Staphylococcus Aureus Prevention Strategies in Cardiac Surgery: A Cost-Effectiveness Analysis

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Background. **Cardiac surgery patients colonized with *Staphylococcus aureus* have a greater risk of surgical site infection (SSI). The purpose of this study was to evaluate the cost-effectiveness of decolonization strategies to prevent SSIs.**

Methods. **We compared three decolonization strategies: universal decolonization (UD), all subjects treated; targeted decolonization (TD), only *S aureus* carriers treated; and no decolonization (ND). Decolonization included mupirocin, chlorhexidine, and vancomycin. We implemented a decision tree comparing the costs and quality-adjusted life-years (QALYs) of these strategies on SSI over a 1-year period for subjects undergoing coronary artery bypass graft surgery from a US health sector perspective. Deterministic and probabilistic sensitivity analyses were conducted to address the uncertainty in the variables.**

Results. **Universal decolonization was the dominant strategy because it resulted in reduced costs at near-equal QALYs compared with TD and ND. Compared with ND, UD decreased costs by $462 and increased QALYs by 0.002 per subject, whereas TD decreased costs by $205 and increased QALYs by 0.001 per subject. For 1,000 subjects, UD prevented 19 SSI and TD prevented 10 SSI compared with ND. Sensitivity analysis showed UD to be the most cost-effective strategy in more than 91% of simulations. For the 220,000 coronary artery bypass graft procedures performed yearly in the United States, UD would save $102 million whereas TD would save $45 million compared with ND.**

Conclusions. **Universal decolonization outperforms other strategies. However, the potential costs savings of $57 million per 220,000 coronary artery bypass graft procedures comparing UD versus TD must be weighed against the potential risk of developing resistance associated with universal decolonization.**

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Surgical site infection (SSI) results in significant morbidity and mortality. Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S aureus* (MSSA) have been implicated in as many as half of SSIs for patients undergoing cardiac surgery [1]. Patients colonized with *S aureus* have a greater likelihood of acquiring health-associated *S aureus* infections [2], and studies have found that bundled prevention strategies with intranasal and topical decolonization as well as glycopeptide antibiotic prophylaxis are effective in reducing SSIs in cardiac surgery [3]. However, as infection prevention programs require significant costs to implement, understanding the economic burden of various prevention strategies is important.

A number of *S aureus* cost-effectiveness analyses have demonstrated that implementing decolonization strategies resulted in decreased costs, reduced SSIs, and increased quality-adjusted life-years (QALYs) [4–6]. However, no cost-effectiveness analysis has included a universal bundled decolonization strategy in a cardiac surgery setting. The purpose of this study was to determine the cost effectiveness of three decolonization strategies to prevent SSI among cardiac surgery patients: universal decolonization (UD), where all subjects are treated; targeted decolonization (TD), where only *S aureus* carriers are treated; and no decolonization (ND), where no subjects are treated.

Material and Methods

Model Overview

We developed a decision analysis model comparing the costs and outcomes of three *S aureus* prevention strategies

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CI = confidence interval
MRSA = methicillin-resistant *Staphylococcus aureus*
MSSA = methicillin-susceptible *Staphylococcus aureus*
ND = no decolonization
QALY = quality-adjusted life-year
SSI = surgical site infection
TD = targeted decolonization
UD = universal decolonization

for subjects undergoing coronary artery bypass graft surgery (CABG [Supplemental Fig 1]). Universal decolonization was defined as the treatment of all subjects with mupirocin intranasal decolonization, chlorhexidine gluconate skin decolonization, and preoperative vancomycin along with the standard regimen of antibiotic. Targeted decolonization identified *S aureus* carriers preoperatively using a polymerase chain reaction screening test. Subjects colonized with *S aureus* were treated with mupirocin intranasal decolonization and chlorhexidine gluconate skin decolonization before surgery. Subjects who screened positive for MRSA colonization received preoperative vancomycin and standard antibiotic prophylaxis. Subjects with no evidence of colonization were not administered additional treatment. In the TD strategy, subjects who presented urgently or emergently for CABG incurred the full cost of decolonization and screening. The ND strategy did not screen or treat subjects for *S aureus*, although all subjects received standard perioperative antibiotic prophylaxis.

