New Choices for Central Venous Catheters*

Potential Financial Implications

Andrew F. Shorr, MD, MPH, FCCP; Christopher W. Humphreys, MD; and Donald L. Helman, MD

Objective: To determine the cost-effectiveness of the newer antiseptic and antibiotic-impregnated central venous catheters (CVCs) relative to uncoated CVCs and to each other.

Design: Decision model analysis of the cost and efficacy of CVCs coated with either chlorhexidine silver sulfadiazine (CSS) or rifampin-minocycline (RM) at preventing catheter-related bloodstream infections (CRBSIs). The primary outcome is the incremental cost (or savings) to prevent one additional CRBSI. Model estimates are derived from prospective trials of the CSS and RM CVCs and from other studies describing the costs of CRBSIs.

Setting and patients: Hypothetical cohort of 1,000 patients requiring placement of a CVC.

Interventions: In the model, patients were managed with either an uncoated CVC, CSS CVC, or RM CVC.

Measurements and main results: The incremental cost-effectiveness of the treated CVCs was calculated as the savings resulting from CRBSIs averted less the additional costs of the newer devices. Sensitivity analysis of the effect of the major clinical inputs was performed. For the base case analysis, we assumed the incidence of CRBSIs was 3.3% with traditional catheters and that the CSS and RM CVC conferred a relative risk reduction for the development of CRBSIs of 60% and 85%, respectively. Despite their significantly higher cost than older catheters, both novel CVCs yield significant savings. Employing either of the treated CVCs saves approximately $10,000 per CRBSI prevented (relative to standard catheters). Comparing the RM CVC to the CSS CVC revealed the RM product to be economically superior, saving nearly $9,600 per CRBSI averted and $81 per patient in the cohort. For sensitivity analysis, we adjusted all model variables by 50% individually and then simultaneously. This demonstrated the model to be most sensitive to the cost of a CRBSI; however, with all inputs skewed by 50% against both the CSS CVC and the RM CVC, these devices remained economically attractive. Under this scenario, use of either treated device was less costly.

Conclusions: Utilization of antiseptic and antibiotic-impregnated CVCs represent an attractive alternative for the prevention of CRBSIs and may lead to significant savings. Of the two newer, coated devices, the RM CVC performs better financially. These observations hold over a range of estimates for our model inputs.

Key words: bacteremia; catheter-related bloodstream infection; central venous catheter; cost; cost-effectiveness; infection; nosocomial; prevention

Abbreviations: CRBSI = catheter-related bloodstream infection; CSS = chlorhexidine silver sulfadiazine; CVC = central venous catheter; LOS = length of stay; RM = rifampin-minocycline; RRR = relative risk reduction

Physicians place central venous catheters (CVCs) for invasive hemodynamic monitoring and to facilitate the delivery of medications, antibiotics, and nutrition. Therefore, CVCs are indispensable in the care of critically ill patients. Recent estimates suggest that >5 million CVCs are inserted each year in the United States.1 Reflecting the growing utilization of CVCs, catheter-related bloodstream infections (CRBSIs) remain a significant burden in the ICU.

*From the Pulmonary and Critical Care Medicine Service, Department of Medicine, Walter Reed Army Medical Center, Washington, DC. The opinions expressed herein are not to be construed as official or as reflecting the policy of either the Department of the Army or the Department of Defense.
CRBSI occurs in approximately 3 to 5% of catheters, and epidemiologic surveillance data indicate that the incidence of CRBSIs is rising. More importantly, the attributable mortality associated with CRBSI has been reported to be as high as 25%, although a meta-analysis suggests it may be as low as 3%. Despite disagreement regarding the attendant risk for death related to the development of a CRBSI, most concur that CRBSIs substantially prolong hospitalization and increase medical costs.

