

Clinical and Economic Outcomes Attributable to Health Care–Associated Sepsis and Pneumonia

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Background: Health care–associated infections affect 1.7 million hospitalizations each year, but the clinical and economic costs attributable to these infections are poorly understood. Reliable estimates of these costs are needed to efficiently target limited resources for the greatest public health benefit.

Methods: Hospital discharge records from the Nationwide Inpatient Sample database were used to identify sepsis and pneumonia cases among 69 million discharges from hospitals in 40 US states between 1998 and 2006. Community-acquired infections were excluded using criteria adapted from previous studies. Because these criteria may not exclude all community-acquired infections, outcomes were examined separately for cases associated with invasive procedures, which were unlikely to result from preexisting infections. Attributable hospital length of stay, hospital costs, and crude in-hospital mortality were estimated from discharge records using a multivariate matching analysis and a supple-

mentary regression analysis. These models controlled for patient diagnoses, procedures, comorbidities, demographics, and length of stay before infection.

Results: In cases associated with invasive surgery, attributable mean length of stay was 10.9 days, costs were \$32 900, and mortality was 19.5% for sepsis; corresponding values for pneumonia were 14.0 days, \$46 400, and 11.4%, respectively ($P < .001$). In cases not associated with invasive surgery, attributable mean length of stay, costs, and mortality were estimated to be 1.9 to 6.0 days, \$5800 to \$12 700, and 11.7% to 16.0% for sepsis and 3.7 to 9.7 days, \$11 100 to \$22 300, and 4.6% to 10.3% for pneumonia ($P < .001$).

Conclusion: Health care–associated sepsis and pneumonia impose substantial clinical and economic costs.

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HEALTH CARE–ASSOCIATED infections (HAIs) affect an estimated 1.7 million hospitalizations in the United States each year.¹ Many of these HAIs result from failures in the process of care at hospitals and may be preventable.² Health care–associated infections have been shown to increase patient morbidity and risk of mortality, to increase the cost of treatment, and to extend hospitalization time. However, previous estimates of the health consequences and economic costs attributable to HAIs remain contentious.³⁻⁷ Differences in estimates of the attributable costs may reflect the small sample sizes used for analysis and the use of varying controls for confounding factors.^{4,5,8-10}

See Invited Commentary at end of article

In this study, we assessed the attributable hospital length of stay (LOS), hospital costs, and in-hospital mortality of a subset of HAIs using 69 million administrative discharge records from hospitals in 40 US states. Administrative databases provide the opportunity for large and generaliz-

able analyses of hospital outcomes.^{11,12} Because the primary purpose of these records is to facilitate billing and management, they do not capture the degree of clinical detail that medical records contain. Previous studies^{13,14} have shown that several specific types of HAIs are poorly identified in administrative records because diagnosis codes used to identify infections are often used improperly and do not distinguish hospital from community acquisition of infection.

To identify infections in administrative data, we focused this analysis on HAIs associated with sepsis and pneumonia, conditions that previous studies^{15,16} have shown to be reliably identified in administrative records. Health care–associated pneumonia is a serious infectious complication of hospitalization that affects approximately 250 000 US hospitalizations each year.¹ Sepsis is a serious systemic response to infection. Sepsis may result from pneumonia, but more often it results from infections at other sites, such as primary bloodstream infections and surgical site infections.¹⁷ All-cause sepsis affects 750 000 US hospitalizations yearly,^{15,18} and approximately half of these cases may be hospital acquired.⁶

Table 1. Criteria for Identifying Health Care–Associated Sepsis and Pneumonia^a

| Infection Type | ICD-9-CM Discharge Diagnosis Codes | Exclusions |
|----------------|---------------------------------------|---|
| Sepsis | 038 ^b | MDC 18; DRGs 20, 68-70, 79-81, 89-91, 126, 238, 242, 277-279, 320-322, 415-417, and 423; HIV/AIDS; immunocompromised states; cancer |
| Pneumonia | 482.0-482.2, 482.4-482.9 ^c | MDCs 18 and 4; secondary diagnosis: 480, 481, 483, 484, 487; HIV/AIDS; immunocompromised states; cancer |

Abbreviations: DRG, diagnosis related group; HIV, human immunodeficiency virus; ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; MDC, major diagnostic category.

