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ORIGINAL RESEARCH

Prior Pneumococcal and Influenza Vaccinations and In-hospital Outcomes for Community-Acquired Pneumonia in Elderly Veterans

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BACKGROUND: Studies of adults hospitalized for community-acquired pneumonia (CAP) reported better outcomes associated with prior pneumococcal vaccination (PV), suggesting potential additional benefits of PV in hospitalized CAP patients. Influenza (flu) vaccination (FV) could independently/additively improve CAP outcomes in hospitalized patients.

OBJECTIVE: To examine the effect of prior PV and FV on in-hospital outcomes in elderly veterans hospitalized for CAP.

DESIGN: Retrospective cohort study.

SETTING AND PATIENTS: A total of 6,723 elderly veterans who were admitted to Veterans Affairs hospitals for CAP between October 1, 2002 and September 30, 2003.

INTERVENTION: PV in the 5 years and FV in the 1 year before admission.

MEASUREMENTS: The association of prior PV and/or FV with inpatient mortality and length of stay (LOS) (primary) and risk of any bacteremia and respiratory complications (secondary) were assessed using logistic regressions and generalized linear model, controlling for patient demographic and clinical characteristics.

RESULTS: Prior PV alone was not associated with shortened LOS, or reduced risk of inpatient mortality or respiratory complications. Lower risk of bacteremia was associated with prior PV (odds ratio: 0.66; 95% confidence interval [CI]: 0.48-0.90). After adjusting for patients' characteristics, risk of inpatient mortality was not statistically significantly different across the vaccination groups, but having had both PV and FV before CAP admission was associated with a 10% reduction in LOS (95% CI: 0.86-0.95) compared to having had neither vaccinations.

CONCLUSION: Significant survival benefit and improved in-hospital outcomes may not be expected among CAP-hospitalized elderly patients with prior PV alone. However, having both PV and FV before CAP admission may reduce LOS. *Journal of Hospital Medicine* 2015;10:287–293.

Community-acquired pneumonia (CAP) ranks fifth among all causes of death and is the leading infectious cause of death among persons 65 years or older (hereafter "elderly") in the US.[1] Of the 1.1 million short-stay hospital discharges for pneumonia in 2010, 55% were for elderly patients.[2] The most common cause of pneumonia in elderly patients leading to hospitalization is infection with *Streptococcus pneumoniae*.[1,3–5] The 23-valent pneumococcal polysaccharide vaccine is recommended (PPSV23) for all elderly persons and has been shown to reduce incidences of invasive pneumococcal bacteremia among immunocompetent elderly individuals.[5] However, its effect on more common manifestations of pneumococcal disease, such as pneumonia, remains controversial.[5–8]

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Several studies examined the association between prior PV and in-hospital outcomes for CAP in adult patients.[9–11] Although the effect of pneumococcal vaccination (PV) on inpatient mortality was inconclusive, the studies found shortened length of stay (LOS),[9,10] lower risk of respiratory failure and other complications,[9] faster resolution of pneumonia symptoms,[10] and fewer intensive care unit (ICU) admissions,[11] among those with prior PV. These findings suggest potential additional benefits of PV in hospitalized CAP patients.

This study examined prior PV on in-hospital outcomes in elderly veterans hospitalized for CAP. Because PV-vaccinated patients are also more likely to have received influenza (flu) vaccination (FV),[9–11] which could independently or additively improve CAP outcomes in hospitalized elderly patients,[12–14] we attempted to separate out the effect of FV by stratifying patients into 4 subgroups: PV alone, FV alone, both, or neither. The priori hypothesis was that PV improves in-hospital outcomes in elderly veterans hospitalized for CAP.

METHODS

Study Cohort

This study is a retrospective cohort study of all elderly veterans admitted to any Veterans Affairs (VA) hospitals for CAP during the fiscal year 2003 (FY'03)

TABLE 1. Baseline Characteristics and In-Hospital Outcomes of Elderly Veterans Hospitalized for Community-Acquired Pneumonia in Fiscal Year 2003

