ORIGINAL ARTICLE

Cost-Effectiveness of Preoperative Nasal Mupirocin Treatment in Preventing Surgical Site Infection in Patients Undergoing Total Hip and Knee Arthroplasty: A Cost-Effectiveness Analysis

Xan F. Courville, MD, MS;[1,4] Ivan M. Tomek, MD, FRCS(C);[1] Kathryn B. Kirkland, MD;[2,4] Marian Birhle, MPH;[4] Stephen R. Kantor, MD;[1] Samuel R. G. Finlayson, MD, MPH[3,4]

OBJECTIVE. To perform a cost-effectiveness analysis to evaluate preoperative use of mupirocin in patients with total joint arthroplasty (TJA).

DESIGN. Simple decision tree model.

SETTING. Outpatient TJA clinical setting.

PARTICIPANTS. Hypothetical cohort of patients with TJA.

INTERVENTIONS. A simple decision tree model compared 3 strategies in a hypothetical cohort of patients with TJA: (1) obtaining preoperative screening cultures for all patients, followed by administration of mupirocin to patients with cultures positive for *Staphylococcus aureus*; (2) providing empirical preoperative treatment with mupirocin for all patients without screening; and (3) providing no preoperative treatment or screening. We assessed the costs and benefits over a 1-year period. Data inputs were obtained from a literature review and from our institution's internal data. Utilities were measured in quality-adjusted life-years, and costs were measured in 2005 US dollars.

MAIN OUTCOME MEASURE. Incremental cost-effectiveness ratio.

RESULTS. The treat-all and screen-and-treat strategies both had lower costs and greater benefits, compared with the no-treatment strategy. Sensitivity analysis revealed that this result is stable even if the cost of mupirocin was over $100 and the cost of SSI ranged between $26,000 and $250,000. Treating all patients remains the best strategy when the prevalence of *S. aureus* carriers and surgical site infection is varied across plausible values as well as when the prevalence of mupirocin-resistant strains is high.

CONCLUSIONS. Empirical treatment with mupirocin ointment or use of a screen-and-treat strategy before TJA is performed is a simple, safe, and cost-effective intervention that can reduce the risk of SSI. *S. aureus* decolonization with nasal mupirocin for patients undergoing TJA should be considered.

LEVEL OF EVIDENCE. Level II, economic and decision analysis.

Infect Control Hosp Epidemiol 2012;33(2):152-159

Surgical site infections (SSIs) are a significant source of patient morbidity and societal expense. Deep SSI after primary total hip or knee arthroplasty complicates 0.5%–2.0% of cases.[1-6] Typically, treatment of deep total joint arthroplasty (TJA) SSI involves a 2-stage revision surgery. In the first stage, all infected implants are removed, an antibiotic-loaded cement spacer is placed, and 6–8 weeks of intravenous antibiotic therapy are administered. The hip or knee components are reimplanted in a second operation if joint aspirations and inflammatory markers suggest that the infection has been eradicated. It is estimated that the direct medical costs of TJA revisions for deep infections are approximately $100,000 per patient, or 3–4 times more than the cost of primary TJA.[7-9] Patients lose functional capabilities and work productivity during months of antibiotic therapy and rehabilitation. Furthermore, even after successful treatment of an SSI, the clinical results are inferior to those achieved with primary TJA that is not complicated by infection.[10]

Strategies to reduce the risk of SSI after TJA include administration of perioperative intravenous antibiotics, surgical site preparation, sterile technique, regulating operating room airflow and traffic,[10] and use of antibiotic-impregnated bone cement.[11] More than half of TJA SSIs are caused by *Staphylococcus aureus*,[12,13] an organism carried in the anterior nares

Affiliations: 1. Department of Orthopaedics, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; 2. Department of Infectious Diseases, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; 3. Department of Surgery, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; 4. The Dartmouth Institute, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire.

Received June 13, 2011; accepted September 22, 2011; electronically published January 4, 2012.

