

# Effect of Pneumococcal Vaccination in Hospitalized Adults With Community-Acquired Pneumonia

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**Background:** Although 23-valent polysaccharide pneumococcal vaccine (PPV) does not prevent community-acquired pneumonia (CAP), it might still improve outcomes in those who develop pneumonia. We tested this hypothesis using a population-based cohort of hospitalized patients with CAP.

**Methods:** From 2000 to 2002, we prospectively collected data on all adults with CAP admitted to 6 hospitals in Capital Health, the largest integrated health delivery system in Canada. Polysaccharide pneumococcal vaccine status was ascertained by interview, medical record review, and contact with physicians and community health offices. The primary outcome was the composite of in-hospital mortality or intensive care unit (ICU) admission. Multivariable regression was used to determine the independent association between PPV use and outcomes, after adjusting for patient characteristics, pneumonia severity, and propensity scores.

**Results:** Of the 3415 patients with CAP (median age,

75 years), 46% were female, 62% had severe pneumonia, and 22% had prior PPV. Overall, 624 patients died or were admitted to an ICU. Polysaccharide pneumococcal vaccine was protective from reaching this composite end point (73/760 [10%] vs 551/2655 [21%] for unvaccinated patients;  $P < .001$ ), mostly a result of reduced ICU admission (2/760 [ $<1\%$ ] vs 349/2655 [13%]). The propensity-adjusted odds of death or ICU admission was 0.62 (95% confidence interval, 0.42-0.92;  $P = .02$ ) for patients who had received PPV. Only 215 of 2416 patients (9%) eligible for PPV at hospital discharge were vaccinated.

**Conclusions:** Patients with CAP who had prior PPV had about a 40% lower rate of mortality or ICU admission compared with those who were not vaccinated. This provides additional support for recommending PPV to those at risk of pneumonia.

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**C**OMMUNITY-ACQUIRED pneumonia (CAP) is a common illness resulting in considerable morbidity and mortality.<sup>1</sup> *Streptococcus pneumoniae* is the most common cause of CAP, accounting for 30% to 50% of all cases.<sup>2</sup> Since 1983, a 23-valent polysaccharide pneumococcal vaccine has been available for use in adults, although vaccination rates in populations at risk (eg, elderly subjects, nursing home residents, and those with chronic pulmonary and nonpulmonary conditions) are still considered to be suboptimal.<sup>3</sup> This may be owing in part to ongoing controversy regarding the actual effectiveness or utility of the vaccine.<sup>4,5</sup>

Randomized clinical trials using the 23-valent pneumococcal polysaccharide vaccine have not demonstrated effectiveness in preventing CAP,<sup>6,7</sup> but most studies have shown that vaccination is effective in preventing invasive pneumococcal disease.<sup>8</sup> Based on this latter evidence and formal health economic models,<sup>9,10</sup> most current guidelines recommend polysaccharide pneumococcal vaccine for those at high risk of pneumococcal pneumo-

nia.<sup>11-14</sup> Despite these widely promulgated guidelines, vaccination rates in those considered eligible remain well under the recommended target goals of 80% to 90%.<sup>15,16</sup> Barriers to the uptake of these recommendations occur at the level of the health care system, the health care provider, and the patient.<sup>17-20</sup> In particular, it may be that providers remain convinced that polysaccharide pneumococcal vaccines do not prevent pneumonia and hence may be of little clinical value.

Recently, it has been suggested that pneumococcal vaccination is associated with improved outcomes, even among those who develop CAP<sup>21-25</sup> (ie, that pneumococcal vaccination is associated with reduced in-hospital and short-term mortality as well as a decreased risk of respiratory failure and other serious complications). It has been postulated that "partial immunity" may lead to an attenuated course of illness among those in whom pneumonia is not actually prevented.<sup>23,24</sup> The few studies published to date have, however, been limited by sample sizes of fewer than 500 patients,<sup>22,24,25</sup> lack of detailed clinical data,<sup>21,23</sup> or incomplete ascertainment of vaccination status.<sup>21</sup> Therefore,

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in a large, population-based, prospective cohort of hospitalized patients with CAP, we sought to determine whether prior pneumococcal vaccination was independently associated with reduced in-hospital mortality or need for intensive care unit (ICU) admission.

