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Is Staphylococcal Screening and Suppression an Effective Interventional Strategy for Reduction of Surgical Site Infection?

Charles E. Edmiston, Jr,[1] Nathan A. Ledeboer,[2] Blake W. Buchan,[2] Maureen Spencer,[3] Gary R. Seabrook,[1] and David Leaper[3,4]

Abstract

Background: *Staphylococcus aureus* has been recognized as a major microbial pathogen for over 100 y, having the capacity to produce a variety of suppurative and toxigenic disease processes. Many of these infections are life-threatening, with particularly enhanced virulence in hospitalized patients with selective risk factors. Strains of methicillin-resistant *Staphylococcus aureus* (MRSA) have rapidly spread throughout the healthcare environment such that approximately 20% of *S. aureus* isolates recovered from surgical site infections are methicillin-resistant, (although this is now reducing following national screening and suppression programs and high impact interventions).

Methods: Widespread nasal screening to identify MRSA colonization in surgical patients prior to admission are controversial, but selective, evidence-based studies have documented a reduction of surgical site infection (SSI) after screening and suppression.

Results: Culture methods used to identify MRSA colonization involve selective, differential, or chromogenic media. These methods are the least expensive, but turnaround time is 24–48 h. Although real-time polymerase chain reaction (RT-PCR) technology provides rapid turnaround (1–2 h) with exceptional testing accuracy, the costs can range from three to 10 times more than conventional culture methodology. Topical mupirocin, with or without pre-operative chlorhexidine showers or skin wipes, is the current ''gold-standard'' for nasal decolonization, but inappropriate use of mupirocin is associated with increasing staphylococcal resistance.

Conclusions: Selection of an effective active universal or targeted surveillance strategy should be based upon the relative risk of MSSA or MRSA surgical site infection in patients undergoing orthopedic or cardiothoracic device related surgical procedures.

Inappropriate antibiotic use, together with the increasing demographics of an ageing population; chronic diseases such as diabetes mellitus; patient contact with healthcare facilities; high bed occupancy rates; and numbers of surgical procedures, have all contributed to the increase in prevalence of Healthcare Associated Infections (HCAIs) caused by selection and emergence of multi-resistant organisms. Infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) have been particularly challenging. Methicillin-resistant *Staphylococcus aureus* surgical site infections (SSIs) have been catastrophic both for patients and for the use of health care resources because of longer post-operative stays, greater treatment costs, and a poorer prognosis [1,2]: The management of MRSA-infected hip and knee prostheses is associated with considerable mortality rates; and morbidities that include prosthetic joint removal and even amputation. Since 2004 in Great Britain, the Health Protection Agency (HPA), now Public Health England (PHE), has coordinated mandatory surveillance of SSIs after major implant, orthopedic operations with an initial finding that almost half the SSIs were attributable to *S. aureus* with almost two thirds of these being because of MRSA (the severity of infection being related to type MRSA15 (ST 20) and MRSA 16 (ST 36) [3]. However, there is evidence that this

[1]Departments of Surgery (Vascular) and [2]Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin.
[3]Infection Prevention Consultants, Boston, Massachusetts.
[4]Institute of Skin Integrity and Infection Prevention, University of Huddersfield, Huddersfield, United Kingdom.

surveillance program considerably underestimates the true rates of SSI as it depends on in-patient and re-admission data [4]. Although the proportion of SSIs relating to MRSA has fallen in line with reductions in bloodstream infection, sensitive forms of *S. aureus* have not fallen at a similar rate.

