Descriptive Epidemiology and Outcomes of Nonventilated Hospital-Acquired, Ventilated Hospital-Acquired, and Ventilator-Associated Bacterial Pneumonia in the United States, 2012–2019

OBJECTIVES: Multiple randomized controlled trials exploring the outcomes of patients with ventilator-associated bacterial pneumonia and hospital-acquired bacterial pneumonia have noted that hospital-acquired bacterial pneumonia patients who require subsequent ventilated hospital-acquired bacterial pneumonia suffered higher mortality than either those who did not (nonventilated hospital-acquired bacterial pneumonia) or had ventilator-associated bacterial pneumonia. We examined the epidemiology and outcomes of all three conditions in a large U.S. database.

DESIGN: Retrospective cohort.

SETTING: Two hundred fifty-three acute-care hospitals, United States, contributing data (including microbiology) to Premier database, 2012–2019.

PATIENTS: Patients with hospital-acquired bacterial pneumonia or ventilator-associated bacterial pneumonia identified based on a slightly modified previously published International Classification of Diseases, 9th Edition/International Classification of Diseases, 10th Edition-Clinical Modification algorithm.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Among 17,819 patients who met enrollment criteria, 26.5% had nonventilated hospital-acquired bacterial pneumonia, 25.6% vHAPB, and 47.9% ventilator-associated bacterial pneumonia. Ventilator-associated bacterial pneumonia predominated in the Northeastern United States and in large urban teaching hospitals. Patients with nonventilated hospital-acquired bacterial pneumonia were oldest (mean 66.7 ± 15.1 yr) and most likely White (76.9%), whereas those with ventilator-associated bacterial pneumonia were youngest (59.7 ± 16.6 yr) and least likely White (70.3%). Ventilated hospital-acquired bacterial pneumonia was associated with the highest comorbidity burden (mean Charlson score 4.1 ± 2.8) and ventilator-associated bacterial pneumonia with the lowest (3.2 ± 2.5). Similarly, hospital mortality was highest among patients with ventilated hospital-acquired bacterial pneumonia (29.2%) and lowest in nonventilated hospital-acquired bacterial pneumonia (11.7%), with ventilator-associated bacterial pneumonia in-between (21.3%). Among survivors, 24.5% of nonventilated hospital-acquired bacterial pneumonia required a rehospitalization within 30 days of discharge, compared with 22.5% among ventilated hospital-acquired bacterial pneumonia and 18.8% ventilator-associated bacterial pneumonia. Unadjusted hospital length of stay after infection onset was longest among ventilator-associated bacterial pneumonia and shortest among nonventilated hospital-acquired bacterial pneumonia patients. Median total hospital costs mirrored length of stay: ventilator-associated bacterial pneumonia 460
pneumonia $77,657, ventilated hospital-acquired bacterial pneumonia $62,464, and nonventilated hospital-acquired bacterial pneumonia $39,911.

**CONCLUSIONS:** Both hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia remain associated with significant mortality and cost in the United States. Our analyses confirm that of all three conditions, ventilated hospital-acquired bacterial pneumonia carries the highest risk of death. In contrast, ventilator-associated bacterial pneumonia remains most costly. Nonventilated hospital-acquired bacterial pneumonia survivors were most likely to require a readmission within 30 days of discharge.

**KEY WORDS:** costs; epidemiology; hospital; nosocomial pneumonia; outcomes

Nosocomial pneumonia (NP) is one of the most common hospital-acquired infections (HAIs). Comprising hospital-acquired and ventilator-associated (VAP) pneumonias, NP accounts for 22% of all HAIs, leads to significant antibiotic use, and is associated with substantial morbidity and mortality (1).

Evidence suggests that ventilated hospital-acquired bacterial pneumonia (vhHABP) differs from nonventilated hospital-acquired bacterial pneumonia (nvHABP). Namely, an analysis of multiple randomized controlled trials exploring the outcomes of patients with ventilator-associated bacterial pneumonia (VABP) and hospital-acquired bacterial pneumonia (HABP) found that those with vhHABP consistently faced higher mortality than those with either nvHABP or VABP (2). Because the analysis was limited to highly regimented randomized controlled trials and performed specifically for the purpose of improving regulatory study designs, it left many questions unanswered. Specifically, it is unclear what patient, infection, and treatment factors may contribute to these disparities (3–10). Additionally, the trials examined were performed over a decade ago, raising the possibility that an evolution in both microbiology and bedside management makes these observations outdated. Though slightly more generalizable, the same can be said for a single-center prospective cohort study from Europe, also conducted over a decade ago, whose findings suggest differences between these entities (11).