## METHODS

### SUBJECTS AND SETTING

Details of our study cohort have been previously published.<sup>26-28</sup> In summary, from 2000 to 2002, a previously validated clinical pathway for managing CAP<sup>29</sup> was implemented in Capital Health (Edmonton, Alberta, Canada). Capital Health is the largest integrated health delivery system in Canada and serves a population of approximately 1 million people.<sup>27,28</sup> Data were collected prospectively on all patients older than 17 years, who were admitted for managing CAP in all 6 regional hospitals. After initial triage and assessment in the emergency department, an inpatient physician was consulted for hospital admission in all patients with a pneumonia severity index (PSI) score of 90 or greater or for those with lower scores if the emergency physician thought that inpatient care was needed. All patients admitted to hospital were treated in a standardized manner according to the aforementioned clinical pathway. This pathway included standardized admission orders related to choice and route of antibiotics, hydration, supplemental oxygenation, thromboembolism prophylaxis, and use of physiotherapy; it also included discharge orders for smoking cessation and pneumococcal vaccination. There were, however, no mandatory orders. Only patients with tuberculosis or cystic fibrosis or who were immunocompromised (using > 10 mg/d of prednisone for > 1 month or other immunosuppressive agents or had human immunodeficiency virus with a CD4 cell count < 250/ $\mu$ L [to convert to  $\times 10^9$ /per liter, multiply by 0.001]) or pregnant were excluded. The Health Research Ethics Board of the University of Alberta approved the study.

### DATA COLLECTION

Six trained research nurses prospectively collected data using standardized abstraction forms. Sociodemographic status, clinical characteristics (ie, premorbid functional status, need for advanced directive, and smoking status), laboratory (ie, findings from blood chemistry and microbiologic analyses) and radiographic data were collected on all patients, and the PSI was calculated. The PSI is a measure of the severity of pneumonia-specific illness at presentation, based on 3 demographic variables, 5 comorbidities, 5 physical findings, and results from 7 laboratory tests.<sup>30</sup> Patients were followed for the duration of their hospital stay.

### EXPOSURE

Our explanatory variable of interest was pneumococcal vaccination status. Vaccination status was collected by highly trained research nurses on each patient's admission to hospital. Thus, the nurses were effectively masked to postadmission outcomes; furthermore, these data were collected for research purposes and entered into case report forms and were thus not accessible to the physicians caring for the patients. Vaccination history was ascertained using multiple complementary methods that included patient and proxy interview, medical record review, contact with primary care physicians, and records from the regional office of community health. An important limitation of the methods that we used is that we were only able to determine if an individual patient had ever received pneumo-

coccal vaccine and not necessarily whether their vaccination status would be considered up-to-date. Similar methods were used to collect influenza vaccination status.

## OUTCOMES

Our primary outcome measure was a composite of in-hospital mortality or admission to an ICU. This primary outcome has been used previously,<sup>27</sup> since it effectively captures the total burden of in-hospital illness for patients with CAP. For example, need for mechanical ventilation, prolonged noninvasive ventilation, use of vasopressors or activated protein C, cardiac monitoring, and 1:1 nursing all require ICU admission in our region and are clinically relevant end points that capture the nonfatal sequelae of severe pneumonia. If a patient both died and was admitted to ICU, only death was counted as an end point. Secondary outcomes included death alone, need for an ICU admission, and receipt of pneumococcal vaccine before discharge from hospital.

