

ORIGINAL ARTICLE

U.S. Hospitalizations for Pneumonia after a Decade of Pneumococcal Vaccination

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ABSTRACT

BACKGROUND

The introduction of 7-valent pneumococcal conjugate vaccine (PCV7) into the U.S. childhood immunization schedule in 2000 has substantially reduced the incidence of vaccine-serotype invasive pneumococcal disease in young children and in unvaccinated older children and adults. By 2004, hospitalizations associated with pneumonia from any cause had also declined markedly among young children. Because of concerns about increases in disease caused by nonvaccine serotypes, we wanted to determine whether the reduction in pneumonia-related hospitalizations among young children had been sustained through 2009 and whether such hospitalizations in older age groups had also declined.

METHODS

We estimated annual rates of hospitalization for pneumonia from any cause using the Nationwide Inpatient Sample database. The reason for hospitalization was classified as pneumonia if pneumonia was the first listed diagnosis or if it was listed after a first diagnosis of sepsis, meningitis, or empyema. Average annual rates of pneumonia-related hospitalizations from 1997 through 1999 (before the introduction of PCV7) and from 2007 through 2009 (well after its introduction) were used to estimate annual declines in hospitalizations due to pneumonia.

RESULTS

The annual rate of hospitalization for pneumonia among children younger than 2 years of age declined by 551.1 per 100,000 children (95% confidence interval [CI], 445.1 to 657.1), which translates to 47,000 fewer hospitalizations annually than expected on the basis of the rates before PCV7 was introduced. The rate for adults 85 years of age or older declined by 1300.8 per 100,000 (95% CI, 984.0 to 1617.6), which translates to 73,000 fewer hospitalizations annually. For the three age groups of 18 to 39 years, 65 to 74 years, and 75 to 84 years, the annual rate of hospitalization for pneumonia declined by 8.4 per 100,000 (95% CI, 0.6 to 16.2), 85.3 per 100,000 (95% CI, 7.0 to 163.6), and 359.8 per 100,000 (95% CI, 199.6 to 520.0), respectively. Overall, we estimated an age-adjusted annual reduction of 54.8 per 100,000 (95% CI, 41.0 to 68.5), or 168,000 fewer hospitalizations for pneumonia annually.

CONCLUSIONS

Declines in hospitalizations for childhood pneumonia were sustained during the decade after the introduction of PCV7. Substantial reductions in hospitalizations for pneumonia among adults were also observed. (Funded by the Centers for Disease Control and Prevention.)

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THE INTRODUCTION OF THE 7-VALENT pneumococcal conjugate vaccine (PCV7) into the U.S. infant immunization schedule in 2000 resulted in major reductions in the incidence of invasive pneumococcal disease in all age groups.^{1,2} The marked decline in disease among unvaccinated persons in addition to those who were vaccinated is attributable to the indirect, or “herd,” protection provided by PCV7. By preventing the acquisition and carriage of vaccine serotypes in the nasopharynx of vaccinated children, PCV7 interfered with this key step in the pathogenesis of pneumococcal disease and reduced the transmission of vaccine serotypes.³⁻⁶

Pneumococcal pneumonia accounts for 20 to 60% of community-acquired cases of pneumonia.⁷ A reduction in pneumonia was an expected outcome of PCV7 vaccination, given that the major U.S. prelicensure trial showed an efficacy of 30% against radiographically defined pneumonia.⁸ (For the purposes of this report, “pneumonia” refers to pneumonia from any cause.) Our previous time-series analysis⁹ estimated a reduction of 39% (95% confidence interval [CI], 22 to 52) in hospitalizations for pneumonia by 2004 among U.S. children younger than 2 years of age, in association with the introduction of PCV7. The more modest declines estimated for other age groups were significant only among adults 18 to 39 years of age.⁹ In a model based on hospital discharge data coupled with vaccine uptake information from 10 states, Simonson et al. estimated that through 2006, the PCV7 vaccination program had prevented 800,000 U.S. hospitalizations for pneumococcal pneumonia.¹⁰

Along with the decline in pneumococcal disease attributed to PCV7, however, there was an increase in disease caused by nonvaccine serotypes, in particular serotype 19A.¹ There is concern that this “serotype replacement” may have eroded some of the gains resulting from the introduction of PCV7.¹¹⁻¹³ To determine whether the early observed reductions in hospitalizations for pneumonia were sustained throughout the first decade of PCV7 use, we performed a comprehensive assessment of U.S. hospitalizations for pneumonia after the introduction of PCV7 and before the switch to the 13-valent pneumococcal conjugate vaccine (PCV13) in 2010.

