Infection Control & Hospital Epidemiology (2018), **39**, 1340–1346
doi:10.1017/ice.2018.228

Original Article

Cost-effectiveness of pre-operative *Staphylococcus aureus* screening and decolonization

Susan E. Kline MD, MPH[1], Erinn C. Sanstead MPH[2], James R. Johnson MD[1,3] and Shalini L. Kulasingam PhD[2]

[1]Division of Infectious Diseases, Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota, [2]Division of Epidemiology, University of Minnesota School of Public Health, Minneapolis, Minnesota and [3]Veterans Affairs Medical Center, Minneapolis, Minnesota

Abstract

Objective: We developed a decision analytic model to evaluate the impact of a preoperative *Staphylococcus aureus* decolonization bundle on surgical site infections (SSIs), health-care–associated costs (HCACs), and deaths due to SSI.

Methods: Our model population comprised US adults undergoing elective surgery. We evaluated 3 self-administered preoperative strategies: (1) the standard of care (SOC) consisting of 2 disinfectant soap showers; (2) the "test-and-treat" strategy consisting of the decolonization bundle including chlorhexidine gluconate (CHG) soap, CHG mouth rinse, and mupirocin nasal ointment for 5 days) if *S. aureus* was found at any of 4 screened sites (nasal, throat, axillary, perianal area), otherwise the SOC; and (3) the "treat-all" strategy consisting of the decolonization bundle for all patients, without *S. aureus* screening. Model parameters were derived primarily from a randomized controlled trial that measured the efficacy of the decolonization bundle for eradicating *S. aureus*.

Results: Under base-case assumptions, the treat-all strategy yielded the fewest SSIs and the lowest HCACs, followed by the test-and-treat strategy. In contrast, the SOC yielded the most SSIs and the highest HCACs. Consequently, relative to the SOC, the average savings per operation was $217 for the treat-all strategy and $123 for the test-and-treat strategy, and the average savings per per SSI prevented was $21,929 for the treat-all strategy and $15,166 for the test-and-treat strategy. All strategies were sensitive to the probability of acquiring an SSI and the increased risk if SSI if the patient was colonized with SA.

Conclusion: We predict that the treat-all strategy would be the most effective and cost-saving strategy for preventing SSIs. However, because this strategy might select more extensively for mupirocin-resistant *S. aureus* and cause more medication adverse effects than the test-and-treat approach or the SOC, additional studies are needed to define its comparative benefits and harms.

(Received 22 June 2018; accepted 19 August 2018; electronically published September 20, 2018)

Staphylococcus aureus is the most common cause of surgical site infection (SSI).[1] A large percentage (25%–33%) of adults in the US population are colonized with *S. aureus*.[2,3] Such *S. aureus* carriers are at 2–10 times greater risk of SSI than noncarriers.[2,3] Consequently, screening for and decolonization of *S. aureus* carriers is a recommended strategy for SSI prevention in selected surgical patients.[4–7] However, optimal *S. aureus* screening and decolonization approaches remain undefined, and practices are highly variable. This is due in part to the scarcity of randomized clinical trial data in outpatients and to doubts that patients will apply decolonization medications as reliably or effectively at home as would nurses in the hospital, as well as concerns about side effects, costs, and possible selection for antimicrobial-resistant bacteria.[6,8,9]

Previous cost-effectiveness analyses concluded that pre-operative *S. aureus* screening and decolonization of *S. aureus* carriers, or administration of an *S. aureus* decolonization regimen to all preoperative patients (without assessing *S. aureus* carrier status), are potentially cost-effective strategies for SSI prevention.[10–13] However, these studies used decolonization efficacy estimates based on earlier trials in which hospital inpatients underwent supervised *S. aureus* decolonization, which is inapplicable to current surgical practice in the United States, where most surgical patients are admitted from home on the day of their scheduled surgery.

To overcome these limitations of the available evidence, we undertook a novel cost-effectiveness analysis based on the results of our recent randomized controlled clinical trial of a self-applied 3-component preoperative *S. aureus* decolonization bundle.[14] In that trial, preoperative 427 outpatients were screened for *S. aureus* carriage at 4 body sites (nares, throat, axillae, and perianal area), and 121 *S. aureus* carriers were randomized to either the standard of care (SOC) consisting of 2 preoperative antiseptic soap showers (n = 53 participants) or the decolonization bundle consisting of 5 days of self-administered nasal mupirocin, chlorhexidine gluconate (CHG) bathing, and CHG mouthwash (n = 57 participants). The trial demonstrated a 47% difference (95% confidence interval [CI], 29.1%–65.7%) in the eradication of *S. aureus* at all screened sites between the decolonization bundle (eradication in 41 of 57 patients, 71.9%) and the SOC (eradication in 13 of 52 patients, 24.5%).[14] The types of surgical patients in this trial were

Author for correspondence: Susan Kline MD, MPH, 420 Delaware St SE, MMC# 250, Minneapolis, MN 55455. E-mail: kline003@umn.edu

PREVIOUS PRESENTATION: This work was reported in preliminary form as a poster at the SHEA 2018 Spring Meeting in Portland, Oregon, on April 18, 2018, Abstract 10081, Poster 209.

