Assessing Pneumococcal Revaccination Safety among New York State Medicare Beneficiaries

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SYNOPSIS

Objective. There have not been adequate studies of the safety of pneumococcal revaccination, especially for revaccination at intervals of less than five years. The objective of this study was to assess revaccination safety by determining whether pneumococcal revaccination is associated with greater utilization of postvaccination health care, compared with initial vaccination.

Methods. The authors conducted a retrospective cohort study of 119,990 New York State Medicare beneficiaries 65 years of age and older who received pneumococcal vaccinations from February 1, 1999, through December 17, 1999. The study used a multivariate regression model with three primary outcome measures—emergency room visits, hospitalizations, and office visits during the two weeks postvaccination. Secondary outcome measures were specific International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes potentially related to adverse vaccine reactions.

Results. Of 119,990 patients, 23,663 had previous claims for pneumococcal vaccination, including 13,466 for whom the revaccination interval was less than five years. After adjustment for demographic and comorbidity factors, revaccination at less than five years was associated with higher rates of emergency room visits (odds ratio [OR] = 1.17; 95% confidence interval [CI] 1.02, 1.34) and office visits (OR = 1.13; 95% CI 1.09, 1.18) during the two-weeks postvaccination, compared with initial vaccination. In addition, several ICD-9-CM codes that might indicate vaccine reactions were recorded more frequently for the revaccination group than for the comparison group.

Conclusions. Because of potential policy implications, further investigation is needed of the causes and consequences of short-interval revaccination.

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For protection against invasive pneumococcal disease, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices recommends use of the 23-valent pneumococcal polysaccharide vaccine (PPV) for people ≥65 years of age and for younger people with an elevated risk of morbidity or mortality from pneumococcal disease.[1]

One-time revaccination is recommended for people ≥65 years of age who received a primary vaccination ≥5 years previously and who were younger than age 65 at the time of primary vaccination. One-time revaccination is also recommended for people younger than age 65 whom the CDC considers at high risk for severe pneumococcal infection (e.g., children with asplenia). In addition, when indicated, PPV vaccine is recommended for those with an unknown vaccination history.[1]

Common adverse reactions to initial PPV administration include mild, local injection-site soreness, erythema, and swelling.[1–3] Systemic symptoms, as well as more serious reactions, are rare, and the benefits of initial vaccination are generally believed to outweigh the costs.[2,4] The data for adverse reactions to revaccination are less clear.[5] Studies with the older 14-valent vaccine suggested a higher incidence of local reactions and fever with revaccination when compared to initial vaccination.[6–8] Subsequent studies were limited because they were generalizable only to children[9] or specialized populations such as postsplenectomy patients,[10] had small sample sizes (<50),[11,12] or lacked appropriate comparison groups.[13]

Even the best studies of PPV revaccination safety to date have several important limitations. The most recent and well-executed study was a comparative intervention with 901 patients receiving an initial vaccination and 513 patients receiving a revaccination.[14] The authors found more frequent local site reactions in the revaccination group but concluded that this risk was not a contradiction to revaccination. In that study, all revaccinations were provided to individuals who had had the initial vaccine ≥5 years previously, congruent with current vaccine guidelines. Snow et al. looked at revaccinations within five years, using hospitalization as the only outcome measure.[15] This not only restricted their ability to detect less severe reactions not requiring hospitalization, but also because of the small sample size (1,006 patients receiving revaccination), the study lacked the statistical power to detect clinically important but small differences in hospitalization rates between patients who received one dose of vaccine and those receiving a second dose.

The purpose of the present study was to better characterize pneumococcal revaccination safety by determining whether pneumococcal revaccination in the Medicare population, particularly at an interval of less than five years from the previous vaccination, is associated with higher rates of outpatient office visits, emergency room visits, or hospitalizations during the two weeks postvaccination, compared with rates among people of comparable health status and demographic characteristics who received initial vaccinations. In addition to these utilization outcomes, we compared initial vaccination and revaccination groups for the two-week postvaccination period in terms of the presence in claims of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)[16] diagnostic codes that may be indicative of vaccine reactions.

METHODS

Sample selection

From Centers for Medicare & Medicaid Services (CMS) Medicare Part A and Part B claims data, we identified all New York State Medicare beneficiaries with claims for PPV doses or administration (defined by a Common Procedural Terminology code of G0009, 90732, or 90669) during the period February 1, 1999, to December 17, 1999.