Several approaches have been advocated to prevent CRBSIs. For example, site selection significantly impacts the rate of infection with less central line-related sepsis reported with the use of the subclavian vein. Similarly, choices regarding skin preparation may alter rates of CRBSI, and investigators have shown the use of full barrier precautions to diminish the risk for CRBSI. A novel approach for the prevention of CRBSI focuses on impregnating the CVC with either antiseptics or antibiotics. Currently, two products employing this strategy are commercially available: one CVC is impregnated with rifampin-minocycline (RM), and the other is treated with chlorhexidine silver sulfadiazine (CSS). By inhibiting bacterial colonization of the CVC, these newer products are thought to lower the incidence of CRBSI. Initially, these products were impregnated only on the extraluminal surface, and both were shown to decrease significantly colonization rates. Device manufacturers have now changed these CVCs so that either the RM or the CSS is applied to both the intraluminal and extraluminal aspects of the CVC. Although effective at preventing CRBSI, these new CVCs are more expensive than standard catheters. A prior cost-effectiveness analysis demonstrated the superiority of antiseptic impregnation relative to standard CVCs but did not assess the two redesigned catheters relative to each other. Unfortunately, no trials comparing the two commercially available innovative CVCs to each other have been conducted. Nonetheless, clinicians must make decisions regarding if and how to utilize these products. Central to any conclusions regarding the newer CVCs will be estimates of the financial consequences of choosing one catheter as opposed to the other. In light of the uncertainty surrounding the effectiveness of the RM and CSS CVCs (relative to each other) combined with the potential economic implications of CRBSI, we conducted a series of cost-effectiveness analyses to compare these new technologies. We applied decision analytic techniques to evaluate the incremental cost-effectiveness of the double-coated RM and CSS CVCs at preventing CRBSI.

Materials and Methods

Our analysis relied on a decision model approach. The recommendations of the Panel on Cost-Effectiveness in Health and Medicine for cost-effectiveness analyses were followed. We present the economic results of all analyses despite the fact that the Panel on Cost-Effectiveness in Health and Medicine suggests that only net health benefits be reported in instances when one option is dominated (eg, more costly and less effective) by another. We compared health and economic outcomes in terms of CRBSI prevention with either the RM or CSS CVCs relative to a standard noncoated CVC, and to each other. In short, we conducted three distinct cost-effectiveness analyses simultaneously. We calculated the incremental cost-effectiveness of impregnated CVCs as the additional costs associated with these catheters less any savings resulting from the use of them divided by the cases of CRBSI prevented. This ratio is expressed as the cost (or savings) per CRBSI prevented. We did not discount costs, as the impact of the potential outcomes was immediate. Since we focused on immediate outcomes, we also performed the analysis from the perspective of large third-party payer or institution rather than assume a societal perspective. All costs are reported in 2002 US dollars. No external funding was received.

Reflecting the design and composition of earlier trials, the target population for the analysis was critically ill patients requiring a CVC that was expected to be in place for > 48 h. We focused on these subjects since CRBSI rates are very low for CVCs that are in place for short durations. We also excluded CVCs placed routinely in the operating room since many are removed quickly. Because CVCs placed during acute resuscitation and during “code” situations are considered by many to be contaminated and because the majority of patients do not survive these efforts, we further excluded these individuals from our target population. We compared two hypothetical cohorts of 1,000 patients each.

Model Structure

We modeled the significant outcomes via a simple decision tree (Fig 1). The only decision node represented the determination whether to employ an impregnated CVC, and if so which one (eg, RM vs CSS). The major health end point was the development of a CRBSI that is represented as a chance node in the decision tree. CRBSI was defined as reported in the trials we relied on for our model inputs (see below). We initially included local infection as an end point for our study. Preliminary analyses, however, revealed the model to be so insensitive to both the cost and incidence of local infections that we excluded local infection from the final model.

We did not model the impact of CRBSI on mortality. First, the randomized trials dealing with the newer CVCs have not examined mortality as a primary outcome. Second, as noted earlier, unlike the data regarding ventilator-associated pneumonia, controversy exists surrounding any potential attributable mortality related to CRBSI. Although one could hypothesize that a reduction in the incidence of CRBSIs would translate into lower mortality, we designed our model to be conservative. In keeping with the goal of being conservative, we further biased our model against the RM CVC by not expressly modeling the potential for hypersensitivity reactions related to the use of CSS. Hypersensitivity reactions to CSS following CVC insertion appear to be rare with < 20 cases reported internationally. Nonetheless, others have estimated that the costs associated with such hypersensitivity reactions are significant ($1,192 per episode in 1998 US dollars).
Data Sources

