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ORIGINAL ARTICLE

Economic Burden of Ventilator-Associated Pneumonia Based on Total Resource Utilization

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OBJECTIVES. To characterize the current economic burden of ventilator-associated pneumonia (VAP) and to determine which services increase the cost of VAP in North American hospitals.

DESIGN AND SETTING. We performed a retrospective, matched cohort analysis of mechanically ventilated patients enrolled in the North American Silver-Coated Endotracheal Tube (NASCENT) study, a prospective, randomized study conducted from 2002 to 2006 in 54 medical centers, including 45 teaching institutions (83.3%).

METHODS. Case patients with microbiologically confirmed VAP ($n = 30$) were identified from 542 study participants with claims data and were matched by use of a primary diagnostic code, and subsequently by the Acute Physiology and Chronic Health Evaluation II score, to control patients without VAP ($n = 90$). Costs were estimated by applying hospital-specific cost-to-charge ratios based on all-payer inpatient costs associated with VAP diagnosis-related groups.

RESULTS. Median total charges per patient were $198,200 for case patients and $96,540 for matched control patients ($P < .001$); corresponding median hospital costs were $76,730 for case patients and $41,250 for control patients ($P = .001$). After adjusting for diagnosis-related group payments, median losses to hospitals were $32,140 for case patients and $19,360 for control patients ($P = .151$). The median duration of intubation was longer for case patients than for control patients (10.1 days vs 4.7 days; $P < .001$), as were the median duration of intensive care unit stay (18.5 days vs 8.0 days; $P < .001$) and the median duration of hospitalization (26.5 days vs 14.0 days; $P < .001$). Examples of services likely to be directly related to VAP and having higher median costs for case patients were hospital care ($P < .05$) and respiratory therapy ($P < .05$).

CONCLUSIONS. VAP was associated with increased hospital costs, longer duration of hospital stay, and a higher number of hospital services being affected, which underscores the need for bundled measures to prevent VAP.

TRIAL REGISTRATION. NASCENT study ClinicalTrials.gov Identifier: NCT00148642.

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The cost of hospitalization has increased by 55% during the past decade. The most important driver of this increase was the greater intensity of services provided during hospitalization.[1] In the intensive care unit (ICU), where costs are nearly 3 times those in the general ward,[2] mechanical ventilation is an important determinant of excess costs.[3] Ventilator-associated pneumonia (VAP) increases length of stay in the ICU and in the hospital, further increasing costs.[4-7] Reimbursement for cases of VAP paid to hospitals by the Centers for Medicare and Medicaid Services (CMS) has changed over time. Before 1983, the CMS reimbursed hospitals for many extra costs associated with VAP on a fee-for-service basis. In 1983, Medicare implemented the prospective payment system and reimbursed hospitals a fixed amount determined by the principal diagnosis on hospital admission. Accordingly, patients are classified into 1 of approximately 500 diagnosis-related groups (DRGs) that are expected to utilize similar hospital resources; patients are classified into a DRG on the basis of *International Classification of Diseases* diagnosis, procedure, age, sex, discharge status, and presence of complications or comorbidities. With this change, the costs of VAP incurred by hospitals began to exceed Medicare reimbursement.[8] This has future implications, because the incidence of VAP will increase as a result of the aging population, and

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quality-of-care initiatives may begin to classify VAP as a preventable complication that is not reimbursable by the CMS.[9]

Estimates of the economic burden of VAP are quite variable and ranged from approximately $10,000[4-6] to $40,000[7] per patient episode in studies published in the early 2000s. Part of the variability depends on whether the perspective is that of the hospital or patient; costs incurred by hospitals[4-6] are lower than charges billed to patients.[7] Variability is also attributable to differences in study design and methods, year(s) when data were collected, hospital location(s), and many other factors. On the basis of a literature review in which previously published estimates were converted to 2005 US dollars, Anderson et al[10] recently estimated that the weight-adjusted mean cost per episode of VAP was $25,000. Data are limited, however, regarding the impact of VAP on different hospital services for patients with VAP.