A total of 128,874 beneficiaries had at least one claim for PPV administration. We excluded 652 beneficiaries for whom the dates of PPV administration were internally inconsistent (i.e., multiple dates for a single claim). We determined prior vaccination status by examining PPV claims for New York State beneficiaries starting with January 1990. To avoid duplicate claims that might represent a single event, we excluded 848 beneficiaries with three or more claims during the study period or a prior vaccination claim during the study period that was closer than 180 days to the latest PPV vaccination. We limited the study to beneficiaries 65 years old or older; thus, we excluded 48 beneficiaries for whom demographic information was not available and 7,304 beneficiaries who were younger than 65 years of age on January 1, 1999. The remaining 119,990 beneficiaries were the study sample.

The revaccination cohort (n = 23,663) consisted of beneficiaries for whom the last (or only) vaccination administered during the study period represented a revaccination. The comparison group (n = 96,327) consisted of beneficiaries who received one PPV vaccination during the study period and for whom there was no other record of PPV vaccination since January 1, 1990, in the CMS claims dataset.

Data collection

The index date for each beneficiary was the date of PPV administration during the study period. For beneficiaries with two vaccinations during this period, the later date of administration was considered the index date. For each beneficiary, we extracted all Medicare Part A and Part B claims data from 30 days prior to the index date through 14 days after the index date.

We abstracted 1998 hospitalization records for the study sample from Medicare claims. We coded the presence or absence of a hospitalization in 1998 as a binomial categorical variable, which we used as a crude index of comorbidity. We searched the 30-day period prior to each beneficiary's index date for an outpatient office visit (Common Procedural Terminology codes 99201–99205, 99211–99215). We coded this as a binomial categorical variable, which was both another index of comorbidity and an indicator for high utilization of care. We used an adaptation of the Charlson Index developed by Deyo and his colleagues for the final comorbidity index.[17,18] For each study subject, we searched all inpatient and outpatient claims for the index date for the comorbid diagnoses identified by Charlson et al.[17] using the ICD-9-CM diagnostic codes used by Deyo et al.[18] We assigned weights by the Charlson method; the adapted Charlson Index was the sum of those weights. We treated this index as a categorical variable with four possible values: 0, 1, 2, ≥3.

The primary outcome variables were office visits, emergency room visits, and hospitalizations in the 14-day post-vaccination period. Secondary outcomes of interest were the presence of specific ICD-9-CM diagnostic codes in any of the first four diagnostic fields of any claim in the 14-day post-vaccination period.

Age, sex, and "race" data were taken from national Medicare enrollment files. Sex and "race" were self-reported at the time of enrollment in Medicare. For the analyses reported here, we reduced age to four categories for analytic simplicity. We included "race" as a variable because it is standard practice to use "race" for demographic adjustment, although we recognize that this variable may be primarily a proxy for other characteristics (e.g., place of residence, access to treatment, wealth) that are not captured in this study. Other than black and white, the remaining "race" categories were grouped into an "other/unknown" category due to small numbers.

Study design and analysis

The design was a retrospective cohort study, with the primary outcomes of interest being emergency room visits, office visits, and hospitalizations during the 14-

Table 1. Characteristics of study subjects (*N* = 119,990)

	Revaccination group (n = 23,663)		*Comparison group (n = 96,327)*	
Variable	*Number*	*Percent*	*Number*	*Percent*
Sex				
Male	9,326	39.4	37,237	38.7
Female	14,337	60.6	59,090	61.3
Age				
≥80	9,540	40.3	26,191	27.2
75–79	6,879	29.1	20,839	21.6
70–74	5,749	24.3	24,279	25.2
65–69	1,495	6.3	25,018	26.0
"Race"				
Black	850	3.6	4,384	4.6
White	21,902	92.6	86,677	90.0
Other/unknown	911	3.8	5,266	5.5
Office visit ≤30 days before index date	10,613	44.9	38,731	40.2
Hospitalization in 1998	4,803	20.3	13,969	14.5
Adapted Charlson Index				
0	16,123	68.1	7,1474	74.2
1	5,777	24.4	19,519	20.3
2	1,398	5.9	4,299	4.5
≥3	365	1.5	1,035	1.1

NOTE: Differences between the revaccination and comparison groups were statistically significant for all variables ($p<0.05$).

