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Review

Staphylococcus aureus and surgical site infections: benefits of screening and decolonization before surgery

H. Humphreys [a,b,*], K. Becker [c], P.M. Dohmen [d,e], N. Petrosillo [f], M. Spencer [g], M. van Rijen [h], A. Wechsler-Fördös [i], M. Pujol [j], A. Dubouix [k], J. Garau [l]

[a] *Department of Clinical Microbiology, Royal College of Surgeons in Ireland, Dublin, Ireland*
[b] *Department of Microbiology, Beaumont Hospital, Dublin, Ireland*
[c] *Institute of Medical Microbiology, University Hospital Münster, Münster, Germany*
[d] *Department of Cardiovascular Surgery, Charité Hospital, Medical University Berlin, Berlin, Germany*
[e] *Department of Cardiothoracic Surgery, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*
[f] *Clinical and Research Department, National Institute for Infectious Diseases 'L. Spallanzani', Rome, Italy*
[g] *Department of Quality and Patient Safety, Universal Health Services, King of Prussia, Pennsylvania, PA, USA*
[h] *Laboratory of Microbiology and Infection Control, Breda, The Netherlands*
[i] *Department of Antibiotics and Infection Control, Rudolfstiftung Hospital, Vienna, Austria*
[j] *Infectious Disease Service, Bellvitge University Hospital, Barcelona, Spain*
[k] *Microbiology Department, Clinique de L'Union, Saint Jean, France*
[l] *Department of Medicine, Mutua de Terassa University Hospital, Barcelona, Spain*

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SUMMARY

Surgical site infections (SSIs) are among the most common healthcare-associated infections, and contribute significantly to patient morbidity and healthcare costs. *Staphylococcus aureus* is the most common microbial cause. The epidemiology of *S. aureus* is changing with the dissemination of newer clones and the emergence of mupirocin resistance. The prevention and control of SSIs is multi-modal, and this article reviews the evidence on the value of screening for nasal carriage of *S. aureus* and subsequent decolonization of positive patients pre-operatively. Pre-operative screening, using culture- or molecular-based methods, and subsequent decolonization of patients who are positive for meticillin-susceptible *S. aureus* and meticillin-resistant *S. aureus* (MRSA) reduces SSIs and hospital stay. This applies especially to major clean surgery, such as cardiothoracic and orthopaedic, involving the insertion of implanted devices. However, it requires a multi-disciplinary approach coupled with patient education. Universal decolonization pre-operatively without screening for *S. aureus* may compromise the capacity to

* Corresponding author. Address: Department of Clinical Microbiology, RCSI Education and Research Centre, Beaumont Hospital, PO Box 9063, Dublin 9, Ireland. Tel.: +3531 8093708/3710; fax: +3531 8092871.
E-mail address: hhumphreys@rcsi.ie (H. Humphreys).

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monitor for the emergence of new clones of *S. aureus*, contribute to mupirocin resistance, and prevent the adjustment of surgical prophylaxis for MRSA (i.e. replacement of a beta-lactam agent with a glycopeptide or alternative).

Introduction

Worldwide, the prevalence of healthcare-associated infections (HAIs) is approximately 4.5–15.5% in hospitalized patients.[1,2] These infections are strongly associated with the resource setting, and the estimated incidence in acute care hospitals in the USA and Europe is 4.5 and 7.1 per 100 hospitalized patients, respectively, corresponding to 1.7 and 4.1 million affected patients.[1,3] Allegranzi *et al.* conducted a meta-analysis on endemic HAIs in resource-poor countries, and documented a rate as high as 15.5 per 100 hospitalized patients.[2]

In resource-rich countries, surgical site infections (SSIs) are the third most common cause of HAIs, but in income-poor settings, they are the most common HAI.[3–5] The incidence of SSIs varies according to operative procedure, with an overall rate of 5.6% in income-poor countries, 2.6% in the USA and 1.6% in Germany.[2,6,7] The incidence of SSIs after major clean surgical procedures differs according to the procedure, with 10.8% for cardiac surgery, 7% for vascular procedures, 2.4% for orthopaedic procedures and 4.8% for breast surgery. *Staphylococcus aureus* is the most common cause, and nasal colonization with *S. aureus* is the most important independent risk factor for the development of an SSI in clean surgery.[4] The rate of *S. aureus* SSI is two to nine times higher in carriers than in non-carriers.[5]

