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Systematic Review and Meta-Analysis

Is Preoperative *Staphylococcus aureus* Screening and Decolonization Effective at Reducing Surgical Site Infection in Patients Undergoing Orthopedic Surgery? A Systematic Review and Meta-Analysis With a Special Focus on Elective Total Joint Arthroplasty

Ana I. Ribau, MD [a, *], Jamie E. Collins, PhD [b], Antonia F. Chen, MD, MBA [b], Ricardo J. Sousa, MD, PhD [a, c]

[a] Department of Orthopedics, Centro Hospitalar do Porto, Porto, Portugal
[b] Department of Orthopaedics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
[c] Porto Bone and Joint Infection Group (GRIP), Centro Hospitalar do Porto and Grupo TrofaSaude - Hospital em Alfena, Portugal

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ABSTRACT

Background: *Staphylococcus aureus* is a major pathogen implicated in orthopedic infections worldwide. Preoperative decolonization has been promoted but different strategies present mixed results. Thus, the goals of this study are to determine (1) whether *S aureus* screening and/or decolonization is effective at reducing surgical site infection in orthopedic surgery, (2) with a special focus on elective total joint arthroplasty (TJA), and (3) which preoperative *S aureus* screening/treatment strategy is most cost-effective for TJA.

Methods: PubMed, Ovid MEDLINE, and Cochrane databases were searched on January 1, 2020, using a systematic strategy. We included papers with data comparing surgical site infection and periprosthetic joint infection rate in orthopedic surgery and/or elective total hip and knee arthroplasty patients before/after *S aureus* screening and/or decolonization protocol and papers evaluating the cost-effectiveness of different *S aureus* screening/treatment strategies.

Results: A total of 1260 papers were screened, and 32 papers were ultimately included. Results showed an increased risk of developing any infection (relative risk [RR] = 1.71 ± 0.16) and *S aureus* infection (RR = 2.79 ± 0.45) after orthopedic surgery without previous nares and whole-body decolonization. Focusing exclusively on elective TJA, there was an increased risk of developing any infection (RR = 1.70 ± 0.17) and *S aureus* infection (RR = 2.18 ± 0.41) if no decolonization is performed. All strategies appeared to be cost-effective, although universal decolonization without screening seemed to be the most advantageous.

Conclusion: Preoperative *S aureus* screening/decolonization protocol lowered the risk of infection after elective orthopedic and TJA surgeries. However, further studies are needed to determine optimal clinical and cost-effective methodologies.

Staphylococcus aureus (*S aureus*) is a major pathogen implicated in orthopedic infections worldwide, and approximately 20%-30% of the general orthopedic population are methicillin-sensitive *S aureus* (MSSA) carriers with 1%-5% methicillin-resistant *S aureus* (MRSA) carriers [1–6]. The anterior nasal cavity is the main site of colonization [5,7]. It has been shown throughout literature that patients who carry this bacteria in their commensal flora are at increased risk of infection in a multitude of clinical scenarios,

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* Reprint requests: Ana I. Ribau, MD, Department of Orthopaedics, Centro Hospitalar do Porto - Hospital de Santo António, Largo Professor Abel Salazar, 4099-001 Porto, Portugal.

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including elective orthopedic surgery [5,8–12]. There is evidence that *S aureus* nasal carriers who develop surgical site infections (SSIs) may present great individual concordance between the nares and infected surgical site isolates, confirming the existence of an important endogenous contamination pathway [13,14].

S aureus nares colonization is a modifiable risk factor, as many elective surgical patients undergo preoperative screening and/or treatment protocols to potentially reduce infection rates, including surgical procedures such as elective total joint arthroplasty (TJA) surgery [15]. However, the efficacy and cost-effectiveness of this intervention have mixed results in literature. Some studies have demonstrated decreased rates of periprosthetic joint infection (PJI) and increased cost-effectiveness with screening and decolonization, while other studies have demonstrated no changes in infection rate (SSI/PJI) when MSSA/MRSA screening and decolonization are implemented [16–18].

Thus, the purposes of this systematic review and meta-analysis are (1) to determine whether preoperative *S aureus* screening and/or decolonization is effective at reducing SSI in orthopedic surgery; (2) to determine whether preoperative *S aureus* screening and/or decolonization is effective at reducing PJI in patients undergoing elective TJA; and (3) to evaluate which preoperative *S aureus* screening/treatment strategy is most cost-effective for reducing PJI in patients undergoing TJA.

Methods

A systematic review and meta-analysis was performed to evaluate the efficacy of preoperative MSSA/MRSA decolonization at reducing infection in orthopedic surgery patients.

Search Methodology

Search terms were developed using PICO methodology and were designed to maximize sensitivity of the literature search: P—(“Knee replacement” OR “Hip replacement” OR “Joint replacement” OR “Knee arthroplasty” OR “Hip arthroplasty” OR “Joint arthroplasty” OR “Knee prost*” OR “Hip prost*” OR “Joint prost*”); AND I—(“Staphylococ* screening” OR “Staphylococ* carrier” OR “aureus”); AND O—(“Periprosthetic joint infection” OR Prosthetic joint infection” OR “Prosthesis-related infections” OR “Surgical site infection” OR “Joint infection”).

A database search was performed on January 1, 2020, through PubMed, Ovid MEDLINE, and Cochrane, and all references were considered regardless of the date of publication. When assessing full text(s) for eligibility, reference list(s) were also screened for additional papers.

Inclusion and Exclusion Criteria

Several different strategies have been adopted in literature regarding the screening and treatment of preoperative *S aureus* colonization. The following inclusion and exclusion criteria were adopted. The inclusion criteria were as follows:

1) Data comparing SSI/PJI rate in orthopedic surgery and/or elective total hip and knee arthroplasty patients before/after *S aureus* screening and/or decolonization protocol
2) Papers evaluating the cost-effectiveness of different *S aureus* screening/treatment strategies
3) Full text availability

The Exclusion Criteria Were as Follows

1) Studies with results on MRSA SSI/PJI rates exclusively and not providing information on overall infection rates (including methicillin-sensitive *S aureus*)
2) Full manuscript not available (eg, abstracts presented at conferences)
3) Language other than those accessible to the authors (English, French, Spanish, or Portuguese)

When discrepancies arose between authors regarding eligibility, a discussion between senior authors (A.C. and R.S.) was used to establish a consensus.

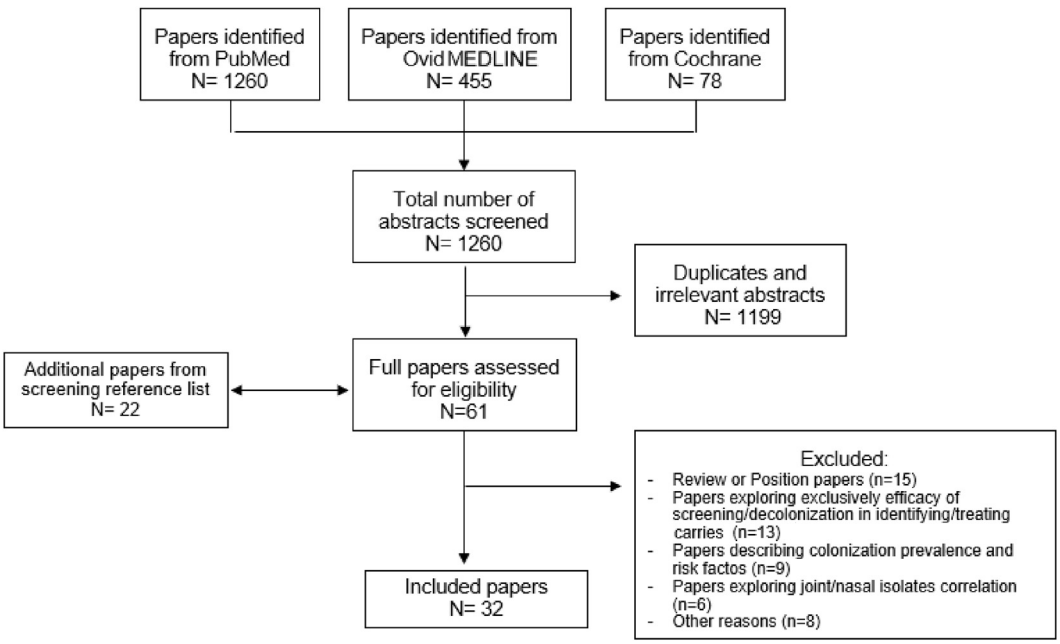

Fig. 1. PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Literature Search

The literature search results are presented in Figure 1, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement. The systematic search identified 1260 potentially relevant articles. After reviewing titles and reading abstracts, 1199 duplicates and irrelevant papers were excluded. Ultimately, 61 papers were retrieved for more detailed analysis and 22 additional papers were selected from screening references. From this selection of 83 papers, 51 papers were excluded.

Fifteen were excluded because they were reviews or position papers. The most common reason for exclusion was not reporting postoperative SSI/PJI rates: (a) 13 papers explored the efficacy of different screening methodologies or the success in achieving *S aureus* eradication in carriers; (b) 9 papers described the prevalence of carriage and risk factors for colonization; and (c) 6 papers explored the correlation between nasal and joint infection isolates exclusively. One paper was excluded because it presented earlier partial results [19] on a similar cohort of patients that were published later [20]. For one other paper, the final results were reported from a bundled triple intervention (*S aureus* preoperative decolonization, vancomycin prophylaxis, and intraoperative betadine irrigation), making it impossible to extract data exclusively evaluating the worth of *S aureus* screening alone [21]. Other papers were

Table 1
Characteristics of Studies Included in the Impact of *Staphylococcus aureus* Screening and Decolonization on SSI in All Orthopedic Procedures Including but Not Limited to Elective Total Joint Arthroplasty.

