Costs associated with delirium in mechanically ventilated patients*

Eric B. Milbrandt, MD, MPH; Stephen Deppen, MA, MS; Patricia L. Harrison, MPH; Ayumi K. Shintani, PhD, MPH; Theodore Speroff, PhD; Renée A. Stiles, PhD; Brenda Truman, RN, MSN; Gordon R. Bernard, MD; Robert S. Dittus, MD, MPH; E. Wesley Ely, MD, MPH

Objective: **To determine the costs associated with delirium in mechanically ventilated medical intensive care unit patients.**

Design: **Prospective cohort study.**

Setting: **A tertiary care academic hospital.**

Patients: **Patients were 275 consecutive mechanically ventilated medical intensive care unit patients.**

Interventions: **We prospectively examined patients for delirium using the Confusion Assessment Method for the Intensive Care Unit.**

Measurements and Main Results: **Delirium was categorized as "ever vs. never" and by a cumulative delirium severity index. Costs were determined from individual ledger-level patient charges using cost-center-specific cost-to-charge ratios and were reported in year 2001 U.S. dollars. Fifty-one of 275 patients (18.5%) had persistent coma and died in the hospital and were excluded from further analysis. Of the remaining 224 patients, delirium developed in 183 (81.7%) and lasted a median of 2.1 (interquartile range, 1–3) days. Baseline demographics were similar between those with and without delirium. Intensive care unit costs (median, interquartile range) were significantly higher for those with at least one episode of delirium ($22,346, $15,083–$35,521) vs. those with no delirium ($13,332, $8,837–$21,471, $p <$ .001). Total hospital costs were also higher in those who developed delirium ($41,836, $22,782–$68,134 vs. $27,106, $13,875–$37,419, $p =$ .002). Higher severity and duration of delirium were associated with incrementally greater costs (all $p <$ .001). After adjustment for age, comorbidity, severity of illness, degree of organ dysfunction, nosocomial infection, hospital mortality, and other potential confounders, delirium was associated with 39% higher intensive care unit (95% confidence interval, 12–72%) and 31% higher hospital (95% confidence interval, 1–70%) costs.**

Conclusions: **Delirium is a common clinical event in mechanically ventilated medical intensive care unit patients and is associated with significantly higher intensive care unit and hospital costs. Future efforts to prevent or treat intensive care unit delirium have the potential to improve patient outcomes and reduce costs of care. (Crit Care Med 2004; 32:955–962)**

KEY WORDS: delirium, mechanical ventilation, critical care, cost, health economics

Delirium is an acute disturbance of consciousness and cognition that fluctuates in severity (1). Also known as acute encephalopathy (2), delirium occurs as many as eight of ten mechanically ventilated medical intensive care unit (ICU) patients. Although most clinicians consider ICU delirium an expected event that is iatrogenic and without consequence (3), it has recently been shown to be associated with increased length of stay, medical complications, and poor outcomes including increased mortality (4–8). What is not known, however, are the costs associated with the development of ICU delirium.

The ICU is an expensive part of the healthcare system, accounting for 1% of the annual U.S. gross domestic product (9). The average cost of ICU care is estimated to be between $20,000 and $30,000 per patient (10–12). Some of the costs of critical care are due to complications such as ventilator-associated pneumonia (13, 14) and catheter-related bloodstream infection (15). Because of the significant clinical and economic impact of these conditions, efforts have been made to identify risk factors for their development and interventions to reduce their incidence. On the other hand, little is known about the economic impact of delirium in critically ill patients, despite the fact that it occurs in the majority of those treated in the ICU (6, 7). We conducted this investigation to determine the costs associated with delirium in mechanically ventilated medical ICU patients.

MATERIALS AND METHODS

Patients. The institutional review board approved this study, and informed consent was obtained from patients or their surrogate. Enrollment criteria included any adult, mechanically ventilated patient admitted to the medical or coronary ICUs of Vanderbilt University's 631-bed medical center from February 2000 to May 2001. During the study period, 555 mechanically ventilated patients

***See also p. 1080.**

From The CRISMA Laboratory (Clinical Research, Investigation, and Systems Modeling of Acute Illness) (EBM), Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA; the Center for Clinical Improvement (SD, TS, RAS), Division of General Internal Medicine and Center for Health Services Research (PLH, AKS, TS, RAS, BT, RSD, EWE), and Division of Allergy, Pulmonary, and Critical Care Medicine (BT, GRB, EWE), Department of Internal Medicine, Vanderbilt University School of Medicine, Nashville, TN; and VA Tennessee Valley Geriatric Research, Education, and Clinical Center (TS, RSD, EWE), Vanderbilt University School of Medicine, Nashville, TN.

Supported, in part, by NIH NRSA Research Training Grant HL07123, Bethesda, MD (EBM); the Vanderbilt University Hospital Pharmacy and Therapeutics Committee, Nashville, TN (EBM); the American Federation for Aging Research Pharmacology in Aging Grant, New York, NY (EWE); the Paul Beeson Faculty Scholar Award from the Alliance for Aging Research, Washington, DC (EWE); and a K23 from the National Institute of Health (AG01023-01A1), Bethesda, MD (EWE).