Table 2. Crude relative risks of emergency room visits, hospitalizations, and physician office visits within the 14-day postvaccination period (*N* = 119,990 study subjects)

	Emergency room visits				*Hospitalizations*				*Office visits*			
Group	*Number*	*Percent*	*RR*	*95% CI*	*Number*	*Percent*	*RR*	*95% CI*	*Number*	*Percent*	*RR*	*95% CI*
Total revaccination cohort (*n* = 23,663)	415	1.8	1.30	1.16, 1.45	348	1.5	1.24	1.10, 1.40	5,754	24.3	1.13	1.10, 1.16
Revaccination <5 years before index date (*n* = 13,466)	252	1.9	1.39	1.21, 1.60	216	1.6	1.35	1.17, 1.56	3,344	24.8	1.15	1.12, 1.19
Revaccination ≥5 years before index date (*n* = 10,197)	163	1.6	1.18	1.01, 1.39	132	1.3	1.09	0.91, 1.31	2,410	23.6	1.10	1.06, 1.14
Comparison group (*n* = 103,036)	1,300	1.3		Reference	1,142	1.2		Reference	20,721	21.5		Reference

RR = relative risk

CI = confidence interval

day period following vaccination or revaccination. The primary exposure of interest was whether the vaccination on the index date was a revaccination, and, if so, whether it occurred less than five years after the previous vaccination. We compared characteristics of the revaccination cohort and comparison group using a two-tailed Pearson's chi square test for independence. We calculated crude relative risks (RRs) for utilization outcomes with 95% confidence intervals (CIs) using EpiInfo Version 6.[19] We performed logistic regression analyses using SPSS Version 9.0[20] to calculate univariate and multivariate odds ratios (ORs). In the multivariate analysis, we used a stepwise logistic regression model, with demographic variables in the first step, prior utilization variables and the adapted Charlson Index in the second step, and the revaccination status in the final step. In addition, we repeated the multivariate analysis stratified by age group to evaluate any interaction effects of age and revaccination status with subsequent outcomes.

To better assess the temporal pattern of the office visit outcome, we performed two additional multivariate logistic regressions: using an office visit during post-index days 1 to 3 as an outcome and using an office visit during post-index days 4 to 14 as an outcome.

Secondary outcomes of interest were claims associated with diagnostic codes that may be directly related to pneumococcal vaccine administration. We searched for ICD-9-CM codes that may be indicative of a vaccine reaction in the first four diagnostic fields of each claim. We calculated crude RRs of these secondary outcomes for the revaccination group compared with the initial vaccination group and 95% CIs with EpiInfo version 6.[19] For significant findings, we repeated the analysis with the stepwise logistic regression model used in the primary outcome analysis.