Author	Year of Publication	Country of Origin	Screening Methodology	Screening Rate	*S aureus* Carriers Overall	MRSA Carriers	Study End Point(s)
Nasal decolonization only							
Gernaat-van der Sluis et al [26]	1998	Netherlands	Screening not performed	—	—	—	Wound infections as set by the CDC
Kalmeijer et al [27]	2002	Netherlands	Nasal swab cultures	91%	91/614 (29.5%)	N/R	SSI according to CDC definition up to 30 d
Wilcox et al [28]	2003	UK	Screening not performed	—	—	—	SSI defined by surgeon and laboratory
Coskun and Aytac [29]	2004	Turkey	Screening not performed	—	—	—	SSI according to CDC definition
Price et al [5]	2008	USA	Nasal swab cultures	N/R	86/284 (30.3%)	5/284 (1.8%)	Deep and superficial SSI according to CDC definition
Hacek et al [30]	2008	USA	Nasal swab PCR confirmed by cultures	84%	223/912 (24.4%)	N/R	Deep and superficial SSI according to CDC definition
Hadley et al [31]	2010	USA	Nasal swab cultures	80%	409/1644 (24.9%)	58/1644 (3.5%)	Deep SSI according to CDC definition
Nasal and skin decolonization							
Pofahl et al [32]	2009	USA	Nasal swab PCR confirmed by cultures	>75%	N/R	367/5094 (7.2%)	SSI according to CDC definition
Kim et al [3]	2010	USA	Nasal swab cultures for MSSA and PCR for MRSA	N/R	1897/7019 (27.0%)	309/7019 (4.4%)	SSI up to 30 d
Bode et al [33]	2010	Netherlands	Nasal swab real-time PCR	N/R	1251/6771 (18.5%)	N/R	Healthcare-associated *S aureus* infections
Rao et al [20]	2011	USA	Nasal swab cultures	89%	321/1285 (25.0%)	43/1285 (3.3%)	SSI up to 2 y
Murphy et al [34]	2011	UK	Nose, throat, and groin swab cultures	N/R	N/R	108/5933 (1.8%)	Deep and superficial SSI according to WHO definition
Barbero Allende et al [35]	2014	Spain	Nasal swab cultures	91.8%	102/382 (26.7%)	N/R	PJI up to 1 y
Schweizer et al [36]	2015	USA	Nasal swab cultures or PCR (hospital discretion)	N/R	1933/13,127 (14.7%)	367/13,127 (2.8%)	SSI according to CDC definition up to 90 d
Baratz et al [1]	2015	USA	Nasal swab cultures for MSSA and PCR for MRSA	N/R	644/3434 (18.8%)	158/3434 (4.6%)	SSI according to CDC definition
Malcolm et al [4]	2015	USA	Nasal swab cultures or PCR	56.7%	573/2291 (25.0%)	115/2291 (5.0%)	Revision arthroplasty for infection
Ramos et al [37]	2016	USA	Nasal swab cultures	N/R	2519/13,828 (18.2%)	N/R	SSI up to 1 y or 90 d
Sporer et al [38]	2016	USA	Nasal swab cultures	99%	2742/9791 (28.0%)	284/9791 (2.9%)	SSI up to 30 d
Sousa et al [6]	2016	Portugal	Nasal swab cultures	79%	228/1028 (22.2%)	8/1028 (0.8%)	PJI up to 1 y
Barbero et al [2]	2017	Spain	Nasal swab cultures	80%	87/384 (22.6%)	16/384 (4.2%)	PJI up to 1 y
Tandon et al [39]	2017	UK	Multiple site cultures	N/R	N/R	83/6613 (1.3%)	Deep SSI up to 1 y
Jeans et al [40]	2018	UK	Nose and groin swab cultures	N/R	N/R	N/R	Public Health England's standard superficial, deep, and organ-space infection
Pelfort et al [41]	2019	Spain	Nasal swab cultures	N/R	15/403 (18.7%)	8/403 (1.9%)	SSI according to CDC definition
Romero-Palacios et al [42]	2019	Canada	Nasal and throat swab cultures	N/R	424/1883 (22.5%)	N/R	Deep/organ-space PJI up to 1 y

SSI, surgical site infection; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; PCR, polymerase chain reaction; N/R, not reported; CDC, Centers for Disease Control and Prevention; PJI, periprosthetic joint infection; WHO, world Health Organization.

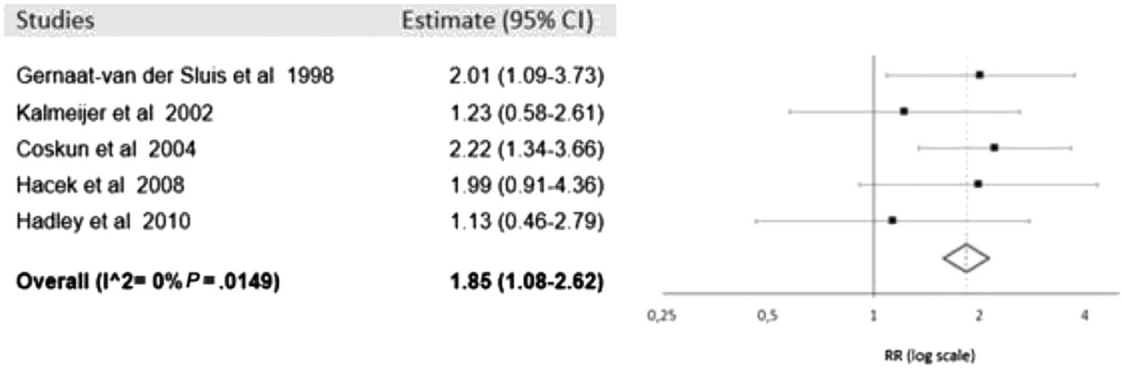

Fig. 2. Forest plots showing the relative risk (RR) of infection control vs nasal decolonization for all orthopedic procedures. CI, confidence interval.

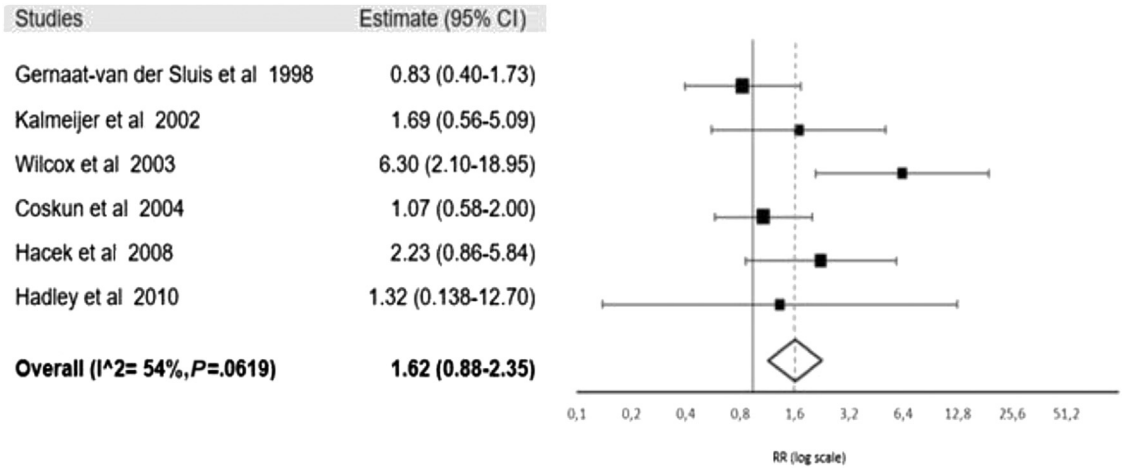

Fig. 3. Forest plots showing the RR of *S aureus* infection control vs nasal decolonization for all orthopedic procedures.

excluded because they evaluated *S aureus* carriage as a risk factor for postoperative infection, but did not supply any information on screening/decolonization results. Three other papers were excluded because they reported on the impact of MRSA exclusively and did not offer any MSSA results [22–24].

Ultimately, 24 papers were included in the analysis for the overall orthopedic surgery, 15 papers for the TJA analysis, and 8 for cost-effectiveness review.

Data Extraction

Two reviewers independently extracted data. Variables recorded included the name of the first author, year of publication, country of origin, targeted population, type of intervention and study design, preoperative treatment regimen, perioperative antibiotic prophylaxis policy, screening methodology and success rate when available, overall *S aureus* and MRSA carriage prevalence, and the end point(s) used in each paper. Data regarding SSI/PJI considering all pathogens and/or considering only *S aureus* SSI/PJI were extracted differentiating MSSA/MRSA carriers from non-carriers and control groups, whenever possible.

Papers included in the cost-effectiveness analysis were also evaluated and the following variables were recorded: name of the first author, year of publication, country of origin, methodology used for analysis, real or assumed prevalence of *S aureus* carriage, real or assumed prevalence of baseline PJI, real or assumed impact

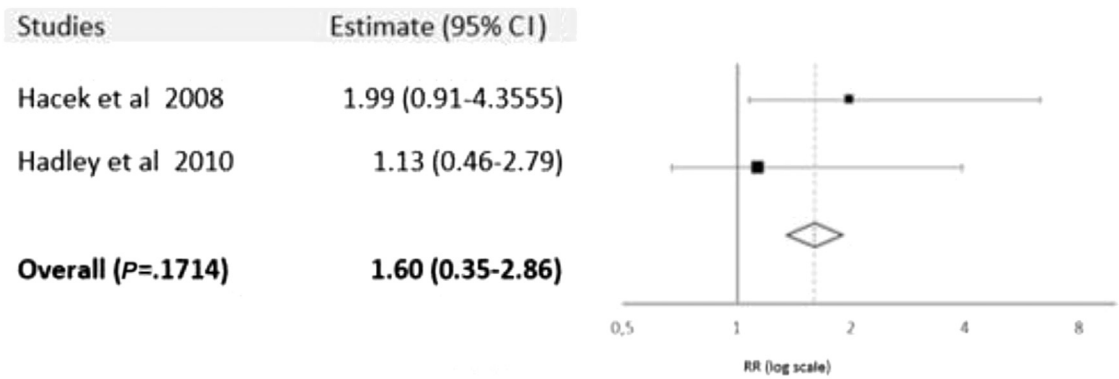

Fig. 4. Forest plots showing the RR of infection control vs nasal decolonization in total joint arthroplasty.

on decrease in SSI/PJI rate and of major cost-effectiveness finding(s).

