2009

Cost-effectiveness analysis of a silver-coated endotracheal tube to reduce the incidence of ventilator-associated pneumonia

Andrew F. Shorr
Washington Hospital Center

Marya D. Zilberberg
EviMed Research Group, LLC

Marin Kollef
Washington University School of Medicine in St. Louis

Cost-Effectiveness Analysis of a Silver-Coated Endotracheal Tube to Reduce the Incidence of Ventilator-Associated Pneumonia •

Author(s): Andrew F. Shorr , MD, MPH, Marya D. Zilberberg , MD, MPH, Marin Kollef , MD

Reviewed work(s):
Source: *Infection Control and Hospital Epidemiology*, Vol. 30, No. 8 (August 2009), pp. 759-763
Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America
Stable URL: http://www.jstor.org/stable/10.1086/599005
Accessed: 08/03/2012 20:47

ORIGINAL ARTICLE

Cost-Effectiveness Analysis of a Silver-Coated Endotracheal Tube to Reduce the Incidence of Ventilator-Associated Pneumonia

Andrew F. Shorr, MD, MPH; Marya D. Zilberberg, MD, MPH; Marin Kollef, MD

OBJECTIVE. To conduct a cost-effectiveness analysis of the economic outcomes of ventilator-associated pneumonia (VAP) prevention associated with silver-coated endotracheal tubes versus uncoated endotracheal tubes.

DESIGN. We used a simple decision model based on a hypothetical 1,000-patient cohort intubated with silver-coated or uncoated endotracheal tubes. The primary end point was marginal hospital savings per case of VAP prevented (savings from using silver-coated endotracheal tubes minus acquisition cost divided by number of VAP cases prevented).

METHODS. We followed each branch of the decision model to VAP or no VAP and conducted Monte Carlo simulations and sensitivity analyses. Inputs for VAP incidence, relative risk reduction, and hospital costs were derived from publicly available sources. Relative risk reduction was derived from the pivotal study of the silver-coated endotracheal tube.

RESULTS. In the base-case analysis, we reduced the pivotal study relative risk in incidence of microbiologically confirmed VAP in patients intubated $\geqslant$24 hours from 35.9% to 24%. Thus, 23 of 97 expected cases of VAP could be prevented with silver-coated endotracheal tubes. The savings per case of VAP prevented was $12,840 in the base case, with assumed marginal VAP cost of $16,620 and costs of $90.00 for coated and $2.00 for uncoated endotracheal tubes. Estimates were most sensitive to assumptions regarding VAP cost and relative risk reduction with silver-coated endotracheal tubes. Nonetheless, in multivariate sensitivity analyses, the silver-coated endotracheal tubes yielded persistent savings (95% confidence interval, $9,630–$16,356) per case of VAP prevented. With other base-case inputs held constant, break-even cost for silver-coated endotracheal tubes was $388.

CONCLUSIONS. The silver-coated endotracheal tube represents a strategy for preventing VAP that may yield hospital savings.

Infect Control Hosp Epidemiol 2009; 30:759-763

Ventilator-associated pneumonia (VAP) places a substantial burden on healthcare systems because of its frequency and associated morbidity and hospital costs. VAP occurs at a rate of 2.5–12.3 episodes per 1,000 ventilator days[1] and occurs in 9.3%–23.5% of patients receiving mechanical ventilation.[2-5] VAP adds 5–7 days to the length of stay in the intensive care unit (ICU)[4] and 10–12 days to the length of hospitalization.[2,3] Specifically, estimates of attributable hospital costs for VAP range from $10,000 to $25,000.[3-6] Because of its high clinical and economic burden, VAP is now a focus of efforts to improve outcomes and patient safety in the ICU. These efforts will become more pertinent if the Centers for Medicare and Medicaid Services adds VAP to the list of conditions that will no longer be eligible for incremental payments.