## STATISTICAL ANALYSIS

Baseline characteristics according to history of pneumococcal vaccination were compared using  $\chi^2$  or Fisher exact test, *t* test, or Wilcoxon rank-sum test as appropriate. Multivariable logistic regression analysis was used to determine the independent association between pneumococcal vaccine use and outcomes, after controlling for patient characteristics, comorbidities, CAP severity (using the PSI), and propensity (to receive pneumococcal vaccine) scores.

With previously described methods,<sup>26,27,31-33</sup> we used multivariable logistic regression to construct a propensity score that predicted the patient's likelihood of receiving pneumococcal vaccination. Of note, only those baseline characteristics that were present before admission to hospital and that could have influenced physicians' decision to provide pneumococcal vaccination were considered potential candidate variables. The propensity score was entered into models using a quintile approach<sup>31,32</sup>; we also examined it as a continuous covariate, but this approach did not materially alter the magnitude or significance of our results and is not presented. As an alternate but often-recommended approach to using the propensity score in a manner that might allow even better control over residual confounding, we used a 5-digit greedy algorithm that matched the propensity score of each patient exposed to pneumococcal vaccine to the patient with the closest propensity score value who had not been vaccinated.<sup>31-33</sup>

Lastly, we conducted 3 prespecified sensitivity analyses. First, we restricted analyses to only patients 65 years or older because this entire population is eligible for pneumococcal vaccination under current guidelines and should thus be much less susceptible to any form of selection bias.<sup>11-14</sup> Second, we restricted analyses to only patients admitted from nursing homes because some have speculated that this population is intrinsically different in terms of pneumococcal vaccine effectiveness.<sup>2</sup> Third, we explored the specificity of our findings by examining outcomes according to vaccination status in those with confirmed pneumococcal pneumonia (ie, those with pneumococcal bacteremia). We considered all other patients to have pneumonia of unknown etiology. All statistical analyses were carried out using SPSS version 14 (SPSS Inc, Chicago Illinois).

## RESULTS

### CLINICAL CHARACTERISTICS

During the study period, 3415 patients with CAP were hospitalized. The median age was 75 years, and 46% were fe-

**Table 1. Characteristics of 3415 Patients With Community-Acquired Pneumonia Admitted to Hospital, Stratified by Pneumococcal Vaccine Use**

Characteristic	Patients, No. (%)		P Value
	Not Vaccinated (n = 2655)	Vaccinated (n = 760)	
Age ≥65 y	1581 (60)	668 (88)	<.001
Male	1434 (54)	369 (49)	.008
Previous comorbidities			
Stroke	214 (8)	92 (12)	.001
Ischemic heart disease	621 (23)	289 (38)	<.001
Heart failure	534 (20)	193 (25)	.002
Cancer	366 (14)	133 (18)	.01
Liver disease	104 (4)	13 (2)	.003
Renal disease	337 (14)	113 (15)	.64
COPD	752 (28)	305 (40)	<.001
Neuropsychiatric illness	515 (19)	186 (25)	.002
Influenza vaccination	239 (9)	666 (88)	<.001
≥5 Medications	373 (14)	117 (23)	<.001
Smoking status			
Nonsmoker	1124 (42)	330 (43)	<.001
Former smoker	795 (30)	317 (42)	
Current smoker	736 (28)	113 (15)	
Nursing home resident	399 (15)	238 (31)	<.001
Advanced directive	247 (9)	138 (18)	<.001
Premorbid functional status			
Independent mobility	2413 (91)	639 (84)	<.001
Wheelchair or prosthesis	146 (6)	85 (11)	
Bedridden	94 (4)	36 (5)	
Pneumonia severity index			
Class I or II	589 (22)	58 (8)	<.001
Class III	510 (19)	130 (17)	
Class IV	987 (37)	375 (49)	
Class V	569 (21)	197 (26)	

Abbreviation: COPD, chronic obstructive pulmonary disease.

male, 31% had chronic obstructive pulmonary disease (COPD), 19% were from nursing homes, and 62% had severe pneumonia (PSI class IV or V). Pneumococcal vaccine status was documented for all patients; 760 (22%) had received prior pneumococcal vaccine. Patient characteristics, stratified according to pneumococcal vaccination status, are given in **Table 1**. In general, those at greater risk of substantial morbidity and mortality from pneumonia appeared more likely to be vaccinated (eg, they were older, had more comorbidity, and were more frail).