In 2003, the Society for Healthcare Epidemiology of America (SHEA) published a guideline indicating, *''Active surveillance cultures are essential to identify the reservoirs for the spread of MRSA and VRE infections and make control possible using the CDC's long-recommended contact precautions''* [5]. The evidence supporting active MRSA surveillance, or screening, is controversial and often supported by ''bad science,'' which only serves to fuel partisan opinions. At present, several states in the US mandate that MRSA surveillance should be undertaken. However, the practice of screening and suppression is not well supported by an evidence-based guideline validating the screening strategy, clinical efficacy, and implementation process. In 2007, as a result of the movement toward legislation mandating active surveillance cultures, as a means of controlling multidrug-resistant organisms (MDROs) within the healthcare environment, the Society for Healthcare Epidemiology of America (SHEA) and the Association of Professional in Infection Control and Epidemiology (APIC) published a joint position paper addressing the rationale for screening, the scientific evidence supporting this endeavor, and unresolved issues surrounding legislatively mandated active surveillance [6]. At present, in the rush to comply with legislative-based mandates, little attention is being given to standardization of practices that would guide individual hospitals in selecting optimal screening and suppression strategies. The cost of development and implementation of an active MRSA surveillance program requires a substantial institutional and fiscal commitment. Therefore, it is reasonable to consider, what is the expected return on investment following implementation of an MRSA active surveillance program, and will the findings serve to improve patient outcomes [7]?

What Is the Role of Nasal Colonization in Overt Infection?

In 1964, a multi-centered clinical study, supported by the National Academy of Science – National Research Council, attempted to resolve the benefits of intra-operative ultraviolet radiation as a strategy to reduce the risk of SSI after clean surgical procedures. The effort of this classical study was unsuccessful in improving outcomes. However, an ancillary component of the study has been responsible for establishing what has come to be viewed as the nasal-baseline colonization rate for *Staphylococcus aureus.* A total of 9,263 healthcare professionals, at the participating six medical centers, had their nares sampled and the baseline colonization rate ranged from 13.4% to 31.0%, giving a standard healthcare worker *S. aureus* colonization rate of approximately 22% [8]. Three patterns of nasal carriage in healthy individuals exist: Persistent carriers, intermittent carriers, and non-carriers [9]. Persistent carriers have been found to have a greater nasal load of *S. aureus* and are therefore viewed as being at a greater risk for developing post-operative infection [10]. The range of individuals who were found to be persistent carriers was between 12%–30%, whereas intermittent carriage is estimated as being somewhere between16%–70% [11,12]. Individuals who have a persistent nasal carriage of *S. aureus* have also been found to have a greater rate of *S. aureus* colonization (two to three times) at distant anatomic sites [9]. Numerous co-dependent risk factors (Table 1) have been identified as increasing the risk of *S. aureus* nasal carriage in medical and surgical patient populations [13–21].

Table 1. Co-Dependent Risk Factors for Methicillin-Resistant *Staphylococcus aureus* Colonization[13–21]

Known MRSA carriage	Antibiotic within past 12 mo
Hospitalization with past 12 mo	Intravenous drug user
Hemodialysis/peritoneal dialysis	Immunocompromised
History of CVA	Elderly
Diabetes mellitus	Obesity
Eczema/psoriasis	HIV positive
End-stage liver disease	

MRSA = methicillin-resistant *Staphylococcus aureus*; CVA = cerebrovascular accident; HIV = human immunodeficiency virus.

Studies conducted in the 1950s and 1960s found that an increased burden of nasal staphylococci correlated with an increased skin burden (carriage), placing hospitalized patients at an increased risk for SSI [22,23]. Nasal carriage of *S. aureus* has been identified as a substantial risk factor for infection in general, orthopedic, and thoracic surgical services [24–26]. Although suppression of the carrier state in at-risk patient populations may decrease the risk of post-operative infection, routine screening to identify persistent carriers is viewed by many practitioners as being controversial [27].

Active Staphylococcal Surveillance from a Laboratory Testing Perspective

In 2012, Jarvis reported on the national prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in in-patients in US healthcare facilities. The analysis found that the prevalence of MRSA, as measured in 2010 (66.4 per 1,000 inpatients), had increased over the 2006 rate (46.3 per 1,000 inpatients) as determined by an APIC national study [28,29]. It was interesting to note that while the rate had increased, whereas the relative proportion of MRSA-infected to MRSA-colonized patients had reversed following the 2006 report. The explanation for this finding is probably related to the large increase in the number of patients undergoing active surveillance testing (75.7%, 2010 compared with 29%, 2006) [29]. The combination of pre-operative identification of MRSA colonization in surgical patients followed by active decolonization has been viewed as a pre-emptive strategy for reducing the risk of SSI [30]. In an effort to combat the risk of MRSA infections in selective surgical patient populations, hospitals have instituted active surveillance programs, screening patients for nasal colonization prior to surgical admission. These methods vary greatly in turnaround-time (TAT), performance, and cost. Therefore, it is important to have an understanding of the methods available for the screening of patient for MRSA as well as the strengths and weaknesses of each strategy.