METHODS

DATA SOURCES

The Agency for Healthcare Research and Quality collects discharge diagnoses for a 20% sample of U.S. hospitals. This Nationwide Inpatient Sample (NIS)¹⁴ is the largest all-payer U.S. inpatient care database, with data from about 8 million hospitalizations annually. The sampling design includes community hospitals as the primary sampling units, and all discharges from these hospitals. In 2009, the sample included 1050 hospitals in 44 states. Stratification and weighting variables enable calculation of national estimates and trends, accounting for the complex sampling design and the expanded sampling framework over time. Up to 15 discharge diagnoses are coded with the use of the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)*, with the first-listed diagnosis regarded as the primary reason for hospitalization.

This study was considered to be exempt research with respect to the requirement for informed consent, as assessed by the Vanderbilt University institutional review board. All authors vouch for the accuracy and completeness of the data presented.

DEFINITION OF HOSPITALIZATION FOR PNEUMONIA

Hospitalization for pneumonia was defined in accordance with the codes in the ICD-9-CM. For the data to qualify for inclusion in the study, the patient had to have a first-listed discharge diagnosis of pneumonia or a first-listed discharge diagnosis of meningitis, septicemia, or empyema in addition to a diagnosis of pneumonia in another diagnostic field. Hospitalization for pneumococcal pneumonia met the criteria for hospitalization for all-cause pneumonia and was also given a specific code for pneumococcal infection or for lobar pneumonia.¹⁵ (For a list of the diagnostic codes used, see the Supplementary Appendix, available with the full text of this article at NEJM.org.)

STATISTICAL ANALYSIS

NIS data from 1997 through 2009 were used to estimate the annual number of hospitalizations for pneumonia among children younger than 2 years of age, 2 to 4 years of age, and 5 to 17 years of age and among adults 18 to 39 years

of age, 40 to 64 years of age, 65 to 74 years of age, 75 to 84 years of age, and 85 years of age or older. Annual total and age-specific hospitalization rates were obtained by dividing the annual number of hospitalizations for pneumonia by the annual population according to the U.S. Census Bureau, with the rates expressed as hospitalizations per 100,000 persons.

We treated the 3 years preceding the introduction of PCV7 (1997 through 1999) as baseline years, since no declines in pneumonia were observed during these years.⁹ PCV7 was licensed in the United States in February 2000, and vaccine uptake increased rapidly after June 2000, when the government purchased PCV7 for the Vaccines for Children Program.⁹ Thus, 2000 was considered a transition year and not included in analyses grouped by year. We estimated the average annual rates of pneumonia for three pre-specified periods: 1997 through 1999 (pre-PCV7 years), 2001 through 2006 (early PCV7 years), and 2007 through 2009 (late PCV7 years). We compared hospitalization rates in late PCV7 years with rates in pre-PCV7 years and estimated age-specific differences in rates and percent declines in annual hospitalizations for pneumonia. The selection of the 2007–2009 period allowed comparison of the most recent 3-year period with the 3-year baseline period. The average annual rate of hospitalization was calculated for each period, with the variance being the sum of each year's variance divided by the number of years squared. Differences in rates were the differences in average annual rates. The variance of the difference in rates was the sum of the variances in the average rate, and the 95% confidence interval was calculated with the use of a normal approximation. The percentage declines in relative rates were derived from the estimates of differences in rates. Age-specific average annual differences in rates were applied to the 2009 U.S. population to estimate the absolute annual reductions in hospitalizations for pneumonia by 2009.