DOI: 10.1097/01.CCM.0000119429.16055.92

were admitted to the ICU, of whom 275 (49.5%) were enrolled whereas 280 were excluded according to criteria defined *a priori*, including a history of psychosis or neurologic disease (e.g., cerebrovascular accident) (n = 86), deafness or inability to understand English (n = 13), extubation before enrollment (n = 69), previously enrolled (n = 27), patient or family refusal (n = 41), or death before study nurses' assessments (n = 44). Other data from this cohort of patients have been published as would be expected from prospective cohort investigations that have the capacity to address multiple issues. Specifically, data regarding the incidence of delirium in first 111 patients were published in the original Confusion Assessment Method for the ICU (CAM-ICU) validation article (6) and for the entire cohort in the Richmond Agitation-Sedation Scale (RASS) validation study (16). Clinical outcomes data from this cohort, however, have only been published in abstract form (8). All of the cost data in this report are entirely original and have not been previously published.

Study Protocol. Study nurses enrolled patients each morning and recorded baseline demographics including Acute Physiology and Chronic Health Evaluation II (17), Sequential Organ Failure Assessment score (18, 19), and Charlson Comorbidity Index (20). Surrogate assessments were used to obtain baseline activities of daily living (21), visual and hearing deficits, and the modified Blessed Dementia Rating Scale (22). Data regarding the presence of nosocomial infection (ventilator-associated pneumonia, catheter-related bloodstream infection, urinary tract infection, and other nosocomial infections) were collected prospectively by trained infection control nurses using Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System criteria (23, 24).

Delirium Assessment. Patients' daily cognitive status was defined as normal, delirious, or comatose using a combined neurologic assessment that took a median 1 min and objectively measured patients' arousal and delirium status. Arousal was measured using the Glasgow Coma Scale (25) and the RASS (16, 26). Delirium was measured using the CAM-ICU (Table 1) (4, 6), a well-validated and highly reliable tool based on *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) criteria for delirium (27). By definition, patients were delirious if they were responsive to verbal stimulation with eye opening and were CAM-ICU positive. Patients were defined as comatose if they a) responded only to physical/painful stimulation with movement but had no eye opening or ability to communicate; or b) had no response to verbal or physical stimulation. This definition of coma (28) corresponded to a median Glasgow Coma Scale of 4 out of possible 15 and a RASS of −4 or −5. Patients were considered normal if they were not delirious or comatose.

To examine cost differences between groups, patients were categorized by a) the clinical distinction of delirium "ever vs. never"; and b) a cumulative delirium severity index. The description of these schemes was as follows: Ever vs. never: If patients ever had delirium while in the ICU (i.e., CAM-ICU positive with a RASS level of −3 or higher), then they were categorized as "ever delirium." All others were categorized as "never delirium." Cumulative Delirium Severity Index: To stratify patients according to severity and duration of delirium, we assigned patients points for each daily assessment (Table 2). On a given day, patients who were CAM-ICU negative received zero points whereas CAM-ICU-positive patients received between 1 and 6 points as determined by the absolute RASS score plus 1. In this way, patients with greater degrees of hyperactive or hypoactive delirium received incrementally greater points. Daily points were totaled to arrive at a cumulative delirium severity index. Patients with zero cumulative points were considered "normal." The remaining patients were grouped by tertiles of cumulative delirium severity (mild, moderate, or severe).

Cost Determination. Costs were determined from individual ledger-level patient charges using cost-center-specific cost-to-charge ratios and were reported in year 2001 U.S. dollars from the hospital perspective. Costs were defined as "ICU related" if they occurred on a day that the patient was in the ICU, with the exception of surgical and emergency department charges that occurred on the day of ICU admission. These exceptions and all other costs were classified as non-ICU related. Average cost per ICU day was calculated by dividing the total ICU cost by the ICU length of stay. ICU costs were further classified by grouping each ICU cost into clinically meaningful cost subcategories (i.e., bed expenses, pharmacy, laboratory, diagnostic radiology).

Statistical Analyses. Baseline characteristics were compared between patients who ever had delirium and never had delirium using Fisher's exact tests, Wilcoxon rank sum tests, or Student's *t*-tests as appropriate. Wilcoxon rank sum tests were also used to compare distributions of ICU cost, total hospital cost, and the duration of mechanical ventilation between those who did and did not develop delirium. Multiple linear regression was used to evaluate the association between delirium and cost after controlling for additional covariates. Because the ICU and total hospital cost data were skewed, the natural log transformation was taken of both response variables, a common practice in the analysis of cost data (29, 30), after trimming exceedingly high total ICU costs (n = 2) and total hospital costs (n = 6) to $100,000 and $200,000, respectively. In this way, outlier patients had their maximum ICU and hospital costs trimmed for the multivariable analyses with assignment of $100,000 and $200,000, respectively. All multivariable analyses were adjusted for the following covariates, which were identified *a priori* as having possible confounding relationships with cost: age, gender, Charlson Comorbidity Index (20), Acute Physiology and Chronic Health Evaluation II score (17), Sequential Organ Failure Assessment score (18, 19), insurance status, race, HIV disease, renal failure, liver disease, congestive heart failure, alcohol abuse, drug abuse, malnutrition, sepsis, and nosocomial infection. One factor not chosen *a priori*, "surviving to hospital discharge," was added to the models following suggestion during peer review. Performing the analyses with or without this variable did not significantly change any of our results, and the current model includes this variable. Estimated ratios of unadjusted and adjusted cost for comparison groups with 95% confidence intervals were calculated. All p values reported are two-sided and all analyses were conducted using SAS release 8.02 (Cary, NC).