ICU practice has evolved dramatically since the previous reports were published. Over the past 15 years, HAIs, in general, and VABP, in particular, have become targets for concerted efforts at eradication, with zero incidence as the goal (12). Although clinicians agree that zero is not a realistic target across the board, efforts at eliminating nosocomial infections have resulted in practice alterations, bearing fruit in such settings as central line-associated infections (13). Unfortunately, the results in VABP have been less convincing (12).

There is a paucity of real-world data describing the current landscape of VABP in the United States, as well little information to clarify the differences among VABP, nvHABP, and vhHABP. Indeed, a 2020 review identified major gaps in our understanding of these entities (14). We recently developed an algorithm for identifying the first episodes of HABP and VABP among hospitalized patients in administrative databases and applied it to a large multicenter U.S. database to explore these conditions and answer these important questions (15).

**MATERIALS AND METHODS**

**Ethics Statement**

Because this study used already-existing fully deidentified data, it was exempt from ethics review under U.S. 45 Code of Federal Regulations 46.101(b)4 (16).

**Study Design and Patient Population**

We conducted a multicenter retrospective cohort study of hospitalized patients with culture-positive nvHABP, vhHABP, or VABP to explore their epidemiology and outcomes. The case identification approach relied on a slight modification of a previously published algorithm (15).

Patients were included if they were adults (age ≥ 18 yr) whose pneumonia diagnosis appeared in a secondary position, whose index respiratory, and/or blood culture had to be obtained on hospital day 3 or later for HABP, or on mechanical ventilation (MV) day 3 or later for VABP, and who were treated with an antibiotic on the day of the index culture and for the next greater than or equal to 3 consecutive days. Patients with the principal diagnosis of pneumonia or one present at admission were excluded, as were those with hospital length of stay (LOS) less than 4 days, whose positive respiratory or blood culture was obtained prior to hospital day 3 for HABP or prior to MV day 3 for VABP, those transferred from another acute care facility, and those whose HABP/VABP episode was a repeat bout during the index hospitalization, as
evidenced by a greater than or equal to 3-day hiatus in pneumonia-specific antimicrobial regimen administration and a new positive culture. To improve the specificity of HABP/VABP diagnosis, we also excluded patients who fit the definition for either a complicated urinary tract infection (cUTI) or a complicated intra-abdominal infection (cIAI) (17, 18).

Data Source

The data source was the Premier Research database, an electronic laboratory, pharmacy, and billing data repository, for years 2012 through the third quarter of 2019. The database has been described in detail previously (15, 17–21). Approximately 200 U.S. institutions submitted microbiology data during the study time frame.

Baseline Measures and Pneumonia Classification

Pneumonia was defined as HABP if at the time of the index culture the patient was not on MV and VABP if at the time the index culture the patient had been on MV for more than 3 days. HAPB was further subdivided into vHABP and nvHABP. Specifically, vHABP designation was given for patients who needed MV less than or equal to 5 days following the onset of index HABP episode and nvHABP if MV was not required.

In addition to infection classification, patient factors examined included history of exposure to antibiotics within 90 days prior to the index admission, antibiotic exposure during the index hospitalization prior to the onset of HABP/VABP, demographic variables, and comorbid conditions. A Charlson comorbidity score was computed as a measure of the burden of chronic illness, whereas ICU admission, presence of severe sepsis or septic shock, dialysis, and vasopressor use were employed as markers for acute disease severity. We also explored hospital structural characteristics (e.g., size, teaching status, and urbanicity) and processes of care (e.g., choices of antimicrobials). We determined whether each patient’s admission was due to medical or surgical diagnosis. Additionally, we identified trauma diagnoses, as well as whether the patient had suffered an acute neurologic insult (22, 23).

Microbiology

We examined common Gram-positive and Gram-negative pathogens that cause bacterial nosocomial pneumonia (NP). Namely, the Gram-negative organisms of interest were *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*, whereas Gram-positive organisms were *Staphylococcus aureus* (both methicillin-susceptible *S. aureus* [MSSA] and methicillin-resistant *S. aureus* [MRSA]), and *Streptococcus pneumoniae*.

