Economic impact of use of chlorhexidine-impregnated sponge dressing for prevention of central line-associated infections in the United States

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Background: The economic impact of adding chlorhexidine gluconate (CHG)-impregnated sponge dressing to standard care (ie, CHG-impregnated sponge dressing + skin preparation and transparent film dressing vs skin preparation and transparent film dressing) for the prevention of central-line infections was evaluated.

Methods: Clinical and economic data were obtained from peer-reviewed published studies to populate the decision model. The efficacy of reducing central-line bloodstream infection (CL-BSI) incidence with CHG-impregnated sponge dressing came from 2 recent randomized controlled trials. One-way and two-way sensitivity analyses were performed on key clinical and economic parameters.

Results: Based on model calculations, a hypothetical 400-bed hospital inserting 3,078 central venous catheters (CVCs) per year is expected to avoid an average of 35 CL-BSIs, 145 local infections, and 281 intensive care unit days annually with the systematic use of CHG-impregnated sponge dressing. Potential hospital net cost savings (mainly because of reduced CL-BSIs with use of the dressing) would be $895,000 annually. Results were robust across a range of values in sensitivity analyses.

Conclusion: CHG-impregnated sponge dressing is a cost-effective CL-BSI prevention treatment option for patients requiring CVCs. The importance of these results should be considered in the context of federal government and insurance company policies that no longer permit enhanced reimbursement for CL-BSI.

Key Words: Chlorhexidine-impregnated sponge dressing; cost; economic; central line-associated infections.

Catheter-related bloodstream infections (CR-BSIs) are a costly subset of health care-associated infections that occur as a result of central venous catheter (CVC) insertion and manipulation. It is estimated that 250,000 to 500,000 CR-BSIs occur annually in the United States.1-5

CR-BSIs are estimated to have an attributable mortality rate of 0% to 11.5% and result in 8 to 12 additional intensive care unit (ICU) days on average.4,6 Decreasing bacterial colonization of the skin at the insertion site is a critical element of CR-BSI prevention.7 The use of chlorhexidine gluconate (CHG)-impregnated sponge dressing for skin antisepsis at catheter insertion results in a short-term reduction of bioburden.8 CHG-impregnated sponge dressing (BIOPATCH Protective Disk with CHG), comprised of a polyurethane foam disk that is impregnated with CHG via a lyophilization process, is uniquely designed to continually release CHG over 7 days, providing 360° protection. CHG-impregnated sponge dressing (BIOPATCH Protective Disk with CHG), comprised of a polyurethane foam disk that is impregnated with CHG via a lyophilization process, is uniquely designed to continually release CHG over 7 days, providing 360° protection. CHG-impregnated sponge dressing has demonstrated its efficacy in reducing both CR-BSIs and local infection rates by prolonged reduction in skin bioburden in a wide variety of patient populations.8-13 After skin antisepsis is completed and the catheter is inserted, a CHG-impregnated sponge dressing is placed 360 degrees around the catheter and stays in contact with the skin for a maximum of 7 days.13 The CHG inhibits bacterial growth on the skin under the dressing.8,9

Before October 2008, CR-BSIs resulted in enhanced reimbursement by the Centers for Medicare and Medicaid
and cost inputs.

METHODS

The target audience is US health care decision makers in the hospital setting, and a hospital perspective was adopted for this analysis. Only the costs of CR-BSIs, local site infections, and CHG-impregnated sponge dressing are included in the analysis. The target patient population includes all inpatients requiring CVC insertion. The comparators in this economic evaluation are CHG-impregnated sponge dressing (ie, CHG-impregnated sponge dressing + chlorhexidine skin preparation + transparent film dressing) versus standard care (ie, chlorhexidine skin preparation and transparent film dressing alone). We used a decision analytic model, a structured representation of “real-world” health care activities incorporating event probabilities, resource utilization, costs, and patient outcomes. A number of outcomes were evaluated and compared between treatment arms including number of CR-BSIs, number of local infections, ICU length of stay, and cost. The decision tree structure is similar to the one used by Crawford et al in their cost-benefit analysis, except that colonization as the intermediate endpoint is removed from the model.