Statistical Analysis

We used a logistic random-effects model to create an overall combined estimate of infection across all studies and to evaluate the effect of intervention on infection. I-square was used to assess heterogeneity. We did this separately for overall infection and *S aureus* infection, for overall elective orthopedic surgery, and TJA only. This approach allows for studies with zero cells (ie, 0% incidence rate) without requiring an ad hoc adjustment [25]. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

A summary of the main characteristics of all studies included in the meta-analyses is presented in Table 1. The overall *S aureus* carriage rate ranged from 15% to 30%, and the MRSA carriage was lower at 1%-7% depending on geography and screening methodology.

Nasal Decolonization Only

Three prospective [5,27,31] and 4 retrospective studies [26,28–30] that focused on preoperative nasal decolonization only (without extensive skin decolonization) were evaluated. Papers where a single preoperative shower with triclosan or chlorhexidine was performed were included in this group, as this single shower is considered routine clinical practice and is not specific to *S aureus* decolonization protocols.

The majority of these papers reported on elective orthopedic surgery, but not necessarily TJA or even those that used metal implants. Most adopted a universal treatment with no screening strategy [26–29,31]. Hacek et al [30] treated carriers exclusively and Price et al [5] offered treatment to identified carriers resulting in a cohort of known untreated carriers. All prospective studies found a trend toward reduced infection rates, but none reached statistical significance [5,27,31]. Retrospective studies demonstrated a significantly reduced overall infection rate [26,29], and *S aureus* infection rates were significantly lower in the intervention group that received *S aureus* screening and nares decolonization [28–30].

When all studies were aggregated together, the relative risk (RR) of developing any infection after orthopedic surgery without *S aureus* nares decolonization was 1.85 ± 0.28 (standard error, 95% confidence interval [CI], 1.08-2.62; I^2 = 0%; $P = .015$) (Fig. 2). The RR for specifically developing an *S aureus* infection after surgery without *S aureus* nares decolonization was 1.62 ± 0.29 (standard deviation, 95% CI, 0.88-2.35; I^2 = 54%; $P = .062$) (Fig. 3). A table summarizing information on papers included in this analysis is available as supplemental material in the appendix (Table A.1).

When focusing on TJA exclusively, the RR of developing any infection after surgery without *S aureus* nares decolonization was 1.60 ± 0.45 (standard error, 95% CI, 0.35-2.86; $P = .171$) (Fig. 4). It was not possible to calculate RR for specifically developing *S aureus* infections in TJA patients as data were only extracted out of 2 papers (Table 2) [30,31].

Nasal and Skin Decolonization

Papers that reported on *S aureus* screening and concomitant nasal and whole-body decolonization procedures for multiple days were mostly before and after intervention studies, although 2 prospective randomized trials [6,33] were found.

Table 2
Staphylococcus aureus Screening and Nasal Decolonization Only Results in Reducing Infection in Total Joint Arthroplasty Patients.

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control	Intervention	*P* Value	Control	Intervention	*P* Value	
Hadley et al, 2010 [31]	Primary total knee or hip arthroplasty	Universal treatment Prospective cohort	5-d Course of intranasal mupirocin regardless of screening result	Cefazolin or clindamycin if ß-lactam allergy (or vancomycin if MRSA carrier)	Unscreened 6/414 (1.45%)	21/1644 (1.28%)	.809	MRSA 1/414 (0.24%)	MRSA 3/1644 (0.18%)	NS	- Staphylococci decolonization led to a 13% decrease in deep SSI which did not reach statistical significance
Hacek et al, 2008 [30]	Elective hip/ knee joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin twice a day	Cefazolin for hip/ vancomycin for knee up to 24 h	Unscreened 14/583 (2.4%)	Noncarriers 7/689 (1.0%) Treated carriers 4/223 (1.8%)	≤.05	Unscreened 10/583 (1.7%)	Noncarriers 4/689 (0.6%) Treated carriers 3/223 (1.3%)	≤.1	- *S aureus* SSI rate in the intervention group was reduced compared to control group—0.8% (7/912) vs 1.7% (10/583), but it did not reach statistical significance - Assuming a similar proportion of carriers and SSI rate among noncarriers, authors calculate about 8 SSI cases were prevented by the intervention

NS, not statistically significant; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; SSI, surgical site infection.

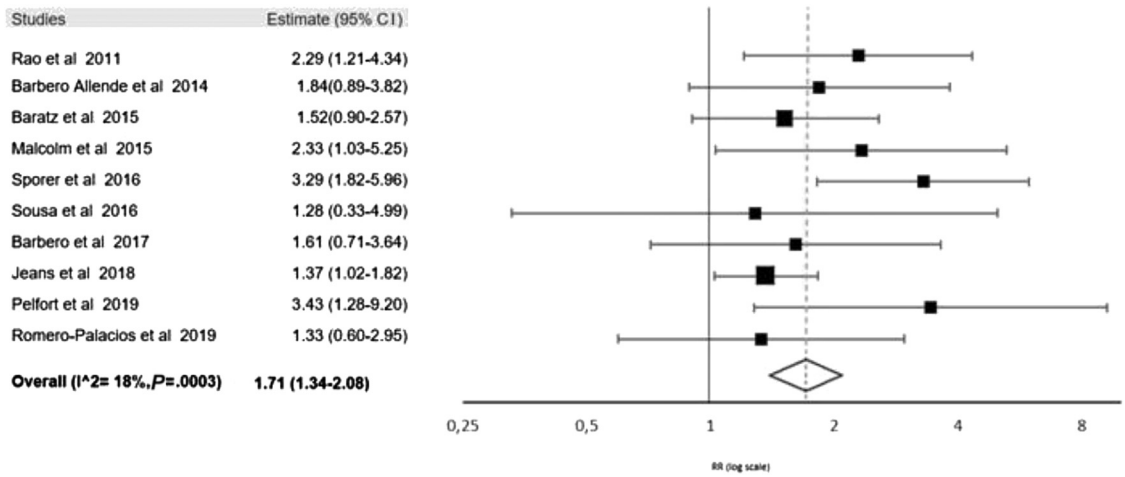

Fig. 5. Forest plots showing the RR of infection control vs nasal and skin decolonization for all orthopedic procedures.

Some studies reported on orthopedic surgery including spine and sports medicine [3,34,37] as well as trauma [2,35] and not elective TJA. Universal screening and selectively treating identified carriers were the widely dominant strategy [1–4,6,20,32–36,38–42], and only 1 paper presented on results after a universal treatment approach [37]. Overall, *S aureus* carriers were mostly evaluated, while some papers specifically focused on MRSA carriers [32,34,39]. The vast majority of decolonization protocols included preoperative nasal mupirocin treatment and chlorhexidine baths, except one study that used nasal povidone-iodine for a portion of the cohort instead of mupirocin [37] and one that used octenidine as an alternative to chlorhexidine baths [40].

When all studies were aggregated together, the RR of developing any infection after orthopedic surgery without *S aureus* nares and whole-body decolonization was 1.71 ± 0.16 (standard error, 95% CI, 1.34-2.08; I^2 = 18%; $P < .001$) (Fig. 5). The RR for specifically developing an *S aureus* infection after surgery without *S aureus* nares and whole-body decolonization was 2.79 ± 0.45 (standard error, 95% CI, 1.78-3.81; I^2 = 19%; $P < .001$) (Fig. 6). A table summarizing information on papers included in this analysis is available as supplemental material in the appendix (Table A.2).

When focusing exclusively on TJA, we were able to extract data out of 13 papers that were included in a specific analysis (Table 3) [1,4,6,20,32,34,36–42]. The RR of developing any infection after TJA without *S aureus* nares and whole-body decolonization was 1.70 ± 0.17 (standard error, 95% CI, 1.32-2.09; I^2 = 27%; $P < .001$) (Fig. 7). The RR for specifically developing an *S aureus* infection after TJA without *S aureus* nares and whole-body decolonization was 2.18 ± 0.41 (standard error, 95% CI, 1.22-3.13; I^2 = 88%; $P = .004$) (Fig. 8).

Risk Reduction on S aureus *Carriers*

A further analysis was made in an attempt to determine whether the risk of infection for treated carriers lowered to baseline noncarrier levels after treatment.

When all studies were aggregated together, the RR of developing any infection after orthopedic surgery was not significantly different when comparing noncarriers and treated carriers—1.31 ± 0.41 (standard error, 95% CI, 0.02-2.60; I^2 = 0%; $P = .445$) (Fig. 9). However, the RR of specifically developing *S aureus* infection carriers was significantly higher—4.64 ± 0.13 (standard error, 95% CI, 1.37-7.91; I^2 = 76%; $P = .002$) even after treatment when compared to noncarriers (Fig. 10).

We were not able to perform a similar analysis focusing exclusively on TJA due to the lack of enough detailed information.