RESULTS

HOSPITALIZATION RATES

From 1997 through 2009, there were 17,892,085 hospitalizations for pneumonia, representing 4.1% of all U.S. hospitalizations other than those

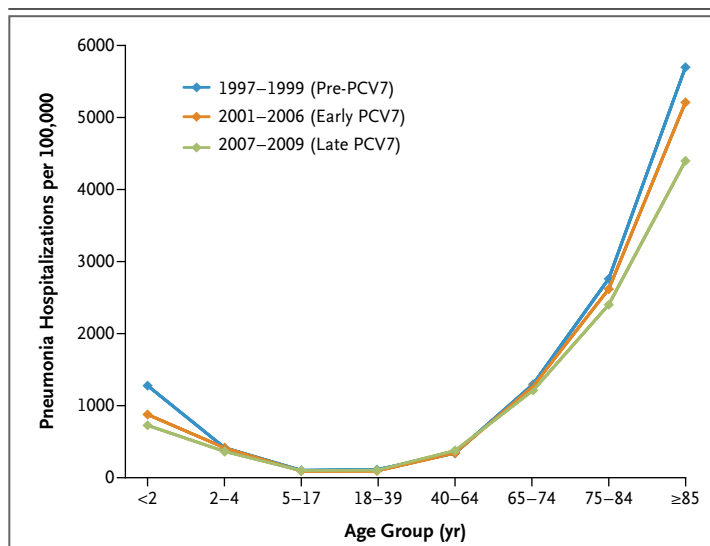


Figure 1. Average Annual Rates of U.S. Hospitalizations for Pneumonia before and after the Introduction of PCV7, According to Age Group. PCV7 denotes 7-valent pneumococcal conjugate vaccine.

for childbirth, including 7.2% of hospitalizations among children and 3.9% of hospitalizations among adults. Pneumonia was the first listed diagnosis for 90% of these hospitalizations, with sepsis as the first listed diagnosis for 9% and meningitis and empyema for less than 1% each.

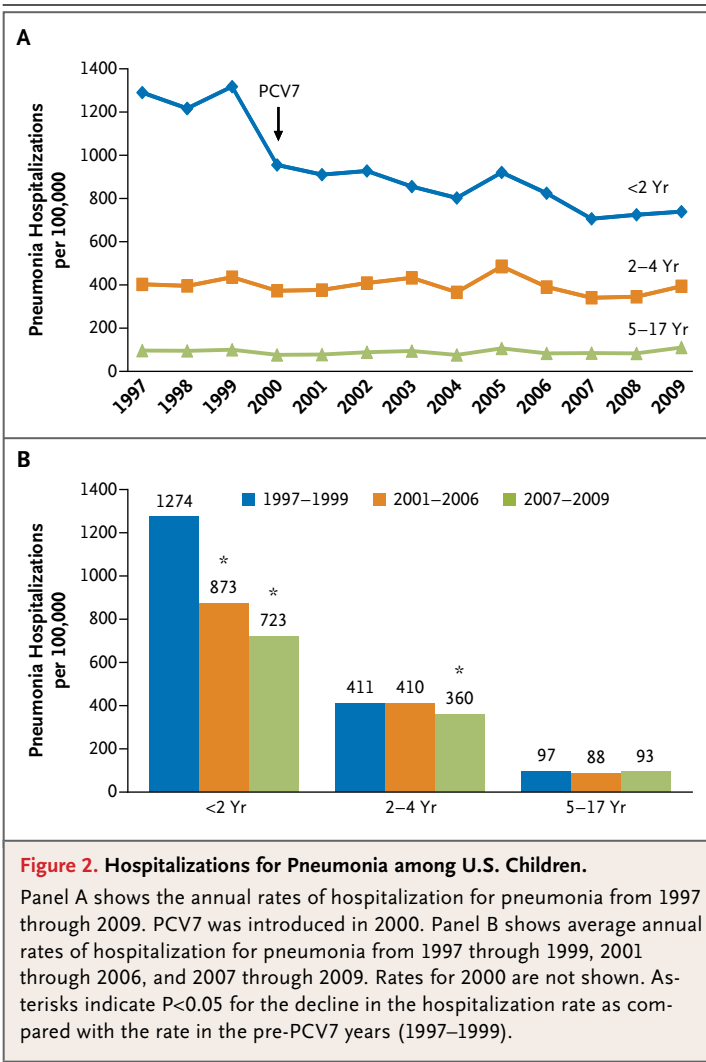
Annual rates of hospitalization for pneumonia were highest at the extreme ends of the age spectrum in all 3-year periods, with rates for children younger than 2 years of age similar to those for adults 65 to 74 years of age, at approximately 1000 hospitalizations per 100,000 persons. Rates for persons 75 years of age or older were two to five times as high. Hospitalization rates declined progressively at the extremes of age from the pre-PCV7 years through the early PCV7 years and the late PCV7 years (Fig. 1).

