Methicillin-Resistant *Staphylococcus aureus*: An Update on Prevention and Control in Acute Care Settings

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KEYWORDS

• Methicillin-resistant *Staphylococcus aureus* • MRSA • Epidemiology
• Infection prevention • Infection control • Active surveillance cultures • Screening
• Decolonization

KEY POINTS

- Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of health-care–associated infections and remains endemic in many health care facilities worldwide.
- Since the 2000s, there has been decreasing clinical and health-economic burden of MRSA compared with multidrug-resistant gram-negative bacteria worldwide, often following implementation of concerted and coordinated multifaceted interventions.
- A change in the epidemiology of MRSA has been noted with increasing introduction of community-associated MRSA into acute care settings (particularly pediatrics), requiring modified infection prevention and control measures (eg, including health care worker screening and contact tracing of household members).
- Despite overall successes in reducing the burden of this multidrug-resistant organism, the optimal approach to MRSA control has been controversial due to limited high-quality evidence to support interventions. However, over the past 15 years, new data from robust large-scale studies have emerged, particularly with regard to MRSA screening and decolonization (targeted and universal) strategies.
- Flexibility to adapt and institute evidence-based measures in the context of local epidemiology, infrastructure, and resources is essential for successful MRSA control.

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA), first described in 1961,[1] has become endemic in health care facilities worldwide. MRSA is a leading cause of skin and soft tissue infections presenting to emergency departments in the United States[2] and in many regions, a significant proportion of invasive infections due to *S aureus* are methicillin resistant (more than 50% in parts of Southern Europe and the Asia-Pacific region).[3,4] The virulence and survival fitness of this pathogen[5] likely contribute to the increased mortality, length of stay, and health care costs associated with MRSA compared with methicillin-sensitive *S aureus* (MSSA).[6] Given its significant impacts on human health, MRSA has been included in the World Health Organization's high priority list of drug-resistant bacteria targeted for the development of new antimicrobials.[7]

Strategies to control MRSA address the reservoir of carriers, routes of transmission, and antibiotic selection pressure (**Fig. 1**). In practice, multiple interventions are often used in an attempt to effectively curb transmission and infection. However, the utility of some control measures is debated due to the inability to eradicate endemic MRSA and the disruption in patient care and costs associated with some strategies.[8,9] Finally, many experts now argue that control of highly resistant gram-negative bacteria, such as carbapenemase-producing Enterobacteriaceae should have higher priority.[7,10,11]

This review provides an update regarding approaches to MRSA control in health care settings with endemic MRSA. Controversies surrounding control measures and recent evidence from rigorously conducted large studies also are discussed. This review does not cover the "search-and-destroy" strategy used in countries with low MRSA prevalence, such as the Netherlands and Denmark (refer to the national policy of the Dutch Working Party on Infection Prevention[12]), or the control of livestock-associated MRSA (see Ref.[13]).

DECLINING METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* RATES IN MANY REGIONS

MRSA epidemiology exhibits marked geographic variation. It is important to note, however, that data from different regions should be compared with caution due to varying definitions used for data collection, study populations, intensity of surveillance, and duration of follow-up. Prospective surveillance networks now exist in many regions, enabling early detection of increasing MRSA rates and facilitating timely

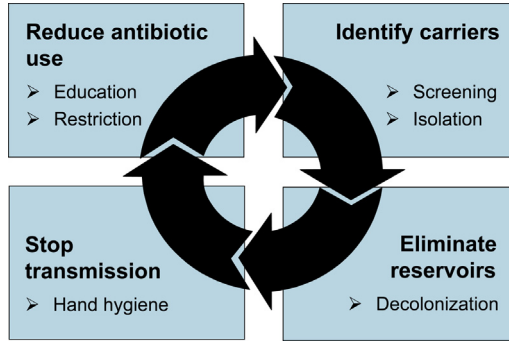


Fig. 1. Approaches to the control of endemic MRSA.

implementation of interventions. These data are also valuable for feedback to institutions, benchmarking and monitoring the success of control strategies.

Trends in Europe

Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net)[3] illustrate the marked variation in Europe in the proportion of *S aureus* isolates that are methicillin resistant. In general, there is an increase in MRSA prevalence from the north to south/east of the continent (**Fig. 2**). These differences are thought to be at least partly explained by varying antibiotic use and infection control practices.[14,15]

It is interesting to note that there have been steady or decreasing MRSA infections rates seen in a number of high-income countries from the early to mid-2000s (see **Fig. 2**). For example, although MRSA rates were high in France in the 1990s, the country subsequently experienced a decline in these rates (**Fig. 3**). This trend seemed to follow a stringent national control program gradually introduced between 1993 and 2004,[16] which included strengthening infection control activities, and mandatory MRSA surveillance and notification of outbreaks.