Propensity score analyses confirmed this impression (**Table 2**). Rates of pneumococcal vaccination increased across quintiles of increasing propensity score: 4% vs 12% vs 20% vs 28% vs 37% of patients (*P* value for trend, <.001). However, when the primary outcome measure (in-hospital mortality or ICU admission) was applied across these same propensity score quintiles, there did not appear to be a robust association between rates of adverse outcomes and increased propensity to be vaccinated: 17% vs 23% vs 23% vs 17% vs 21% (*P* value for trend, .30).

#### IN-HOSPITAL DEATH OR ICU ADMISSION

Overall, 334 patients (10%) died in hospital, 351 (10%) were admitted to an ICU, and 624 (18%) achieved the

**Table 2. Independent Correlates of Receiving Pneumococcal Vaccine: Propensity Score Model<sup>a</sup>**

Variable	OR (95% CI)	P Value
Age ≥65, y	3.47 (2.69-4.48)	<.001
Male	0.77 (0.65-0.92)	.005
Previous comorbidities		
Ischemic heart disease	1.48 (1.23-1.79)	<.001
Heart failure	0.75 (0.61-0.93)	.007
COPD	1.38 (1.14-1.68)	.001
Smoking status		
Nonsmoker	1 [Reference]	
Former smoker	1.33 (1.08-1.62)	.007
Current smoker	0.76 (0.59-0.99)	.04
Nursing home resident	1.82 (1.46-2.27)	<.001
Premorbid functional status		
Independent mobility	1 [Reference]	
Wheelchair or prosthesis	1.67 (1.21-2.31)	.002

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

<sup>a</sup>All presented ORs adjusted for each variable in the Table, as well as adjusted for number of medications and history of stroke, cancer, liver disease, renal disease, and neuropsychiatric illness. C statistic for model = 0.78.

primary composite end point of death or admission to the ICU. Pneumococcal vaccination was protective from reaching this composite end point (73 of 760 [10%] vs 551 of 2655 [21%] for unvaccinated patients; unadjusted odds ratio [OR] of 0.41 [95% confidence interval {CI}, 0.31-0.53]; *P* <.001). In a standard multivariable model that included numerous potential confounders, the adjusted odds of death or ICU admission was 0.61 (95% CI, 0.41-0.91) (*P* = .02) for patients who had received prior pneumococcal vaccination. The same model with the inclusion of propensity score quintiles yielded almost identical results: the adjusted odds of death or ICU admission with pneumococcal vaccination was 0.62 (95% CI, 0.42-0.92) (*P* = .02), with a C statistic of 0.83 (**Table 3**). In terms of the propensity score matched analysis, with 99% efficiency we were able to successfully match 753 of 760 pneumococcal vaccination patients with 753 unvaccinated patients. In this restricted subgroup analysis, the magnitude of benefit was greater, 95% CIs narrower, the results more statistically significant, and the C statistic increased to 0.86. Specifically, the adjusted OR for death or ICU admission with pneumococcal vaccination was 0.50 (95% CI, 0.31-0.83) (*P* = .007).

In examining the individual components of our composite outcome, it is apparent that our results were driven by nonfatal rather than fatal events. Namely, we found that pneumococcal vaccine recipients were not significantly less likely to die compared with patients who were not vaccinated (71 of 760 [9%] vs 263 of 2655 [10%]; propensity score adjusted OR for death 0.82 [95% CI, 0.52-1.30]; *P* = .40), but they were much less likely to require admission to the ICU (2 of 760 [ $<$ 1%] vs 349 of 2655 [13%]; propensity score adjusted OR for ICU admission, 0.08 [95% CI, 0.02-0.37]; *P* <.001).