	PV Only, n = 1,347	FV Only, n = 1,698	Both, n = 1,668	Neither, n = 2,010	*P* Value*
Age, median (IQR)	77 (71–81)	77 (72–81)	77 (71–81)	77 (72–82)	0.0418
65–74 years	539 (40.0%)	619 (36.5%)	670 (40.2%)	733 (36.5%)	0.0051
75–84 years	635 (47.1%)	892 (52.5%)	836 (50.1%)	1058 (52.6%)	
≥85 years	173 (12.8%)	187 (11.0%)	162 (9.7%)	219 (10.9%)	
Male	1318 (97.8%)	1657 (97.6%)	1638 (98.2%)	1964 (97.7%)	0.6378
Race					
White	848 (63.0%)	1149 (67.7%)	1097 (65.8%)	1272 (63.3%)	<0.0003
Nonwhite	229 (17.0%)	214 (12.6%)	271 (16.2%)	289 (14.4%)	
Unknown	270 (20.0%)	335 (19.7%)	300 (18.0%)	449 (22.3%)	
Married	726 (53.9%)	951 (56.0%)	930 (55.8%)	1043 (51.9%)	0.0419
No. of non-mental health VA outpatient visits last year, median (IQR)	17 (10–27)	21 (13–32)	22 (14–34)	15 (9–26)	<0.0001
CAP hospitalization last year	87 (6.5%)	106 (6.2%)	100 (6.0%)	106 (5.3%)	0.4689
Respiratory conditions in past 30 days	149 (11.1%)	183 (10.8%)	173 (10.4%)	263 (13.1%)	0.0424
Charlson Comorbidity Index, median (IQR)	2 (1–4)	3 (1–4)	3 (1–4)	2 (1–4)	<0.0001
Inpatient outcomes					
LOS, d, median(IQR)	6 (4–10)	5 (3–9)	5 (3–9)	6 (4–9)	0.0077
Death	130 (9.7%)	119 (7.0%)	113 (6.8%)	166 (8.3%)	0.0127
Bacteremia	31 (2.3%)	56 (3.3%)	40 (2.4%)	68 (3.4%)	0.1204
Respiratory complications	200 (14.8%)	192 (11.3%)	185 (11.1%)	253 (12.6%)	0.0073

NOTE: **Abbreviations:** CAP, community-acquired pneumonia; FV, influenza vaccine; IQR, interquartile range; LOS, length of stay; PV, pneumococcal vaccine; VA, Veterans Affairs. **P* values were based on Kruskal-Wallis test for continuous variables and χ^2 test for categorical variables.

(October 1, 2002 to September 30, 2003). Inpatient admissions for pneumonia were defined based on the principal diagnosis of nonviral pneumonia (International Classification of Diseases, 9th Revision [ICD-9], codes 481.xx–487.0x). The principal diagnosis was defined as the "condition determined to be the reason for the admission."[15] To select only CAP cases, we included admissions where patients were admitted either directly or through a VA outpatient clinic. We excluded transfers from another hospital, skilled nursing facilities, intermediate care facilities, or another healthcare facility. All patients were 65 years or older on the first day of the first admission in FY'03 (index admission) and had at least 1 outpatient visit to a VA facility each year during the 5 years prior to the index admission.

Data Source

Data were drawn from Veterans Health Administration medical SAS datasets (SAS Institute Inc., Cary, NC). Demographic characteristics, inpatient and outpatient care utilization, and related medical diagnoses and procedure codes were extracted from national patient data extracts. Selected lab test results were drawn from the Decision Support System national extracts. This study was approved by institutional review boards at the University of Arkansas for Medical Sciences and the Central Arkansas Veterans Healthcare System.

Prior Vaccination Status

Prior PV status was determined within 5 years prior to the index admission using: ICD-9 codes V06.6, V06.8, and V03.82, ICD-9 procedure code 99.55, or Current Procedure Terminology (CPT) codes 90732 and 90669.[16] This 5-year time frame was chosen for 2 reasons: (1) the Centers for Disease Control and Prevention (CDC) recommends a second dose for elderly persons if the first dose was before age 65 years and more than 5 years have passed[17]; (2) effectiveness of PV decreases over time in elderly persons, especially after 5 years since vaccination.[5,18] Consistent with the CDC's vaccination recommendation,[18] patients with no record of prior PV were classified as "not vaccinated." Prior FV status was determined in the year before the index admission using: ICD-9 code V04.8, ICD-9 procedure code 99.52, or CPT codes 90655–90660.[16] Based on prior vaccinations, patients were classified into 4 groups: PV alone, FV alone, both, or neither.

Outcome Variables

The primary outcomes were LOS and inpatient mortality. LOS, measured in days, was the duration of a hospital stay from admission to discharge, censored at death or transfer, the occurrence of which was ascertained via the discharge type field. Inpatient mortality was defined as death from any cause that occurred before discharge or transfer. The secondary outcomes were respiratory complications and any bacteremia identified via the diagnosis field of discharge records (see Supporting Information, Appendix Table A.1, in the online version of this article for a list of ICD-9 codes).