The impact of SSIs includes significant morbidity and mortality, and increased direct healthcare costs.[8] The mean postoperative length of stay (LOS) is 10 days for SSIs, with a resultant additional healthcare cost of €19 billion for European health services.[9] In the USA, it is estimated that out of 80 million procedures carried out annually, SSIs occur in approximately 1.9%, and account for 69,475 HAIs.[10] Jenks *et al.* calculated the economic cost for additional LOS due to SSIs in the UK to be 23 days for cardiac procedures, 10 days for vascular procedures, 17 days for hip replacement, and three days for breast surgery, reflecting healthcare-acquired costs of £11,003, £2480, £3214 and £1469, respectively.[4] In a multicentre study of 659 surgical patients, Anderson *et al.* compared patients with meticillin-resistant *Staphylococcus aureus* (MRSA) SSIs or meticillin-susceptible *S. aureus* (MSSA) SSIs with uninfected controls.[11] While meticillin resistance was not associated with increased mortality, it was associated with 10 days of additional hospitalization. Patients with SSIs also required more visits by hospital providers (46/89 vs 61/178 for patients without SSIs; $P=0.008$), had greater need for home help [55/89 vs 84/178; $P=0.009$), and had a greater requirement for medical equipment (33/89 vs 39/178; $P=0.008$).[12]

There are various strategies to minimize SSIs, and these can be classified as those interventions occurring before, during and after surgery. One is to decolonize patients with *S. aureus*, especially before elective surgery. However, another approach recommends that all patients due for surgery should be decolonized without prescreening for *S. aureus*.[13,14]

A literature review was conducted regarding recent changes in the epidemiology of *S. aureus*, especially MRSA, and the consequences of screening and decolonization of patients who were positive for *S. aureus*. Relevant studies published in PubMed from 2000 to February 2016 were reviewed, as well as key studies published before this time using the following search terms: surgical site (wound) infection, *S. aureus*, MRSA, surveillance, screening, surgery, decolonization, cost effectiveness and related topics. Emphasis was placed on sourcing and reviewing original papers describing controlled clinical trials or quasi-experimental studies involving interventions to prevent SSIs due to *S. aureus*. In addition, the reference lists of papers were reviewed to determine if there were other studies that should be included, but which were not detected in the original literature search.

Changing epidemiology of MRSA and its implications

Regarding the molecular epidemiology of *S. aureus*, one must distinguish between its genomic background based on a relatively stable core genome, and the gain or loss of mobile elements, including the MRSA-determining SCC*mec* element, whereby evolution of both do not necessarily correlate.[15] Due to MRSA being a major nosocomial pathogen with more limited therapeutic options compared with MSSA, there have been more reports on MRSA subsequent to its worldwide emergence. This holds true despite MSSA accounting for the majority of *S. aureus* bloodstream infections (BSIs).[16] In contrast to other pathogens, such as pneumococci or meningococci, the population structure of *S. aureus* is highly clonal, and while there is an overlap between the genetic backgrounds of MRSA and MSSA, the latter are more genetically diverse and more widespread geographically.[17–19] Despite a decrease in the prevalence of MRSA in several countries, the global impact of MRSA on healthcare systems continues with significant morbidity, mortality and associated socio-economic burden.[20–23]

Changes in clonal lineages

There is often an erroneous view that MRSA represents a uniform subpopulation of *S. aureus*. While this is justified for many, but not all, MRSA control measures, therapeutic aspects and antibiotic stewardship concerns require a differentiated approach. In fact, MRSA comprise a multitude of more or less epidemiologically successful clonal lineages with huge differences in resistance patterns and virulence factors.[24,25] Thus, local infection prevention and control specialists and clinicians caring for patients should know the current and emerging MRSA strains. Regular screening of patients at risk for MRSA and the characterization of isolates is therefore mandatory in providing details of the local, national and international epidemiology.[26]

While some pandemic or epidemic lineages may persist globally or locally for years, others may emerge or disappear

