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Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guidelines for the prevention and control of meticillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities

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Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guidelines for the prevention and control of meticillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities.

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Authors' contribution:

All authors except AB/GM and MS provided advice and contributed to writing; AB/HL/GM/MS/JW conducted searches, evidence syntheses, and contributed to writing.

"NICE has accredited the process used by the Healthcare Infection Society to produce: Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guidelines for the prevention and control of meticillin-resistant Staphylococcus aureus (MRSA) in healthcare facilities." The NICE accreditation of HIS methodology is valid for five years from March 2020. More information on accreditation can be viewed at <http://www.nice.org.uk/about/what-we-do/accreditation>"

1. Executive summary

Meticillin-resistant *Staphylococcus aureus* (MRSA) infections remain a serious cause of healthcare-associated infection (HCAI) in many countries. MRSA is easily spread by multiple routes and can persist in the environment for long periods. In health and care settings, transmission via staff hands remains the most important route for patient MRSA acquisition. Infection prevention and control (IPC) measures and control of the use of antimicrobials are effective in reducing prevalence of MRSA. There have been many publications related to MRSA since the last guideline was published in 2006 and this update contains further measures that are clinically effective for preventing transmission when used by healthcare workers.

Methods for systematic review were in accordance with National Institute for Health and Care Excellence (NICE) approved methodology and critical appraisal followed Scottish Intercollegiate Guidelines Network (SIGN) and other standard checklists. Articles published between 2004 and February 2021 were included. Questions for review were derived from a stakeholder meeting, which included patient representatives in accordance with the Population Intervention Comparison Outcome (PICO) framework. Recommendations are made in the following areas: screening, management of colonised healthcare staff, environmental screening and cleaning/disinfection, surveillance, IPC precautions (including isolation and movement of patients and equipment), and patient information.

Table 1: Summary of the changes to the recommendations from previous guidelines

Please see the separate document

2. Lay summary

'MRSA' stands for meticillin-resistant *Staphylococcus aureus*, which is a type of bacteria that can cause infection. Infection with MRSA mainly occurs in people who are already ill and can occur wherever care is given. This can be in hospital or in the community such as in residential or nursing care homes or in your own home. Treating MRSA is difficult because the bugs are resistant to some types of antibiotics (penicillins) that would often be used to fight *Staphylococcus aureus*. This means these types of antibiotics will not work for MRSA infections.

The good news is that the number of MRSA infections in the UK has fallen since 2008, but it does still remain a problem. This guideline is intended to help doctors and other health and social care staff to try and prevent patients from getting MRSA and becoming ill. It may also be of use to patients who already have MRSA, those who care for them (relatives, care staff, etc.) and the general public, by helping them to understand which things work and which do not work to prevent MRSA in hospitals and other care settings.

The guideline contains an explanation, scientific evidence, and a glossary of terms to make it easy to read and use (Supplementary Materials A).

3. Introduction

Infections due to methicillin-resistant *Staphylococcus aureus* (MRSA, also referred to as methicillin-resistant *Staphylococcus aureus*) have decreased significantly in the UK and elsewhere but they continue to cause significant morbidity and mortality. Hence, infection prevention and control (IPC) measures remain essential.

There has been significant progress in recent years in managing MRSA in healthcare settings. Despite these advances the control of MRSA remains demanding, and should be based on the best available evidence to ensure the appropriate use of healthcare resources. This document is an update of the previously published recommendations for the IPC of MRSA in healthcare facilities.

A Joint Working Party of the Healthcare Infection Society (HIS) and the Infection Prevention Society (IPS) has updated the previous guidelines and has prepared the following recommendations to provide advice on the procedures and precautions needed to prevent the spread of MRSA. This includes recommendations on patient and staff screening, patient management, testing strategies, decolonisation, reduction of environmental contamination, surveillance and feedback to minimise transmission and drive system improvement, and the information needs of patients and healthcare professionals.

The process used for the development of this updated version of the guidance was accredited by the National Institute for Health and Care Excellence (NICE). This is an important step in the evolution of the guidance and helps to ensure that users of the document have confidence in the underlying basis for the recommendations made. Although the guidance is most relevant in the UK context, the recommendations will be relevant to healthcare settings in other countries and are based upon a systematic review of UK-based and international literature.

4. Guideline Development Team

4.1 Acknowledgements

APRW was supported, in part, by the National Institute for Health Research University College London Hospitals Biomedical Research Centre. AD was supported by Public Health England (soon to become UK Health Security Agency, UKHSA).

4.2 Source of funding

There was no external funding for this work.

4.3 Disclosure of potential conflicts of interest

HH has been in receipt of research funding from Astella and Pfizer in recent years and has received a consultancy fee from Pfizer in the last three years.

APRW: Consultant on Drug Safety Monitoring Board for Roche, Advisory Board for Pfizer.

JRP received consultancy fee from Imperial College London.

DAE received consultancy fees and speaker fees from commercial organisations.

LB received consultancy fee from a commercial organisation.

All declarations of interest are available in Supplementary Materials B.

4.4 Relationship of authors with sponsor

The Healthcare Infection Society (HIS) and the Infection Prevention Society (IPS) commissioned the authors to undertake the Working Party Report. The authors are members of both societies.

4.5 Responsibility for guidelines

The views expressed in this publication are those of the authors and have been endorsed by HIS and IPS and following a four-week external consultation.

5. Working Party Report

Date of publication: XXX (published online XXX).

5.1 What is the Working Party Report?

The report is a set of recommendations covering key aspects of the IPC of MRSA in healthcare settings. The guidelines review the evidence for screening, surveillance and management of the individuals who are found to be colonised or infected with MRSA. The treatment of MRSA infections is outside of the scope of these guidelines.