The model required four major inputs: the incidence of CRBSI with standard, noncoated CVCs; the relative risk reduction (RRR) for CRBSI with both the RM and CSS CVCs relative to an uncoated CVC; the accrual costs for each type of catheter; and the financial sequelae of CRBSI. Table 1 summarizes the baseline values used for this analysis. For the baseline estimate of CRBSI with standard CVCs, we relied on the findings of a meta-analysis by Kluger and Maki. They reviewed 61 prospective trials and estimated that the weighted overall rate of CRBSI with traditional CVCs is 3.3%. As no trial exists directly comparing the RM and CSS devices to each other, we developed estimates of the RRR for CRBSI from randomized trials comparing either of the modified catheters to standard CVCs. To identify these randomized studies, we searched MEDLINE using the following key words: bacteremia, bloodstream, catheter, central line, colonization, nosocomial, and sepsis. The search was not restricted to the English language, and we exploded each key word. We also contacted the manufacturers of the RM CVC (Cook Critical Care; Bloomington, IN) and the CSS CVC (Arrow International; Reading, PA) and reviewed published abstracts of recent scientific meetings. For the RM dual-impregnated catheter, one randomized controlled trial has been published. Darouiche et al18 noted that the incidence of CRBSI with the newer RM CVC was 0.28%. The CVCs in this trial were in place for mean of 8.4 days. For a control arm, the authors compared the RM CVC not to standard, uncoated catheters, but to the original CSS catheter in which the antiseptic material was placed only on the external surface. With the single-bonded CSS, there were 13 CRBSIs among 382 catheters, resulting in a RRR of 91.8% favoring the RM product. To be conservative, to bias the model against the RM CVC, and despite earlier studies showing the original CSS CVC to be superior to an uncoated catheter, we assumed that the RRR for CRBSI with the RM CVC vis-à-vis a standard CVC would be the same as the RRR seen with the older CSS CVC (with the antiseptic only on the external surface). Since the impact

Table 1—Model Inputs

<table>
<thead>
<tr>
<th>Variables</th>
<th>Base-Case Estimate</th>
<th>Ranges Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of CRBSIs with standard CVCs, %</td>
<td>3.3</td>
<td>1.65–4.95</td>
</tr>
<tr>
<td>RRR for CRBSIs with CSS CVC (vs standard CVC), %</td>
<td>60.0</td>
<td>30.0–90.0</td>
</tr>
<tr>
<td>RRR for CRBSIs with RM CVC (vs standard CVC), %</td>
<td>95.0</td>
<td>42.5–92.5</td>
</tr>
<tr>
<td>Cost of standard CVC, $</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Cost of CSS CVC, $</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Cost of RM CVC, $</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Cost of CRBSI, $</td>
<td>10,920</td>
<td>5,460–16,380</td>
</tr>
</tbody>
</table>
of interventions formally studied under the rubric of a clinical trial may not directly translate into clinical practice, we adjusted downward the point estimate for the RRR to 55%.

We found no published trials of the dual-treated CSS CVC, although several have been presented as abstracts. The largest of these projects (n = 742 catheters) was a multicenter, randomized trial comparing the intraluminally and extraluminally treated CSS CVC against a standard, untreated catheter.16 The RRR for colonization was 50.0% with the newer product. Despite its efficacy in decreasing colonization rates, the investigators found that the enhanced CSS CVC did not alter CRBSI rates. With the traditional CVC: the incidence of CRBSIs was 0.87% as opposed to 0.31% with the re-engineered catheter (p = 0.65). The inability to detect differences in the frequency of CRBSIs in part reflects the fact that the rate of CRBSI in the standard arm was exceedingly low. The catheters in this trial, unlike those in the study by Darouiche and coworkers,19 remained in place on average < 7 days. In a study of 1,006 patients with a diagnosis of either leukemia, lymphoma, or multiple myeloma, Karthans and colleagues22 observed that the newer CSS CVC resulted in fewer CRBSIs (1.96% vs 14.55% of catheters). This population, though, is not directly comparable to the subjects of interest for the present analysis; therefore, we opted to accept the RRR found in the larger CSS CVC trial (60%) for the initial estimate of our model despite it being a “negative” study. This approach, again, is consistent with our effort to bias the model in favor of the CSS CVC relative to the RM CVC.