To characterize the current economic burden of VAP on hospitals and to determine which services increase its cost, we performed a retrospective cohort analysis of patients enrolled in the North American Silver-Coated Endotracheal Tube (NASCENT) study.[11] The NASCENT study was a prospective, randomized study conducted from 2002 to 2006 in 54 medical centers in North America that included 45 teaching institutions (83.3%). Adults requiring mechanical ventilation were randomly assigned to undergo intubation with a silver-coated tube (Agento I.C.; Bard) or an uncoated tube (Hi-Lo Endotracheal Tube; Mallinckrodt). Of the 1,509 patients who were intubated for 24 hours or longer, 93 (6.2%) developed microbiologically confirmed VAP (ie, 37 [4.8%] of 766 patients using the silver-coated tube and 56 [7.5%] of 743 patients using the uncoated tube [$P = .03$]). The preliminary results of this cohort analysis of the NASCENT study have been reported elsewhere.[12]

METHODS

To characterize the economic burden of VAP on hospitals and to determine which services increase its cost, we performed a retrospective matched cohort analysis of patients enrolled in the NASCENT study.[11] Each medical center's institutional review board approved the NASCENT study. Written informed consent was required and obtained from patients or their legally authorized representatives.

Patients with medical insurance claim forms and *International Classification of Diseases, Ninth Revision, Clinical Modification* procedural codes for mechanical ventilation (codes 96.70–96.72 for mechanical ventilation or codes 96.01–96.05 for nonsurgical intubation of the respiratory tract) were eligible for inclusion in our retrospective cohort analysis. The diagnosis of VAP was based on the presence of 10^4 colony-forming units or more per milliliter of a pathogen in quantitative bronchoalveolar lavage fluid obtained from patients intubated for 24 hours or longer. Standard diagnostic criteria[13,14] were used for determining when to obtain samples for culture, namely, suspicion of VAP or the presence of a new radiographic infiltrate, plus 2 of the following 3 qualifying clinical signs: fever or hypothermia, leukocytosis or leukopenia, and/or purulent tracheal aspirate. Case patients were defined as patients with microbiologically confirmed VAP; control patients were defined as patients without microbiologically confirmed VAP. Each case patient was matched to as many control patients as possible by primary diagnostic code at admission, receipt of mechanical ventilation services, and microbiological evidence and was subsequently matched by Acute Physiology and Chronic Health Evaluation (APACHE) II score at ICU admission.

The primary economic outcome was hospital cost, which was computed for each patient by linking charge data to a source of accounting data with the ratio of hospital cost to patient charge (hereafter the cost-to-charge ratio) for each hospital and multiplying the hospital-specific cost-to-charge ratio by the charges for each case. The cost-to-charge ratios were obtained from CMS historical impact files for the fiscal years 2003–2005, with the appropriate annual impact file determined by patient discharge date.

Medicare reimbursement was based on DRG payments and computed for each patient according to the following formula: [(standardized labor share × operating wage index) + (standardized nonlabor share × operating COLA adjustment for hospitals)] × (1 + operating IME + operating DSH adjustment factor) × (DRG weight)].[15] Standardized labor-related and nonlabor-related amounts were based on the Federal Register rules and regulations files for each year. Data on the operating wage index, the cost-of-living adjustment (COLA), the indirect medical education (IME) payment, and the disproportionate share hospital (DSH) adjustment were obtained from CMS historical impact files for the fiscal years 2003–2005[16] and were used to adjust payment impacts of policy changes to DRG payments. A hospital that qualifies for the DSH adjustment receives higher Medicaid reimbursement than do other hospitals because it treats a disproportionate share of Medicaid patients. The difference in the number of nonzero charge events was computed by adding the number of nonzero charge events within each CMS revenue category for each patient, which allows for between-group comparison of the number of events occurring in each service unit.

Patients' characteristics and their risk factors for VAP within 30 days of hospital admission were compared between groups at baseline. Median hospital charges were calculated for each service category. Costs were estimated by applying hospital-specific cost-to-charge ratios based on all-payer inpatient costs. The median duration of intubation and the median duration of length of stay were calculated for each cohort. Between-group differences were analyzed by use of the Wilcoxon-Mann-Whitney test and 1-way analysis of variance for continuous variables and by use of the χ^2 test for categorical variables. A P value of less than .05 was considered to be statistically significant. SAS (SAS Institute) and Stata (StataCorp) were used for statistical analysis.

