ORIGINAL ARTICLE

Outcomes of Patients with Healthcare-Associated Pneumonia: Worse Disease or Sicker Patients?

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BACKGROUND. Healthcare-associated pneumonia (HCAP) is an entity distinct from community-acquired pneumonia (CAP). HCAP has a higher case-fatality rate, due either to HCAP organisms or to the health status of HCAP patients. The contribution of HCAP criteria to case-fatality rate is unknown.

METHODS. We conducted a retrospective review of adult patients admitted with a diagnosis of pneumonia from July 2007 through November 2011 to 491 US hospitals. HCAP was defined as having at least 1 of the following: prior hospitalization within 90 days, hemodialysis, admission from a skilled nursing facility, or immune suppression. We compared characteristics of patients with CAP and patients with HCAP and explored the contribution of HCAP criteria to case-fatality rate in a hierarchical generalized linear model.

RESULTS. Of 436,483 patients hospitalized with pneumonia, 149,963 (34.4%) had HCAP. Compared to CAP patients, HCAP patients were older, had more comorbidities, and were more likely to require intensive care unit (ICU) care. In-hospital case-fatality rate was higher among patients with HCAP, compared to those with CAP (11.1% vs 5.1%, $P < .001$). After adjustment for demographics, comorbidities, presence of other infections, early ICU admission, chronic and acute medications, early tests and therapies, and length of stay, HCAP remained associated with increased case-fatality rate (odds ratio [OR], 1.35 [95% confidence interval (CI), 1.32–1.39]); odds of death increased for each additional HCAP criterion (OR [95% CI]: 1 criterion, 1.27 [1.23–1.31], 2 criteria, 1.55 [1.49–1.62], and 3 or more criteria, 1.88 [1.72–2.06]).

CONCLUSIONS. After adjustment for differences in patient characteristics, HCAP was associated with greater case-fatality rate than CAP. This difference may be due to HCAP organisms or to HCAP criteria themselves.

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Pneumonia is the eighth-leading cause of death in the United States,[1] with a case-fatality rate that is estimated to be between 4% and 10%.[2] Pneumonia can be categorized by the conditions under which it develops: community acquired (CAP), hospital acquired (HAP), and ventilator associated (VAP). In 2005, the American Thoracic Society and the Infectious Diseases Society of America jointly published guidelines[3] for the management of a distinct group of patients with recent exposure to the healthcare system who are at increased risk of harboring multidrug-resistant organisms (MDROs). Healthcare-associated pneumonia (HCAP) is identified by the following criteria: hemodialysis, admission to an acute care hospital in the prior 90 days, residence in a skilled nursing facility (SNF), home infusion or wound care therapy, family members with MDRO, and immune suppression. The distinction of HCAP is important because, although these patients develop pneumonia while living in the community, their outcomes more closely resemble those of HAP or VAP than those of CAP, and it is recommended that they be treated empirically for MDRO infection.[4]

Previous studies have shown that patients with HCAP comprise a heterogeneous population with varying rates of MDRO infection.[5] It is not known, however, whether outcomes vary according to the setting in which HCAP is acquired. Studies have also shown that outcomes for patients with HCAP are worse than outcomes for patients with CAP, but it is not clear whether this difference is due to a more virulent infection, inappropriate antimicrobial coverage, or simply the higher comorbidity burden among the chronically ill who are susceptible to HCAP.

Using a national database from 491 US hospitals, we examined a large cohort of pneumonia patients. We aimed to assess the degree to which comorbidities and presenting severity of illness explain the higher case-fatality rate seen

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among HCAP patients, compared to CAP patients, and to assess the effect that the specific HCAP criteria have on outcomes of HCAP patients.

METHODS

Setting and Patients

We used Premier's inpatient database, which was developed for measuring healthcare quality and utilization and is frequently used for health services research.[6,7] The database contains a date-stamped log of all items and services charged to the patient or insurer, including medications, laboratory tests, and procedures, as well as all elements derived from the uniform billing 04 (UB-04) form, such as sociodemographics, ICD-9-CM (*International Classification of Diseases, Ninth Revision, Clinical Modification*) diagnosis codes, and hospital and physician information. Premier member hospitals are drawn from all regions of the United States and are generally reflective of US acute care hospitals, with slight overrepresentation of larger hospitals, the southern region, and urban facilities. This study was submitted to the institutional review board at Baystate Medical Center and deemed not "human subjects research," as the Premier data are deidentified.

