



# SEPSIS IN THE CONTEXT OF NONVENTILATOR HOSPITAL-ACQUIRED PNEUMONIA

By Karen K. Giuliano, PhD, RN, MBA and Dian Baker, PhD, RN, APRN-BC

**Background** Sepsis is a leading cause of mortality among hospitalized patients and is the most expensive condition affecting the US health care system. Pneumonia is associated with about half of sepsis cases, yet limited research has described the incidence of sepsis in the context of nonventilator hospital-acquired pneumonia (NV-HAP). Persons with NV-HAP who are at risk for sepsis must be identified so that interventions to reduce the burden of NV-HAP and improve outcomes among patients with sepsis can be designed.

**Objectives** To determine the proportion of persons with NV-HAP in whom sepsis develops and to describe the demographic and clinical characteristics of persons with NV-HAP in whom sepsis develops.

**Methods** In this retrospective, population-based study, data were extracted from the National Inpatient Sample from the 2012 Healthcare Cost and Utilization Project dataset. *International Classification of Diseases, Ninth Revision, Clinical Modification* codes were used to identify adult patients at least 18 years of age who had a stay of at least 48 hours, had no documented diagnosis of ventilator-associated pneumonia, and had secondary diagnoses of both NV-HAP and sepsis, neither of which was present on admission.

**Results** In the 2012 calendar year, 119 075 adults had NV-HAP develop; sepsis developed in 36.3% of these cases. Male and black patients were overrepresented in the sample, and patients had a mean of 7 comorbid conditions (SD, 3.3).

**Conclusions** Sepsis in the context of NV-HAP is a key concern. Additional research is needed to identify factors associated with the development of sepsis among patients with NV-HAP. (*American Journal of Critical Care*. 2020;29:9-14)

**CE** 1.0 Hour

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Sepsis is a systemic response to infection that can cause acute organ dysfunction, disability, and death.<sup>1,2</sup> Despite focused efforts for more than a decade to curtail mortality and morbidity, sepsis remains a significant health care challenge.<sup>3</sup> In the United States alone, sepsis affects 2% of all patients admitted to hospitals and has an associated 25% mortality.<sup>1,4</sup> Furthermore, sepsis is the most expensive condition facing the US health care system,<sup>5</sup> with costs exceeding \$23 billion in 2013. In Europe and Central Asia, the impact of sepsis is comparable to that in the United States, but East Asia and the Pacific battle against an even higher incidence rate.<sup>6</sup>

Even with the extensive worldwide efforts to decrease sepsis, the incidence and mortality of sepsis are continuing to increase.<sup>6,7</sup> Current efforts remain focused on early recognition and treatment, but preventive strategies have not been as aggressively deployed. Although the US Centers for Disease Control and Prevention recognizes the fundamental benefits of prevention-oriented strategies,<sup>8</sup> prevention of sepsis through prevention of infection, particularly hospital-acquired infection, remains a clinical challenge.

The most common type of infection leading to sepsis is pneumonia, including community-acquired pneumonia and hospital-acquired pneumonia.<sup>4,9</sup>

The risk of sepsis associated with nonventilator hospital-acquired pneumonia continues to be underappreciated.

Hospital-acquired pneumonia comprises both ventilator-associated pneumonia (VAP) and nonventilator hospital-acquired pneumonia (NV-HAP). Ventilator use is a risk factor for hospital-acquired pneumonia,<sup>10,11</sup> and the use

of evidence-based prevention strategies has led to significant decreases in VAP incidence.<sup>12-15</sup> Unfortunately, in comparison with VAP, NV-HAP has been inadequately studied and underreported; thus, the risk of sepsis associated with NV-HAP continues to be underappreciated.<sup>16-20</sup> In spite of recent reductions in VAP incidence, data still indicate that 50% of sepsis cases are associated with pneumonia.<sup>1</sup> Moreover, emerging data suggest that the incidence

of NV-HAP and its associated morbidity and mortality are substantial, with the overall impact exceeding that of VAP.<sup>16,17</sup> There is, therefore, a need to improve understanding of sepsis in the context of NV-HAP. Identification of persons with NV-HAP who are at risk for sepsis is necessary to design interventions to reduce the burden of NV-HAP and improve outcomes among those with sepsis.