^aAdapted from Needleman et al¹⁹ and Iezzoni.²⁰

^bThree new ICD-9-CM codes were introduced in 2002 and 2003 to clarify the severity of sepsis cases: 995.91 (sepsis), 995.92 (severe sepsis), and 785.52 (septic shock). These newer codes were introduced only to clarify the severity of sepsis cases and were not intended to replace the 038 code for sepsis due to bacterial infection.²⁴ Thus, these codes should not have substantially altered the accuracy of sepsis identification based on the 038 code.

^cThis analysis was restricted to include only pneumonia cases with a bacterial pneumonia diagnosis code.

To distinguish HAIs from community-acquired infections, which may impose different costs, we used criteria adapted from earlier studies^{19,20} to exclude cases in administrative data likely to be community acquired. Furthermore, we conducted a separate analysis of outcomes in cases associated with invasive surgical procedures because these cases were unlikely to result from preexisting infections.

METHODS

DATA

We used hospital discharge records from the 1998-2006 Nationwide Inpatient Sample (NIS) database developed by the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. The NIS is the largest all-payer database of hospitalization records in the United States and has been shown to accurately reflect hospital and patient characteristics in the nation as a whole.¹¹ Each year, the NIS approximates a 20% sample of all US hospitalizations through stratified random sampling of hospitals.²¹ During each sample year, the NIS provides records on all patient discharges from the sampled hospitals, totaling approximately 7 to 8 million discharges yearly between January 1, 1998, and December 31, 2006. The NIS provides information on each patient's diagnoses (≤ 15 *International Classification of Diseases, Ninth Revision, Clinical Modification*²² discharge diagnosis codes are reported), procedures performed in the hospital (≤ 15 are recorded using *International Classification of Diseases, Ninth Revision, Clinical Modification* procedure codes), time between inpatient admission and each procedure, urgency of admission, demographics, and insurers. Hospital LOS, in-hospital mortality, and hospital charges were recorded directly on patient discharge records. Hospital costs were estimated by multiplying hospital charges by institution type- and state-specific cost conversion factors derived for 90% of hospitals in the 2001-2006 NIS by the Agency for Healthcare Research and Quality.²³ Missing charge-to-cost conversions were extrapolated by regressing conversions on year and state. Costs for years before 2006 were adjusted to year 2006 dollars using the Consumer Price Index for Medical Care, Hospital, and Related Services.¹²

IDENTIFYING HAIs

Sepsis and pneumonia have been determined to be reliably identified using administrative records; the specificity and positive predictive value of sepsis coding in administrative data are 99% and 89%, and those of pneumonia coding are 99% and 85%, respectively.^{15,16}

Although coding for these conditions is reliable, administrative data do not directly distinguish between HAIs and community-acquired infections. We addressed this problem in 2 ways. First, we used HAI identification criteria adapted from Needleman et al¹⁹ and Iezzoni²⁰ to exclude preexisting infections (**Table 1**). The present criteria excluded any hospitalization with a primary diagnosis related to infectious diseases (major diagnostic category 18) because primary diagnoses of infectious disease indicate preexisting infections as opposed to infections that arise as nosocomial complications.^{11,24-26} We also excluded patients identified as being immunocompromised, those with cancer or human immunodeficiency virus/AIDS, and all incoming hospital transfers because of difficulty identifying and attributing HAIs for these hospitalizations.