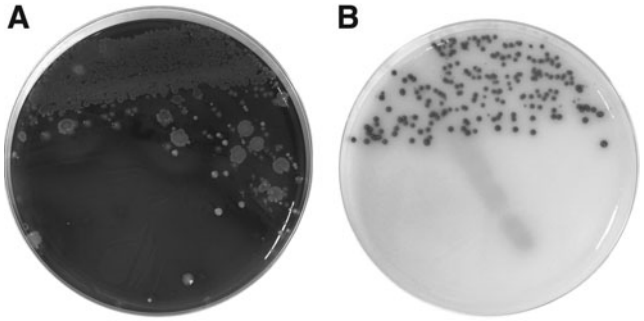

FIG. 1. Example of routine screening for MRSA on chromogenic medium, nasal swab specimen was plated to non-selective blood agar **(A)** and chromogenic medium **(B)**. Chromogenic medium inhibits the growth of nasal flora and methicillin susceptible *S. aureus* (MSSA). MRSA appears as blue colonies on this medium following 18–24 h incubation.

Culture-based strategies

There are a number of culture-based screening methods that can be used to identify MRSA and MSSA. Basic methods rely on a two-step identification algorithm. Specimens are inoculated to non-selective medium and incubated for 18–24 h. Colonies demonstrating a characteristic beta-hemolytic pattern are confirmed as *S. aureus* using simple biochemical tests including gram stain, catalase and coagulase tests, or latex agglutination. Methicillin resistance of these strains is then determined using an oxacillin or cefoxitin disk diffusion assay [31]. Although simple and cost-effective, this approach can take 48 h or longer to definitively identify MRSA. This processing time can be reduced by 18–24 h if the disk test is replaced by an agglutination assay targeting the methicillin resistance determinant MecA (pbp2a).

These pbp2a agglutination tests have demonstrated high sensitivity and specificity characteristics, but add considerable cost compared with the disk diffusion method (Table 1) [32–34]. The major drawback to culture methods is a lack of sensitivity when compared with broth enriched samples or molecular methods. When broth enriched cultures are used as the gold standard, direct culture methods demonstrate a sensitivity of only 80%, whereas molecular methods attain sensitivity of approximately 93% [35]. Alternatively, incorporation of 4.0% NaCl and 6 mcg/mL oxacillin as selective agents into culture medium can speed presumptive identification of MRSA and is recommended by the Clinical and Laboratory Standards Institute (CLSI) [35]. Recently, an array of chromogenic media have been developed, which are specifically aimed at high-throughput MRSA screening from nasal swabs. These media contain a concentration of oxacillin or cefoxitin, which is inhibitory to *mecA*-negative staphylococci. A chromogenic substrate utilized specifically by *S. aureus* gives these media specificity for MRSA, which appear as pigmented colonies (Fig. 1). The sensitivity and specificity of these screening media are high, ranging from 88–98% and 98%–100%, respectively when compared with standard culture methods (Table 2) [36–38]. These media provide results within 18–24 h and the method is relatively inexpensive for screening large numbers of patients for nasal carriage. The major drawback to culture methods is a lack of sensitivity when compared with broth-enriched samples or molecular methods. When broth-enriched cultures are used as the gold standard, direct culture methods demonstrate a sensitivity of only 80%, whereas molecular methods attain a sensitivity of approximately 93% [39].

Nucleic acid tests

These tests are based on nucleic acid amplification and are used primarily for testing nasal swabs collected in transport medium. Identification of MRSA involves amplification and detection of the *SCCmec* junction with *orfX* in *S. aureus*. All nucleic acid amplification tests (NAATs) have similar sensitivity and specificity characteristics ranging from 86–96% and 93–98%, respectively (Table 2). The major difference between the available NAATs is the level of automation, throughput, and on-demand capabilities.