Cite this article: Kline SE. *et al* (2018). Cost-effectiveness of preoperative *Staphylococcus aureus* screening and decolonization. *Infection Control & Hospital Epidemiology* 2018, 39, 1340–1346. doi: 10.1017/ice.2018.228

© 2018 by The Society for Healthcare Epidemiology of America. All rights reserved.

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

general surgery (17.3%), neurologic surgery (20%), orthopedic surgery (56.4%), and urologic surgery (6.4%).[14] However, the trial was powered to evaluate the decolonization bundle only for *S. aureus* eradication, not SSI prevention. Given the low incidence of SSI (~2%–3%), evaluation for SSI prevention would have required a much larger sample size.[15]

Because the "test-and-treat" strategy used in our decolonization trial would miss some *S. aureus* carriers (ie, due to the imperfect sensitivity of screening cultures and to newly acquired colonization between screening and surgery) and would impose screening costs and complexity, we envisioned a third approach in which all preoperative patients would receive the decolonization bundle without screening (ie, regardless of *S. aureus* carrier status).[14,16,17] Thus, we conducted a formal analysis of the costs and benefits of 3 different SSI prevention strategies: the SOC, "test and treat," and "treat all."

Methods

Model overview

We developed a decision analytic model to evaluate the impact of a novel preoperative decolonization bundle on reducing SSIs, healthcare-associated costs (HCACs), and death due to SSI. The decision tree was built in OpenTree (Fig. 1) and was converted to R code.[18] Analyses were performed using R Studio version 3.1.3 software (R Core Development Team, Vienna, Austria).

Population modeled

Our model population included men and women aged 18 years or older in the United States who were to undergo elective surgery, including orthopedic, urologic, neurologic, colorectal, cardiovascular, and general surgery.

Strategies modeled

We evaluated 3 preoperative treatment strategies: (1) the SOC; (2) the test-and-treat strategy consisting of administration of the decolonization bundle to surgical patients who screen positive for *S. aureus* at any of 4 swabbed body sites (ie, nasal, throat, axillary, and perianal area); and (3) a treat-all strategy consisting of administration of the decolonization bundle to all surgical patients. The self-administered decolonization bundle consisted of daily showering with CHG soap, twice daily gargling with CHG mouth rinse, and twice daily application of mupirocin nasal ointment, for 5 days prior to surgery. The SOC consisted of 2 self-administered disinfectant soap showers prior to surgery: 1 the night before and 1 the morning of surgery.

Model parameters

Model parameters were derived primarily from the Kline et al[14] randomized controlled trial of the decolonization bundle for eradicating *S. aureus* from the 4 screened body sites (Table 1). Parameters not available from the trial were obtained from the literature and expert opinion. The prevalence of *S. aureus* at any of the 4 screened body sites was estimated from the trial, and plausible were ranges obtained from the literature to account for lower prevalence estimates from studies in which fewer body sites were swabbed.[19] We assumed that all patients attended a baseline appointment at which 1 of the 3 treatment strategies was assigned and screening was performed (if applicable). The average number of days between the baseline appointment and surgery was estimated to be ~60 days.[14] We assumed that patients had a low but nonzero probability of spontaneously acquiring or clearing *S. aureus* between treatment assignment and preoperative treatment administration.[14] Spontaneous acquisition and clearance rates were derived from a longitudinal study of community-dwelling adult outpatients who underwent nasal swab culturing at 1 and 2 months post baseline and subsequently every 2 months for a median of 2 years.[17]

The efficacies of the decolonization bundle and the SOC in eliminating *S. aureus* from all 4 sites were obtained from the recent trial.[14] Adherence to treatment assignment was not modeled explicitly, given that treatment efficacy estimates were based on the results of the trial, in which 80%–90% of the decolonization-bundle group participants reported applying >80% of prescribed medication doses and 100% of the SOC group participants reported taking both preoperative showers.[14] Patients with *S. aureus* colonization were assumed to be at 4.5-fold greater risk of acquiring an SSI relative to patients without *S. aureus* colonization.[20,21] The baseline risk of SSI among patients without *S. aureus* colonization was estimated from a multistate prevalence survey in which the medical records of hospitalized patients were reviewed for documentation of SSI.[15] Estimates for sensitivity and specificity of culture screening were derived from a systematic review and meta-analysis of methicillin-resistant *S. aureus* detection assays.[16]