Whereas rates of hospitalization for pneumonia among children younger than 2 years of age declined substantially after the introduction of PCV7 in 2000, the rates among older children were much lower and stable throughout (Fig. 2A). Most of the decline in hospitalizations among young children occurred soon after the introduction of PCV7. The decline was sustained through the late PCV7 years, and rates for children younger than 2 years of age and those 2 to

PRE-PCV7 YEARS VERSUS LATE PCV7 YEARS

In both the pre-PCV7 and late PCV7 years, the length of the hospital stay increased with increasing age (Table 1), but it was consistently shorter in the late PCV7 years for all age groups. The proportion of pneumonias coded as pneumococcal was smaller at the extremes of age in both periods, but this proportion declined in all age groups over time. In-hospital mortality was lowest among children 2 to 4 years of age (0.2%) and increased with increasing age. Over time, in-hospital mortality remained similar or declined at the extremes of age, whereas mortality increased modestly in the three age groups encompassing persons 18 to 74 years of age.

The largest absolute and relative reductions in rates of hospitalization for pneumonia were at the extremes of age (Table 2). For children younger than 2 years of age, the reduction of 551.1 hospitalizations (95% CI, 445.1 to 657.1) per 100,000, or 43.2% (95% CI, 34.9 to 51.6), translated into 47,000 fewer hospitalizations in 2009 than would have been expected if rates had remained unchanged from those in the pre-PCV7 years. The decline in hospitalizations per 100,000 adults 85 years of age or older, which was 1300.8 (95% CI, 984.0 to 1617.6), or 22.8% (95% CI, 17.3 to 28.4), translated into 73,000 fewer hospitalizations than would have been expected in 2009. Although the absolute reductions were smaller among younger adults — 8.4 (95% CI, 0.6 to 16.2), 85.3 (95% CI, 7.0 to 163.6), and 359.8 (95% CI, 199.6 to 520.0) hospitalizations per 100,000 adults 18 to 39 years, 65 to 74 years, and 75 to 84 years of age, respectively, they nonetheless represented substantial declines in annual numbers of hospitalization for pneumonia. The overall, age-adjusted annual reduction in hospitalization rates from the pre-PCV7 years was 54.8 hospitalizations per 100,000 (95% CI, 41.0 to 68.5), representing an estimated 168,000 fewer hospitalizations in 2009 than would have been expected.



4 years of age were lower in the late PCV7 years than in pre-PCV7 years. Rates of hospitalization for pneumonia among children 5 to 17 years of age were the lowest of those in all age groups and changed little over the study period (Fig. 2B).

Hospitalization rates for pneumonia in most adult age groups also appeared to decline beginning in 2000 (Fig. 3A). For adults 65 years of age or older, rates declined progressively, and rates in the late PCV7 years were lower than those in pre-PCV7 years. Soon after PCV7 was introduced, small declines occurred among adults 18 to 39 years of age, and rates in the late PCV7 years remained significantly lower than those in pre-PCV7 years for this age group; however, the rates actually increased modestly among adults aged 40 to 64 years of age (Fig. 3B).