A silver-coated endotracheal tube (Agento I. C., C. R. Bard) has been developed to reduce VAP incidence. The silver coating provides broad-spectrum antimicrobial activity,[7] reduces bacterial adhesion to the endotracheal tube,[8,9] and blocks biofilm formation on the endotracheal tube.[10] The silver ions are microdispersed in a proprietary polymer that may enhance antimicrobial activity by blocking bacterial adhesion to the endotracheal tube.[11-14] The North American Silver-Coated Endotracheal Tube (NASCENT) study[15] provided clinical evidence of efficacy in 2,003 patients expected to require mechanical ventilation for $\geqslant$24 hours. In this randomized, controlled, pivotal trial, the silver-coated endotracheal tube resulted in a 35.9% relative risk reduction of VAP ($P = .03$), with a cumulative incidence of microbiologically confirmed VAP of 7.5% in patients managed with uncoated endotracheal tubes and 4.8% in patients managed with silver-coated endotracheal tubes. Therefore, the estimated number of patients that must be treated with the silver-coated endotracheal tube to prevent 1 case of VAP is approximately 37 based on the 2.7% absolute risk reduction in patients intubated for $\geqslant$24 hours.

We hypothesized that use of silver-coated endotracheal tubes would be cost effective in patients requiring mechanical ventilation for $\geqslant$24 hours. Given the economic burden as-

From Washington Hospital Center, Washington, DC (A.F.S.); EviMed Research Group, LLC, Goshen, MA (M.D.Z.); and Washington University School of Medicine, St. Louis, MO (M.K.)

Received December 5, 2008; accepted March 6, 2009; electronically published June 19, 2009.

 0899-823X/2009/3008-0007$15.00. DOI: 10.1086/599005

sociated with VAP,[2-5] routine use of an endotracheal tube capable of reducing the incidence of VAP might offset the acquisition cost of the device, resulting in savings to the hospital. To test this hypothesis, we developed a decision model to compare the costs of silver-coated and uncoated endotracheal tubes relative to those associated with the development of VAP.

METHODS

We compared economic outcomes in terms of VAP prevention with the use of silver-coated endotracheal tubes to outcomes with the use of uncoated endotracheal tubes in a hypothetical cohort of 1,000 patients expected to require mechanical ventilation for $\geqslant$24 hours. The primary end point was marginal hospital savings associated with prevention of 1 case of VAP, and it was calculated as savings in VAP hospital costs associated with use of the silver-coated endotracheal tube minus direct hospital acquisition cost of the endotracheal tube divided by the number of VAP cases prevented. This ratio represented the cost (or savings) per 1 case of VAP prevented. The secondary end point was marginal hospital savings (or costs) associated with reduced incidence of VAP over the entire 1,000-patient cohort. We followed the recommendations of the Panel on Cost-Effectiveness in Health and Medicine.[16]

Model structure and inputs. We used a simple decision tree to model the outcomes. The only decision node represented the determination to use silver-coated or uncoated endotracheal tubes. We passed the 1,000-patient cohort through each branch of the decision tree separately to development of VAP or no development of VAP. The model required the following inputs: incidence of VAP, relative risk reduction of VAP with silver-coated endotracheal tube, hospital costs associated with VAP, and costs of silver-coated and uncoated endotracheal tubes (Table 1). We used the medical care component of the Consumer Price Index[17] to adjust the estimated cost of VAP to 2007 US dollars.