Culture and susceptibility results represented the results as reported by the local microbiology laboratories at the participating hospitals.

Outcome Variables

The primary outcome of interest was hospital mortality. Secondary outcomes included postinfection onset MV duration, postinfection ICU LOS, hospital LOS (total and postinfection onset), hospital costs, discharge destination, and 30-day readmission rates among survivors.

Statistical Analyses

We report descriptive statistics to compare nvHABP, vHABP, and VABP groups across all demographics, comorbidities, infection characteristics, hospital characteristics and processes, and hospital outcomes. Continuous variables are reported as means with standard deviations and as medians with interquartile ranges. Differences between mean values were tested via a one-way analysis of variance test and between medians using the Kruskal-Wallis test. Categorical data are summarized as proportions, with the chi-square test used to examine intergroup differences unless a cell count was less than five, wherein the Fisher exact test was used. *p* values of less than 0.05 were considered statistically significant. We note, however, that because of the large sample size, statistical significance may not indicate clinical significance.

RESULTS

Among 17,819 patients who met enrollment criteria, 26.5% had nvHABP, 25.6% vHAPB, and 47.9% VABP (Table 1). VABP accounted for the majority of pneumonias in the Northeastern United States (54.0%), and in large (55.5%) urban (92.3%) teaching (68.6%) hospitals.

Demographically, patients with nvHABP were oldest (mean 66.7 ± 15.1 yr) and most likely White (76.9%),
whereas those with VABP were youngest (59.7 ± 16.6 yr) and least likely White (70.3%). vHABP was associated with the highest comorbidity burden (mean Charlson score 4.1 ± 2.8) and VABP with lowest (3.2 ± 2.5). Though many individual comorbidities were similarly distributed across the groups, paralysis and neurologic disorders were substantially more common in vHABP than nvHABP, and in VABP than in vHABP (Table S1, http://links.lww.com/CCM/G793). Although obesity was subject to the same pattern, the frequencies were reversed for chronic pulmonary disease and cancer, with the highest prevalence of each in nvHABP.

On average, time to pneumonia onset from admission was longest in nvHABP (10.2 ± 11.2 d) and shortest in VABP (6.5 ± 6.6 d) (Table 1). Acute illness severity was highest in the vHABP group and lowest in the nvHABP, as evidenced by the prevalence of such markers as early vasopressor use, and evidence of severe sepsis or septic shock at any time during hospitalization (Table 1). In contrast, and not surprisingly, patients with VABP were more likely than others to be in the ICU within the first 2 days of infection (95.7%) and nvHABP the least (58.0%). This was inversely proportional to the patient’s code status at admission, with nvHABP group having the highest prevalence of “do-not-resuscitate” orders (8.1%) and VABP the lowest (3.4%) (Table 1).

The most common pathogens that together accounted for over 80% of all pneumonia cases were similar across all pneumonia types, though some of their rankings differed. Although overall S. aureus was the most commonly isolated organism, methicillin-resistant (MRSA) was likeliest in nvHABP and methicillin-susceptible (MSSA) in VABP (Fig. 1). P. aeruginosa was most prevalent in vHABP, and least in VABP. K. pneumoniae and E. coli were the next predominant bacteria isolated with some variation across the conditions. Notably, E. coli was one-third and one-fourth less common in VABP than in vHABP and nvHABP, respectively. A. baumannii, though rare