Furthermore, we separately examined sepsis and pneumonia cases associated with invasive surgical procedures because these cases were unlikely to result from preexisting infections.¹² We used the National Healthcare Safety Network list of operative procedures associated with substantial risk of infection²⁷ to identify cases associated with invasive surgery. We subdivided the procedures into abdominal, orthopedic, thoracic (noncardiac), cardiac, neurologic, and other based on National Healthcare Safety Network groupings to assess HAI costs by group. We also examined infections in the subgroup of surgical patients admitted for elective invasive procedures. These elective surgery patients were even less likely than were other invasive surgery patients to have serious preexisting infections.⁷

ANALYTICAL APPROACH

To determine the hospitalization costs attributable to HAIs, we conducted a multivariate matching analysis in which patients with HAIs were matched to similar control patients who did not have HAIs. We identified potential control hospitalizations as those that did not contain diagnoses in their records that could indicate the presence of HAIs using broader criteria than those used to identify the HAIs selected for analysis in this study (**Table 2**). We then attempted to match each HAI case to a control with the same primary diagnosis, principal procedure (if ≥ 1 procedure was conducted), age group (in intervals of 10 years), urgency of admission (elective, urgent, or emergency), and year of discharge. To account for the effect of preexisting patient comorbidities on hospital outcomes, we also matched case and control hospitalizations on the Charlson Comorbidity Index score of mortality risk.^{28,29} Cases and controls associated with invasive surgical procedures were matched on the first invasive surgery performed on the patient to control for operative characteristics that could affect patient resource consumption, cause morbidity, or increase the risk of mortality. Cases of HAI that could not be matched to any control hospitalizations were excluded from this part of the analysis.

Longer hospital stays and higher costs associated with HAI cases may, in part, be due to extended preinfection hospital exposure. Because extended LOS is an independent risk factor for infection, the preinfection LOS of patients with HAIs may be expected to exceed that of similar patients who did not acquire an HAI. Attributing preinfection LOS to HAIs would overstate the true costs of HAIs. Some studies^{3,5,8} have directly controlled for LOS before HAI onset to address this potential bias. Because the NIS database does not record time of infection onset, we used 2 other methods to correct for this bias. First, among patients who underwent invasive procedures, we required that the number of days between hospital admission and the first invasive surgery be the same in HAI cases and matched controls. The HAIs in these surgical patients were most likely to be postoperative infections,²⁷ and, thus, controlling for preoperative LOS should substantially control for time to infection. Second, we approximated controlling for preinfection LOS in patients with HAI who did not undergo invasive procedures by excluding control hospitalizations that had an LOS of less than 40% of the LOS of matched HAI cases. A study⁶ of 490 nosocomial sepsis cases from 8 tertiary care centers found that the mean preonset LOS was approximately 40% of the total LOS for these hospitalizations. Other estimates indicate that this proportion of preonset LOS may be similar or lower in nosocomial pneumonia cases.^{30,31} Therefore, this adjustment may be suitable to use for pneumonia cases as well. We present results with and without this 40% adjustment.

We estimated LOS, hospital costs, and mortality attributable to the presence of health care–associated sepsis and pneumonia in the following manner. For each HAI case, attributable LOS, hospital costs, and mortality rates were calculated as the difference between the outcome of the case and the mean outcome in all matched controls. Deaths were excluded to calculate attributable LOS and hospital cost estimates. Outgoing hospital transfers and discharges against medical advice were excluded for all outcomes because the results of these hospitalizations may not reflect the full course of treatment required. Means and medians were used to summarize attributable LOS and hospital costs in HAI cases. Only means were used to summarize attributable mortality rates because mortality is a binary outcome. We used Wilcoxon rank sum tests to determine whether outcomes were significantly different in cases vs controls. We interpreted $P < .05$ to be statistically significant. Statistical analyses were performed using a software package (STATA version 10.0; StataCorp, College Station, Texas).

