ABSTRACT Respiratory syncytial virus (RSV) infection is the most common cause of hospitalization for bronchiolitis and pneumonia in the winter for children younger than one year of age. After reviewing our hospital cost data for RSV hospitalization from the 1997–1998 RSV season and after accounting for the different numbers of patients in each group, we found that the weighted mean charges were $15,841; the mean cost was $10,613; and the average length of stay was 3.9 days.

INTRODUCTION
Respiratory syncytial virus (RSV) is the most common cause of hospitalization for bronchiolitis and pneumonia (infections of the lower respiratory tract) in infants and children under one year of age during the winter.1-3 Earlier studies had indicated that 0.1% to 1% of all RSV infections resulted in hospitalization,4,5 with higher rates seen in children born before 32 weeks of gestation and in children with bronchopulmonary dysplasia.

In 2001, Shay and associates estimated that there were between 73,400 and 126,300 hospitalizations per year for RSV bronchiolitis and/or pneumonia in the U.S. in children younger than one year of age from 1994 to 1996, with substantial increases noted since 1980.6 A case–fatality rate of 2.5% has been reported for children hospitalized with RSV infection younger than one year of age. Most of the deaths occurred in children with chronic underlying diseases (e.g., congenital heart disease, sickle cell disease, cystic fibrosis),7,8 although recent mortality rates appear to be decreasing.1

Palivizumab (Synagis®, MedImmune) can effectively prevent hospitalizations caused by RSV infection in infants; it is commonly used only for the following patients:9,10

- children at high risk for severe disease (i.e., those younger than two years of age with chronic lung disease who have required medical therapy in the previous six months)
- infants younger than one year of age, born at or less than 28 weeks of gestation
- infants younger than six months of age, born between 29 and 32 weeks of gestation
- infants younger than six months of age, born between 33 and 35 weeks of gestation with additional risk factors for RSV infection

Despite the generally accepted safety and efficacy of palivizumab, the decision to provide prophylaxis for RSV infection is influenced by its cost–benefit ratio. The objective of our study was to evaluate the actual charges and costs associated with hospitalizations caused by infection with RSV at a tertiary-care medical center. From the results, we hope to accurately determine the true expenditures of hospital-based RSV care so that future cost–benefit analysis of prophylaxis can be even more comprehensive and rigorous.

METHODS
From the fall of 1997 through the spring of 1998, we reviewed the available medical records of all patients with RSV, confirmed by enzyme-linked immunoassay (ELISA) or viral culture, at Children’s Memorial Medical Center in Chicago. At the center, acute respiratory infections in all admitted infants and children of all ages require a rapid test for RSV; these infections include the clinical diagnoses of bronchiolitis, bronchitis, cold, croup, asthma with fever, influenza, and viral pneumonia.

The patients were divided into three groups: children admitted to the ward only (ward), children admitted to the ward and the pediatric intensive-care unit (PICU) (ward + PICU), and children admitted to the PICU who also required mechanical ventilation (ward + PICU + ventilation). Children whose RSV infection was judged to play no role in their hospitalization were excluded from analysis (see Results), and children with a known risk factor for RSV infection were analyzed separately.

Total hospital charges, PICU expenses, and ventilator costs—excluding physician charges—were ascertained for each patient from the Business Development Office. If RSV was not both the admitting and the discharge diagnosis, we determined what role, if any, RSV played in that child’s hospitalization and we used only that part of the cost attributable to RSV. For example, if a hospitalized child’s condition worsened and subsequent testing confirmed a newly acquired RSV infection, we used only the amount of time required to return to the baseline state to calculate the cost of the patient’s RSV-related hospitalization. Data abstracted from the charts for each patient included age, sex, race, gestational age, type of insurance (private or public aid), and length of stay (or the portion of the length of stay attributable to RSV).

We calculated the mean charge per case, the mean cost per case (with a cost/charge ratio of 0.67 at Children’s Memorial), and the mean length of stay for each group. We then calculated the weighted mean charge, cost, and length of stay for each group. Because of the differences in the size of each subgroup, we used weighted averages. For instance, multiplying the mean charge for each group by the percentage of patients in the study from that group and adding the results yields the weighted mean charge. We used public aid as a crude surrogate for socioeconomic status.

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RESULTS

Ninety-three patients were hospitalized at Children’s Memorial from fall 1997 through spring 1998 with an admitting or a discharge principal or a secondary diagnosis of RSV infection. Five of these cases were classified as nosocomial infections, as defined by the lack of respiratory symptoms on admission, the development of RSV infection more than 96 hours after admission, or the occurrence of RSV infection within 96 hours of a previous hospital admission, based on the usual incubation period for RSV and on our hospital’s infection-control policies.

The charts of four patients were unavailable for review (two in the ward group and two in the ward + PICU + ventilation group). In nine instances, a confirmed RSV infection was an incidental finding and was not the cause of the patient’s hospitalization. This was true for eight patients in the ward group and for one patient in the ward + PICU + ventilation group; thus, these patients were not included in our analysis.

