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

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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 ≥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.

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 and occurs in 9.3%–23.5% of patients receiving mechanical ventilation. VAP adds 5–7 days to the length of stay in the intensive care unit (ICU) and 10–12 days to the length of hospitalization. Specifically, estimates of attributable hospital costs for VAP range from $10,000 to $25,000. 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, reduces bacterial adhesion to the endotracheal tube, and blocks biofilm formation on the endotracheal tube. The silver ions are microdispersed in a proprietary polymer that may enhance antimicrobial activity by blocking bacterial adhesion to the endotracheal tube. The North American Silver-Coated Endotracheal Tube (NASCENT) study provided clinical evidence of efficacy in 2,003 patients expected to require mechanical ventilation for ≥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 ≥24 hours.

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

**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 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 and hospital cost of VAP were bound by their corresponding published 95% confidence intervals. We varied the relative risk reduction of VAP by ±50% and the cost estimate of the silver-coated endotracheal tube by ±$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

<table>
<thead>
<tr>
<th>Input variable</th>
<th>Point estimate</th>
<th>Range tested</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled cumulative VAP risk with uncoated endotracheal tube</td>
<td>9.7%</td>
<td>7.0%–12.5%</td>
<td>Safdar et al¹</td>
</tr>
<tr>
<td>VAP relative risk reduction with silver-coated endotracheal tube</td>
<td>24%</td>
<td>12%–36%</td>
<td>Kollef et al¹³</td>
</tr>
<tr>
<td>Marginal VAP hospital costs³</td>
<td>$16,620</td>
<td>$7,355–$36,621</td>
<td>Warren et al⁷</td>
</tr>
<tr>
<td>Silver-coated endotracheal tube cost</td>
<td>$90.00</td>
<td>$80.00–$100.00</td>
<td>Assumption</td>
</tr>
<tr>
<td>Uncoated endotracheal tube cost</td>
<td>$2.00</td>
<td>$0.00–$5.00</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>

**NOTE.** VAP, ventilator-associated pneumonia.

¹ Actual relative risk reduction of 36% seen in the NASCENT study reduced by 33% to 24% in the base case.
³ Reported values adjusted to 2007 US dollars.
银涂层气管插管

**图解。** 气管插管相关性肺炎（VAP）预防的医院节省。垂直线表示基线情景中的节省。水平条表示随着每个输入在上、下限之间变化时医院节省的范围，同时保持其他变量不变。

医院节省（表2）。例如，降低VAP的成本从基线的7,355美元/例至2,315美元/例，持续有利于银涂层气管插管，节省3,575美元/例VAP预防。同样，降低相对风险降低从基线的24%至12%的结果为医院节省9,060美元/例VAP预防。

在多变量蒙特卡罗模拟中，每项输出涉及10,000次试验。每个结果的95%置信区间为VAP预防的医院节省9,630至16,356美元。这转化为95%置信区间为195,104至424,809美元的节省，对整个1,000名患者群体有效。

在盈亏平衡敏感性分析中，需要将银涂层气管插管的成本提高到388美元/例，以抵消所有其他输入保持不变时的节省。在其他输入的盈亏平衡敏感性分析中，VAP风险降低至2.2%，相对VAP风险降低与银涂层气管插管的降低从24%至5.5%，或边际VAP成本降低至16,620至3,780以抵消所有其他输入保持不变的节省。

在最坏情况下，每个输入最大化反对银涂层气管插管，医院预防1例VAP的成本为4,550美元，假设VAP风险为9.7%，相对VAP风险降低为12%，边际VAP成本为7,355美元，以及银涂层气管插管的100美元成本。在最坏情况下，未涂层气管插管必须免费（成本为0.00美元）。

**讨论。**

我们的发现表明银涂层气管插管的设计减少了VAP的发生。虽然银涂层气管插管的获取成本远高于未涂层气管插管，但这种成本差异被VAP感染的额外医院成本所抵消。3-6具体而言，边际医院节省每例VAP预防为12,840美元，确认银涂层气管插管与显著节省有关。尽管模型输入相关的不确定性，我们的结论关于银涂层气管插管的成本影响仍然有效，适用于广泛的假设。

根据已发表的推荐，16我们有意将模型假设偏向未涂层气管插管。例如，我们降低了在NASCENT研究15中观察到的相对风险降低的一半。我们这样做是为了模拟实际实践，其中的效应大小往往小于受试者设计中试图通过精确的入院标准来限制变异性而报告的临床研究。与我们保守的方法一致，我们的估计来自38项前瞻性或非随机临床研究的综合分析。4这些研究的VAP发病率是9.7%，接近一个大型美国数据库。2同样，我们的边际VAP成本基于一个保守估计约为12,000美元，5这在基于综合分析的VAP住院成本范围4内。

我们进行了广泛的敏感性测试来捕捉模型输入和结果的不确定性的重大影响。

### 表2。使用银涂层气管插管预防VAP的边际医院节省

<table>
<thead>
<tr>
<th>成本VAP/例，美元</th>
<th>12% RRR</th>
<th>18% RRR</th>
<th>24% RRR</th>
<th>30% RRR</th>
<th>36% RRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>7,355</td>
<td>-205</td>
<td>2,315</td>
<td>3,575</td>
<td>4,331</td>
<td>4,835</td>
</tr>
<tr>
<td>11,988</td>
<td>4,428</td>
<td>6,948</td>
<td>8,208</td>
<td>8,964</td>
<td>9,468</td>
</tr>
<tr>
<td>16,620</td>
<td>9,060</td>
<td>11,580</td>
<td>12,840</td>
<td>13,596</td>
<td>14,100</td>
</tr>
<tr>
<td>26,621</td>
<td>19,061</td>
<td>21,581</td>
<td>22,841</td>
<td>23,597</td>
<td>24,101</td>
</tr>
<tr>
<td>36,621</td>
<td>29,061</td>
<td>31,581</td>
<td>32,841</td>
<td>33,597</td>
<td>34,101</td>
</tr>
</tbody>
</table>

**注。** RRR，相对风险降低；VAP，气管插管相关性肺炎。
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.\(^1\)\(^8\) Consequently, clinical criteria can lead to inaccurate diagnosis and overestimation of the incidence, whereas the microbiologic criteria used in the NASCENT study\(^1\)\(^5\) 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.\(^1\)\(^9\) An infection control strategy comprising intensive surveillance and interventions saves approximately $5,300 per case.\(^2\)\(^0\) Oral decontamination with various antibiotic preparations saves $13,430 per case.\(^2\)\(^1\) 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,\(^2\)\(^2\)\(^2\)\(^3\)\(^4\)\(^2\)\(^4\)\(^2\) and adequate staffing levels,\(^2\)\(^5\)\(^2\)\(^6\)\(^2\)\(^7\) all followed by continuous vigilance and surveillance to maintain success.\(^2\)\(^8\) Unfortunately, nonadherence is common among both physicians and nurses,\(^2\)\(^9\) 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\(^1\)\(^5\) 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.\(^1\)\(^5\) 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 \textit{Pseudomonas aeruginosa} may not be the same as those due to methicillin-susceptible \textit{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\(^2\)\(^9\) and more than 75% of tubes are removed before 10 days.\(^3\)\(^0\)\(^3\)\(^1\)

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 $\geq 24$ hours could have important public health implications.

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**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 research funding 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.

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REFERENCES


