Impact of RSV: Implications for Managed Care

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Respiratory syncytial virus (RSV) disease is the leading cause of infant hospitalization, and premature infants are particularly at high risk. Timely RSV management strategies can help reduce costly RSV hospitalizations.

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infections — particularly bronchiolitis — in infants and young children in the United States, and is the leading cause of hospitalization of infants younger than 1 year of age (Leader 2002, Shay 1999). Up to 126,000 infants are hospitalized each year because of severe RSV disease, 20 percent of whom are premature infants, and the number and rate of hospitalizations may be increasing (Leader 2002, Shay 1999). In addition, it is estimated that up to 400 children younger than 1 year of age die each year due to severe RSV infection (Shay 2001, Thompson 2003). RSV disease contracted in infancy may also be associated with respiratory ailments later in life, such as recurrent wheezing and physician-diagnosed asthma in childhood (Sigurs 2005, Stein 1999).

The economic burden on the U.S. health care system is significant. Direct medical costs of RSV-associated hospital care for infants (emergency department visits and inpatient stays) over a 4-year period, 1997 to 2000, amounted to an estimated $3 billion, or an annual average cost of $750 million (Leader 2003a). Between 1997 and 2002, the RSV hospitalization rate among infants younger than 1 year of age increased by 25 percent, with the highest hospitalization rate being among infants during the first 3 months of life (45.3 per 1,000) (McLaurin 2005). Mean hospital charges for RSV increased by 39 percent between 1997 and 2002 and totalled more than $1.1 billion in 2002 (McLaurin 2005). Furthermore, RSV hospitalization of infants is associated with substantial time, out-of-pocket, and productivity losses for the affected families and, by extension, society in general (Leader 2003b).

These data underscore the need for the early and careful identification, evaluation, and management of infants younger than 1 year of age — particularly premature infants — who may be at high risk of severe RSV disease.

Why are premature infants at high risk?

Acute infection of the lower respiratory tract, which manifests clinically as bronchiolitis or pneumonia, is the hallmark of severe RSV disease. RSV outbreaks generally occur during the annual RSV season of November through April, although the season can vary greatly throughout the country or during any 1 year, and even among close communities (AAP 2006, Mullins 2003, Panozzo 2007).

Infection is easily transmitted, usually hand to hand or by contact with contaminated surfaces, such as kitchen and bathroom countertops, and even toys, clothing, and other objects (AAP 2006, Hall 1980). Spread in households and child-care centers is common, as is reinfection (AAP 2006, Hall 2001).

Preterm infants (35 weeks or less gestational age [GA]); infants with congenital heart disease (CHD); and premature infants with chronic lung disease (CLD) are known populations at an increased risk of developing severe RSV disease (AAP 2006, Boyce 2000, Law 2004).

Premature infants have an elevated risk of RSV susceptibility primarily because they have fewer disease-fighting antibodies — maternal antibody transfer generally occurs during the third trimester or after 28 weeks (Yeung 1968). Also, their lungs are less mature than the lungs in full-term infants (Langston 1984). As shown in Figure 1, preterm infants have about half the lung volume of full-term infants, with a thicker air-space wall, which results in impaired gas exchange; alveoli, the distal, tiny grape-
like structures that are the principal site of gas exchange in the lungs are not uniformly present until 36 weeks GA (Langston 1984).

Preterm birth rates vary among racial, ethnic, and socioeconomic groups (Martin 2007). Of infants born preterm, approximately 75 percent are born 32 to 35 weeks GA (Figure 2), and about two thirds of these infants are likely to have two or more documented RSV risk factors (Figure 3).

Although prematurity alone can significantly increase the risk for severe RSV disease, the presence of one or more other risk factors listed in the Table on page 4 may also increase susceptibility. Strong recent evidence cited in the literature (Table) supports that exposure to tobacco smoke, young chronological age, and crowded living conditions are linked to an increased risk of RSV disease.