RESULTS

Patient Characteristics. Fifty-one of 275 patients (18.5%) had persistent coma and died in the hospital after a median of 8 (range, 4–12) hospital days. Due to their 100% mortality rate and the inability to ever evaluate them for delirium, these persistent coma patients were not included in the remainder of the analyses. Of the remaining 224 patients, delirium developed in 183 (81.7%) for a median of 2.1 (interquartile range, 1–3) days. At enrollment there were no significant differences between the "ever delirium" and "never delirium" groups in terms of age, race, gender, severity of illness, degree of organ dysfunction, or admitting diagnosis (Table 3). Patients who developed delirium had longer ICU (median, 8 vs. 5 days) and hospital length of stay (median, 21 vs. 11 days) (all $p < .001$).

Univariate Analysis of Cost. More than 395,000 individual line item charges were converted to costs and analyzed. Median (interquartile range) ICU and total hospital costs were $20,654 ($13,478–$32,760) and $36,936 ($21,066–$65,340), respectively. ICU costs (median, interquartile range) were significantly higher for patients with at least one episode of delirium ($22,346, $15,083–$35,521) compared with those who were never delirious ($13,332, $8,837–$21,471, $p < .001$, Fig. 1). Total hospital costs were also higher in those who developed delirium ($41,836, $22,782–$68,134) than in those who did not ($27,106, $13,875–$37,419, $p = .002$). Delirious patients had significantly higher costs in most major

Table 1. Confusion Assessment Method for Intensive Care Unit (CAM-ICU)

CAM-ICU Features and Descriptions		
1. Acute onset or fluctuating course	**Absent**	**Present**
A. Is there evidence of an acute change in mental status from the baseline? **OR** **B.** Did the (abnormal) behavior fluctuate during the past 24 hrs, that is, tend to come and go, or increase and decrease in severity as evidenced by fluctuation on a sedation scale (e.g. RASS), GCS, or previous delirium assessment?		
2. Inattention	**Absent**	**Present**
Did the patient have difficulty focusing attention as evidenced by scores <8 on either the auditory or visual component of the ASE?		
3. Disorganized thinking	**Absent**	**Present**
Is there evidence of disorganized or incoherent thinking as evidenced by incorrect answers to two or more of the four questions and/or inability to follow the commands? **Questions** (alternate set A and set B): **Set A** 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does 1 lb weigh more than 2 lbs? 4. Can you use a hammer to pound a nail? **Set B** 1. Will a leaf float on water? 2. Are there elephants in the sea? 3. Do 2 lbs weigh more than 1 lb? 4. Can you use a hammer to cut wood? **Other:** 1. Are you having any unclear thinking? 2. Hold up this many fingers. (Examiner holds two fingers in front of patient) 3. Now do the same thing with the other hand. (Not repeating the number of fingers)		
4. Altered level of consciousness	**Absent**	**Present**
Is the patient's level of consciousness anything other than alert, such as vigilant, lethargic, or stupor? (e.g., RASS other than "0" at time of assessment) **Alert** Spontaneously fully aware of environment and interacts appropriately **Vigilant** Hyperalert **Lethargic** Drowsy but easily aroused, unaware of some elements in the environment or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded minimally **Stupor** Becomes incompletely aware when prodded strongly; can be aroused only by vigorous and repeated stimuli, and as soon as the stimulus ceases, stuporous subject lapse back into the unresponsive state		
Overall CAM-ICU (features 1 and 2 and either feature 3 or 4):	**Yes**	**No**

RASS, Richmond Agitation-Sedation Scale; GCS, Glasgow Coma Scale; ASE, Attention Screening Examination.

subcategories of ICU cost, including bed expenses, pharmacy, and laboratory (Table 4). Patients who developed delirium had similar average cost per ICU day ($4,592, $3,662–$6,417) compared with their nondelirious counterparts ($5,177, $3,993–$7,540, $p = .25$). Patients who did not survive hospitalization had greater ICU ($24,848 vs. $19,556, $p = .004$) and total hospital costs ($46,683 vs. $34,737, $p = .007$) than did hospital survivors.

Using the cumulative delirium severity index, we found that greater severity and duration of delirium were associated with significantly higher ICU and total hospital costs (Fig. 2). No significant cost differences were found between

Table 2. Delirium severity index determination[a]

CAM-ICU	RASS	Delirium Severity Index
—		0
+	+4	5
+	+3	4
+	+2	3
+	+1	2
+	0	1
+	−1	2
+	−2	3
+	−3	4
+	−4	5
+	−5	6

CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; RASS, Richmond Agitation-Sedation Scale.

[a]Delirium severity index determination: Nondelirious (i.e., CAM-ICU negative) patients received zero delirium severity index points for a given day whereas delirious (i.e., CAM-ICU positive) patients received between 1 and 6 points on that day as determined by the absolute RASS score plus 1. In this way, patients with greater degrees of hyperactive or hypoactive delirium receive incrementally greater delirium severity index points. Daily points were then summed to arrive at a cumulative delirium severity index.