In the United Kingdom, MRSA bloodstream infections (BSIs) rose during the 1990s, peaking in 2003 with subsequent yearly reduction, then more recent plateauing in rates (**Fig. 4**). As was the case in France, this favorable trend followed implementation of a national strategy, including universal screening on hospital admission.[17] Although the national hand hygiene campaign is considered a major contributor to the decline in MRSA,[18] it is likely that the multifaceted approach, together with a clear target and support from the Department of Health, resulted in the marked improvement.

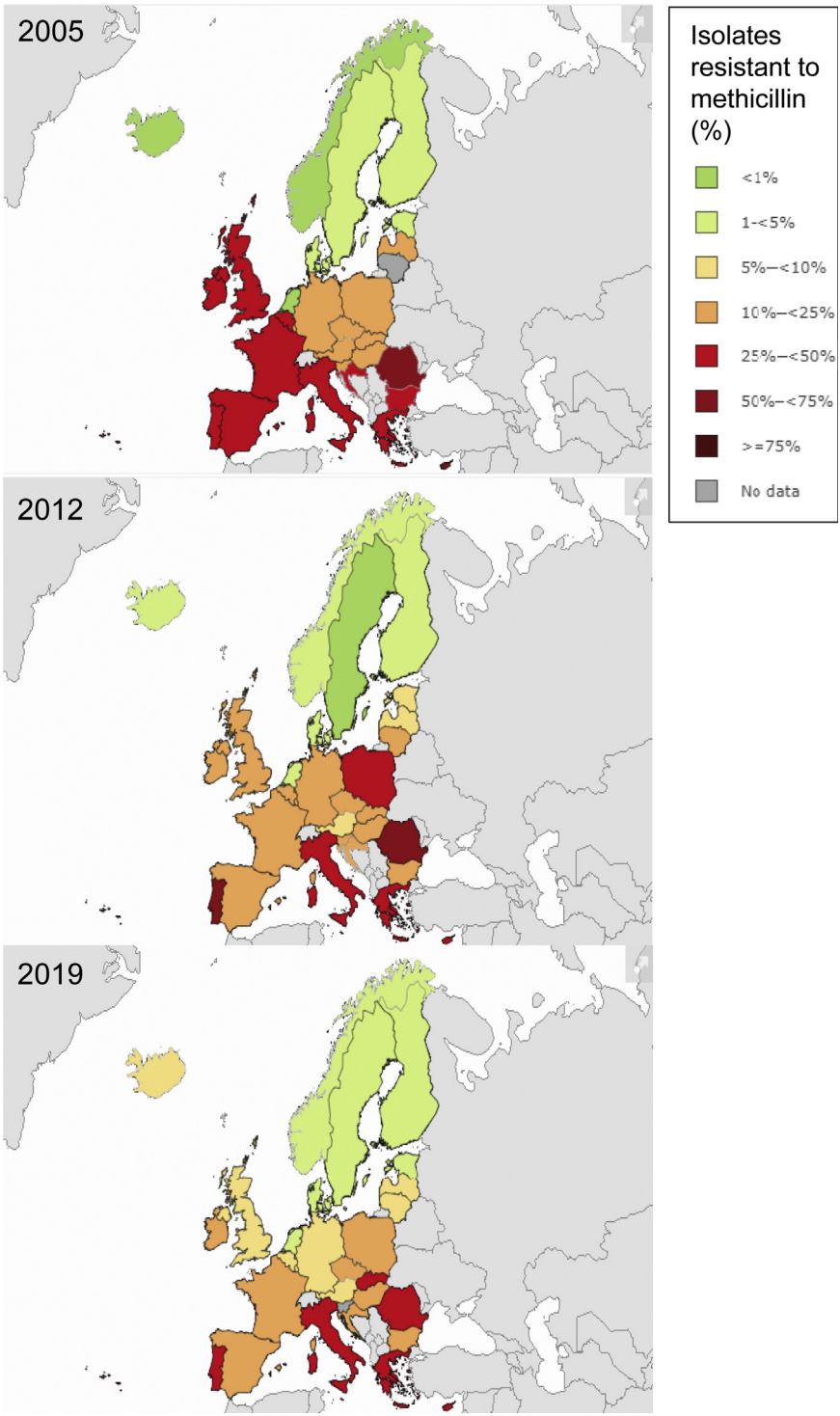
In addition to France and the United Kingdom, there is now a diverse group of European countries, with varying baseline MRSA prevalence, that have been able to reverse previously increasing trends in MRSA (see **Fig. 2**). Although the proportion of MRSA among *S aureus* isolates decreased in Europe from 27% in 2007 to 17% in 2015, a study of the burden of antibiotic-resistant bacteria in this region has estimated that the incidence of MRSA infections has actually increased by 1.28 times during this period, mainly due to infections in infants and older individuals (>55 years).[11]