 0899-823X/2012/3302-0008$15.00. DOI: 10.1086/663704

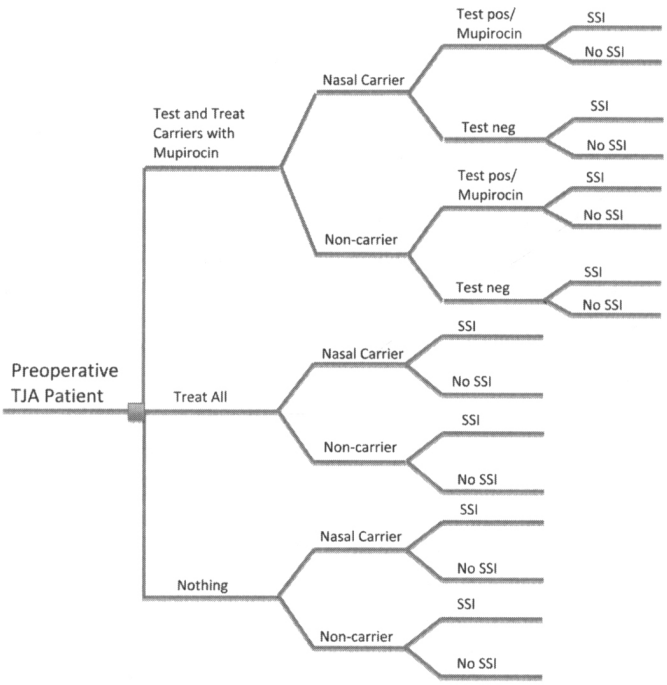

FIGURE 1. Simple decision model for patients undergoing total joint arthroplasty (TJA) to have no treatment, be treated preoperatively with mupirocin, or be screened and then, if *Staphylococcus aureus* carriage is detected, treated with mupirocin. SSI, surgical site infection.

of 20%–30% of patients who undergo TJA.[14-16] In a large study, 84.6% of *S. aureus* infections were caused by bacterial strains of *S. aureus* identical to those found in the patient's nares,[17] which suggests that most SSIs after TJA are caused not by hospital-acquired pathogens but by patients' endogenous flora. Therefore, decolonization strategies have been studied,[12-14,18,19] including mupirocin calcium ointment. This agent inhibits bacterial protein and RNA synthesis and is active against methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) as well as other gram-positive and some gram-negative bacteria. The ointment is applied intranasally twice daily for 5 days and is associated with an *S. aureus* eradication rate of 83% over the short term.[17] The treatment reduces SSI rates associated with nonorthopedic and orthopedic procedures,[20] including among patients who undergo TJA.[21,22] The adverse effects of mupirocin are generally limited to local irritation, and most patients tolerate the therapy with ease.[20,23]

We assessed the cost-effectiveness of 3 preoperative strategies for treating *S. aureus* colonization in patients undergoing TJA to prevent deep SSI using a cost-effectiveness decision model. Our goal was to compare the following strategies: (1) preoperative nasal screening of all patients for *S. aureus* colonization, followed by mupirocin treatment only for patients with positive cultures; (2) empirical treatment of all preoperative patients with mupirocin, with no *S. aureus* screening; and (3) standard infection prevention measures without *S. aureus* screening or mupirocin decolonization.

The question of whether mupirocin is a cost-effective alternative to no therapy is an ideal question for a decision analysis, because there is uncertainty regarding the efficacy of mupirocin as a result of emerging mupirocin resistance, which can be evaluated in the sensitivity analysis.

METHODS

Patient Population

Two decision models were created that were based upon hypothetical cohorts of 65-year-old patients with end-stage hip or knee osteoarthritis for whom medical management had failed and TJA had been recommended. The cohort age was chosen to coincide with the mean age of patients undergoing TJA from a large multihospital database.[24] Separate models for patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA) were run, although demographic data and infection rates in large registries are similar between the 2 populations.[1-6] The analysis was performed from a societal perspective but was limited to costs and health effects directly affecting the target population (eg, it did not include caregiver time or future health problems).

Model Design

The model depicting the risks of revision surgery for deep SSI within 1 year of the primary operation is shown in Figure 1. The model begins with the decision in the target population of 65-year-old patients to use one of the following strategies: (1) preoperative nasal screening of all patients for *S. aureus* colonization, followed by administration of mupirocin treat-

https://doi.org/10.1086/663704 Published online by Cambridge University Press

ment to patients with positive culture results (the screen-and-treat strategy); (2) preoperative mupirocin administration to all patients and no screening (the treat-all strategy); and (3) no administration of mupirocin and no screening for *S. aureus* (the no-treatment strategy).