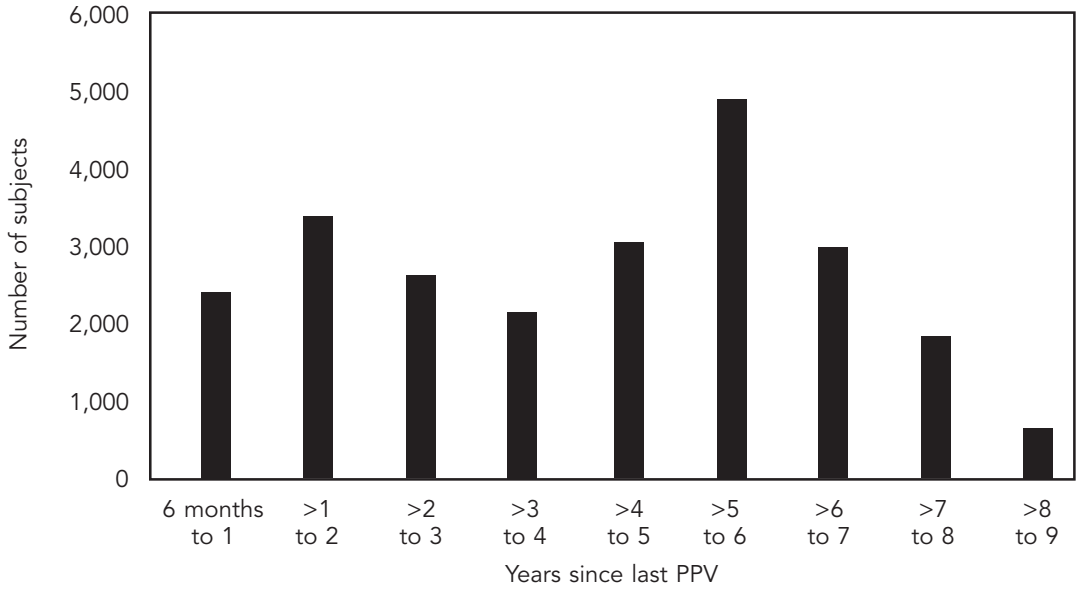
RESULTS

The characteristics of the study groups are presented in Table 1. Compared with the comparison group, the revaccination cohort had a higher proportion of males and higher rates of hospitalizations in 1998 and office visits in the 30-day period before the index date. The two groups also differed in age, "race," and comorbidities as measured by the Charlson Index. All of these differences were statistically significant ($p<0.05$).

Crude New York State rates and RRs for the primary outcome measures are presented in Table 2. The revaccination group was 1.30 times as likely as the comparison group to have an emergency room visit (95% CI 1.16, 1.45), 1.24 times as likely to be hospitalized (95% CI 1.10, 1.40), and 1.13 times as likely to have an office visit (95% CI 1.10, 1.16) in the 14-day postvaccination period. For all outcomes, revaccination within five years was associated with higher RRs than revaccination after five years.

The Figure shows the distribution of the length of time between revaccination during the study period and previous vaccination for the revaccination cohort

Figure. Interval between pneumococcal vaccinations in the revaccination cohort (*n* = 23,663)



PPV = pneumococcal polysaccharide vaccine

(*n* = 23,663). Fifty-seven percent of the revaccination cohort (*n* = 13,466) were revaccinated less than five years after the previous vaccination.

In the univariate logistic regression analysis for emergency room visits as an outcome (Table 3), statistically significant positive predictors were revaccination at an interval of <5 or ≥5 years, ages 75–79 or ≥80 years, black "race," having been hospitalized in 1998, having had an office visit ≥30 days prior to the index vaccination date, and having an adapted Charlson Index >0.

All of these variables except revaccination at ≥5 years remained statistically significant positive predictors in the multivariate model. The OR for revaccination at <5 years, after adjustment for the demographic and morbidity variables was 1.17 (95% CI 1.02, 1.34) in the multivariate model, representing an approximate excess emergency room utilization rate of 2.2 per 1,000 beneficiaries.

In the univariate logistic regression analysis for hospitalization as an outcome (Table 4), revaccination at an interval of <5 years, ages 70–74 and 75–79, black "race," male sex, an adapted Charlson Index >0, hospitalization in 1998, and recent office visit were statistically significant positive predictors. All of these variables except revaccination status and black "race" remained statistically significant in the multivariate model. The adjusted OR for revaccination at <5 years was 1.09, which did not reach statistical significance (95% CI 0.94, 1.27).

In the univariate logistic regression analysis for office visits as an outcome (Table 5), revaccination at <5 years and at ≥5 years, ages 70–79, "race" other than black or white, male sex, an adapted Charlson Index >0, hospitalization in 1998, and recent office visit were statistically significant positive predictors. The OR for the age category 70–74 became nonsignificant in the multivariate model. The adjusted OR for the revaccination at <5 year group was 1.13 (95% CI 1.09, 1.18), representing an approximate excess office visit rate of 28 per 1,000 beneficiaries, and for the ≥5 year group the OR was 1.09 (95% CI 1.04, 1.15), representing an approximate excess office visit rate of 20 per 1,000 beneficiaries.

For each of the three outcomes (emergency room visits, hospitalizations, and office visits), multivariate analyses stratified by age did not show significant differences in the adverse effects of revaccination across the four age categories.

When the office visit outcome was split into post-index days 1 to 3 and post-index days 4 to 14, the multivariate logistic regression model yielded adjusted ORs for the revaccination groups that were greater, although not significantly greater, for office visits during the first 3 days than for visits during the following 11 days. For revaccination at <5 years, the adjusted ORs were 1.19 (95% CI 1.10, 1.30) for an office visit during days 1–3 and 1.12 (95% CI 1.10, 1.23) for an office visit during days 4–14. For revaccination at ≥5 years, the adjusted ORs were 1.10 (95% CI 1.05, 1.15)

Table 3. Logistic regression analysis on emergency room visits as outcome (*N* = 119,990 study subjects)