### Table 1. Hospital Events

| Event/Factor                           | Nonventilated Hospital-Acquired Bacterial Pneumonia | Ventilated Hospital-Acquired Bacterial Pneumonia | Ventilator-Associated Bacterial Pneumonia | p  |
|----------------------------------------|-----------------------------------------------------|-------------------------------------------------|-----------------------------------------|----|
| Time to pneumonia (d)                  |                                                     |                                                 |                                         |    |
| Mean (sd)                              | 10.2 (11.2)                                         | 8.7 (9.0)                                       | 6.5 (6.6)                               | <0.001 |
| Median (IQR)                           | 7 (5–12)                                            | 4 (6, 10)                                       | 4 (3, 8)                                | <0.001 |
| Illness severity measures by day 2     |                                                     |                                                 |                                         |    |
| from infection onset                   |                                                     |                                                 |                                         |    |
| ICU admission                          | 2,742                                               | 4,287                                           | 8,162                                   | <0.001 |
|                                         | 57.99                                               | 93.99%                                          | 95.69                                   | <0.001 |
| Time from hospitalization to ICU       |                                                     |                                                 |                                         |    |
| admission (d)                          |                                                     |                                                 |                                         |    |
| Mean (sd)                              | 5.0 (11.4)                                          | 4.4 (5.7)                                       | 2.1 (3.5)                               | <0.001 |
| Median (IQR)                           | 1 (1–5)                                             | 2 (1–6)                                         | 1 (1, 2)                                | <0.001 |
| Vasopressors                           | 365                                                 | 1,770                                           | 2,103                                   | 24.65 |
| Time from hospitalization to           |                                                     |                                                 |                                         |    |
| vasopressors (d)                       |                                                     |                                                 |                                         |    |
| Mean (sd)                              | 6.0 (6.3)                                           | 6.4 (8.1)                                       | 4.2 (5.2)                               | <0.001 |
| Median (IQR)                           | 5 (2–8)                                             | 5 (2–8)                                         | 2 (1–5)                                 | <0.001 |
| Severe sepsis                          | 627                                                 | 1,166                                           | 1,393                                   | 16.33 |
|                                          | 13.26                                               | 25.56%                                          | 18.79                                   | <0.001 |
| Septic shock                           | 557                                                 | 1,472                                           | 1,603                                   | 18.79 |
|                                          | 11.78                                               | 32.27%                                          | 18.79                                   | <0.001 |

IQR = interquartile range.
across types, was over two times more common in VABP than either of the other two conditions (Fig. 1). VABP (17.8%) was more likely than either vHABP (15.2%) or nvHABP (11.7%) to be polymicrobial.

Unadjusted hospital mortality was highest among patients with vHABP (29.2%) and lowest in nvHABP (11.7%) (Table 2). Among patients discharged alive, 20.7% of nvHABP, 12.1% of vHABP, and 11.7% of VABP groups were able to be sent home without home healthcare. The remaining were discharged to another healthcare facility or required home healthcare. Of note, the likelihood of going to hospice was highest in the vHABP group (29.2%) and lowest in the nvHABP group (11.7%). Combined, hospital deaths and hospice discharges in the vHABP group (36%) exceeded those in the nvHABP (19%) by a factor of nearly 2 and were ~1/3 more likely than that in the VABP group (26%). In contrast, among survivors, nvHABP patients were most likely and VABP patients least likely to require a repeat hospitalization within 30 days of discharge. Finally, and not surprisingly, the costs of hospitalization in the VABP group were nearly double of, and in vHABP one-third higher than, those in nvHABP.

Although many studies have explored both HABP and VABP over the past decade, few have differentiated between those who do versus those who do not require MV support to manage their HABP. Esperatti et al (11) conducted a single-center prospective cohort study performed in six ICUs in a large institution in Europe, enrolling 315 patients with HABP and VABP whose infection onset occurred in the ICU. Interestingly, although the investigators combined both vHABP and nvHABP together into a group they called nonventilated ICU-acquired pneumonia, the distribution of pneumonia types reported by these investigators was almost identical to the current study’s: 52% VABP, and, among remaining HABP, 52% required MV. Though their study was too small to reveal many potentially significant differences between the groups, it is worth pointing to some numeric disparities. Directionally, additional similarities to our findings include older age and higher prevalence of comorbidities. The most common Gram-negative (P. aeruginosa) and Gram-positive (S. aureus) organisms were also the same, though their distributions require MV. Overall, those diagnosed with vHABP appeared most ill, both chronically and acutely, whereas VABP patients were youngest and had the lowest burden of illness. Commensurate with this, hospital mortality was also highest in the vHABP group and lowest among the nvHABP. Combined, hospital deaths and hospice discharges in the vHABP group (36%) exceeded those in the nvHABP (19%) by a factor of nearly 2 and were ~1/3 more likely than that in the VABP group (26%). In contrast, among survivors, nvHABP patients were most likely and VABP patients least likely to require a repeat hospitalization within 30 days of discharge. Finally, and not surprisingly, the costs of hospitalization in the VABP group were nearly double of, and in vHABP one-third higher than, those in nvHABP.