The LightCycler MRSA Advanced Test is an FDA-cleared molecular test capable of batch testing one to 30 samples with a run time of ~75 min, but requires manual pre-processing of specimens. In contrast, the BD MAX/GeneOHM platform offers completely automated sample extraction, amplification, and detection for up to 24 specimens simultaneously. Results are available in 45 min to 2 h, depending on the number of specimens tested. The GeneXpert MRSA test offers the benefit of complete automation along with a rapid time to a result (45 min) and on-demand capabilities, making the Xpert MRSA an attractive choice for real-time screening of emergency department or trauma admissions. In general,

TABLE 2. SCREENING METHODS FOR DETECTION OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

Test type	*Batch/On Demand*	*TAT*[a]	*Cost per test*	*Sensitivity*	*Specificity*	*Citation*
Culture[b]						
Non-Selective medium, oxacillin disk $35–$50	Either	36–48 h	<$1	80%–100%	99%–100%	[37,49]
Non-selective medium, pbp2a agglutination	Either	18–24 h	$4–$6	100%	97%–99%	[32–34]
Chromogenic medium	Either	18–24 h	$3–$5	85%–96%	99–100%	[36–37,49]
Nucleic acid detection						
LightCycler MRSA	Batch(1–30)	2 h	$18–$30	92%	98%	[39]
GeneOHM MRSA	Batch(1–24)	45 min–2 h	'$22–$35	92%–96%	94%–95%	[37,47,48]
Xpert MRSA	On Demand	45 min		86%–94%	93%–94%	[45,48]

[a]TAT = Turn-around-time
[b]Comparison to non-enriched gold standard culture methods

the cost per test is lower for platforms geared toward batch processing or which lack complete automation as compared with fully automated on-demand tests (Table 2).

Culture methods share some distinct advantages over nucleic acid-based tests. First, methicillin resistance is determined phenotypically by assessing the ability of *S. aureus* to grow in the presence of methicillin or a methicillin derivative. This allows for greater specificity than NAATs, which are designed to detect the *SCCmec-orfX* junction as an indicator of methicillin resistance in *S. aureus*. Mutations within the *mecA* gene can result in a susceptible phenotype while maintaining a MRSA-positive NAAT result. Conversely, *SCCmec* rearrangement events can occur that truncate or alter the NAAT primer/probe target site. This can lead to false negative NAAT results [39–41]. Most common among these are deletions of the right end junction of the SCC*mec* cassette with *orfX*. A second advantage of culture methodology is that it will detect only live bacteria. In contrast, NAATs can remain positive even after effective decolonization treatment because of residual *S. aureus* DNA in the specimen. This makes NAATs a poor choice for confirmation of MRSA decolonization. Similarly, culture methods can identify borderline resistance phenotypes attributed to hyper-production of beta-lactamases or other non-*mecA* mediated mechanisms [36,42–44]. Lastly, culture-based screening methods are inexpensive and do not require skilled molecular technologists to perform the analysis.

The primary advantage of the current molecular screening methods is high sensitivity and rapid turn-around time (TAT). When compared with direct culture, NAATs are up to 13% more sensitive and have limits of detection as low as 100 bacteria per swab [39,45]. In some cases increased sensitivity is the result of non-viable bacteria, but recovery of MRSA from broth enrichment of specimens often indicates the presence of a low concentration of MRSA. The average TAT using molecular tests is 69–75 h faster than routine culture methods [46]. In most surgical applications, pre-screening may occur seven or more days prior to surgery and therefore the initial screening process is not necessarily time sensitive. But subsequent screening at the time of surgical admission does pose a time-sensitive dilemma, because patients who are not adequately decolonized will need to be flagged for contact isolation. Therefore, for surgical patients a tiered approach may be appropriate, which involves a hybrid culture/molecular screening strategy.