Variable	Emergency room visits		Univariate		Multivariate	
	Number	Percent	OR	95% CI	OR	95% CI
Revaccination status						
<5 years before index date	252	1.9	1.39	1.22, 1.60	1.17	1.02, 1.34
≥5 years before index date	163	1.6	1.19	1.01, 1.40	0.99	0.84, 1.17
No previous PPV > January 1, 1990	1,300	1.3	Reference		Reference	
Sex						
Male	649	1.4	0.96	0.87, 1.06	0.96	0.87, 1.06
Female	1,066	1.5	Reference		Reference	
Age						
≥80	742	0.2	2.08	1.80, 2.34	1.79	1.55, 2.07
75–79	396	1.4	1.42	1.21, 1.66	1.25	1.07, 1.47
70–74	309	1.0	1.02	0.86, 1.20	0.93	0.79, 1.10
65–69	268	1.0	Reference		Reference	
"Race"						
Other	97	1.6	1.12	0.91, 1.38	1.16	0.94, 1.42
Black	98	1.9	1.34	1.09, 1.65	1.25	1.02, 1.54
White	1,520	1.4	Reference		Reference	
Hospitalization in 1998						
Yes	515	2.7	2.35	2.12, 2.61	2.00	1.80, 2.22
No	1,200	1.2	Reference		Reference	
Office visit ≥30 days prior to index date						
Yes	886	1.8	1.54	1.40, 1.69	1.45	1.32, 1.59
No	829	1.2	Reference		Reference	
Adapted Charlson Index						
≥3	41	2.9	2.49	1.81, 3.42	2.04	1.49, 2.81
2	140	2.5	2.08	1.74, 2.48	1.76	1.47, 2.11
1	485	1.9	1.61	1.45, 1.80	1.49	1.33, 1.66
0	1,049	1.2	Reference		Reference	

OR = odds ratio

CI = confidence interval

PPV = pneumococcal polysaccharide vaccine

for an office visit during days 1–3 and 1.07 (95% CI 1.02, 1.13) for an office visit during days 4–14.

ICD-9-CM codes that we believed a priori might be indicative of a vaccine reaction are shown in Table 6. The RR of their presence in claims for the 14 days postvaccination for the revaccination cohort vs. the comparison group was significant for the codes representing limb pain (RR = 1.41; 95% CI, 1.16, 1.70), unspecified allergic/adverse reactions (RR = 1.61; 95% CI 1.20, 2.15), and adverse reactions to vaccines or other biological substances properly administered (RR = 6.11; 95% CI 1.02, 36.54). In multivariate logistic regression analysis, the adjusted ORs were 1.27 (95% CI 1.05, 1.55) for limb pain and 1.70 (95% CI 1.26, 2.29) for unspecified allergic/adverse reaction.

DISCUSSION

The results of this study have potentially important public health practice and policy implications. These findings suggest that Medicare beneficiaries who receive PPV revaccination at an interval of less than five years have higher rates of emergency room visits and office visits during the 14 days postvaccination than do beneficiaries with only an initial vaccination. This finding persists even after adjustment for specific demographic and comorbidity factors in a multivariate model. In addition, although the adjusted OR for hospitalization (1.09) for beneficiaries with revaccination at <5 years compared with the initial vaccination group is not statistically significant (95% CI 0.94, 1.27), it approaches significance. Our sample size, though the

Table 4. Logistic regression analysis on hospitalizations as outcome (*N* = 119,990 study subjects)

Variable	Hospitalizations		Univariate		Multivariate	
	Number	Percent	OR	95% CI	OR	95% CI
Revaccination status						
<5 years before index date	216	1.6	1.36	1.17, 1.57	1.09	0.94, 1.27
≥5 years before index date	132	1.3	1.09	0.91, 1.31	0.87	0.73, 1.05
No previous PPV > January 1, 1990	1,142	1.2	Reference		Reference	
Sex						
Male	641	1.4	1.19	1.08, 1.32	1.18	1.06, 1.31
Female	849	1.2	Reference		Reference	
Age						
≥80	631	1.8	2.37	2.02, 2.79	2.11	1.79, 2.49
75–79	361	1.3	1.74	1.46, 2.07	1.56	1.31, 1.87
70–74	299	1.0	1.33	1.11, 1.59	1.23	1.02, 1.47
65–69	199	0.8	Reference		Reference	
"Race"						
Other	65	1.1	0.85	0.66, 1.09	0.86	0.67, 1.11
Black	83	1.6	1.29	1.03, 1.61	1.21	0.96, 1.51
White	1,342	1.2	Reference		Reference	
Hospitalization in 1998						
Yes	534	2.7	2.44	2.18, 2.72	1.99	1.77, 2.22
No	1,057	1.0	Reference		Reference	
Office visit ≥30 days prior to index date						
Yes	841	1.7	1.87	1.69, 2.07	1.74	1.57, 1.93
No	649	0.9	Reference		Reference	
Adapted Charlson Index						
≥3	51	3.6	3.63	2.73, 4.84	2.87	2.14, 3.83
2	151	2.7	2.62	2.20, 3.12	2.16	1.81, 2.58
1	386	1.5	1.49	1.32, 1.68	1.37	1.21, 1.54
0	902	1.0	Reference		Reference	

