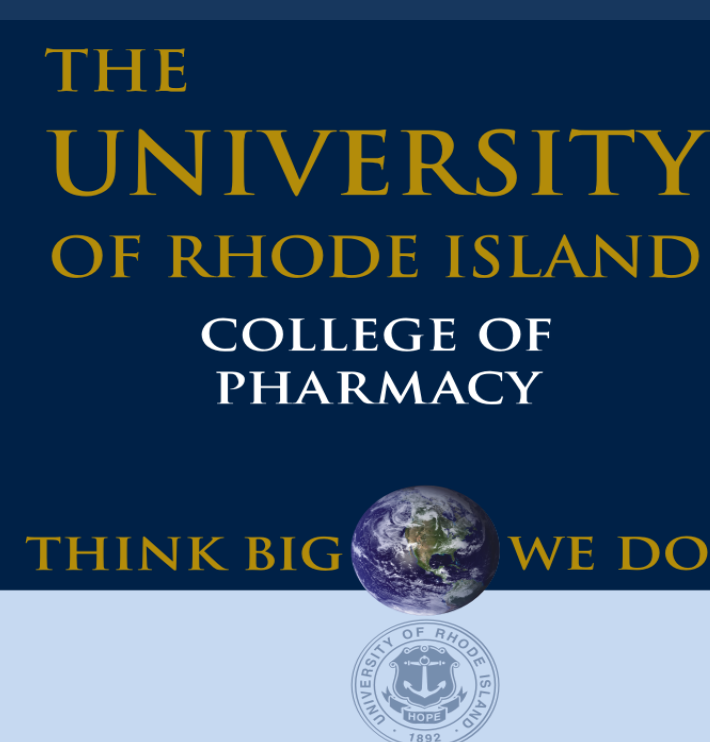
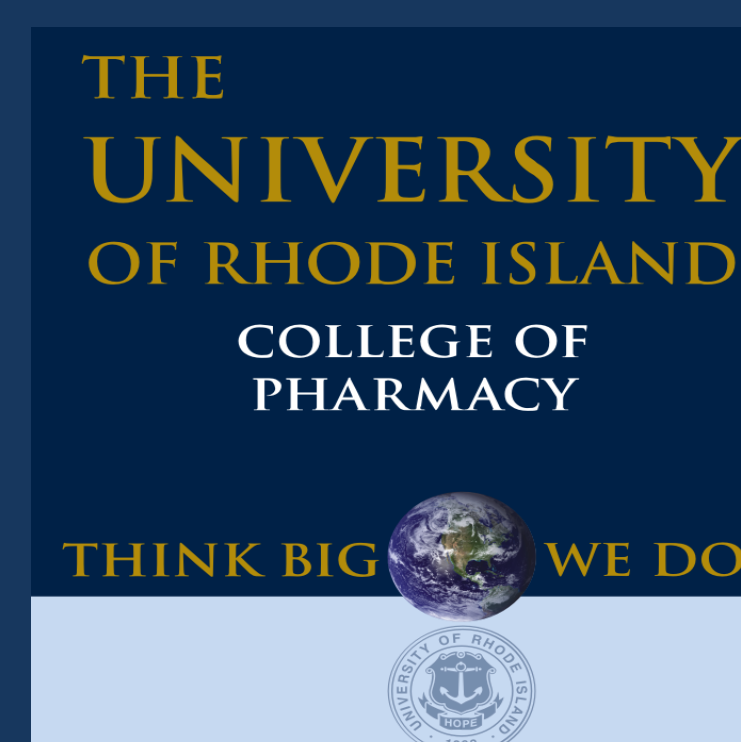


Predictors of Mortality Among Unvaccinated Veterans with Serious *Streptococcus pneumoniae* Infections



Jacob B Morton, PharmD, MBA, BCPS¹, Haley J Morrill, PharmD¹, Kerry L LaPlante, PharmD, FCCP^{1,2}, and Aisling R Caffrey, Ph.D., MS^{1,2}



College of Pharmacy, University of Rhode Island, Kingston, RI¹, USA and Alpert Medical School of Brown University, Providence, RI, USA²

ABSTRACT

Background: Serious *S. pneumoniae* infections are a major cause of mortality worldwide. However, factors influencing mortality have not been fully elucidated. We sought to identify predictors of mortality among unvaccinated Veterans with serious pneumococcal disease.