Monte Carlo simulations and sensitivity analyses. We performed Monte Carlo simulations and sensitivity analyses to identify important model uncertainties and to assess the robustness of our findings across the wide range of VAP incidence in different patient populations. Each outcome was tested in 10,000 simulation trials, while the estimates were simultaneously and randomly varied across the ranges specified in Table 1. The ranges for the incidence of VAP[4] and hospital cost of VAP[5] were bound by their corresponding published 95% confidence intervals. We varied the relative risk reduction of VAP by $\pm$50% and the cost estimate of the silver-coated endotracheal tube by $\pm$\$10. To bias the model against the silver-coated endotracheal tube, we set the lower bound of the acquisition cost for the uncoated endotracheal tube at \$0.00. We conducted sensitivity analyses to assess the univariate contribution of uncertainty in each model parameter to the variability in outcomes and subsequently completed a 2-way sensitivity analysis—simultaneously varying the 2 most influential inputs on the outcome estimate. We also tested break-even scenarios to determine circumstances under which each input was no longer associated with hospital savings and a worst-case scenario with all inputs maximally biased against the silver-coated endotracheal tube.

RESULTS

In the base-case analysis, we estimated that use of silver-coated endotracheal tubes would prevent 23 of 97 expected cases of VAP. Despite the higher acquisition cost of the silver-coated endotracheal tube, we calculated a marginal hospital savings of \$12,840 per 1 case of VAP prevented, with assumed marginal VAP cost of \$16,620 (in 2007 US dollars) and costs of \$90.00 for silver-coated and \$2.00 for uncoated endotracheal tubes. This translated to a total annualized marginal hospital savings of \$298,914 for the entire 1,000-patient cohort, reducing VAP-specific hospital costs by 18.5%.

In the univariate sensitivity analysis, the model was most sensitive to VAP hospital cost, VAP relative risk reduction associated with the silver-coated endotracheal tube, and pooled cumulative risk of VAP assumptions (Figure). Varying the hospital cost of VAP across the 95% confidence interval led to less than 25% variability in the point estimate for savings with the silver-coated endotracheal tube. Similarly, varying the relative risk reduction across the prespecified range of 12%–36% led to less than 25% variability in savings with the silver-coated endotracheal tube. The model was relatively insensitive to the acquisition costs of the silver-coated and the uncoated endotracheal tubes.

In a 2-way sensitivity analysis of the most influential inputs, use of the silver-coated endotracheal tube continued to yield

TABLE 1. Model Input Estimates and Sources

Input variable	Point estimate	Range tested	Source
Pooled cumulative VAP risk with uncoated endotracheal tube	9.7%	7.0%–12.5%	Safdar et al[4]
VAP relative risk reduction with silver-coated endotracheal tube[a]	24%	12%–36%	Kollef et al[15]
Marginal VAP hospital costs[b]	\$16,620	\$7,355–\$36,621	Warren et al[5]
Silver-coated endotracheal tube cost	\$90.00	\$80.00–\$100.00	Assumption
Uncoated endotracheal tube cost	\$2.00	\$0.00–\$5.00	Expert opinion

NOTE. VAP, ventilator-associated pneumonia.

[a] Actual relative risk reduction of 36% seen in the NASCENT study[15] reduced by 33% to 24% in the base case.

[b] Reported values adjusted to 2007 US dollars.[5]

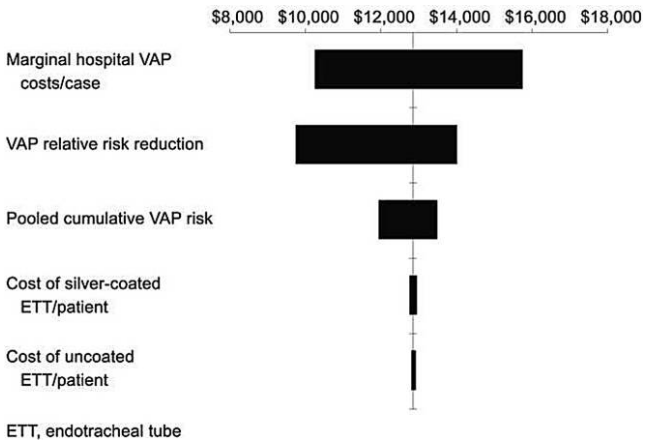

FIGURE. Hospital savings per 1 case of ventilator-associated pneumonia (VAP) prevented. The vertical line represents the savings in the base-case scenario. The horizontal bars represent the range in hospital savings associated with varying each input between the upper and lower limits while holding other variables constant.

hospital savings (Table 2). For example, diminishing the cost of VAP from the base case to $7,355 yielded a persistently favorable profile for the silver-coated endotracheal tube with cost savings of $3,575 per 1 case of VAP prevented. Similarly, lowering the magnitude of VAP relative risk reduction from the base case of 24% to 12% resulted in hospital savings of $9,060 per 1 case of VAP prevented.