OR = odds ratio

CI = confidence interval

PPV = pneumococcal polysaccharide vaccine

largest to date for any study addressing this issue, does not have adequate statistical power to detect an OR <1.20 because the prevalence of hospitalization is low.

Examination of the diagnostic codes intuitively specific to local or systemic vaccine reaction revealed some excess diagnoses in the revaccination group, but this effect was small in comparison with the overall excess utilization. Most diagnostic codes for the post-index period reflected the chronic cardiovascular, pulmonary, and diabetic illnesses expected in this age group. It is biologically plausible, however, that vaccine reactions exacerbate underlying conditions, leading to the higher utilization that we observed for the revaccination group.

There are several limitations to our study. Medicare claims data do not reflect all vaccinations and may contain errors. Some beneficiaries in the comparison group might have had a previous PPV vaccination during the time period examined that was not billed to Medicare, in which case their index vaccination was in fact a revaccination. This may have occurred if individuals paid for vaccinations out-of-pocket at local pharmacies, visited physician practices that did not consistently or correctly bill for vaccinations, or were enrolled in managed care plans and their vaccinations were not billed to Medicare. Although present author JQ has calculated, using Medicare claims data, that claims were filed for PPV vaccination for 33% of non–managed care–enrolled seniors in New York State in 1991–1999 (Unpublished data, Health Care Quality Improvement Department, IPRO, November 2000), Behavioral Risk Factor Surveillance Survey data on

Table 5. Logistic regression analysis on office visits as outcome (*N* = 119,990 study subjects)

Variable	Office visits		Univariate		Multivariate	
	Number	Percent	OR	95% CI	OR	95% CI
Revaccination status						
<5 years before index date	3,344	24.8	1.21	1.16, 1.26	1.13	1.09, 1.18
≥5 years before index date	2,410	23.6	1.13	1.08, 1.19	1.09	1.04, 1.15
No previous PPV > January 1, 1990	20,721	21.5	Reference		Reference	
Sex						
Male	10,751	23.1	1.10	1.07, 1.13	1.07	1.04, 1.10
Female	15,724	21.4	Reference		Reference	
Age						
≥80	7,553	21.1	0.99	0.96, 1.03	0.92	0.89, 0.96
75–79	6,534	23.6	1.14	1.10, 1.19	1.05	1.00, 1.10
70–74	6,760	22.5	1.08	1.04, 1.12	1.01	0.97, 1.05
65–69	5,628	21.2	Reference		Reference	
"Race"						
Other	1,615	26.1	1.27	1.20, 1.35	1.23	1.16, 1.31
Black	1,170	22.4	1.03	0.97, 1.10	0.99	0.93, 1.06
White	23,690	21.8	Reference		Reference	
Hospitalization in 1998						
Yes	5,008	26.7	1.35	1.30, 1.40	1.24	1.19, 1.29
No	21,467	21.2	Reference		Reference	
Office visit ≤30 days prior to index date						
Yes	15,044	30.5	2.27	2.21, 2.34	2.22	2.15, 2.28
No	11,431	16.2	Reference		Reference	
Adapted Charlson Index						
≥3	432	30.9	1.69	1.51, 1.89	1.50	1.33, 1.69
2	1,758	30.9	1.69	1.59, 1.79	1.53	1.45, 1.63
1	5,971	23.6	1.17	1.13, 1.21	1.12	1.08, 1.16
0	18,314	20.9	Reference		Reference	

OR = odds ratio

CI = confidence interval

PPV = pneumococcal polysaccharide vaccine

New York State seniors revealed a cumulative PPV coverage rate of 50%.[21] While the groups and techniques are not exactly comparable, it is clear that over time, many pneumococcal vaccinations do not enter the Medicare claims files. In addition, some claims for PPV may, in fact, be miscoded claims for influenza vaccine or other services. In either case, misclassification to revaccination or comparison groups would have artificially reduced rather than increased our estimate of the difference in outcomes.