CONFIRMATORY REGRESSION ANALYSIS

A limitation of the matching process is that only a subset of patients can be matched to suitable controls, especially when many matching criteria are included.^{11,12} We, therefore, conducted linear regression analysis using the 1998-2006 NIS database to estimate the effects of health care–associated sepsis and pneumonia on LOS, hospital costs, and mortality in all non-excluded hospitalizations in the sample. The regression models, one for each outcome, included as covariates all variables considered in the main analysis and hospital identifiers, patient primary insurers, sex, age, race, and the individual comorbidity indicators used to compose the Charlson Comorbidity Index score^{28,29} to address the possible bias caused by omitted variables in the matching analysis. The models did not control for preinfection hospital exposure in patients not undergoing invasive surgical procedures. Accordingly, these models were likely to have overestimated hospitalization costs in this group. Standard errors were clustered at the hospital level to control for intrahospital correlation in outcomes.

Table 2. Exclusion Criteria for Control Hospitalizations^a

| ICD-9-CM Discharge Diagnosis Codes | Further Exclusions |
|--|--|
| 00.8.45, 038, 320, 321, 322, 324, 420, 421, 422, 480, 481, 482, 483, 485, 486, 487.0, 507, 513.1, 514, 519.2, 590.1, 590.2, 590.3, 590.80, 590.9, 595.0, 595.3, 595.81, 595.89, 595.9, 599.0, 682, 711.0, 728.0, 730 (not including 730.1, 730.7, 730.8), 790.7, 958.3, 995.90, 995.91, 995.92, 996.6, 997.3, 997.5, 998.0, 998.3, 998.5, 998.6, 998.83, 999.3 | MDC 18, HIV/AIDS, immunocompromised states, cancer |

Abbreviations: HIV, human immunodeficiency virus; ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; MDC, major diagnostic category.

^a Adapted from Noskin et al,¹² Sherman et al,¹³ Stevenson et al,¹⁴ and Needleman et al.¹⁹

RESULTS

This analysis was based on a cohort of 58 701 608 hospitalization records that met the inclusion criteria, of which 557 967 hospitalizations were identified as health care–associated sepsis or pneumonia cases. Sepsis was identified in 493 250 cases, pneumonia was identified in 79 835 cases, and 15 118 hospitalizations were associated with both sepsis and pneumonia. Hospitalizations associated with invasive procedures accounted for 8 690 418 of all hospitalizations (15%) and 130 848 of case hospitalizations (23%). The proportion of cases matched to at least 1 control varied from 30% for invasive surgery patients (who were matched using more criteria than were other patients) to 65% for patients who did not undergo invasive surgery.

OUTCOMES IN INVASIVE SURGERY PATIENTS

Table 3 provides information on cases identified using the present methods in invasive surgery patients for different surgical patient groups. Overall attributable mean LOS was 10.9 days, hospital costs were \$32 900, and crude in-hospital mortality was 19.5% for sepsis cases and 14.0 days, \$46 400, and 11.4%, respectively, for pneumonia cases.

OUTCOMES IN ELECTIVE SURGERY PATIENTS

Compared with the broader group of all invasive surgery patients, elective surgical admissions were generally associated with higher attributable LOS, hospital costs, and mortality (data not shown). Mean estimates of LOS, hospital costs, and mortality were higher by 4.6 days, \$13 000, and 3.6%, respectively, for matched sepsis cases. Mean LOS and hospital cost estimates for pneumonia cases were higher by 0.6 days and \$1000, respectively, although mortality was lower by 0.1%.

OUTCOMES IN PATIENTS WHO DID NOT HAVE INVASIVE SURGERY

Table 4 provides information on cases in patients who did not undergo invasive surgery. The LOS and hospital

Table 3. Attributable Outcomes of Health Care–Associated Sepsis and Pneumonia Associated With Invasive Surgery for Different Surgical Patient Groups, 1998-2006^a

