Health Care Utilization for Pneumonia in Young Children After Routine Pneumococcal Conjugate Vaccine Use in the United States

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Objective: To estimate the effect of 7-valent pneumococcal conjugate vaccine (PCV7) on rates of pneumonia-related health care utilization and costs in children younger than 2 years.

Design: Retrospective population study.

Setting: Approximately 40 large employers each year, from 1997 to 2004.

Participants: Enrollees in the MarketScan databases collected by Thomson Medstat.

Main Exposure: Pneumococcal conjugate vaccine immunization program.

Main Outcome Measures: Rates of International Classification of Diseases, Ninth Revision–coded hospitalizations and ambulatory visits due to all-cause and pneumococcal pneumonia and their medical expenditures.

Results: Comparing the rates in 2004 with those in the baseline period of 1997 to 1999 among children younger than 2 years, hospitalizations due to all-cause pneumonia declined from 11.5 to 5.5 per 1000 children (52.4% decline; P < .001) and ambulatory visits due to all-cause pneumonia declined from 99.3 to 58.5 per 1000 children (41.1% decline; P < .001). Rates of hospitalizations due to pneumococcal pneumonia declined from 0.6 to 0.3 per 1000 children (57.6% decline; P < .001) and rates of ambulatory visits declined from 1.7 to 0.9 per 1000 children (46.9% decline; P < .001). Projecting from these data to the US population, the total estimated direct medical expenditures for all-cause pneumonia-related hospitalizations and ambulatory visits in young children were reduced from an annual average of $688.2 million during the period of 1997 to 1999 to $376.7 million in 2004 (45.3% decline and approximately $310 million decrease).

Conclusions: In children younger than 2 years, the age group targeted for vaccination, pneumonia-related health care utilization in a privately insured population declined substantially following PCV7 introduction. These results suggest that PCV7 may play an important role in reducing the burden of pneumonia, resulting in major savings in medical care cost.

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Pneumonia is the leading cause of childhood morbidity and mortality worldwide. Each year, it accounts for 2 million deaths in children, mainly in developing countries. Before introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), the incidence of community-acquired pneumonia in Europe and North America was estimated to be 34 to 40 cases per 1000 children younger than 5 years. Streptococcus pneumoniae is considered the most common bacterial cause of childhood pneumonia, accounting for an estimated 17% to 44% of pneumonia hospitalizations in children.

In 2000, PCV7 was introduced in the routine childhood immunization schedule in the United States. The vaccine is recommended for all children aged 2 to 23 months and children aged 24 to 59 months at increased risk for pneumococcal disease. The National Immunization Survey indicates that uptake of 3 or more doses of PCV7 increased from 41% in 2002 to 83% in 2005 among children aged 19 to 35 months (ie, children born in 1999-2004). Postlicensure studies have shown that the immunization program has dramatically reduced rates of invasive pneumococcal disease in children. The vaccine has also been shown to be effective in protecting children who did not receive all of the rec-
ommended doses. Economic evaluations concluded that routine use of PCV7 in young children is cost-effective for prevention of invasive disease. Clinical trials in the United States, Gambia, and South Africa provided evidence that pneumococcal conjugate vaccine also protects against pneumonia. The Northern California Kaiser Permanente trial reported PCV7 efficacy of 4.3% for all-cause pneumonia, 9.8% for pneumonia in which radiography was performed, and 20.5% for pneumonia with a positive radiographic finding. A 9-valent conjugate vaccine trial in Gambia found vaccine efficacy of 37% for radiography-confirmed pneumonia. These data suggest that widespread PCV7 immunization could have an effect on pneumococcal-related community-acquired pneumonia, but few studies have evaluated the population impact of PCV7 on all-cause pneumonia and pneumococcal pneumonia and no studies to our knowledge have assessed the economic implications associated with potential reductions in childhood pneumonia.

We compared outcome rates in 2004 with the baseline rates from 1997 to 1999 to estimate the potential effect of PCV7 on disease incidence and medical care expenditures in children younger than 2 years, the age group targeted for vaccination.