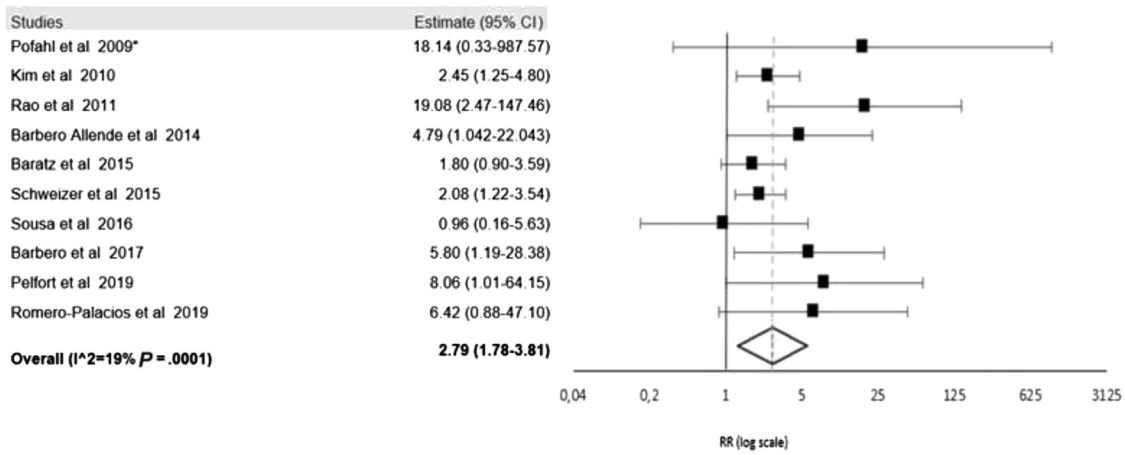

Fig. 6. Forest plots showing the RR of *S aureus* infection control vs nasal and skin decolonization for all orthopedic procedures (*approximate RRs—study with zero cells, applying a continuity correction of 0.25).

Table 3
Staphylococcus aureus Screening With Concomitant Nasal and Skin Decolonization Results in Reducing Infection in Total Joint Arthroplasty Patients.

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control (%)	Noncarriers (%)	Treated Carriers (%)	Control (%)	Noncarriers (%)	Treated Carriers (%)	
Pofahl et al, 2009 [32]	Elective hip/ knee joint arthroplasty[a]	Selective MRSA carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice daily 5 d before surgery + chlorhexidine baths on days 1, 3, and 5	Prophylaxis changes in MRSA carriers at surgeon discretion	—	—		6/1979 (0.3%)	0/1436 (0.0%)		- Reduction in MRSA SSI was most pronounced in orthopedics (hip and knee prostheses) where it reached statistical significance - The rate in MSSA SSI did not change significantly in any group
Rao et al, 2011 [20]	Elective total joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin (vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	Historic 20/741 (2.7%)	17/1440 (1.2%)		Historic 11/741 (1.5%) Concurrent 19/2284 (0.8%)	1/964 (0.1%)	0/321 (0.0%)	- This paper has 2 control groups: historic before intervention of the same surgeons and concurrent in the same time period of a different group of surgeons - Overall infection rate (including superficial and deep infection and nonstaphylococcal infections) decreased significantly during the intervention period - Considering only deep SSI rate of the same surgeons before and after the intervention, overall infection rate— 1.2% (9/741) vs 0.6% (8/1440) and *S aureus* infection rate—0.7% (5/741) vs 0.1% (2/1440) were both reduced
Murphy et al, 2011 [34]	Elective hip/ knee joint arthroplasty[b]	Selective MRSA carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine body wash and shampoo	Cefuroxime (vancomycin if MRSA carrier)	—			—	15/1993 (0.8%)	4/56 (7.1%)	- Patients with negative rescreening after treatment underwent surgery within 3 mo (positive rescreens were excluded) - Deep sepsis rate in lower-limb joint arthroplasties was significantly higher among MRSA previously carriers—7.4% (2/27) in total hip and 6.9% (2/29) in total knee—than among non-carriers—1.1% (11/982) in total hip and 0.4% (4/1011) in total knee—despite confirmed successful preoperative decolonization
Schweizer et al, 2015 [35]	Primary hip or knee arthroplasty[c]	Selective carrier's treatment Multicenter retrospective before and after intervention	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin or cefuroxime (vancomycin if MRSA carrier)	—	—		66/20,642 (0.32%)	17/11,059 (0.15%)		- The rate of complex *S aureus* SSI, but not all *S aureus* SSI, decreased significantly after hip or knee arthroplasties (17/10,000 operations) - The decrease in overall SSI rate considering all

											pathogens and all surgeries did not reach statistical significance
Baratz et al, 2015 [1]	Elective primary and revision hip or knee arthroplasty	Selective carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin (plus vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	33/3080 (1.1%)	17/2763 (0.6%)	All carriers 7/644 (1.1%) MRSA carriers 4/158 (2.5%) MSSA carriers 2/486 (0.4%)	21/3080 (0.7%)	13/3434 (0.4%)		- There were no differences in infection risk between the protocol group and the historic control group
Malcolm et al, 2016 [4]	Primary hip or knee arthroplasty	Selective carrier's treatment Retrospective after intervention	Topical mupirocin twice daily for 3 d + chlorhexidine body wipes preoperatively	Cefazolin (or vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	Unscreened 16/1751 (0.9%)	8 cases (0.4%)	MRSA carriers 0 cases (0.0%) MSSA carriers 1 case (0.3%)	—	—	—	- Rates of revision arthroplasty for any reason after at least 1 y was similar among screened and unscreened cohorts—1.0% (22/2291) vs 1.4% (25/1751) - Risk of revision due to PJI was significantly higher in unscreened compared to screened patients—0.9% (16/1751) vs 0.4% (9/2,2291) - After screening and decolonization, there were no differences in overall or revision due to PJI between preoperative carriers and noncarriers
Ramos et al, 2016 [37]	Elective primary hip or knee arthroplasty[d]	Universal treatment Retrospective after intervention	5-d Course of intranasal mupirocin or nasal povidone-iodine the day of surgery + chlorhexidine gluconate wipes the night before surgery	Vancomycin if MRSA carrier	—	THA (0.4%) TKA (0.7%)	THA 8/939 (0.8%) TKA 18/912 (2.0%)	—	—	—	- *S aureus* preoperative colonization was a significant risk factor for SSI among total knee but not total hip - MRSA carriers had higher risk of infection than MSSA carriers—2.7%(10/367) vs 1.2% (26/2152)
Sporer et al, 2016 [38]	Elective primary total joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice daily + daily chlorhexidine baths 5 d before admission	Cefazolin (vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	16/1443 (1.1%)	33/9791 (0.34%)		—	—		- SSI rate was significantly lower after initiation of nasal screening—0.34% vs 1.1%. - SSI rate dramatically decreased in the first year of implementation - *S aureus* was involved in PJI less frequently after intervention although it did not reach statistical significance—66.7% vs 33.3%
Sousa et al, 2016 [6]	Elective primary hip/ knee joint arthroplasty	Selective carrier's treatment Single-center randomized controlled trial	Intranasal mupirocin twice a day + daily chlorhexidine baths in the 5 d before surgery	Cefazolin (plus vancomycin if MRSA carrier or ß-lactam allergy) up to 24h	Untreated carriers 6/139 (4.3%)	16/800 (2.0%)	3/89 (3.4%)	Untreated carriers 3/139 (2.2%)	9/800 (1.1%)	2/89 (2.2%)	- Overall PJI rate was higher among *S aureus* carriers than noncarriers—3.9% (9/228) vs 2.0% (16/800), but it did not reach statistical significance - Treated and untreated carriers showed no

(*continued on next page*)

Table 3 (*continued*)

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control (%)	Noncarriers (%)	Treated Carriers (%)	Control (%)	Noncarriers (%)	Treated Carriers (%)	
											significant difference either in *S aureus* or all pathogens infections
Tandon et al, 2017 [39]	Elective hip or knee arthroplasty	Selective MRSA carrier's treatment Retrospective after intervention	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine baths + hair shampoo on days 1 and 3	Several different regimens; teicoplanin alone or with gentamicin in 58% of cases	—	—		—	81/6530 (1.2%)	5/79 (6.3%)	- Patients with negative rescreening after treatment underwent surgery within 3 mo—mean time interval 2.93 wk - Four patients with MRSA-positive rescreens after treatment were excluded - The relative risk of deep SSI in MRSA carriers was significantly higher despite treatment both in hip (4.46) and knee (5.6) patients
Jeans et al, 2018 [40]	Elective hip or knee arthroplasty	Retrospective study Case-control	Daily octenidine wash + intranasal mupirocin 4 times a day 5 d before and after the procedure		69/3593 (1.92%)	131/9318 (1.41%)					- PJI fell from 1.92% to 1.41% with the screening and decolonization protocol ($P = .03$) - The screening program was most effective in MSSA prevention in THA (3% to 1.5%, $P = .002$)
Pelfort et al, 2019 [41]	Elective primary knee arthroplasty	Retrospective study Case-control	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine baths	2 g of cefazolin or 1g vancomycin if MRSA carrier or ß-lactam allergy	17/400 (4.25%)	5/403 (1.24%)		8/400 (2%)	1/403 (0,24%)		- Incidence of 20.6% of *S aureus* nasal carriers, with an incidence of only 1.9% for MRSA. - No nasal carrier who was decolonized presented a SSI by this microorganism. - Reduction in global SSIs of 71% and a reduction in specific *S aureus* SSIs of 88%
Romero-Palacios et al, 2019 [42]	Primary or revision hip or knee arthroplasty	Retrospective before and after intervention	5-d Course of intranasal mupirocin twice daily + chlorhexidine baths	—	42/8505 (0.5%)	7/1883 (0.4%)		29/8505 (0.3%)	1/1883 (0.05%)		- No nasal carrier who was decolonized presented a SSI by this microorganism - Significant reduction in PJIs due to *S aureus* by screening for and decolonizing *S aureus* carriers before total joint arthroplasties - No significant difference in overall infection rates was observed

NS, not statistically significant; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; PJI, periprosthetic joint infection; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a] This paper also reported on cardiac surgery and hysterectomy but data presented here concerns joint arthroplasty exclusively.

[b] This paper also reported on other elective inpatient orthopedic surgery but data presented here concerns joint arthroplasty exclusively.

[c] This paper also reported on cardiac operations but data presented here concerns joint arthroplasty exclusively.

[d] This paper also reported on primary spinal fusion but data presented here concerns joint arthroplasty exclusively.