There are also the inherent limitations of the retrospective study design. Exposure to revaccination is not a random event, and therefore the two study groups were not comparable at baseline. The beneficiaries in the revaccination cohort were older and had more comorbidities than those in the comparison group, and we attempted to adjust for these variables in the multivariate model. Prior office visits, hospitalizations, and the adapted Charlson Index were the strongest predictors of the outcomes, but these did not fully account for the statistically significant association of revaccination with emergency room and office visits. Some of the observed excess utilization may be due to baseline differences not captured by our risk adjustment model. It is also possible that the excess office visits attributable to revaccination may represent only a fraction of the visits estimated by our model. However, several observations support the conclusion that at least some of the excess utilization observed is attributable to revaccination rather than to unmeasured confounding variables. The appearance of larger effects among those with more recent revaccination and

Table 6. Relative risk of select ICD-9-CM diagnostic codes for the revaccination group vs. the comparison group

		Revaccination group (n = 23,663)	*Comparison group (n = 96,327)*		
ICD-9-CM code	*Brief description*	*Number*	*Number*	*RR*	*95% CI*
7806	Fever	42	128	1.34	0.94, 1.89
7807, 7809	Malaise	66	246	1.09	0.83, 1.43
71941, 71942	Pain–upper arm/shoulder	31	137	0.92	0.62, 1.36
7295	Limb pain	145	420	1.41	1.16, 1.70
72981	Limb swelling	24	62	1.58	0.98, 2.52
7821	Rash	14	53	1.08	0.60, 1.94
7089, 708, 7081	Urticaria	3	11	1.11	0.31, 3.98
7820	Change in skin sensation	14	53	1.08	0.60, 1.94
9953, 9952	Allergic/adverse reaction, unspecifed	64	162	1.61	1.20, 2.15
9994	Anaphylactic shock	1	0		—
9993	Infection following injection, vaccination, and transfusion	4	5	3.26	0.87, 12.13
9951	Angioneurotic edema	2	3	2.71	0.45, 16.24
E9499, E9488	Adverse reaction to vaccine/other	3	2	6.11	1.02, 36.54

ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification

RR = relative risk

CI = confidence interval

an increase in vaccine reaction-associated diagnostic codes in revaccinees support a true excess utilization due to revaccination. However, excess utilization is a crude indicator of morbidity or adverse consequences due to revaccination, and further exploration, perhaps with medical chart review, would be warranted to explore the precise nature of the excess visits.

Note that the ORs calculated for the "race" variable in the present study should be interpreted with extreme caution. The "race" variable was most likely a proxy for other factors such as urban vs. rural residence, differential access to care, and differential treatment by providers.

Our findings are consistent with those of other investigators. As previously described, the best study to date examined revaccinations at an interval of >5 years, finding a higher rate of local reactions in the revaccination group, consistent with the results of earlier studies.[14] Snow et al.[15] performed a similar study to ours, but looked only at hospitalization as an outcome. Although their data showed no difference in hospitalization rates between Medicare enrollees receiving one dose of vaccine and those receiving a second dose, their sample size was much smaller than that in the current study.

The public health implications of the findings reported here need to be carefully assessed. This study only considered excess health care utilization associated with PPV revaccination, and does not have any bearing on the current policy to encourage initial PPV vaccination for high-risk individuals. Revaccination after five years, recommended to maintain protection for selected individuals at higher risk, was associated with less excess utilization than revaccination within five years and so may be justified. Current CDC recommendations do not call for revaccination at intervals of less than five years for immunocompetent individuals, and do not recommend revaccinations at all for people who received their initial pneumococcal vaccination after age 65. They do recommend PPV vaccination of patients who cannot remember their prior vaccination status, even if their medical records are not available for examination. This is justified if a large proportion of the high-risk population has never been vaccinated with PPV, if many opportunities for PPV vaccination are in settings in which medical records are not available, and if the number or the adverse consequences of PPV revaccinations occurring as a result of this policy are small in comparison with the benefit. In the present study, we found that the number of PPV revaccinations in the Medicare population in New York State was substantial and that these were associated with a measurably higher health care utilization among patients receiving revaccina-

tions within five years than among those who received only an initial vaccination. Further exploration is required to determine the extent to which excess revaccinations are a consequence of the current recommendations and to better characterize the size and nature of the excess utilization associated with revaccination. These issues are vital for accurately weighing the costs and benefits of the current revaccination recommendations and considering future policy revisions.