**RSV is costly**

Actuarial cost analyses show that health care costs for infants 33 to 36 weeks GA who have a history of RSV hospitalization are substantially higher than

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**FIGURE 2**

32 to 35 weeks GA infants — a birth cohort at high risk for RSV

- Of the 7.9% of U.S. infants born preterm (≤35 weeks GA) in 2005, approximately 75% were born 32 to 35 weeks GA.1,2
- Preterm birth rates vary among racial-ethnic and socioeconomic groups. Rates are highest for African-Americans and have increased by one third among whites and by 9% among Hispanics since 1990.1

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**FIGURE 3**

Infants born 32 to 35 weeks GA are likely to have two or more documented RSV risk factors

- Approx. 75% of those preterm infants are 32 to 35 weeks GA.1
- Two thirds of these infants have two or more documented risk factors.1

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*1 Survey included a review of 905 patient charts from pediatricians who manage patients ≤35 weeks GA.1

1 Risk factors include school-aged siblings, daycare attendance, exposure to environmental air pollutants or tobacco smoke, severe neuromuscular disease, congenital abnormalities of the airways, low birthweight (<2500 g), crowded living conditions (≥4 in household), multiple births, and family history of asthma.1

*1 Data on file, MedImmune, LLC.

health care costs for infants 33 to 36 weeks GA with no history of RSV hospitalization, or even with full-term infants who have a history of RSV hospitalization (Figure 4). In addition, as shown in Figure 5, the RSV hospitalization rate for preterm infants is nearly double the rate for low-risk, full-term infants. Also, infants born 33 to 35 weeks GA have double the hospital length of stay, double the length of stay in the neonatal intensive care unit (NICU), and more than triple the intubation rate of full-term infants (Figure 6).

Managing RSV
Prematurity is associated with a greater use of hospital resources and poorer clinical outcomes during RSV hospitalization (Boyce 2000, Horn 2003, Law 2002). A comprehensive

<table>
<thead>
<tr>
<th>TABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors associated with an increased risk of RSV hospitalization</strong></td>
</tr>
<tr>
<td><strong>Risk factor</strong></td>
</tr>
<tr>
<td>Multiple births(^{14,15})</td>
</tr>
<tr>
<td>Low birthweight (&lt;2500 g)(^{14,16,17,18,22})</td>
</tr>
<tr>
<td>Crowded living conditions(^{3,11,15,19})</td>
</tr>
<tr>
<td>Family history of asthma(^{3,11,20,21})</td>
</tr>
<tr>
<td>Young chronological age (&lt;12 wks)(^{1,2,3,22})</td>
</tr>
<tr>
<td>Exposure to environmental smoke(^{1,2,11,12,13,21,23})</td>
</tr>
<tr>
<td>*School-age siblings(^{1,2,3})</td>
</tr>
<tr>
<td>*Day care attendance(^{2,3,5})</td>
</tr>
<tr>
<td>*Exposure to environmental air pollutants(^7)</td>
</tr>
<tr>
<td>*Severe neuromuscular disease(^8,9)</td>
</tr>
<tr>
<td>*Congenital abnormalities of the airways(^6)</td>
</tr>
</tbody>
</table>

\(^*\) AAP identified risk factors.

PICU=pediatric intensive care unit.


FIGURE 4
Infants with a history of RSV hospitalization are associated with increased health care costs

In the first year of life, infants 33 to 36 weeks GA with a history of RSV hospitalization cost:
- Nearly 5 times as much as infants 33 to 36 weeks GA with no history of RSV hospitalization
- Nearly 4 times as much as full-term infants with a history of RSV hospitalization

Average total cost per infant during the first year of life (excluding the birth hospitalization)*

<table>
<thead>
<tr>
<th>Average payment ($)</th>
<th>No history of RSV hospitalization</th>
<th>History of RSV hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;33 weeks</td>
<td>$26,167</td>
<td>$82,822</td>
</tr>
<tr>
<td>33–36 weeks</td>
<td>$7,827</td>
<td>$37,168</td>
</tr>
<tr>
<td>Full term</td>
<td>$2,143</td>
<td>$10,298</td>
</tr>
</tbody>
</table>

* The results shown are based on a study of 50,184 commercially insured infants born in calendar year 2004 who survived their first year of life. The results reflect the mix of risk characteristics underlying the study population. Care should be used when generalizing the results to other infant populations. The costs associated with the first year of life are influenced by factors which could result in material differences in observed results, including the delivery system and overall cohort morbidity (i.e., presence of other significant medical conditions).

GA=gestational age.

sive and proactive RSV management program for infants younger than 1 year at high risk of RSV infection, with an emphasis on preterm infants, can help reduce NICU admissions and RSV hospitalizations and their associated costs.

Optimally, such a program should ensure the care of an infant prior to hospital discharge and throughout the infant’s first RSV season, which can be determined by accessing local RSV epidemiology data. Case management should be encouraged. Hospital case managers can quickly identify and evaluate high-risk infants. Managed care case managers can facilitate the prompt and smooth transition of these infants from the hospital or NICU setting to the clinical setting or home so that RSV management can continue. Parent education is also important, and parents and other caregivers should be counseled on the importance of hand washing and other sanitation safeguards in the home.