Table 3. Baseline characteristics at ICU admission

Characteristic	Never Delirium (n = 41)	Ever Delirium (n = 183)	p Value
Age, mean (SD), yrs	54 (17)	56 (17)	.35
Men, %	44	52	.35
Race			.87
White, %	78	79	
Black, %	22	21	
Charlson Comorbidity Index, mean (SD)[a]	3.2 (2.8)	3.2 (2.8)	.19
Vision deficits, %	70	68	.85
Hearing deficits, %	16	19	.65
Blessed Dementia Rating Scale, mean (SD)[b]	0.14 (0.6)	0.23 (0.8)	.45
Activities of daily living, mean (SD)[c]	0.81 (2.4)	0.91 (2.3)	.58
APACHE II score, mean (SD)[d]	23.2 (9.6)	25.6 (8.1)	.06
SOFA score, mean (SD)[e]	9.5 (2.9)	9.6 (3.4)	.93
ICU admission diagnosis, %[f]			
Sepsis/acute respiratory distress syndrome	59	43	.06
Pneumonia	15	19	.50
Myocardial infarction/congestive heart failure	10	8	.75
Hepatic or renal failure	0	6	.11
Chronic obstructive pulmonary disease	5	10	.31
Gastrointestinal bleeding	5	4	.76
Malignancy	0	4	.20
Drug overdose	7	4	.43
Other	29	27	.85

APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit.

[a]Charlson Comorbidity Index (20) represents the sum of a weighted index that takes into account the number and seriousness of preexisting comorbidities; [b]Blessed Dementia Rating Scale (22) was validated as an instrument to be completed by surrogates to determine the presence of dementia. Scores range from 0 (best) to 17 (worst), with ≥4.5 representing the most widely used threshold for dementia; [c]activities of daily living scale (21) was completed by surrogates to estimate the baseline performance of the patient during the period just prior to the acute illness requiring admission to the intensive care unit. The scale ranges from 0 (best) to 12 (worst); [d]APACHE II (17) is a severity of illness scoring system, and these data were calculated using the most abnormal variables during the first 24 hrs following admission to the intensive care unit. APACHE II scores range from 0 (best) to 71 (worst); [e]SOFA (18, 19) is an organ failure scoring system that was also calculated using the most abnormal variables during the first 24 hrs following admission to the intensive care unit. SOFA scores range from 0 (best) to 24 (worst); [f]the admission diagnoses were recorded by the patients' medical team as the diagnoses most representative of the reason for ICU admission.

those with a cumulative delirium severity classification of "normal" and those classified as "mild" (p = .29, data not shown); therefore, the "normal" and "mild" categories were pooled. ICU costs (median, interquartile range) were greatest for those in the severe category ($34,330, $48,056–$25,087), followed by those for the moderate ($19,693, $26,836–$15,861) and normal/mild ($12,642, $8,129–$19,383) categories (all $p < .001$). Total hospital costs were similarly disbursed across the severe ($49,054, $38.827–$85,321), moderate ($36,720, $23,117–$54,208), and normal/mild ($21,289, $12,178–$50,848) categories.

Multivariable Analysis of Cost. Figure 3 presents the relative increase in ICU and total hospital costs obtained from the univariate and multivariable analyses. After adjustment for age, comorbidity, severity of illness, degree of organ dysfunction, nosocomial infection, hospital mortality and other covariates, the development of delirium was associated with a relative cost of ICU and total hospital care of 1.39 (95% confidence interval, 1.12–1.72; p = .003) and 1.31 (confidence interval, 1.01–1.70; p = .04), respectively. This correlates with a 39% increase in ICU cost and 31% increase in total hospital cost. When analyzed according to cumulative delirium severity and compared with normal and mild category, patients in the moderate (relative cost, 1.44; 95% confidence interval, 1.21–1.72; $p \leq .001$) and severe (relative cost, 2.25; confidence interval, 1.86–2.72; $p < .001$) categories had incrementally greater ICU costs. Likewise, total hospital costs were increased in the moderate (relative cost, 1.37; confidence interval, 1.09–1.74; p = .01) and severe groups (relative cost, 1.67; confidence interval, 1.29–2.15; $p < .001$).

DISCUSSION

This is the first report of the costs associated with delirium in mechanically ventilated ICU patients. We have shown that the severity and duration of delirium were independently associated with increased ICU and total hospital costs. Even after we controlled for important potentially confounding variables, such as baseline comorbidities and severity of illness, we found that delirium was associated with a 1.4-fold and 1.3-fold increase in ICU and total hospital costs, respectively. In addition, the data demonstrated a "dose-response" in which cumulative delirium severity was associated with incrementally greater cost.