In sensitivity analyses restricted to patients 65 years or older (*n* = 2249), the adjusted OR for pneumococcal vaccination protection from death or ICU admission was essentially unchanged (71 of 425 [17%] vs 597 of 1824

**Table 3. Independent Correlates for Death or ICU Admission in Patients With Community-Acquired Pneumonia Admitted to Hospital: Multivariable Logistic Regression Analyses<sup>a</sup>**

Variable	Adjusted OR (95% CI)	P Value
Pneumococcal vaccination	0.62 (0.42-0.93)	.02
Influenza vaccination	0.42 (0.29-0.61)	<.001
Smoking status		
Nonsmoker	1 [Reference]	
Former smoker	0.71 (0.54-0.93)	.01
Current smoker	0.79 (0.61-1.03)	.09
Advanced directive	1.50 (1.14-2.09)	.005
Premorbid functional status		
Independent	1 [Reference]	
Wheelchair or prosthesis	1.86 (1.27-2.73)	.001
Bedridden	2.85 (1.87-4.34)	<.001
Pneumonia severity index		
Class I or II	1 [Reference]	
Class III	2.45 (1.60-3.75)	<.001
Class IV	5.00 (3.35-7.46)	<.001
Class V	15.23 (9.79-23.75)	<.001

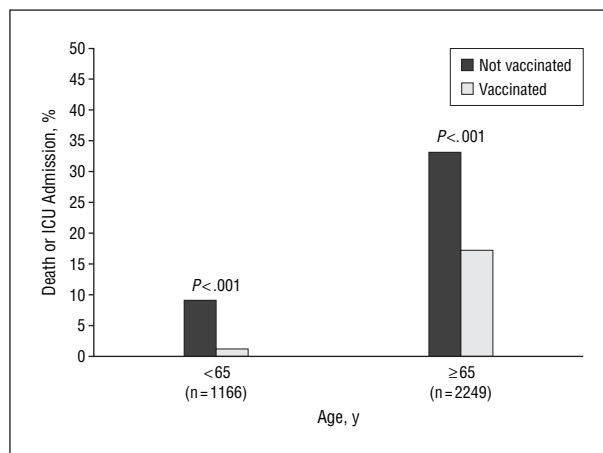
Abbreviations: CI, confidence interval; ICU intensive care unit; OR, odds ratio.

<sup>a</sup>All ORs adjusted for each variable presented in the Table, as well as for propensity score (quintiles), age, sex, stroke, ischemic heart disease, heart failure, cancer, liver disease, renal disease, chronic obstructive pulmonary disease, neuropsychiatric illness, number of medications, and nursing home residence. C statistic for model = 0.83.

[33%] for unvaccinated patients; adjusted OR, 0.63 [95% CI, 0.41-0.97];  $P = .04$  (**Figure**). In sensitivity analyses restricted to nursing home patients ( $n = 637$ ), we observed similar reductions in death or ICU admission associated with receipt of pneumococcal vaccine, although these findings were not significant (adjusted OR, 0.56 [95% CI, 0.28-1.12];  $P = .11$ ).

#### PNEUMOCOCCUS-SPECIFIC ANALYSES

Rates of pneumococcal bacteremia were significantly lower among those who had blood cultures drawn and who had been vaccinated against pneumococcus compared with those who had not been vaccinated (10/534 [2%] vs 85 of 1816 [5%];  $P = .004$  for difference). We considered these 95 patients with pneumococcal bacteremia to have confirmed pneumococcal pneumonia. None of the 10 patients with confirmed pneumococcal pneumonia who received the pneumococcal vaccine died or went to the ICU compared with 27 of 85 (32%) of those with confirmed pneumococcal pneumonia who were not vaccinated ( $P = .06$ ) (**Table 4**). In terms of further attempting to establish the specificity of the benefit of the vaccine to those with pneumococcal pneumonia, we also examined outcomes among the 3320 patients with pneumonia of unknown etiology (Table 4). Among these patients, there was no difference in mortality ( $P = .78$ ) and a much smaller reduction in the composite outcome of death or ICU admission (10% absolute reduction compared with a 32% reduction among those with confirmed pneumococcal pneumonia) (Table 4). Lastly, of the 85 unvaccinated patients with confirmed pneumococcal pneumonia who were clearly eligible for vaccination at the time of discharge, only 6 (7%) were actually vaccinated. This is no