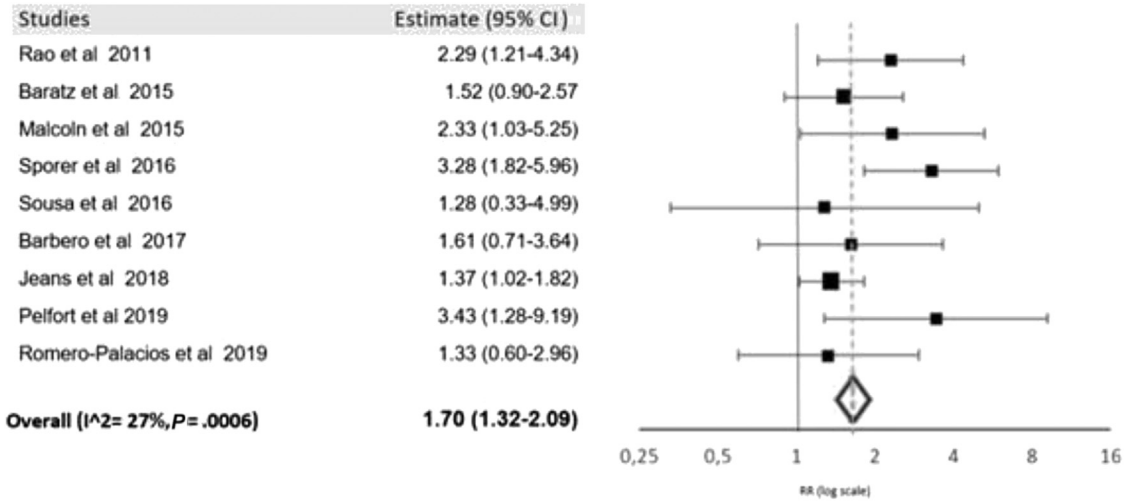

Fig. 7. Forest plots showing the RR of infection control vs nasal and skin decolonization in total joint arthroplasty.

Cost-Effectiveness

One letter to the editor [18] and 7 other papers [16,17,43–47] focused on the cost-effectiveness of preoperative screening and decolonization strategies before elective TJA procedures and are summarized in Table 4.

Slover et al [45] conducted a Markov decision analysis to assess the cost savings associated with preoperative *S aureus* screening and decolonization program on 365 TJAs and 287 spine fusions in the United States, with an assumed 1.5% baseline risk of infection. Data from their own cohort were used to determine the probability of positive MSSA and MRSA cultures and patient compliance with the prescribed mupirocin treatment, along with costs of nasal culture and mupirocin treatment. The authors concluded that a universal *S aureus* screening and decolonization protocol for TJA and spinal fusion needed to produce a modest reduction (35% reduction in the revision rate for TJA and 10% for spine fusion) in the SSI rate would save costs [45].

Courville et al [17] used a simple decision tree model comparing 3 different screening strategies in a hypothetical cohort of TJA patients: (1) nasal screening of all patients and treatment for *S aureus* culture-positive patients (screen-and-treat strategy); (2) preoperative mupirocin treatment for all patients and no screening (treat-all strategy); and (3) no screening and no mupirocin treatment (no-treatment strategy). The authors found that empirical treatment of all patients without previous screening for nasal *S aureus* carriage was associated with lower costs and greater expected benefit with a high range interval of costs for testing, *S aureus* prevalence, mupirocin treatment, RR of PJI, and costs for primary and septic revision surgeries [17]. However, differences in cost and benefit between the 3 strategies were relatively small.

Meda et al [18] evaluated the cost-effectiveness of MSSA decolonization based on their rates of infection after TJA. Of 5156 TJA patients, there were 29 deep incisional/organ-space infections, excluding those likely to have a hematogenous origin. In 2 of those infections, *S aureus* was the isolated pathogen. Considering only primary and not revision surgery and assuming a 20% colonization rate, the authors determined that MSSA screening and treatment would not be cost-effective in their unit where *S aureus* infection is responsible for less than 5% of all identified PJI [18].

Williams et al [47] evaluated the cost-effectiveness of 3 different screen-and-treat protocols (4 swabs, 2 swabs, and nasal swab alone) and compared them to no-screening and universal decolonization (treat-all) strategies. The prevalence of *S aureus* colonization and sensitivity of swab protocols were derived from institutional data from a retrospective analysis of 1641 patients. Results showed that universal decolonization and the 4-swab strategies provided the largest reduction in PJI [47]. Cost-

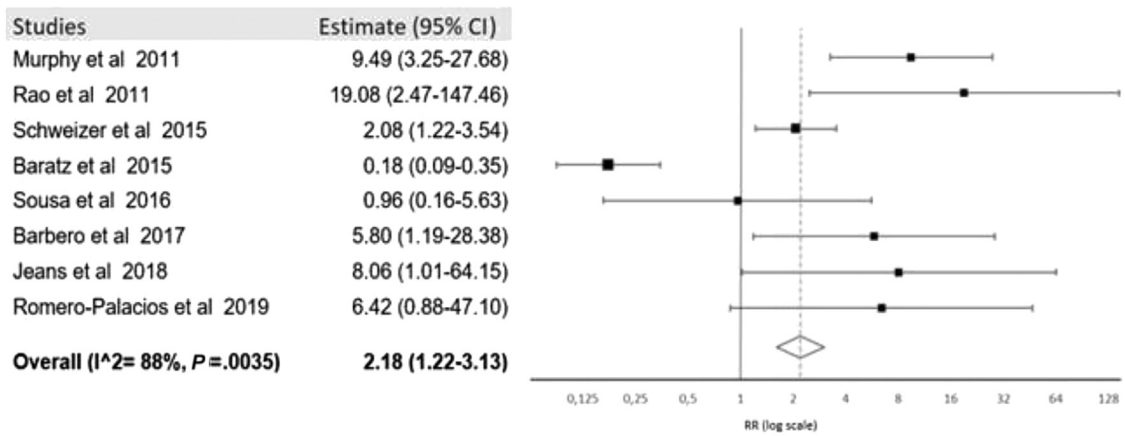

Fig. 8. Forest plots showing the RR of *S aureus* infection control vs nasal and skin decolonization in total joint arthroplasty.

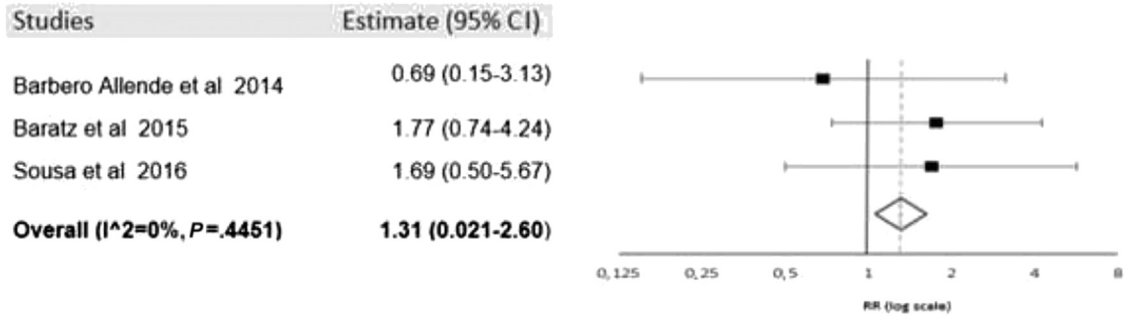

Fig. 9. Forest plots showing the RR of developing any infection after surgery in treated carriers vs noncarriers.

effectiveness was viewed from different perspectives depending on the payer. From the societal perspective, universal decolonization was the most cost-effective at an incremental cost of USD 14,229 per infection prevented. From a hospital-only perspective, the universal decolonization strategy dominated in the base case and across a range of values in sensitivity analyses. From a patient perspective, 2 swabs (nares and pharynx) dominated at an incremental cost of USD 4773 per infection prevented. From the societal perspective, the universal decolonization strategy was the most effective. The authors also found that regardless of the payer perspective considered, as the risk of PJI in an untreated carrier increased, the incremental cost per infection prevented decreased [47].

Stambough et al [46] performed a similar study comparing 1981 patients who underwent a screen-and-treat strategy and 2205 patients who underwent a treat-all strategy. Patients were treated using a combination of nasal mupirocin and chlorhexidine scrubs in both groups. The study found a significant decrease in the 90-day overall and *S aureus* infection rates using the universal decolonization protocol compared with screen-and-treat strategy, and a cost analysis accounting for the cost to administer the universal regimen demonstrated an actual savings in excess of USD 700,000 [46].

In a break-even analysis, Kerbel et al [44] reported on different absolute risk reduction (ARR, ie, difference between the before and after intervention infection rates) that would be necessary to make different screening/treatment strategies cost-effective. Naturally, screening and selective treatment require much higher ARR reductions (0.56% for total knee arthroplasty and 0.45% for total hip arthroplasty) than universal treatment strategies. The latter required a minimum of 0.02% ARR and a maximum of 0.15% ARR, depending on the cost of the universal treatment adopted [44]. Hadi et al [43] reported on the prevalence of *S aureus* and MRSA colonization on their TJA cohort and determined that if screening and treatment would reduce 1 infection in 100 patients (1% ARR), it would lead to 80% reduction in costs.

Recently, Rennert-May et al [16] performed a Markov model to assess the efficiency of implementing a decolonization protocol before TJA in Alberta (Canada) using mupirocin ointment and chlorhexidine sponges. The effectiveness of such a protocol at reducing *S aureus* complex SSI was derived from a preintervention and postintervention trial [36]. They figured such a protocol would save USD 161 per person, which in Alberta would translate into savings of USD 1.26 million annually.