To better understand the incidence and impact of sepsis among persons with NV-HAP, we conducted a retrospective, population-based study in which we analyzed data from the National Inpatient Sample (NIS) from the 2012 Healthcare Cost and Utilization Project (HCUP) data set. The purpose of this study was to determine the proportion of individuals with NV-HAP in whom sepsis develops and to describe the demographic and clinical characteristics of persons with NV-HAP who have sepsis develop.

## Methods

This study is part of our hospital-acquired pneumonia prevention initiative program of research.<sup>19-23</sup> The institutional review board at the principal investigator's institution granted this secondary analysis project exempt status.

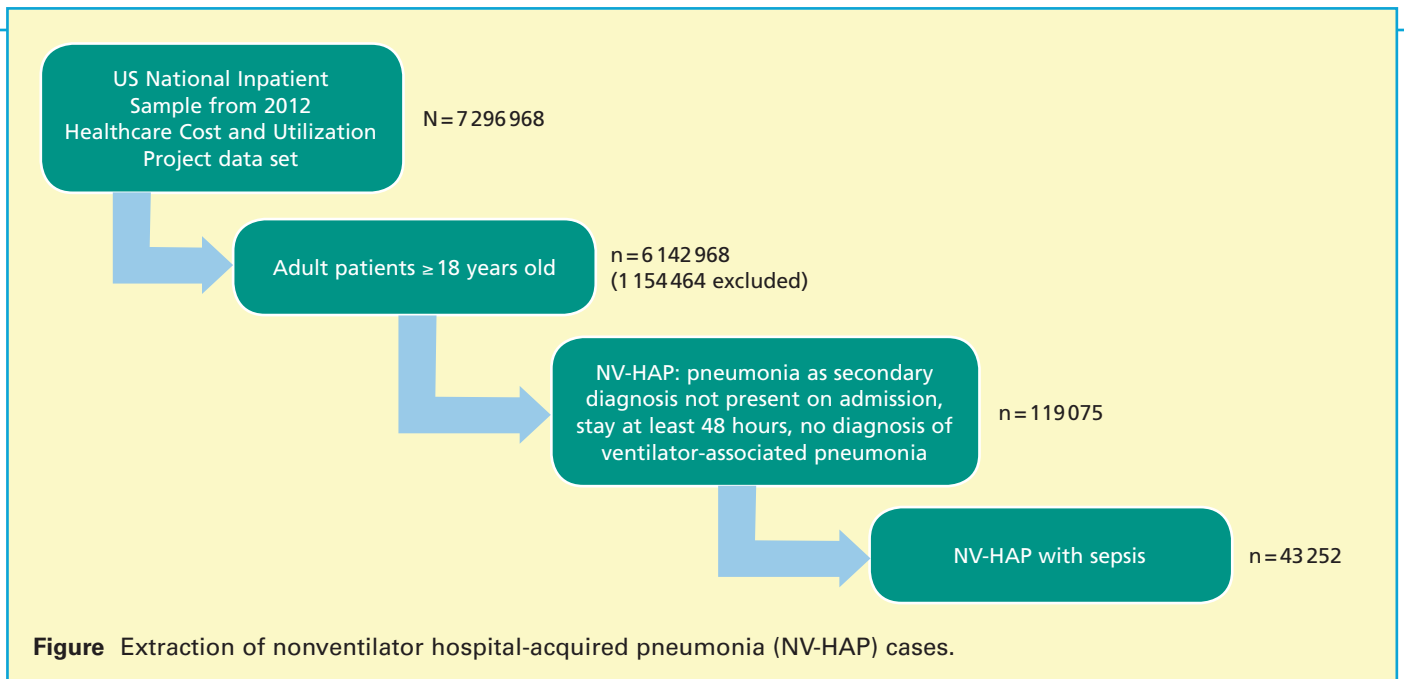
## Data Source

Data were extracted from the HCUP NIS data set. The data extraction process is shown in the Figure. The HCUP NIS data set is a public-use data set that supports analyses on US hospital trends. The HCUP is a partnership of federal and state health care agencies and the Agency for Healthcare Research and Quality.<sup>24</sup> The NIS is the largest all-payer, inpatient care database of the United States, with a 20% stratified sample of all inpatient discharges from community hospitals (excluding rehabilitation and long-term acute care hospitals). Forty-four states participate in HCUP, representing more than 96% of the US population. As required for use of the NIS dataset, data use agreement training was completed by the principal investigator (April 27, 2015; HCUP-318K72CUW).