| Infection Type and Outcome | Invasive Surgical Procedures | | | | | | |
|----------------------------|------------------------------|-----------|------------|-----------------------|---------|------------|--------|
| | All | Abdominal | Orthopedic | Thoracic (Noncardiac) | Cardiac | Neurologic | Other |
| Sepsis | | | | | | | |
| Mean LOS, d | 10.9 | 10.7 | 8.9 | 16.3 | 19.0 | 19.5 | 9.3 |
| Median LOS, d | 6.1 | 5.6 | 5.4 | 10.0 | 14.4 | 15.0 | 6.0 |
| Mean costs, \$ | 32 900 | 32 500 | 23 200 | 64 000 | 66 800 | 51 600 | 22 200 |
| Median costs, \$ | 16 100 | 15 100 | 11 700 | 38 200 | 48 100 | 36 800 | 12 500 |
| Mortality, % | 19.5 | 17.3 | 21.0 | 26.2 | 32.1 | 14.2 | 19.6 |
| No. of cases | 108 610 | 63 082 | 21 500 | 4853 | 9628 | 4573 | 9282 |
| Incidence, % | 1.2 | 1.9 | 0.7 | 4.4 | 1.5 | 2.5 | 0.8 |
| Pneumonia | | | | | | | |
| Mean LOS, d | 14.0 | 14.8 | 12.1 | 22.2 | 15.3 | 18.0 | 9.7 |
| Median LOS, d | 9.3 | 9.0 | 8.3 | 15.7 | 10.9 | 14.0 | 7.0 |
| Mean costs, \$ | 46 400 | 48 000 | 36 600 | 88 900 | 56 800 | 55 500 | 27 800 |
| Median costs, \$ | 29 200 | 28 200 | 22 000 | 65 900 | 39 200 | 44 700 | 18 700 |
| Mortality, % | 11.4 | 9.9 | 18.0 | 19.2 | 11.5 | 2.8 | 12.4 |
| No. of cases | 28 469 | 11 765 | 5835 | 1096 | 5693 | 4120 | 1800 |
| Incidence, % | 0.3 | 0.3 | 0.2 | 1.0 | 0.9 | 2.2 | 0.1 |

Abbreviation: LOS, hospital length of stay.

^a $P < .001$ for all differences between outcome and zero by means of the Wilcoxon rank sum test.

Table 4. Attributable Outcomes of Health Care–Associated Sepsis and Pneumonia Not Associated With Invasive Surgery, 1998-2006^a

| Infection Type and Outcome | Unadjusted | Adjusted for Preinfection LOS ^b |
|----------------------------|------------|--|
| Sepsis | | |
| Mean LOS, d | 6.0 | 1.9 |
| Median LOS, d | 2.9 | 1.5 |
| Mean costs, \$ | 12 700 | 5800 |
| Median costs, \$ | 4400 | 2200 |
| Mortality, % | 11.7 | 16.0 |
| No. of cases | 384 640 | 384 640 |
| Incidence, % | 0.8 | 0.8 |
| Pneumonia | | |
| Mean LOS, d | 9.7 | 3.7 |
| Median LOS, d | 4.7 | 2.6 |
| Mean costs, \$ | 22 300 | 11 100 |
| Median costs, \$ | 8100 | 4500 |
| Mortality, % | 4.6 | 10.3 |
| No. of cases | 51 366 | 51 366 |
| Incidence, % | 0.1 | 0.1 |

Abbreviation: LOS, hospital length of stay.

^a $P < .001$ for all differences between outcome and zero by means of the Wilcoxon rank sum test.

^b Longer hospital stays and costs associated with health care–associated infection (HAI) cases may be due, in part, to extended preinfection hospital exposure because extended LOS is an independent risk factor for infection. To address this potential bias, we excluded control hospitalizations from the matching analysis that had a total LOS of less than the expected preinfection LOS of matched HAI cases, estimated to be 40% of the LOS of each HAI case. This adjustment was not used for infections associated with invasive surgery (Table 3), for which we controlled for this bias using length of preoperative hospital stay.

cost estimates obtained after excluding control hospitalizations with less than the expected preinfection LOS of case hospitalizations declined by as much as 70% of the values obtained without the adjustment for LOS. Attributable mortality estimates, however, increased after the ex-

clusions. Estimates of the attributable costs of hospitalization in the group of patients who did not undergo invasive surgery were lower than were those in the invasive surgical group even without these exclusions. For example, the mean attributable LOS due to sepsis was approximately 11 days and that due to pneumonia was approximately 14 days in the surgical group, but they were not longer than 6 and 10 days, respectively, in other patients.