Delirium could be related to increased cost through a variety of mechanisms, such as greater severity of illness or degree of organ dysfunction (31–33), admitting diagnosis, or the presence of nosocomial infection (13–15). However, inclusion of these variables in the multivariable analyses had little effect on the costs attributable to delirium. Another potential mechanism could be through increased intensity of resource use (34–39), although this seems unlikely given

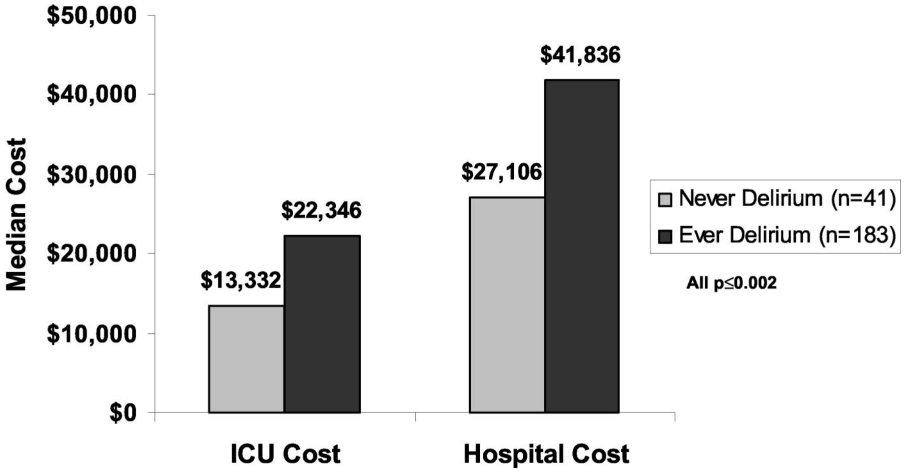

Figure 1. Median intensive care unit (*ICU*) and hospital cost per patient. This histogram shows cost according to clinical categorization of "ever delirium" vs. "never delirium." Delirium was significantly associated with increased ICU and hospital cost.

Delirium is a common clinical event in mechanically ventilated medical intensive care unit patients and is associated with significantly higher intensive care unit and hospital costs.

Table 4. Patient costs for major subcategories of ICU care

Characteristic	Never Delirium (n = 41)	Ever Delirium (n = 183)	*p* Value
Bed expenses	6,278 (3,791–8,804)	10,061 (6,312–16,016)	<.001
Pharmacy	1,641 (918–3,319)	3,293 (1,993–5,106)	<.001
Laboratory	1,303 (665–2,369)	2,262 (1,011–4,260)	.003
Diagnostic radiology	1,106 (451–1,946)	1,732 (885–2,834)	.002
Respiratory therapy[a]	897 (650–1,467)	1,466 (1,019–2,441)	<.001
Central supply	760 (411–1,301)	1,234 (586–2,245)	.001
Biomedical monitoring	105 (53–330)	178 (53–390)	.32
PT/OT/speech therapy	0 (0–141)	175 (0–429)	.001
Dialysis[b]	0 (0–0)	0 (0–0)	.61

ICU, intensive care unit; PT, physical therapy; OT, occupational therapy. Values are median patient costs (US$) with interquartile ranges given in parentheses. Subcategories of ICU cost were based on the general ledger category assigned to each cost item in the hospital billing system.

[a]Includes costs of mechanical ventilation; [b]27 of 183 (14.8%) delirious patients and 4 of 41 (12.2%) nondelirious patients required dialysis. Because so few required dialysis, the median (interquartile range) cost of dialysis for both patient groups was $0 ($0–$0).

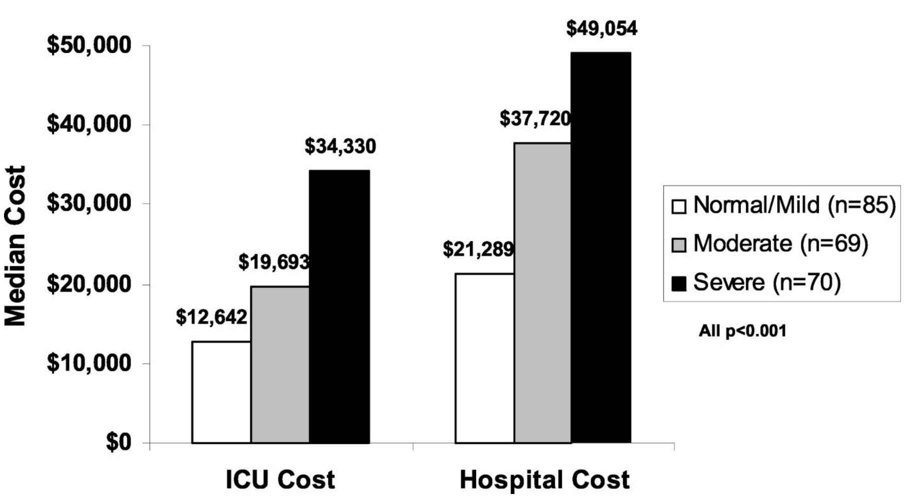

Figure 2. Median intensive care unit (*ICU*) and hospital cost per patient. This histogram shows cost according to cumulative delirium severity indexes. Increasing delirium severity was significantly associated with incrementally greater ICU and hospital cost.

that there were no differences in cost per ICU day between delirious and nondelirious patient groups. A more plausible mechanism to explain the delirium-cost relationship is found in length of stay, which is known to be a major cost driver (12) and which was greater in delirious patients in our study. Because of the observational nature of this study, we cannot determine whether delirium caused longer lengths of stay or if longer lengths of stay simply resulted in greater time at risk for developing delirium. However, delirium could easily lead to increased length of stay and cost if it resulted in the administration of excess sedation or if it otherwise interfered with liberation from mechanical ventilation. The salient question is whether reducing the incidence and/or severity of delirium will alter clinical outcomes and improve cost. To address this question, future work should include trials of delirium prevention and treatment interventions that target modifiable risk factors such as sedation and analgesia practices (40) and early patient mobilization.