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over a few years.[23,27,28] For decades, multi-resistant, healthcare-associated (HA) MRSA was synonymous with MRSA. However, the sudden arrival of hitherto less significant lineages, and the subsequent epidemiological success of community-associated (CA)[29,30] and livestock-associated (LA) MRSA[31,32] lineages within a few short years, are prime examples of the adaptability of MRSA as a pathogen. Moreover, there are two, not necessarily linked, molecular evolutionary processes: (i) the macro- and micro-evolution of the clonal lineage itself, as traceable by genotyping methods (e.g. multi-locus sequencing, *spa* typing or whole-genome sequencing); and (ii) the uptake/loss and evolution of the genetic element encoding meticillin resistance on the staphylococcal cassette chromosome *mec* (SCC*mec*).[33,34] Different types and subtypes of the SCC*mec* element may occur in the same clonal lineage, and different clonal lineages may harbour identical SCC*mec* elements.[35] These mobile elements not only determine beta-lactam resistance, with the exception of newer cephalosporins with MRSA activity, but also carry additional genes encoding virulence factors and/or resistance to non-beta-lactam antibiotics, metals (e.g. cadmium, copper) and metalloids (arsenic). Consequently, knowledge of commonly occurring SCC*mec* is relevant for clinical decisions.

New clonal MRSA lineages may be epidemiologically different, such as those occurring in patients not previously thought to be at risk of acquisition, or there may be different routes of transmission. They may even carry fewer common virulence factors, with the consequence of reduced rates of infection, or they may exhibit different resistance patterns. The recent global spread of CA-MRSA lineage USA300, which carries the prophage-located Panton-Valentine leucocidin (PVL), is a good example of this. This toxin and altered genome-encoded toxins, such as alpha-toxin and phenol-soluble modulins, have been associated with previously uncommon MRSA-caused infections such as necrotizing pneumonia and necrotizing fasciitis/myositis.[35,36] In contrast to classical HA-MRSA, CA-MRSA can occur in young healthy individuals. The causative strains are typically not multi-resistant, and therefore there are more therapeutic options.[37] Moreover, knowledge of special MRSA clonal lineages known to be associated with PVL or other virulence factors (e.g. pyrogenic toxin, superantigens, exfoliative toxins) may also influence clinical management, such as the use of immunoglobulins in addition to antibiotics.

The ongoing spread of the most successful LA-MRSA clonal complex (CC) CC398 has a number of important features: it has novel transmission routes as a zoonotic pathogen; it exhibits resistance to arsenic, cadmium, copper and/or zinc; and it is usually tetracycline resistant, an important consideration for empiric treatment.[38–40] The proportion of CC398 in Europe ranges from $<$10% to $>$30% in pig-dense regions.[28,41] As with CA-MRSA, the differing epidemiology of LA-MRSA and their introduction into hospitals has led to changed guidelines for MRSA screening.[42] Individuals with professional livestock contact are at risk for MRSA colonization, and are considered to need screening in some countries.[43] There is increasing evidence for the transmission of LA-MRSA in the human population without known contacts with livestock or involvement in agriculture.[38,43]

Another new challenge is the discovery of MRSA isolates containing a novel SCC*mec*, type XI, encoding the highly divergent *mecC*, originally described as *mecA*$_{LGA251}$, which shares only 70% DNA homology with *mecA*.[44–46] Particularly challenging is the laboratory detection and identification of *mecC*-MRSA, as well as the determination of meticillin resistance.[47] A livestock origin is probable for these *mecC* strains.[34,44,48] While the prevalence of *mecC*-MRSA is currently $<$1% amongst humans, this gene and its related variants are widely distributed in *S. aureus* and coagulase-negative staphylococci recovered from wild and companion animals.[44,49–52]

To detect major outbreaks earlier and to identify potentially fatal clones, changes in antibiotic resistance and virulence properties should be monitored regularly amongst hospital and community isolates. Different clonal lineages may present typical resistance patterns or may be equipped with certain virulence factors, such as PVL-positive CA-MRSA. This is vital for optimal empiric therapy (i.e. to choose agents that act on protein biosynthesis to inhibit toxin production). Moreover, knowledge on the composition of the circulating clones is crucial for the investigation of MRSA transmission events, to determine populations at risk (e.g. farm workers colonized with LA-MRSA), and to quickly recognize those strains that may cause diagnostic difficulties.