Covariates

Covariates included patients' demographic characteristics (age, gender, race, marital status) and Charlson Comorbidity Index scores. Comorbidities were

identified during the year prior to the index admission using ICD-9 diagnoses codes based on Deyo et al. adaptation.[19] Additionally, we included prior admission for CAP within the year preceding index admission, the number of outpatient visits (excluding mental health visits; ICD-9 codes 290.xx–319.xx) within the year preceding index admission, and acute respiratory conditions experienced within 30 days preceding index admission. Development of bacteremia and respiratory complications may increase LOS, and risk of mortality and were adjusted in the regression models for these outcomes.

Race

Missing race in VA administrative data is a well-documented problem.[20] When available, missing race was imputed using information reported during a patient's other inpatient stays available in our data as follows. We first imputed it using the most frequently reported race category. If unavailable, race was imputed by the most recently reported race category whenever available. This imputation algorithm reduced the proportion of patients with missing race information in our data to from 76% to 20%. Remaining patients with missing race information after imputation were analyzed as a separate category.

Pneumonia Severity Index Score

For patients with available lab values, we constructed an abbreviated pneumonia severity index (PSI) score adapted from Escobar et al.[21] The original PSI score developed by the Pneumonia Patient Outcomes Research Team (PORT) is a validated clinical prediction tool that permits risk stratification with regard to the likelihood of adverse outcomes in CAP patients.[22] Calculation of the PORT score requires information on patient's physical examination and radiographic findings at admission,[22] which was unavailable to us. Escobar et al. developed and validated an abbreviated form of the PORT score (PSI-E) in CAP patients that does not incorporate physical examination and radiographic findings.[21] We calculated the PSI-E developed by Escobar et al. with the exception that arterial pH and PaO_2 test results were omitted because they were not available in the VA lab result files for the years we examined.

Data Analysis

Patients' baseline characteristics (see Covariates) were compared across the 4 vaccination groups using the Kruskal-Wallis test for continuous variables and χ^2 test for categorical variables. Multiple regression analyses were used to assess the effect of prior PV and FV on inpatient outcomes during the index admission while adjusting for covariates. LOS was analyzed using a generalized linear model (GLM) with a negative binomial distribution and a logarithmic link function,[23] and incidence rate ratios (IRRs) were reported. IRRs were calculated by taking the exponential of the estimated coefficients from the GLM and are interpretable as the relative change in mean LOS associated with a 1-unit change in a predictor variable. Risk of inpatient mortality, and development of respiratory complications or bacteremia, were analyzed using logistic regressions, and odds ratios (ORs) were reported. All regression models adjusted for covariates as described earlier. In addition, we conducted propensity score matching of PV-vaccinated (n = 2937) and unvaccinated (n = 2937) patients using the GMATCH algorithm.[24] Propensity scores were estimated using a logistic regression to predict prior PV based on covariates listed earlier and prior FV status. GLM or logistic regression models were applied to the matched sample, with PV as the only predictor to generate IRRs or ORs, respectively. To account for the matched nature of the data, analyses were stratified by matched pairs.[25]

Sensitivity Analysis

Many sensitivity analyses were performed that: (1) included patients admitted from nursing homes or other inpatient facilities (n = 7296); (2) excluded 0-night admissions (n = 6678); (3) varied the minimum number of VA outpatient visits to 2, 3, 4, or 5 visits each year in the previous 5 years; and (4) adjusted for the abbreviated PSI score only in patients with available information (n = 3689).

Flu Season

Defining prior FV status during the previous year may have included individuals who received FV for the previous flu season (eg, a patient was admitted in December 2003, but his or her last FV was in January 2003). We conducted 2 sensitivity analyses: (1) recoded patients who were last vaccinated in the previous flu season as unvaccinated and (2) restricted to index admissions occurred during the flu season (n = 5311). A flu season was defined as from September to May of the following year.

Time Since Last PV

To determine if the effectiveness of PV varies by the years elapsed since vaccination, among those with prior PV, we further classified prior PV as within 1 year ($\leq$1 year), 2 years (>1 but $\leq$2 years), 3 years (>2 but $\leq$3 years), 4 years (>3 but $\leq$4 years), or 5 years (>4 but $\leq$5 years) preceding the index admission. Two-thirds of patients received PV more than 2 years ago. We re-estimated the regression models with indicators for the number of years since the last PV (as defined above, PV within 1 year preceding index admission as the reference group).