Costs

The analytic perspective of this study was the medical sector. As such, only direct costs pertaining to healthcare were included in the model (Table 2). Costs associated with the treatment strategies (ie, decolonization bundle, SOC, and screening cultures) were obtained from the trial.[14] We assumed that, on average, a nurse needed 30 minutes per patient to collect swabs for screening and to report patient results. The median wage for a registered nurse was obtained from the US Bureau of Labor Statistics.[22] The plausible range for the attributable cost of an SSI was obtained from the Centers for Disease Control (CDC) evidence-based guidelines for the prevention of SSI and a study of healthcare claims following major elective surgery.[7,23] All costs were adjusted to 2016 US dollars using the Consumer Price Index.[24] Costs were not discounted, due to the limited model time horizon (see the following section). Patients under the test-and-treat strategy who lacked *S. aureus* carriage but falsely screened positive (estimated as 3%) accrued the same decolonization-bundle treatment costs as did actual *S. aureus* carriers.[14] Patients with *S. aureus* colonization who falsely screened negative (estimated as 12%) accrued the same SOC treatment costs as non–*S. aureus* carriers.[16]

Model outcomes and analysis

We assessed the model outcomes of SSIs, deaths due to SSI, and direct costs for each treatment strategy using the base-case values of model parameters. A time horizon of 150 days was modeled, based on the assumed time between baseline visit and surgery, plus 90 days post surgery to capture outcomes directly related to surgery.[1] Using the SOC as the reference, we calculated the number of SSIs prevented, the number of deaths from SSI prevented, and the total savings under the treat-all and the test-and-treat strategies.

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

We conducted a cost-effectiveness analysis in which the SOC was the reference strategy. If a strategy was more costly and less effective than an adjacent strategy, it was considered a less favorable approach.[25] We conducted 1-way sensitivity analyses of model parameters to examine the impact of extreme values on predicted SSIs per 10,000 population. We also conducted a