The decision analysis systematically assigns probabilities and values to each alternative. These values are based on a reasonable range of evidence-based data gathered from the literature. The potential pathways are reflected in the branches of the tree. Utilities were measured in quality-adjusted life-years (QALYs), and costs were measured in 2005 US dollars. The model was constructed with the use of decision analysis software (TreeAge Pro 2009; TreeAge Software).

Model Parameters

The following assumptions were made in construction of the model: (1) deep SSI as defined by the Centers of Disease Control and Prevention[25] will be recognized within 1 year after surgery; (2) patients who need a revision TJA for a deep SSI will undergo a 2-stage revision operation within the year after the procedure; (3) the adverse effects from receipt of mupirocin are negligible, and most patients complete the course of therapy. The specific values used in the decision model are shown in Table 1 and are described below.

The 7 studies on preventing *S. aureus* SSI with mupirocin therapy in patients undergoing orthopedic procedures were reviewed to estimate the therapy's effectiveness. The literature consists of a small number of clinical series with 172–12,000 patients who underwent a variety of orthopedic procedures with prosthetic implants.[12-14,18,19,21,22] In the only systematic review, Kallen et al[21] performed a subgroup analysis on 2 orthopedic studies that included 1 randomized controlled trial (RCT) with an evidence level of I.[13,18] Pooling these studies, they found a relative risk (RR) of 0.61 for SSI among *S. aureus* carriers who were treated with mupirocin, compared with untreated patients.[21] Since this review was published, 5 additional primary studies (with evidence levels ranging from I through III) that have included orthopedic patients have been published. These 5 studies estimated RRs for *S. aureus* SSI of 0.10–0.49 for patients decolonized with mupirocin.[12,14,19,20,22] For the sensitivity analysis, a broad range of 0.1–0.9 was used to account for the possibility that these studies underestimated the risk reduction. In a larger study, the authors estimated the probability of *S. aureus* SSI in *S. aureus* carriers who were treated with mupirocin to be 1.3%, compared with 0.58% among noncarriers who were untreated.[14] We used these probabilities for one branch in the model, because this was the only study to report rates of *S. aureus* SSI stratified by colonization and treatment status.

We used the *S. aureus* colonization rate from our local population of patients with TJA for the base case. From January 2007 through June 2008, 153 (26%) of 587 screened patients who underwent TJA were colonized with *S. aureus*, including 12 patients with MRSA, which is consistent with reported colonization rates among populations of patients undergoing orthopedic procedures (24%–30%).[12-14,22] For the sensitivity analysis, this range was expanded to 1%–70%.

We used the least expensive screening test for *S. aureus* in our model, a nasal swab sample culture incubated on selective media. The nasal swab sample incubation period is 24–48 hours, and carriers can then be treated with mupirocin. The test for *S. aureus* has a sensitivity and specificity of 85% and 52%, respectively.[26]

Utilities were based on quality of well-being index scores reported in the literature. All health states were assigned utility factors along a continuum, with 0.0 representing death and 1.0 representing perfect health.[27] From a longitudinal cohort study involving 1,356 patients, a quality of well-being index score of 0.65 was established for 75–84-year-old patients with arthritis,[27] and a score of 0.71 was established for 75–84-year-

TABLE 1. Model Variables for the Base Case Analysis

Variable	Base case value	Range reported in the literature	Reference(s)
SSI risk reduction from mupirocin	0.61	0.1–0.64	12-14, 18-22
Probability of SSI among mupirocin-treated carriers, %	1.3	...	14
Probability of SSI among untreated noncarriers, %	0.58	...	14
Probability of carrying *Staphylococcus aureus*, %	26	24–30	12-14, 22, this study
Test sensitivity, %	52	50–54	26
Test specificity, %	85	80–100	26
Utility after primary TKA	0.68	...	27, 28
Utility after septic knee revision	0.53	...	28
Utility after primary THA	0.80	...	11
Utility after septic hip revision	0.64	...	29
Cost of primary TJA[a]	23,508	...	30
Cost of septic hip revision[a]	104,398	...	7, 30
Cost of septic knee revision[a]	117,441	...	9
Cost of mupirocin treatment[a]	6.23	6–58	31, this study
Cost of *S. aureus* screening test[a]	96.00	24–96	31, this study

NOTE. THA, total hip arthroplasty; TJA, total joint arthroplasty; TKA, total knee arthroplasty; SSI, surgical site infection.
[a] Cost is given in 2005 US dollars.