The associated annual cost of ICU delirium could be enormous. In our study, delirium occurred in 82% of mechanically ventilated patients and was associated with an incremental increase in ICU cost of $9,014 per patient. In the United States, there are approximately 880,000–2,760,000 ICU admissions annually for respiratory failure requiring mechanical ventilation (41–45). At the rate of delirium detected in our cohort, the estimated number of cases of ICU delirium could range from 721,600 to 2,263,200 per year with an associated increase in healthcare costs ranging between $6.5 and $20.4 billion. If we use

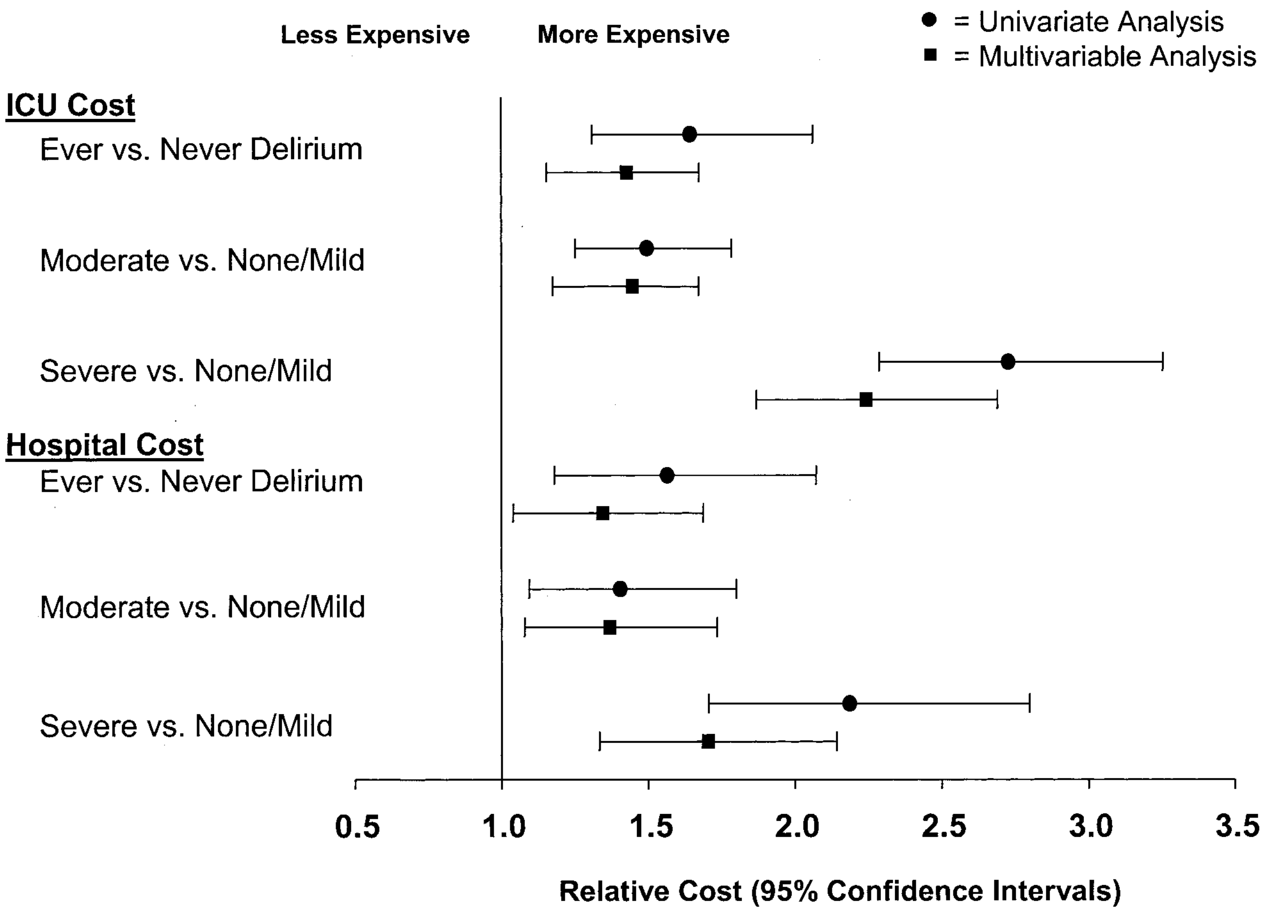

Figure 3. Univariate and multivariable analyses of delirium vs. cost. Point estimates of relative cost for univariate and multivariable analyses are indicated by solid circles and squares, respectively, and the 95% confidence intervals by horizontal lines. Patients were compared by clinical categorization (ever vs. never delirium) and by cumulative delirium severity index (moderate and severe vs. none/mild). A relative cost ratio of >1.0 indicates increased cost over comparison group. *ICU*, intensive care unit.

the incidence of delirium from a less severely ill ICU cohort in which delirium occurred in only 19% of patients (46), the estimated annual costs would still be in the range of $1.5–$4.7 billion. Since some of the additional cost associated with delirium in this study could be attributable to unmeasured differences between patient groups, these estimates represent the upper limit of the cost attributable to ICU delirium. If only 20% of the difference we noted was in fact due to delirium, then we would still find delirium to be a significant public health concern with $300 million to $4 billion in annual attributable costs.

