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Major Article

# The epidemiology of nonventilator hospital-acquired pneumonia in the United States

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Hospital cost
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***Background:*** Nonventilator hospital-acquired pneumonia (NV-HAP) is among the most common hospital-acquired infections. The purpose of our study was to quantify the incidence and influence of NV-HAP in the United States using a national dataset.

***Methods:*** The 2012 US National Inpatient Sample dataset was used to compare an NV-HAP group to 4 additional group cohorts: pneumonia on admission, general hospital admissions, matched on mortality and disease severity, and ventilator-associated pneumonia (VAP). The main outcome was NV-HAP incidence. The secondary outcome was to compare hospital length of stay, total hospital charges, and mortality between the NV-HAP group and the 4 additional group cohorts.

***Results:*** The overall incidence of NV-HAP was 1.6%, which represents a rate of 3.63 per 1,000 patient-days. NV-HAP was associated with increased total hospital charges, a longer hospital length of stay, and greater likelihood of death in comparison to all groups except patients with VAP.

***Conclusion:*** NV-HAP is an underappreciated and serious patient safety issue, resulting in significant increases in cost, length of stay, and mortality. Efforts toward prevention of NV-HAP should be raised to the same level of concern as VAP prevention.



Hospital-acquired pneumonia (HAP) is a common health care-acquired infection (HAI) worldwide,[1] occurring at a rate of up to 21 cases per 1,000 hospital admissions.[2] HAP includes 2 distinct subgroups: nonventilator HAP (NV-HAP) and ventilator-associated pneumonia (VAP).[3] Results from a multistate point-prevalence survey using the National Healthcare Safety Network criteria for HAIs suggest that NV-HAP and VAP combined accounted for 21.8% (95% confidence interval, 18.4-25.6) of all HAIs in the United States during 2011. This is equivalent to 157,500 infections (95% confidence interval, 50,800-281,400), with 60.9% of these classified as NV-HAP.[4] Both NV-HAP and VAP are associated with substantial clinical and economic burdens, including prolonged hospital length of stay (LOS), higher overall health care costs, and increased morbidity and mortality.[5-7]

The majority of research during the past 2 decades has focused primarily on VAP. VAP is an identifiable, trackable event for which evidence-based preventive care bundles have been developed and widely implemented.[8-10] These efforts have produced significant declines in VAP rates, resulting in improved patient outcomes and decreased health care costs related to VAP.[11-13]

However, a recent statewide study in Pennsylvania found that NV-HAP is more common than VAP, NV-HAP is associated with similar risk factors and complications to VAP, and was associated with a greater overall economic burden.[14] Data from 2009-2011 revealed 5,597 NV-HAP cases compared with 2,299 VAP diagnoses, with equivalent mortality (18.7% and 18.9%, respectively). The total cost for NV-HAP cases was $156 million compared with $86 million for VAP.[14] These findings are consistent with data from other studies that found an incidence of 1.22-8.9 per 1,000 patient-days and mortality of 13.9%-19%.[4,15-17]

The purpose of this study was to determine the incidence, total hospital charges, and mortality associated with NV-HAP in US hospitals, and compare these findings to 4 group cohorts

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without NV-HAP. The following research questions were addressed:

1. What is the overall incidence of NV-HAP in US acute care hospitals?
2. Do significant differences exist in total hospital charges, LOS, and mortality between acute care patients with NV-HAP and patients with a primary diagnosis of pneumonia?
3. Do significant differences exist in total hospital charges, LOS, and mortality between acute care patients with NV-HAP and the general population of acute care patients?
4. Do significant differences exist in total hospital charges, LOS, and mortality between acute care patients with NV-HAP and patients matched for illness acuity and mortality risk?
5. Do significant differences exist in total hospital charges, LOS, and mortality between acute care patients with NV-HAP and patients with VAP?