Methods: This was a case-control study of older Veterans (≥ 50 years) with positive *S. pneumoniae* cultures (blood, cerebrospinal fluid, respiratory) during admissions to Veterans Affairs medical centers between 2002 and 2011. Patients with a pneumococcal vaccine within 5 years of culture were excluded. Using multivariable logistic regression, we identified independent predictors of all-cause 30-day mortality (significant at $p < 0.05$). Potential predictors included patient demographics, as well as comorbidities during admission and medical history with the year prior to culture, identified by diagnosis codes.

Results: Among 9,730 severe pneumococcal infections, 18% died within 30 days of culture (1,764 cases, 7,966 controls). Pneumonia (62%), bacteremia (26%), and bacteremic pneumonia (11%) were the most common infections. Predictors of mortality present during the pneumococcal admission included invasive pneumococcal disease (odds ratio [OR] 2.10, confidence interval [CI] 1.85-2.39), intensive care (OR 2.26, CI 1.99-2.57), dialysis (OR 3.35, CI 2.37-4.72), endocarditis (OR 2.74, CI 1.28-5.90), neutropenia (OR 2.67, CI 1.32-5.42), non-metastatic (OR 2.34, CI 1.91-2.87) or metastatic malignancy (OR 2.54, CI 1.89-3.41), and moderate or severe liver disease (OR 2.47, CI 1.53-3.99). Corticosteroid use within 30 days of admission (OR 1.30, CI 1.13-1.50) was also a predictor of mortality.

Conclusion: Organ or immune system dysfunction-related conditions were the most common predictors of 30-day mortality among unvaccinated Veterans. Increased vaccination efforts among patients with these conditions may improve outcomes.

BACKGROUND

- Pneumococcal pneumonia, bacteremia, and meningitis lead to substantial morbidity and mortality.^{1,2}
- Pneumococcal pneumonia: 400,000 hospitalizations and 5-7% mortality annually, but mortality for hospitalized and older patients likely underestimated.³
- Surprisingly, studies examining mortality often exclude non-bacteremic pneumonia, focusing only on invasive disease.
- Predictors of mortality in serious pneumococcal disease are largely unknown.

OBJECTIVES

- **Objectives:** To determine predictors of 30-day mortality among unvaccinated, older Veterans.

METHODS

- National case-control study of Veterans age ≥ 50 years hospitalized for pneumococcal bacteremia, meningitis, or pneumonia from 2002-2011.
- Pneumonia: Positive sputum culture and ICD-9 code for pneumonia; bacteremia/meningitis: positive blood/cerebrospinal fluid culture.
- Exclusion: received pneumococcal vaccine within 5 years of culture.
- Cases: not alive 30 days after culture; controls: alive at 30 days.
- Identified predictors (during hospitalization and within one year prior) of 30-day all-cause mortality using multivariable logistic regression.

RESULTS

- 9,730 serious pneumococcal infections; 18% 30-day mortality
- Cases significantly more likely to have comorbidities and history of chronic conditions compared to controls ($p < 0.05$).

Table 1. Predictors of 30-day mortality in unvaccinated adults.