Active Staphylococcal Surveillance in Surgical Patients: Some Objective Considerations

In addressing the benefits of an active staphylococcal surveillance program, a key question that warrants evidence-based consideration is, how effective has this strategy been in reducing risk and improving patient outcomes? Several published studies have suggested that eradication of the MRSA carrier state is effective in reducing surgical site infections caused by MRSA in selective surgical disciplines. In a study conducted in 2007, all patients admitted to a tertiary medical center for elective surgery were screened (nasal) for MRSA. Positive patients were treated with topical intranasal 2% mupirocin (twice a day for 5 d) and in addition were instructed to take three 4% chlorhexidine gluconate (CHG) showers (days one, three, and five before surgery). Peri-operative antimicrobial prophylaxis was altered based on screening results. Patients were not screened again prior to surgery. The MRSA colonization rate in surgical patients was 6.8% and the rate of MRSA colonization in a comparator (control) group (universal surveillance) was 7.2%. Whereas a reduction was observed in MRSA infections in patients undergoing selective cardiac procedures and hysterectomies, the findings were not statistically significant. However, a substantial reduction in MRSA SSI was observed in patients undergoing knee and hip (prostheses) procedures ($p < 0.04$) [50]. Whether or not active surveillance is beneficial in reducing the risk of infection in cardiac surgery is at-present unresolved. A separate study published in 2007 suggested that active surveillance provided little if any benefit in reducing the risk of MRSA mediastinitis [51]. However, it should be pointed out that in this study MSSA colonization was 15.5%, whereas MRSA colonization was found to be 0.4%. Therefore, the incidence of MSSA mediastinitis was closely correlated with pre-operative MSSA colonization ($p < 0.0001$).

This study clearly suggests that focusing solely on MRSA practitioners may be missing the fact that MSSA is responsible for the vast majority of SSIs and therefore, when present, should warrant intervention. This perspective was validated in a recent study from the Netherlands. Patients undergoing cardiothoracic or orthopedic surgery were screened for *S. aureus* nasal carriage and carriers were treated with mupirocin and chlorhexidine gluconate showers. The authors documented that identifying and treating nasal carriage of *S. aureus* resulted in a substantial reduction in hospital cost post-surgery because of a reduction in patient morbidity [52].

In the study by Kim et al. published in 2010, an active surveillance program (PCR-based) was implemented to detect *S. aureus* (MSSA and MRSA) nares colonization in elective orthopedic surgery patients. A total of 1,588 patients were identified as *S. aureus* carriers (22.6%); 309 (4.4%) were characterized as MRSA. All positive patients were treated with 2% mupirocin (twice a day for 5 d) and instructed to take 2% CHG total body-shower for 5 d prior to surgery. At admission, the MRSA-colonized patients were rescreened by PCR and repeat positives were flagged for contact isolation. There was a substantial reduction in MRSA infections ($p < 0.032$) compared with a baseline pre-intervention control group [53]. Although the number of MSSA infections decreased, the results were not statistically significant ($p < 0.094$); however, the overall decline in *S. aureus* infections was statistically significant [$p < 0.009$]. These findings suggest that although active *S. aureus* (MRSA and MSSA) screening may demonstrate a benefit in selective patient populations, exogenous (occult) sources of staphylococci may contaminate the wound prior to closure [54]. A prospective Swiss study that included 21,754 surgical patients found no substantial reduction in nosocomial MRSA infections after implementing a PCR-based universal surveillance program in the surgical wards. Patients positive for MRSA were placed in isolation, with suppression using mupirocin and given daily body-washes with CHG (for 5 d) [55].

This study has been criticized, as only 43% of the patients known to be MRSA carriers before surgery received effective peri-operative antimicrobial prophylaxis against MRSA. It is also worth noting that 31% of the MRSA carriers undergoing elective surgery were identified after surgery because of the