## MATERIALS AND METHODS

Before receiving the Healthcare Cost and Utilization Project (HCUP) US National Inpatient Sample (NIS) dataset from the Agency for Healthcare Research and Quality (AHRQ), Data Use Agreement (DUA) training is required. On April 27, 2015, the principal investigator (PI) completed the DUA training and a DUA was executed between the PI and the AHRQ (HCUP-318K72CUW), with records kept by both AHRQ and the PI. The NIS is a public-use dataset commonly used for secondary analyses on US hospital trends. Although no institutional review board approval is required for use of the dataset, an institutional review board determination of exemption was obtained from the PI's hospital system.

### *Data source*

The NIS was developed as part of the HCUP, a partnership between federal and state agencies and the health care industry, with sponsorship provided by AHRQ. The NIS is the largest all-payer, inpatient care database in the United States, consisting of a 20% stratified sample of all inpatient discharges from community hospitals, excluding rehabilitation units, long-term acute care hospitals, psychiatric hospitals, and alcoholism or chemical dependency units.[18,19]

Discharges are stratified by hospital, census division, ownership status, urban or rural location, teaching status, bed size, patient diagnosis-related group, and month of admission. Patients covered by Medicare, Medicaid, private payers, and those who are uninsured are included in the NIS. The data are sampled from state inpatient databases, which include all inpatient data reported to the HCUP.

A total of 46 states participate in HCUP, which represents more than 95% of the US population. The NIS contains anonymized information about each hospital admission, including patient demographic characteristics, admission status, primary and secondary diagnosis and procedure codes, hospital characteristics, expected source of payment, total charges, LOS, disease severity, comorbidity measure, locations from which patients were admitted, and transfer information at the time of discharge. The 2012 HCUP NIS contains a total of 7,296,968 unweighted patient records and was the most recent year data were available from NIS when the secondary data analyses were conducted. The self-weighted NIS data estimates patterns and trends for more than 36 million inpatient hospital stays nationally.

### *Sample*

The diagnosis codes in the 2012 HCUP NIS database distinguish between a primary diagnosis and up to 24 secondary diagnoses. The dataset was mined for patient records of adults aged 18 years or older) with a secondary diagnosis of pneumonia. Because we sought to calculate the incidence of NV-HAP, we used ICD-9-CM codes 480.8, 481, 482.1, 482.0, 482.2, 482.39, 482.41, 482.42, 482.82, 482.83, 483.8, 484.6, 484.7, and 486.0 to identify the NV-HAP cases. ICD-9 codes have been used in previous research to determine NV-HAP incidence.[15,20] This effort resulted in a sample (N = 133,595) of patients with NV-HAP. Because NV-HAP is defined as an episode of pneumonia unassociated with mechanical ventilation that is not incubating at the time of hospital admission and occurs ≥48 hours following admission,[3,21] we excluded all patients without a hospital LOS of at least 48 hours. This resulted in a final sample for analysis of 119,075.

To create clinically relevant comparisons, four comparison groups were generated from the remaining records (Fig 1). For groups 2-4, random sampling was performed without replacement to ensure that duplicate records did not appear in >1 group. The sequential process used to create all 4 groups is shown in Figure 1. Group 2 (n = 119,075) was a randomly generated sample of patients admitted with pneumonia as a primary diagnosis (research question 2). Group 3 (n = 119,075) was a randomly generated sample of any patient in the NIS dataset (research question 3). Group 4 (n = 119,075), was a randomly generated sample of cases for which each patient was matched to the NV-HAP group on both disease severity and mortality score. In the NIS dataset, the disease severity and mortality risk data elements are both recorded using an ordinal scale, with scores ranging from 0-4 (0 = not specified, 1 = minor, 2 = moderate, 3 = major, and 4 = extreme). Thus, the combined total score had a possible range of 0-8. Patients in group 4 were matched to patients in the NV-HAP group on the combined score for disease severity and mortality risk (research question 4). Group 5 (N = 3,260) was created using the ICD-9 code 997.31 to capture all cases of VAP (research question 5).