RESULTS

Of the 2,003 patients enrolled in the NASCENT study, 524 (26.2%) had medical insurance claims data.[11] Of these 524 patients, 30 (5.7%) had microbiologically confirmed VAP and were matched by diagnostic code to 90 control patients without VAP (Figure 1). There were no statistically significant differences between cohorts in demographic characteristics at baseline or in risk factors for VAP within 30 days of admission (Table 1).

Median total hospital charges were $198,200 for case patients with VAP and $96,540 for control patients without VAP ($P < .001$) (Table 2). The average derived cost-to-charge ratios were similar for case patients and control patients (0.38 vs 0.41; $P = .203$), resulting in median costs of $76,730 for case patients and $41,250 for control patients ($P = .001$). After adjusting for DRG payments, median losses to hospitals were $32,140 for case patients and $19,360 for control patients ($P = .151$). Between-cohort differences remained statistically significant in the subset of patients who survived, except for median losses to hospitals ($P = .054$).

Services with the highest median costs for case patients and control patients were hospital services ($23,190 vs $11,110; $P = .004$), pharmacy services ($10,990 vs $6,310; $P = .101$), laboratory services ($8,512 vs $6,102; $P = .271$), and respiratory therapy ($4,838 vs $2,787; $P = .018$) (Table 3). Additional services with higher median costs for case patients than for control patients included cardiology services ($P = .046$), operating room services ($P < .001$), electrocardiogram services ($P = .017$), nuclear medicine services ($P = .042$), and recovery room services ($P = .030$).

The duration of intubation, the duration of ICU stay, and the duration of hospitalization were longer for case patients with VAP than they were for control patients without VAP (Table 4). Between-cohort differences remained statistically significant in the subset of patients who survived.

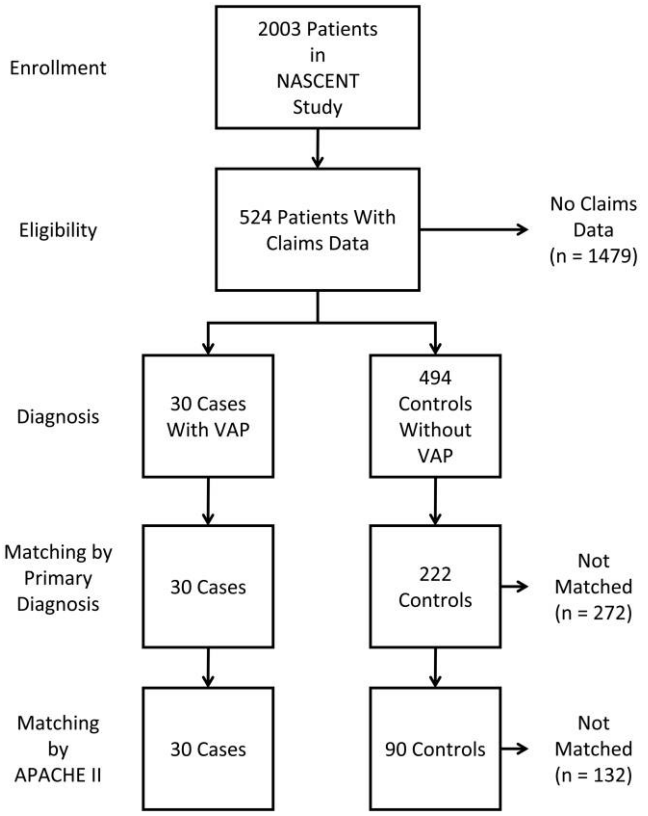

FIGURE 1. Flowchart summarizing enrollment of participants from the North American Silver-Coated Endotracheal Tube (NASCENT) study into the present study. APACHE, Acute Physiology and Chronic Health Evaluation; VAP, ventilator-associated pneumonia.