DISCUSSION

Remarkable early declines in hospitalizations for pneumonia among young children⁹ were sustained during the past decade of PCV7 use, alleviating concerns that disease caused by pneumococcal serotype replacement would erode the benefits of vaccination.¹¹ Hospitalizations also

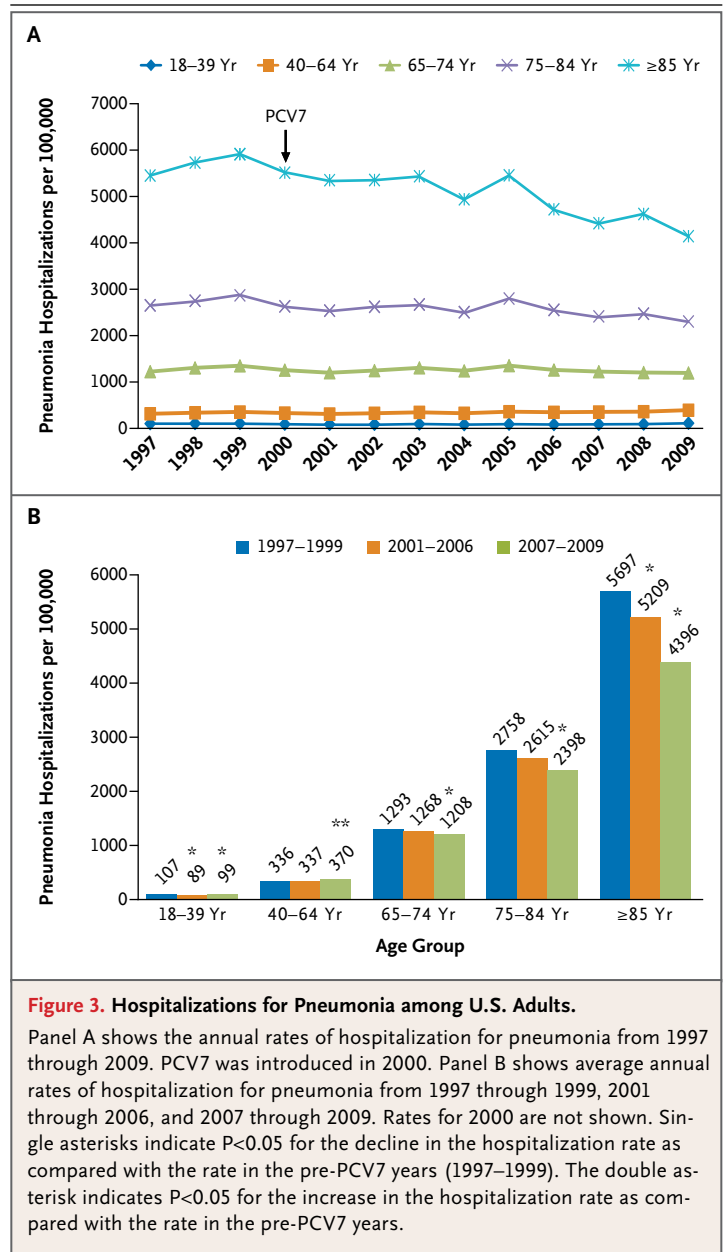
declined in other age groups, most notably in older adults, an age group in which the disease burden from pneumonia is substantial and in-hospital mortality ranges from 7 to 12%. Overall, in 2009, there were about 168,000 fewer hospitalizations for pneumonia than would have been expected on the basis of hospitalization rates in the 3 years preceding the introduction of PCV7. This estimated annual reduction in hospitalizations is five times as high as the annual reduction in cases of invasive pneumococcal disease.¹

Although 20 to 60% of cases of community-acquired pneumonia are thought to be pneumococcal, only a small proportion of pneumonias are diagnosed as pneumococcal (Table 1), and serotype information is usually unavailable.⁷ The attribution of trends in rates of disease to the PCV7 vaccination program requires an understanding of expected changes in rates among young children that are based on the results of randomized vaccine trials performed before licensure and on changes in pneumococcal nasopharyngeal carriage, which account for the indirect effects of vaccination.