Discussion

It has been shown that a significant proportion of patients carry *S aureus* in their commensal flora and they seem to be at increased risk of infection in multiple clinical settings [48,49]. This has driven many centers to adopt screening/decolonization before elective medical procedures including surgery [33]. Results in orthopedic surgery are encouraging but high-level evidence regarding TJA specifically is still scarce. A different aspect deserving our attention is the cost-effectiveness of the different screening/decolonization strategies that have been described. Thus, the purposes of this study were to (1) determine whether preoperative *S aureus* screening and/or decolonization is effective at reducing SSI in orthopedic surgery; (2) determine whether preoperative *S aureus* screening and/or decolonization is effective at reducing PJI in patients undergoing elective TJA; and (3) evaluate which preoperative

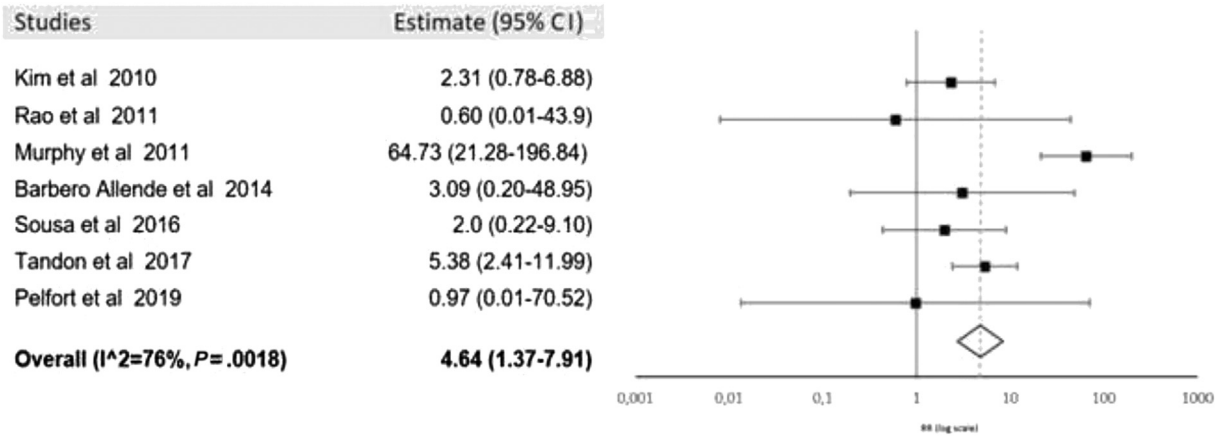

Fig. 10. Forest plots showing the RR of developing *S aureus* infection after surgery in treated carriers compared to noncarriers.

Table 4
Cost-Effectiveness Studies of *Staphylococcus aureus* Screening in Total Joint Arthroplasty Patients.

Author	Year	Country	Methodology	Overall *S aureus* (MRSA) Carriage Rate Real or Presumed	Overall PJI (*S aureus*) Rate Real or Presumed	Reduction/Impact on PJI Rate Real or Presumed	Major Finding(s)
Slover et al [45]	2011	USA	Markov decision analysis	23.3% (MRSA 3.3%)	1.5%	10% Reduction on revision rate	Combined with an average cost of septic revisions greater than USD 70,000 would make the screen-and-treat protocol cost saving for the institution
Courville et al [17]	2012	USA	Decision models based	26% (MRSA 2%)	1.3% for mupirocin-treated carriers 0.58% for untreated noncarriers	0.61 relative risk among mupirocin-treated (vs untreated carriers)	Both the treat-all strategy and the screen-and-treat strategy are cost-effective alternatives compared with no decolonization Treat-all strategy was associated with lower costs and greater expected benefit
Meda at al [18].	2016	UK	Retrospective	20%	0.56% (*S aureus* 0.02%)	-	Hypothetical implementation of a screen-and-treat protocol was considered not to be cost-effective (extremely low *S aureus* infection rate)
Williams et al [47]	2017	USA	Decision analytic model	33.5%	3.3% for untreated carriers 1.3% for treated carriers 0.58% for untreated noncarriers	45% decrease (treat-all) 45% decrease (4-swab screen) 41% decrease (2-swab screen) 38% decrease (1-swab screen)	Treat-all decolonization is most cost-effective from a societal perspective across a broad range of rates of PJI risk and decolonization efficacy
Stambough et al [46]	2017	USA	Retrospective	20%	0.76% (MRSA 0.30%)	0.76% (screen-and-treat) to 0.23% (treat-all)	Treat-all decolonization demonstrates significant decrease in both the overall SSI and *S aureus* infection rate compared to a screen-and-treat historic control Universal decolonization saved USD 717,205.59 (2205 vs 1981 TJA)
Kerbel et al [44]	2018	USA	Break-even analysis	—	1.10% for TKA 1.63% for THA	0.56% ARR for TKA and 0.45% for THA 0.02% ARR for both TKA and THA 0.15% ARR for TKA and 0.12% for THA	*S aureus* nasal screen-and-treat Most inexpensive treat-all protocol (ie, mupirocin ointment) Most expensive treat-all protocol (ie, mupirocin + chlorhexidine wipes, chlorhexidine shower + prophylactic vancomycin)
Hadi et al [43]	2018	Iran	Prospective cross-sectional	20.8% (MRSA 1.8%)	2%-7%	1% ARR	Screen-and-treat decolonization program leads to 80% reduction in costs
Rennert-May et al [16]	2019	Canada	Markov model	—	1.04% (*S aureus* 0.4%)	50% reduction in PJI rate	USD 153 savings per person with a screen-and-treat decolonization program

MRSA, methicillin-resistant *S aureus*; PJI, periprosthetic joint infection; SSI, surgical site infection; TJA, total joint arthroplasty; TKA, total knee arthroplasty; THA, total hip arthroplasty; ARR, absolute risk reduction (ie, difference between the initial and final infection rates).

S aureus screening/treatment strategy is most cost-effective for reducing PJI in patients undergoing TJA.

Earlier decolonization protocols focused solely on nasal decontamination using mupirocin ointment. Retrospective studies comparing before and after universal treatment protocols for overall orthopedic surgery found encouraging significant improvements in infection rates [26,29]. Prospective studies however, including 1 randomized controlled trial, were not able to show a similar statistically significant advantage [5,27]. If one analyzes evidence of nares decolonization specifically on TJA patients, no studies were able to show true effectiveness [30,31]. The results of the present meta-analysis showed that nares decolonization only marginally offered some advantage considering infections in all orthopedic surgical cases, but the same trend did not hold in *S aureus* infections alone or in elective TJA.

Recognizing the relevance of other body site colonization, preoperative treatment protocols have evolved to include not only nares but also whole-body decontamination mostly by using daily chlorhexidine baths 5 days before surgery. Most papers in this category have adopted the screening and selective carrier's treatment approach and the overwhelming majority of data come from before-and-after intervention studies. Results of this meta-analysis showed that the current methodology of nares and whole-body decolonization seems to be effective for reducing the overall risk of *S aureus* infections in orthopedic surgical cases, and a similar conclusion was found when pooling results for elective TJA.

It is nevertheless important to recognize that results also suggest decolonization is not fully protective. The RR of *S aureus* infection after surgery is still 4.64 times higher than that of non-colonized patients. This finding is in line with the results of a small underpowered but unique prospective randomized controlled trial focusing exclusively on TJA. Sousa et al [6] reported on 1028 elective TJA with 228 identified carriers that were randomized to preoperative treatment. Treated and untreated carriers showed no

significant differences in overall or *S aureus* PJI, but PJI among carriers considered together was higher than among noncarriers [6]. Multiple studies have demonstrated that *S aureus* carriers are at increased risk of infection in a variety of clinical scenarios, including TJA. Whether this increased risk is exclusively due to the carrier state is not entirely clear, as some known medical factors that increase the risk of being *S aureus* carriers are also known independent risk factors for PJI, including diabetes, obesity, renal insufficiency, inflammatory arthritis, or immunosuppression [6,50,51]. In fact, Maoz et al [52] also found *S aureus* colonization was associated with a higher infection rate in 3672 primary and 406 revision hip arthroplasties, but it was not demonstrated to be an independent risk factor in a multivariate analysis.

Despite its apparent merit, implementing an effective screening and targeted decolonization strategy in daily practice is laborious and complex in present-day practice, raising questions about its cost-effectiveness. Several different methods for assessing cost-effectiveness were used in literature, making it impossible to perform a meta-analysis. Based on the results of our systematic review, it seems that adopting a universal decolonization rather than a screen-and-treat protocol was the most cost-effective approach and also the most effective in decreasing PJI in a wide range of *S aureus* carriage prevalence, costs of screening and treatment, PJI rate, and socioeconomic costs of dealing with infection. It is also easier and less resource-consuming to implement and more importantly, no carrier would be left untreated due to screening sensitivity issues or timely identification. However, the treat-all approach is associated with theoretical costs that are not considered in the economic models, such as risks of emerging resistance to topical antibiotics like mupirocin [53]. An alternative approach to obviate this problem would be to use antiseptics, such as octenidine or povidone-iodine, rather than antibiotics to achieve *S aureus* decolonization [54–56]. Despite this, 1-swab or 2-swab screen-and-treat strategies still offer cost-effective results. Ultimately, choosing the most appropriate strategy may depend on the baseline PJI risk in each institution and patient subpopulations. In this regard, it is important to stress that although specific medical and demographic risk factors for *S aureus* and MRSA colonization among TJA candidates can be found, there is a significant proportion of carriers with no known risk factor(s) and therefore selective screening of high-risk population subgroups is not an effective approach to accurately identify carriers [34,50,51,57,58].

Other meta-analyses have already been performed on this topic. Past meta-analyses have focused on overall orthopedic surgery [59] or even orthopedic and cardiac surgery [60]. More recently, Sadigursky et al [61] and Zhu et al [62] specifically examined the TJA population and Ning et al [63] performed a similar study focusing on spinal surgery. During the Second International Consensus Meeting on Musculoskeletal Infection held in Philadelphia in 2018, a recommendation was also issued on this topic [64]. The current paper represents an update and attempts to overcome a couple of limitations identified in the aforementioned recommendation. We were able to include a larger number of studies with several thousand patients and did not limit our report to overall orthopedic surgical cases but also included subgroup analysis on elective TJA cases. Additionally, we also performed a meta-analysis of the extracted data to grasp a better perception of its real impact. We also combined a systematic review investigating the cost-effectiveness of different strategies.