For the cost of each catheter, we ascertained the price our institution pays the manufacturers for these devices. The charge for a traditional CVC is $43, as opposed to $70 for a CSS CVC and $81 for a RM CVC. The cost for the CVCs reflects the price for directly comparable kits with each containing chlorhexidine skin preparation and full barrier drapes. The costs of a CRBSI comprises the costs associated with the following: (1) diagnosis of this process, (2) its treatment, and (3) the degree to which it prolongs hospitalization. To determine these variables, we multiplied the component charges our institution bills to third-party payers by department-specific cost-to-charge ratios. We obtained charge data from our the billing service of our hospital.

For the diagnosis of a CRBSI, we assumed each patient had both blood cultures and cultures of the CVC performed. Although an evaluation for fever in an ICU patient will likely include other cultures and perhaps radiographs, we did not include the costs of these in our estimate of the cost of diagnosing a CRBSI. With respect to treatment, we assumed that patients would require 10 days of antibiotics at an approximate cost of $170 (this is based on the belief that there would be little need for either vancomycin, other expensive agents such as linezolid, or antifungal therapy). As Table 2 demonstrates, six earlier reports have documented the attributable ICU length of stay (LOS) following a CRBSI.23–25 In these studies, the additional ICU LOS related to development of a CRBSI ranged from 6.5 to 20 days; therefore, we based our financial calculation on an extra ICU LOS of only 6 days. Similarly, we determined that a CRBSI would lead to an additional ward hospitalization of 5 days. The cost for the added ICU LOS equaled $7,830, while the costs of the longer ward hospitalization totaled $2,340. We also projected that professional fees during the extended hospitalization would come to $500 and that patients would still require a CVC. In light of a CRBSI, we assumed clinicians would opt to replace all infected CVCs with traditional, inexpensive catheters. Summing these values reveals the cost of a CRBSI to be $10,920. Prior estimates of the cost of a CRBSI vary widely (Table 2).2,3,23–25 Nonetheless, our baseline cost for a CRBSI is significantly less than what has been reported in more recent literature.

### Table 2—Prior Estimates of the Attributable Morbidity and Cost of CRBSIs

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Extra ICU LOS, d</th>
<th>Extra Ward LOS, d</th>
<th>Cost per CRBSI, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMWR20</td>
<td>1992</td>
<td>NR</td>
<td>NR</td>
<td>3,517</td>
</tr>
<tr>
<td>Arows et al5</td>
<td>1995</td>
<td>NR</td>
<td>NR</td>
<td>4,830</td>
</tr>
<tr>
<td>Pittet et al23</td>
<td>1994</td>
<td>6.5</td>
<td>6.0</td>
<td>25,690</td>
</tr>
<tr>
<td>DiGivone et al24</td>
<td>1999</td>
<td>10.3</td>
<td>2.7</td>
<td>34,508</td>
</tr>
<tr>
<td>Rello et al25</td>
<td>2000</td>
<td>19.6 (combined)</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Slouin et al26</td>
<td>2001</td>
<td>14.6</td>
<td>6.5</td>
<td>46,133</td>
</tr>
<tr>
<td>Renaud and 26</td>
<td>2001</td>
<td>9.5</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Brun-Buisson27</td>
<td>2001</td>
<td>20</td>
<td>22</td>
<td>56,167</td>
</tr>
</tbody>
</table>

*MMWR = Morbidity and Mortality Weekly Report. NR = not reported.

### Sensitivity Analysis

We used sensitivity analysis to identify important model uncertainties and to assess the robustness of our conclusions. Since uncertainty exists regarding both the effectiveness of the newer CVCs and the costs of a CRBSI, sensitivity analysis also affords a mechanism to assess the cost implications of the regular use of the newer CVCs across a range of estimates for these model inputs. We varied base case estimates by 50% individually in order to identify variables that substantially affected the results. We also adjusted all model inputs by 50% simultaneously to provide a multivariate assessment of a best-case and worst-case scenario. In other words, for the multivariate sensitivity analyses, each model input was simultaneously skewed by 50% to capture the potential for uncertainty in each of our point estimates for model inputs. For example, we tested the model with a concurrently 50% lower incidence of CRBSIs, cost for CRBSIs, and RRR for CRBSIs. Finally, we calculated threshold values for each variable to determine at what point there was no incremental cost (or savings) with either the RM or CSS CVC relative to the standard CVC.