The 43.2% decline in annual hospitalizations for pneumonia among children younger than 2 years of age is consistent with clinical trial results. In a precensure trial of PCV7 in children enrolled in Northern California by Kaiser Permanente,⁸ rates of radiographically defined pneumonia fell by 30% (95% CI, 11 to 46). Randomized trials conducted in South Africa, the Philippines, and Gambia showed declines of 17 to 37% in rates of pneumonia.¹⁶

PCV7 also had a major effect on pneumococcal carriage. The carriage of PCV7 serotypes was markedly reduced by 2009, and nonvaccine serotypes became the predominant colonizers.^{5,17,18} Indirect protection against invasive pneumococcal disease in unvaccinated groups has also been reported.¹⁹

Before the introduction of PCV7, vaccine serotypes caused 80% of invasive pneumococcal disease in young children. The proportion of invasive pneumococcal disease caused by vaccine serotypes was considerably lower in adults, but it increased with increasing age, reaching 51% in those 85 years of age or older.²⁰ Seven years after the introduction of PCV7, invasive pneumococcal disease caused by vaccine serotypes was almost eliminated in children younger than 5 years of age and declined by more than 85% in all unvac-



inated age groups. Total cases of invasive pneumococcal disease, which include cases caused by vaccine serotypes and cases caused by nonvaccine serotypes, declined by 76% among children younger than 5 years of age and by 43%, 40%, 18%, and 37% among persons 5 to 17 years of age, 18 to 49 years of age, 50 to 64 years of age, and 65 years of age or older, respectively.¹ These total reductions in invasive pneumococcal disease encompass the decline in vaccine-serotype disease and the increase in nonvaccine serotype disease.¹¹

Table 1. Rates of Hospitalization, Length of Hospital Stay, and Rates of In-Hospital Death Related to Pneumonia from Any Cause 3 Years before and 7 to 9 Years after the Introduction of PCV7.*

Characteristic	Age Group							
	<2 yr	2–4 yr	5–17 yr	18–39 yr	40–64 yr	65–74 yr	75–84 yr	≥85 yr
Average annual hospitalizations — no./100,000 (95% CI)								
Pre-PCV7	1274 (1185–1364)	411 (383–439)	97 (91–104)	107 (102–113)	336 (321–351)	1293 (1239–1348)	2758 (2643–2873)	5697 (5457–5937)
Late PCV7	723 (666–780)	360 (329–391)	93 (85–101)	99 (93–104)	370 (351–388)	1208 (1152–1264)	2398 (2287–2510)	4396 (4189–4603)
Length of hospital stay — days								
Pre-PCV7								
Median	2.3	2.0	2.3	3.2	4.0	4.6	4.9	5.2
Interquartile range	1.4–3.6	1.2–3.1	1.4–3.8	1.9–5.4	2.4–6.6	2.8–7.5	3.0–7.9	3.2–8.2
Late PCV7								
Median	1.9	1.8	2.0	3.0	3.8	4.2	4.3	4.4
Interquartile range	1.1–3.2	1.1–2.9	1.2–3.6	1.7–5.7	2.1–6.9	2.4–7.4	2.6–7.5	2.6–7.2
Reason for admission coded as pneumococcal disease — % (95% CI)								
Pre-PCV7	2.2 (1.9–2.5)	3.2 (2.8–3.5)	4.2 (3.9–4.6)	8.4 (7.6–9.2)	7.4 (7.0–7.8)	5.6 (5.4–5.8)	4.6 (4.5–4.8)	3.7 (3.6–3.9)
Late PCV7	1.5 (1.3–1.7)	2.7 (2.3–3.0)	2.9 (2.6–3.2)	4.6 (4.4–4.8)	4.8 (4.6–4.9)	3.5 (3.3–3.6)	2.6 (2.5–2.7)	2.2 (2.1–2.4)
In-hospital deaths — % (95% CI)								
Pre-PCV7	0.2 (0.2–0.3)	0.2 (0.1–0.3)	0.4 (0.3–0.5)	1.8 (1.6–1.9)	4.3 (4.2–4.5)	6.8 (6.7–7.0)	9.3 (9.2–9.4)	13.0 (12.8–13.2)
Late PCV7	0.2 (0.1–0.2)	0.1 (0.1–0.2)	0.4 (0.3–0.5)	2.2 (2–2.4)	4.9 (4.7–5.1)	7.0 (6.9–7.2)	8.7 (8.6–8.8)	11.5 (11.3–11.7)