The strengths of this study include the prospective use of valid and reliable measures of levels of arousal and delirium that were specifically designed for mechanically ventilated patients and that are recommended for routine use in the ICU (47). To determine costs, we used department-specific cost-to-charge ratios and detailed day-specific billing data. This approach has been shown to be accurate compared with even more rigorous cost-accounting methodologies (38, 48). Furthermore, since all costs were analyzed by the day in which they occurred, we were able to distinguish between ICU- and non-ICU-related costs, something that many ICU cost studies have been unable to do.

Several limitations of this study are important to consider. The data obtained from this observational cohort study were not intended to establish a causal link between delirium and cost. In addition, this analysis was limited to the hospital perspective and therefore did not include physician fees or costs that occurred after discharge. Given emerging data suggesting that patients who experience ICU delirium may also have ongoing neurocognitive deficits and decreased long-term survival (8, 49–52), an analysis of the long-term societal costs of ICU delirium is warranted. Furthermore, this study was limited to medical ICU patients. Whether these findings apply to other patient populations, such as surgical ICU patients, deserves additional study.

CONCLUSIONS

Delirium is a common clinical event in mechanically ventilated medical ICU patients and is independently associated with significantly higher ICU and hospital costs. These data underscore the importance of recent national recommendations for delirium assessment in all critically ill patients (47). Future efforts to prevent or treat ICU delirium have the potential to improve patient outcomes and reduce costs of care.

ACKNOWLEDGMENTS

We thank Derek Angus, MB, ChB, MPH; Tom Elasy, MD, MPH; Richard Wall, MD; Eric Grogan, MD; and Christianne Roumie, MD, for their insights and helpful contributions that guided us in our approach to this manuscript.