DISCUSSION

We have demonstrated that among patients with NP, roughly half have VABP, whereas the other half have HABP, which can be further divided into roughly equal groups of those who do and those who do not
The outcomes in our study and the one from Spain are worth comparing as well. Hospital mortality in particular was higher in VABP (42%) than in HABP (36%) in the analysis by Esperatti et al (11), though both groups exhibited strikingly high rates of death, or about double those within our cohort. These rates, however,
are not dissimilar to the mortality rate observed in one of the seven studies examined by Talbot et al (2) in an effort to inform NP regulatory trial design. The specific study performed in Barcelona reported a relatively higher rate of 28-day mortality in all three types of pneumonia: 21.7% in nvHABP, 39.4% in vHABP, and 27.0% in VABP. Save for a single other trial examined, these mortality rates were approximately double those seen in other studies (2). This may be consistent with the regional differences in rates also seen in the study by Esperatti et al (11). In general, our observed hospital mortality is well within the range of what has been previously reported in these conditions (24).

One surprising pattern emerged among the three groups we explored. Of all the patients, those who survived nvHABP had the highest likelihood of needing a repeat hospitalization within 30 days of discharge. Nearly one-fourth of these patients were readmitted, whereas under one-fifth of all those who had survived VABP required additional admissions. Since the gap between the rates of readmission in vHABP and nvHABP groups was not substantial, the disparities in this outcome are likely related to the greater survivorship in nvHABP, and higher age and burden of comorbidities in these two groups than in the VABP group. A possible additional explanation is that a higher proportion of both vHABP and VABP than nvHABP survivors had been discharged to another healthcare facility, giving them access to more comprehensive care than available at home.

All other economic outcomes comported with prior literature (24). That is, hospital LOS and its various components were highest in VABP and lowest in nvHABP, as were all the components of the corresponding costs. Although literature is replete with estimates of costs related to both HABP and VABP, much of it is not contemporary and, thus, may not reflect the current prevention, treatment, and reimbursement environment. More importantly, to the best of our knowledge, no study has addressed the potential differential in resource utilization between nvHABP and vHABP. The fact that it is significant further confirms that these are two distinct entities whose management may require different approaches. At the very least, it can help institutions that care for these patients to understand resources they need depending on their own patient mix.

Our study has a number of limitations and strengths. As an observational study, it is subject to multiple threats to validity, particularly selection bias. Defining the enrollment criteria prospectively mitigates this bias. Misclassification is of particular concern when using administrative data. To deal with this, we used a previously published, though not clinically validated, algorithm that identifies the first episode of pneumonia. We also excluded other potential sources of infection, such as cUTI and cIAI. Although these criteria improved the specificity of our case finding approach, they reduced its sensitivity, and thus likely led to undercounting of cases. Including microbiology specimens from specific sources, pharmacy data, and dates of cultures and treatments further improved the specificity at the expense of sensitivity. Although this strategy likely misclassified some patients, it was nondifferential across the comparator groups and, thus, would have driven the differences between the groups toward null. At the same time, it is possible that only the most severe cases of both HABP and VABP were coded as pneumonia, in which case the outcomes we report may be worse across the three groups than those seen in clinically defined NP. However, the agreement in mortality rates with other literature lends face validity to our methods (24). The data did not allow us to differentiate between infection and colonization. Although confounding is present in all observational studies, we did not attempt to adjust it away, as the aim of the current study was to provide a comparative description of these three types of NPs. As a large multicenter geographically representative database, it is only minimally prone to lack of generalizability. At the same time, our results capture only the events that occur in the hospital and lack such data points as postdischarge death. Because we preferred to err on the side of specificity and required a positive culture and no evidence of cUTI or cIAI, our results may not generalize to the excluded groups. Despite these limitations, this is the largest and most contemporary multicenter cohort study to examine the epidemiology and outcomes of NP in the United States.

CONCLUSIONS

In summary, we have demonstrated that there are substantial differences between populations who suffer nvHABP, vHABP, and VABP, both demographically and clinically. Similarly, their hospital outcomes also diverge. Further studies are needed to explore
more granular determinants of outcomes in these populations, as well as potential ways to mitigate them. The current study provides a contemporary benchmark for future analyses geared at improving both understanding and management of these distinct conditions.