### Results

#### Base Case

In the base case, utilizing a standard CVC results in 31 CRBSIs. The total costs for this approach are $414,280, or $414.28 per patient. Nearly 90% of the costs arise because of infection. Table 3 summarizes the results of the base case model. With the CSS CVC, overall costs are significantly lower ($218,512) because only 13.6 CRBSIs develop. This approximately 50% reduction in total costs yields an incremental savings of $9,596.47 per CRBSI prevented. Utilizing the base case estimates demonstrates the RM CVC to be superior in terms of cost-effectiveness to both the standard and the CSS catheters. Routinely employing the RM CVC leads to fewer CRBSIs. Base case costs with the RM CVC total only $136,692, or $136.69 per patient; therefore, the incremental savings with the RM CVC as opposed to a standard catheter is $9,605.12 per CRBSI pre-
vented. The incremental savings of the RM CVC when directly compared to the CSS CVC is similar ($9,625.88 per CRBSI prevented).

On a per-patient basis when evaluated relative to an untreated CVC, the use of the RM CVC yields $277.59 in savings for each individual in the cohort. This per patient savings arises despite the fact that RM CVC is approximately twice as expensive as a conventional catheter. Similarly, regular insertion of RM CVCs rather than a CSS CVCs saves $81.82 per line placed, even though the RM CVC is 15% more costly than the CSS CVC.

Sensitivity Analysis

As shown in Figure 2, varying each model input by 50% revealed the model to be most sensitive to the cost of a CRBSI. For example, if the cost of a CRBSI were only $5,460.00, the incremental savings with the CSS CVC relative to a standard catheter would fall to $4,136.47 per CRBSI prevented. For a standard CVC as compared to RM CVC, a 50% decrease in the financial implications of a CRBSI leads to a similar 57% decline in the incremental savings. Analyzing incremental savings also showed the model to be mildly sensitive to the estimated incidence of CRBSIs and the RRR of the newer CVCs (Fig 2); however, halving either the incidence of CRBSIs or the efficacy of the impregnated CVCs results in a < 15% shift in the point estimate for the incremental savings.

The comparison of the RM CVC to the CSS CVC followed a parallel pattern. When we manipulated model inputs so that the RRR for either of the new CVCs was 50% less than baseline, the efficacy of the RM CVC fell disproportionately. In order to create a scenario where the RRR with the CSS CVC relative to the traditional catheter was now only 30% rather than 60%, and simultaneously the RRR with the RM CVC relative to the traditional catheter was reduced to 42.5%—while maintaining a background incidence of CRBSIs of 3.3%—led to a situation where the superiority of the RM CVC was greatly diminished (a 17.9% RRR vs the CSS CVC). In the face of this nearly 72% drop in effectiveness, the RM CVC remained more cost-effective. Specifically, the incremental savings per CRBSI prevented was now $8,331.76 favoring the RM CVC over the CSS device. From the individual patient’s vantage, adjusting the model this severely against the RM CVC still yielded a savings of $35.41 per patient.

In the multivariate sensitivity analysis (Table 3) with all variables adjusted simultaneously by 50%, the re-engineered catheters remained dominant relative to the standard CVC. When we halved the model inputs along with like reductions in the costs of a CRBSI, placing a regular CVC results in 17 CRBSIs. We compute the overall cost of this strategy to be $135,820.00. In this situation, placing the CSS CVC is associated with an incremental savings $165.88 per CRBSI prevented. Per-patient charges have increased to, but remain below, those noted with a standard CVC. When all inputs are similarly biased against the RM CVC, the incremental savings per CRBSI prevented falls to $200.48. Comparing the RM to the CSS CVC in this fashion shows the RM catheter to perform better economically. Using the RM CVC as opposed to the CSS product, despite all model inputs skewed by 50% in favor of the CSS CVC, leads to a incremental savings of $283.53 per CRBSI avoided. Put another way, even if our baseline model estimates are severely askew, the RM CVC remains the most economically attractive option.