In a multivariate Monte Carlo simulation involving 10,000 trials for each outcome, the 95% confidence interval for the point estimate was $9,630–$16,356 saved per 1 case of VAP prevented. This translated to a 95% confidence interval of $195,104–$424,809 in savings for the entire 1,000-patient cohort.

In the break-even sensitivity analysis, the cost of the silver-coated endotracheal tube had to be increased to $388 to offset the savings when all other inputs were held constant at the base-case point estimates. In break-even sensitivity analyses of other inputs, VAP risk had to be decreased from 9.7% to 2.2%, relative VAP risk reduction with the silver-coated endotracheal tube had to decrease from 24% to 5.5%, or marginal VAP cost had to decline from $16,620 to $3,780 to offset the savings when all other inputs were held constant.

In the worst-case scenario with each input maximally skewed against the silver-coated endotracheal tube, the hospital cost to prevent 1 case of VAP was $4,550, with assumed VAP risk of only 7%, relative VAP risk reduction of 12%, marginal VAP cost of $7,355, and cost of $100 for the silver-coated endotracheal tube. In the worst-case scenario, the uncoated endotracheal tubes had to be free (cost of $0.00).

DISCUSSION

Our findings demonstrated the cost effectiveness of a silver-coated endotracheal tube designed to reduce VAP incidence. Although the acquisition cost of the silver-coated endotracheal tube far exceeds that of an uncoated endotracheal tube, this difference in cost was offset by the excess hospital costs associated with VAP infection.[3-6] Specifically, the marginal hospital savings per 1 case of VAP prevented was $12,840, confirming that the silver-coated endotracheal tube was associated with substantial savings. Despite uncertainty associated with specific model inputs, our conclusions regarding the cost implications of the silver-coated endotracheal tube remained valid across a wide range of assumptions.

In accordance with published recommendations,[16] we intentionally biased model assumptions to favor uncoated endotracheal tubes. For example, we diminished the relative risk reduction observed in the NASCENT study[15] by one-third. We did this to simulate actual practice, where the effect size is often smaller than what is reported in controlled clinical studies that (by design) try to limit variability through precise entry criteria. Consistent with our conservative approach, we also chose the estimate for incidence of VAP from a meta-analysis of 38 prospective cohort or nonrandomized studies of 48,112 patients.[4] The pooled cumulative incidence of VAP in that population was 9.7%, which approximated the incidence in a large US database.[2] Similarly, our marginal hospital cost of VAP was based on a conservative estimate of approximately $12,000,[5] which was within the range of attributable costs calculated in the meta-analysis.[4] Higher values have been reported for both VAP incidence and VAP hospital cost.[3,6] Of course, use of these higher inputs would have made the intervention even more cost effective.

We performed extensive sensitivity testing to capture the substantial uncertainty surrounding model inputs and the

TABLE 2. Marginal hospital savings per 1 case of VAP prevented with use of silver-coated endotracheal tube in a 2-way sensitivity analysis

Cost of VAP per case, US$	Marginal hospital savings, US$				
	12% RRR	18% RRR	24% RRR	30% RRR	36% RRR
7,355	−205	2,315	3,575	4,331	4,835
11,988	4,428	6,948	8,208	8,964	9,468
16,620	9,060	11,580	12,840	13,596	14,100
26,621	19,061	21,581	22,841	23,597	24,101
36,621	29,061	31,581	32,841	33,597	34,101