Data sources for populating the model

The clinical and economic data used to populate the decision analytic model were obtained from the published literature.

Clinical inputs

The base case number of implanted CVCs per year was set at 5,078 based on market research data for a 400-bed hospital with 60 ICU beds, 340 non-ICU beds, and a 72% occupancy rate (Table 1).

The rate of CR-BSIs in standard care used the median pooled rate of 1.95 per 1,000 CVC-days based on the Centers for Disease Control and Preventions’ National Healthcare Safety Network report for hospital ICUs. This rate of CR-BSIs was allocated differentially among patients using standard nonimpregnated and impregnated catheters. Crnich and Maki found that the risk of a CR-BSI with a standard versus an impregnated catheter was 0.65. Using this odds ratio, it was estimated that the rate of CR-BSIs was 2.49 per 1,000 CVC-days with a standard catheter and 1.62 per 1,000 CVC-days with an impregnated catheter. Because the rate of CR-BSIs differs depending on whether the catheters used are standard or impregnated, it was necessary to make an assumption about the proportion of standard versus impregnated CVCs. The number of standard versus impregnated CVCs was assumed to be equal for the baseline analysis (ie, 50% of CVCs were standard catheters, and 50% were impregnated catheters).

CHG-impregnated sponge dressing efficacy rates were applied to the estimated number of CR-BSIs and local site infections occurring with standard care to quantify CHG-impregnated sponge dressing clinical impact. The efficacy of adding CHG-impregnated sponge dressing to standard care in reducing the incidence of CR-BSIs came from 2 randomized controlled trials. Both trials compared CR-BSI rates for CVCs in ICU patients with or without CHG-impregnated sponge dressing. The first trial compared CHG-impregnated sponge dressing and standard care versus standard care alone in regular CVCs, and the second study measured CHG-impregnated sponge dressing efficacy when used in addition to CHG-silversulfadiazine-impregnated CVCs. CHG-impregnated sponge dressing demonstrated a reduction of CR-BSIs by 69% in standard CVCs when compared with standard care in critically ill patients. When used in combination with impregnated catheters, CHG-impregnated sponge dressing delivered an incremental reduction of 44% in CR-BSIs compared with impregnated catheters alone. Because the efficacy of CHG-impregnated sponge dressing differs depending on whether it is used with standard or impregnated catheters and because the assumption was that the proportion of standard versus impregnated catheters was equal, efficacy estimates for CHG-impregnated sponge dressing with standard or impregnated catheters were weighted equally in calculating the clinical impact of CHG-impregnated sponge dressing.

The rate of local site infection was assumed to be 10% under standard CVC management based on Pemberton et al. Vokurka et al found a rate of local site infection of 30% in impregnated catheters and 29% in standard catheters. The lower infection rate...
from Pemberton et al\textsuperscript{19} was used as a more conservative estimate, but the Vokurka et al\textsuperscript{20} values were implemented as a sensitivity analysis in the model. Rates of colonization from the meta-analysis by Ho and Litton\textsuperscript{21} were used as a proxy for rates of local infection, and we assumed a 47\% reduction in risk of local infection with use of antiseptic/impregnated CVCs based on the meta-analysis. This efficacy estimate was applied to both standard and impregnated CVCs. Local cutaneous reactions to CHG-impregnated dressings were not considered in the model because these are rare and minor and typically resolve spontaneously. These reactions are treated by either just removing the dressing or by using emollients for local site care; therefore, they do not result in additional health care resource consumption.

To determine the number of CHG-impregnated sponge dressings required per CVC, an assumption about the average duration of CVC implantation per patient was required. This value was set at 10 days based on Ho and Litton.\textsuperscript{21}

\textbf{Economic inputs}

Costs of CR-BSIs, local site infection, and CHG-impregnated sponge dressing were included in the analysis. The maximum CHG-impregnated sponge dressing wear time (7 days) was based on prescribing information for the product.\textsuperscript{13} Based on a mean duration of CVC implantation of 10 days, it was estimated that 2 CHG-impregnated sponge dressing were used per CVC (Table 1).