Efforts to identify threshold points (Table 3) at which one no longer saves funds with either enhanced catheter reveals the CSS CVC to be better financially until the RRR for a CRBSI compared to a standard CVC falls to 7.3% or the cost of a CRBSI is only $1,323.50. A RRR of 7.3% implies that the CSS CVC achieves only 12% of the effectiveness reported in clinical trials. Employing the base case RRR, we

<table>
<thead>
<tr>
<th>Variables</th>
<th>Standard vs CSS CVC</th>
<th>Standard vs RM CVC</th>
<th>CSS vs RM CVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case incidence of CRBSIs</td>
<td>33.0 vs 13.6</td>
<td>33.0 vs 5.1</td>
<td>13.6 vs 5.1</td>
</tr>
<tr>
<td>Base case incremental savings per CRBSI prevented, $</td>
<td>9,596.47</td>
<td>9,605.12</td>
<td>9,625.88</td>
</tr>
<tr>
<td>Base case incremental savings per patient in cohort, %</td>
<td>165.88</td>
<td>277.59</td>
<td>81.82</td>
</tr>
<tr>
<td>Incremental savings per CRBSI prevented with all variables adjusted by 50% against newer device, $*</td>
<td>0.85</td>
<td>1.45</td>
<td>0.60</td>
</tr>
<tr>
<td>Incremental savings per patient with all variables adjusted by 50% against newer device, $*</td>
<td>7.3</td>
<td>10.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Threshold break-even point for incidence of CRBSI, %</td>
<td>0.62</td>
<td>0.41</td>
<td>0.16</td>
</tr>
<tr>
<td>Threshold break-even point for cost of CRBSI, $</td>
<td>1,323.50</td>
<td>1,314.90</td>
<td>1,294.10</td>
</tr>
</tbody>
</table>

*For purposes of comparison, the RM CVC is considered the newer device relative to the CSS CVC.

Table 3—Results From Cost-effectiveness Analysis

www.chestjournal.org CHEST / 124/1 / JULY, 2003 279
FIGURE 2. Tornado diagram. Top: One-way sensitivity analysis of the CSS CVC vs the standard CVC. Middle: One-way sensitivity of the RM CVC vs the standard CVC. Bottom: One-way sensitivity analysis of the RM CVC vs the CSS CVC. The solid vertical lines designate the marginal cost-effectiveness of the "novel" intervention for the base case scenario. The horizontal bars demonstrate the range in the incremental cost-effectiveness resulting when a particular input varies between its upper and lower limit while other variables remain constant.
calculated that the incidence of CRBSIs in an ICU would have to fall to < 6.2 per 1,000 devices (0.62%) in order for this approach to no longer save costs. The RM CVC requires additional outlays if the RRR falls to 10.2% (a relative effectiveness of 12% of what has been shown in clinical trials) or if the cost of a CRBSI drops to $1,314.90. When the rate of CRBSIs is 0.41%, routinely employing the RM CVC necessitates financial expenditures.

For the RM CVC to no longer be financially attractive relative to the CSS device, the RM CVC would have to result in a RRR of < 7.4%. As long as the RM CVC prevents one additional CRBSI per every 13 catheters placed, it remains economically appealing when contrasted with the CSS CVC. Similarly, when the cost of a CRBSI is < $1,294.10 per event, the CSS CVC becomes financially superior to the RM-treated product.

**Discussion**

This decision model reveals that both the RM and CSS CVCs are economically attractive alternatives for the prevention of CRBSIs in critically ill patients. Regular use of these catheters may, in fact, result in significant savings. Although both of the newer CVCs are more expensive than traditional catheters, the additional acquisition charges are outweighed by the substantial costs of a CRBSI. Comparing the RM product to the redesigned CSS CVC, we found the RM CVC to perform better financially.

Sensitivity testing underscores that our conclusions regarding the cost-effectiveness of the CSS and RM CVCs are robust over a wide range of values for each of the uncertainties of the model. The most important variable with regard to our conclusions was the cost of a CRBSI. Varying the cost of CRBSI by 50%, though, did not alter our principal finding that the efficacy of these newer technologies compensates for their expense. Similar sensitivity analyses confirm that the comparison of the RM to the CSS CVC is most sensitive to the cost of a CRBSI. Nonetheless, with the cost of CRBSI halved, use of the RM device remains financially dominant. In accordance with the recommendations of the Panel on Cost-Effectiveness in Health and Medicine, we also performed multivariate sensitivity analysis. When every variable was simultaneously adjusted by 50% to favor traditional CVCs, utilizing treated catheters still yielded savings. In this scenario, per-patient costs remain lowest if one employs the RM CVC.