Despite these strengths, there were weaknesses associated with this study. As with all other meta-analyses, the results were only as reliable as the quality of the papers included. Although the heterogeneity among different study results was low for most major findings, only 5 of the studies included were prospective [5,6,27,31,33]. The overwhelming majority of papers included in this study came from before-and-after intervention studies with historic control groups. In itself this study design increases the possibility of certain bias such as changes in perioperative antibiotic prophylaxis regimen, surgical duration or surgical technique changes such as irrigation before closure or even postoperative protocols such as dressing, decreased blood transfusion policy with or without the use of tranexamic acid, etc. that may not be specifically mentioned. There were also significant differences among screening methodologies, including some papers that exclusively screened MRSA carriers [32,34,39], with inherent differences in their ability to identify and subsequently treat all potential *S aureus* carriers. In some studies, the perioperative antibiotic prophylaxis in MRSA carriers was changed [1,3,4,6,20,33,34,36–38,41], which may or may not influence the outcomes of these specific subgroup of patients [65,66]. Due to the different strategies involved in the studies, we were unable to conduct a meta-analysis comparing noncarriers to treated carriers and to nontreated carriers in the TJA group. Our analysis, as the studies included, did not take into account patient characteristics, such as age and comorbidities, and intervention specificities, such as the duration of surgery that can influence SSI and PJI rates. Thus, the authors believe that more prospective studies with standardized methodologies and including other types of data may provide higher levels of evidence for this topic of study.

Conclusion

Nasal colonization of *S aureus* at the time of surgery is a risk factor for SSI/PJI in orthopedic and elective TJA surgery. This systematic review and meta-analysis determined that the implementation of a traditional *S aureus* screening and whole-body decolonization protocol using mupirocin and chlorhexidine can reduce infection after TJA. However, this finding is mostly based upon retrospective studies, so larger-scale prospective multicenter studies are needed to further scrutinize its real value. The actual impact of such intervention may in part depend on the preponderance of the endogenous contamination route over the traditional exogenous mode of acquiring infection in each specific epidemiological setting. The concept of genetic predisposition for endogenous routes such as the microbiome concept is emerging with experimental data suggesting the gut microbiota may influence susceptibility to PJI [67]. Further studies are also needed to determine clinically effective methodologies potentially using antiseptics to reduce *S aureus* colonization to obviate antibiotic resistance associated with implementing the most cost-effective universal treatment strategy.

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Appendix

Table A.1
Staphylococcus aureus Screening and Nasal Decolonization Only Results in Reducing SSI in All Orthopedic Procedures.

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control	Intervention	*P* Value	Control	Intervention	*P* Value	
Prospective studies											
Kalmeijer et al, 2002 [27]	Elective orthopedic surgery with implants (ie, hip, knee, or back)	Universal treatment Randomized, placebo-controlled trial	Topical intranasal mupirocin ≥2 doses before surgery	Cefamandole 2 g within 1 h before and 8 and 16 h after surgery	Historic 14/299 (4.7%)	12/315 (3.8%)	NS	Historic 8/299 (2.7%)	5/315 (1.6%)	NS	- Relative risk ratio of overall or *S aureus* infections was not significantly reduced - Endogenous *S aureus* infections were 5 times less likely to occur in the mupirocin group but difference was not statistically significant
Price et al, 2008 [5]	Elective orthopedic surgery	Selective carrier's treatment by choice Cross-sectional analysis	Topical intranasal mupirocin ≥6 doses before surgery	Cefazolin (or clindamycin if cephalosporin allergy)	—	—	—	Noncarriers 2/196 (1.0%) Untreated carriers 2/43 (4.7%)	Treated carriers 0/43 (0.0%)	NS	- No statistically significant SSI rate between groups - SSI resulting from *S aureus* was significantly higher among arthroplasty surgery ($P = .02$) - Both infections in the untreated carriers group were MSSA phenotypically similar to the nares isolate
Hadley et al, 2010 [31]	Primary total knee or hip arthroplasty	Universal treatment Prospective cohort	5-d Course of intranasal mupirocin regardless of screening result	Cefazolin or clindamycin if ß-lactam allergy (or vancomycin if MRSA carrier)	Unscreened 6/414 (1.45%)	21/1644 (1.28%)	.809	MRSA 1/414 (0.24%)	MRSA 3/1644 (0.18%)	NS	- Staphylococci decolonization led to a 13% decrease in deep SSI which did not reach statistical significance
Retrospective studies											
Gernaat-van der Sluis et al, 1998 [26]	Arthroplasties, endoprosthetic surgery, and internal fixation	Universal treatment Retrospective before and after intervention	Topical intranasal mupirocin 3 times before surgery	Cefazolin 1g within 1 h before and 4 h after surgery	Historic 34/1260 (2.7%)	14/1044 (1.3%)	.02	Historic 14/1260 (1.1%)	7/1044 (0.7%)	NS	- Relative risk ratio of overall infection significantly decreased by 50% after intervention - *S aureus* infections were also reduced but not statistically significant
Wilcox et al, 2003 [28]	Orthopedic surgery with insertion of metal prosthesis and/ or fixation	Universal treatment Retrospective before and after intervention	Topical intranasal mupirocin 5 d (ie, from day −1 to day +4)	Three doses of Cefadrine 1 g	—	—	—	MRSA[a] 23/1000	MRSA[a] 3.3-4.0/1000	<.001	- The incidence of MRSA infections was significantly reduced but not SSI caused by other pathogens (including MSSA) - Of 11 MRSA SSI cases occurring in the

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Table A.1 (*continued*)

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control	Intervention	*P* Value	Control	Intervention	*P* Value	
											intervention period, only 1 actually received treatment - Prevalence of MRSA carriage in the orthopedic wards decreased regularly after intervention
Coskun and Aytac, 2004 [29]	Orthopedic operations not otherwise specified	Universal treatment Retrospective after intervention	Topical intranasal mupirocin 3 times daily 3 d before surgery	Cefazolin or cefuroxime	Historic 28/920 (3.0%)	32/2329 (1.4%)	<.001	Historic 14/920 (1.5%)	32/2329 (0.4%)	<.001	- There was a significant decrease in overall, *S aureus*, and MRSA SSI rates - MRSA decreased from 10/920 (1.1%) to 3/2329 (0.1%)
Hacek et al, 2008 [30]	Elective hip/ knee joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin twice a day	Cefazolin for hip/ vancomycin for knee up to 24 h	Unscreened 14/583 (2.4%)	Noncarriers 7/689 (1.0%) Treated carriers 4/223 (1.8%)	≤.05	Unscreened 10/583 (1.7%)	Noncarriers 4/689 (0.6%) Treated carriers 3/223 (1.3%)	≤0.1	- *S aureus* SSI rate in the intervention group was reduced compared to control group − 0.8% (7/912) vs 1.7% (10/583), but it did not reach statistical significance - Assuming a similar proportion of carriers and SSI rate among noncarriers, authors calculate about 8 SSI cases were prevented by the intervention

NS, not statistically significant; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; SSI, surgical site infection.

[a] Incidence of MRSA infections per 1000 operations.

Table A.2
Staphylococcus aureus Screening With Concomitant Nasal and Skin Decolonization Results.

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control (%)	Noncarriers (%)	Treated Carriers (%)	Control (%)	Noncarriers (%)	Treated Carriers (%)	
Pofahl et al, 2009 [32]	Elective hip/ knee joint arthroplasty[a]	Selective MRSA carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice daily 5 d before surgery + chlorhexidine baths on days 1,3, and 5	Prophylaxis changes in MRSA carriers at surgeon discretion	—	—		6/1979 (0.3%)	0/1436 (0.0%)		- Reduction in MRSA SSI was most pronounced in orthopedic (hip and knee prostheses) where it reached statistical significance - The rate in MSSA SSI did not change significantly in any group
Kim et al, 2010 [3]	Elective inpatient orthopedic surgery (arthroplasty, spine, sports medicine)	Selective carrier's treatment Retrospective before and after	Intranasal mupirocin twice a day + daily chlorhexidine baths initiated 5 d before surgery	Cefazolin (vancomycin if MRSA carrier)	—	—	—	24/5293 (0.45%)	7/5122 (0.14%)	MRSA 3/309 (0.97%) MSSA 3/1588 (0.19%)	- The rate of SSI during the intervention period was significantly lower than observed during the historic control period—0.19% (13/ 7019) vs 0.454% (24/5293) - The risk reduction was greater for MRSA SSI (0.06% vs 0.19%) than for MSSA SSI (0.13% vs 0.26%) - SSI rate among MRSA carriers (0.97%) but not MSSA carriers (0.45%) was significantly higher than that of noncarriers (0.14%)
Bode at al [33]	Orthopedic surgery[b]	Selective carrier's treatment Multicenter randomized placebo-controlled trial	5-d Course of intranasal mupirocin twice a day + daily chlorhexidine baths starting at the time of admission	Not specified				4/87[c] (4.6%)		1/85 (1.2%)	- Considering all surgical patients, *S aureus* deep SSI rate was significantly lower among mupirocin-chlorhexidine vs placebo—0.9% (4/504) vs 4.4% (16/413) - Among orthopedic surgery patients, mupirocin-chlorhexidine-treated patients vs placebo presented lower *S aureus* SSI rate but it did not reach statistical significance - SSI rate due to microorganisms other than *S aureus* was not significantly lower in mupirocin-chlorhexidine-treated patients—11% vs 12%
Rao et al, 2011 [20]	Elective total joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin (vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	Historic 20/741 (2.7%)	17/1440 (1.2%)		Historic 11/741 (1.5%) Concurrent 19/2284 (0.8%)	1/964 (0.1%)	0/321 (0.0%)	- This paper has 2 control groups: historic before intervention of the same surgeons and concurrent in the same time period of a different group of surgeons - Overall infection rate (including superficial and deep infection and nonstaphylococcal infections) decreased significantly during the intervention period