emergent nature of the intervention and delays in reporting screening results [56]. A recent evidence-based review of universal screening for MRSA, in patients undergoing elective surgery, cited the Swiss study as an example of the conflicting nature of this interventional practice [57]. Two large institutional studies, one conducted in the Veterans Affairs Hospitals and the other in a critical care patient population have added further to the ambiguity surrounding the benefit of active surveillance in medical and surgical patient populations. The Huskin study (Star*ICU) targeted ICU patients (n = 5,435 admission), and surveillance cultures (nasal) were obtained after admission and processed in a remote laboratory. The study emphasized an expanded use of barrier precautions in addition to contact precautions. The study did not, however, use nasal mupirocin in culture-positive patients, nor did the study attempt to reduce the density of body site contamination using CHG body-washes or cleansing. Consequently, merely identifying carriers and expanding the use of barrier precautions did not effectively reduce MRSA transmission [58]. Another criticism of this study is that culture reports were delayed for 5 d because of remote processing. In addition, 55% of the patients were excluded from the study because their ICU stay was less than 3 d, omitting patients who may have served as a salient source of contamination. Furthermore, the authors noted that staff compliance to the institution's barrier precaution policy was judged as poor.

The general consensus is that the Star*ICU study is a poor example of an effective interventional effort to reduce the risk of MRSA infection within a healthcare patient population. Alternatively, the nationwide VA study, which was published in the same journal as the Star*ICU study, is a remarkable contrast in design and execution. Over a 3-y period, 1,934,598 patients were enrolled in an ''MRSA bundle'' that included universal nasal screening (PCR-based), contact precautions for colonized or infected patients, enhanced hand hygiene practices and a change in ''institution culture'' surrounding aseptic practices. The mean prevalence of MRSA was 13.6% and the incidence of MRSA healthcare-associated infections declined in the ICUs from 1.64 per 1,000 patient days to 0.62 per 1,000 patient days ($p < 0.001$). A concomitant decrease in MRSA infections in the non-ICU patient population followed a similar trend [59]. The risk-reduction benefit derived from an active staphylococcal surveillance program would appear to depend on two factors: A ''robust'' surveillance methodology that delivers results in a timely fashion and the level of institutional compliance to evidence-based interventional strategies that are triggered upon positive (MSSA or MRSA) surveillance findings.

Unfortunately, the majority of active surveillance studies have been conducted in medical (ICU) patient populations and studies that focus strictly on surgical populations are limited in both scope of practice and effective evidence-based interventions. The current paucity of well-designed clinical trials effectively limits a global consensus endorsing active staphylococcal surveillance as a general risk reduction practice across surgical disciplines.

Although peer-reviewed evidence suggests that active screening may play a role in reducing risk in selective, at-risk patient populations, applying this strategy to all surgical patient populations is viewed by many as unwarranted because: (a) Mandating universal surveillance precludes local assessment of risk and prioritization of healthcare resources, (b) it limits the ability of local officials to develop an integrated program based upon specific need, and (c) it does not take into account the ''moving target'' nature of evidence-based medicine, which may over time altering the scope and focus of organism-specific surveillance.

Suppression, Current, and Alternative Regimens

Nasal mupirocin has been widely used for the suppression of nasally carried *S. aureus* (MSSA and MRSA) in surgical patients or high risk patients for over 20 y [60,61]. However, the clinical studies documenting the benefit in surgical patients are often poorly designed, lacking adequate control groups and generally of poor scientific quality. A prospective study published in 2001 reported on the use of nasal mupirocin in open heart procedures in non-diabetic and diabetic patients. Overall, nasal mupirocin was effective in reducing the sternal SSI rate (2.7% vs. 0.9%, $p < 0.005$) and post-operative stay (12.1 compared with 38.4 d, $p < 0.004$) compared with a control (untreated) group. The authors concluded that mupirocin was safe, inexpensive, and effective in reducing the overall risk of sternal surgical site infections [62]. Unfortunately, the study was not designed as a randomized control trial and therefore a selection bias could not be ruled out. In a separate prospective study by Kalmeijer et al., 614 orthopedics patients were randomized to mupirocin versus placebo. The suppression rate was substantially more effective in the treatment group compared with the control group (27.8% compared with 83.5%, $p < 0.05$). However, no substantial difference was noted either in the SSI rate between the mupirocin treatment and placebo groups or in the length of post-operative stay [63]. A careful analysis of the baseline infection rate in this patient population suggests that the study was not adequately powered for discerning a substantial difference between treatment and control groups.