Trends in the United States

In the United States, MRSA rates steadily increased from 1998, with MRSA accounting for 53% of *S aureus* clinical isolates in 2005.[19] Since that year, there has been a decrease in hospital-onset BSIs due to MRSA (17% annual reduction between 2005 and 2012, with a slower decline seen between 2013 and 2016).[20] As was the case in parts of Europe, a series of infection control interventions during this period may have contributed to the decline. In 2007, Veterans Affairs hospitals throughout the United States introduced a multimodal strategy involving universal MRSA screening, contact precautions, hand hygiene promotion, and institutional culture change.[21] Between 2005 and 2017, there was a 55% decrease in MRSA infections in Veterans Affairs hospitals.[22] Many US states also mandated specific MRSA control interventions,[23] and in 2008, the Centers for Medicare and Medicaid Services introduced financial penalties, declining additional payment to hospitals for preventable health-care–acquired complications such as health-care–associated infections (HAIs).[24]

Potential Explanations for Declines in Methicillin-Resistant Staphylococcus aureus

It is often difficult to identify the precise determinants of successful MRSA control. Decreasing MRSA rates may reflect improved infection control practices and enhanced antibiotic stewardship. Some argue, however, that widespread declines



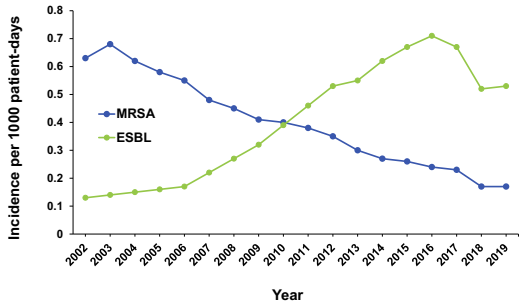


Fig. 3. French national surveillance data showing changes in the incidence of MRSA and extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (2002–2019). (Data *from* Santé publique France. Available at: www.santepubliquefrance.fr. Accessed March 26, 2021)

in MRSA are attributable to changes in the organism itself, including shifts in circulating clones.[25] An observational study in Oxford (United Kingdom) found that MRSA rates fell in line with national trends from 2003, but this decline preceded local roll-out of enhanced infection control interventions in 2006.[26] Typing data showed that the decline was strain-specific, particularly involving ST36. Similarly, areas of France where enhanced interventions were not implemented also experienced decreasing MRSA rates.[27]

Biological factors, such as reduced bacterial fitness manifesting as decreased survival and/or growth rate,[28] could explain the decline in particular strains. A Danish study explored this hypothesis by typing stored isolates from the first MRSA epidemic in Denmark (1957–1980). They found a significant fitness cost associated with multiple antibiotic resistances, which, based on mathematical modeling, could explain declines in phage complex 83A observed in Denmark.[29] The relative contribution of infection control strategies versus biological factors on declining MRSA rates remains an area of debate.

IMPORTATION OF COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* INTO HEALTH CARE SETTINGS

The importation of virulent and transmissible community-associated (CA-MRSA) into acute care settings poses challenges around the globe. Indeed, a growing body of evidence suggests that CA-MRSA lineages are increasingly responsible for HAIs.[30] Although no precise international surveillance data are currently available on this worrisome trend, several studies have reported epidemiologic data on CA-MRSA infections among hospitalized patients.

First, several US investigators have found an increase in the relative proportion of MRSA BSIs due to the endemic CA-MRSA USA300 strain, including hospital-onset BSIs, despite overall decreasing trends of MRSA BSI in the United States.[31,32] Second, many nosocomial CA-MRSA outbreaks have been reported, highlighting the

Fig. 2. Proportion of invasive *S aureus* isolates with methicillin resistance from 2005 to 2019 in countries participating in the European Antimicrobial Resistance Surveillance Network (EARS-Net). (*From* EARS-Net data. Available at: http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx. Accessed March 26, 2021; with permission)

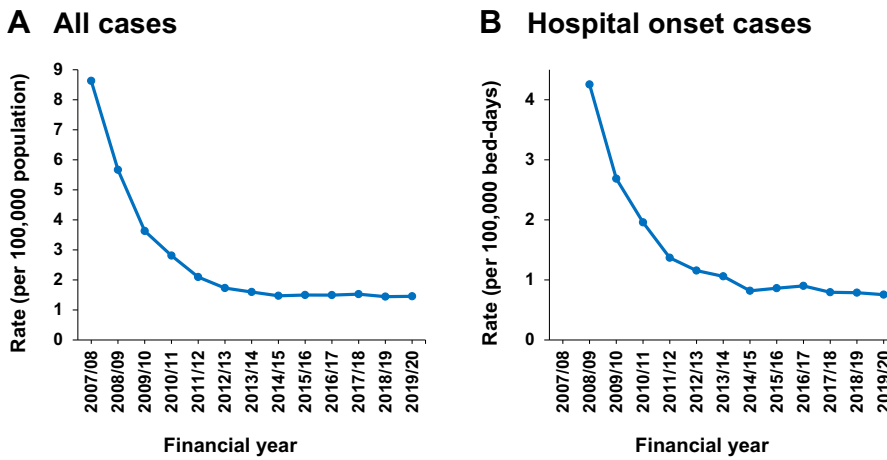


Fig. 4. Trends in rates of MRSA bacteremia in England per 100,000 population (*A*) and hospital-onset cases per 100,000 bed-days (*B*) (2007–2020). (*From* Public Health England. Available at: https://www.gov.uk/government/statistics/mrsa-mssa-and-e-coli-bacteraemia-and-c-difficile-infection-annual-epidemiological-commentary. Accessed March 26, 2021)