Resistance to mupirocin and other topical agents

Administration of mupirocin to the nares and chlorhexidine (CHG) to the skin represents the cornerstone of decolonization in patients colonized with MRSA. The polyketide antibiotic, mupirocin, is a naturally occurring antibiotic compound produced by the soil bacterium *Pseudomonas fluorescens* as a mixture of pseudomonic acids A, B, C and D. Its rapid hydrolysis in body fluids and its low activity at higher pH levels leads to rapid breakdown in tissues, and precludes systemic administration. Thus, it was developed as a topical antibiotic primarily for bacterial infections of the skin. While initial in-vitro studies confirmed good activity against clinical isolates of *S. aureus*, Kavi *et al.* described that its frequent use/abuse, including its use without prescription in some countries, has been quickly followed by resistance and even outbreaks of mupirocin-resistant MRSA.[53]

There are currently two categories of mupirocin resistance: (i) chromosomal low-level mupirocin resistance (LMupR) with minimum inhibitory concentrations (MICs) from 8 to 64 (up to 256) μg/mL; and (ii) plasmid-borne high-level mupirocin resistance (HMupR) with MICs $\geq$512 μg/mL. Isolates carrying both LMupR and HMupR resistance have been described.[54] Low-level mupirocin resistance occurs via a variety of amino acid changes in the native isoleucyl-tRNAsynthetase due to non-synonymous mutations in the respective gene, *ileS*.[54] While the mutation frequency is approximately 10^{-8} to 10^{-9} per bacterium per generation, administration of mupirocin mimics the effect of amino acid starvation, which results in an increase in the mutation rate.[55] The clinical significance of LMupR in terms of decolonization has yet to be determined.[56] This is in contrast to the more clinically significant HMupR, which is generated by the acquisition of the plasmid-located *mupA* (*ileS-2*) gene encoding another isoleucyl RNA synthetase.[54] Respective plasmids can be conjugative, and the *mupA* gene is flanked by insertion sequences, both of which may facilitate HMupR exchange between plasmids and staphylococcal isolates.[57] Particularly worrying are in-vivo transfers of *mupA* plasmids within different clonal lineages of *S. aureus*, as well as between *S. aureus* and *Staphylococcus epidermidis*.[58,59] There is evidence that such conjugative transfer of HMupR from

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S. epidermidis to *S. aureus* can occur in a clinical situation following mupirocin treatment. Thus, nosocomial mupirocin-resistant coagulase-negative staphylococci may act as a reservoir for the transmission of HMupR.[60] Moreover, HMupR-bearing plasmids often confer resistance to aminoglycosides, tetracyclines, macrolides, lincosamides, streptogramin B, penicillin and trimethoprim, which leads to the spread of multi-drug-resistant clones.[61]

In recent years, increasing mupirocin resistance amongst *S. aureus* isolates, particularly MRSA, has been recognized in many countries (Table I). Mupirocin resistance varies from 3% to 10%, but some studies report overall rates (LMupR and HMupR) of 60–90%. In the University of Geneva Hospitals, mupirocin resistance among blood culture isolates peaked at 95% in 2005, and variations in resistance rates correlated with mupirocin consumption.[62] This strong association with mupirocin exposure holds true for both LMupR and HMupR. Increased use of mupirocin also leads to the emergence of mupirocin-resistant coagulase-negative staphylococci (CoNS).[63,64] When both *S. aureus* and CoNS were studied, a higher prevalence of mupirocin resistance was recorded amongst CoNS.[63,64] In epidemiological studies, single HA- and CA-MRSA as well as CoNS clonal lineages were found to be associated with HMupR, substantially increasing the overall prevalence.[65,66] Also, Ahmed *et al.* demonstrated mupirocin-resistant MRSA isolates detected in nasal swabs from healthcare workers.[67] Mupirocin administration should be integrated into local antibiotic stewardship programmes to avoid selection pressure arising from inappropriate use. Thus, this agent should be restricted to targeted nasal MRSA and MSSA decolonization purposes, and its use should be preceded by screening. Knowledge of the circulating MRSA strains in the hospital and community is important to detect HMupR-associated clonal lineages quickly.

Poovelikunnel *et al.* recommend that increasing mupirocin resistance, and the consequent limitations in its use, warrants the discovery and evaluation of other topical agents, such as CHG, octenidine dihydrochloride, polyhexanide, sodium hypochlorite, omiganan pentahydrochloride, ethanol, tea tree oil, honey, probiotics and silver, as reviewed recently.[68] Also, lysostaphin, recombinant bacteriophage endolysins and, possibly, alcohol-based nasal antiseptics, which are supported by some good in-vitro data, may represent alternatives in the future.[69–71] However, clinical trials for these agents are awaited.