The cost of CR-BSIs was conservatively estimated as $25,000 per episode, as previously used by Crawford et al.\textsuperscript{16} Based on other estimates by the Centers for Disease Control and Prevention,\textsuperscript{22} costs per CVC-BSI episode range from $34,508 to $56,167. The cost of local site infection was estimated as $399 per event by Saint et al based on the cost of blood, catheter tip, cultures, intravenous or oral antimicrobials, and the cost of replacing a CVC.\textsuperscript{23} Their conservative estimate excludes nursing time, other laboratory tests, and the cost of other supplies such as gauze or transparent dressing.

\textbf{Sensitivity analysis}

Because the model contains a number of assumptions, it was necessary to conduct sensitivity analyses to determine how changes in the values of uncertain parameters may affect the results of the model. Alternate plausible estimates or confidence interval values of estimates were used when available. When other parameter estimates were not available or appropriate, a range of \pm 25\% of the base case value was implemented. The number of CVCs was not evaluated in a sensitivity analysis because the results were directly proportionate to the number of CVCs. The following clinical parameters were tested to measure the

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\begin{table}[h]
\centering
\begin{tabular}{|l|c|l|}
\hline
\textbf{Clinical inputs} & \textbf{Value} & \textbf{Source} \\
\hline
No. of implantable CVCs per year & 3,078 & Assumes 400-bed hospital (60 ICU, 340 non-ICU with 72\% occupancy) \\
Impregnated CVCs & 50\% & Assumption \\
Non-impregnated CVCs & 50\% & Assumption \\
Average duration of implantation & 10 days & Ho and Litton,\textsuperscript{21} 2006 \\
CR-BSIs per 1,000 CVC-days & 1.93 & Edwards et al,\textsuperscript{17} 2009 \\
Rate of local site infection per CVC & 10\% & Pemberton et al,\textsuperscript{19} 1996 \\
Percent decrease risk of CR-BSIs with CHG-impregnated sponge dressing & 69\% & Timsit et al,\textsuperscript{8} 2009 \\
Impregnated CVCs & 44\% & Ruschulte et al,\textsuperscript{9} 2009 \\
Nonimpregnated CVCs & 69\% & Timsit et al,\textsuperscript{8} 2009 \\
Impregnated CVCs & 44\% & Ruschulte et al,\textsuperscript{9} 2009 \\
Nonimpregnated CVCs & 47\% & Ho and Litton,\textsuperscript{21} 2006 \\
Economic inputs & & \\
Additional length of stay because of CR-BSI (days) & 8.0 & Pittet et al,\textsuperscript{4} 1994 \\
Maximum CHG-impregnated sponge dressing wear time (days) & 7.0 & CHG-impregnated sponge dressing package insert recommendation\textsuperscript{13} \\
Average number of CHG-impregnated sponge dressings per CVC & 2 & Calculated based on duration of CVC and maximum wear time \\
Cost per CR-BSI & $25,000 & Crawford et al,\textsuperscript{16} 2004, and O’Grady et al,\textsuperscript{22} 2002 \\
Cost of a local site infection & $399 & Saint et al,\textsuperscript{23} 2000 \\
Price of CHG-impregnated sponge dressing per unit & $6.56 & J & J Wound Management Price List, February 2009\textsuperscript{29} \\
\hline
\end{tabular}
\caption{Base case input parameters used in the model}
\end{table}

CHG, chlorhexidine gluconate; CR-BSI, catheter-related bloodstream infection; CVC, central venous catheter; ICU, intensive care unit.
robustness of the model and to determine the importance of the individual parameters in model results:

- proportion of impregnated versus standard CVCs (±25%);
- average duration of CVC implantation (minimum and maximum values found in the literature: 4.5 days was implemented as a lower estimate per Levy et al11 and 17 days was implemented as an upper estimate per Garland et al12);
- CR-BSIs rate (0.54 CR-BSIs per 1,000 CVC-days was implemented as a lower estimate and 5.63 CR-BSIs per 1,000 CVC-days was implemented as an upper estimate per Edwards et al’s17 minimum and maximum rates depending on the location of the line);
- rate of local infections (Vokurka et al20) found a rate of 30% in impregnated catheters and 29% in standard catheters);
- percent decrease risk of CR-BSIs with CHG-impregnated sponge dressing (95% confidence interval from Ho and Litton21 meta-analysis: 29%-114% [altered to 100% for calculation of sensitivity analysis]); and
- percent decrease risk of local infections with CHG-impregnated sponge dressing (95% confidence interval from Ho and Litton meta-analysis21: 34%-65%).

The following economic parameters were evaluated in sensitivity analyses on the model:

- cost of a local infection (±25%); and
- price of CHG-impregnated sponge dressing (±25%).

**Software**

The economic model was developed in Adobe Flash Player 10 (Adobe, San Jose, CA). The model is interactive, and assumptions of the model are easily modifiable for sensitivity analyses and to adjust for differences across hospitals and health care systems.

**RESULTS**

**Base case**

Based on the model calculations, a hospital inserting 3,078 CVCs per year is expected to avoid an average of 35 CR-BSIs, 145 local infections, 281 ICU days, and 4 deaths with the use of CHG-impregnated sponge dressing. The annual cost of CHG-impregnated sponge dressing would be approximately $40,000 for this sample hospital. The cost savings to the hospital because of reduced CR-BSIs and local infections with CHG-impregnated sponge dressing amount to nearly $936,000 per year, thereby resulting in a net cost savings of > $895,000 with the use of CHG-impregnated sponge dressing (Table 2). Cost-effectiveness studies often report cost-effectiveness ratios as results of the evaluation. This is necessary when the treatment being evaluated is more effective and also less costly overall (when dressing costs and infection costs were considered) than the comparator. Therefore, a cost-effectiveness ratio does not need to be calculated because it would not cost health care payers incremental dollars to derive the additional benefit (ie, economically “dominant” strategy).

### Table 2. Base case clinical and economic consequences

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Standard CVC management</th>
<th>CVC management with CHG-impregnated sponge dressing</th>
<th>Events avoided/cost savings with CHG-impregnated sponge dressing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical consequences</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual number of CR-BSIs</td>
<td>59</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>Annual number of local site infections</td>
<td>308</td>
<td>163</td>
<td>145</td>
</tr>
<tr>
<td>Number of additional ICU days because of CR-BSI</td>
<td>475</td>
<td>194</td>
<td>281</td>
</tr>
<tr>
<td>Annual CR-BSI mortality, n</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><strong>Economic consequences</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of CHG-impregnated sponge dressing</td>
<td>$0</td>
<td>$40,383</td>
<td>−$40,383</td>
</tr>
<tr>
<td>Cost of CR-BSIs</td>
<td>$1,485,135</td>
<td>$606,655</td>
<td>$878,480</td>
</tr>
<tr>
<td>Cost of local site infections</td>
<td>$122,812</td>
<td>$65,090</td>
<td>$57,722</td>
</tr>
<tr>
<td>Total costs/savings</td>
<td>$1,607,947</td>
<td>$712,129</td>
<td>$895,818</td>
</tr>
</tbody>
</table>

CHG, chlorhexidine gluconate; CR-BSI, catheter-related bloodstream infection; CVC, central venous catheter; ICU, intensive care unit.
Sensitivity analyses

Clinical variable input parameters. Figure 1 presents a tornado diagram that illustrates the relative affect that changing the various input variable values had on the model. Changing the proportion of impregnated versus nonimpregnated CVCs only affected the number of CR-BSIs because the efficacy of CHG-impregnated sponge dressing in CR-BSIs varies depending on the type of catheter used. Modifying the value ± 25% had a moderate effect on model results. Increasing the proportion of nonimpregnated catheters resulted in fewer CR-BSIs and more cost savings for CHG-impregnated sponge dressing because the product demonstrates slightly greater efficacy with nonimpregnated CVCs.