All analyses were conducted using SAS software (SAS Institute, Inc.). A 2-sided *P* value of <0.05 was used to determine statistical significance.

TABLE 2. Adjusted Incident Rate Ratio or Odds Ratios for In-Hospital Outcomes Among Elderly Veterans Hospitalized for Community-Acquired Pneumonia in Fiscal Year 2003

	Length of Stay (Days)			Inpatient Death		
Vaccination status	IRR	95% CI	*P* Value	OR	95% CI	*P* Value
PV in previous 5 Years	1.02	0.97-1.07	0.4561	1.15	0.89-1.50	0.2901
FV last year	0.97	0.92-1.02	0.1920	0.90	0.69-1.17	0.4193
Both	0.90	0.86-0.95	<0.0001	0.88	0.67-1.16	0.3646
Neither	Ref			Ref		

	Bacteremia			Respiratory Complications		
Vaccination status	OR	95% CI	*P* Value	OR	95% CI	*P* Value
PV in previous 5 Years	0.67	0.43-1.03	0.0673	1.23	1.01-1.51	0.0429
FV last year	0.99	0.69-1.42	0.9536	0.90	0.74-1.10	0.3085
Both	0.72	0.48-1.07	0.1047	0.87	0.71-1.07	0.1860
Neither	Ref			Ref		

NOTE: All analyses have been adjusted for patient's age, gender, race, marital status, comorbidity index score, non–mental health outpatient visits, and CAP hospitalization in the previous year, and any acute respiratory conditions experienced in the previous 30 days. Analyses of length of stay and inpatient death was additionally adjusted for development of bacteremia and respiratory complications. **Abbreviations:** CI, confidence interval; FV, influenza vaccine; IRR, incidence rate ratio; OR, odds ratio; PV, pneumococcal vaccine.

RESULTS

In FY'03, 10,540 elderly VA patients had at least 1 inpatient admission for nonviral pneumonia. Among them, 3242 were excluded due to lack of VA outpatient visits in at least 1 of the 5 years prior to the index admission. Additionally, 574 patients were excluded because they were transferred from nursing homes or other inpatient facilities. The final sample consisted of 6723 elderly patients; among them, 1347(20%) had only PV, 1698(25%) had only FV, 1668 (25%) had both, and 2010 (30%) had neither prior to admission (see Supporting Information, Appendix 1, in the online version of this article) (see Supporting Information, Appendix Figure A.1, in the online version of this article).

Table 1 compares patients' baseline characteristics and inpatient outcomes across vaccination groups. Patients with prior PV and FV had the shortest LOS and were least likely to experience respiratory complications or die during the inpatient stay. They also tended to be younger, had more frequent VA non–mental health outpatient visits in the previous year, and more medical comorbidities than other groups. Although these differences were statistically significant, the actual differences were small across the groups.

Table 2 presents findings from the adjusted regression analyses. After adjusting for covariates, having prior PV alone, FV alone, or both did not significantly affect the risk of inpatient mortality, compared to patients without records of either vaccination. However, having both prior PV and FV was associated with 10% reduction in LOS (IRR: 0.90; 95% confidence interval [CI]: 0.86-0.95; $P < 0.0001$). PV alone were associated with an increased risk of respiratory complications (OR: 1.23; 95% CI: 1.01-1.51; $P = 0.0429$) and trended toward a reduced risk of bacteremia (OR: 0.67; 95% CI: 0.43-1.03; $P = 0.0673$). After matching on patient characteristics including prior FV status, prior PV significantly lowered the risk of developing bacteremia (OR: 0.66; 95% CI: 0.48-0.90; $P = 0.0088$) but was not statistically significantly associated with the other outcomes (Table 3).

TABLE 3. Propensity Score–Matched Sample of PV Vaccinated and Unvaccinated Elderly Veterans Hospitalized for Community-Acquired Pneumonia in Fiscal Year 2003

In-Hospital Outcomes, Matched Sample (n = 5 874)	PV vs No PV		
	IRR/OR	95% CI	*P* Value
Length of stay	0.97	0.93-1.01	0.1502
Inpatient death	1.13	0.94-1.37	0.2027
Bacteremia	0.66	0.48-0.90	0.0088
Respiratory complications	1.11	0.95-1.30	0.2018

NOTE: Patients were propensity matched 1:1 using the greedy match algorithm.[24] The IRRs/ORs were generated after matching using either generalized linear regression model or logistic regression models with PV as the only predictor and were stratified by matched pairs.[25] **Abbreviations:** CI, confidence interval; IRR, incidence rate ratio; OR, odds ratio; PV, pneumococcal vaccine.