	Predictors During Hospitalization		Predictors within One Year	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pneumococcal Vaccine Currently Recommended				
Age	1.03 (1.02-1.03)	1.03 (1.03-1.04)	-	-
Congestive heart failure	1.56 (1.36-1.78)	1.5 (1.25-1.81)	-	-
CS use previous 30 days	-	-	1.27 (1.12-1.43)	1.3 (1.13-1.50)
Dialysis	3.27 (2.53-4.22)	3.35 (2.37-4.72)	-	-
Metastatic malignancy	3.35 (2.72-4.14)	2.54 (1.89-3.41)	3.11 (2.62-3.69)	1.53 (1.19-1.97)
Mild liver disease	1.61 (1.32-1.97)	1.63 (1.20-2.22)	1.98 (1.69-2.32)	1.35 (1.07-1.71)
Moderate/severe liver disease	4.12 (2.87-5.91)	2.47 (1.53-3.99)	3.20 (2.39-4.28)	1.49 (1.01-2.20)
Myocardial Infarction	2.08 (1.67-2.58)	1.75 (1.35-2.27)	2.08 (1.74-2.48)	1.31 (1.06-1.62)
Neutropenia	4.56 (2.55-8.15)	2.67 (1.32-5.42)	-	-
Non-metastatic malignancy	2.21 (1.95-2.50)	2.34 (1.91-2.87)	-	-
Pneumococcal Vaccine Not Currently Recommended				
Cardiac arrhythmia	1.73 (1.53-1.94)	1.41 (1.21-1.63)	-	-
Cerebrovascular disease	-	-	1.92 (1.66-2.22)	1.25 (1.05-1.49)
Chronic pressure ulcers	2.17 (1.685-2.80)	1.42 (1.04-1.92)	2.15 (2.08-3.05)	2.04 (1.48-2.82)
Coagulopathy	2.45 (1.98-3.03)	2.3 (1.75-3.01)	-	-
Dementia	2.49 (1.81-3.44)	1.8 (1.23-2.61)	-	-
Elixhauser comorbidity score	-	-	1.19 (1.17-1.21)	1.16 (1.12-1.20)
Endocarditis	2.35 (1.23-4.50)	2.74 (1.28-5.90)	-	-
Fluid or electrolyte disorders	1.33 (1.18-1.50)	1.69 (1.43-1.99)	2.24 (2.01-2.51)	1.2 (1.03-1.39)
Gram-negative infection	-	-	2.33 (1.74-3.11)	1.48 (1.05-2.07)
MRSA infection	-	-	2.54 (1.88-3.44)	1.59 (1.12-2.25)
Neurological disorders	1.91 (1.55-2.35)	1.86 (1.42-2.45)	2.03 (1.72-2.40)	1.28 (1.02-1.59)
VRE infection	5.28 (1.77-15.74)	3.78 (1.02-14.17)	-	-
Weight loss	-	-	2.06 (1.79-2.37)	1.21 (1.02-1.44)
Other Predictors				
Hospitalized in NE US	1.31 (1.11-1.55)	1.29 (1.06-1.56)	-	-
Hospitalized in southern US	1.30 (1.14-1.49)	1.33 (1.14-1.56)	-	-
ICU Level of Care	2.20 (1.97-2.45)	2.26 (1.99-2.57)	-	-
IPD	1.93 (1.74-2.14)	2.1 (1.85-2.39)	-	-

CI, Confidence interval; ICU, Intensive Care Unit; IPD, invasive pneumococcal disease; MRSA, methicillin-resistant *Staphylococcus aureus*; NE, northeast; OR, odds ratio; US, United States; VRE, Vancomycin-resistant *Enterococcus*. Other variables controlled for in the final model (OR < 1): length of stay, Elixhauser comorbidity score, hypertension, streptococcal spp. infection, amputation, infective arthritis, history of peripheral vascular disease, cigarette smoking, drug abuse, dialysis, obesity, race, hospitalization in the midwestern and western US (reference).

CONCLUSIONS

- Many predictors of mortality were organ or immune system-related dysfunction, and were consistent with current pneumococcal vaccination recommendations.
- Several predictors identified are not specifically recommendations for pneumococcal vaccination, including dementia and neurological disorders.
 - These patients may also benefit from pneumococcal vaccination

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