ROBUSTNESS OF COST ESTIMATES

The attributable LOS and mortality for the HAIs selected for analysis did not change substantially across time (**Figure**). Attributable LOS for pneumonia and sepsis associated with invasive surgery increased somewhat, whereas mortality attributable to pneumonia decreased slightly. Mortality attributable to sepsis that was not associated with invasive surgery decreased between 2002 and 2003 and then increased after 2003.

Hospitalization costs also did not change substantially across time (data not shown). For example, among invasive surgical hospitalizations, sepsis costs increased 11%, from \$29 900 to \$33 200, from 1998 to 2006, and pneumonia costs decreased less than 1%, from \$47 700 to \$47 500, during the same period.

Regression analysis, which included all matched and unmatched HAI cases and controls in the cohort, produced results similar to those obtained from the matching analysis (**Figure**). Including deaths in the calculations of attributable LOS and hospital costs resulted in estimates that differed by no more than 10% for hospital costs and 9% for LOS, except that attributable LOS decreased from 1.9 days to 1.3 days in patients with sepsis who did not undergo invasive procedures when using the 40% adjustment for preinfection LOS. Further sensitivity analysis, which reduced the number of variables included in the matching analysis to increase the number of HAI cases that could be matched to at least 1 control,

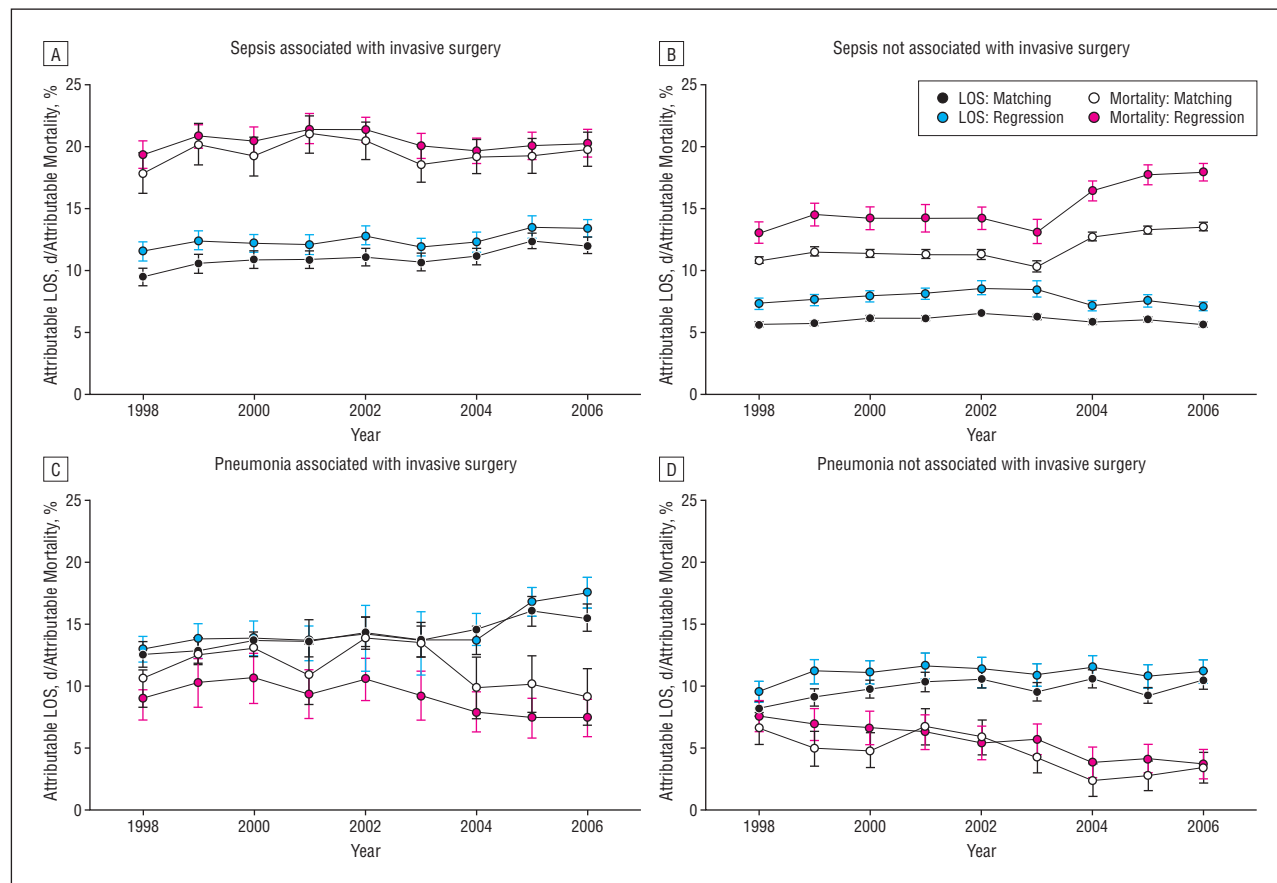


Figure. Variations across time in mean attributable length of stay (LOS) and mortality estimates between matching and regression models. Error bars indicate 95% confidence intervals. Results for the matching analysis for cases not associated with invasive surgery did not include adjustment for time to infection for consistency with the regression models.

produced similar or higher estimates of the attributable costs of HAIs.

COMMENT

Previous estimates of the economic and clinical costs of HAIs may reflect the use of small sample sizes and the absence of controls for important confounders.^{4,5,8-10} We estimated the attributable outcomes of health care–associated sepsis and pneumonia cases using detailed matching and regression analyses of more than 500 000 HAI-associated hospital discharges originating from 40 US states between January 1, 1998, and December 31, 2006. This sample of hospitalizations is much larger than those used in previous studies, and it captures a greater diversity of hospitals and geographic locations. The analytical approach included controls for patient diagnoses, demographics, comorbidities, and hospital treatment and approximate controls for preinfection hospital exposure. These estimates demonstrate that the national impact of hospitalization attributable to HAIs is substantial.