epidemic potential of CA-MRSA transmission in acute care settings.[33,34] Finally, mathematical models predict that CA-MRSA strains harboring smaller SCC*mec* elements will eventually displace traditional hospital-acquired MRSA strains in hospitals, with significant clinical and public health implications.[35]

Although this emerging trend is of concern, it does not fundamentally change preventive measures to control MRSA in hospitals, described later in this article in more detail. The only major exception may be the more aggressive staff screening policies implemented in the context of a documented CA-MRSA outbreak in a hospital ward, especially in the absence of an identified reservoir of patients colonized with CA-MRSA.[36]

RECENT EVIDENCE AND CONTROVERSIES REGARDING METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* CONTROL STRATEGIES

Before discussing research regarding MRSA control, it is important to highlight issues to consider before applying research findings to clinical practice. Studies often report the effect of multiple simultaneously implemented interventions, making it difficult to determine the relative contribution of each intervention. It is also noteworthy that studies have been conducted in the context of varying baseline MRSA prevalence. Thus, results may not be generalizable to all settings. Reporting bias, where negative studies are less likely to be published, must also be considered. In addition, many studies have suboptimal design and analysis. In the past, most studies have been observational or quasi-experimental, with few randomized controlled trials. Fortunately, data from several high-quality intervention studies are now available.

Research concerning MRSA control interventions has resulted in ongoing debate with regard to the utility of MRSA screening, isolation, decolonization, and environmental cleaning. The importance of hand hygiene and antibiotic stewardship is less controversial. The potential advantages and disadvantages of various interventions are summarized in **Table 1** and discussed in the following sections.

Table 1
Advantages and disadvantages of various methicillin-resistant *Staphylococcus aureus* control strategies

Infection Control Measure	Mode of Action	Potential Advantages	Potential Disadvantages/ Barriers to Implementation
Hand hygiene	Reduces cross-transmission	Simple Inexpensive Not organism specific	Requires behavior change Difficult to sustain high hand hygiene compliance rates
MRSA screening of patients	Early identification of carriers	Identifies reservoir Reduces infection risk for the individual patient (eg, appropriate perioperative antibiotic prophylaxis)	Costs Resources MRSA-specific Needs to be linked with other measures (eg, isolation, decolonization) Optimal population and method controversial
MRSA screening and decolonization of health care workers	Reduces reservoir	Complete assessment of reservoir Interruption of MRSA transmission to patients Reduction of infection risk for the individual health care worker Decreased transmission risk to close contacts/ community reservoir	Disruption to patient care False reassurance of noncolonized or nonidentified health care workers Ethical considerations (stigmatization) Costs
Isolation	Increased barrier to cross-transmission	Not organism specific	Costs Potential negative psychological effects Possible decrease in quality of care of patient
Targeted decolonization	Reduces reservoir	Interruption of MRSA transmission to other patients Reduces infection risk for the individual patient	Not feasible for all patients Risk of mupirocin and chlorhexidine resistance Side effects of decolonization treatment
Universal decolonization (routine chlorhexidine bathing)	Reduces reservoir	Reduces infection risk for the individual patient Not organism specific	Risk of chlorhexidine resistance Side effects of decolonization treatment
Antibiotic stewardship	Reduces selection pressure	Not organism specific (includes *Clostridium difficile*)	Opposition from physicians and pharmaceutical industry Most effective interventions unclear Long-term effects unclear
Enhanced environmental cleaning	Reduces environmental reservoir	Not organism specific	Strong evidence for efficacy lacking Best strategy unclear

Abbreviation: MRSA, methicillin-resistant *S aureus*.

Hand Hygiene

As MRSA is most commonly transmitted between patients via the contaminated hands of health care workers (HCWs), a multimodal approach to improving hand hygiene practices is an integral part of standard infection control measures.[37] The effectiveness of hand hygiene promotion has been demonstrated in terms of reductions in MRSA transmission and infections at local and national levels.[18,38–40] Although efforts to improve hand hygiene practices in health care facilities are important, controversy exists regarding the utility of attempts to further increase hand hygiene compliance in settings where baseline compliance is already high (>50%). In this situation, studies, including dynamic modeling, suggest that this intervention alone may not result in further significant reduction in MRSA transmission.[41,42]

Screening for Methicillin-Resistant Staphylococcus aureus

Most MRSA carriage is asymptomatic and therefore not identified using routine clinical cultures. The latter alone may only identify 18% of actual MRSA patient-days.[43] A significant number of colonized patients will subsequently develop infection, with estimates of up to 25% of patients in intensive care units (ICUs).[44] Active MRSA surveillance may identify this large asymptomatic reservoir of transmission and infection risk using screening cultures or more rapid nucleic acid amplification tests (NAATs), which are often polymerase chain reaction (PCR)-based assays. Patients identified to be colonized may then be placed on contact precautions and decolonization treatment, usually in the form of topical antibiotics and antiseptics, may be instituted in an attempt to eradicate carriage and/or reduce risk of MRSA infection.