### *Study variables*

Three main outcome variables were compared between the NV-HAP group and each of the 4 comparison groups. These variables included total inpatient charges, LOS (up to a maximum of 365 days), and mortality.

Demographic variables provided by the dataset included age, sex, payer source, and race/ethnicity.

Additional clinical variables of interest that were available in the dataset included admission status (elective/nonelective), admission history (transferred in or not, and if so from what type of facility), discharge disposition (where patients went immediately after hospital discharge), the total number of comorbid conditions, and whether patients underwent a surgical procedure.

### *Statistical analysis*

Data were analyzed using SPSS version 23 (IBM-SPSS Inc, Armonk, NY). Mean differences for the continuous outcome and descriptive variables between the NV-HAP group (group 1) and each of the comparison groups were analyzed with *t* tests with Bonferroni corrections. The $\chi^2$ test was used for significance testing for the noncontinuous variables.

Second, multivariate regressions were run using patient group as the key independent variable and total charges, LOS, and mortality as the dependent variables. Analyses were run adjusting for demographic and other clinical variables. Ordinary least squares regression was used to analyze total cost and length of stay. Logistic regression was used to analyze patient death.

Listwise deletion was used for missing data. Nominal-scale variables were dummy-coded to be included for analyses. Residuals for total hospital charges, and length of stay violated assumptions of