NOTE. RRR, relative risk reduction; VAP, ventilator-associated pneumonia.

unique costs and epidemiologic situations of individual institutions. For example, VAP risk is difficult to estimate because accurate diagnosis is confounded by other frequent ICU complications that mimic the clinical appearance of VAP.[18] Consequently, clinical criteria can lead to inaccurate diagnosis and overestimation of the incidence, whereas the microbiologic criteria used in the NASCENT study[15] are not likely to be associated with this limitation. Each of our sensitivity analyses confirmed the robustness of the hospital savings associated with the silver-coated endotracheal tube over a wide range for each model input. The most influential input on the outcome estimate was marginal hospital cost of VAP. Diminishing this input to its lower 95% confidence bound,[5] however, did not alter the principal finding. Only the extreme scenario of lowest VAP cost combined with lowest VAP relative risk reduction failed to yield savings. Nonetheless, the additional expenditures required for use of the silver-coated endotracheal tube were modest and totaled only $205 to prevent 1 case of VAP.

The marginal hospital savings associated with use of the silver-coated endotracheal tube was at least comparable to that of other prevention strategies generally employed in the ICU and to that of specific VAP prevention strategies. For example, continuous subglottic suctioning saves $1,924 per case of VAP prevented.[19] An infection control strategy comprising intensive surveillance and interventions saves approximately $5,300 per case.[20] Oral decontamination with various antibiotic preparations saves $13,430 per case.[21] In contrast with other prevention strategies, the use of the silver-coated endotracheal tube was supported by data from a large prospective randomized trial, whereas the quality of the data supporting these alternative strategies is more limited.

Successful implementation of prevention strategies typically requires a multidisciplinary team,[22] staff education,[23,24] and adequate staffing levels,[25] all followed by continuous vigilance and surveillance to maintain success.[26] Unfortunately, nonadherence is common among both physicians[27] and nurses,[28] suggesting a practical advantage for use of the silver-coated endotracheal tube. Because its efficacy does not rely on behavioral changes by healthcare providers or procedural changes within the ICU, the silver-coated endotracheal tube becomes user independent after placement. This in turn removes an important component of process of care from the patient safety equation and is consistent with efforts to alter culture in the ICU.

Our pharmacoeconomic analysis had several limitations. First, only 1 clinical study was used to estimate relative risk reduction of VAP with use of silver-coated endotracheal tubes; however, the NASCENT study[15] was the largest randomized study of the impact of an endotracheal tube on incidence of VAP. Use of the silver-coated endotracheal tube was not associated with decreased length of hospital stay in the NASCENT study.[15] Failure to detect between-group differences in length of stay, one of the most important drivers of economic outcome, is not surprising in view of the low incidence of microbiologically confirmed VAP. Furthermore, the pivotal study was not powered to detect between-group differences in secondary end points.

Second, the model assumed that all types of VAP have similar financial implications. In other words, the costs of VAP due to *Pseudomonas aeruginosa* may not be the same as those due to methicillin-susceptible *Staphylococcus aureus*. To address this, we altered the cost estimates for VAP extensively and found that the hospital savings persisted. Similarly, the model did not differentiate between early- and late-onset VAP, which also may have different financial implications. In clinical practice, however, most cases of VAP occur during the first 7–8 days of intubation because the median duration of intubation is less than 10 days[29] and more than 75% of tubes are removed before 10 days.[30,31]

Third, we quantified cost effectiveness from the hospital perspective. Modeling from the societal perspective would not necessarily have diminished the cost effectiveness of the silver-coated endotracheal tube because it is unclear whether VAP is associated with attributable mortality. In fact, consideration of long-term, patient-reported complications of VAP probably would have augmented our findings.

Finally, there are likely hidden costs that we could not consider. Conversely, there are potential savings that we could not specifically model. For example, decreased VAP rates may help prevent the spread of antimicrobial resistance. From the throughput perspective, preventing VAP may facilitate bed turnover in the ICU and thus help eliminate bottlenecks that impede access to appropriate care.