As examples, one patient who had been admitted with nephrotic syndrome and Streptococcus pneumoniae bacteremia, a second patient who had been admitted with a complication of sickle cell disease, a third patient who had been admitted with Henoch-Schönlein purpura, and a neonate who had been admitted with indirect hyperbilirubinemia were found to be RSV-positive but required no oxygen and were not in respiratory distress throughout their hospitalizations. A fifth patient, who had recently undergone liver transplantation, was admitted for portal vein thrombosis and was found to be RSV-positive; she too required no oxygen and experienced no respiratory distress throughout her hospitalization. Our analysis focuses on the remaining 80 patients.

The demographics of the study population are shown in Table 1. About two-thirds of the patients were black or Hispanic, accurately reflecting the demographics of the population at Children’s Memorial and the demographics of RSV infection. There was a predominance of boys (47 of 80, or 59%) and children receiving public aid (52 of 80, or 65%), again, as would be expected from the demographics. The median age of the patients studied was 23.2 months, with slightly older children (median age, 34 months) requiring PICU monitoring and younger children (median age, eight months) requiring mechanical ventilation.

Nine of the 12 patients (75%) who experienced respiratory failure that necessitated mechanical ventilation had a known risk factor for increased complications because of RSV (mainly pre-existing heart disease). The same was true for four of the 13 patients (31%) who had been admitted to the PICU but who were not undergoing ventilation and for nine of the 55 patients (16%) who had been admitted to the ward service alone.

Children who required ventilation were thus more likely to have risk factors for RSV infection than children who had been admitted to the hospital (either to the ward or to the PICU) and who did not receive ventilation (the chi square for this distribution was equal to 0.001). Two of the 55 patients (4%) who had been admitted to the ward only, one of 13 patients who had been admitted to the PICU but who had not received ventilator therapy (8%), and three of the 12 patients admitted to the PICU who needed mechanical ventilation (25%) had been born at less than 36 weeks of gestation.

Bronchiolitis was the diagnosis in two of 13 patients in the PICU (15%), in four of 12 patients who required mechanical ventilation (33%), and in all but 11 patients admitted to the ward (80%). Other diagnoses associated with RSV infection in our population included croup, pneumonia, and prolonged intubation.

Table 2 lists the mean charges per case, mean costs per case (using our institution’s RSV charge x 0.67), and mean length of stay for each group. The weighted mean charge, mean cost, and mean length of stay overall for the entire study population was $15,841; $10,613; and 3.9 days, respectively.

DISCUSSION

RSV is one of the most common causes of hospitalization and emergency room care among children in the first few years of life. RSV typically causes bronchiolitis but can also result in pharyngitis, laryngotracheobronchitis, pneumonia, and prolonged intubation. Studies of children hospitalized with RSV infection that include a substantial number of nonbronchiolitis RSV-related conditions also report higher median ages.

Determining true expenditures related to RSV infection requires diagnostic confirmation, a chart review, and an analysis of billing costs. One previous study used a U.S. database to estimate the nationwide hospital charges of RSV pneumonia; in 1998 dollars, the hospital charges for RSV pneumonia were $295,100,000 in 1993; $392,300,000 in 1994; and $295,800,000 in 1995. Individual records were not validated in that study, however, because all identifiers were removed; RSV bronchiolitis was not included in the analysis because that diagnosis was not assigned a separate International Classification of Diseases (9th revision) (ICD-9) code until 1996.

A study at a U.S. tertiary-care center, published in 2001, showed...
a comparable average cost of $4,338 per patient for fiscal year 1997 for patients with acute RSV bronchiolitis,12 similar to our mean cost of $5,037 for patients admitted to the ward only. Another study that estimated the economic burden of RSV-associated bronchiolitis hospitalizations yielded similar data.13 Studies from other countries have tended to yield lower figures.14,15 Our intent was to measure the direct costs of hospitalization attributable to RSV at a single, tertiary-care facility. In our analysis, we did not calculate indirect costs, such as those related to secondary cases, and we did not include physician charges or the costs of outpatient follow-up care. An earlier study that had used indirect costs16 had been criticized for inflating the potential cost savings of products designed to prevent RSV infection. Our information thus provides a dataset of direct costs upon which to base future cost–benefit analyses.

RSV immune globulin and palivizumab have proved effective as prophylactic therapy for RSV illness in high-risk children.9,17 Although most of the patients admitted to our ward service were not in a group previously identified to be at high risk for RSV infection, nine in 12 (75%) of those children who ultimately received ventilation and four in 13 (31%) of those children admitted to the PICU were in such a group. Thus, many of the children at high risk for RSV infection require intensive care or ventilation, at a significant cost. Approximately 55% of these cases of RSV might be prevented if prophylaxis were used in a timely manner in eligible children.9 Had all eligible children received prophylaxis and had these preventive measures been 55% effective, the estimated cost savings during the season we studied at our institution could have been more than $250,000.

Potential cost savings at the hospital level, of course, must be balanced against the cost of prescribing palivizumab for about 17 healthy individuals to prevent a single hospitalization.9 For the season we studied, prophylactic measures to prevent the high-risk eligible cases could have cost as much as $970,000, based on one vial of palivizumab per dose (about $950 per vial in 1998 at our institution) and five doses per season. More important than cost, however, is the 50 patient-days of hospitalization that might have been avoided during the season studied. Our estimated cost–benefit ratio of 3.88 ($970,000/$250,000) can be compared with that of Shireman and Braman (6.67) using data from the 1999–2000 season in Kansas.18

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