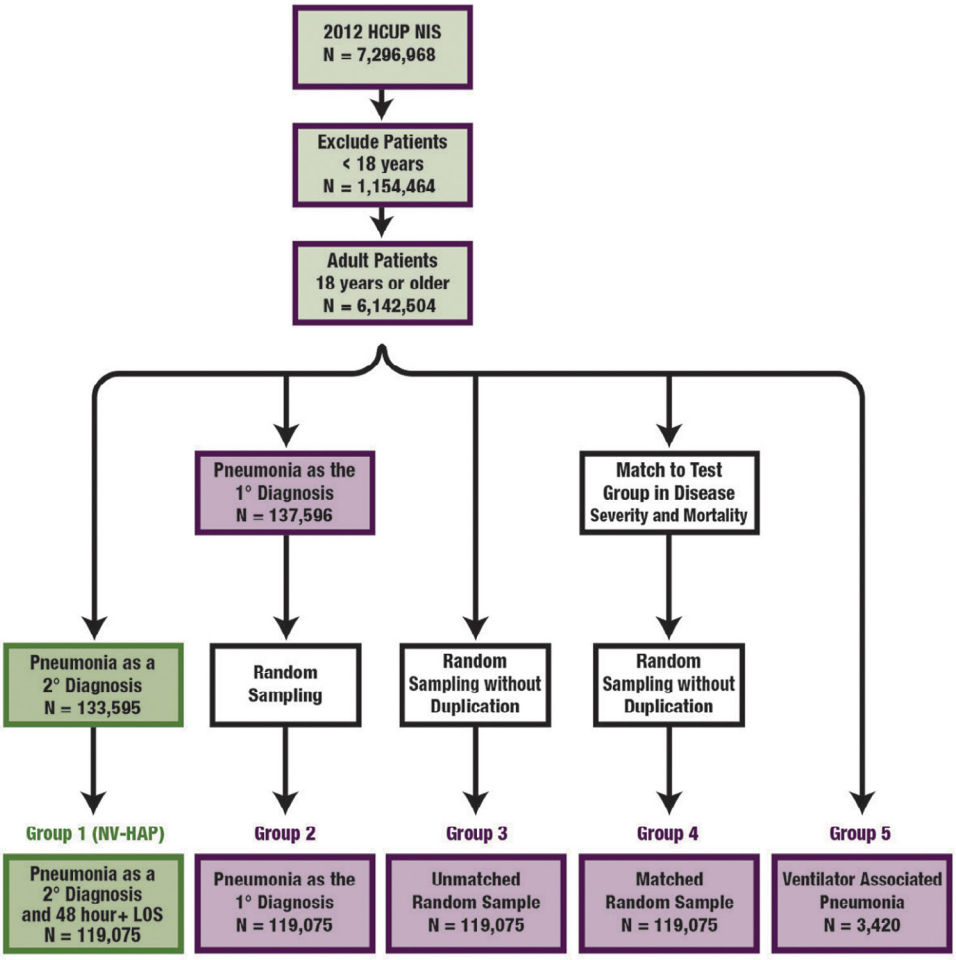


**Fig 1.** Sampling procedure. *HCUP-NIS*, Healthcare Cost and Utilization Project-National Inpatient Database.

normality. Therefore, parallel analyses were run using nonparametric tests. These analyses produced the same results with minor exceptions and in the interest of parsimony are not presented here. All significance tests were 2-tailed with $\alpha = 0.05$.

## RESULTS

### *Research question 1*

The overall incidence of NV-HAP in our sample was 1.6%, which represents a rate of 3.63 per 1,000 patient-days.

### *Research questions 2-5*

Descriptive data showing the unadjusted differences in total hospital charges, length of stay, patient mortality, and the demographic and clinical variables are shown in Table 1. Because most variables had some missing data, data are reported as valid percentages. Significant differences were found between the NV-HAP group and the 4 comparison groups for almost all variables. Therefore, it is important to look at both statistically significant and clinically meaningful differences as we interpret the findings.

### *Total hospital charges, LOS, and mortality*

Given the large number of demographic and other clinical variables on which the NV-HAP group varied from the 4 comparison groups, multivariate analyses were conducted to ensure that group differences were not influenced by confounding variables, with results shown in Table 2.

### *Limitations*

The sampling strategy using ICD-9 codes to identify the NV-HAP cases has been used in previous research.[15,20] However, variations in the accuracy of administratively coded data (ACD) are well-documented in the literature, including 2 recent systematic reviews that used ACD for HAI detection.[22,23] The review by van Mourik et al[23] included 7 studies that looked at NV-HAP, and found that both sensitivity and positive predictive value were each around 40%. Unfortunately, the interpretation of these findings is further complicated by the varying methodologies used. Because this was a secondary analysis, we were not able to perform any measurements of sensitivity, specificity or positive predictive value. There is a general consensus that much of the currently used ACD, specifically ICD-9 coding, has limited and variable accuracy for the identification and surveillance of HAI. However, until better methods can be developed and assessed, current ACD will continue to serve as a common benchmark for HAI surveillance and payment. The recent migration from ICD-9 to ICD-10 in the United States will hopefully represent an improvement.

Because of our matching procedure, there should have been no difference in mortality between the NV-HAP patients (group 1)

