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Flu-Related Hospitalizations in Children

Editor's note: An estimated 20,000 children are hospitalized each year with influenza-related illnesses. Children with certain chronic conditions are at higher risk for serious influenza (flu) complications, and recommendations for annual flu vaccines have been targeted at these children. Over the past four years, public health officials have expanded their recommendations about which children should be immunized against the flu. This Issue Brief summarizes clinical outcomes and costs from the largest study to date of children hospitalized with the flu. These findings should help inform clinicians and policymakers in prioritizing their efforts to implement the new recommendations.

Flu vaccine now recommended for children ages 6 months to five years

In the United States, influenza outbreaks typically occur during the winter months, and are responsible for about 36,000 deaths and 200,000 hospitalizations each year. Influenza-related deaths in children are rare, but hospitalization rates for children are similar to those for the elderly and for adults with chronic conditions. Annual influenza vaccination is the primary way to prevent infection and its complications.

- Population-based studies suggest that people with certain chronic medical conditions are at increased risk of serious flu complications. These conditions include asthma and other respiratory diseases, cardiac disease, immunosuppression, chronic kidney disease, and metabolic and endocrine conditions.
- National guidelines indicate that children with high-risk conditions receive annual flu vaccines. Last year, this recommendation was extended to all children 6-23 months of age. This year, the recommendation was extended to all children ages 6 months to five years.
- Actual vaccination rates lag far behind these recommendations. Estimates from 2005 suggest 48% vaccination coverage among children aged 6-23 months and 35% coverage among children aged 2-17 years who had one or more high-risk medical conditions.

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Study of hospitalized children sheds light on flu-related complications

To understand the clinical course and serious complications in children with the flu, Keren and colleagues studied 745 children 21 years and younger who were hospitalized for influenza at the Children's Hospital of Philadelphia in four consecutive flu seasons (July 2000-June 2004). All patients had acquired the flu in the community. The diagnosis was confirmed by laboratory tests.

Chronic medical conditions in children hospitalized with the flu

Known high-risk conditions (as of 2004)	
Asthma	24%
Immunosuppressive disorder	8%
Cardiac disease	7%
Hemoglobinopathy	6%
Chronic pulmonary disease (other than asthma)	4%
Metabolic disease	3%
Long-term salicylate therapy	2%
Chronic renal dysfunction	1%
Suspected high-risk conditions	
Neurological/neuromuscular disease	12%
Gastroesophageal reflux disease	14%

- About 25% were infants less than six months old, a group for whom neither flu vaccines nor antiviral medications are currently licensed. About 77% of patients were under age 5.
- More than half of the patients were African-American, in part reflecting the racial composition of the surrounding neighborhood (see neighborhood analysis on next page).
- Forty-three percent of patients had at least one chronic condition recognized as a risk factor for severe flu infection. The most prevalent appear in the table at left. The researchers also analyzed the prevalence of two other conditions suspected of being risk factors for flu complications at that time: neurological/neuromuscular disease and gastroesophageal reflux disease.
- The vaccination status of the patients in the study was not known.

Neurological/neuromuscular conditions and cardiac disease are risk factors for flu complications or prolonged hospital stays

Of greatest concern to parents and health professionals is the potential for serious flu-related complications, such as respiratory failure and death. The researchers analyzed risk factors for these complications and prolonged hospitalizations (more than six days).

- A total of 132 patients (25%) experienced at least one flu-related complication. Pneumonia was most common (15%).
 - Thirty-two children (4.3%) had respiratory failure, defined as the need for mechanical ventilation. Of those patients, five died.
 - Adjusting for other factors, patients with neurological/neuromuscular disease, chronic pulmonary conditions other than asthma, and cardiac disease were at much higher risk of respiratory failure than other patients. Overall, patients with any of these conditions had about a 10% chance of respiratory failure. Having two of the three chronic conditions increased that probability to 31%-39%.
 - The median length of stay was 2 days, but 12% of patients were hospitalized for more than six days. Patients with neurological/neuromuscular or cardiac disease had a much higher likelihood of a prolonged hospitalization than other patients.
 - These results support the decision in 2005 to add neurological/neuromuscular disease to the list of chronic conditions in children that warrant annual flu vaccination.
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Each flu hospitalization costs more than \$13,000, much higher than previously estimated

Keren and colleagues calculated the direct medical costs of influenza-related hospitalizations. From hospital billing records, the average hospital charge was \$26,172 (not including physician services), and the average total reimbursement for the hospital was \$14,770. The researchers used cost-to-charge ratios and other standards to estimate direct medical costs, including physician services, in 2004 dollars.