We identified all adult (age ≥18 years) patients admitted with pneumonia to participating hospitals between July 1, 2007, and November 30, 2011. Cases were identified by an ICD-9-CM principal-diagnosis code of pneumonia or a secondary-diagnosis code of pneumonia paired with a principal diagnosis of respiratory failure, acute respiratory distress syndrome, respiratory arrest, sepsis, or influenza; in addition, each patient had to undergo a chest radiograph and receive antimicrobials by the second hospital day. We excluded patients who were transferred in from or out to other acute care facilities because we could not assess their antimicrobial therapy or outcomes. We also excluded patients with a length of stay of 1 day or less, patients with cystic fibrosis, those whose attending physician of record was in a specialty that would not be expected to treat pneumonia (eg, psychiatry), those whose diagnosis-related group was inconsistent with pneumonia, and those with pneumonia clearly designated as "not present on admission."

Patients were considered to have HCAP if they were admitted from an SNF or a long-term care facility, had been hospitalized in the previous 90 days, were dialysis patients, or were receiving immunosuppressing medications, such as chemotherapy or steroids, equivalent to at least 20 mg of prednisone per day. We did not assess for family members with MDRO colonization or patients on home infusion therapy because markers for these conditions were not available in the database. Patients who did not meet any of the HCAP criteria were classified as having CAP.

Demographics and Comorbidities

For each patient, we extracted age, sex, race/ethnicity, insurance status, principal diagnosis, and specialty of the attending physician. Using software provided by the Healthcare Costs and Utilization Project of the Agency for Healthcare Research and Quality (ver. 3.1), we recorded the presence of comorbid conditions.[8] We also created a numerical comorbidity summary score based on the work of Gagne et al.[9]

Diagnostic Testing and Treatments

We identified acute medications, such as antimicrobials, vasopressors, and steroids, and therapies, such as mechanical ventilation and blood transfusions. We assessed whether patients were able to take oral medication on hospital day 1 or 2 by the administration of medications that are available only in oral preparations. We also examined use of diagnostic testing, such as bronchoscopy, *Legionella*/*Mycoplasma* testing, blood cultures, arterial blood gas, and serum lactate, as well as early (hospital day 1 or 2) intensive care unit (ICU) admission, use of vasopressors, invasive mechanical ventilation (IMV), or noninvasive ventilation (NIV). A full list of the variables assessed has been published elsewhere.[10]

Outcomes

Outcomes included in-hospital case-fatality rate; late (day 3+) initiation of IMV, NIV, or vasopressors; hospital length of stay; cost of hospitalization; and discharge disposition.

Analysis

Summary statistics are presented as frequencies and percentages for categorical variables and as medians with interquartile ranges for continuous variables. Associations between patient demographics, clinical characteristics, and HCAP/CAP status are assessed with χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables.

To predict the case-fatality rate for each patient, we constructed a hierarchical generalized linear model (SAS GLIMMIX) with a random hospital effect, using a logit link that included demographics, comorbidities, medications (excluding antimicrobials), and treatments administered in the first 2 days of hospitalization.[10] This model had good discrimination (*c* statistic, 0.86) and calibration. We then adjusted for the patient's length of stay and added an indicator of HCAP status to this model to assess its additional value in predicting death. In additional models, we explored the independent contribution of individual HCAP criteria to case-fatality rate. Finally, we assessed the independent effect of HCAP versus CAP on the following secondary outcomes: all-cause readmissions, late ICU admission, late IMV, length of stay, and cost. This was done with multivariable hierarchical generalized linear models, as described above, but not adjusted for length of stay. Length of stay and cost were trimmed at 3 standard deviations above the mean, and natural log–transformed values were modeled to account for extreme positive skew. Binary outcome models were assessed via logit link, and identity link models were used for continuous outcome models.

All tests were 2-sided, with a significance level of 0.05. All analyses were performed in the Statistical Analysis System (ver 9.3, SAS Institute) and STATA (release 12, StataCorp).