**Table 1**
Group descriptive statistics

| | Group 1: Patients with NV-HAP (n = 119,075) | | | Group 2: Pneumonia as primary diagnosis (n = 119,075) | | | Group 3: Unmatched random sample (n = 119,075) | | | Group 4: Matched random sample (n = 119, 075) | | | Group 5: Patients with VAP (n = 3,420) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | μ | n | % | μ | n | % | μ | n | % | μ | n | % | μ | n | % |
| Main outcome variable | | | | | | | | | | | | | | | |
| Total charges, $ in thousands | 132.99 | | | 33.17* | | | 37.96* | | | 100.38* | | | 368.20* | | |
| Length of stay, d | 13.1 | | | 5.1* | | | 4.5* | | | 10.6* | | | 28.4* | | |
| Patient died | | 15,593 | 13.1 | | 4,197 | 3.5* | | 2,123 | 1.8* | | 12,597 | 11.3* | | 631 | 19.4* |
| Demographic variable | | | | | | | | | | | | | | | |
| Age, y | 67.0 | | | 68.5* | | | 57.1* | | | 67.9* | | | 58.2* | | |
| Female | | 57,305 | 48.1 | | 63,119 | 53.0* | | 70,782 | 59.4* | | 55,788 | 49.8* | | 1,202 | 36.9* |
| Male | | 61,765 | 51.9 | | 55,944 | 47.0 | | 48,286 | 40.6 | | 56,172 | 50.2 | | 2,058 | 63.1 |
| Clinical variable | | | | | | | | | | | | | | | |
| Number of chronic conditions | 7.5 | | | 6.0* | | | 4.8* | | | 7.7* | | | 7.1* | | |
| Elective admission | | 11,438 | 9.6 | | 8,109 | 6.8 | | 30,675 | 25.9 | | 13,182 | 11.8 | | 366 | 11.3 |
| Transferred in | | | | | | | | | | | | | | | |
| Not transferred in | | 101,292 | 85.5 | | 110,594 | 93.4 | | 109,698 | 92.7% | | 95,230 | 85.5 | | 2,395 | 73.9 |
| Transferred from a different acute care hospital | | 10,660 | 9.0 | | 2,744 | 2.3 | | 5,455 | 4.6% | | 9,948 | 8.9 | | 582 | 18.0 |
| Transferred from another type of health facility | | 6,496 | 5.5 | | 5,034 | 4.3 | | 3,233 | 2.7 | | 6,144 | 5.5 | | 262 | 8.1 |
| Transferred out | | | | | | | | | | | | | | | |
| Not transferred out | | 70,173 | 58.9 | | 89,855 | 75.5 | | 98,436 | 82.7 | | 75,587 | 63.5 | | 1,277 | 39.2 |
| Transferred out to a different acute care hospital | | 4,461 | 3.7% | | 2,661 | 2.2 | | 2,381 | 2.0% | | 4,770 | 4.0% | | 216 | 6.6 |
| Transferred out to another type of health facility | | 44,407 | 37.3 | | 26,522 | 22.3 | | 18,212 | 15.3 | | 38,683 | 32.5 | | 1,764 | 54.1 |
| Operating room procedure | | 27,181 | 22.8 | | 2,779 | 2.3 | | 35,369 | 29.7 | | 30,626 | 27.4 | | 1,684 | 51.7 |

NOTE. Differences in means and proportions were analyzed comparing the test group (NVHAP) and the four comparison groups, using *t* tests with Bonferroni corrections, or $X^2$ where appropriate.
*NVHAP*, nonventilator hospital-acquired pneumonia; *VAP*, ventilator-associated pneumonia.
*$P < .001$.

**Table 2**
Multivariate analyses of main outcome variables

| | Cost ($ in thousands) | | Length of stay, d | | Death | |
|---|---|---|---|---|---|---|
| Group | *β* | CI | *β* | CI | Odds ratio | CI |
| NVHAP | – | – | – | – | – | – |
| Pneumonia as primary diagnosis | –68.66 | –69.72-–67.61* | –5.93 | –6.02-–5.85* | 0.26 | 0.25-0.27* |
| Unmatched random sample | –93.22 | –94.29-–92.14* | –8.07 | –8.15-–7.99* | 0.16 | 0.15-0.17* |
| Matched random sample | –36.47 | –37.50-–35.43* | –2.69 | –2.77-–2.61* | 0.82 | 0.80-0.84* |
| VAP | 195.92 | 191.50-200.33* | 13.05 | 12.71-13.39* | 1.71 | 1.56-1.87* |

NOTE. For groups, NVHAP was the comparison group.
*CI*, confidence Interval of the coefficient; *LL*, lower limit; *NVHAP*, nonventilator hospital-acquired pneumonia; *UL*, upper limit; *VAP*, ventilator-associated pneumonia.
*$P < .001$.

and the group matched on mortality and severity of illness (group 4). Because our matching procedure used a combined score that weighted both mortality risk and illness severity equally, it is possible that the influence of NV-HAP may not have been adequately accounted for in the illness severity rating.