DISCUSSION

Our study examined the costs associated with patients with VAP diagnosed on the basis of microbiologic criteria, thereby avoiding the limitations of clinically diagnosed VAP and helping to delineate excess costs associated with this diagnosis. Unlike economic studies that focus on major cost determinants, such as length of stay, our approach provides a comprehensive analysis of the many different services that contribute to the economic burden of VAP. In addition, our approach includes both costs based on the cost-to-charge ratio and Medicare payments based on DRG, allowing calculation of the loss to hospitals for patients with VAP. Most economic outcomes, including charges, costs, and DRG payments, were significantly higher for case patients with VAP than for control patients without VAP. For example, the median total hospital cost was $35,480 higher for case patients with VAP than for control patients without VAP. The total hospital cost was higher for case patients with VAP because of the increased utilization of services, such as those provided by the hospital, respiratory department, and other patient-service units that may contribute indirectly. In addition, the duration of intubation, the duration of ICU stay, and the duration of hospitalization were longer for case patients with VAP than for control patients without VAP.

Other studies[4-7] have also reported that costs were significantly increased among case patients with VAP, compared with control patients without VAP. The highest estimate of approximately $40,000 was based on mean charges of $100,000 for case patients and $60,000 for control patients in a retrospective, matched cohort study of patients hospitalized in the late 1990s.[7] As expected, estimates of costs were lower than those of charges. For example, mean attributable costs from the same time period were approximately $10,000 in a retrospective, matched cohort study[4] and $12,000 in a prospective surveillance of patients with costs estimated by use of a step-down allocation method with multiple linear regression modeling to adjust costs for significant variables.[6] Safdar et al[5] estimated that the additional costs were approximately $10,000 on the basis of a quantitative systematic literature review of studies published from 1991 to 2003 and on the basis of microcosting that used attributable length of

TABLE 1. Data on Case Patients with Ventilator-Associated Pneumonia (VAP) and Control Patients without VAP from the North American Silver-Coated Endotracheal Tube Study, 2002–2006

Characteristic	Case patients ($n = 30$)	Control patients ($n = 90$)	P
Male sex	18 (60.0)	43 (47.8)	.246
Age			.413
Median ± SD, years	68.0 ± 15.6	64.5 ± 17.6	
Range, years	32–87	24–98	
APACHE II score, median (range)	18.0 (11–40)	18.0 (9–40)	.925
Risk factors for VAP within 30 days of hospitalization			
Functional dependency	7 (23.3)	11 (12.2)	.140
Smoking	1 (3.3)	15 (16.7)	.063
Impaired sensorium	6 (20.0)	11 (12.2)	.290
COPD	3 (10.0)	9 (10.0)	>.99
Long-term steroid use	2 (6.7)	9 (10.0)	.584
Emergency surgery or trauma	1 (3.3)	11 (12.2)	.160
None	3 (10.0)	18 (20.0)	.212
Immunodeficiency[a]	4 (13.3)	26 (28.9)	.088
Use of silver-coated endotracheal tube	16 (53.3)	45 (50.0)	.752
Duration of intubation[b]			
Median (range), days	3.7 (1.0–11.4)	4.7 (1–21.8)	.332
⩽4 days	16 (53.3)	36 (40.0)	.202[c]
>4 days	14 (46.7)	54 (60.0)	
Mortality	5 (16.7)	29 (32.2)	.102

NOTE. Data are no. (%) of patients, unless otherwise indicated. APACHE, Acute Physiology and Chronic Health Evaluation; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

[a] Defined as >2 weeks of high-dose steroids, presence of human immunodeficiency virus antibody, chemotherapy within 45 days, chemotherapy-induced neutropenia, or immunosuppression for organ transplantation.

[b] For case patients, we determined the duration of intubation before the onset of VAP.

[c] Determined from χ^2 analysis of case patients and control patients for group values.

stay data. More recently, Anderson et al[10] estimated that the weight-adjusted mean costs were $25,000 per episode of VAP on the basis of a literature review, with costs standardized to US dollars in 2005. Collectively, findings from previous studies combined with our findings suggest that the economic burden of VAP incurred by hospitals is increasing.