RESULTS

Patient Characteristics and Severity of Illness

After exclusions, we identified 436,483 eligible patients from 491 hospitals (Figure 1). Among these, 149,963 (34.4%) were identified as HCAP patients and 286,520 (65.6%) as CAP patients. HCAP patients were older (median age, 73 vs 70 years, $P < .001$), had a higher comorbidity burden (combined comorbidity score, 4 vs 2, $P < .001$), and were more likely to have a principal diagnosis of sepsis/respiratory failure (38% vs 25%, $P < .001$) than CAP patients (Table 1). Of all patients, 112,071 (25.7%) met only 1 criterion for HCAP, 33,380 (7.7%) met 2 criteria for HCAP, and 4,512 (1.0%) met 3 or more criteria for HCAP. HCAP patients were more likely than CAP patients to be initially admitted to an ICU (25% vs 16%) and to be treated with norepinephrine (9.8% vs 3.8%) or IMV (14% vs 8%).

Outcomes

Unadjusted outcomes for patients with HCAP and CAP appear in Table 1. HCAP patients had a higher case-fatality rate (11.1% vs 5.1%), longer length of stay, and higher costs. They were also more likely to require late (day 3 or later) admission to the ICU (4.7% vs 3.1%, $P < .001$) and IMV. Finally, discharge disposition was significantly different between HCAP and CAP groups. HCAP patients were more likely to be discharged to an SNF (31.2% vs 16.8%) or hospice (5.7% vs 2.7%) and had more all-cause readmission (13.8% vs 7.3%, $P < .001$) than CAP patients.

After adjustment for demographics, comorbidities, length of stay, need for initial ICU admission, ability to take oral medications, chronic and acute medications, and early tests and procedures to indicate more severely ill patients, the odds ratio (OR) of in-hospital death remained higher among HCAP patients than among CAP patients (OR, 1.35 [95% confidence interval (CI), 1.32–1.39]). Adjustment for these same factors minus length of stay also attenuated, but did not extinguish, differences in length of stay, cost, and readmission (Figure 2).

Among the different HCAP subgroups (Table 2), the adjusted case-fatality rate was highest for patients undergoing hemodialysis (OR, 1.71 [95% CI, 1.58–1.86]) and lowest for patients who were immune suppressed (OR, 1.21 [95% CI, 1.15–1.27]; Figure 3). Reducing the HCAP criteria to an admission within the past 30 days did not affect the adjusted case-fatality rate for HCAP versus CAP (OR. 1.27 [95% CI,