Active surveillance may be universal, where all patients admitted to hospital are screened, or targeted, where screening is limited to patient groups at increased risk of colonization, such as those with prior antibiotic use, prolonged hospitalization, ICU admission, hemodialysis, or contact with a known MRSA carrier. Risk factors for MRSA colonization may vary in different regions[45,46]; therefore, targeted screening approaches should be tailored to local MRSA epidemiology. HCWs who are MRSA carriers can also act as reservoirs for outbreaks and ongoing transmission within hospitals, especially for CA-MRSA. HCW screening in settings with endemic MRSA is beyond the scope of this review but is discussed elsewhere.[36]

Until recently, universal MRSA screening has been one of the most controversial issues in infection control due to questions about its effectiveness, pathogen-specific approach, and costs, particularly for screening using NAATs.[9] Active surveillance is considered most useful in patients at high risk of MRSA infection, such as in outbreak settings.[47] More recently, studies have focused on universal screening in endemic settings to reduce infection risk, with conflicting results (**Table 2**).

In 2008, a hospital-wide observational study conducted in the United States showed that universal MRSA screening was associated with reduction in MRSA disease.[43] In contrast, a prospective crossover study in surgical wards of a Swiss hospital published the same year did not find a reduction in MRSA infections or acquisition.[48] Other studies have compared molecular-based and culture-based screening, also with varying results.[49,50] A large prospective multicenter study, reported in 2013 in 33 surgical wards in Europe and Israel, did not find that screening was associated with a reduction in MRSA infections overall.[51] However, screening combined with contact precautions and decolonization was associated with decreasing MRSA infection rates in the subgroup of clean surgery wards.

There have been a number of high-quality studies exploring the utility of MRSA screening in ICUs. Previous reports, predominantly retrospective or quasi-

Table 2
Selected studies of universal methicillin-resistant *Staphylococcus aureus* screening

Study, Country	Setting	Design	Control Group	Total Duration (mo)	Rapid Screening	Decolonization[a]	Admission MRSA Prevalence (%)	Baseline MRSA Infection Rate (per 1000 Patient-days)	Additional Interventions	Findings	Primary Outcome
Robicsek et al,[32] 2008, US	Hospital-wide	Before-after	No	45	Molecular (commercial) modified in-house	Targeted (at physician discretion)	6.3	0.89	Staged ICU screening then universal screening	Reduction in MRSA disease	Positive
Harbarth et al,[38] 2008, Switzerland	Surgery	Crossover	Yes	24	Molecular (in-house)	Targeted	5.1	0.91	Modified perioperative prophylaxis	No reduction in MRSA infections	Negative
Jeyaratnam et al,[39] 2008, UK	Geriatrics, Oncology, Surgery	Crossover	Yes	14	Molecular (commercial) vs selective broth/ chromogenic agar	Targeted	6.7	1.09	Preemptive isolation if high risk; discharge screening	No reduction in MRSA transmission	Negative
Hardy et al,[40] 2010, UK	Surgery	Crossover	Yes	16	Molecular (commercial) vs chromogenic agar	Targeted (with naseptin if high-level mupirocin resistance)	3.6	Not stated	Rescreening every 4 d; decolonization in 71% molecular vs 41% culture arms	Reduction in MRSA transmission	Positive
Huskins et al,[44] 2011, US	ICU	Cluster-randomized trial	Yes	17	Selective broth/ selective agar (mannitol salt agar with oxacillin)	No (but some targeted use at physician discretion)	9.5–12.4	13.7–13.9 (colonization and infection)	Rescreening weekly and on discharge	No reduction in MRSA transmission or infection	Negative