TABLE 2. Results of the Analysis for the Base Case of Total Hip Arthroplasty (THA) and Total Knee Arthroplasty (TKA)

Variable	Average cost, 2005 US$	Average QALY	Average cost-effectiveness, $ per QALY
THA base case			
Treat all patients	24,258	0.7985	$24,258 ÷ 0.7985 QALY = $30,379 per QALY
Screen and treat *S. aureus*–positive patients with mupirocin	24,471	0.7983	$24,471 ÷ 0.7983 QALY = $30,655 per QALY
No treatment	24,506	0.7980	$24,506 ÷ 0.7980 QALY = $30,709 per QALY
TKA base case			
Treat-all patients	24,378	0.6787	$24,378 ÷ 0.6787 QALY = $35,916 per QALY
Screen and treat *S. aureus*–positive patients with mupirocin	24,611	0.6785	$24,611 ÷ 0.6785 QALY = $36,270 per QALY
No treatment	24,667	0.6783	$24,667 ÷ 0.6783 QALY = $36,365 per QALY

NOTE. QALY, quality-adjusted life-year.

old patients without arthritis. [27] Consistent with another cost-effectiveness analysis,[27,28] we estimated a utility of 0.68 after TKA, and we estimated that a septic revision would have 80% of the utility of a TKA.[28] For THA, a time-trade-off technique has determined a utility value of 0.80.[29] After a revision for infection, a conservative 20% decrease in utility was assigned (80% of 0.80 is 0.64).[29] Ranges from 0.1 through 0.9 were tested in sensitivity analyses.

The costs of TJA and revision operations were estimated in 2005 US dollars from the orthopedic literature[7] and accounted for the costs associated with the procedure and acute hospitalization. Costs for caregivers' time and lost wages were not included. A primary TJA in our model was assigned a cost of $23,508, and a revision infected THA was assigned a cost of $104,398 (converted from 2002 to 2005 US dollars from the Bureau of Labor Statistics). The cost estimates, calculated in 2005 dollars, were from Bozic et al[7,30] and were based on the assumption that most patients will be treated with a 2-stage revision and 6–8 weeks of intravenous antibiotics. The charges for TKA revisions attributable to infection were also estimated from the literature at $117,441.[9] For sensitivity analyses, we used the cost ranges of $10,000–$100,000 for primary TJA and $20,000–$250,000 for revision surgery, which are within plausible ranges.

We used the costs at our medical center of the bacterial culture ($96) and a 5-day course of mupirocin ointment ($6.23) for the base case. The bacterial culture costs include the test and supplies, 30 minutes of nursing time for teaching and checking the test results, and 11 minutes of laboratory technician time. For sensitivity analyses, we used a range of published cost estimates for the culture ($10–$200),[31] which would include the costs of polymerase chain reaction and the mupirocin ointment ($5–$100).

Analysis

We used a decision analysis model with a hypothetical cohort to evaluate the cost-effectiveness of mupirocin to prevent deep SSI after TJA. Our model reflects a 1-year time frame. Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in cost between 2 strategies by the difference in effectiveness and were reported in dollars per QALY. An ICER expresses how much money must be spent to gain 1 QALY using a proposed treatment strategy, compared with an established treatment strategy. When a treatment strategy provides benefit and no additional cost, the proposed treatment strategy is reported as "dominant" and no ICER is calculated. Using the Panel on Cost-effectiveness in Health and Medicine Recommendations, medical interventions with an ICER less than $50,000 per QALY are considered to be cost-effective, and this value was used in threshold analysis.[32] In contrast to ICER, "average cost-effectiveness" is the total cost of a proposed treatment strategy per QALY without reference to any other treatment strategy. Average cost-effectiveness is useful for comparing the relative costs of alternative treatment strategies per unit benefit, but when reported alone (without reference to an established alternative), it does not allow one to determine whether the additional benefit of a treatment is worth the cost.

Sensitivity analyses were performed on all variables in the model to determine the effect of a wide range of values on the cost-effectiveness ratio. Ranges for the model were based upon reported ranges from the literature if possible (Table 1). If no ranges were found in the literature, plausible ranges were established by expert opinion. Any variable that had a significant effect on the results of the model and the potential to alter the preferred strategy is reported.