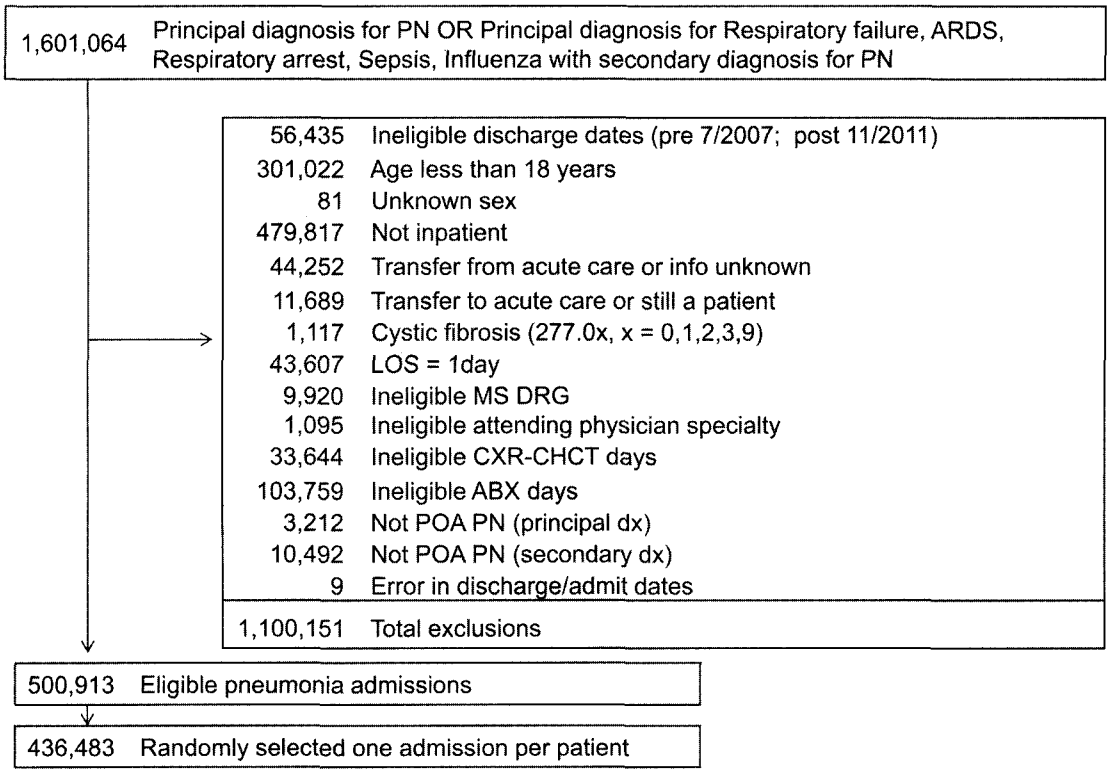

FIGURE 1. Patient selection flow chart. ABX, antimicrobial; ARDS, acute respiratory distress syndrome; CHCT, chest computed tomography; CXR, chest X-ray; dx, diagnosis; LOS, length of stay; MS DRG, Medicare severity diagnosis-related group; PN, pneumonia; POA, present on admission.

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TABLE 1. Demographics, Comorbidities, Tests, and Procedures among Patients with CAP and HCAP

Characteristic	Overall	CAP	HCAP	CAP vs HCAP, *P* (2-sided)[a]
Total patients	436,483 (100)	286,520 (65.6)	149,963 (34.4)	
Age, median (IQR), years	71 (57–82)	70 (56–82)	73 (61–83)	<.001[b]
Sex				<.001
Female	230,810 (52.9)	153,737 (53.7)	77,073 (51.4)	
Male	205,673 (47.1)	132,783 (46.3)	72,890 (48.6)	
Race/ethnicity				<.001
White	305,994 (70.1)	201,616 (70.4)	104,378 (69.6)	
Black	50,030 (11.5)	31,068 (10.8)	18,962 (12.6)	
Hispanic	18,031 (4.1)	12,249 (4.3)	5,782 (3.9)	
Other	62,428 (14.3)	41,587 (14.5)	20,841 (13.9)	
Marital status				<.001
Married	169,252 (38.8)	113,196 (39.5)	56,056 (37.4)	
Single	225,891 (51.8)	145,983 (51)	79,908 (53.3)	
Other/missing	41,340 (9.5)	27,341 (9.5)	13,999 (9.3)	
Insurance payor				<.001
Medicare	298,338 (68.4)	184,100 (64.3)	114,238 (76.2)	
Medicaid	36,233 (8.3)	24,143 (8.4)	12,090 (8.1)	
Managed care	55,512 (12.7)	42,016 (14.7)	13,496 (9)	
Commercial indemnity	16,198 (3.7)	11,858 (4.1)	4,340 (2.9)	
Other	30,202 (6.9)	24,403 (8.5)	5,799 (3.9)	
Discharge disposition				<.001
Home	223,938 (51.3)	171,613 (59.9)	52,325 (34.9)	
Home health	60,505 (13.9)	38,910 (13.6)	21,595 (14.4)	
Hospice	16,267 (3.7)	7,736 (2.7)	8,531 (5.7)	
Other	9,315 (2.1)	5,331 (1.9)	3,984 (2.7)	
Expired	31,421 (7.2)	14,715 (5.1)	16,706 (11.1)	
SNF/ICF	95,037 (21.8)	48,215 (16.8)	46,822 (31.2)	
Comorbidities				
Combined comorbidity score, median (IQR)	2 (1–5)	2 (1– 4)	4 (2–6)	<.001[b]
Congestive heart failure	118,502 (27.1)	64,920 (22.7)	53,582 (35.7)	<.001
Valvular disease	38,544 (8.8)	19,126 (6.7)	19,418 (12.9)	<.001
Peripheral vascular disease	34,228 (7.8)	18,973 (6.6)	15,255 (10.2)	<.001
Hypertension	267,204 (61.2)	169,505 (59.2)	97,699 (65.1)	<.001
Neurological disorders	59,454 (13.6)	35,501 (12.4)	23,953 (16)	<.001
Chronic pulmonary disease	210,309 (48.2)	139,302 (48.6)	71,007 (47.3)	<.001
Diabetes	139,020 (31.9)	84,112 (29.4)	54,908 (36.6)	<.001
Hypothyroidism	66,322 (15.2)	41,282 (14.4)	25,040 (16.7)	<.001
Metastatic cancer	17,363 (4)	8,745 (3.1)	8,618 (5.7)	<.001
Obesity	49,389 (11.3)	34,424 (12)	14,965 (10)	<.001
Weight loss	44,532 (10.2)	24,052 (8.4)	20,480 (13.7)	<.001
Anemia	137,978 (31.6)	76,611 (26.7)	61,367 (40.9)	<.001
Depression	59,646 (13.7)	37,660 (13.1)	21,986 (14.7)	<.001
End-stage renal disease	38,895 (8.9)	22,750 (7.9)	16,145 (10.8)	<.001
Principal diagnosis				<.001
Pneumonia/influenza	306,465 (70.2)	213,697 (74.6)	92,768 (61.9)	
Sepsis	96,211 (22)	52,295 (18.3)	43,916 (29.3)	
Respiratory failure/arrest	33,807 (7.7)	20,528 (7.2)	13,279 (8.9)	
Urinary tract infection	61,850 (14.2)	34,583 (12.1)	27,267 (18.2)	<.001
Treatments or tests on hospital day 1 or 2				
ICU	81,388 (18.6)	44,563 (15.6)	36,825 (24.6)	<.001
IMV	44,590 (10.2)	23,308 (8.1)	21,282 (14.2)	<.001
NIV	39,323 (9)	22,699 (7.9)	16,624 (11.1)	<.001
Vasopressors				