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Table 2
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Study, Country	Setting	Design	Control Group	Total Duration (mo)	Rapid Screening	Decolonization[a]	Admission MRSA Prevalence (%)	Baseline MRSA Infection Rate (per 1000 Patient-days)	Additional Interventions	Findings	Primary Outcome
Lee et al,[41] 2013, Europe and Israel	Surgery	Prospective interventional cohort	Yes	24	Molecular (commercial) and chromogenic agar	Targeted	2.1	0.56	Universal screening vs hand hygiene vs combination	No reduction in MRSA infection (except for clean surgery)	Negative
Huang et al,[45] 2013, US	ICU	Cluster-randomized trial	Yes	33	Not stated	Group 2 – Targeted Group 3 - Universal	10.2–11.5	3.4–4.3 (MRSA clinical cultures); 0.5–0.6 (bacteremia)	Group 1 – screening, isolation; Group 2 – screening, targeted decolonization; Group 3 – no screening, universal decolonization	No reduction in MRSA infection in Group 1	Negative (for screening without decolonization)
Derde et al,[46] 2014, Europe	ICU	Cluster-randomized trial	Yes	27	Molecular (commercial) vs chromogenic agar	Universal	3.6	Not stated	Hand hygiene and universal decolonization phase followed by screening phase	No reduction in MRSA transmission (for screening)	Negative
Roth et al,[108] 2016, Canada	Hospital-wide	Quasi-experimental	Yes	44	Selective broth/ molecular (commercial) with culture (nonselective agar) confirmation	No	2.6	0.47 (colonization and infection)	Nil	No reduction in MRSA transmission	Negative

Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant *S aureus*.

[a] Decolonization refers to topical antibiotic and/or antiseptic treatment. Targeted decolonization refers to treatment of known MRSA carriers; universal decolonization refers to treatment of all patients in the study group, regardless of colonization status.

experimental in design, have largely shown that screening was associated with decreased incidence of MRSA BSIs, not only in the ICU but hospital-wide.[52,53] However, 3 more recent robust cluster-randomized controlled trials did not find that screening was associated with a decrease in MRSA transmission or infections.[54–56] It must be noted, however, that the long turnaround time for screening results (mean 5.2 ± SD 1.4 days) in the first study conducted in 19 ICUs in the United States,[54] where all screening swabs were processed at a central laboratory, may have delayed institution of control measures, decreasing the effectiveness of the screening strategy. The second study, also conducted in the United States in 74 ICUs, showed that MRSA screening and isolation without decolonization was only partially effective in reducing the rate of MRSA clinical isolates or MRSA BSIs.[55] The third study involved 13 European ICUs.[56] It compared PCR-based and culture-based screening and found that in the setting of high compliance with hand hygiene and universal chlorhexidine bathing, the addition of screening did not further reduce the acquisition of multiresistant bacteria, including MRSA.

The costs and adverse effects of universal MRSA screening have also prompted much discussion, particularly with regard to laboratory resources, decolonization, and isolation policies. Some argue that resources are better used for "horizontal" strategies that target all HAIs rather than MRSA alone.[57] A study evaluating the costs and benefits of universal MRSA screening in England found that this strategy was not cost-effective due to the fall in MRSA prevalence in the United Kingdom.[58] Screening admissions to high-risk specialties was likely to represent better resource use in terms of cost per quality-adjusted life-year gained.[58]

Although many recent studies cast doubt on the utility of MRSA screening over non–pathogen-specific approaches such as universal decolonization in the ICU setting, changes in practice should be implemented with caution. There are several important considerations at a local level when assessing the need to screen for MRSA (**Fig. 5**). In certain populations, such as patients undergoing clean surgical procedures, preoperative screening linked with targeted decolonization and surgical prophylaxis with MRSA activity is likely to reduce postoperative MRSA infections.[59] Based on the accumulating evidence, mandates for universal MRSA screening introduced in 2009 to 2010 in the United Kingdom have been modified to recommend a targeted risk-based approach.[60] The authors found that such an approach (predominantly using cultures with selective media) is reasonable and should be based on local MRSA prevalence, risk factors for colonization, and the vulnerability of the patient population.

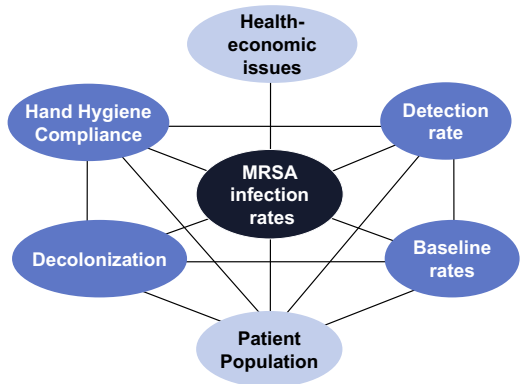

Fig. 5. Important issues to consider when introducing a screening program for MRSA.

Contact Precautions and Isolation

Identifying carriers without additional interventions to reduce the risk of transmission or progression to infection is unlikely to have an impact on MRSA infections. Placing those with MRSA on contact precautions (ie, using gown and gloves for contact with the patient or their environment) may delay colonization of other patients and thereby reduce infection rates.[61] Although studies have found that contact precautions reduce MRSA acquisition, most of these studies are of low quality.[62] A more rigorous cluster-randomized trial in ICUs found that universal glove and gown use did not reduce the overall acquisition of multiresistant gram-positive organisms.[63] There was, however, a small reduction in MRSA acquisition, a secondary outcome of the study.