Emerging resistance to the widely used antiseptic CHG and other biocides has been reported. The possession of genes encoding resistance to CHG (*qacA* and/or *qacB*) ranges from 65% to 91% among MRSA isolates.[68,72] CoNS are also affected by biocide resistance and, in a French study, more than 40% of CoNS isolated from catheter-associated BSIs in preterm neonates exhibited decreased susceptibility to at least one antiseptic tested.[73] Moreover, the concurrent spread of MRSA and MSSA with low-level mupirocin resistance and elevated MICs for antiseptics has been reported recently.[74]

The ever-changing local, national and international epidemiology of MRSA, and the threat of antibiotic and biocide resistance require regular, broader characterization of isolates from carriers and from patients with infection. This will help to inform new therapeutic approaches and enhanced infection prevention and control measures, but is predicated on having isolates that are not available in the absence of surveillance screening.

Table I
Global threat of mupirocin resistance in staphylococci: selection of studies published in the past decade

Country	Source	Species	Percentage (%) of mupirocin-resistant isolates		Reference
			LMupR[a]	HMupR	
France	Nasal swabs from ICU and orthopaedic surgery patients	*S. aureus*	0.0	0.0	75
		CoNS	1.9	4.9	
India	Various clinical specimens	*S. aureus* (MRSA)	16.7	36.1	76
USA	Mainly deep swabs from outpatients with SSSIs	*S. aureus*	1.8	8.7	77
France	Catheter-associated BSIs in very preterm neonates	CoNS	2.0	58.8	73
UK	Nasal swabs from elderly care home residents	*S. aureus* (MRSA)	1.4	3.9	65
France	Various clinical specimens, mainly from	*S. aureus* (MRSA)	0	0.8	64
	BSIs and osteoarticular infections	CoNS	0.8	5.6	
Brazil	Mainly BSIs	*S. haemolyticus*	1.6	7.8	78
Netherlands	Blood culture isolates	CoNS	5.5	12.8	63
China	Various clinical specimens	*S. aureus* (MRSA)	0.0	6.6	79
Germany	Various clinical specimens	*S. aureus* (MSSA)	0.5	0.0	80
		S. aureus (MRSA)	6.9	2.5	
		S. epidermidis	17.5	4.0	
		S. haemolyticus	2.4	0.0	
Ireland	Blood, wound and MRSA screening specimens	*S. aureus* (MRSA)	0.0	3.0	81
		S. aureus (MSSA)	0.0	1.0	
		CoNS	10.0	22.0	
South Africa	Various clinical specimens	*S. aureus*	7.0	0.9	82

BSIs, bloodstream infections; CoNS, coagulase-negative staphylococci; HMupR, high-level mupirocin resistance; ICU, intensive care unit; LMupR, low-level mupirocin resistance; MRSA, meticillin-resistant *S. aureus*; MSSA, meticillin-susceptible *S. aureus*; SSSIs, skin and skin structure infections.
[a] Designated as 'mupirocin intermediate' in some publications.

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Impact of decolonization on *S. aureus* surgical site infections

Evidence

A recent systematic literature analysis has confirmed key components in the prevention and control of MRSA and the evidence underpinning them.[83] According to macro-epidemiological data and mathematical models, infection control measures that do not incorporate screening may fail to reduce MRSA spread effectively, most likely due to a failure in the full implementation of targeted infection control measures.

Decolonization with mupirocin has been shown to be effective in reducing SSIs due to antibiotic-resistant and -susceptible *S. aureus*.[84] Lee *et al*. undertook a prospective control study on clean surgery wards with a combination of MRSA screening, contact precautions and decolonization which resulted in decreased MRSA rates.[85] Many of the studies involved elective cardiothoracic and prosthetic joint surgery. While some focused on MRSA, many of the measures implemented were effective in reducing both MRSA and MSSA.[84] Other studies describing a series of measures, including screening and decolonization, have shown these measures to be effective.[5,86–92] Schweizer *et al*. undertook a study to reduce SSIs among patients undergoing cardiac, hip and knee surgery in nine US states involving 20 hospitals.[86] Adherence to the protocol was 83%, and there was a significant decline in *S. aureus* infections in both orthopaedic and cardiothoracic surgery. van Rijen *et al*. showed that screening patients undergoing cardiothoracic or orthopaedic surgery for *S. aureus* nasal carriage, with a subsequent decolonization protocol, resulted in a substantial reduction in hospital costs.[90] In another study, the nares were screened at least one week before orthopaedic surgery using rapid polymerase chain reaction (PCR) for both MRSA and MSSA.[5] Positive patients completed a five-day decolonization protocol with 2% nasal mupirocin twice per day and daily bathing with CHG before surgery in their home. If a repeat nasal specimen was MRSA positive, contact precautions (CPs) were introduced in the operating room and nursing units, and all such patients received adjusted surgical prophylaxis to cover for MRSA, such as a glycopeptide. Approximately 96% of 7338 patients were screened before elective orthopaedic surgery and, following decolonization of carriers, the SSI rate fell significantly to 0.19% compared with historical controls, for whom the rate was already low at 0.45%.[87]