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TABLE 1 (*Continued*)

Characteristic	Overall	CAP	HCAP	CAP vs HCAP, *P* (2-sided)[a]
Dopamine	14,952 (3.4)	6,884 (2.4)	8,068 (5.4)	<.001
Norepinephrine	25,596 (5.9)	10,889 (3.8)	14,707 (9.8)	<.001
Other[c]	11,667 (2.7)	4,886 (1.7)	6,781 (4.5)	<.001
Loop diuretics	123,383 (28.3)	72,569 (25.3)	50,814 (33.9)	<.001
Insulin	119,467 (27.4)	70,989 (24.8)	48,478 (32.3)	<.001
Arterial or venous blood gas	168,496 (38.6)	102,618 (35.8)	65,878 (43.9)	<.001
Blood lactate level	104,538 (24)	60,534 (21.1)	44,004 (29.3)	<.001
Foley catheter	54,166 (12.4)	31,024 (10.8)	23,142 (15.4)	<.001
Outcomes				
In-hospital case-fatality rate	31,421 (7.2)	14,715 (5.1)	16,706 (11.1)	<.001
All-cause readmission (30 days)	38,128 (9.4)	19,795 (7.3)	18,333 (13.8)	<.001
Late ICU[d] (day 3+)	12,780 (3.6)	7,489 (3.1)	5,291 (4.7)	<.001
Late IMV[d] (day 3+)	15,905 (4.1)	9,097 (3.5)	6,808 (5.3)	<.001
Length of stay, median (IQR), days	5 (3–8)	5 (3–7)	6 (4–10)	<.001[b]
Cost, median (IQR), US $	7,906 (4,900–14,263)	7,005 (4,489–12,204)	10,049 (6,080–18,309)	<.001[b]

NOTE. Data are no. (%) of patients unless otherwise indicated. CAP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; ICF, intermediate care facility; ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; NIV, noninvasive ventilation; SNF, skilled nursing facility.

[a] Except as indicated, *P* value based on χ^2 test.

[b] *P* value based on Kruskal-Wallis test.

[c] Includes vasopressin, epinephrine, and phenylephrine.

[d] Among patients who were not treated early (days 0–2).

1.24–1.31]). Presence of multiple HCAP criteria increased the odds of death. For each additional criterion, the adjusted case-fatality rate increased by about 3%.