REFERENCES

1. Inouye SK, Bogardus ST Jr, Charpentier PA, et al: A multicomponent intervention to prevent delirium in hospitalized older patients. *N Engl J Med* 1999; 340:669–676
2. Kirshner HS. Behavioral Neurology. Second Edition. New York, Butterworth-Heinemann, 2001
3. Ely EW, Stephens RK, Jackson JC, et al: Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: A survey of 912 healthcare professionals. *Am J Respir Crit Care Med* 2002; 167:969
4. Ely EW, Margolin R, Francis J, et al: Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001; 29:1370–1379
5. Ely EW, Siegel MD, Inouye SK: Delirium in the intensive care unit: an under-recognized syndrome of organ dysfunction. *Semin Respir Crit Care Med* 2001; 22:115–126
6. Ely EW, Inouye SK, Bernard GR, et al: Delirium in mechanically ventilated patients: Validity and reliability of the confusion assessment method for the intensive care unit (CAM- ICU). *JAMA* 2001; 286:2703–2710
7. Ely W, Gautam S, Margolin R, et al: The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med* 2001; 27:1892–1900
8. Ely EW, Shintani A, Bernard G, et al: Delirium in the ICU is associated with prolonged length of stay in the hospital and higher mortality. *Am J Respir Crit Care Med* 2002; 165:A23
9. Socioeconomic Status and Health Chartbook (U.S. Department of HHS publication PHS 98–1232). Hyattsville, MD, U.S. Dept of Health and Human Services, 1998
10. Chelluri L, Mendelsohn AB, Belle SH, et al: Hospital costs in patients receiving prolonged mechanical ventilation: Does age have an impact? *Crit Care Med* 2003; 31: 1746–1751
11. Ely EW, Baker AM, Evans GW, et al: The distribution of costs of care in mechanically ventilated patients with chronic obstructive pulmonary disease. *Crit Care Med* 2000; 28: 408–413
12. Moerer O, Schmid A, Hofmann M, et al: Direct costs of severe sepsis in three German intensive care units based on retrospective electronic patient record analysis of resource use. *Intensive Care Med* 2002; 28:1440–1446
13. Rello J, Ollendorf DA, Oster G, et al: Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. *Chest* 2002; 122:2115–2121
14. Warren DK, Shukla SJ, Olsen MA, et al: Outcome and attributable cost of ventilator-associated pneumonia among intensive care unit patients in a suburban medical center. *Crit Care Med* 2003; 31:1312–1317
15. Marciante KD, Veenstra DL, Lipsky BA, et al: Which antimicrobial impregnated central venous catheter should we use? Modeling the costs and outcomes of antimicrobial catheter use. *Am J Infect Control* 2003; 31:1–8
16. Ely EW, Truman B, Shintani A, et al: Monitoring sedation status over time in the ICU: the reliability and validity of the Richmond Agitation Sedation Scale (RASS). *JAMA* 2003; 289:2983–2991
17. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818–829
18. Vincent JL, Moreno R, Takala J, et al: The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996; 22:707–710
19. Vincent JL, De Mendonca A, Cantraine F, et al: Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med* 1998; 26:1793–1800
20. Deyo RA, Cherkin DC, Ciol MA: Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992; 45:613–619
21. Katz S, Ford AB, Moskowitz RW, et al: Studies of illness in the aged—the index of ADL: A standardized measure of biological and psychosocial function. *JAMA*1963; 185:94–99
22. Blessed G, Tomlinson BE, Roth M: The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiat* 1968; 114:797–811
23. Emori TG, Edwards JR, Culver DH, et al: Accuracy of reporting nosocomial infections in intensive-care-unit patients to the National Nosocomial Infections Surveillance System: A pilot study. *Infect Control Hosp Epidemiol* 1998; 19:308–316
24. Gaynes RP, Horan TC. Surveillance of Nosocomial Infections. Hospital Epidemiology and Infection Control. Third Edition. Philadelphia, Lippincott Williams & Wilkins, 1999, pp 1285–1318
25. Teasdale G, Jennett B: Assessment of coma and impaired consciousness: A practical scale. *Lancet* 1974; 1:81–84
26. Sessler CN, Gosnell MS, Grap MJ, et al: The Richmond agitation-sedation scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002; 166:1338–1344
27. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. Washington, DC, American Psychiatric Association, 1994
28. Simpson DA: Clinical examination and grading. In: The Pathophysiology and Management of Severe Closed Injury. Reilly P, Bullock R (Eds). London, Chapman and Hall Medical, 1997, pp 145–165
29. Fischer LR, Wei F, Rolnick SJ, et al: Geriatric depression, antidepressant treatment, and healthcare utilization in a health maintenance organization. *J Am Geriatr Soc* 2002; 50:307–312
30. Oderda GM, Evans RS, Lloyd J, et al: Cost of opioid-related adverse drug events in surgical patients. *J Pain Symptom Manage* 2003; 25:276–283
31. Civetta JM, Hudson-Civetta JA, Nelson LD: Evaluation of APACHE II for cost containment and quality assurance. *Ann Surg* 1990; 212:266–274
32. Oye RK, Bellamy PE: Patterns of resource consumption in medical intensive care. *Chest* 1991; 99:685–689
33. Rapoport J, Teres D, Lemeshow S, et al: Explaining variability of cost using a severity-of-illness measure for ICU patients. *Med Care* 1990; 28:338–348
34. Brimhall BB, Dean T, Hunt EL, et al: Age and laboratory costs for hospitalized medical patients. *Arch Pathol Lab Med* 2003; 127: 169–177
35. Perls TT, Wood ER: Acute care costs of the oldest old: they cost less, their care intensity is less, and they go to nonteaching hospitals. *Arch Intern Med* 1996; 156:754–760
36. Perlstein PH, Atherton HD, Donovan EF, et al: Physician variations and the ancillary costs of neonatal intensive care. *Health Serv Res* 1997; 32:299–311
37. Studnicki J, Honemann D: Analyzing inpatient hospital duration and intensity: A methodology. *Qual Rev Bull* 1982; 8:15–26
38. Chalom R, Raphaely RC, Costarino AT Jr: Hospital costs of pediatric intensive care. *Crit Care Med* 1999; 27:2079–2085
39. Two-month mortality and functional status of critically ill adult patients receiving prolonged mechanical ventilation. *Chest* 2002; 121:549–558
40. Kress JP, Pohlman AS, O'Connor MF, et al: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000; 342: 1471–1477
41. Birkmeyer JD, Birkmeyer CM, Wennberg DE, et al: Leapfrog Safety Standards: Potential Benefits of Universal Adoption. Washington, DC, The Leapfrog Group, 2000
42. Lewandowski K, Metz J, Deutschmann C, et al: Incidence, severity, and mortality of acute respiratory failure in Berlin, Germany. *Am J Respir Crit Care Med* 1995; 151:1121–1125
43. Roupie E, Lepage E, Wysocki M, et al: Prevalence, etiologies and outcome of the acute respiratory distress syndrome among hypoxemic ventilated patients. SRLF Collaborative Group on Mechanical Ventilation. Societe de Reanimation de Langue Francaise. *Intensive Care Med* 1999; 25:920–929
44. Vincent JL, Akca S, De Mendonca A, et al: The epidemiology of acute respiratory failure in critically ill patients. *Chest* 2002; 121: 1602–1609
45. Dennett SL, Zeiher BG, Bowman L, et al: Who receives mechanical ventilation in the

U. S.: Diagnoses and resource use. *Crit Care Med* 2003; 30:A128
46. Dubois MJ, Bergeron N, Dumont M, et al: Delirium in an intensive care unit: A study of risk factors. *Intensive Care Med* 2001; 27: 1297–1304
47. Jacobi J, Fraser GL, Coursin DB, et al: Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002; 30:119–141
48. Shwartz M, Young DW, Siegrist R: The ratio of costs to charges: How good a basis for estimating costs? *Inquiry* 1995; 32:476–481
49. Dolan MM, Hawkes WG, Zimmerman SI, et al: Delirium on hospital admission in aged hip fracture patients: Prediction of mortality and 2-year functional outcomes. *J Gerontol* 2001; 55A:M527–M534
50. Jackson JC, Hart RP, Gordon SM, et al: Six-month neuropsychological outcome of medical intensive care unit patients. *Crit Care Med* 2003; 31:1226–1234
51. Katz IR, Curyto KJ, TenHave T, et al: Validating the diagnosis of delirium and evaluating its association with deterioration over a one-year period. *Am J Geriatr Psychiatry* 2001; 9:148–159
52. Rockwood K, Cosway S, Carver D: The risk of dementia and death after delirium. *Age Ageing* 2001; 28:551–556