## About the Authors

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### Case Identification

The 2012 HCUP NIS data set allows extraction of principal diagnosis and up to 24 secondary diagnoses based on the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis codes. In addition, HCUP includes a present-on-admission indicator to distinguish between medical conditions that are present when patients enter the hospital and those that occur during the hospital stay. To identify cases of NV-HAP with data available in HCUP, we queried the database for adult patients at least 18 years of age who had a stay of at least 48 hours; had no diagnosis of VAP; and had secondary diagnoses of both NV-HAP and sepsis, neither of which was present on admission.

Consistent with the HCUP Clinical Classifications Software recommendations,<sup>24</sup> NV-HAP cases were identified using the following *ICD-9-CM* codes: 480.80, 481.00, 482.00, 482.10, 482.20, 482.39, 482.41, 482.42, 482.82, 482.83, 483.80, 484.60, 484.70, and 486.00.<sup>25</sup> Given that hospital-acquired pneumonia is defined as pneumonia that occurs more than 48 hours after hospital admission,<sup>10</sup> we excluded cases in which pneumonia occurred less than 48 hours after hospital admission. Sepsis cases were identified by *ICD-9-CM* codes 995.91 and 995.92.

### Demographic and Clinical Characteristics

Data describing the demographic and clinical characteristics of each case were extracted from the database. These characteristics included age, sex, race, number of chronic conditions, elective versus nonelective hospital admission, length of hospital

stay, total hospital charges, operating room procedure (yes/no), admission and discharge transfer status, and in-hospital mortality.

### Statistical Analyses

Descriptive statistics were used to summarize the characteristics of NV-HAP cases with sepsis. All statistical analyses were performed using SPSS v23.0.

### Results

In the 2012 calendar year, 133 595 adults in the HCUP NIS database had a secondary diagnosis of pneumonia. After excluding cases with a length of stay less than 48 hours, we obtained a sample of 119 075 NV-HAP cases (see Figure). Sepsis developed in 36.3% of these cases. Descriptive data are shown in the Table. The amount of missing data was 4% for race and less than 1% for all other variables.

### Discussion

Our goal was to add to the body of knowledge describing sepsis within the context of NV-HAP. In the current study, 36.3% of patients with NV-HAP had sepsis develop. This proportion is comparable to the proportion of patients with VAP who have sepsis develop, which previous reports<sup>26,27</sup> have indicated ranges from 37% to 50%. Because NV-HAP usually occurs outside of the intensive care unit and occurs more often in medical than in surgical patients, the sepsis risk associated with NV-HAP may be

**Sepsis developed in 36.3% of 119 075 cases of nonventilator hospital-acquired pneumonia.**

**Table****Descriptive characteristics of 43 252 patients with nonventilator hospital-acquired pneumonia and sepsis**

Characteristic	Value <sup>a</sup>
Age, mean (SD), y	66.4 (16.3)
Male sex	52.9 (22874)
Race (n=41 525)	
White	67.9 (28 191)
Black	15.3 (6374)
Hispanic	9.4 (3907)
Asian or Pacific Islander	3.4 (1396)
Native American	0.7 (286)
Other	3.3 (1371)
Chronic conditions (n=43 252)	
Number of conditions, mean (SD)	7.4 (3.2)
Elective versus nonelective hospital admission (n=43 146)	
Patients who did not elect for hospital admission	92.7 (40 084)
Patients who elected for hospital admission	7.1 (3062)
Receipt or not of operating room procedure (n=43 252)	
Patients who did not undergo an operating room procedure	78.8 (34 061)
Patients who underwent an operating room procedure	21.2 (9191)
Patient's preadmission setting (n=43 018)	
Another acute care facility	8.3 (3605)
Another type of health care facility	7.3 (3156)
A non-health care setting	83.8 (36 257)
Patient transfer disposition at discharge (n=43 241)	
To a different acute care facility	3.8 (1654)
To another type of health care facility	39.4 (17 029)
To a non-health care setting	56.8 (24 558)
In-hospital mortality (n=43 241)	20.5 (8847)

<sup>a</sup> Values are percentage (number) of patients unless otherwise indicated in first column.