Summary

Severe RSV disease, manifested as bronchiolitis or pneumonia, is the leading cause of hospitalization of infants younger than 1 year of age in the United States. Infants born 35 weeks or less GA are particularly at high risk of severe RSV disease, which may result in frequent NICU admissions or long hospital stays and additional health care utilization over the first 12 months of life. This care is costly — infants 33 to 36 weeks GA with a history of RSV hospitalization incur costs that are nearly 5 times as much as costs for 33 to 36 weeks GA infants with no history of RSV hospitalization.

FIGURE 5
RSV hospitalizations in Tennessee Medicaid infants*

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD</td>
<td>56.3</td>
</tr>
<tr>
<td>CHD</td>
<td>12.1</td>
</tr>
<tr>
<td>≤ 28 weeks GA</td>
<td>9.4</td>
</tr>
<tr>
<td>29 to &lt;33 weeks GA</td>
<td>8.2</td>
</tr>
<tr>
<td>33 to &lt;36 weeks GA</td>
<td>8.0</td>
</tr>
<tr>
<td>Low-risk**</td>
<td>4.4</td>
</tr>
</tbody>
</table>

*Data derived from a retrospective analysis of 3,553 hospitalizations for RSV-related illness in children <3 years of age enrolled in the Tennessee Medicaid system between July 1989 and June 1993.

**Low-risk defined as children born at term with no underlying medical conditions.

BPD=bronchopulmonary dysplasia, CHD=congenital heart disease, GA=gestational age.

Source: Adapted from Boyce 2000

FIGURE 6
Effects of prematurity on RSV-related hospital resource use and outcomes*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Days</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU LOS</td>
<td>8.4 days*</td>
<td>38.7%*</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>4.1 days</td>
<td>12.1%</td>
</tr>
</tbody>
</table>

*Based on a retrospective multicenter study that measured the severity of illness in 304 infants aged ≤1 year who were admitted to the hospital with confirmed RSV from April 1995 to September 1996.

**Statistically significant difference from full-term infants (Duncan multiple range test).

ICU=intensive care unit, LOS=length of stay.

4.1 days

Full term (n=215) 33–35 wks GA (n=31)

(P<.0001)*

3.8 days

Full term (n=215) 33–35 wks GA (n=31)

(P=.021)*

12.1%

Full term (n=215) 33–35 wks GA (n=31)

(P=.002)*

Adapted from Horn 2003
Steps to creating an effective RSV program for high-risk infants

 managed care analysis by Norman White, MD
 Medical Director, Presbyterian Health Plan, Albuquerque, N.M.

Through the use of successive quality-improvement cycles, Presbyterian Health Plan (PHP) has evolved an effective process to reduce the impact of RSV disease in the high-risk infant population. Timely and appropriate identification of high-risk infants, particularly infants born 35 weeks gestation and less who have two or more documented risk factors, is the first step and requires the participation of the neonatology treatment team, including the physician, nurse, pharmacist, and discharge planner, as well as the NICU team and hospital case managers. RSV management begins prior to hospital discharge and continues throughout an infant’s first RSV season.

The use of standardized forms, originating in contracted NICUs and primary care offices, is an important component of PHP’s RSV management process. Initial information about a high-risk infant is conveyed to the primary care provider prior to outpatient follow-up using common forms that have been developed in collaboration with local pediatric clinicians and health care insurers.

Continuity of care is reinforced by the PHP program coordinator and home health agencies that work with the identified infants and their parents or caregivers to follow through with the RSV management program during the first RSV season.

The program’s season is determined by the historical time frame for RSV occurrence in New Mexico, together with current season information provided by the local virology lab in Albuquerque. The anticipated onset of the season is November 1, while monitoring of current data allows for the ability to initiate program activity sooner if warranted. Similarly, the end of the RSV season is monitored for the decreasing incidence of RSV isolates, with termination of the program typically at the end of April.

Managed care payers should be cognizant of the potential ramifications of severe RSV disease in infants. Developing a proactive RSV management strategy can help improve health outcomes and reduce unnecessary hospital resource use.

References


**Disclosures:**

Doris Makari, MD, is an employee of MedImmune. J Michael Hoopes, PharmD, is an employee of MedImmune. He is also a member of the American Society of Health-System Pharmacists and the Drug Information Association. Norman White, MD, is a Medical Director with Presbyterian Health Plan, Albuquerque, New Mexico. He reports no financial arrangements or affiliations that may constitute a conflict of interest with his commentary.