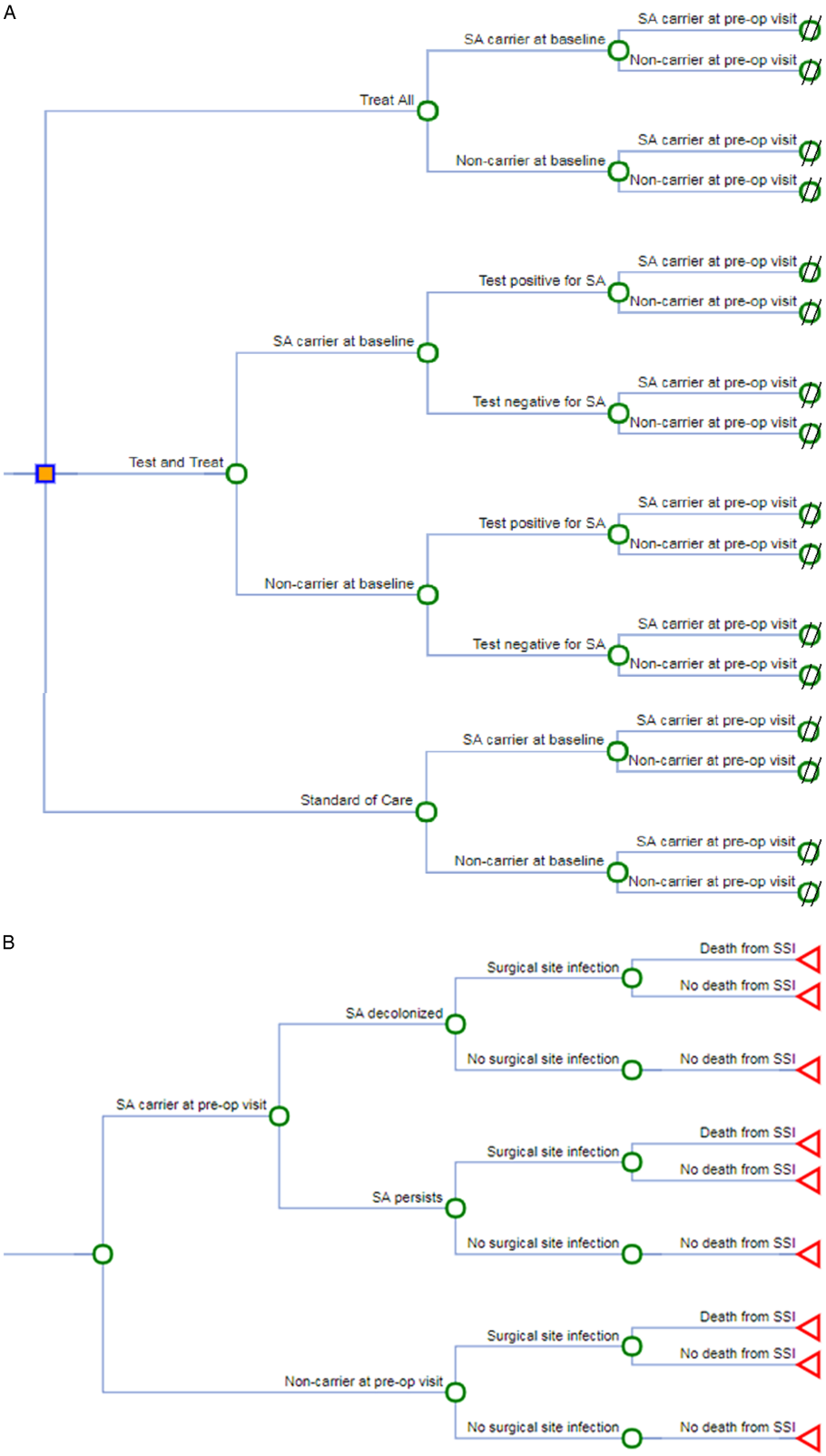


Fig. 1. Decision analytic trees. The trees were designed to evaluate the impact of a preoperative (pre-op) decolonization bundle on reducing surgical site infections (SSIs), healthcare-associated costs, and death due to SSI. Carrier and noncarrier refer to carriage of *Staphylococcus aureus* (SA). (A) 3 strategies. (B) Subtree of strategy efficacy.

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

Table 1 . Parameter Estimates for Decision Analytic Model

Parameter	Base-Case Value, % (Range)	Reference(s)
Prevalence of *Staphylococcus aureus* colonization[a]	30.0 (15.0–36.0)	Kline et al,[14] Wertheim et al,[19] Tong et al,[28] Botelho-Nevers et al[9]
Monthly probability of natural *S. aureus* clearance	3.6 (2.5–6.7)	Miller et al[17]
Monthly probability of *S. aureus* acquisition	1.5 (1.3–1.8)	Miller et al[17]
S. aureus culture sensitivity	88.0 (82.0–92.0)	Luteijn et al[16]
S. aureus culture specificity	95.0 (91.0–97.0)	Luteijn et al[16]
Probability of SSI given no colonization with *S. aureus*	2.0 (1.0–5.0)	Magill et al,[15] Urban et al.[29]
RR of SSI given colonization with *S. aureus*	4.5 (2.0–10.0)[b]	Simor[20] Bode et al[21]
Bundle efficacy	71.9 (58.5–83.0)	Kline et al[14]
Standard of care efficacy	24.5 (13.8–38.3)	Kline et al[14]
Probability of death from SSI	1.0 (0.3–5.0)	Berger et al,[23] Kirkland et al[30]

Note. SSI, surgical site infection; RR, relative risk.
[a]Nasal, throat, axillary, and/or perianal area.
[b]This is a multiplier of probability of SSI given no colonization with *S. aureus* (relative risk).

Table 2. Costs for Decision Analytic Model

Parameter	Base-Case Value, $ (Range)	Reference(s)
Cost of SOC treatment	9.00 (6.75–11.25)	Kline et al[14]
Cost of bundle treatment	25.33 (19.00–31.66)	Kline et al[14]
Cost of *Staphylococcus aureus* screening culture[a]	63.58 (54.63.26–81.46)	Kline et al[14]
Cost of surgical site infection	23,573 (10,209–34,174)	Berger et al,[23] Berrios-Torres et al[7]
Spine surgery	(42,845–91,999)[b]	Emohare et al[26]
Total knee arthroplasty	(27,154–84,043)[b]	Kurtz et al[27]
Total hip arthroplasty	(33,999–105,025)[b]	Kurtz et al[27]

Note. SOC, standard of care.
[a]Includes labor.
[b]Used for secondary base-case analysis only.

probabilistic sensitivity analysis in which we sampled values randomly from parameter distributions to account for the uncertainty in the parameter estimates used in the model. In total, 10,000 sets of parameter values were sampled for the probabilistic sensitivity analysis.