DATA SOURCE

Data were obtained from the 1997 to 2004 MarketScan databases that contain information from approximately 40 self-insured employers each year, including large private employers and state governments. Together, these employers offer more than 100 health insurance plans, and data are available for more than 500 million claims for employees, retirees, and their dependents. All states except Alaska and Hawaii are included, as is Washington, DC. The 2004 MarketScan databases included data obtained from some health plan contributors combined with the data from the employer customers. More than 40,000 covered children younger than 2 years are represented per year. The longitudinal databases enable patient follow-up and contain patient demographics, provider characteristics, dates of services for ambulatory and hospital visits, length of stay in the hospital, payments, diagnostic codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]), procedure codes (Current Procedural Terminology ‘98), and other variables. Total payments reported in MarketScan databases represent actual amounts paid by insurance companies and patients to providers (eg, physicians and hospitals).

STUDY POPULATION

The enrollment tables of MarketScan databases contain person-level enrollment records (including demographic and insurance plan information) on most enrollees (from an average of 73% in 1997-1999 to >99% in 2004). We included all of the enrollees younger than 2 years from the MarketScan enrollment tables in our analysis of hospitalizations and ambulatory visits per 1000 person-years. Persons who were not in the enrollment tables were excluded from analysis.

This study was reviewed by the human subjects coordinator at the National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, and an analysis of secondary data without identifiers was determined to not require institutional review board review.

DATA ANALYSIS

Rates of Pneumonia-Related Hospitalizations and Ambulatory Visits

The study sample consisted of all of the inpatient admissions and ambulatory visits (outpatient clinic and emergency department) from January 1, 1997, to December 31, 2004. An all-cause pneumonia-related hospitalization was defined as a pneumonia ICD-9 code listed as the primary (discharge) diagnosis (003.22, 011.6, 055.1, 073.0, 115.15, 115.95, and 480-487.0) or as a meningitis or septicemia ICD-9 code as the primary diagnosis and a pneumonia ICD-9 code as the secondary diagnosis (003.21, 013.0, 036.0, 036.1, 047.0, 049.0, 049.1, 053.0, 054.72, 072.1, 090.42, 091.81, 094.2, 098.82, 100.81, 112.83, 114.2, 115.01, 115.11, 115.91, 130.0, 320, 321, 322, 003.1, 020.2, 022.3, 031.2, 036.2, 038, 054.5, 785.52, and 790.7). Some of these hospitalizations included a Current Procedural Terminology code indicating that radiography was performed. Pneumococcal pneumonia–related hospitalizations were identified by a specific pneumococcal pneumonia ICD-9 code or by unspecified pneumococcal codes with other codes indicating pneumococcal disease. We excluded all of the pneumonia hospitalizations associated with birth (ie, the inpatient admission record included both pneumonia and delivery ICD-9 codes). If a patient with pneumonia had an ambulatory visit that later resulted in hospital admission, this was counted as 1 pneumonia hospitalization and 1 pneumonia ambulatory visit. To capture complete medical care cost information for ambulatory visits, we did not distinguish between first and follow-up visits in our analysis. We estimated the number of prevented pneumonia-related hospitalizations by the end of 2004 by multiplying the estimated rate differences by the specific 2004 population estimate from the census. Dehydration, a common cause of hospital admission in children, was used as a control condition to assess possible changes in admission practices.

We conducted stratified analyses of all-cause pneumonia-related hospitalizations by insurance plan type and sex. The sample size was too small to conduct stratified analyses for pneumococcal pneumonia (19-48 pneumococcal pneumonia-related hospitalizations each year).

We compared pneumonia-related hospitalization rates between managed care and nonmanaged care insurance plans. Five types of insurance plans were categorized as managed care: exclusive provider organization, health maintenance organization, noncapitated point of service, preferred provider organization, and capitated or partially capitated point of service. Two types of insurance were categorized as nonmanaged care: basic or major medical and comprehensive.