Changing the duration of catheterization had a significant impact on model results; the greater the duration, the greater the effect of CHG-impregnated sponge dressing. A similar effect was observed with an increase in the baseline rate of CR-BSIs; with higher rates, the impact of CHG-impregnated sponge dressing was even greater. The rate of CR-BSIs and the percentage decrease risk in CR-BSIs had a significant impact on the cost savings with CHG-impregnated sponge dressing. Changing the rate of local infections and the percentage decrease risk of local infections did not affect results significantly.

Economic variable input parameters. Sensitivity analyses on economic parameters do not influence the clinical outcomes; therefore, only the economic outcomes of these sensitivity analyses are presented (Fig 1). The model was only sensitive to the cost of CR-BSIs. Altering the average number of CHG-impregnated sponge dressing per CVC, the cost per local site infection, or the cost of the CHG-impregnated sponge dressing did not affect the model results significantly.

The 2 parameters that the model results were most sensitive to were the rate of CR-BSIs and the cost per CR-BSI. A 2-way sensitivity analysis was conducted to see how the model results (cost savings) changed when the values of these 2 variables were varied (Table 3). The model showed that CHG-impregnated sponge dressing was cost savings in all instances tested (only positive values of cost savings were obtained in the analyses).

DISCUSSION

The challenge to both payers and providers of health care is to maximize the net benefit obtained from health care expenditures. Health economic models help to identify, measure, and compare relevant costs and outcomes, providing a tool for evaluating the economic impact of alternate therapies and/or medical interventions. Economic models are not intended to replace health care providers’ insight and judgment because they summarize only a subset of information needed to make decisions about resource allocation. However, because they provide details regarding the implications of alternative decisions, they can be valuable during that decision-making process.

Prevention of CR-BSIs has become a high priority nationally. Multiple preventative strategies are being implemented concomitantly to decrease the incidence of these infections. Because of the reduced rate of these infections, it was not clear whether new technical devices used to decrease the risk of infection confer further advantages. A meta-analysis of CHG-impregnated sponge dressing (Ho and Litton21) showed a significant
decrease in catheter colonization and a nonsignificant decrease in CVC-BSIs, indicating a need for a large randomized controlled trial. Recently, Timsit et al. and Ruschulte et al. showed that the use of CHG-impregnated sponge dressing reduced the risk of infection even when background infection rates were low. The Ruschulte et al. study showed that a statistically significant reduction in infection rates was seen not only with standard catheters but also with impregnated catheters, which already provide infection control benefits. We believed that incorporation of this new clinical evidence in a cost-effectiveness model would enable determination of whether this product provides value for money.

This study applied modeling techniques to evaluate the cost-effectiveness of CHG-impregnated sponge dressing versus standard care alone. The approach used expresses the clinical and economic findings in terms that are meaningful for target audiences (eg, hospital administrators, physicians, infection preventionists, nurses, and other clinicians). Overall, this evaluation was conducted using a limited number of assumptions and relied on high level of evidence for inputs. Extensive 1-way sensitivity analyses were performed on the model. The objective was to conduct a straightforward, easily interpretable analysis of the input parameters to which the model was most sensitive (ie, what were the key cost drivers in the model and how did uncertainty around these parameter estimates affect the key results and conclusions).

The results of CHG-impregnated sponge dressing being a cost-saving treatment strategy held true when tested through a multitude of sensitivity analyses. The results of the cost-effectiveness model were found to be most sensitive to the duration of catheterization, the number of CR-BSIs, the rate of CR-BSI reduction with CHG-impregnated sponge dressing, and the cost of CR-BSIs. However, regardless of what alternate plausible parameter values were implemented in the model, CHG-impregnated sponge dressing remained more effective and less costly than standard care alone.