In addition to conducting a base-case analysis with an average SSI cost for general surgery, we conducted a sensitivity analysis using surgery-specific SSI costs. This analysis accounted for the higher costs of SSIs associated with certain procedures, including spinal surgery, total knee arthroplasty (TKA), and total hip arthroplasty (THA).[26,27] We used the patient distribution from Kline et al[14] to determine the percentage of all surgical patients undergoing these procedures. We assessed both extremes of the ranges of these surgery-specific SSI costs. The general surgery SSI cost was applied to patients undergoing a procedure of any type other than those listed above.

Mupirocin resistance and medication side effects modeled

We used estimates from the recent Kline et al[14] trial to estimate for each strategy the number of patients who would experience an adverse drug event or develop mupirocin resistance.

Results

Base case

Under base-case assumptions, the treat-all strategy prevented the most SSIs and resulted in the lowest healthcare-associated costs, followed by the test-and-treat strategy. Compared to the treat-all and test-and-treat strategies, the SOC was the least favorable because it resulted in both the most SSIs and the highest healthcare-associated costs. The base-case results from the decision analytic model are shown in Table 3.

For the 2 more favorable strategies, the average savings per patient were $217 for the treat-all strategy and $123 for the test-and-treat strategy, a difference of $94 per patient, whereas the average savings per SSI prevented were $21,929 for the treat-all strategy and $15,166 for the test-and-treat strategy. Compared to the test-and-treat strategy, the treat-all strategy prevented 18 more SSIs per 10,000 patients undergoing surgery. In a threshold analysis based on the decolonization bundle, the efficacy thresholds below which the particular strategy would no longer be cost saving were 42% for the test-and-treat strategy and 28% for the treat-all strategy. For comparison purposes, the efficacies for *S. aureus* eradication in the

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

Kline et al[14] study were 71.9% for the decolonization bundle and 24.5% for the SOC.

Inclusion of surgery-specific costs for spinal surgery, TKA, and THA increased the total savings for the treat-all and the test-and-treat strategies. Specifically, the ranges of savings per SSI prevented were $30,694–$58,626 for the treat-all strategy and $23,931–$51,863 for the test-and-treat strategy. The ranges of savings per patient undergoing surgery were $305–$582 for the treat-all strategy and $195–$422 for the test-and-treat strategy.

One-way sensitivity analyses

In a 1-way sensitivity analyses for the outcome of SSIs, all 3 strategies were highly sensitive to both the probability of acquiring an SSI and the risk of SSI given colonization with *S. aureus*, but they were relatively less sensitive to treatment efficacy. Parameters pertaining to SSI risk similarly had the greatest impact on costs. When the prevalence of *S. aureus* carriage was set at the lowest plausible value (15%), the SOC remained less favorable than the treat-all and the test-and-treat strategies. However, when the relative risk of SSI among *S. aureus*–colonized patients was <3.5 and the prevalence of *S. aureus* was ≤15% or the risk of SSI was ≤1%, the test-and-treat strategy became more costly than the SOC while remaining more effective in preventing SSIs. With test-and-treat strategy, the use of the highest plausible values for culture sensitivity and specificity increased the savings per infection prevented by $363 and the number of infections prevented per 10,000 population undergoing surgery by 4. Under no combination of extreme screening or treatment costs was the test-and-treat strategy less expensive than the treat-all strategy.

Probabilistic sensitivity analysis

In 10,000 simulations of the decision analytic model, based on the different parameter sets that were generated for probabilistic sensitivity analysis, the median savings per infection prevented were $20,355 (IQR, $14,488–$26,615) for the treat-all strategy and $14,480 (IQR, $8,103–$21,407) for the test-and-treat strategy. The respective median numbers of infections prevented per 10,000 population undergoing surgery were 164 (IQR, 81–281) for the treat-all strategy and 120 (IQR, 70–223) for the test-and-treat strategy. The respective median numbers of deaths prevented per 10,000 population undergoing surgery were 4 (IQR, 2–8) for the treat-all strategy and 3 (IQR, 2–6) for the test-and-treat strategy. The most costly strategy was the SOC in 91% of simulations and the test-and-treat strategy in the remaining 9% of simulations. In 100% of simulations, the treat-all strategy both prevented the most SSIs and was least costly.

Mupirocin resistance and adverse drug events

Using estimates from the recent trial, the number of instances of mupirocin-resistant *S. aureus* per 10,000 patients treated would be 52 for the treat-all strategy and 46 for the test-and-treat strategy, whereas the SOC would yield no mupirocin resistance (Fig. 2).[14] Adverse drug events from applied medications would be most numerous in the treat-all strategy, with 3,460 patients per 10,000 treated experiencing at least 1 adverse drug event, compared to 3,039 for the test-and-treat strategy and 2,860 for the SOC (Fig. 2). These include all participant-reported adverse drug events from the recent trial (as recorded by patients in a drug diary), including minor complaints such as dry skin and unpleasant taste.[14] Because no serious adverse drug events occurred in the recent trial,[14] none were projected here.