In a randomized, double-blinded, placebo-controlled trial conducted in a surgical patient population (n = 3,864; general, gynecologic, neurological and cardiothoracic surgical patients), 23.1 percent of study participants were colonized with *S. aureus* in their anterior nares. Although the study documented that topical mupirocin had a substantial impact on reducing the risk of healthcare-acquired *S. aureus* infections (bacteremia, $p < 0.02$), topical treatment did not substantially reduce the overall rate of SSIs [64]. The authors did note that the overall rate of *S. aureus* SSI was quite low and less than half of the infections occurred in patients with *S. aureus* nasal carriage, which was lower than the original estimate. Finally, the authors found using molecular analysis (PFGE) that some of the infections were likely associated with strains transmitted from healthcare workers or other patients rather than endogenous nasal carriage strains. The authors concluded that mupirocin suppression was safe, exerting a protective benefit against selective healthcare-acquired infections and was a ''reasonable adjunctive agent to prevent such infections after surgery'' [64].

Keshtgar et al. documented using rapid MSSA PCR screening and suppression within 24 h of admission found that there was a statistically significant reduction in both MSSA-related SSIs and length of hospital stay [65]. A study by Bode et al. that included almost 7,000 patients proposed

that there was a benefit for MSSA screening and suppression. However, there were several flaws in the study methodology, which included selective operational deficiencies; for example, only a small proportion of patients were actually randomized, which opens up the possibility of investigational bias [66]. The overall benefits of designing a surveillance and decolonization strategy that includes methicillin-sensitive *S. aureus* (MSSA) is controversial but advocates would suggest that given the high percentage of device-related SSIs caused by MSSA including these organisms in a comprehensive risk reduction strategy is warranted.

Although mupirocin has been viewed as the ''gold-standard'' for ''short-term'' suppression of MRSA, it has been less effective as a ''long-term'' agent. A separate analysis evaluated the efficacy of a 7-d combined course of topical and systemic agents that include 2% chlorhexidine gluconate body-cleansing, 2% mupirocin topical application to the anterior nares (twice daily), rifampin (300 mg bid) and doxycycline (100 mg, bid) in a hospitalized patient population. Combination therapy was initiated within 4 d of positive (MRSA) culture result and the comparator group was no intervention. Follow-up cultures were obtained from the anterior nares, perineum, skin lesion site, vascular access sites and other sites that may have initially yielded MRSA. At 3 and 8 mo, 74% and 54% of treated patients, respectively, were culture negative for MRSA compared with the non-treatment group ($p < 0.0001$). The study suggests that in hospitalized patients, MRSA can be successfully suppressed (long-term) using a 7-d combination therapy of CHG cleansing, topical mupirocin, and oral rifampin/doxycycline [67]. The implication of this approach for surgical patients undergoing elective surgery is unknown. However, in those hospitalized surgical patients who have documented persistent staphylococcal (MRSA) carriage, this may be an effective (alternative) suppression strategy, especially in high-risk surgical patients.

A cautionary comment on mupirocin is warranted. Current epidemiologic trends, in combination with the push to improve clinical outcomes, have in part led to an increased usage of mupirocin to suppress MRSA colonization in selected surgical patient populations. In most cases, this practice has been combined with institutional-initiated, active surveillance programs, documenting MRSA carriage. The decision to use topical mupirocin, when confronted with a positive MRSA surveillance culture, would in those circumstances be deemed appropriate. What should be considered questionable, however, is the ''routine'' use of mupirocin in medical, surgical, or high-risk patient populations where there is no documentation of MRSA or MSSA carriage [68]. Although data quantifying the risk associated with the emergence of mupirocin resistance in short-term or long-term, empiric use would appear to be ambiguous. In general we have observed resistance develop in those healthcare facilities which have unrestricted policies allowing use of mupirocin for prolonged periods of time. A recent analysis from Great Britain has looked at the relative transmissibility of mupirocin-resistant (MupR) strains of *Staphylococcus aureus* within the ICU and general patient population and found that resistant strains were less transmissible than sensitive (MupS) strains [69]. That said, the authors urge caution in adopting a widespread or universal approach to decolonization with mupirocin. Given, that at present, mupirocin is the only topical agent documented to have a benefit in eliminating MRSA carriage, institutional efforts should be taken to insure that inappropriate use is limited and subject to review under ''antibiotic stewardship'' guidelines.