The outcomes of health care–associated sepsis and pneumonia may vary across different patient groups (Tables 3 and 4), a finding consistent with other research.¹⁸ We found that the attributable hospital LOS and hospital costs of health care–associated sepsis and pneu-

monia cases were at least 40% higher in patients who underwent invasive procedures than in those who did not. In the subgroup of electively admitted invasive surgery patients, the attributable costs of HAIs were even higher. Cases associated with invasive surgery, especially elective surgery, were unlikely to have resulted from preexisting infections. Thus, it is possible that outcomes between the patient groups are as different as observed, or it is possible that better identification of HAIs in the surgical patient groups may have contributed to the observed differences in hospitalization outcomes. Some HAI cases identified by this analysis may have been misidentified community-acquired infections, which may have lower associated costs than HAIs.^{6,32} Such a bias would likely result in underestimating the true costs of HAIs.

The overall mean LOS and hospital costs, but not mortality, of sepsis cases were lower than those of pneumonia cases. These findings may be explained by the costs of sepsis cases varying by underlying cause of infection, with the combination of pneumonia and sepsis having particularly high attributable costs.^{33,34} Among invasive surgery patients, for example, sepsis associated with pneumonia had attributable mean LOS, hospital costs, and in-hospital mortality of 23.7 days, \$80 000, and 27.9%, respectively, whereas these outcomes were 10.3 days, \$30 800, and 18.7%, respectively, for cases of sepsis not associated with pneumonia (data not shown). Out-

comes in pneumonia cases that were not also coded as sepsis cases in the results were 12.5 days, \$41 500, and 8.1%, respectively (data not shown). The high LOS and hospital costs of the pneumonia cases we identified may partially be a result of restricting the analysis to pneumonia cases with bacterial pneumonia diagnosis codes, which may select for more severe cases. These costs should also reflect the relatively high costs of health care–associated pneumonia compared with community-acquired pneumonia.³²