Table 3. Base-Case Results per 10,000 Population Undergoing Surgery

Variable	Decolonization Strategy		
	SOC	Test and Treat	Treat All
Surgical site infections, no.	358	277	259
Prevented SSIs, no.	N/A	81	99
Deaths due to SSI, no.	4	3	3
Prevented deaths due to SSI, no.	N/A	1	1
Total cost savings, $	N/A	1,235,114	2,178,307

Note. SOC, standard of care; N/A, not applicable; SSI, surgical site infection.

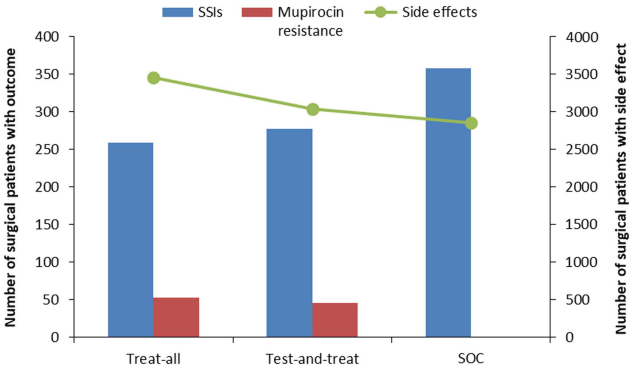


Fig. 2. Surgical site infections (SSIs), muprocin resistance, and side effects from medications modeled for a population of 10,000 surgical patients. Modeled patients assigned to 1 of 3 preoperative treatment strategies: "treat all," "test and treat," and the standard of care (SOC).

Discussion

In this study, we developed a decision analytic model to evaluate the impact on healthcare-associated costs, SSIs, and deaths due to SSI of a preoperative decolonization bundle directed toward *S. aureus* colonization in outpatient surgery clinic patients. To our knowledge, this study is the first to use clinical trial data to inform a cost-effectiveness analysis of this 3-component, self-applied, outpatient decolonization bundle in SSI prevention. Based on the decolonization efficacy estimates from the recent trial, and other parameters taken from the literature, our decision analytic model showed that screening and decolonization with the decolonization bundle (ie, the test-and-treat strategy) is cost-saving. Moreover, a treat-all strategy in which all preoperative patients receive the decolonization bundle (regardless of *S. aureus* status) was cost-saving compared to both the SOC and the test-and-treat strategy.[14]

Despite the limited evidence from randomized clinical trials involving outpatients that preoperative *S. aureus* screening and decolonization prevents SSIs, several studies involving hospitalized patients have demonstrated potential benefits with this approach.[21,31–36] The recent Kline et al[14] trial involving outpatients that served as the basis for the present cost-effectiveness

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

analysis demonstrated that the 3-drug decolonization bundle was significantly more effective than 2 showers in eradicating *S. aureus* carriage from 4 body sites prior to surgery. Although the trial demonstrated that patients were able to apply the multidrug, multidose regimen reliably and effectively at home, it did not assess the clinical outcome of SSIs. The results of our decision analytic model provide evidence that supports conducting a larger clinical trial to assess experimentally the impact of this decolonization bundle on SSIs.

From a medical cost perspective, our findings support offering the decolonization bundle to all preoperative elective surgery patients for self-administration at home for 5 days prior to surgery. However, this approach would expose non–*S. aureus* carriers to medication unnecessarily, with attendant risks of side effects (eg, allergic reactions and irritated or dry skin) and possible selection for resistance to CHG and/or mupirocin, as can occur in *S. aureus* with prolonged administration of these drugs.[37,38] In addition, only *S. aureus* carriers would be at risk for developing these drug-resistant *S. aureus* strains.