RESULTS

Empirical treatment of all patients without screening for nasal *S. aureus* carriage was the dominant strategy and was associated with lower costs and greater expected benefit than the 2 other strategies in both the THA and TKA models. However, differences in cost and benefit between the 3 strategies were relatively small. In the THA model, the average cost-effectiveness was $30,380 per QALY for the treat-all strategy, $30,660 per QALY for the screen-and-treat strategy, and $30,710 per QALY for the no-treatment strategy (Table 2).

TABLE 3. Sensitivity Analyses Demonstrating the Range Applied to Each Sensitivity Analyses and the Average Cost-Effectiveness for the Most Cost-Effective Strategy in Both the Total Hip Arthroplasty (THA) and Total Knee Arthroplasty (TKA) Models

Variable, range for sensitivity analysis	Most cost-effective strategy	THA model average cost-effectiveness, $ per QALY	TKA model average cost-effectiveness, $ per QALY
Cost of mupirocin			
$5–$100	Treat all[a]	30,377–30,496	35,915–36,055
Cost of test			
$10–$200	Treat all[a]	30,379	35,916
Cost of TJA surgery			
$10,000–$39,250	Treat all[a]	13,619–49,912	16,200–58,897
$39,500–$100,000	Treat all[a]	52,704–125,000	58,897–147,576
Cost of septic revision surgery			
<$26,000	No treatment	29,371–29,482	34,227–34,676
$26,000–$250,000	Treat all[a]	29,471–32,058	34,676–37,715
Prevalence of *S. aureus* in target population			
0.1%–70%	Treat all[a]	30,027–31,000	35,440–36,757
Relative risk of SSI with treatment compared with no treatment			
0.1–0.98	Treat all[a]	29,938–30,700	36,184–35,856
>0.99	No treatment[a]	30,709	35,857
Utility of TJA			
0.1–0.48	Treat all[a]	50,000–240,000	50,882–254,400
0.49–0.9	Treat all[a]	27,000–49,800	27,137–49,843
Utility of SSI after TJA			
0.1–0.9	Treat all[a]	30,573–30,288	35,744–36,134

NOTE. SSI, surgical site infection; QALY, quality-adjusted life-year; TJA, total joint arthroplasty.
[a] Dominant strategy (both lower costs and greater expected benefit) in the sensitivity analysis.

Similarly, in the TKA model, the average cost-effectiveness was $35,916 per QALY for the treat-all strategy, $36,270 per QALY for the screen-and-treat strategy, and $36,365 per QALY for the no-treatment strategy (Table 2).

Sensitivity analyses are reported in Table 3. The sensitivity analyses revealed that, if the cost of mupirocin were as high as $100 (base case cost is $6.23), treating all patients would still dominate the other strategies (range, $5–$100). If the cost of septic revision surgery were as low as $26,000 and as high as $250,000, treating all patients would remain the dominant strategy. If the cost of septic revision were very low (<$26,000), the no-treatment strategy would no longer be dominated (ie, it would cost less than the treatment strategies); however, treating all patients would still be a cost-effective approach to decreasing deep SSI incidence (ICER, <$50,000 per QALY). If the cost of the screening test were as low as $10 or as high as $200, the treat-all strategy would remain the dominant strategy in the model.

Treating all patients remained the dominant strategy when the prevalence of *S. aureus* colonization in the target population ranged from 0.1% though 70%. The RR of SSI associated with mupirocin treatment, compared with no treatment, was also tested across a wide range in the sensitivity analysis (RR, 0.1–0.9), and the treat-all strategy remained the dominant strategy until mupirocin was no longer effective (RR, >0.99).

The treat-all strategy is not cost-effective (ICER, >$50,000 per QALY) when the utility of life after TJA is less than 0.48. When the utility of TJA is between 0.49 and 0.9, the treat-all strategy is the most cost-effective strategy in the model. The treat-all strategy is dominant across all potential ranges of utility of life after TJA septic revision surgery (0.1–0.9).

DISCUSSION

Our analysis demonstrates that both the treat-all strategy and the screen-and-treat strategy for a TJA preoperative *S. aureus* decolonization program with nasal mupirocin are cost-effective alternatives, compared with no decolonization. The treat-all and screen-and-treat strategies have similar average cost-effectiveness ratios, with only trivial differences between the strategies. A treat-all strategy is simpler to implement and avoids missing potential carriers because of false-negative test results. However, hospitals with a high prevalence of mupirocin resistant strains may prefer a screen-and-treat strategy. The sensitivity analyses demonstrate that using mupirocin preoperatively is cost-effective across a wide range of conditions, including in settings in which there is a high prevalence of mupirocin-resistant strains.