* Pre-PCV7 refers to the 3-year period (1997 through 1999) preceding the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2000, and late PCV7 refers to the 3-year period beginning 7 years after its introduction (2007 through 2009).

The reduction in hospitalizations for pneumonia among unvaccinated persons is perhaps more remarkable than the decline among young children, who were targeted for vaccination. Indeed, older adults accounted for more than half the decline in overall hospitalizations for pneumonia. The patterns of decline in hospitalizations for pneumonia are similar to those observed for all cases of invasive pneumococcal disease, with the largest relative and absolute reductions at the extremes of age.^{1,2} For both invasive pneumococcal disease and pneumonia, the potential for disease reduction was highest at the extremes of age, because the rates of vaccine-serotype disease were highest in these age groups before PCV7 was introduced.²⁰

Substantial reductions in rates of childhood

pneumonia have been reported in other countries where PCV7 has been introduced. In Australia, a time-series analysis showed reductions of 38% and 29% in pneumonia among children younger than 2 years of age and those 2 to 4 years of age, respectively, within 2 years after the introduction of the vaccine in 2005.²¹ In the United Kingdom, hospitalizations for pneumonia among children younger than 15 years of age, which had increased through 2006, when PCV7 was introduced there, fell by 19% by 2008.²² The association of declines in rates of pneumonia with the timing of vaccine introduction in multiple countries supports a causal association.

The attribution of changes in pneumonia to the PCV7 vaccination program also requires consideration of changes in coding practices,

Table 2. Differences in Rates of Hospitalization for Pneumonia from Any Cause 3 Years before and 7 to 9 Years after the Introduction of PCV7.*

Age	U.S. Population, 2009 <i>millions</i>	Difference in Hospitalization Rates per 100,000 Population, Pre-PCV7 vs. Late PCV7 <i>no. (95% CI)</i>	Reduction in Hospitalizations, Pre-PCV7 to Late PCV7 <i>% (95% CI)</i>	Estimated Absolute Reduction in Hospitalizations, 2009 <i>no. (95% CI)</i>
<2 yr	8.6	551.1 (445.1 to 657.1)	43.2 (34.9 to 51.6)	47,000 (38,000 to 56,000)
2–4 yr	12.7	51.3 (9.8 to 92.8)	12.5 (2.4 to 22.6)	7,000 (1,000 to 12,000)
5–17 yr	53.2	4.4 (–5.9 to 14.7)	4.5 (–6.1 to 15.1)	2,000 (–3,000 to 8,000)
18–39 yr	92.5	8.4 (0.6 to 16.2)	7.8 (0.6 to 15.1)	8,000 (<1,000 to 15,000)
40–64 yr	100.4	–33.8 (–57.4 to –10.2)	–10.1 (–17.1 to –3.0)	–34,000 (–58,000 to –10,000)
65–74 yr	20.8	85.3 (7.0 to 163.6)	6.6 (0.5 to 12.7)	18,000 (1,000 to 34,000)
75–84 yr	13.1	359.8 (199.6 to 520.0)	13.0 (7.2 to 18.9)	47,000 (26,000 to 68,000)
≥85 yr	5.6	1300.8 (984.0 to 1617.6)	22.8 (17.3 to 28.4)	73,000 (55,000 to 91,000)
All age groups†	307.0	54.8 (41.0 to 68.5)	10.5 (7.9 to 13.1)	168,000 (126,000 to 210,000)

* Pre-PCV7 refers to the 3-year period (1997 through 1999) preceding the introduction of PCV7 in 2000, and late PCV7 refers to the 3-year period beginning 7 years after its introduction (2007 through 2009).