In a systematic review of 19 studies involving orthopaedic patients screened for *S. aureus*, and decolonized if positive, Chen *et al*. showed an overall reduction in SSI rates ranging from 13% to 200%, including a reduction in *S. aureus* SSI rates from 40% to 200%, and a reduction in MRSA SSI rates from 29% to 149%.[89] Finally, in a Swiss study of 12 surgical wards when rapid screening for MRSA was undertaken pre-operatively amongst a variety of surgical specialties, 94% of 10,844 patients were screened.[91] However, a combination of screening and decolonization of positive patients did not lead to a reduction in MRSA SSIs. In this study, CPs were only introduced after a positive result and not on suspicion, there was significant movement of patients between care units, and not all high-risk patients were screened.

Bode *et al*. conducted a randomized clinical trial with a treatment group that was screened by rapid PCR at the time of admission.[92] While no positive MRSA screens were noted, 18.8% were positive for MSSA. Positive patients received a five-day course of mupirocin/CHG for decolonization during hospitalization; negative patients received placebo (nasal ointment and regular soap). The SSI rate was 3.4% in the treatment group compared with 7.7% in the placebo group, with a reduction in mean hospital stay of almost two days.

Reduced costs are also associated with screening and decolonization in some areas of elective surgery. van Rijen *et al*. performed an economic evaluation of the Dutch study referred to above.[86,90] Despite the additional costs of screening and decolonization, the reduced infection rate meant that €2841 was saved per cardiothoracic patient and €955 was saved per orthopaedic patient in the screened patients.[90] Furthermore, the same authors recorded a reduction in one-year mortality from 7% to 3% in patients undergoing clean procedures (i.e. cardiothoracic, orthopaedic, vascular and others).[93] All the economic models in a review of 19 studies involving orthopaedic patients favoured the implementation of an *S. aureus* decolonization protocol.[89]

Logistical issues

S. aureus decolonization regimens require a multidisciplinary approach with the support of hospital administrators, nursing personnel, surgeons, hospital hygienists, medical microbiologist/infectious disease specialists and ancillary staff.[94] The programme challenges include:

- appropriate diagnostics in the microbiology laboratory or in other testing settings, the training of staff, and the communication of positive screen results and their significance;
- a system to facilitate pre-operative screening using nasal screening tests and ensuring patient compliance;
- creation of a multi-disciplinary group to include the pre-admission unit, presurgery unit, operating room, post-operative care unit, hospital hygienists, medical microbiologists/infectious disease specialists, and pharmacy/nursing/ancillary departments; and
- support or development of information systems for the rapid reporting of positive and negative screening results to patients, caregivers and relevant departments.

A patient education programme is essential, and the key features are outlined in Table II.

Another benefit of early detection is the potential for a greater focus on environmental contamination with MRSA and its eradication. Villamaria *et al*. sampled 32 non-contact precaution rooms (NCPRs) and 68 contact precaution rooms (CPRs). They found a higher burden of MRSA in the CPRs, as might be expected. The detection of MRSA in NCPRs may be due to residual contamination from prior occupants due to inadequate cleaning, or the shedding of MRSA from patients with intermittent colonization or extranasal colonization not detected at admission.[95] Hardy *et al*. conducted a study in a nine-bed intensive care unit over 14 months that showed widespread contamination of the hospital environment with MRSA, and highlighted the need for more effective cleaning of the environment to eliminate MRSA.[96]

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Table II
Education requirements for patients undergoing screening and decolonization before surgery

Theme	Specifics
Hand hygiene	Importance of personal hygiene
	Asking healthcare workers if they have decontaminated their hands
Staphylococcus aureus	What is MRSA/MSSA?
	Measures to prevent transmission
	Importance of environmental cleaning
Decolonization	What are mupirocin and CHG?
	Where to access and how to apply decolonization agents
	Importance of compliance

MRSA, meticillin-resistant *S. aureus*; MSSA, meticillin-susceptible *S. aureus*; CHG, chlorhexidine.