The experience of individual ICUs in terms of either their baseline CRBSI rate or their estimated cost of a CRBSI may differ from our initial model inputs. For example, certain institutions may have exceedingly few CRBSIs. When trying to apply our findings to their situations, the results of our threshold analysis may serve as general guidelines to such hospitals. The model showed the CSS and RM to lead to savings until the incidence of CRBSIs falls below approximately 0.5%. Based on the results of the epidemiologic studies, few ICUs achieve CRBSI rates this low; therefore, most hospitals should investigate adopting these new catheters. Additionally, both novel devices are financially superior until the cost of a CRBSI reaches what one would expect if each CRBSI essentially only prolonged ICU length of stay by one day. Given that the attributable length of stay reported with CRBSI is much greater, our findings are applicable to most ICUs in the United States.

Several informal studies have examined the cost-effectiveness of impregnated CVCs at preventing CRBSIs. Marin and co-workers, for example, concluded that these newer devices saved costs as long as the cost per CRBSI exceeded $3,495. Because their primary goal was to determine the relative effectiveness of the newer products, they pooled the results from the CSS and RM trials to compare any bonding or coating vs standard catheters. Their project only focused on the older impregnated devices (eg, the CVCs treated on only the extraluminal surface) and had no formal sensitivity testing.

Veenstra et al compared the older, extraluminally treated CSS product to regular catheters. In their sensitivity analysis, they observed that the savings with the CSS CVC ranged from $68 to $391 per line placed. Our decision modeling builds on these earlier efforts in several ways. First, we explored the implications of the CVCs that are now commercially available. Catheters with either the antiseptic or antibiotic applied only to one side are not currently manufactured. Second, we directly compared the newer, treated devices to each other. Prior research on cost-effectiveness and the prevention of CRBSIs only explored the CSS approach vis-à-vis standard catheters. Third, we did not attempt to include mortality in our model. In order to be conservative, we did not expressly add death as an end point. As noted earlier, there is controversy regarding the attributable mortality resulting from CRBSIs, and none of the trials proving the effectiveness of the impregnated CVCs explored death from
CRBSI. Finally, in contrast to Veenstra et al., we excluded both hypersensitivity to CSS and local infection resulting from colonization from our assessment. We believed it was necessary to do this in order to bias the model against the RM device because it was the most expensive option. Despite this persistent bias favoring the CSS CVC over the RM catheter, utilizing the RM device remains economically superior over a wide range of potential uncertainties.

Coating the CVC with either CSS or RM represents one approach for the prevention of CRBSIs. Other alternatives for avoiding CRBSIs include limiting site selection to the subclavian vein, educating housestaff to improve sterile technique, using full drapes, and preparing the site with chlorhexidine as opposed to povidone-iodine. Opting for the subclavian vein over the femoral vein is an alternative without direct medical costs other than the concern for pneumothorax. Educational efforts to enhance compliance with the use of full barriers and appropriate sterile technique are also relatively cost free. As such, employment of either the RM or CSS CVC should not be seen as replacements for strategies of this sort. The ability of chlorhexidine as site care to reduce the risk for CRBSI is a similar intervention that is likely to be extremely cost-effective. The RRR for CRBSI with chlorhexidine is nearly 50% vs povidone-iodine, and it costs only 50 cents more per day. Readers should note that in both the trials, we used to determine the effectiveness of the treated catheters, chlorhexidine skin preparation, and full drapes were included in the study protocols; therefore, the cost-effectiveness of the interventions modeled in this study are likely additive to the benefits of these other options. Future promising technologies for averting CRBSIs comprise the use of antibiotic flush solutions, anti-septic hubs, and needle-less lock connectors. Preliminary data for each of these methods are encouraging but none have yet been subjected to formal cost-effectiveness analysis.

In comparison to other prophylactic interventions in critically ill patients, impregnated CVCs provide similar, if not potentially greater, savings. Reddy et al concluded that the regular use of amiodarone perioperatively, for the prevention of atrial fibrillation complicating cardiac surgery, yielded $1,676 in savings per case of atrial fibrillation avoided. Corwin and coworkers suggested that treatment with erythropoietin in order to preclude the transfusion of an additional unit of blood would cost between $300 and $500 for the patient in the ICU. Continuous aspiration of subglottic secretions in order to avoid ventilator-associated pneumonia may save $4,992 for each case averted.