† The values for all age groups were adjusted to the U.S. population in accordance with the age-group distribution in 2009.

hospital admission thresholds, and other factors. Despite stable overall hospitalization rates among older adults in the years 2000 through 2009, there were major declines in hospitalizations for which the diagnostic codes were pneumonia, congestive heart failure, and coronary atherosclerosis.¹⁴ Lindenauer et al. explored changes in hospital coding for pneumonia in the years 2003 through 2009 and found increasing use of sepsis as the first listed diagnosis and of pneumonia as a secondary rather than primary (first-listed) diagnosis.²³ Our definition of hospitalization for pneumonia included hospitalizations for which sepsis was the primary diagnosis, so our reported rates were not influenced by such coding changes.

Pneumonia is the only common childhood condition for which hospitalizations declined during the study period,¹⁴ and the decline was temporally associated with the introduction of PCV7.⁹ Among children, the decline in hospital-

izations for pneumonia was not accompanied by a “compensatory” increase in outpatient visits for pneumonia²⁴; in fact, decreases in outpatient visits for pneumonia were reported.^{25–28} In addition, the decline in the length of stay and the stability of in-hospital rates of death from pneumonia (Table 1) suggest no major increases in admission thresholds.

It seems unlikely that influenza vaccination was a major contributor to these declines in childhood pneumonia, since influenza vaccination of healthy young children was uncommon before the initial (2004) and expanded (2006) recommendations for it were made by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices. By 2009, only 30% of healthy children were being vaccinated for influenza.²⁹ Among adults, the major increases in pneumococcal and influenza vaccination predate the introduction of PCV7. Among adults 65 years of age or older, the rates of both

pneumococcal polysaccharide vaccination and influenza vaccination had more than doubled between 1989 and 1999 (from 14% to 50% and from 30% to 66%, respectively).³⁰ Similarly, the rate of smoking fell from 40% of the adult population in the 1970s to 26% in the 1990s.³¹ During this period in which major changes in immunization practices and smoking behavior occurred, hospitalizations for pneumonia in adults actually increased.³² Since the introduction of PCV7 in 2000, there have been much more modest changes, with the percentage of adults 65 years of age or older who received pneumococcal polysaccharide vaccine increasing to 60% and the percentage who received influenza vaccine increasing to 67% by 2008.³⁰ During this same period, the percentage of adults who smoked fell to 24%.³¹

Notwithstanding the substantial reductions in pneumonia observed after the introduction of PCV7, unvaccinated age groups have a residual burden of pneumococcal disease due to serotypes covered by the vaccine.¹³ In the United Kingdom, a novel urinary immunoassay was used to diagnose serotype-specific pneumococcal pneumonia in hospitalized adults 2 years after PCV7 was introduced. Investigators estimated that 40% of cases of pneumonia were pneumococcal, that at least 20% of these cases were caused by PCV7 serotypes, and that this portion increased with increasing age.³³ Thus, even 2 years after the introduction of the vaccine and despite a rapid decline in cases of childhood invasive pneumococcal disease, a substantial portion of cases of pneumonia in adults were

still due to vaccine serotypes. This finding is consistent with the slower rate of decline in cases of invasive pneumococcal disease caused by PCV7 serotypes in U.S. adults¹ and with the modest decline in all cases of pneumonia in adults during the early PCV7 period.

It is not known whether the direct vaccination of adults with PCV13 would prevent pneumonia in adults and whether such efforts would add substantially to the indirect benefits generated by the ongoing PCV13 vaccination program in infants, which may now be reducing the transmission of the additional six vaccine serotypes.^{34,35} PCV13 has recently been recommended for immunocompromised adults in the United States,³⁶ a group for which efficacy data are already available,³⁷ and indirect benefits are likely to be modest.^{13,38}

In summary, the reduction initially observed in hospitalizations for childhood pneumonia was sustained in the decade after 2000, when PCV7 was introduced. More modest relative declines in hospitalizations for pneumonia among older adults emerged more slowly and resulted in large absolute overall reductions in hospitalizations for pneumonia.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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