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REFERENCES

1. Nuroti PJ, Butler JC, Brieman RF. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 1997;46:1-24.
2. Fine MJ, Smith MA, Carson CA, Meffe F, Sankey SS, Weissfeld LA, et al. Efficacy of pneumococcal vaccination in adults. Arch Intern Med 1994;154:2666-77.
3. Nichol KL, MacDonald R, Hauge M. Side effects associated with pneumococcal vaccination. Am J Infect Control 1997;25:223-8.
4. Fiebach N, Beckett W. Prevention of respiratory infections in adults: influenza and pneumococcal vaccines. Arch Intern Med 1994;154:2545-57.
5. Spika JS, Fedson DS, Facklam RR. Pneumococcal vaccination: controversies and opportunities. Infect Dis Clin North Am 1990;4:11-27.
6. Carlson AJ, Davidson WL, McLean AA, Vela PP, Weibel RE, Woodhour AF, et al. Pneumococcal vaccine: dose, revaccination, and coadministration with influenza vaccine. Proc Soc Exp Biol Med 1979;161:558-63.
7. Borgono JM, Mclean AA, Vella PP, Woodhour AF, Canepa I, Davidson WL, et al. Vaccination and revaccination with polyvalent pneumococcal polysaccharide vaccines in adults and infants. Proc Soc Exp Biol Med 1978;157:148-54.
8. Hilleman MR, Carlson AJ, Mclean AA, Vella PP, Weibel RE, Woodhour AF. *Streptococcus pneumoniae* polysaccharide vaccine: age and dose responses, safety, persistence of antibody, revaccination, and simultaneous administration of pneumococcal and influenza vaccines. Rev Infect Dis 1981;3 Suppl:S31-S42.
9. Kaplan J, Sarnaik S, Schiffman G. Revaccination with polyvalent pneumococcal vaccine in children with sickle cell anemia. Am J Pediatr Hematol Oncol 1986;8:80-2.
10. Rutherford EJ, Livengood J, Higginbotham M, Miles WS, Koestner J, Edwards KM, et al. Efficacy and safety of pneumococcal revaccination after splenectomy for trauma. J Trauma 1995;39:448-52.
11. Mufson MA, Hughey DF, Turner CE, Schiffman G. Revaccination with pneumococcal vaccine of elderly persons 6 years after primary vaccination. Vaccine 1991; 9:403-7.
12. Davidson M, Bulkow LR, Grabman J, Parkinson AJ, Chamblee C, Williams WW, et al. Immunogenicity of pneumococcal revaccination in patients with chronic disease. Arch Intern Med 1994;154:2209-14.
13. Rodriguez R, Dyer PD. Safety of pneumococcal revaccination. J Gen Intern Med 1995;10:511-12.
14. Jackson LA, Benson P, Sneller VP, Butler JC, Thompson RS, Chen RT, et al. Safety of revaccination with pneumococcal polysaccharide vaccine. JAMA 1999;281: 243-8.
15. Snow RS, Babish JD, McBean AM. Is there any connection between a second pneumonia shot and hospitalization among Medicare beneficiaries? Public Health Rep 1995;110:720-5.
16. Department of Health and Human Services (US). International classification of diseases, ninth revision, clinical modification. 6th ed. Washington: DHHS; 1996.
17. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987;40:373-83.
18. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613-19.
19. Centers for Disease Control and Prevention (US). EpiInfo: version 6. Atlanta: CDC; 1994.
20. SPSS Inc. SPSS: version 9.0. Chicago: SPSS Inc.; 1999.
21. Centers for Disease Control and Prevention (US), National Center for Chronic Disease Prevention and Health Promotion, Division of Adult and Community Health, Behavioral Surveillance Branch. 1999 BRFSS summary prevalence report. June 2000 [cited 2002 May 13]. Available from: URL: http://www.cdc.gov/nccdphp/brfss/pdf/99prvrpt.pdf