underappreciated.<sup>16,19</sup> Additionally, it is possible that recognition and treatment of NV-HAP for patients admitted with another principal diagnosis may be delayed, further increasing their risk for sepsis as well as other related complications. This notion is further strengthened by findings from published research on rapid response teams, in which data support respiratory compromise as the most common reason for deterioration in a patient's condition and initiation of the rapid response team.<sup>28-30</sup>

In our descriptive review of patient characteristics, we found a high need for postdischarge care in another health care facility for NV-HAP patients with

sepsis, with a total of 17 029 patients with NV-HAP and sepsis requiring additional care in a health care facility upon hospital discharge. These findings are consistent with previous research and provide evidence to highlight that hospital-

based length of stay and total charges represent only a portion of the total economic impact of sepsis following NV-HAP.<sup>25</sup>

**Sepsis in the context of nonventilator hospital-acquired pneumonia is a significant concern.**

Male patients and black patients were overrepresented in the current sample of individuals with NV-HAP and sepsis in comparison to the population demographic characteristics of the United States as a whole.<sup>31</sup> This finding is consistent with previous reports of a higher incidence of sepsis among male patients<sup>1</sup> and black patients.<sup>32,33</sup> Similarly, patients in the current sample had a mean of 7 comorbid conditions (SD, 3.3), a finding that is supported by previous research suggesting a positive association between chronic disease burden and risk of sepsis.<sup>2</sup>

The results of this study indicate that sepsis in the context of NV-HAP is a significant concern, perhaps particularly among individuals who are male, identify as black, or have multiple chronic health conditions. Additional research is needed to identify factors associated with the development of sepsis among patients with NV-HAP and to design and test interventions aimed at the prevention and early recognition and treatment of sepsis in this patient population.

### Limitations

While the sampling strategy of using ICD-9 codes to identify the NV-HAP cases has been used in previous research,<sup>19,25</sup> variations in the accuracy of administratively coded data (ACD) have been well-documented.<sup>34,35</sup> Data indicate that currently used ACD, specifically ICD-9 coding, may have limited and variable accuracy for the identification and surveillance of hospital-acquired infection. In a recent study<sup>36</sup> conducted at 47 acute care hospitals in California, researchers looked at both traditional surveillance and claims-based surveillance for surgical site infection. These researchers found that the overall sensitivity for traditional surveillance was 50% whereas that of claims-based surveillance was 84%, and that surveillance using both ICD-9 and ICD-10 codes provided a standardized approach.<sup>36</sup> Nevertheless, given that the identification of surgical site infection can occur in either the acute care setting before discharge or in the outpatient setting where the surveillance process is less defined, these findings may have limited applicability for the acute care infection surveillance used to identify NV-HAP.

Because of the secondary nature of our analyses and the use of ACD, we were unable to confirm that all cases included in our analyses were correctly classified. Thus, we were unable to identify the impact of any incorrectly classified cases in our sample because they would be the result of a coding error. One example is related to our exclusion of patients with a VAP diagnosis. In doing so, it is possible that we may have eliminated some of the most severe NV-HAP

cases, that is, those patients who had NV-HAP develop, required mechanical ventilation, and were coded at discharge as VAP. Again, because of the secondary nature of our analyses, we cannot be sure that the patients in this important group were all correctly classified, and this may potentially have resulted in an underestimation of the incidences of both NV-HAP and sepsis in this subset of our sample.<sup>37,38</sup>

All things considered, because ACD is the approach currently used by US hospitals for payment, ACD will continue to serve as the common benchmark for health care–associated infection surveillance and payment until better methods can be developed and assessed.<sup>36</sup> The transition in US health care from ICD-9 to ICD-10 and the increased number of diagnostic codes associated with ICD-10 should provide improvements in the coding accuracy for ACD.

## Conclusions

In the past decade, evidence-based care practices, including early mobilization, head-of-bed elevation, judicious use of proton-pump inhibitor medications, and standardized oral care, have reduced the incidence of VAP.<sup>39-41</sup> However, because the risk of NV-HAP has been underappreciated, patients who are not undergoing mechanical ventilation do not routinely receive care to prevent hospital-acquired pneumonia. Clearly, additional research is needed to translate the achievements of VAP prevention into evidence-based strategies for NV-HAP prevention.

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## FINANCIAL DISCLOSURES

None reported.

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