It is recommended that patients with MRSA are isolated in single rooms or cohorted depending on the availability of single rooms.[64] Where facilities are limited, patients may be isolated based on a risk assessment of the likelihood of transmission and possible impact of MRSA spread to vulnerable patients.[64] Observational studies have shown that single-room isolation reduces MRSA acquisition and infections among hospitalized patients.[65] However, a prospective study of isolation in the ICU did not show a difference in MRSA transmission.[66]

There is debate regarding the utility of contact precautions and isolation.[67] Concerns have been raised about social isolation, feelings of depression, patient satisfaction, and the quality of care provided by HCWs for patients in isolation.[68] It is reassuring to note, however, that an increase in adverse events was not seen in a cluster-randomized controlled ICU trial conducted by Harris and colleagues.[63]

Duration of MRSA colonization in individuals is variable and there is a lack of consensus regarding when contact precautions can be discontinued.[69] A framework guiding discontinuation of contact precautions, including requirements for the number of negative screening cultures over a specified period of time (eg, 3 consecutive negative weekly surveillance cultures), with extension of contact precautions for high-risk patients, including those with chronic wounds or from long-term care facilities, has been suggested.[70]

In view of the limited evidence for isolation of MRSA carriers and potential harms, recommendation of this intervention in all settings may no longer be warranted, particularly where there is good adherence to standard precautions, including hand hygiene, and where MRSA rates are not high or increasing. Experts have called for a review of the necessity of this intervention or, at a minimum, for guidelines to highlight the uncertainties regarding the value of contact precautions and isolation for MRSA control.[9,67]

Targeted Decolonization of Methicillin-Resistant Staphylococcus aureus Carriers

There is increasing interest in the use of decolonization to suppress or eradicate MRSA carriage to reduce transmission and subsequent infection risk.[71] Decolonization is commonly performed with topical intranasal antibiotics (eg, mupirocin) with or without antibacterial body washes (eg, chlorhexidine), although a variety of other agents can been used.[72] Short-term nasal mupirocin is the most effective treatment for eradicating nasal MRSA carriage, with a success rate of up to 90% 1 week after treatment, and between 30% and 60% after longer follow-up, depending on the patient profile and colonization of extranasal body sites.[73,74] It must be noted that eradication of MRSA can be challenging due to the presence of chronic wounds, medical devices, and comorbidities. Compliance with decolonization protocols also influences success rates.[75]

There is insufficient evidence for routine targeted decolonization of all MRSA carriers. Decolonization is often used during MRSA outbreaks, particularly if linked to

transmission by HCWs. Data looking specifically at ICUs show that the incidence of MRSA colonization and/or infections was reduced after initiation of decolonization.[76] Other reports have also demonstrated that decolonization of *S aureus* carriers (including predominantly MSSA carriers) with mupirocin reduces infection rates, particularly in surgical and dialysis patients.[59,77] However, decolonization of MRSA carriers did not reduce infection rates in patients who were predominantly cared for on medical services.[78] As infections may develop after patients leave hospital, a recent study assessed the effectiveness of post-discharge decolonization of MRSA carriers for 5 days twice a month for 6 months and found that it led to a 30% lower risk of MRSA infection at 12 months.[79]

Although there has been demonstrated benefit in some patient groups, the use of decolonization therapy has also raised some concerns. Resistance may emerge with uncontrolled use of mupirocin.[80,81] Treatment failure has been associated with colonization with mupirocin-resistant and/or chlorhexidine-resistant strains at baseline, or recovery of resistant strains after treatment when baseline strains were sensitive.[82,83] Some also question the utility of this intervention due to significant rates of patient recolonization.[72] In health care facilities with high rates of HAIs due to *S aureus*, it may be reasonable to use decolonization therapy in *S aureus* carriers who are at high risk of infection, particularly short-term use in those undergoing clean surgical procedures (eg, cardiothoracic and orthopedic surgery) where the evidence for benefit of this intervention is most robust.[59]

Universal Decolonization with Routine Chlorhexidine Bathing

By decreasing the bacterial load on patients' skin, universal decolonization (ie, decolonizing all patients regardless of known MRSA colonization status) with routine chlorhexidine bathing may reduce MRSA transmission and infection. There are several multicenter cluster-randomized controlled trials that have evaluated this intervention in ICU patients.[55,84,85] They have shown that universal decolonization (with chlorhexidine bathing, and the addition of intranasal mupirocin in one study[55]) was effective in reducing acquisition of multidrug-resistant organisms and health-care–associated BSIs.[55,84,86] However, the reduction in BSIs was mostly due to skin commensals, with failure to demonstrate significant decreases in MRSA acquisition or infection.