We used a generalized linear model to compare the all-cause pneumonia–related hospitalization rates in 2004 with those in 1997 to 1999 using PROC GLIMMIX (SAS Institute, Inc, Cary, North Carolina). We used sandwich variance estimators to account for possible multiple visits per patient. The covariates included insurance plan type (managed care vs nonmanaged care), sex, and 2 interaction terms (insurance × year and sex × year). P ≤ 0.05 was considered statistically significant. As the prevaccination baseline, we combined data for 1997, 1998, and 1999 to reduce the effect of year-to-year variation in rates. We calculated the percentage of declines for hospitalizations and ambulatory visits due to all-cause pneumonia and pneumococcal pneumonia from the baseline period to 2004. For consistency, the 95% confidence intervals (CIs) for all of these declines were computed using the 8 method. Analyses were performed with SAS version 9.1 statistical software (SAS Institute, Inc).
Table 1. Number and Rates per 1000 Person-Years of Hospitalizations and Ambulatory Visits for All-Cause and Pneumococcal Pneumonias Among Children Younger Than 2 Years From the 1997 to 2004 MarketScan Databases

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<td>All-cause pneumonia</td>
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<td>Rate/1000 person-years (95% CI)</td>
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<td>(10.1-12.0)</td>
<td>(10.6-12.5)</td>
<td>(7.8-9.2)</td>
<td>(7.3-8.7)</td>
<td>(5.1-6.2)</td>
<td>(5.3-6.2)</td>
<td>(5.2-5.8)</td>
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<td>Ambulatory visits</td>
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<td>5228</td>
<td>6136</td>
<td>4636</td>
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<td>10523</td>
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<td>Rate/1000 person-years (95% CI)</td>
<td>(94.3-99.8)</td>
<td>(92.9-98.3)</td>
<td>(102.4-108.0)</td>
<td>(98.3-103.4)</td>
<td>(96.2-100.9)</td>
<td>(59.1-62.5)</td>
<td>(64.9-67.9)</td>
<td>(57.4-59.6)</td>
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<td>Pneumococcal pneumonia</td>
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<td>Rate/1000 person-years (95% CI)</td>
<td>(0.4-0.8)</td>
<td>(0.4-0.8)</td>
<td>(0.5-0.9)</td>
<td>(0.2-0.5)</td>
<td>(0.2-0.5)</td>
<td>(0.2-0.4)</td>
<td>(0.2-0.4)</td>
<td>(0.2-0.3)</td>
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<td>100</td>
<td>76</td>
<td>111</td>
<td>97</td>
<td>103</td>
<td>111</td>
<td>165</td>
</tr>
<tr>
<td>Rate/1000 person-years (95% CI)</td>
<td>(1.0-1.7)</td>
<td>(1.8-2.6)</td>
<td>(1.2-2.0)</td>
<td>(1.7-2.5)</td>
<td>(1.2-1.9)</td>
<td>(1.1-1.6)</td>
<td>(0.8-1.2)</td>
<td>(0.8-1.1)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

Medical Expenditures

We estimated expenditures for hospitalizations and ambulatory visits from the total payments to providers. Expenditures were standardized to 2004 US dollars using the medical consumer price index. We calculated the mean and median length of stay and payments per hospitalization as well as the mean payments per ambulatory visit. For pneumococcal pneumonia, we used combined 2003 and 2004 data to obtain the estimates for 2004. We multiplied the average of 1997, 1998, and 1999 US census data and 2004 US census data by the rates and mean payments from the MarketScan databases to estimate national medical expenditures (hospitalizations and ambulatory visits only) for pneumonia in children younger than 2 years in the prevaccine years of 1997 to 1999 and in 2004. We also used the 1997 to 1999 and 2004 Medical Expenditure Panel Survey population estimates to determine the medical expenditures for pneumonia among children with private insurance during these periods.

RESULTS

The number of covered children younger than 2 years who met the inclusion criteria in the MarketScan databases increased from about 43,000 in 1997 to 180,000 in 2004 as more companies were included in the MarketScan databases. Throughout the study period, there were slightly more enrolled boys (51.3%) than girls (48.7%). The proportion of enrollees covered by managed care plans (including exclusive provider organization, health maintenance organization, preferred provider organization, and point of service) increased gradually over time (from 71.8% in 1997 to 92.8% in 2004).