Preoperative decolonization of patients undergoing TJA is rational, because endogenous *S. aureus* is the causative agent of many deep prosthetic SSIs. A single course of mupirocin is effective in eradicating *S. aureus* colonization[20,21,33] with an adverse effect profile limited to irritation or itching.[20,23] Al-

https://doi.org/10.1086/663704 Published online by Cambridge University Press

though *S. aureus* recolonization can occur, the timing of this would not likely occur within the perioperative period. Importantly, the prevalence of mupirocin resistance and decolonization failure appears to be increasing.[34,35] Higher rates of resistance seem to occur among patients with long-term daily use,[31] including older patients, those with prior hospitalization, those with wound or pressure sores, those with exposure to MRSA-inactive antibiotics, and those with central venous catheters.[35] Some studies have found that resistance can develop after a single, short-term course of therapy.[13,17,36] Our analysis assumes that mupirocin has a persistent efficacy over time. If mupirocin resistance increases in the future, the results of this analysis would not be applicable.

The limitations to this cost-effectiveness analysis include the 1-year time course, which does not take into account the long-term effects of SSI or therapies. Were the analyses extended to longer-term outcomes, it is likely that the treated group would have the advantage of fewer revision surgeries over their lifetime and an associated improved QALY score. Our model is limited by the paucity of literature on *S. aureus* decolonization and SSI in patients who undergo orthopedic procedures. Estimates of the effectiveness of mupirocin treatment may be limited by publication bias, with studies that have negative findings being less likely to have been published. Also, there was heterogeneity within the studies as to the outcomes reported (all SSIs, SSIs due to *S. aureus* only, or other infections), additional infection prophylaxis given (antibiotics or chlorhexidine washes), and the patient populations that may influence the generalizability of the results. Although there is uncertainty surrounding some of our assumptions, we tested the less certain assumptions broadly in sensitivity analysis, and the model conclusions remained robust.

Seven studies were found involving patients who had undergone orthopedic procedures and the use of mupirocin treatment for *S. aureus* carriers, and the results of these studies tend to favor decolonization. To our knowledge, only a single meta-analysis has specifically examined the relationship between mupirocin use and SSI rates among patients who underwent orthopedic procedures.[21] This review pooled only 2 articles[13,18] and concluded that mupirocin use led to a significant risk reduction of 0.61 ($P < .05$) for SSI. A Cochrane Review on this topic did show improvements in *S. aureus* infection rates, but it did not show significant changes in overall rates of SSI after decolonization.[33] One study with 1,700 patients treated with mupirocin showed no difference in either the rate of SSI or the rate of *S. aureus* SSI, compared with the rates among 400 historic control subjects.[19] Two large orthopedic studies found a statistically significant difference between SSI rates among decolonized patients and untreated *S. aureus* carriers, with SSI rates 3–4-fold lower among decolonized patients.[12,14] These 2 reports did not find significant risk reductions in *S. aureus* SSI in the mupirocin group (including both *S. aureus* carriers and noncarriers), compared with control groups,[12,14] although there were trends that suggested that mupirocin was protective against *S. aureus* SSI. The most recent case-control trial, which included 12,000 patients, showed a 0.41 risk reduction ($P < .05$) in *S. aureus* SSI in the study group, compared with the historical cohort. The study group was screened for *S. aureus* nasal carriage, and the carriers received preoperative treatment with mupirocin, chlorhexidine scrub, and vancomyocin.[22] A large RCT demonstrated a statistically significant 0.21 reduction in relative risk ($P < .05$) among surgical patients (including patients who underwent cardiothoracic, vascular, gastrointestinal, general surgical, and orthopedic surgical procedures) who were treated with mupirocin and chlorhexidine scrub, compared with the placebo group.[20]

It has been estimated that 7,000–14,000 patients would be needed to demonstrate a 20% reduction in SSI rate after mupirocin decolonization if the baseline SSI rate were 5%.[21] Future studies need to compare homogeneous patient populations or stratify results according to the type of orthopedic implant (cemented vs uncemented) and the type of surgery (primary vs revision). A large multicenter RCT would be the best study design to confirm the effectiveness of mupirocin treatment in preventing SSI, and centers should continue to monitor for mupirocin resistance, because this could change the balance of cost and benefit for this intervention.