**Figure.** Rates of death or intensive care unit (ICU) admission stratified by pneumococcal vaccination status and age.

different than the overall 9% rate of pneumococcal vaccination among all 2416 patients who were potentially eligible at the time of their discharge from hospital.

#### COMMENT

In this large, population-based “real-world” cohort of more than 3000 hospitalized patients with pneumonia, only one-fifth had received previous pneumococcal vaccination. Importantly, however, we observed that patients with prior pneumococcal vaccination had about a 40% lower adjusted rate of mortality or ICU admission compared with those who had not been vaccinated, a benefit derived primarily because of reduced need for ICU admission. The estimate of benefit remained essentially unchanged when the analyses were restricted to patients 65 years or older or patients admitted from nursing homes—both groups for whom “universal” pneumococcal vaccination is currently recommended.<sup>11-14</sup> Furthermore, in what we consider to be exploratory analyses, we demonstrated substantially larger and more pneumococcus-specific benefits of vaccination among the patients with confirmed pneumococcus pneumonia compared with the patients with pneumonia of unknown etiology. Some benefit is still seen in the “pneumonia of unknown etiology” cohort, since at least 30% to 50% are believed to have (undiagnosed) pneumococcal pneumonia.<sup>1,2</sup>

Our finding that there appears to be benefit from pneumococcal vaccination, even in populations who develop pneumonia, is broadly consistent with prior studies that have tried to examine this question.<sup>21-23,25</sup> That said, we believe our study has been able to overcome some of the collective limitations of these previous efforts, and provides further assurance that the results of those studies were not a result of selection bias or confounding. In contrast to our findings on mortality, recent observational studies by Fisman et al<sup>21</sup> and Vila-Córcoles et al<sup>25</sup> reported that prior pneumococcal vaccination also provided a significant survival benefit in those with CAP. We believe that these differences are not because of residual confounding in these studies, but rather more likely relate to issues around power: the study by Fisman et al<sup>21</sup> study had a total sample size 4 to 5 times as large as ours, while the cohort in the study by

**Table 4. Characteristics of 3415 Patients With Community-Acquired Pneumonia According to the Confirmation of Pneumococcus as the Cause**

Characteristic	Patients With Pneumonia of Unknown Etiology (n = 3320)			Patients With Confirmed Pneumococcal Pneumonia (n = 95)		
	Not Vaccinated, No. (%) (n = 2570)	Vaccinated, No. (%) (n = 750)	P Value	Not Vaccinated, No. (%) (n = 85)	Vaccinated, No. (%) (n = 10)	P Value
Age ≥ 65 y	1553 (60)	659 (88)	<.001	28 (33)	9 (90)	<.001
Male	1382 (54)	367 (49)	.02	52 (61)	2 (20)	.02
Influenza vaccination	236 (9)	656 (88)	<.001	3 (4)	10 (100)	<.001
Pneumonia severity index						
Class I or II	569 (22)	58 (8)	<.001	20 (24)	0	.31
Class III	494 (19)	128 (17)		16 (19)	2 (20)	
Class IV	962 (37)	370 (49)		25 (29)	5 (50)	
Class V	545 (21)	194 (26)		24 (28)	3 (30)	
Admission to ICU	326 (13)	2 (<1)	<.001	23 (27)	0	.11
Death	252 (10)	71 (10)	.78	11 (13)	0	.60
Death or admission to ICU	524 (20)	73 (10)	<.001	27 (32)	0	.06

Abbreviation: ICU, intensive care unit.