DISCUSSION

In this large retrospective cohort study of patients with HCAP and CAP, we observed that the risk of death was higher among HCAP patients than among CAP patients even after we adjusted for multiple markers of comorbid illness, indicating that HCAP carries a case-fatality rate that appears to be independent of comorbidities. HCAP patients were also sicker on admission, but even after adjustment for initial treatments—a measure of severity of illness that accurately predicts inpatient outcomes[10]—they still had a higher case-fatality rate. This difference in case-fatality rate between the two groups may be due to more virulent or resistant organisms or to additional unmeasured confounders. Finally, we found that with each additional HCAP criterion, the absolute adjusted case-fatality rate increased by approximately 3%.

Since HCAP was first described as a unique entity almost a decade ago,[11] a number of studies have compared HCAP to CAP in hospitalized patients.[2,11-17] Most studies include several hundred patients at a single institution. The largest study to date was conducted at 59 US hospitals and included 3,209 patients with culture-proven pneumonia, 31% of whom had HCAP.[11] Mortality was 19.8% for HCAP and 10.0% for CAP patients. After adjustment for age and physiologic derangements associated with mortality, the OR for mortality with HCAP, compared to that with CAP, was 1.65. The increased mortality was attributed at least in part to infection with more severe organisms, in particular methicillin-resistant *Staphylococcus aureus* (MRSA), which was isolated in 27% of HCAP cases. *Pseudomonas* was isolated from an additional 25% of patients. A more recent study conducted at

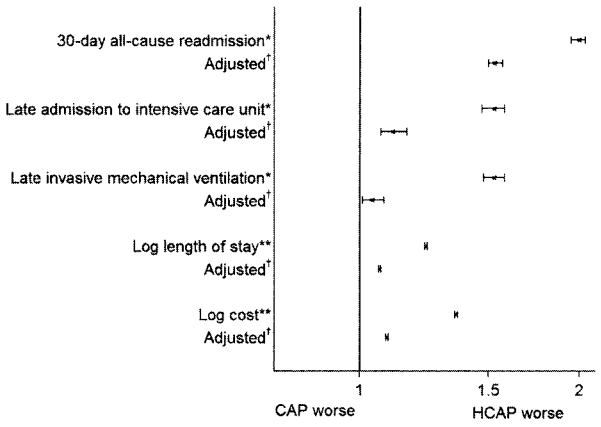

FIGURE 2. Odds ratios and risk ratios for HCAP, compared to CAP, for secondary outcomes. All analyses account for clustering of patients in hospitals. *Odds ratio (95% confidence interval [CI]). †Adjusted for patient demographics, comorbidities, medications, and treatments in first 2 days of hospitalization. **Risk ratio (95% CI). CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia.

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TABLE 2. Early Treatments and Outcomes by HCAP Criteria

	Admitted from SNF	Hemodialysis	Hospitalized within past 90 days	Immune suppressed	2 or more components
Total patients	14,667 (3.4)	9,110 (2.1)	60,685 (13.9)	27,609 (6.3)	37,892 (8.7)
Early treatments					
Early IMV	2,112 (14.4)	1,355 (14.9)	6,443 (10.6)	4,659 (16.9)	6,713 (17.7)
Early NIV	1,426 (9.7)	887 (9.7)	7,170 (11.8)	2,633 (9.5)	4,508 (11.9)
Early vasopressors					
Dopamine	562 (3.8)	517 (5.7)	2,087 (3.4)	2,200 (8.0)	2,702 (7.1)
Norepinephrine	963 (6.6)	889 (9.8)	3,104 (5.1)	4,566 (16.5)	5,185 (13.7)
Other[a]	358 (2.4)	421 (4.6)	1,350 (2.2)	2,248 (8.1)	2,404 (6.3)
Early admission to ICU	3,179 (21.7)	2,246 (24.7)	12,010 (19.8)	8,218 (29.8)	11,172 (29.5)
Outcomes					
Late IMV (day 3+)[b]	457 (3.6)	449 (5.8)	2,418 (4.5)	1,397 (6.1)	2,087 (6.7)
Late NIV (day 3+)[b]	602 (4.6)	428 (5.2)	3,021 (5.7)	1,557 (6.2)	2,293 (6.9)
Late vasopressors[b]					
Dopamine	171 (1.2)	266 (3.1)	864 (1.5)	500 (2.0)	864 (2.5)
Norepinephrine	291 (2.1)	407 (5.0)	1,369 (2.4)	822 (3.6)	1,397 (4.3)
Other[a]	316 (2.2)	533 (6.1)	1,772 (3.0)	1,162 (4.6)	1,814 (5.1)
Late admission to ICU (day 3+)[b]	338 (2.9)	381 (5.6)	2,036 (4.2)	1,019 (5.3)	1,517 (5.7)
Length of stay, median (IQR), days	6 (4–9)	6 (3–10)	6 (4–9)	6 (4–10)	7 (4–11)
Cost, median (IQR), US $	9,113 (5,748–15,970)	10,601 (6,340–20,837)	9,044 (5,663–15,572)	10,137 (5,873–20,093)	12,284 (7,292–22,268)
Discharge disposition					
Home	1,392 (9.5)	4,836 (53.1)	23,700 (39.1)	14,261 (51.7)	8,136 (21.5)
Home health	589 (4.0)	1,184 (13.0)	11,724 (19.3)	4,022 (14.6)	4,076 (10.8)
Hospice	836 (5.7)	214 (2.4)	3,863 (6.4)	1,001 (3.6)	2,617 (6.9)
SNF/ICF	9,959 (67.9)	1,691 (18.6)	14,427 (23.8)	4,501 (16.3)	16,244 (42.9)
Expired	1,483 (10.1)	967 (10.6)	5,419 (8.9)	3,138 (11.4)	5,699 (15.0)
Other	408 (2.8)	218 (2.4)	1,552 (2.6)	686 (2.5)	1,120 (3.0)