This cost-effectiveness analysis demonstrates that, in the context of a low prevalence of mupirocin resistance among *S. aureus* isolates, either of 2 interventions—treating all patients who undergo TJA with a 5-day course of preoperative mupirocin or screening all patients with use of nasal cultures and then treating *S. aureus* carriers—is cost-effective when implemented to prevent deep SSI. However, from an operational perspective, incorporating a routine course of preoperative mupirocin before TJA procedures is easier than implementing a screen-and-treat strategy. The latter requires multiple steps, including a visit to obtain a specimen for culture, follow-up of culture results, and a prescription of mupirocin for colonized patients. Each step introduces the potential for error or omission. Moreover, imperfect sensitivity of testing would result in additional missed decolonization opportunities. For this reason, for surgeons wishing to decolonize *S. aureus*–colonized patients before TJA surgery, we believe that the treat-all approach is the most likely to achieve this aim. Periodic reassessment of trends in mupirocin resistance among *S. aureus* isolates will be important in determining whether this approach continues to be cost-effective.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Xan F. Courville, MD, MS, Department of

Orthopaedics, Dartmouth Hitchcock Medical Center, 1 Medical Center Drive, Lebanon, NH 03756 (xcourville@gmail.com).

REFERENCES

1. Jamsen E, Huhtala H, Puolakka T, Moilanen T. Risk factors for infection after knee arthroplasty: a register-based analysis of 43,149 cases. *J Bone Joint Surg Am* 2009;91(1):38–47.
2. Khatod M, Inacio M, Paxton EW, et al. Knee replacement: epidemiology, outcomes, and trends in southern California: 17,080 replacements from 1995 through 2004. *Acta Orthop* 2008;79(6): 812–819.
3. Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005;87(7):1487–1497.
4. Ong KL, Kurtz SM, Lau E, Bozic KJ, Berry DJ, Parvizi J. Prosthetic joint infection risk after total hip arthroplasty in the Medicare population. *J Arthroplasty* 2009;24(6):105–109.
5. SooHoo NF, Lieberman JR, Ko CY, Zingmond DS. Factors predicting complication rates following total knee replacement. *J Bone Joint Surg Am* 2006;88(3):480–485.
6. Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. *Clin Orthop Relat Res* 2010;468:52–56.
7. Bozic KJ, Ries MD. The impact of infection after total hip arthroplasty on hospital and surgeon resource utilization. *J Bone Joint Surg Am* 2005;87-A:1746–1751.
8. Hebert CK, Williams RE, Levy RS, Barrack RL. Cost of treating an infected total knee replacement. *Clin Orthop Relat Res* 1996; 331:140–145.
9. Lavernia C, Lee DJ, Hernandez VH. The increasing financial burden of knee revision surgery in the United States. *Clin Orthop Relat Res* 2006;446:221–226.
10. Barrack RL, Engh G, Rorabeck C, Sawhney J, Woolfrey M. Patient satisfaction and outcome after septic versus aseptic revision total knee arthroplasty. *J Arthroplasty* 2000;15(8):990–993.
11. Rorabeck CH, Bourne RB, Mulliken BD, et al. The Nicolas Andry award: comparative results of cemented and cementless total hip arthroplasty. *Clin Orthop Relat Res* 1996(325):330–344.
12. Rao N, Cannella B, Crossett LS, Yates AJ Jr, McGough R III. A preoperative decolonization protocol for *Staphylococcus aureus* prevents orthopaedic infections. *Clin Orthop Relat Res* 2008; 466(6):1343–1348.
13. Kalmeijer MD, Coertijens 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.
14. Hacek DM, Robb WJ, Paule SM, Kudrna JC, Stamos VP, Peterson LR. *Staphylococcus aureus* nasal decolonization in joint replacement surgery reduces infection. *Clin Orthop Relat Res* 2008;466(6):1349–1355.
15. Price CS, Williams A, Philips G, Dayton M, Smith W, Morgan S. *Staphylococcus aureus* nasal colonization in preoperative orthopaedic outpatients. *Clin Orthop Relat Res* 2008;466(11): 2842–2847.