Findings from sensitivity analyses are included in the online appendices. Results were generally robust to various sensitivity analyses. However, in the analysis using the subset of patients with available lab information to define the PSI-E score, having prior FV alone was also found to be associated with reduced LOS (IRR: 0.92; 95% CI: 0.86-0.98; $P < 0.05$). The relationship between PV and in-patient outcomes did not vary by the time since vaccination, which is consistent with Jackson et al.[11]

DISCUSSION

Consistent with previous findings,[7–11] elderly VA patients hospitalized for CAP were found to have an association between prior PV and reduced risk of bacteremia. However, no associations of prior PV alone with other in-hospital outcomes (LOS, inpatient mortality, or development of respiratory complications) were consistently found. Although, FV was not associated with a decrease in inpatient mortality in this study, having had both prior PV and FV (not necessarily given at the same time) was found to be associated with shortened LOS.

Our findings were inconsistent with 3 previous studies of prior PV on in-hospital outcomes among adult CAP patients. Those studies found shortened LOS,[9,10] lower risk of respiratory failure and other complications,[9] faster resolution of pneumonia symptoms,[10] and fewer ICU admissions[11] among PV-vaccinated patients. Subanalysis of elderly patients performed in 2 of the 3 studies demonstrated a comparable survival benefit[9] or protective effect on the composite outcome of ICU admission or death[11] among elderly patients

compared to nonelderly patients. However, unlike our analysis, neither study excluded patients admitted from nursing home facilities. Our database, including patients admitted from nursing homes or other inpatient facilities, estimated a slightly more favorable effect of PV alone on inpatient mortality compared to our main analysis, although the estimate remained statistically insignificant (see Supporting Information, Appendix Table A.2, in the online version of this article).

In all 3 previous studies,[9–11] an overwhelming majority of PV vaccinated patients also received FV (Mykietiuk[10]: 90.2% in PV vaccinated vs 39.9% in unvaccinated; Fisman[9]: 70% vs 2.2%; Johnstone[11]: 88% vs 9%), making it harder to distinguish the effect of having only PV from that of having both PV and FV. By defining a separate group for having both vaccinations, we found that having both PV and FV reduced LOS relative to PV alone or having had neither vaccinations. This suggests that PV alone may not be as effective in improving inpatient outcomes as shown in the previous studies, although limitations of our study prevented us from making a deterministic conclusion.

Our findings of no beneficial effects of PV alone on in-hospital outcomes for CAP other than bacteremia in the elderly VA patients are supported by previous findings of no effect of PV on all-cause pneumonia and all-cause mortality,[4,7,8] decreasing antibody response to PV,[26–28] and decreasing vaccine effectiveness over time in the elderly patients.[5,18] Also, in a study of patients who were previously hospitalized for CAP, PV at discharge was not associated with prevention of subsequent hospitalization for CAP or death from all causes.[29]

PV alone was found to be associated with an increased risk of respiratory complications using an unmatched sample, and this finding appears to be robust to several variations in the sample selection process (see Supporting Information, Appendix, in the online version of this article). This paradoxical finding may be a result of residual confounding despite our efforts to control for baseline differences in patients' characteristics. Using propensity matching where only those with similar observed characteristics, including comorbidity burden, were compared, the result was no longer statistically significant, although still trended in the same direction.

Up until recently, PPSV23 was the only pneumococcal vaccine recommended for all elderly individuals 65 years or older. Since September 2014, 13-valent pneumococcal conjugate vaccine (PCV13) has also been recommended for all elderly persons in the United States. PCV13 became available in 2010 and was initially recommended only for routine use in children ages 2 to 59 months. Early evidence indicated some herd effect in adults associated with the use of PCV13 in children; however, the effect was not statistically significant in all age groups.[30] Because at the time of the study elderly patients were not vaccinated by other pneumococcal vaccines, and PCV13 was not yet in use in children, this strengthens the findings in terms of evaluating the efficacy of PPSV23, because the association was not attenuated by the herd effect of PCV13 in children or having both PPSV23 and PCV13 in the elderly population. The recent recommendation to vaccinate all elderly adults with PCV13 was based on findings from an industry-supported placebo-controlled trial of pneumococcal vaccine naïve patients.[31] It is unknown whether PCV13 is more effective than PPSV23 in elderly adults and whether giving both would have any additional benefit in the elderly population. Future studies with population wide data on PCV13 use in elderly adults are needed.