NOTE. Data are no. (%) of patients unless otherwise indicated. HCAP, healthcare-associated pneumonia; ICF, intermediate care facility; ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; NIV, noninvasive ventilation; SNF, skilled nursing facility.

[a] Includes vasopressin, epinephrine, and phenylephrine.

[b] Each of these outcomes is assessed among patients who were not treated early (days 0–2).

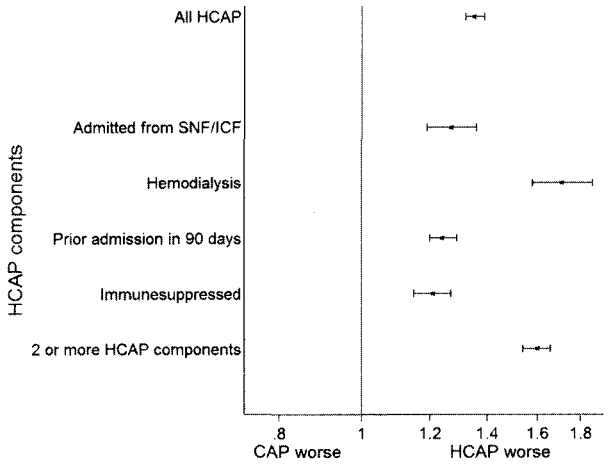

FIGURE 3. Odds ratios (95% confidence intervals) for in-hospital death with HCAP, compared to CAP, in a multivariable adjusted model. The model accounts for clustering of patients in hospitals and is adjusted for patient demographics, comorbidities, length of stay, and medications and treatments in first 2 days of hospitalization. CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; ICF, intermediate care facility; SNF, skilled nursing facility.

66 Spanish hospitals found similar case-fatality rates for HCAP as well as high rates of infection with MRSA and *Pseudomonas* sp.[17] Both studies confirmed the need to differentiate HCAP from CAP in prescribing guidelines.

In contrast, a more recent study from the United Kingdom[16] found that although HCAP patients had a 30-day mortality rate more than twice that of CAP patients, after adjustment for baseline pneumonia severity index, comorbidities, and antimicrobial therapy, the odds of mortality with HCAP fell to 1.29 and were no longer significant. With further adjustment for aspiration risk and functional status, the odds of mortality with HCAP were 0.97. However, rates of infection with both MRSA and *Pseudomonas* were low (<2% each). The authors concluded that, for their cohort, there was no need for broad-spectrum antimicrobials for HCAP patients.