PNEUMONIA-RELATED HOSPITALIZATIONS

Annual hospitalization rates for all-cause and pneumococcal pneumonias from 1997 to 2004 are presented in Table 1. The changes in these rates for 1997 to 1999 vs 2004 are illustrated in the Figure. On average, about 60.6% of patients hospitalized with an all-cause pneumonia code had radiography performed, about 4.9% of the all-cause pneumonia cases were coded as pneumococcal pneumonia, and about 59.0% of hospitalized patients with all-cause pneumonia were boys. Comparing rates in 2004 with those in the baseline period, we observed 6.0 (95% CI, 5.4-6.7) fewer hospitalizations for all-cause pneumonia per 1000 children younger than 2 years—a 32.4% decline from 11.5 to 5.5 hospitalizations per 1000 children (P < .001). There were 0.4 (95% CI, 0.2-0.5) fewer hospitalizations due to pneumococcal pneumonia per 1000 children—a decline of 57.6% from 0.6 to 0.3 hospitalizations per 1000 children (P < .001) (Table 1). About 2.1% to 10.7% of the pneu-
Pneumococcal pneumonia hospitalizations included a concurrent diagnosis code for bacteremia or sepsis. The rates for all-cause pneumonia hospitalization in which radiography was performed declined from 6.9 to 3.5 hospitalizations per 1000 children (P < .001), a 48.4% decline. We estimated that routine use of PCV7 prevented about 49,000 hospitalizations for all-cause pneumonia by 2004 in children younger than 2 years. Dehydration hospitalizations constituted an average of 3.0% of all of the annual hospitalizations for children younger than 2 years—a 46.9% decline from 1.7 to 0.9 ambulatory visits per 1000 children (P < .001).

**MEDICAL EXPENDITURES CORRESPONDING TO PNEUMONIA**

The mean length of stay and the mean payments per hospitalization and ambulatory visit for all-cause and pneumococcal pneumonias in young children are summarized in [Table 2](#). The mean length of stay per all-cause pneumonia hospitalization was significantly shorter in the postvaccination era compared with the prevaccination baseline period (3.01 days vs 3.44 days, respectively; P = .008 for t test). The median lengths of hospital stay were 2 and 3 days, respectively. Although the mean payments per all-cause pneumonia hospitalization were lower in the postvaccination era, this difference was not significant ($6296 vs $6392, respectively; P = .89). The related median payments were $3760 and $3868, respectively. In contrast, the mean payments per all-cause pneumonia ambulatory visit were significantly higher in the postvaccination era than in the prevaccination baseline ($201 vs $175, respectively; P < .001). There were no significant differences in the pneumococcal pneumonia length of stay and payments in the prevaccination and postvaccination periods.

On the basis of the observed decline in all-cause pneumonia rates and projecting from MarketScan data to the US population using 1997 to 1999 and 2004 census data, the estimated annual national medical expenditures for hospitalizations and ambulatory visits in children younger than 2 years declined from an average of $688.2 million in 1997 to 1999 to $376.7 million in 2004, a 45.3% decline. For the subset of pneumococcal pneumonia, annual medical expenditures declined from an average of $122.0 million in 1997 to 1999 to $88.9 million in 2004 (27.1% decline). The cost of vaccination was not con-

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**Table 2. Mean Length of Hospital Stay and Payments per Hospitalization and Ambulatory Visit Among Children Younger Than 2 Years From the MarketScan Databases**

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>1997–1999</th>
<th>2004</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td><strong>All-cause pneumonia</strong></td>
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<tr>
<td>Length of stay, mean (95% CI), d</td>
<td>3.44 (2.73-3.23)</td>
<td>3.01 (2.69-3.33)</td>
<td>.008</td>
</tr>
<tr>
<td>Length of stay, mean (95% CI), d</td>
<td>8.53 (7.10-9.16)</td>
<td>10.33 (8.58-14.08)</td>
<td>.49</td>
</tr>
<tr>
<td><strong>Pneumococcal pneumonia</strong></td>
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<td></td>
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<tr>
<td>Length of stay, mean (95% CI), d</td>
<td>8.53 (6.97-10.10)</td>
<td>10.33 (8.58-14.08)</td>
<td>.49</td>
</tr>
<tr>
<td><strong>Ambulatory visits</strong></td>
<td></td>
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<tr>
<td>Payments, mean (95% CI), $</td>
<td>218 (169-275)</td>
<td>263 (163-364)</td>
<td>.44</td>
</tr>
</tbody>
</table>
| Abbreviation: CI, confidence interval.
We reported a comprehensive evaluation of pneumonia-related health care utilization in young children including trends in hospitalizations, ambulatory visits, and related expenditures over a period that spanned the introduction and maturation of the pneumococcal conjugate vaccination program in the United States. We found that by 2004, rates of hospitalization and ambulatory visits as well as resulting medical expenditures for all-cause pneumonia and pneumococcal pneumonia had decreased markedly from the prevaccination years. These results add to the growing evidence base of benefits of PCV7 vaccination and suggest an important role for the vaccine in reducing the burden of pneumonia and associated medical costs.