Limitations

The major limitation for generalizing to all elderly population is that we studied elderly veterans who are almost exclusively males (98%). Previous studies have found males are at higher risk of acquiring CAP,[32] to die from CAP,[33] and to be hospitalized for CAP.[34] Vaccine effectiveness was also found to be higher in women than men.[35] These suggest that our finding may not generalize to female patients admitted for CAP.

Another important limitation is that if PV and/or FV are truly effective in reducing hospitalizations for pneumonia, then those who were hospitalized despite prior vaccinations potentially may have more severe disease and/or be less responsive to the vaccines than unvaccinated patients. If so, this potential selection bias would bias our results toward null, and may partially explain our insignificant findings of PV alone on inpatient outcomes and the low vaccination rates observed in this study.

By focusing on elderly patients admitted for CAP, our cohort is more homogeneous than many previous studies, given that PV was recommended for all elderly persons at the time of the study, and all patients in our study had CAP. Nonetheless, unmeasured selection bias may exist and could partially explain the lack of estimated beneficial effect. In particular, the PSI score could not be calculated for the whole sample due to lack of data availability. In a subsample of patients with available information to calculate the abbreviated PSI score, we continued to find no significant beneficial effect of PV on outcomes other than bacteremia.

Other limitations included the possibility that prior vaccination status may have been misclassified because of (1) the use of diagnosis and procedure codes to identify prior vaccination status and (2) the lack of linked Medicare data to obtain the complete medical service utilization history of the elderly patients with dual coverage. To address the second issue, we selected patients with at least 1 VA outpatient visit

each year in the previous 5 years of the index admission, hoping to identify patients who were more likely to be VA service users. In sensitivity analyses, we further restricted our data to only patients with at least 2, 3, 4, or 5 visits per year, respectively, in the previous 5 years, and the results were generally robust to these variations (see Supporting Information, Appendix Tables A.2 and A.3, in the online version of this article). Although higher vaccination rates have been reported previously (PV: 81%–89%; FV: 79%–80%) for all elderly veterans in 2003,[36,37] a lower vaccination rate may be expected among hospitalized patients for CAP, if PV and/or FV are effective in reducing hospitalizations for pneumonia as reported in previous studies.[36,38,39] The lower PV rate observed among hospitalized elderly patients in this study is similar to another study of hospitalized elderly patients (50% prior PV rate),[40] and is consistent with the low prior PV rates reported in other studies of CAP-hospitalized patients, which ranges from 11% to 22%.[9–11]

Cases of CAP admissions were identified based on principal diagnosis of pneumonia. This increased precision in the identified cases but may have underidentified CAP admissions. ICD-9 code 481.0x (influenza with pneumonia) was also used for case identification, similar to other studies[4,9,12,41]; excluding this code only excluded a few and did not affect the findings. Relying exclusively on diagnosis codes to detect pneumonia may also lead to misclassification due to coding errors. The gold standard to confirm pneumonia was with x-ray. However, such information was not available in our data.

We did not have bacteriological data to study the pneumococcal-specific outcomes, such as pneumococcal pneumonia or pneumococcal bacteremia, which the pneumococcal vaccine is designed to protect against. Diagnosis codes for the pneumococcal-specific outcomes have low sensitivity,[42] and will significantly underidentify those cases. This limitation will bias our result toward null, which may partially explain the insignificant findings.

CONCLUSIONS

In this study of elderly VA patients admitted for CAP, we did not find significant effects of prior PV on LOS, inpatient mortality, or respiratory complications. Although given the limitations of this study, we could not conclusively say that PV has no effect on these outcomes. Nonetheless, our findings and the findings of no significant protective effect on overall mortality and decreasing antibody response to vaccines in the elderly from other studies, does raise the question of whether the previously reported beneficial effects on in-hospital outcomes for CAP in adults could be generalized to elderly patients. Larger electronic medical record databases with more complete information on patients' vaccination history are needed to confirm these findings. Nonetheless, given its protective effect against invasive diseases,[7,8] the economic benefits shown,[43,44] and relative safety, PV should still be recommended for all elderly persons, especially very old and frail nursing home residents.[45] However, significant survival benefit and improved in-hospital outcomes for CAP as reported in previous studies may not be expected in elderly patients with prior PV, particularly if vaccination was given more than 5 years ago. This study also supports the recommendation of FV in the elderly population. Although, FV was not associated with a decrease in inpatient mortality in this study, having both PV and FV was found to be associated with shortened LOS.