REFERENCES

1. Magill SS, Edwards JR, Bamberg W, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team: Multistate point-prevalence survey of health care-associated infections. N Engl J Med 2014; 370:1198–1208
2. Talbot GH, Das A, Cush S, et al; Foundation for the National Institutes of Health Biomarkers Consortium HABP/VABP Project Team: Evidence-based study design for hospital-acquired bacterial pneumonia and ventilator-associated bacte-
rional pneumonia. J Infect Dis 2019; 219:1536–1544
3. Freire AT, Melnyk V, Kim MJ, et al; 311 Study Group: Comparison of tigecycline with imipenem/cilastatin for the treatment of hospital-acquired pneumonia. Diagn Microbiol Infect Dis 2010; 68:140–151
4. Kollef MH, Chastre J, Clavel M, et al; A randomized trial of 7-day doripenem versus 10-day imipenem-cilastatin for ventil-
lator-associated pneumonia. Crit Care 2012; 16:R218
5. Ramirez J, Dartois N, Gandjini H, et al; Randomized phase 2 trial to evaluate the clinical efficacy of two high-dosage tige-
cycline regimens versus imipenem-cilastatin for treatment of hospital-acquired pneumonia. Antimicrob Agents Chemother 2013; 57:1756–1762
6. Réa-Neto A, Niederman M, Lobo SM, et al; Efficacy and safety of doripenem versus piperacillin/tazobactam in nosocomial pneumonia: A randomized, open-label, multicenter study. Curr Med Res Opin 2008; 24:2113–2126
7. Chastre J, Wunderink R, Prokocimer P, et al; Efficacy and safety of intravenous infusion of doripenem versus imipenem in ventilator-associated pneumonia: A multicenter, randomized study. Crit Care Med 2008; 36:1089–1096
8. Rubinstein E, Lalani T, Corey GR, et al; ATTAIN Study Group: Telavancin versus vancomycin for hospital-acquired pneumonia due to Gram-positive pathogens. Clin Infect Dis 2011; 52:31–40
9. Wunderink RG, Niederman MS, Kollef MH, et al; Linezolid in methicillin-resistant Staphylococcus aureus nosocomial pneu-
monia: A randomized, controlled study. Clin Infect Dis 2012; 54:621–629
10. Wunderink RG, Rello J, Cammarata SK, et al; Linezolid vs van-
comycin: Analysis of two double-blind studies of patients with methicillin-resistant Staphylococcus aureus nosocomial pneu-
monia. Chest 2003; 124:1789–1797
11. Esperatti M, Ferrer M, Theessen A, et al; Nosocomial pneu-
monia in the intensive care unit acquired by mechanically ventilated versus nonventilated patients. Am J Respir Crit Care Med 2010; 182:1533–1539
12. Vazquez Guilamet C, Kollef MH: Is zero ventilator-associated pneumonia achievable?: Practical approaches to ventilator-
associated pneumonia prevention. Clin Chest Med 2018; 39:809–822
13. Pronovost P, Needham D, Berenholtz S, et al; An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med 2006; 355:2725–2732
14. Vallecoccia MS, Dominoe C, Cutuli SL, et al; Is ventilated hospital-acquired pneumonia a worse entity then ventilator-
associated pneumonia?: A retrospective cohort study. Chest 2019; 155:1119–1130
15. US Department of Health and Human Services Office for Human Research Protections. Human Subject Regulations Decision Charts. 2020. Available at: https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html. Accessed February 3, 2021
16. Zilberberg MB, Nathanson BH, Sulham K, et al; Development and validation of a bedside instrument to predict carbapenem resistance among patients with hospital-acquired and ventila-
tor-associated pneumonia: A prospective cohort study. Open Forum Infect Dis 2019; 6:ofz504
19. Rothberg MB, Pekow PS, Priya A, et al: Using highly detailed administrative data to predict pneumonia mortality. *PLoS One* 2014; 9:e87382

20. Rothberg MB, Haessler S, Lagu T, et al: Outcomes of patients with healthcare-associated pneumonia: Worse disease or sicker patients? *Infect Control Hosp Epidemiol* 2014; 35(Suppl 3):S107–S115

21. Lagu T, Stefan MS, Haessler S, et al: The impact of hospital-onset *Clostridium difficile* infection on outcomes of hospitalized patients with sepsis. *J Hosp Med* 2014; 9:411–417

22. American College of Surgeons. National Trauma Data Bank User Manual, 2011. Available at: https://www.facs.org/~/media/files/quality%20programs/trauma/ntdb/ntdbmanual2010.ashx. Accessed February 21, 2017

23. McCormick N, Bhole V, Lacaille D, et al: Validity of diagnostic codes for acute stroke in administrative databases: A systematic review. *PLoS One* 2015; 10:e0135834

24. Kalil AC, Metersky ML, Klompas M, et al: Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016; 63:e61–e111