An additional consideration for the treat-all strategy is that patients would not know their *S. aureus* carrier status and consequently might be less motivated to apply the decolonization-bundle medications compared to patients who test positive for *S. aureus* in the test-and-treat strategy. Decreased adherence to the decolonization-bundle medications would be expected to lower the efficacy of the decolonization bundle. Our threshold analysis, however, suggested that resistance (or other factors, including nonadherence to the decolonization bundle) would need to reduce the efficacy of the decolonization bundle to <28% (from the 71.9% observed in the recent trial) before the treat-all strategy would no longer be cost-saving in comparison to the SOC.[14]

The potential long-term adverse health impacts resulting from the unintended consequence of widespread *S. aureus* decolonization efforts need to be balanced against the costs and deaths caused by *S. aureus* SSIs.[23,26,27,39] Our analysis suggests that this balance may differ by surgery type. Total joint replacement and spine surgeries can result in deep SSIs that lead to prolonged hospitalization and disability. Our analysis showed that the savings per SSI prevented by the treat-all strategy increased by 40%–167% for THA and TKA procedures compared to general surgery. We acknowledge that the mix of surgical patients across institutions varies widely. Each institution would need to consider case mix when deciding what strategy to use.

From a societal perspective, the human and heath economic burden of SSIs should be balanced against the costs, potential side effects, and selection for *S. aureus* resistant to mupirocin or CHG that could result from the decolonization bundle. A clinical trial to study these outcomes in the real-world setting of busy surgical clinics, surgery centers, and acute-care hospitals is warranted.

Acknowledgments.

Financial support. This work was supported by the Agency for Healthcare Research and Quality (AHRQ grant no. 1R03HS022912-01), the National Institutes of Health (NIH grant no. UL1TR000114); by matching funds and pilot study funds from the University of Minnesota and the University of Minnesota Medical Center; and by the Office of Research and Development, US Department of Veterans Affairs.

Conflicts of interest. All authors report no conflict of interest relevant to this article.

References

1. Hidron A, Edwards J, Patel J, *et al*. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect Control Hosp Epidemiol* 2008;29:996–1011.
2. Perl TM, Golub JE. New approaches to reduce *Staphylococcus aureus* nosocomial infection rates: treating *S. aureus* nasal carriage. *Ann Pharmacother* 1998;32:S7–S16.
3. Wenzel RP, Perl TM. The significance of nasal carriage of *Staphylococcus aureus* and the incidence of postoperative wound infections. *J Hosp Infect* 1995;31:13–24.
4. Ban KA, Minei JP, Laronga C, *et al*. American college of surgeons and surgical infection society: surgical site infection guidelines, 2016 update. *Am Coll Surg* 2017;224:59–74.
5. Global guidelines for the prevention of surgical site infection. World Health Organization website. http://www.who.int/gpsc/ssi-guidelines/en/. Published 2016. Accessed July 21, 2017.
6. Parvizi J, Shohat N, Gehrke T. Prevention of periprosthetic joint infection: new guidelines. *Bone Joint J* 2017;99-B 4 Supple B:3–10.
7. Berríos-Torres SI, Umscheid CA, Bratzler DW, *et al*. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg* 2017;152:784–791.
8. Chlebicki M, Safdar N, O'Horo JC. Preoperative chlorhexidine shower or bath for prevention of surgical site infection: a meta-analysis. *Am J Infect Control* 2013;41:167–173.
9. Botelho-Nevers E, Gagnaire J, Verhoeven PO, *et al*. Decolonization of *Staphylococcus aureus* carriage in 2016. *Med Mal Infect* 2016:1–6.
10. Courville XF, Tomek IM, Kirkland KB, *et al*. Cost-effectiveness of preoperative nasal mupirocin treatment in preventing surgical site infection in patients undergoing total hip and knee arthroplasty: a cost-effectiveness analysis. *Infect Control Hosp Epidemiol* 2012:33:152–159.
11. Wassenberg MWM, Wit GA De, Bonten MJM. Cost-effectiveness of preoperative screening and eradication of *Staphylococcus aureus* carriage. *PLoS One* 2011;6:e14815.
12. Young LS, Winston LG. Preoperative use of mupirocin for the prevention of healthcare-associated *Staphylococcus aureus* infections: a cost-effectiveness analysis. *Infect Control Hosp Epidemiol* 2006;27:1304–1312.
13. Noskin GA, Rubin RJ, Schentag JJ, *et al*. Budget impact analysis of rapid screening for *Staphylococcus aureus* colonization among patients undergoing elective surgery in US hospitals. *Infect Control Hosp Epidemiol* 2008;29:16–24.
14. Kline S, Neaton J, Lynfield R, *et al*. Effectiveness of screening and decolonization of *S. aureus* in surgery outpatients. *Infect Control Hosp Epidemiol* 2018 Jul 24:1–9. doi: 10.1017/ice.2018.151.
15. Magill S, Edwards J, Bamberg W, *et al*. Multistate point-prevalence survey of health care-associated infections. *Nat Rev Microbiol* 2014;370:1198–1208.
16. Luteijn JM, Hubben GAA, Pechlivanoglou P, *et al*. Diagnostic accuracy of culture-based and PCR-based detection tests for methicillin-resistant *Staphylococcus aureus*: a meta-analysis. *Clin Microbiol Infect* 2010;17:146–154.
17. Miller RR, Walker AS, Godwin H, *et al*. Dynamics of acquisition and loss of carriage of *Staphylococcus aureus* strains in the community: the effect of clonal complex. *J Infect* 2014;68:426–439.
18. Jalal H, Alarid-Escudero F, Hunink MGM. PS 1-58 DTree: an open source tool for building decision trees and cost-effectiveness analyses. In: 38th Annual North American Meeting of the Society for Medical Decision Making; 2016:E57.
19. Wertheim HFL, Melles DC, Vos MC, *et al*. The role of nasal carriage in *Staphylococcus aureus* infections. *Lancet Infect Dis* 2005;5:751–762.
20. Simor AE. Staphylococcal decolonization: an effective strategy for prevention of infection? *Lancet Infect Dis* 2011;11:952–962.
21. Bode L, Kluytmans J, W H, *et al*. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 2010;362:9–17.
22. Occupational outlook handbook, 2016–2017. US Department of Labor Bureau of Labor Statistics website. https://www.bls.gov/ooh/healthcare/registered-nurses.htm. Published 2017. Accessed August 1, 2017.