In our study, we also found that HCAP was an independent risk factor for death, but after adjustment for multiple comorbidities, the risk associated with a single HCAP criterion was 1.35—similar to that seen in the UK study. However, because of our much larger sample size, the findings were highly significant. This estimate does not include adjustment for direct measures of aspiration risk or functional status, but we did adjust for comorbidities and treatments that are surrogate markers for both aspiration risk and functional status, including paralysis, neurological disorders, tube feeds, medications for Alzheimer's and Parkinson's diseases, nutritional supplements, appetite stimulants, use of restraints, antipsychotic medications, and Foley catheters, all of which were significantly more common among HCAP patients. The excess case-fatality rate associated with HCAP and the fact that patients who met multiple HCAP criteria had an even higher case-fatality rate imply that HCAP may be caused by the more virulent pathogens encountered in the healthcare environment. However, because we did not have access to microbiology data, we were unable to ascertain whether the differences in case-fatality rate were due to specific organisms or to inappropriate initial antimicrobial coverage.[18] Moreover, we cannot exclude the possibility of residual confounding due to functional status or advanced directives.

Our study adds to the findings of previous studies in several ways. First, we examined more than 400,000 patients at almost 500 hospitals that are broadly representative of US hospitals as a whole. This large sample allowed us to adjust for numerous patient comorbidities to better isolate the effects of HCAP on case-fatality rate, complications, cost, length of stay, and readmissions. We found that HCAP patients were fundamentally different from CAP patients in terms of demographics, comorbidities, and medications and treatments received in the hospital. After adjustment for these, HCAP was still strongly associated with increased risk of death and readmission, but less so for complications of pneumonia, length of stay, and cost. The effect on readmissions has been noted by others in a small, single-institution cohort.[19] Second, this is the first study that we are aware of to describe the relationship between the number of HCAP criteria and the case-fatality rate. Each additional criterion appears to increase the adjusted case-fatality rate by 3%. This is similar to the finding by Maruyama et al[20] that patients with 2 or more multidrug-resistant risk factors have higher 30-day mortality than those with 1 risk factor or none. Finally, we were able to compare the effects of the different HCAP criteria on case-fatality rate and found that hemodialysis is a stronger predictor of death than other HCAP factors. Whether the risk of hemodialysis is due to repeated exposures to resistant organisms or due to hemodialysis itself cannot be determined from this data set.

There were several limitations to our study. First, the data are derived from administratively coded ICD-9-CM diagnoses rather than from clinical data or individual chart review. We did require supporting evidence of pneumonia based on chest radiographs and the administration of antimicrobials, but it is possible that some patients in our sample did not have pneumonia. It is also possible that some CAP patients actually had HCAP, but we were unable to obtain their exposure status in our database (eg, if they had been previously hospitalized at a non-Premier hospital or if they were admitted from an SNF but the admission source was recorded as the emergency department). In contrast, our specificity for HCAP was high, because exposure is determined by admission from an SNF, hemodialysis, or recent admission, all of which are reliable if present. We may also have missed cases of HCAP if they were coded as aspiration pneumonitis (ICD-9-CM code 507.0) rather than as pneumonia. These cases would have been excluded rather than misclassified in our data set. We did not have access to microbiologic results, so we were unable to

determine whether the increased case-fatality rate from HCAP was due to antimicrobial-pathogen mismatching or to more virulent organisms. Similarly, we did not have access to advanced directives, which may have been more common among HCAP patients and could have influenced the intensity of care. Although HCAP patients in general were more likely than CAP patients to be admitted to intensive care, individual HCAP patients may have chosen to forego life-sustaining therapy. Finally, our mortality outcome was limited to inpatient case-fatality rate. However, it is unlikely that other measures of mortality, such as 30-day mortality, would yield a lower relative risk associated with HCAP, as HCAP patients had more comorbid illness and would therefore be more likely to die within 30 days than CAP patients.

In conclusion, we found that HCAP patients had outcomes that were worse than those of CAP patients, even after adjustment for comorbidities and presenting severity of illness, although the difference appears to be less than has been observed by others. The difference might be due to the specific HCAP organisms or to unmeasured confounders such as functional status or do-not-resuscitate orders. Patients who met multiple HCAP criteria appear to be at highest risk for death and might be expected to benefit most from broad-spectrum empirical antimicrobials. Further studies are required to determine the extent to which antimicrobial resistance contributes to the increased case-fatality rate associated with HCAP in the United States.

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