Vila-Córcoles et al,<sup>25</sup> though smaller, had almost twice the rate of short-term mortality as our population.

If the findings of this observational study are not a result of selection bias and confounding, what might be the mechanism of benefit? We speculate that even when the antibody response following vaccination is not sufficient to prevent pneumonia, the hosts' response may still be sufficient enough to moderate outcomes once pneumonia establishes itself. The vaccine-generated immune response has previously been shown to facilitate opsonization, activate complement, and promote bacterial phagocytosis in animal models,<sup>2</sup> which may in part explain a plausible mechanism of attenuation, even among patients who do not have pneumococcal bacteremia.

In addition to improved clinical outcomes, our results suggest that there may also be an associated reduction in costs associated with pneumococcal vaccination, a health economic benefit that has not been captured in previous cost-effectiveness analyses of this vaccine.<sup>9</sup> Specifically, much of the benefit in our study was in terms of reduction in the need for costly ICU admissions; previous cost analyses have been restricted to examining the benefits of preventing pneumococcal disease but may have not adequately captured the possibility of attenuating the severity or mitigating the cost of disease in those for whom pneumonia is not prevented. Our results imply that the cost-effectiveness of pneumococcal vaccine on a population-wide basis has probably been underestimated.

This was an observational study, and it carries the inherent limitations of any nonrandomized study, particularly as it relates to selection bias and confounding. We attempted to minimize this using several strategies. First, we extensively adjusted for a host of clinical and laboratory parameters that are not usually available in administrative studies.<sup>21,23-25</sup> Second, we used propensity scores to minimize, though not eliminate, selection bias. Indeed, vaccinated patients were older, frailer, and sicker on admission compared with unvaccinated patients, im-

plying that we may have somewhat underestimated the benefits of pneumococcal vaccination. This last possibility is supported by the fact that in our propensity score-matched analysis, in which our sample size was only 44% of the total cohort, the estimates of benefit were greater, the 95% CIs narrower, and the results more statistically significant. Lastly, we restricted analyses to groups for whom universal vaccination is recommended (ie, groups less subject to a healthy vaccine recipient effect) and demonstrated benefits similar to the population as a whole. Other limitations specific to our study include the fact that we did not have specific measures of immunity or information regarding how long ago vaccines had been received; that information regarding the cause of pneumonia was incomplete and that only two-thirds of patients even had blood cultures drawn; that our ability to make inferences with respect to confirmed pneumococcal disease was limited by a sample of only 95 patients; that our outcomes were restricted to the period of hospitalization only; and that certain populations (eg, pregnant or nursing women and patients with human immunodeficiency virus) were excluded.

In conclusion, in a large population-based cohort of patients hospitalized with pneumonia, we found that previous pneumococcal vaccination was associated with a significant 40% relative reduction in hospital mortality or need for ICU admission, a benefit primarily related to nonfatal events. Although the totality of published evidence to date indicates that pneumococcal vaccination does not prevent CAP,<sup>8</sup> our results are consistent with the possibility that pneumococcal vaccination leads to better outcomes in those who go on to eventually develop pneumonia. We believe that our results further emphasize the importance of adopting current adult pneumococcal vaccination guidelines, particularly since only 22% of our population were vaccinated before their hospitalization and less than 10% of eligible patients were vaccinated before hospital discharge.

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**Author Contributions:** Dr Majumdar had full access to all the data in the study and had final responsibility for the decision to submit for publication. *Study concept and design:* Johnstone, Marrie, and Majumdar. *Acquisition of data:* Marrie and Majumdar. *Analysis and interpretation of data:* Johnstone, Marrie, Eurich, and Majumdar. *Drafting of the manuscript:* Johnstone. *Critical revision of the manuscript for important intellectual content:* Marrie, Eurich, and Majumdar. *Statistical analysis:* Eurich and Majumdar. *Obtained funding:* Marrie and Majumdar. *Study supervision:* Majumdar.

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