Community-acquired pneumonia is an important cause of hospital admissions and outpatient visits in children, and estimating the burden of vaccine-preventable pneumonia and pneumococcal-related illnesses has important implications for immunization policy. Although several studies have documented substantial reductions in the incidence of invasive pneumococcal disease following routine use of PCV7,11–13,32 data on the immunization program’s effect on all-cause pneumonia or pneumococcal pneumonia in the population are currently limited.22,23 We found that in the MarketScan databases, rates of all-cause pneumonia hospitalizations and ambulatory visits declined by 52.4% and 41.1%, respectively. This suggests that S pneumoniae was a major contributor to the burden of pneumonia hospitalizations and ambulatory visits in children younger than 2 years. The observed decline in pneumonia after introduction of PCV7 is consistent with the increasing vaccination coverage during the study period,9,10,33,34 and it occurred despite vaccine shortages during early implementation of the PCV7 immunization program. Reductions in pneumonia hospitalizations were noted earlier than those in ambulatory settings. The reasons for this are unknown, but it is possible that pneumococci is associated with a larger proportion of patients with pneumonias who are hospitalized as compared with those who are treated as outpatients.

Our measures for the costs of all-cause pneumonia and pneumococcal pneumonia included the complete hospital, emergency department, and outpatient visits for the patients with these clinical syndromes from the same data set. Thus, our estimates for the direct medical costs due to these illnesses are likely to be reasonable and can be used in updating cost-effectiveness studies for PCV7. In addition, such data on reduction of health care costs after introduction of a new vaccine have policy implications. Pneumococcal illnesses are associated with considerable economic burden in the United States and other countries. One US study35 estimated that pneumococcal-associated diseases caused $2.5 billion in direct medical costs and $3 billion in work-loss and productivity costs for each US birth cohort. Thus, reduction of pneumococcal-related illnesses should have a profound effect on reducing total costs. Our data showed that compared with costs in the prevaccination period, direct medical costs for hospitalizations and outpatient visits due to all-cause pneumonia were reduced in the postvaccination period by $311 million annually. One study35 projected that implementation of pneumococcal conjugate vaccine in infants and young children could reduce direct medical costs of pneumococcal-associated diseases (including otitis media) by $342 million. The total net savings from the vaccine would be much greater if indirect costs such as work loss by parents or productivity loss by disability or death due to the disease were included. In addition, our data are consistent with other studies showing that rates of all-cause pneumonia are several-fold higher than the incidence of invasive pneumococcal disease (1.88 and 0.34 cases per 1000 children younger than 2 years for the prevaccination period and 2004, respectively36). If our findings are confirmed by other studies, the use of PCV7 to prevent pneumococcal disease is likely to be even more cost-effective than previously estimated.15,16 A significant reduction in the length of stay for all-cause pneumonia was observed when prevaccine years were compared with postvaccine years. It is possible that this reflects changes in treatment practices or diagnostic criteria for pneumonia now.

The declines in rates of pneumonia observed in our study exceeded the vaccine efficacy estimates (4.3%–20.5%) reported in clinical trials17–19 but are consistent with results of other national studies22,23 evaluating the PCV7 program effect. It is possible that herd effects that have been demonstrated for invasive pneumococcal disease may also extend to noninvasive pneumococcal-related disease.22,23 Several other factors, however, may also have influenced the observed disease reductions: first, uptake of PCV7 in this privately insured population may have been higher than in the general population37; second, there may be a trend of decreasing use of clinical diagnostics for community-acquired pneumonia (eg, obtaining blood cultures) during the post-PCV7 era, particularly in managed care38; and third, the definition of pneumonia we used was based on ICD-9–coded diagnosis of pneumonia and may be different from case definitions used in clinical trials.39