Our study updates the body of evidence used to characterize the economic burden of VAP and to determine which services increase cost; this body of evidence is essential because CMS reimbursement is based on DRGs, not on each of the services utilized. In addition, our study provides data to incentivize the use of preventive strategies in North American hospitals, which will become more important if the CMS classifies VAP as a nonreimbursable, preventable complica-

TABLE 2. Total Hospital Charges and Costs for Case Patients with Ventilator-Associated Pneumonia (VAP) and Control Patients without VAP from the North American Silver-Coated Endotracheal Tube Study, 2002–2006

Type of patients, charges and costs	Case patients ($n = 30$)	Control patients ($n = 90$)	P
All patients			
Charges, US$	198,200 (46,480–579,700)	96,540 (28,920–531,800)	<.001
CCR costs, US$	76,730 (9,713–276,500)	41,250 (8,247–171,600)	.001
Average derived CCR	0.38 (0.18–0.54)	0.41 (0.18–0.62)	.203
DRG payment, US$	39,840 (7,151–152,400)	17,840 (4,374–126,200)	.001
CCR cost minus DRG payment, US$	32,140 (−34,330 to 191,600)	19,360 (−84,860 to 126,300)	.151
Survivors[a]			
Charges, US$	202,500 (88,180–579,700)	102,300 (31,030–531,800)	<.001
CCR costs, US$	89,550 (33,860–276,500)	43,020 (8,247–171,600)	<.001
Average derived CCR	0.38 (0.19–0.54)	0.40 (0.18–0.62)	.683
DRG payment, US$	40,370 (30,000–152,400)	20,510 (4,374–109,400)	.004
CCR cost minus DRG payment, US$	36,920 (−10,590 to 191,600)	25,300 (−67,490 to 114,000)	.054

NOTE. Data are median values (range). CCR, (hospital) cost–to–(patient) charge ratio; DRG, diagnosis-related group.

[a] There were 25 case patients and 61 control patients who survived.

TABLE 3. Hospital Costs for Case Patients with Ventilator-Associated Pneumonia (VAP) and Control Patients without VAP from the North American Silver-Coated Endotracheal Tube Study, 2002–2006, by Selected Types of Service

Service (CMS codes)	Median cost (range), US$		P
	Case patients ($n = 30$)	Control patients ($n = 90$)	
Hospital (110–214)	23,190 (2,079–76,070)	11,110 (661–90,330)	.004
Pharmacy (250–259)	10,990 (1,376–70,580)	6310 (306–47,220)	.101
Laboratory (300–309)	8,512 (1,541–43,340)	6,102 (935–29,500)	.271
Respiratory therapy (410–419)	4,838 (0–20,070)	2,787 (0–17,500)	.018
Radiology (320–333)	1,531 (287–5,426)	1,179 (188–8,760)	0.146
Cardiology (480–489)	968 (0–14,040)	491 (0–6,029)	0.046
Computed tomography (350–359)	737 (0–9,300)	818 (0–5,644)	.167
Operating room (369–371)	717 (0–1,515)	0 (0–1,882)	<.001
Blood (380–391)	512 (0–33,430)	385 (0–37,620)	.544
Electrocardiogram (730–740)	291 (0–2,016)	126 (0–2,571)	.017
Pulmonary diagnostic, unlisted (460)	196 (0–10,770)	0 (0–5,994)	.108
Orthopedic diagnostic (920–924)	145 (0–3,177)	0 (0–1,900)	.134
Occupational therapy (430–434)	17 (0–2,021)	0 (0–852)	.067
Orthopedic rehabilitation (940–949)	0 (0–8,023)	0 (0–1,199)	.210
Renal (800–809, 881)	0 (0–5,165)	0 (0–5,707)	.668
Ambulatory (490)	0 (0–4,479)	0 (0–1,364)	.379
Nuclear medicine (340–343)	0 (0–1,557)	0 (0–1,131)	.042
Recovery room (710–719)	0 (0–1,060)	0 (0–1,173)	.030

NOTE. CMS, Centers for Medicare and Medicaid Services.

tion. Preventive strategies[13,17,18] are often bundled, but implementation is challenging. Educational interventions have been shown to be successful at encouraging the use of bundled preventive strategies, and the use of these interventions has been shown to significantly reduce infection rates in prospective observational studies.[19-21] Unfortunately, these benefits tend to subside when there is a lack of continuous educational reinforcement, and nonadherence is common among clinicians.[22-24] Barriers to adherence include a lack of resources and an increase in costs.[22,24] To maximize the likelihood of success, Craven[25] advocates a team approach comprising infection control professionals, infectious disease specialists, critical care nurses and physicians, respiratory care staff, administrators, risk management staff, microbiologists, and other stakeholders—all under the direction of an advocate or "champion" who can market preventive strategies to decision makers responsible for allocating resources. Our findings provide economic support for this multidisciplinary approach, and the diversity of services impacted by VAP suggests that the list of team members and services may need to be expanded.