Consequences of universal decolonization

There is debate about whether universal decolonization in the absence of screening is easier and more effective. Courville *et al.* compared selective screening with decolonization of positive patients alone, universal screening with decolonization of positive patients, and no screening but universal decolonization.[97] While decolonizing all patients was the best strategy to maintain a low rate of MRSA, screening was cost-effective in certain categories of patients, but the risk of mupirocin resistance remained.[97] In a study using a Dutch database of patients undergoing prosthetic joint or cardiopulmonary surgery, selective decontamination (assuming 100% compliance) was calculated to prevent seven SSIs from a base case of 14, and save €47,746 per 1000 patients; in contrast, decontamination of all patients prevented 11 infections and saved €178,970 per 1000 patients.[98] Other economic models have made a strong case for screening and decolonization in cardiac surgery; vascular surgery; and heart, lung and transplant surgery.[99–101] For cardiac surgery, the incremental cost-effectiveness ratio was under $15,000 per quality-adjusted life year, and was less than $50,000 for vascular surgery.[99,101]

Decolonization without prior screening of all patients in other clinical settings is a component of some MRSA control strategies (i.e. a horizontal infection prevention and control measure). In a large cluster-randomized trial conducted by Huang *et al.* in US intensive care units, the application of mupirocin to the nares in combination with daily CHG bathing of all patients (i.e. universal decolonization) reduced all BSIs, but not MRSA BSIs or MRSA rates overall. However, the emergence of mupirocin resistance was not investigated.[102]

The widespread use of mupirocin can engender resistance, and mupirocin resistance has been reported in some studies of MRSA decolonization.[103–105] In a Brazilian teaching hospital, Vivoni *et al.* showed that resistance peaked at 65% of MRSA isolates when patients were treated empirically, but resistance rates fell when mupirocin was restricted to MRSA-colonized patients alone.[106] In a Swiss hospital, a hospital-wide policy to decolonize MRSA carriers with intranasal mupirocin application started in 1994. The proportion of MRSA blood culture isolates with mupirocin resistance, mostly low-level resistance, increased from 0% in 1999 to 95% in 2005, and was 89% in 2008.[62] The increased resistance levels correlated with mupirocin use during those periods. There is therefore a clear correlation between empirical mupirocin use and the emergence of mupirocin resistance amongst MSSA, MRSA and *S. epidermidis*. Finally, in a simulation based on real hospital data, Deeny *et al.* recently confirmed that a 'screen and treat' strategy maintains a low level of mupirocin resistance, whereas 'universal mupirocin use' leads to an increase in mupirocin resistance in 50–75% of simulations.[107] Additional issues to consider are that universal decontamination in the absence of screening is likely to result in suboptimal data on resistance, the potential emergence of new but unrecognized clones, and, finally, the absence of the opportunity to adjust pre-operative antibiotic prophylaxis to cover for MRSA in patients who screen positive.

Conclusions

SSIs due to *S. aureus* are significant in terms of patient outcome, and consume precious healthcare resources. This is particularly true in orthopaedic and cardiothoracic surgery. The pre-operative identification of carriers of MSSA and MRSA, followed by decolonization before surgery, is associated with reduced SSI rates and cost savings. Recent studies confined to intensive care units have advocated universal decolonization, and have shown reductions in overall BSI rates and healthcare costs. While there may well be a case for such a horizontal infection prevention strategy in critically ill patients who may be colonized with multi-drug-resistant microbes, it should be considered with caution elsewhere because of the risk of the emergence of resistance. Screening and selective decolonization of patients positive for *S. aureus* have the benefits of preventing SSIs, helping to contain costs, monitoring changes in circulating isolates of MSSA and MRSA, and minimizing the emergence of resistance.

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Conflict of interest statement

HH is in receipt of research support from Pfizer and Astellas, and has received lecture and other fees from Novartis, AstraZeneca and Astellas. KB has received research support from Cepheid and Pfizer; and lecture, travel and other fees from Cepheid, Cubist Pharmaceuticals, Merck Sharp & Dohme (MSD), Novartis Pharma, Oxoid, Pfizer and Siemens Healthcare Diagnostics; and has participated in scientific boards for Roche Molecular Systems. PMD has received

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