Our pharmacoeconomic findings, combined with previous data demonstrating clinical benefit, indicated that use of a silver-coated endotracheal tube represents a strategy for preventing VAP that may result in savings to the hospital or healthcare system. Importantly, the silver-coated endotracheal tube becomes user independent after intubation and does not add to the burden of the healthcare provider. Collectively, these findings suggested that routine use of the silver-coated endotracheal tube among patients expected to require mechanical ventilation for $\geqslant$24 hours could have important public health implications.

ACKNOWLEDGMENTS

We thank Cindy W. Hamilton, PharmD, ELS (Hamilton House, Virginia Beach, VA), for assisting with manuscript preparation.

Financial support. This study, including the pharmacoeconomic analysis and manuscript preparation, was supported by a research grant from C. R. Bard. The pharmacoeconomic analysis was performed by EviMed Research Group, LLC, Goshen, MA, and was based on the NASCENT study.

Potential conflicts of interest. All authors report that they are consultants to and have received research funding from C. R. Bard. In addition, A.F.S. reports that he is a consultant to Pfizer, Johnson and Johnson, and Astellas and has received speaking fees from Pfizer, Merck, and Johnson and Johnson. M.D.Z. reports that she is a consultant to Ortho-McNeil, is a shareholder in Johnson and Johnson, and has received grants from Johnson and Johnson. M.K. reports that he has received speaking fees from Merck, Elan, and Pfizer and has received grants from Pfizer, Merck, and Elan. Cindy W. Hamilton

reports that Hamilton House received compensation from C. R. Bard for its contributions.

Role of the sponsor. C. R. Bard had no control or comment over the study design as to the methods chosen or inputs selected, the form of modeling, the analysis of the results, the interpretation of our findings, or the drafting of the manuscript. A copy of the manuscript was provided to Bard, but no feedback was solicited or received from them.

Address reprint requests to Andrew Shorr, MD, MPH, Pulmonary and Critical Care Medicine Service, Washington Hospital Center, Washington, DC 20010 (afshorr@mail.dnamail.com).

Presented in part: International Conference of the American Thoracic Society, Toronto, ON, Canada, May 16–21, 2008 (poster 4582).