This study has several limitations that are primarily associated with the inability of administrative records to provide as much clinical detail and precision as medical records. First, although we used various methods to differentiate HAIs from community-acquired infections, these methods may not exclude all community-acquired infections from this analysis. Second, we included approximate controls for time to infection, but these were not exact and could not explicitly model the time-dependent nature of HAIs.⁵ Third, we included controls for diagnoses, procedures, comorbidities, and demographics, but a lack of further clinical detail in the administrative records limited our ability to risk-adjust outcomes of HAI cases for potential confounders, including more detailed indicators of patient severity of illness and procedures known to be conducted on patients before the onset of infection.

These economic and clinical cost estimates provide new evidence that the burden of HAIs in the United States is high.^{1,35,36} To obtain crude aggregate estimates of the national attributable costs of health care–associated sepsis and pneumonia, we multiplied estimates of hospitalization costs by estimates of the number of cases occurring nationwide in 2006. We estimated 290 000 sepsis cases in 2006 based on the results after adjusting for the 20% sampling scheme of the NIS database. Because the sensitivity of administrative databases for identifying pneumonia is not as strong as for sepsis,¹⁶ we used an external estimate of 200 000 for pneumonia cases,¹ adjusted to exclude the proportion of pneumonia cases that were also identified as sepsis in the results. We applied mean estimates from Table 3 and the lowest mean estimates from Table 4 in proportion to the share of cases that were and were not associated with invasive surgery in the results. We adjusted for the different costs of pneumonia without sepsis, and we included deaths in calculations of LOS and hospital costs to reflect aggregate hospitalization costs in all cases. Based on these methods, there were 2.3 million patient hospitalization days, \$8.1 billion in-hospital costs, and 48 000 deaths attributable to health care–associated sepsis and pneumonia in 2006. These figures are likely to be underestimates because they focus on infections that were acquired and diagnosed during the same hospitalization, although many HAIs, including most surgical site infections, are not diagnosed until after hospital discharge.³⁷

The economic costs of health care–associated sepsis and pneumonia are substantial, but high rates of these infections persist in US hospitals. It is unclear whether hospitals or patient insurers bear the greater share of the costs of HAIs: some estimates suggest that less than 20% of HAI cases receive additional reimbursement and that patient insurers may bear

as little as 5% of the total costs of HAIs,³⁸ whereas other estimates suggest that hospitals may bear the lighter burden.³⁹ The effect of the attributable costs of HAIs on hospital decision making is also difficult to assess because most hospital costs, such as labor, are fixed in the short term,⁴⁰ meaning that hospitals are using resources that do not cost more in the short term for their use. Regulations that deny additional reimbursement to hospitals for HAIs may not adequately incentivize infection control because of the aforementioned factors, and furthermore, they may not work if hospitals knowingly misclassify HAIs to avoid financial penalties⁴¹ or if existing problems with documenting HAIs prevent adequate enforcement of these regulations.

In summary, the attributable costs and outcomes of hospitalization due to health care–associated sepsis and pneumonia in the United States are substantial, although they may vary in different patient groups. Further study is needed to assess the outcomes of other types of HAIs and to examine incentives and regulatory options to reduce HAI incidence.

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INVITED COMMENTARY

Reducing Preventable Harm

The Institute of Medicine shocked the nation in 1999 by reporting that 98 000 people die of preventable harm each year in the United States alone.¹ Since then, other countries have documented that a substantial number of people experience preventable harm.²

These estimates likely contain uncertainty because measuring preventable harm is a difficult task. Many stud-

ies lack clear definitions of adverse events (the numerator) and those at risk for these events (the denominator) as well as surveillance systems to identify the events and those at risk. Definitions and surveillance systems are needed to accurately measure a rate of harm. Yet, even if we could accurately measure a rate, researchers still need to embark on the difficult task of disentangling preventable and inevitable harm. Although we may not know