Active Screening from a Cost-Effectiveness Perspective

Active screening is viewed by many healthcare practitioners as an effective strategy for identifying colonized patients who may be at risk for healthcare-associated infections, including SSI [70]. Whether or not this practice is cost-effective in the current environment of ''value-added purchasing'' is another matter. Two recent publications have attempted to address this question by using two different modeling strategies. In a study by Kang et al., cost-effectiveness was evaluated in a simulation model of an 800-bed tertiary care academic hospital. The three screening strategies were universal surveillance, targeted screening or no screening. The model captured the cost associated with use of PCR technology to rapidly identify patients with MRSA carriage. In this analysis, targeted screening was found to be the most effective strategy, preventing 59 MRSA HAIs with an associated total cost saving of $282,770 compared with no surveillance. Compared with no screening, a universal screening strategy was projected to prevent 93 MRSA but at a substantially greater cost ($1,391,742). Targeted screening was assessed as a cost-effective strategy in healthcare institutions where MRSA infections are ''highly endemic'' [71].

A second study using an alternative simulation model to estimate cost associated with active MRSA screening concurred with the previous study, suggesting that under high or medium (MRSA) prevalence conditions the most cost-effective screening strategy was a targeted (selective) screening process using either PCR or chromogenic media [72]. Based upon these two findings, it would appear that targeted screening is the most cost-effective strategy when compared with universal MRSA screening. Unfortunately, most published cost-effectiveness studies looking at averting MRSA dissemination and related infections have been conducted in general or ICU patients not surgical patient populations. However, it is conservatively estimated that a patient who develops an MRSA healthcare-associated infection incurs excess medical expenses of approximately $24,000 [73]. Using that metric as a baseline, Peterson et al. documented, after 4 y of an active MRSA screening program, a total 406 ''avoided'' MRSA infections (compared with baseline), resulting in a potential $8.8 million in preventable savings [74]. At present, the optimum strategy for preventing MRSA surgical site infections is unknown, given the myriad of intrinsic and extrinsic patient risk factors. Future studies are warranted, identifying the sentinel role that active MRSA screening plays as an adjunctive component of a comprehensive multi-faceted risk-reduction strategy in the surgical patient population.

A Pragmatic Consideration of Active Staphylococcal Surveillance in the Surgical Patient as a Risk Reduction Strategy

The 2015 CDC Guidelines for the Prevention of Surgical Site Infections does not include active staphylococcal (MRSA or MSSA) surveillance/suppression in either the ''Core'' or ''Arthroplasty'' sections of the guideline. In light of the current

evidence-based literature, the following considerations are warranted:

- Selection of an efficacious (risk-reduction, cost-effective) active screening strategy (universal or targeted) should be based upon the relative risk of MSSA or MRSA healthcare-associated infection in selective surgical patient populations.
- In the absence of targeted or universal screening, routine topical mupirocin or systemic antimicrobial agents is not currently recommended for the elimination of MSSA or MRSA carriage in surgical patients.
- In the case of targeted screening, preoperative decolonization may be considered for MSSA and MRSA colonized patients undergoing selective surgical procedures, such as cardiovascular, vascular procedures with implantation of prosthetic graft and orthopedic total joint procedures. The benefit of targeted screening-preoperative decolonization in other device-related surgical procedures (i.e., implantation of neurosurgical hardware, hernia repair with mesh, etc.) is unknown and currently not supported by the medical/surgical literature.
- The optimal suppression regimen is unclear, but a standardized regimen of topical nasal mupirocin (twice a day for 5 d) and 2% or 4% chlorhexidine gluconate-body cleansing (once a day for 2–3 d) prior to surgical admission is recommended [75].

Author Disclosure Statement

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Address correspondence to:
Dr. Charles E. Edmiston, Jr
Division of Vascular Surgery
Department of Surgery
9200 West Wisconsin Avenue
Milwaukee, WI 53226

E-mail: edmiston@mcw.edu