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Table A.2 (*continued*)

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control (%)	Noncarriers (%)	Treated Carriers (%)	Control (%)	Noncarriers (%)	Treated Carriers (%)	
											- Considering only deep SSI rate of the same surgeons before and after the intervention, overall infection rate—1.2% (9/741) vs 0.6% (8/1440)—and *S aureus* infection rate—0.7% (5/741) vs 0.1% (2/1440)—were both reduced
Murphy et al, 2011 [34]	Elective inpatient orthopedic surgery	Selective MRSA carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine body wash and shampoo	Cefuroxime (vancomycin if MRSA carrier)	—	—	—	—	6/5825 (0.3%)	6/90 (6.7%)	- Patients with negative rescreening after treatment underwent surgery within 3 mo (positive rescreens were excluded) - Deep sepsis rate in lower-limb joint arthroplasties was significantly higher among MRSA previously carriers—7.4% (2/27) in total hip and 6.9% (2/29) in total knee, than among noncarriers—1.1% (11/982) in total hip and 0.4% (4/1011) in total knee despite confirmed successful preoperative decolonization
Barbero Allende et al, 2015 [35]	Joint arthroplasty (total or partial, primary or revision, elective or trauma)	Selective carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin twice a day + daily chlorhexidine bath	Cefazolin or vancomycin if ß-lactam allergy up to 24 h	19/384 (4.9%)	9/309 (2.9%)	2/100 (2.0%)	9/384 (2.3%)	1/309 (0.3%)	1/100 (1.0%)	- Overall PJI rate was lower, albeit not significantly compared to historic controls—2.9% (12/49) vs 4.9% (19/384) - *S aureus* PJI was significantly reduced compared to historic control—0.5% (2/409) vs 2.3% (9/384) - Overall PJI and *S aureus* PJI rates were similar between noncarriers and treated *S aureus* carriers
Schweizer et al, 2015 [36]	Primary hip or knee arthroplasty[d]	Selective carrier's treatment Multicenter retrospective before and after intervention	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin or cefuroxime (vancomycin if MRSA carrier)	—	—		66/20,642 (0.32%)	17/11,059 (0.15%)		- The rate of complex *S aureus* SSI, but not all *S aureus* SSI, decreased significantly after hip or knee arthroplasties (−17/10,000 operations) - The decrease in overall SSI rate considering all pathogens and all surgeries did not reach statistical significance
Baratz et al, 2015 [1]	Elective primary and revision hip or knee arthroplasty	Selective carrier's treatment Retrospective	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin (plus vancomycin if MRSA carrier or ß-lactam	33/3080 (1.1%)	17/2763 (0.6%)	All carriers 7/644 (1.1%) MRSA carriers 4/158	21/3080 (0.7%)	13/3434 (0.4%)		- Both overall infections considering all pathogens—1.1% (33/3080) vs 0.8% (27/3434)—and *S aureus* infection rate—0.7% (21/3080)

		before and after intervention		allergy) up to 24 h			(2.5%) MSSA carriers 2/486 (0.4%)				vs 0.4%(13/3434)—did not decrease significantly after the intervention - Risk of infection in overall *S aureus* carriers was not significantly higher than noncarriers - MRSA carriers were significantly more likely to develop SSI than noncarriers or even MSSA carriers
Malcolm et al, 2016 [4]	Primary hip or knee arthroplasty	Selective carrier's treatment Retrospective after intervention	Topical mupirocin twice daily for 3 d + chlorhexidine body wipes preoperatively	Cefazolin (or vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	Unscreened 16/1751 (0.9%)	8 cases (0.4%)	MRSA carriers 0 cases (0.0%) MSSA carriers 1 case (0.3%)	—	—	—	- Rates of revision arthroplasty for any reason after at least 1 y was similar among screened and unscreened cohorts—1.0% (22/2291) vs 1.4% (25/1751) - Risk of revision due to PJI was significantly higher in unscreened compared to screened patients—0.9% (16/1751) vs 0.4% (9/2,2291) - After screening and decolonization, there were no differences in overall or revision due to PJI between preoperative carriers and noncarriers
Ramos et al, 2016 [37]	Elective primary hip or knee arthroplasty or primary spinal fusion	Universal treatment Retrospective after intervention	5-d Course of intranasal mupirocin or nasal povidone-iodine the day of surgery + chlorhexidine gluconate wipes the night before surgery	Vancomycin if MRSA carrier	—	11,309 THA (0.4%) TKA (0.7%) Spine (1.3%)	THA 8/939 (0.8%) TKA 18/912 (2.0%) Spine 10/668 (1.5%)	—	—	—	- *S aureus* preoperative colonization was a significant risk factor for SSI among total knee but not total hip or spine patients - MRSA carriers had higher risk of infection than MSSA carriers—2.7%(10/367) vs 1.2% (26/2152)
Sporer et al, 2016 [38]	Elective primary total joint arthroplasty	Selective carrier's treatment Retrospective before and after intervention	Intranasal mupirocin twice daily + daily chlorhexidine baths 5 d before admission	Cefazolin (vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	16/1443 (1.1%)	33/9791 (0.34%)		—	—		- SSI rate was significantly lower after initiation of nasal screening—0.34% vs 1.1%. - SSI rate dramatically decreased in the first year of implementation - *S aureus* was involved in PJI less frequently after intervention although it did not reach statistical significance—66.7% vs 33.3%
Sousa et al, 2016 [6]	Elective primary hip/knee joint arthroplasty	Selective carrier's treatment Single-center randomized controlled trial	Intranasal mupirocin twice a day + daily chlorhexidine baths 5 d before surgery	Cefazolin (plus vancomycin if MRSA carrier or ß-lactam allergy) up to 24 h	Untreated carriers 6/139 (4.3%)	16/800 (2.0%)	3/89 (3.4%)	Untreated carriers 3/139 (2.2%)	9/800 (1.1%)	2/89 (2.2%)	- Overall PJI rate was higher among *S aureus* carriers than noncarriers—3.9% (9/228) vs 2.0% (16/800), but it did not reach statistical significance - Treated and untreated carriers showed no significant difference either in *S aureus* or all pathogen infections

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Table A.2 (*continued*)

Author	Target Population	Type of Intervention/ Study	Treatment Regimen	Perioperative Antibiotic Prophylaxis	Overall Infection			*S aureus* Infection			Major Finding(s)
					Control (%)	Noncarriers (%)	Treated Carriers (%)	Control (%)	Noncarriers (%)	Treated Carriers (%)	
Barbero et al, 2017 [2]	Total or partial hip arthroplasty for femoral neck fracture	Selective carrier's treatment Retrospective before and after intervention	5-d Course of intranasal mupirocin twice a day + daily chlorhexidine wash (most starting after surgery)	Cefazolin or vancomycin if ß-lactam allergy up to 24 h	Historic 10/138 (7.2%)	12/267 (4.5%)		Historic 6/138 (4.3%) Unscreened 2/62 (3.2%)	2/267 (0.7%)		- 83 of 87 identified carriers underwent decolonization treatment after surgery - *S aureus* infections were significantly reduced in the intervention period compared to historic control—0.7% vs 4.3% - Both cases of *S aureus* infections in the intervention group occurred in noncarriers
Tandon et al, 2017 [39]	Elective hip or knee arthroplasty	Selective MRSA carrier's treatment Retrospective after intervention	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine baths + hair shampoo on days 1 and 3	Several different regimens; teicoplanin alone or with gentamicin in 58% of cases	—	—		—	81/6530 (1.2%)	5/79 (6.3%)	- Patients with negative rescreening after treatment underwent surgery within 3 mo—mean time interval 2.93 wk - 4 patients with MRSA positive rescreens after treatment were excluded - The relative risk of deep SSI in MRSA carriers was significantly higher despite treatment both in hip (4.46) and knee (5.6) patients
Jeans et al, 2018 [40]	Elective hip or knee arthroplasty	Retrospective study Case-control	Daily octenidine chlorhexidine wash + intranasal mupirocin 4 times 5 d before procedure, and 5 d after	—	69/3593 (1.92%)	131/9318 (1.41%)		—	—	—	- PJI fell from 1.92% to 1.41% with the screening and decolonization protocol ($P = .03$) - The screening program was most effective in MSSA prevention in THA (3% to 1.5%, $P = .002$)
Pelfort et al, 2019 [41]	Elective hip joint arthroplasty	Retrospective study Case-control	5-d Course of intranasal mupirocin 3 times a day + daily chlorhexidine baths	Cefazolin (vancomycin if MRSA carrier or ß-lactam allergy)	17/400 (4.25%)	5/403 (1.24%)		8/400 (2%)	1/403 (0.24%)		- Incidence of 20.6% of *S aureus* nasal carriers, with an incidence of only 1.9% for MRSA - No nasal carrier who was decolonized presented a SSI by this microorganism - Reduction in global SSIs of 71% and a reduction in specific *S aureus* SSIs of 88%
Romero-Palacios et al, 2019 [42]	Primary or revision hip or knee arthroplasty	Retrospective before and after intervention	5-d Course of intranasal mupirocin twice daily + chlorhexidine baths	—	42/8505 (0.5%)	7/1883 (0.4%)		29/8505 (0.3%)	1/1883 (0.05%)		- No nasal carrier who was decolonized presented a SSI by this microorganism - Significant reduction in PJIs due to *S aureus* by screening for and decolonizing *S aureus* carriers before total joint arthroplasties - No significant difference in overall infection rates was observed

MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; PJI, periprosthetic joint infection; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a] This paper also reported on cardiac surgery and hysterectomy but data presented here concerns joint arthroplasty exclusively.

[b] This paper also reported on medical and other surgical patients but data presented here concerns orthopedic surgery exclusively.