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press

23. Berger A, Edelsberg J, Yu H, *et al*. Clinical and economic consequences of post-operative infections following major elective surgery in US hospitals. *Surg Infect (Larchmt)* 2014;15:322–327.
24. CPI inflation calculator. US Department of Labor Bureau of Labor Statistics website. https://data.bls.gov/cgi-bin/cpicalc.pl. Accessed August 23, 2018.
25. Gillian S, Neiumann P, Basu A, *et al*. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA* 2016;316:1093–1103.
26. Emohare O, Ledonio CG, Hill BW, *et al*. Cost savings analysis of intrawound vancomycin powder in posterior spinal surgery. *Spine J* 2014;14:2710–2715.
27. Kurtz SM, Lau E, Watson H, *et al*. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty* 2012;27:61–65.
28. Tong SYC, Davis JS, Eichenberger E, *et al*. *Staphylococcus aureus* infections: epidemiology, pathophysiology, clinical manifestations, and management. *Clin Microbiol Rev* 2015;28:603–661.
29. Urban JA. Cost analysis of surgical site infections. *Surg Infect (Larchmt)* 2006;7:19–22.
30. Kirkland KB, Briggs JP, Trivette SL, *et al*. The impact of surgical-site infections in the 1990's: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999;20:725–730.
31. Perl TM, Cullen JJ, Wenzel RP. Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infection. *New Engl J Med* 2002;346:1871–1877.
32. Segers P, Speekenbrink R, Ubbink D, *et al*. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate a randomized controlled trial. *JAMA* 2006;296:2460–2466.
33. Kluytmans JA, Mouton JW, Marjolein FQ. Reduction of surgical site infections in cardiothoracic surgery by elimination of nasal carriage of *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 1996;17:780–784.
34. Schweizer ML, Chiang H, Septimus E, *et al*. Association of a bundled intervention with surgical site infections among patients undergoing cardiac, hip, or knee surgery. *JAMA* 2015;313:2162–2171.
35. Kalmeijer MD, Coertjens H, van Nieuwland-Bollen PM. Surgical site infections in orthopedic surgery: the effect of mupirocin nasal ointment in a double-blind, randomized, placebo-controlled study. *Clin Infect Dis* 2002;35:353–358.
36. Konvalink A, Erret L, Fong IW. Impact of treating *Staphylococcus aureus* nasal carriage on wound infections in cardiac surgery. *J Hosp Infect* 2006;64:162–168.
37. Irish D, Eltringham I, Teall A, *et al*. Control of an outbreak of an epidemic methicillin-resistant *Staphylococcus aureus* also resistant to mupirocin. *J Hosp Infect* 1998;39:19–26.
38. Hayden MK, Lolans K, Haffenreffer K, *et al*. Chlorhexidine and mupirocin susceptibility of methicillin-resistant *Staphylococcus aureus* isolates in the REDUCE-MRSA trial. *J Clin Microbiol* 2016;54:2735–2742.
39. Noskin GA, Rubin RJ, Schentag JJ, *et al*. National trends in *Staphylococcus aureus* infection rates: impact on economic burden and mortality over a 6-year period (1998–2003). *Clin Infect Dis* 2007;45:1132–1140.

https://doi.org/10.1017/ice.2018.228 Published online by Cambridge University Press