Our study had several limitations, some of which are inherent to retrospective cohort analyses. First, our findings were subject to selection bias due to the retrospective design, but data were obtained from a large, prospective, multicenter, randomized study.[11] To limit bias, we matched case patients to control patients by primary diagnostic code and APACHE II score; on the basis of baseline demographic characteristics of patients and their risk factors for VAP, the cohorts appeared to be balanced (ie, all P values greater than .05). Our findings were also subject to selection bias inherent to a randomized, controlled study performed primarily at teaching hospitals in the United States, and therefore they may not be generalizable to nonteaching hospitals or to other countries. In addition, we

TABLE 4. Duration of Intubation and Length of Stay (LOS) for Case Patients with Ventilator-Associated Pneumonia (VAP) and Control Patients without VAP from the North American Silver-Coated Endotracheal Tube Study, 2002–2006

Type of patient and variable	Median no. of days (range)		P
	Case patients ($n = 30$)	Control patients ($n = 90$)	
All patients			
Intubation duration[a]	10.1 (3–25)	4.7 (1–22)	<.001
VAP onset ⩽4 days	9.1 (3–20)		
VAP onset >4 days	12.9 (5–25)		
Intensive care unit LOS[a]	18.5 (5–33)	8.0 (2–33)	<.001
VAP onset ⩽4 days	11.5 (5–29)		
VAP onset >4 days	23.5 (6–33)		
Hospital LOS[a]	26.5 (5–36)	14.0 (3–50)	<.001
VAP onset ⩽4 days	18.5 (5–31)		
VAP onset >4 days	31.5 (20–36)		
Survivors[b]			
Intubation duration	10.2 (3–25)	4.8 (1–22)	<.001
Intensive care unit LOS	19.0 (5–33)	8.0 (2–33)	<.001
Hospital LOS	29.0 (12–36)	16.0 (3–50)	<.001

[a] Duration after VAP onset.

[b] There were 25 case patients and 61 control patients who survived.

focused on microbiologically documented VAP, as described in the NASCENT study[11]; other studies[4-7] have reported the economic burden of clinically suspected VAP, with and without microbiologic confirmation, as aggregate findings.

Second, claims data were available for only one-fourth of patients in the NASCENT study,[11] but the 30 case patients represent the largest economic study of patients with microbiologically confirmed VAP. Third, the two-fold increase in mortality among control patients was unexpected and could have contributed to between-cohort differences in cost and length of stay; however, between-cohort differences remained statistically significant among survivors. Fourth, microcosting was not feasible for this large multicenter study, so costs were estimated by summing charges from individual services and then applying the estimated cost-to-charge ratios on the basis of matched CMS DRGs. We were not able to obtain service-specific ratios or patient-specific actual costs but did use hospital-specific ratios and charges for each hospital. Fifth, sample size precluded statistical evaluation of the onset of VAP on economic burden, but the higher cost of late-onset, as opposed to early-onset, VAP has already been reported.[6] Sixth, we performed an unmatched statistical analysis on matched data, which would tend to increase estimates of standard error and make it more difficult to detect between-group differences. An unmatched approach almost certainly resulted in a conservative analysis of between-group differences. Seventh, an estimation of attributable costs, including each of the services shown in Table 3, was not feasible, but other studies have shown that patients with VAP have higher attributable costs than do patients without VAP.[4-6]

In conclusion, case patients with microbiologically confirmed VAP had a longer duration of mechanical ventilation, a longer ICU stay, and a longer hospital stay than did control patients without VAP, which led to significantly higher charges, hospital costs, and DRG payments. Our findings add to the current body of literature regarding the economic burden of VAP and the types of services that play a role in increasing the cost of hospital care for patients with VAP. The increased total costs and the diversity of resources utilized underscore the need for bundled measures to prevent VAP.

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