The seasonal occurrence of severe influenza epidemics could increase pneumonia hospitalizations and outpatient visits. During our study period, the highest influenza activity in the United States occurred in 1999 to 2000 and 2003 to 2004. Although this was not accounted for in our analysis, we did not detect major effects on the pneumonia hospitalization rates during these periods. Vaccination with PCV7 has been suggested to reduce pneumonias associated with influenza infections.40 Furthermore, as the recommendation for routine influenza immunization of children aged 6 to 23 months began only in 2004, influenza immunization in children is unlikely to affect our results, particularly because full 2-dose coverage in this age group was very low.21,41

Several limitations to our data and analysis should be considered when interpreting the results. First, a well-recognized limitation of our study design is that ecologi-
cal analyses cannot prove causality between PCV7 immunization and the observed decline in pneumonia-related health care utilization. Second, MarketScan obtains its data mostly from employer-sponsored insurance, particularly from large employers. The study population is therefore somewhat homogeneous and may not be nationally representative. Nonetheless, with an average of 77,000 enrolled children per year during the 1997 to 2004 study interval, the MarketScan population is large, draws from numerous medical settings, and represents a wide variety of geographic, social, and economic strata. Third, rates of pneumonia, health care utilization, and medical expenditures per case for pneumonia may be greater for persons with Medicaid or without insurance, making national projections conservative (perhaps underestimating costs). However, because the proportion of the US population with private insurance only slowly declined during the study interval, any bias in our analysis is likely to have been consistent over time and our estimates should reflect the degree of reduction in pneumonia health care utilization and expenditures in an insured population. Fourth, claims data that are collected for different, ie, administrative, purposes should be interpreted with caution. As there is no mechanism to validate MarketScan diagnostic codes through direct medical record reviews, misclassification is possible. Our study may have missed some pneumonia health care utilization owing to the incompleteness of the databases, incomplete coding, or multiple insurance plans for some enrollees. In general, these last instances likely would be rare. Finally, the MarketScan population has almost tripled during our study period, and trends for pneumonia events could be affected by secular changes in the MarketScan population or in insurance or associated utilization patterns. We showed that pneumonia hospitalizations among all of the MarketScan enrollees declined by 60.4% as a proportion of total hospitalizations. Thus, this analysis controls at least partially for any changes in practice standards for hospitalization that might have occurred over time, and we did not observe a shift to outpatient management of pneumonia. In addition, evaluation of a control condition (hospitalizations for dehydration) suggested that changes in pneumonia hospitalizations were unlikely to be associated with changes in admission practices in general. Declines in hospitalization occurred among both managed care and nonmanaged care insurance plans, although more quickly in nonmanaged care plans, also suggesting that the declines were not artifacts of secular changes in insurance coverage. Further study is needed to understand why changes for nonmanaged care plans were larger than for managed care plans.

In conclusion, our data suggested that routine use of PCV7 has markedly reduced the rates of all-cause pneumonia and pneumococcal pneumonia in children younger than 2 years. These findings are consistent with other recent studies documenting the impact of pneumococcal conjugate vaccine on noninvasive pneumococcal syndromes and add additional evidence of the benefits of this vaccine in the population. The decline of disease as shown in our study highlights the further health and economic benefits of PCV7 vaccination in young children in the United States.

References


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34. Centers for Disease Control and Prevention. National, state, and urban area vacci-

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**Announcement**

Trial Registration Required. In concert with the International Committee of Medical Journal Editors (ICMJE), Archives of Pediatrics and Adolescent Medicine will require, as a condition of consideration for publication, registration of all trials in a public trials registry (such as http://ClinicalTrials.gov). Trials must be registered at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment before this date, registration will be required by September 13, 2005, before considering the trial for publication. The trial registration number should be supplied at the time of submission.

For details about this new policy, and for information on how the ICMJE defines a clinical trial, see the editorials by DeAngelis et al in the September 8, 2004 (2004; 292:1363-1364) and June 15, 2005 (2005;293:2927-2929) issues of JAMA. Also see the Instructions to Authors on our Web site: www.archpediatrics.com.