Our study has several limitations. First, our model did not incorporate duration of catheterization as a risk factor for development of a CRBSI. CVCs that remain in place for greater periods of time are more prone to lead to infection. We addressed this limitation by expressly excluding from the analysis patients for whom the CVC would be in place for < 48 h. Additionally, from the perspective of the ICU clinician deciding which catheter to use, it is often not possible to estimate the expected duration of catheterization. Our decision analysis accepts this uncertainty in order to better reflect “real world” scenarios in hopes of making our conclusions generalizable. Second, we had to indirectly estimate the effectiveness of the RM CVC relative to the CSS CVC. Clearly, data from a project directly comparing these devices would be superior for cost-effectiveness analysis. Nonetheless, no such trial exists. Based on the variable inputs we used, such a trial would be large and therefore difficult to conduct. We estimate that for a trial to have an 80% power to detect a 50% decrease in the RRR for CRBSIs with the RM CVC (given a baseline CRBSI rate of 2% with the CSS CVC), the study would require > 2,500 catheters in each arm. To partially address this limitation, we consistently biased the model against the RM device. Our point estimates for the effectiveness of the RM CVC were low compared to published reports, and we employed data not from a trial contrasting the RM CVC with a standard catheter but from one examining the older, single-coated CSS CVC. Multiple sensitivity analyses also demonstrated that the RM CVC need only be slightly superior to the CSS catheter in order for it to appear financially attractive. Third, uncertainty exists regarding the cost of a CRBSI. Studies reporting either the actual costs to infection resulting from colonization from our assessment patients or the impact of a CRBSI on LOS have been retrospective. Likewise, the projects reporting the attributable morbidity for CRBSI come from major academic hospitals and the results from specialized centers may not apply to other clinical settings.

With either newer device, there is also concern that the types of organisms causing CRBSIs will change and this may affect the cost of a CRBSI. As a corollary, some investigators have expressed concern that, although the RM CVC may be effective, it will lead to more CRBSI resulting from fungi. From any perspective, however, the costs of CRBSIs appear to be increasing despite growing economic pressure to rapidly transfer patients out of the ICU. In essence, a central limitation with our decision analysis specifically—and modeling, more generally—is that it relies on the quality of the published data for deriving inputs. Conversely, decision analysis helps to make explicit, as the present
case illustrates, the imperfect information available to guide clinicians. Furthermore, we were conservative in our estimate of the cost of a CRBSI and performed several different sensitivity analyses to address such concerns directly by specifically altering the cost of a CRBSI across a wide range of inputs. Finally, we did not explore the possibility of resistance. The prevalence of organisms resistant to multiple antibiotics continues to grow, particularly in the ICU. In vitro resistance to either CSS or RM has not been reported. In vitro studies, however, reveal that resistance may be seen with either CSS or RM. Long-term studies will be required in order to conclusively determine if resistance will be an issue with these devices and if this will have economic consequences.

In conclusion, an economic analysis of CRBSIs demonstrates that both of the newer, redesigned CVCs save costs compared to older, standard CVCs. Irrespective of their greater cost, antiseptic and antibiotic-impregnated catheters yield significant savings because of their demonstrated efficacy at decreasing the incidence of CRBSIs. This observation holds across a range of assumptions. Of the two coated catheters, the RM CVC results in greater savings than the CSS catheter.

ACKNOWLEDGMENT: We thank Curtis Sessler, MD, FCCP, and Gregory Susla, Pharm D, for helpful comments on earlier versions of this manuscript.

REFERENCES

5 Arnow PM, Quinosing EM, Beach M. Consequences of intravascular catheter sepsis. Clin Infect Dis 1993; 16:778–784
29 Public Health Focus: surveillance, prevention, and control of nosocomial infection. MMWR Morb Mortal Wkly Rep 1992; 41:783–787
36 Dauenhauer SA, Brooks KL, Nelson SM. Analysis of a reduction in bloodstream infections as related to use of untreated vs. silver/chlorhexidine vs. rifampin/minocycline central venous catheters. American Society of Microbiology meeting. Orlando, FL: May 20–24, 2000

CHEST Journal On-line
Access CHEST on-line (www.chestjournal.org) – full text available from January 1999 to present; abstracts from 1970s to present. Post electronic comments to articles, link to MEDLINE abstracts from reference lists, track article citations and more! Activate your on-line access today!