In contrast, other cluster-randomized controlled trials have failed to reproduce these findings.[85] In addition, a recent study conducted in non–critical care settings showed that universal chlorhexidine bathing and targeted intranasal mupirocin for MRSA carriers did not significantly reduce MRSA or vancomycin-resistant *Enterococcus* clinical cultures or BSIs, except in a post hoc analysis of a subgroup of patients with devices.[87] It is important to bear in mind that chlorhexidine resistance may result in failure of chlorhexidine bathing protocols,[82,88] and chlorhexidine allergy/intolerance and increased costs should also be considered.[89] Thus caution must be exercised with widespread use of chlorhexidine bathing.

Antibiotic Stewardship

Selective pressure from prior antibiotic use is a risk factor for MRSA acquisition.[90] A meta-analysis assessed 76 studies and found a 1.8-fold (95% confidence interval [CI] 1.7–1.9, $P<.001$) increase in the risk of acquiring MRSA in patients with recent antibiotic use, particularly fluoroquinolones (risk ratio 3, 95% CI 2.5–3.5).[90] More recent studies using robust statistical methods have also shown an association between antibiotic use and MRSA incidence at hospital and country levels.[15,91,92]

There is also evidence to suggest that reduction in antibiotic use can result in reduction in MRSA infections.[93] A nonlinear time-series study, conducted across a region in

Scotland, found that a national antibiotic stewardship and infection control program was associated with a reduction in MRSA prevalence density of 50% ($P = .006$) in hospitals as well as a 47% decline ($P<.0001$) in the community over a 16-year period.[94] As antibiotic use is also linked to the incidence of other nosocomial pathogens, the promotion of appropriate antibiotic use should be a priority for all health care facilities.[95]

Environmental Cleaning

MRSA is frequently found in the environment close to colonized patients,[96] with numerous surfaces (eg, keyboards, tourniquets, and files) becoming contaminated. This organism can survive on surfaces for months,[97] acting as an ongoing reservoir for transmission long after a colonized patient has been discharged. Small-scale studies have shown that enhanced cleaning can reduce environmental MRSA contamination.[98,99] Observational studies also suggest that environmental contamination can play a role in MRSA transmission. One such study found that a cleaning intervention was associated with a reduction in MRSA transmission, including from prior room occupants.[100]

Recently, "no touch" cleaning techniques such as ultraviolet (UV) light, hydrogen peroxide, or antibacterial surface materials (such as copper) have been promoted as more efficient and less labor-intensive methods of environmental decontamination.[97] However, most studies evaluating these modalities have been limited to their effect on detectable MRSA contamination of the environment or have used suboptimal study designs that are susceptible to numerous sources of bias when assessing clinical outcomes. Two recent more robust cluster-randomized trials of cleaning interventions, including UV-C[101] and a cleaning bundle,[102] showed a reduction in acquisition of pathogens or HAIs. However, the effects were mainly seen for vancomycin-resistant *Enterococcus* rather than MRSA. Strong clinical evidence correlating cleaning (by any method) or environmental decontamination with a reduction in HAIs due to MRSA remains, therefore, lacking.[103]

Whole Genome Sequencing for Methicillin-Resistant Staphylococcus aureus Control

Whole genome sequencing (WGS) has traditionally been used for demonstrating the population biology of organisms including MRSA.[104] However, over the past decade, this technology has also been a useful tool for investigating MRSA transmission in hospital and community settings.[105–107] The added insights from WGS data, beyond collection of epidemiologic information alone, can assist in refining infection control interventions so they are tailored to local transmission dynamics. However, the lack of widespread and timely access to this technology at present limits its routine clinical use.

SUMMARY

The control of MRSA is paramount in health care settings. Reducing the burden of this pathogen is an important public health priority that has attracted increasing public and political interest. The decline in invasive MRSA infections in many countries seems to correlate with the introduction of multifaceted infection control approaches coupled with strong leadership and administrative support, often at a national level, to facilitate implementation of interventions. With accumulation of high-quality studies evaluating these interventions, flexibility to adapt and institute evidence-based measures in the context of local epidemiology and available resources remains important to optimize MRSA control.

CLINICS CARE POINTS

- Widespread implementation of multifaceted infection prevention and control interventions has been associated with decreases in the clinical burden of MRSA in geographically diverse acute care settings.
- However, there is increasing importation of community-associated MRSA into health care facilities. If associated with hospital outbreaks, additional interventions (eg, health care worker screening and contact tracing of household members) may be required.
- The utility of universal MRSA screening and contact precautions is unclear, particularly when non–pathogen-specific approaches such as universal decolonization are used. Moreover, universal MRSA screening is not cost-effective in low-prevalence settings.
- Screening and targeted decolonization of *S aureus* (including MRSA) carriers can decrease infections in selected high-risk groups, particularly surgical patients undergoing cardiac and orthopedic procedures.
- Universal decolonization using chlorhexidine bathing with or without intranasal mupirocin can reduce acquisition of multidrug-resistant organisms (including MRSA) and health-care–associated BSIs when used in the ICU.
- Local epidemiology, health infrastructure, and available resources are important to consider when developing MRSA control strategies, to ensure that they are optimized and relevant for local needs.

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