In 2004, Crawford et al compared the costs with the benefits of using the CHG-dressing in the prevention of CR-BSI on a national level. These authors used a very similar approach to our current study (ie, same perspective, target patient population, outcomes evaluated, comparators, cost of CR-BSIs, cost of local infection, length of ICU stay, and number of CHG-impregnated sponge dressing per patient) and reached similar conclusions about the cost-effectiveness of the CHG-impregnated sponge dressing. Crawford et al.’s population-level analysis primarily differed from our model because there have been published clinical trial data subsequent to their analysis.

Nosocomial infection with methicillin-resistant *Staphylococcus aureus* (MRSA) has become a major problem worldwide. The incidence or prevalence of CHG resistance in the United States is unknown. In some Asian countries, 40% to 60% of MRSA strains are believed to carry the QAC A/B gene (coding for CHG resistance). The prevalence in the United Kingdom is reported to be approximately 10%. We are not aware of any reports of such resistance in the United States. The clinical significance of these levels of resistance is not known.

There are a few limitations of this modeling evaluation. First, simplifying assumptions are required in decision analytic models. A balance in determining reasonable clinical treatment pathways and creating a transparent model based on published evidence is strived for. Patients in the Timsit et al study were critically ill, but rates of efficacy from this study were applied to both non-ICU and ICU patients. Rates of local infections were obtained from the meta-analysis by Ho and Litton, who reported rates of colonization. However, this method of estimating infection rates is often seen in clinical trials where rates of colonization are commonly used as primary end points and

<table>
<thead>
<tr>
<th>Cost per CR-BSI</th>
<th>CR-BSIs per 1,000 CVC-days</th>
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<tbody>
<tr>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>$6,000</td>
<td>$71,959</td>
</tr>
<tr>
<td>$11,000</td>
<td>$217,966</td>
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<td>$21,000</td>
<td>$208,510</td>
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<td>$299,544</td>
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<tr>
<td>$36,000</td>
<td>$345,061</td>
</tr>
<tr>
<td>$41,000</td>
<td>$390,579</td>
</tr>
<tr>
<td>$46,000</td>
<td>$436,096</td>
</tr>
</tbody>
</table>

CR-BSI, catheter-related bloodstream infection; CVC, central venous catheter.
sensitivity analysis showed local infection rates have little impact on the cost outcomes.

The importance of skin flora in contributing to CR-BSI in patients is believed to be dependent on the dwell time of the catheter. It is generally accepted that the intraluminal route of infection becomes more predominant in longer term catheters. One published article examined CVC-related BSI pathogenesis in short-term catheters. Their study was based on a population of 1,263 catheters and 6,075 CVC-days and found that, overall, 45% of infections were extraluminally acquired, 26% were intraluminally derived, and the mechanism of infection was indeterminate in 29% of infections.

A second limitation of this modeling evaluation is that the model was built by combining data from multiple sources to identify inputs for efficacy, resource utilization, and costs. This lack of homogeneity of data sources is a common critique of economic evaluations based on modeling techniques. Data obtained from a retrospective claims analysis might have provided a more homogenous representation of actual costs and utilization; however, properly adjusting for covariates in administrative claims analyses is very difficult. A prospective, randomized, cost-effectiveness evaluation would be another approach to collecting economic evidence first-hand. Finally, care should be taken in generalizing results found in this modeling evaluation to other patient populations. The results of this study may not be applicable to smaller hospitals or hospitals with lower rates of CVC insertion. This analysis was also conducted from the perspective of a US hospital payer, and the results of the evaluation would differ from a different payer perspective or in a different country.

CHG-impregnated sponge dressing is a cost-effective and cost savings treatment option for patients requiring CVCs. The use of the CHG-impregnated sponge dressing with standard care will result in better clinical outcomes for patients and lower total health care costs compared with standard care alone. These results are considered to be robust because the conclusions were not affected by implementing alternate values in sensitivity analyses of the parameters.

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References