REFERENCES

1. Edwards JR, Peterson KD, Andrus ML, et al. National Healthcare Safety Network (NHSN) report, data summary for 2006, issued June 2007. *Am J Infect Control* 2007; 35:290–301.
2. 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.
3. Hugonnet S, Eggimann P, Borst F, Maricot P, Chevrolet JC, Pittet D. Impact of ventilator-associated pneumonia on resource utilization and patient outcome. *Infect Control Hosp Epidemiol* 2004; 25:1090–1096.
4. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005; 33:2184–2193.
5. 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.
6. Anderson DJ, Kirkland KB, Kaye KS, et al. Underresourced hospital infection control and prevention programs: penny wise, pound foolish? *Infect Control Hosp Epidemiol* 2007; 28:767–773.
7. Petering HG. Pharmacology and toxicology of heavy metals: silver. *Pharmacol Ther* 1976; 1:127–130.
8. Ahearn DG, Grace DT, Jennings MJ, et al. Effects of hydrogel/silver coatings on in vitro adhesion to catheters of bacteria associated with urinary tract infections. *Curr Microbiol* 2000; 41:120–125.
9. Gabriel MM, Sawant AD, Simmons RB, Ahearn DG. Effects of silver on adherence of bacteria to urinary catheters: in vitro studies. *Curr Microbiol* 1995; 30:17–22.
10. Berra L, De Marchi L, Yu ZX, Laquerriere P, Baccarelli A, Kolobow T. Endotracheal tubes coated with antiseptics decrease bacterial colonization of the ventilator circuits, lungs, and endotracheal tube. *Anesthesiology* 2004; 100:1446–1456.
11. Chandra J, Patel JD, Li J, et al. Modification of surface properties of biomaterials influences the ability of *Candida albicans* to form biofilms. *Appl Environ Microbiol* 2005; 71:8795–8801.
12. Cunliffe D, Smart CA, Alexander C, Vulfson EN. Bacterial adhesion at synthetic surfaces. *Appl Environ Microbiol* 1999; 65:4995–5002.
13. Patel JD, Ebert M, Ward R, Anderson JM. *S. epidermidis* biofilm formation: effects of biomaterial surface chemistry and serum proteins. *J Biomed Mater Res A* 2007; 80:742–751.
14. Tebbs SE, Elliott TS. Modification of central venous catheter polymers to prevent in vitro microbial colonisation. *Eur J Clin Microbiol Infect Dis* 1994; 13:111–117.
15. Kollef MH, Afessa B, Anzueto A, et al. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. *JAMA* 2008; 300:805–814.
16. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine. *JAMA* 1996; 276:1253–1258.
17. Bureau of Labor Statistics of the US Department of Labor. Consumer Price Index. Available at: http://www.bls.gov/data. Accessed August 10, 2007.
18. Klompas M, Platt R. Ventilator-associated pneumonia—the wrong quality measure for benchmarking. *Ann Intern Med* 2007; 147:803–805.
19. Shorr AF, O'Malley PG. Continuous subglottic suctioning for the prevention of ventilator-associated pneumonia: potential economic implications. *Chest* 2001; 119:228–235.
20. Lai KK, Baker SP, Fontecchio SA. Impact of a program of intensive surveillance and interventions targeting ventilated patients in the reduction of ventilator-associated pneumonia and its cost-effectiveness. *Infect Control Hosp Epidemiol* 2003; 24:859–863.
21. van Nieuwenhoven CA, Buskens E, Bergmans DC, van Tiel FH, Ramsay G, Bonten MJ. Oral decontamination is cost-saving in the prevention of ventilator-associated pneumonia in intensive care units. *Crit Care Med* 2004; 32:126–130.
22. Craven DE. Preventing ventilator-associated pneumonia in adults: sowing seeds of change. *Chest* 2006; 130:251–260.
23. Babcock HM, Zack JE, Garrison T, et al. An educational intervention to reduce ventilator-associated pneumonia in an integrated health system: a comparison of effects. *Chest* 2004; 125:2224–2231.
24. Zack JE, Garrison T, Trovillion E, et al. Effect of an education program aimed at reducing the occurrence of ventilator-associated pneumonia. *Crit Care Med* 2002; 30:2407–2412.
25. Needleman J, Buerhaus P, Mattke S, Stewart M, Zelevinsky K. Nurse-staffing levels and the quality of care in hospitals. *N Engl J Med* 2002; 346: 1715–1722.
26. Kollef MH. The prevention of ventilator-associated pneumonia. *N Engl J Med* 1999; 340:627–634.
27. Rello J, Lorente C, Bodi M, Diaz E, Ricart M, Kollef MH. Why do physicians not follow evidence-based guidelines for preventing ventilator-associated pneumonia? a survey based on the opinions of an international panel of intensivists. *Chest* 2002; 122:656–661.
28. Ricart M, Lorente C, Diaz E, Kollef MH, Rello J. Nursing adherence with evidence-based guidelines for preventing ventilator-associated pneumonia. *Crit Care Med* 2003; 31:2693–2696.
29. Esteban A, Anzueto A, Alia I, et al. How is mechanical ventilation employed in the intensive care unit? an international utilization review. *Am J Respir Crit Care Med* 2000; 161:1450–1458.
30. Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002; 287:345–355.
31. Freeman BD, Borecki IB, Coopersmith CM, Buchman TG. Relationship between tracheostomy timing and duration of mechanical ventilation in critically ill patients. *Crit Care Med* 2005; 33:2513–2520.