16. Kluytmans JA, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and assoicated risks. *Clin Microbiol Rev* 1997;10:505–520.
17. Perl TM, Cullen JJ, Wenzel RP, et al. Intranasal mupirocin to prevent postoperative *Staphlococcus aureus* infections. *New Engl J Med* 2002;346:1871–1877.
18. Gernaat-van der Sluis A, Hoogenboom-Verdegaal A, Edixhoven P. Prophylactic mupirocin could reduce orthpaedic wound infections: 1,044 patients treated with mupirocin compared with 1,260 hopsital controls. *Acta Orthop Scand* 1998;69:412–414.
19. Wilcox MH, Hall J, Pike H, et al. Use of perioperative mupirocin to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) orthopaedic surgical site infections. *J Hosp Infect* 2003;54(3): 196–201.
20. Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 2010;362(1):9–17.
21. Kallen AJ, Wilson CT, Larson RJ. Perioperative intranasal mupirocin for the prevention of surgical-site infections: systematic review of the literature and meta-analysis. *Infect Control Hosp Epidemiol* 2005;26:916–922.
22. Kim D, Spencer M, Davidson S, et al. Institutional prescreening for detection and eradication of methicillin-resistant *Staphylococcus aureus* in patients undergoing elective orthopaedic surgery. *J Bone Joint Surg Am* 2010;92:1820–1826.
23. Ammerlaan HS, Kluytmans JA, Wertheim HF, Nouwen JL, Bonten MJ. Eradication of methicillin-resistant *Staphylococcus aureus* carriage: a systematic review. *Clin Infect Dis* 2009;48(7):922–930.
24. DeFrances C, Cullen KA, Kozak LJ. 2007 National hospital discharge survey: 2005 annual summary with detailed diagnosis and procedure data. http://www.cdc.gov/nchs/data/series/sr_13/sr13_165.pdf. Accessed August 26, 2011.
25. Horan T, Andrus M, Dudeck M. CDC/NHSN surveillance definition of health care associated infection and criteria for specific types of infections in the acute setting. *Am J Infect Control* 2008; 36:309–332.
26. Noskin GA, Rubin RJ, Schetag JJ, et al. Budget impact analysis of rapid screening for *Staphlococcus aureus* colonization among patients undergoing elective surgery in US hospitals. *Infect Control Hosp Epidemiol* 2008;29:16–24.
27. Fryback DG, Dasbach EJ, Klein R, et al. The Beaver Dam health outcomes study: initial catalog of health-state quality factors. *Med Decis Making* 1993;13:89–102.
28. Slover J, Espehaug B, Havelin LI, et al. Cost-effectiveness of unicompartmental and total knee arthroplasty in elderly low-demand patients. *J Bone Joint Surg Am* 2006;88:2348–2355.
29. Cummins JS, Tomek IM, Kantor SR, Furnes O, Engesaeter LB, Finlayson SRG. Cost-effectiveness of antibiotic-impregnated bone cement used in primary total hip arthroplasty. *J Bone Joint Surg Am* 2009;91:634–641.
30. Bozic KJ, Katz P, Cisternas M, Ono L, Ries MD, Showstack J. Hospital resource utilization for primary and revision total hip arthroplasty. *J Bone Joint Surg Am* 2005;87:570–576.
31. 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.
32. Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine.* New York: Oxford University Press, 1996.
33. van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing *Staphylococcus aureus* infections in nasal carriers. *Cochrane Database Syst Rev* 2008(4):CD006216.

34. Deshpande LM, Fix AM, Pfaller MA, Jones RN; SENTRY Antimicrobial Surveillance Program Participants Group. Emerging elevated mupirocin resistance rates among staphylococcal isolates in the SENTRY Antimicrobial Surveillance Program (2000): correlations of results from disk diffusion, Etest and reference dilution methods. *Diag Microbiol Infect Dis* 2002;42:283–290.
35. Lee AS, Macedo-Vinas M, Francois P, et al. Impact of combined low-level mupirocin and genotypic chlorhexidine resistance on persistent methacillin-resistant *Staphylococcus aureus* carriage after decolonization therapy: a case-control study. *Clin Infect Dis* 2011;52:1422–1430.
36. McConeghy KW, Mikolich DJ, LaPlante KL. Agents for the decolonization of methicillin-resistant *Staphylococcus aureus*. *Pharmacotherapy* 2009;29(3):263–280.