Multi-Year Data Tape Information, 1979–2001*. Hyattsville, MD: National Center for Health Statistics; 2003
- Indian Health Service. *Regional Differences in Indian Health 2000–2001*. Rockville, MD: Indian Health Service; 2003
- Kaufman SF. *Utilization of IHS and Tribal Direct and Contract General Hospitals, FY 1996 and U.S. Non-Federal Short-Stay Hospitals, 1996*. Rockville, MD: Indian Health Service; 1998
- Kozak LJ, Hall MJ, Owings MF. National Hospital Discharge Survey: 2000 annual summary with detailed diagnoses and procedure data: National Center for Health Statistics. *Vital Health Stat* 13. 2002;(153):1–194
- Public Health Service and Health Care Financing Administration. *International Classification of Diseases, 9th Revision, Clinical Modification*. 6th ed. Washington, DC: US Department of Health and Human Services; 1997. CD-ROM
- Rhoades DA, D'Angelo AJ, Rhoades ER. Data sources and subsets of the Indian population. In: Rhoades ER, ed. *American Indian Health: Innovations in Health Care, Promotion, and Policy*. Baltimore, MD: Johns Hopkins University Press; 2000:93–102
- Cunningham PJ, Altman BM. The use of ambulatory health care services by American Indians with disabilities. *Med Care*. 1993;31:600–616
- US Department of Health and Human Services. *Detailed Data 1979–2001: Public Use Data Tape Documentation: Natality*. Hyattsville, MD: Centers for Disease Control and Prevention, National Center for Health Statistics; 2003
- Shah BV, Barnell BC, Bieler GS. *SUDAAN Users Manual, Release 7.0*. Research Triangle Park, NC: Research Triangle Institute; 1996
- Curns AT, Holman RC, Shay DK, et al. Outpatient and hospital visits associated with otitis media among American Indian and Alaska Native children younger than 5 years. *Pediatrics*. 2002;109(3). Available at: www.pediatrics.org/cgi/content/full/109/3/e41
- Bulkow LR, Singleton RJ, Karron RA, Harrison LH, Alaska RSV Study Group. Risk factors for severe respiratory syncytial virus infection among Alaska Native children. *Pediatrics*. 2002;109:210–216
- Indian Health Service. *The Sanitation Facilities Construction Program of the Indian Health Service, Public Law 86–121: Annual Report for 1998*. Rockville, MD: US Public Health Service; 1999
- US Bureau of the Census. *US Census Statistical Briefs: Housing of American Indians on Reservations: Plumbing*. Washington, DC: US Bureau of the Census; 1995
- Robin LF, Less PS, Winget M, et al. Wood-burning stoves and lower respiratory illnesses in Navajo children. *Pediatr Infect Dis J*. 1996;15:859–865
- Morris K, Morgenlander M, Coulehan JL, Gahagen S, Arena VC, Morganlander M. Wood-burning stoves and lower respiratory tract infection in American Indian children. *Am J Dis Child*. 1990;144:105–108
- Holman RC, Parashar UD, Clarke MJ, Kaufman SF, Glass RI. Trends in diarrhea-associated hospitalizations among American Indian and Alaska Native children, 1980–1995. *Pediatrics*. 1999;103(1). Available at: www.pediatrics.org/cgi/content/full/103/1/e11
- Ellestad-Sayed J, Coodin FJ, Dilling LA, Haworth JC. Breast-feeding protects against infection in Indian infants. *Can Med Assoc J*. 1979;120:295–298
- Butler JC, Crengle S, Cheek JE, et al. Emerging infectious diseases among indigenous peoples. *Emerg Infect Dis*. 2001;7:554–555
- Wright AL, Bauer M, Naylor A, Sutcliffe E, Clark L. Increasing breast-feeding rates to reduce infant illness at the community level. *Pediatrics*. 1998;101:837–844
- Bachrach VRG, Schwarz E, Bachrach LR. Breastfeeding and the risk of hospitalization for respiratory disease in infancy: a meta-analysis. *Arch Pediatr Adolesc Med*. 2003;157:237–243
- Oddy NH, Sly PD, de Klerk NH, et al. Breast feeding and respiratory morbidity in infancy: a birth cohort study. *Arch Dis Child*. 2003;88:224–228
- McCusker D, Clifton H, Miller-Korth N. Native American infant mortality in Wisconsin. *Wis Med J*. 2000;99:50–52
- Coultas DB, Gong H Jr, Grad R, et al. Respiratory diseases in minorities of the United States. *Am J Respir Crit Care Med*. 1994;149(suppl):S93–S131
- Pedreira FA, Guandolo VL, Feroli EJ, Mella GW, Weiss IP. Involuntary smoking and incidence of respiratory illness during the first year of life. *Pediatrics*. 1985;75:594–597
- Holman RC, Shay DK, Curns AT, Lingappa JR, Anderson LJ. Risk factors for bronchiolitis-associated deaths among infants in the United States. *Pediatr Infect Dis J*. 2003;22:483–490
- Anderson LJ, Parker RA, Strikas RA, et al. Day care center attendance and hospitalization for lower respiratory tract illness. *Pediatrics*. 1988;82:300–308
- Law BJ, Carbonell-Estrany X, Simoes EA. An update on respiratory syncytial virus epidemiology: a developed country perspective. *Respir Med*. 2002;96(suppl B):S1–S7

43. Centers for Disease Control and Prevention. Respiratory syncytial virus activity: United States, 2000–01 season. *MMWR Morb Mortal Wkly Rep*. 2002;51:26–28
44. Black S, Shinefield H, Fireman B, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children: Northern California Kaiser Permanente Vaccine Study Center Group. *Pediatr Infect Dis J*. 2000;19:187–195
45. Singleton R, Dooley L, Bruden D, Raelson S, Butler JC. Impact of palivizumab prophylaxis on respiratory syncytial virus hospitalizations in high risk Alaska Native infants. *Pediatr Infect Dis J*. 2003;22:540–545
46. Meissner HC, Welliver RC, Chartrand SA, et al. Immunoprophylaxis with palivizumab, a humanized respiratory syncytial virus monoclonal antibody, for prevention of respiratory syncytial virus infection in high risk infants: a consensus opinion. *Pediatr Infect Dis J*. 1999;18:223–231
47. Sorrentino M, Powers T, Palivizumab Outcomes Study Group. Effectiveness of palivizumab: evaluation of outcomes from the 1998 to 1999 respiratory syncytial virus season. *Pediatr Infect Dis J*. 2000;19:1068–1071
48. Meissner HC, Long SS, American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Fetus and Newborn. Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus. *Pediatrics*. 2003;112:1447–1452
49. Cunningham PJ. Access to care in the Indian Health Service. *Health Aff (Millwood)*. 1993;12:224–233

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