We were not able to look at the hospital all-cause readmission rates specifically for our NV-HAP cases because all-cause readmission is not part of the 2012 HCUP-NIS dataset. For patients with pneumonia, in 2012 all-cause readmission was 15.7.[24] Beginning in 2013, HCUP has created a national readmissions database that is available for use by researchers. Data on hospital all-cause readmissions, especially between NV-HAP and pneumonia as admitting diagnosis groups, would have provided additional context regarding the overall health care costs associated with NV-HAP.

## DISCUSSION

Empirical data that detail the current incidence, risk, and outcomes associated with NV-HAP are beginning to emerge.[25] Data support that risk factors do exist for NV-HAP, some of which include age, immunocompromised status, intensive care unit admission, prolonged duration of intensive care unit or hospital stay, illness severity, underlying chronic lung disorders, and comorbid health conditions.[16,26-30] However, Quinn et al[15] found NV-HAP in patients with few to no risk factors, including patients on maternity wards and healthy young adults. Given this finding, the identification of patients with NV-HAP presents a challenge for both researchers and clinicians due to the dispersion of cases throughout all clinical areas of the hospital. To optimize the identification and prevention of NV-HAP, it is important for clinicians to understand that every acute care patient has some risk; there are simply no patients without risk.

We found that after adjusting for other demographic and clinical variables (Table 2), the total hospital charges, hospital LOS, and odds of death for the NV-HAP group were significantly higher than all comparison groups, except those patients with VAP.

Even with the limitations associated with secondary analyses, our findings on the overall incidence of 1.6% (3.63 per 1,000 patient-days) are similar to reports by other researchers. Reported incidence ranges from 0.49-2.12 per 100 patients and 1.25-5.9 per 1,000 patient-days.[15,31] Additional hospital days associated with NV-HAP range from 4-15.9 days.[17,32] Reported estimated NV-HAP acute care costs range from $28,000-$40,000.[4,14,26] Although we reported total hospital charges as provided by using the 2012 HCUP median cost-to-charge ratio of 30%, our estimated acute care cost be $39,897, again consistent with other published research. Furthermore, because of the higher incidence of NV-HAP compared with VAP, the overall cost of NV-HAP was much higher, a finding also consistent with previous research.[14]

Our mortality rate of 13.1% is consistent with the NV-HAP mortality ranges of 13.9%-30% reported by other researchers.[4,14,17,33,34] Although the odds of death for patients with NV-HAP were significantly lower than patients with VAP, the absolute number of patient deaths from NV-HAP in our sample was 15,593 compared with 631 patients with VAP. Thus, the overall mortality influence associated with NV-HAP was much greater than VAP, a finding consistent with previous research.[14]

When comparing the differences between transfer-in and transfer-out status (Table 1), patients with NV-HAP had the greatest overall need for postdischarge care. Although a higher percentage of VAP patients required transfer out to another health care facility, the absolute number of VAP patients was only 1,764 compared with 44,407 patients with NV-HAP. For patients with NV-HAP, 5.5% were transferred in from another type of health care facility, whereas 37.3% were transferred out to another health care facility, the cost of which is not included in our analyses.

## CONCLUSIONS

The hidden harm from NV-HAP in acute care is a significant patient safety issue. Our study describes the substantial influence of NV-HAP on health care use, costs, and patient morbidity and mortality. Currently, NV-HAP is not widely monitored as a preventable HAI because hospitals are not required to report or implement standards to decrease the incidence of NV-HAP. Findings from our study indicate that more national epidemiologic data are needed to further define the scope and influence of NV-HAP.

Finally, pragmatic studies are needed to determine the safest and most effective methods for NV-HAP prevention. In the meantime, hospitals can and should monitor NV-HAP rates and use the current, best-available evidence for NV-HAP prevention.

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