Disclosures

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References

1. Stupka JE, Mortensen EM, Anzueto A, Restrep MI. Community-acquired pneumonia in elderly patients. *Aging Health*. 2009;5(6):763–774.
2. CDC/NCHS National Hospital Discharge Survey, 2010. Number of discharges from short-stay hospitals, by first-listed diagnosis and age: United States, 2010. National Center for Health Statistics. Available at: http://www.cdc.gov/nchs/data/nhds/3firstlisted/2010first3_numberage.pdf. Accessed July 14, 2014.
3. Fung HB, Monteagudo-Chu MO. Community-acquired pneumonia in the elderly. *Am J Geriatr Pharmacother*. 2010;8(1):47–62.
4. Jackson LA, Neuzil KM, Yu O, et al. Effectiveness of pneumococcal polysaccharide vaccine in older adults. *N Engl J Med*. 2003;348:1747–1754.
5. Jackson LA, Janoff EN. Pneumococcal vaccination of elderly adults: new paradigms for protection. *Clin Infect Dis*. 2008;47(10):1328–1338.
6. Melegaro A, Edmunds WJ. The 23-valent pneumococcal polysaccharide vaccine. Part 1. Efficacy of PPV in the elderly: a comparison of meta-analysis. *Eur J Epidemiol*. 2004;19:353–363.
7. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. *Cochrane Database Syst Rev*. 2008;(1):CD000422.
8. Huss A, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. *CMAJ*. 2009;180(1):48–58.
9. Fisman DN, Abrutyn E, Spaude KA, Kim A, Kirchner C, Daley J. Prior pneumococcal vaccination is associated with reduced death, complications, and length of stay among hospitalized adults with community-acquired pneumonia. *Clin Infect Dis*. 2006;42:1093–1101.
10. Mykietiuk A, Carratalà J, Domínguez A, et al. Effect of prior pneumococcal vaccination on clinical outcome of hospitalized adults with community-acquired pneumococcal pneumonia. *Eur J Clin Microbiol Infect Dis*. 2006;25:257–462.
11. Johnstone J, Marrie T, Eurich D, Majumdar S. Effect of pneumococcal vaccination in hospitalized adults with community-acquired pneumonia. *Arch Intern Med*. 2007;167:1938–1943.
12. Spaude KA, Abrutyn E, Kirchner C, Kim A, Deley J, Fisman DN. Influenza vaccination and risk of mortality among adults hospitalized with community-acquired pneumonia. *Arch Intern Med*. 2007;167:53–59.
13. Jefferson T, Rivetti D, Rivetti A, Rudin M, DiPietrantanj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet*. 2005;366:1165–1174.

14. Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. *N Engl J Med*. 2007;357:1373–1381.
15. *VIReC Research User Guide: FY2002 VHA Medical SAS Inpatient Datasets*. Hines, IL: Veterans Affairs Information Resource Center; 2003.
16. Immunization Information Systems, Centers for Disease Control and Prevention. CPT codes mapped to CVX codes. Available at: http://www2a.cdc.gov/vaccines/iis/iisstandards/vaccines.asp?rpt=cpt. Accessed December 2, 2014.
17. Centers for Disease Control and Prevention. Pneumococcal polysaccharide vaccine information statement. Available at: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/ppv.html. Accessed December 2, 2014.
18. Shapiro ED, Berg AT, Austrian R, et al. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. *N Engl J Med*. 1991;325:1453–1460.
19. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM Administrative Databases. *J Clin Epidemiol*. 1992;45(6):613–619.
20. Long JA, Bamba MI, Ling B, Shea JA. Missing race/ethnicity data in Veterans Health Administration based disparities research: a systematic review. *J Health Care Poor Underserved*. 2006;17:128–140.
21. Escobar GJ, Fireman BH, Palen TE, et al. Risk adjusting community-acquired pneumonia hospital outcomes using automated databases. *Am J Manag Care*. 2008;14(3):158–166.
22. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336:243–250.
23. Austin PC, Rothwell DM, Tu JV. A comparison of statistical modeling strategies for analyzing length of stay after CABG surgery. *Health Serv Outcomes Res Methodol*. 2002;3:107–133.
24. Kosanke J, Bergstralh E. GMATCH SAS macro. Available at: http://www.mayo.edu/research/documents/gmatchsas/DOC-10027248. Accessed December 2, 2014.
25. Faries D, Leon A, Haro J, Obenchain R. *Analysis of Observational Health Care Data Using SAS*. Cary, NC: SAS Institute; 2010.
26. Schenkein JG, Park S, Nahm MH. Pneumococcal vaccination in older adults induces antibodies with low opsonic capacity and reduced antibody potency. *Vaccine*. 2008;26:5521–5526.
27. Lee H, Nahm MH, Kim KH. The effect of age on the response to the pneumococcal polysaccharide vaccine. *BMC Infect Dis*. 2010;10:60.
28. Park S, Nahm MH. Older adults have a low capacity to opsonize pneumococci due to low IgM antibody response to pneumococcal vaccinations. *Infect Immun*. 2011;79(1):314–320.
29. Johnstone J, Eurich DT, Minhas JK, Marrie TJ, Majumda SR. Impact of the pneumococcal vaccine on long-term morbidity and mortality of adults at high risk for pneumonia. *Clin Infect Dis*. 2010;51(1):15–22.
30. Simonsen L, Taylor RJ, Schuck-Pain C, Lutig R, Haber M, Klugman KP. Effect of 13-valent pneumococcal conjugate vaccine on admissions to hospital 2 years after its introduction in the USA: a time series analysis. *Lancet Respir Med*. 2014;2(5):387–394.
31. American Academy of Family Physicians. ACIP recommends routine PCV13 immunization for adults 65 and older. Available at: http://www.aafp.org/news/health-of-the-public/20140827pcv13vote.html. Accessed December 2, 2012.
32. Jackson LA, Neuzil KM, Thompson WW, et al. The burden of community-acquired pneumonia in seniors: results of a population-based study. *Clin Infect Dis*. 2004;39:1642–1650.
33. Christensen JS, Jensen TG, Kolmos HJ, et al. Bacteremia with Streptococcus pneumoniae: sepsis and other risk factors for 30-day mortality-a hospital-based cohort study. *Eur J Clin Microbiol Infect Dis*. 2012;13(10):2719–2725.
34. Fry Am, Shay DK, Holman RC, Curns AT, Anderson LJ. Trends in hospitalizations for pneumonia among persons aged 65 years or older in the United States, 1988–2002. *JAMA*. 2005;294(21):2712–2719.
35. Wiemken TL, Carrico RM, Klein SL, et al. The effectiveness of the polysaccharide pneumococcal vaccine for the prevention of hospitalizations due to Streptococcus pneumoniae community-acquired pneumonia in the elderly differs between the sexes: results from the Community-Acquired Pneumonia Organization (CAPO) international cohort study. *Vaccine*. 2014;17:32(19):2198–2203.
36. Jha Ak, Wright SM, Perlin JB. Performance measures, vaccinations, and pneumonia rates among high-risk patients in Veterans Administration health care. *Am J Public Health*. 2007;97(12):2167–2172.
37. Chi RC, Reber GE, Neuzil KM. Influenza and pneumococcal vaccination in older veterans: results from the Behavioral Risk Factor Surveillance System. *J Am Geriatr Soc*. 2006;54:217–223.
38. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med*. 1994;331:778–784.
39. Nichol KL, Baken L, Wuorenma J, Nelson A. The health and economic benefits associated with pneumococcal vaccination of elderly persons with chronic lung disease. *Arch Intern Med*. 1999;159:2437–2442.
40. Wong-Beringer A, Brodetsky E, Quist R. Pneumococcal vaccination in hospitalized elderly patients: role of the pharmacist. *Pharmacotherapy*. 2003;2(23):199–208.
41. Aronsky D, Haug PJ, Lagor C, Dean NC. Accuracy of administrative data for identifying patients with pneumonia. *Am J Med Qual*. 2005;30:319–328.
42. van de Garde EM, Oosterheert JJ, Bonten M, Kaplan RC, Leufkens HG. International classification of diseases codes showed modest sensitivity for detecting community-acquired pneumonia. *J Clin Epidemiol*. 2007;60(8):834–838.
43. Ament A, Baltussen R, Duru G, et al. Cost-effectiveness of pneumococcal vaccination of older people: a study in 5 western European countries. *Clin Infect Dis*. 2000;31:444–450.
44. Evers SM, Ament AJ, Colombo GL, et al. Cost-effectiveness of pneumococcal vaccination for prevention of invasive pneumococcal disease in the elderly: an update for 10 Western European countries. *Eur J Clin Microbiol Infect Dis*. 2007;26(8):531–540.
45. Maruyama T, Taguchi O, Niederman MS, et al. Efficacy of 23-valent pneumococcal vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial. *BMJ*. 2010;340:c1004.