- The average cost was \$13,159, although costs were much higher for the 19% of patients admitted to an intensive care unit (ICU). These more seriously ill patients had total costs of \$39,792, compared with \$7,030 for patients cared for on wards only.
- Room charges accounted for most of the costs in both ward and ICU patients (75% and 58% respectively). Diagnostic tests and therapeutic costs (mostly lab tests and pharmaceuticals) for ICU patients were nearly ten times greater than for ward patients.
- Children with cardiac, metabolic, and neurologic/neuromuscular disease, and those 18 to 21 years old, had the greatest likelihood of having high-cost hospitalizations.
- These cost estimates are three to four times higher than estimates derived from previous smaller studies.

Neighborhood analysis estimates the rate of flu hospitalizations in the population

To estimate the overall incidence of flu-related hospitalization in children, the researchers defined a neighborhood “cohort” of children living in 9 contiguous zip codes that surround the hospital. Among the 745 patients, 231 (31%) lived in the neighborhood.

- Compared to the entire group of children in the study, hospitalized children from the neighborhood were more likely to be African-American (90% vs. 55%) and more likely to have asthma (31% vs. 24%). Hospitalized children from the neighborhood were also more likely to be African American than the underlying population of children in the neighborhood (90% vs. 77%).
- Using U.S. Census data to calculate the population of children in the neighborhood, the researchers estimated that the incidence of flu-related hospitalization was 7-8 per 10,000 child-years of observation. Children 0-23 months of age had the highest rate of flu-related hospitalizations (41.6 per 10,000 child-years).

POLICY IMPLICATIONS

Influenza is a common cause of hospitalization among both healthy and chronically ill children. How vaccination status affected the children in this study, or will affect hospitalization rates in the future, is not known. However, these findings should help clinicians and policymakers prioritize their vaccination efforts.

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POLICY IMPLICATIONS

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- Because children with cardiac or neurologic/neuromuscular disease are at risk of serious complications and prolonged hospitalization from the flu, children with these conditions and their close contacts should be a high priority to receive the vaccine.
- The neighborhood analysis supports the public health recommendation to give priority to children aged 6-23 months for receiving the vaccine because they are at increased risk for hospitalization compared to children over 24 months of age.
- The cost findings strengthen the economic case for vaccinating children with high-risk conditions against the flu. In estimating the cost-effectiveness of flu vaccination, researchers should incorporate these higher inpatient cost estimates into their analyses.
- Further research is needed to assess the effectiveness, and cost-effectiveness, of the flu vaccine in preventing hospitalizations and serious complications in children now recommended for annual vaccination.

This Issue Brief is based on the following articles: R. Keren, T.E. Zaoutis, S. Saddlemire, X.Q. Luan, S.E. Coffin. Direct medical cost of influenza-related hospitalizations in children. Pediatrics, November 2006, vol. 188, pp. E1321-E1327; R. Keren, T.E. Zaoutis, C.B. Bridges, G. Herrera, B. Watson, A.B. Wheeler, D.J. Licht, X.Q. Luan, S.E. Coffin. Neurological and neuromuscular disease as a risk factor for respiratory failure in children hospitalized with influenza infection. Journal of the American Medical Association, November 2, 2005, vol. 294, pp. 2188-2194. See also S.E. Coffin, T.E. Zaoutis, A. Wheeler, K. Heydon, G. Herrera, C.B. Bridges, B. Watson, R. Localio, R.L. Hodinka, R. Keren. Incidence, complications, and risk factors for prolonged stay in children hospitalized with community-acquired influenza. Pediatrics 2007 (in press).

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