The model estimated the effect of the decolonization strategies on the probability of a SSI, QALYs, and total costs. An incremental cost-effectiveness ratio was calculated, and a willingness-to-pay threshold of $50,000 per QALY was used. We used a health care sector perspective and a 1-year time horizon. All costs were adjusted for inflation to 2016 US dollars, and measures were not discounted. A budget impact analysis was conducted for the United States where the cost savings from a decolonization strategy was extrapolated to the number of CABG procedures performed annually. All analysis was performed using TreeAge Pro 2016 (Williamstown, MA). This study was deemed not human research by the Johns Hopkins Institutional Review Board.

Data Sources

Probabilities, costs, and quality-of life-weights were derived from searches of the literature indexed in MEDLINE (Table 1) [4, 6–18]. The base case was the average patient undergoing CABG in the United States. The probability of SSI was estimated from the Centers for Disease Control and Prevention and stratified into superficial, deep, and mediastinitis SSI [8]. We updated a recent systematic review and meta-analysis to determine the effect of bundled decolonization interventions in cardiac surgery (Appendix) [3]. Four studies met the eligibility criteria of a cardiac surgery study population, included SSI as an outcome measurement, and used a bundled decolonization treatment strategy with intranasal mupirocin, chlorhexidine, and glycopeptide preoperative antibiotics. The relative risk of SSI for UD was estimated to be 0.35 (95% confidence interval [CI]: 0.26 to 0.46) [11, 19]. This relative risk UD variable was derived from two studies that approximated our UD strategy whereby all patients were treated with mupirocin but only MRSA carriers were given vancomycin. The relative risk of SSI for TD was estimated to be 0.65 (95% CI: 0.48 to 0.89) [10, 20].

The costs of *S aureus* prevention strategies include the medication, material, and labor costs. For TD, labor costs were calculated by multiplying the average estimated time taken by a nurse to obtain a screening test (5 minutes) and a technician to conduct the polymerase chain reaction screening test (7.5 minutes) with the average hourly wage [13]. Similarly, if subjects tested positive for *S aureus*, the labor costs were calculated by multiplying the estimated time taken by a physician assistant to notify the subject and arrange for the medications to be available at a pharmacy (5 minutes) with the average hourly wage for a physician assistant [13]. Only the costs and QALYs of SSIs were considered in the model. The QALYs for superficial, deep, and mediastinitis SSI were obtained by multiplying the SSI health utility by 2 months, 8 months, and 1 year, respectively [6].

Analysis of Uncertainty

The uncertainty of our model was assessed using univariate and Bayesian multivariate probabilistic sensitivity analysis. The one-way and two-way sensitivity analyses were conducted by varying clinical inputs and quality-of-life weights across a range of values to account for differences in the input parameters across surgical sites. The uncertainty ranges for probabilities, relative risks, and costs were calculated by halving and doubling the published estimates. The uncertainty ranges for the relative risks had an upper bound of no effect (1.0). For the probabilistic sensitivity analysis, we performed 10,000 Monte Carlo simulations, allowing us to vary the model parameters simultaneously (costs, effectiveness of decolonization, probabilities, and quality-of-life weights). Beta distributions were applied to probabilities and quality-of-life weights, triangular distributions for relative risks, and gamma distributions for costs. Each simulation was plotted on cost-effectiveness planes, and the probability that a strategy was cost effective was calculated for a range of willingness-to-pay thresholds.

Results

The costs and QALYs of competing *S aureus* prevention strategies are given in Table 2. In our base case (average scenario), UD was the dominant strategy because it reduced costs and increased QALYs compared with TD and ND. Compared with ND, UD decreased costs by $462 and increased QALYs by 0.002 per subject, whereas TD decreased costs by $205 and increased QALYs by 0.001.