5.2 Why do we need a Working Party Report for this topic?

The previous guidelines relating to this topic were published in 2006. MRSA is still an important healthcare-associated pathogen which can be controlled effectively by evidence-based IPC and quality improvement methods. There have been many publications on the subject since 2006 and new technologies have emerged. The effect of these studies on recommended practice needs to be reviewed.

5.3 What is the purpose of the Working Party Report's recommendations?

The main purpose of these guidelines is to inform IPC practitioners about the current UK policy and best available options for preventing and controlling MRSA. This document also highlights current gaps in knowledge, which will help to direct future areas of research.

5.4 What is the scope of the guidelines?

The main scope of the guidelines is to provide advice for the optimal provision of an effective and safe healthcare service while reducing the risk of MRSA transmission in healthcare settings. The guidelines are suitable for patients of all age groups. These guidelines were largely developed with hospitals in mind but may be useful in other settings where MRSA is a concern, for example long-stay units. The guidelines' main focus was the prevention of transmission to patients, thus pre- and perioperative care was not included. Antibiotic stewardship and treatment are covered in a separate publication.²

5.5 What is the evidence for these guidelines?

Topics for these guidelines were derived from stakeholder meetings including patient representatives and were designed in accordance with the Population Intervention Comparison Outcomes (PICO) framework (Appendix 1). To prepare these recommendations, the Working Party collectively reviewed relevant evidence from peer-reviewed journals subject to validated appraisal. Methods, which were in accordance with NICE methodology for developing guidelines, are described fully below.

5.6 Who developed these guidelines?

The Working Party included infectious diseases/microbiology clinicians, IPC experts, systematic reviewers, and two lay member representatives.

5.7 Who are these guidelines for?

Any healthcare practitioner may use these guidelines and adapt them for their use. It is anticipated that users will include clinical staff and, in particular, IPC teams. These guidelines aim to provide recommendations for all health and care settings and to include available evidence for all settings where MRSA is a concern. However, the available reported studies were predominantly conducted in hospital settings. The Working Party believes that while many sections of these guidelines are particularly relevant to hospitals, some evidence and recommendations can be extrapolated to other health and social care settings (e.g. the sections on environment and equipment decontamination, use of personal protective equipment (PPE), transfer of patients and patient information).

5.8 How are the guidelines structured?

Each section comprises an introduction, a summary of the evidence with levels (known as evidence statements), and a recommendation graded according to the available evidence.

5.9 How frequently are the guidelines reviewed and updated?

The guidelines will be reviewed at least every four years and updated if change(s) are necessary or if new evidence emerges that requires a change in practice.

5.10 Aim

The primary aim of these guidelines is to assess the current evidence for all aspects relating to the IPC of MRSA. A secondary aim is to identify those areas in particular need of further research to inform future MRSA guidelines.

6. Implementation of these guidelines

6.1 How can these guidelines be used to improve clinical effectiveness?

Primarily, these guidelines will inform the development of local protocols for preventing MRSA transmission and managing patients colonised or infected with MRSA. They also provide a framework for clinical audit, which will aid in improving clinical effectiveness. In addition, the future research priorities identified by the Working Party will allow researchers to refine applications to funding bodies.

6.2 How much will it cost to implement these guidelines?

Provided that existing practice follows current recommendations, it is not expected that significant additional costs would be generated by the recommendations in this document. However, failure to follow best practice, for example by not screening in a population with high prevalence, the hospital should expect to incur higher costs due to MRSA infections.

6.3 Summary of audit measures

Regular audit remains an important part of any guideline implementation. Audit is effective only when the results are fed back to staff and when there is a clear plan for the implementation of improvements. Many NHS Trusts also require that the results of audits and interventions are reported through clinical governance structures and to Hospital IPC Committees to help reduce the MRSA burden. The MRSA Working Party suggests the following aspects of patient care to be audited:

- Compliance with screening protocol.

- Compliance with decolonisation regimens.

- Compliance with prescribed isolation precautions.

- Cleaning/disinfection standards.

- Antimicrobial Stewardship (please refer to recent MRSA treatment guidelines²).

- Emergence of resistance, especially to mupirocin and chlorhexidine (CHG), if used extensively.

- IPC practices, e.g. hand hygiene, aseptic technique.

- Compliance with informing the receiving ward/unit/care home and the ambulance/transport service that patient is colonised/infected with MRSA.

6.4 Supplementary tools

Lay materials and continuing professional development questions (CPD) are available in the Supplementary Materials (files C and D).

7. Methodology

7.1 Evidence appraisal

Topics for these guidelines were derived from stakeholder meetings including patient representatives. To prepare these recommendations, the Working Party collectively reviewed relevant evidence from published, peer-reviewed journals. Methods were in accordance with NICE-approved methodology for developing guidelines (Supplementary Materials B).

7.2 Data sources and search strategy

Three electronic databases (Medline, CINAHL/EMCare and EMBASE) were searched for articles published between July 2004 and February 2021. The searches were restricted to English language studies, non-animal studies and non-in vitro studies. Search terms were constructed using relevant MeSH and free text terms (provided in appendices for each question cluster). The reference lists of identified systematic reviews, guidelines and included papers were scanned for additional studies. Search strategies and the results are available in Appendix 1.

7.3 Study eligibility and selection criteria

Search results were downloaded to Endnote database and screened for relevance. Two reviewers (MS, AM, AB, GM, JW or HL) independently reviewed the title and abstracts. Disagreements were addressed by a third reviewer. Two reviewers (MS, AM, AB, GM, JW or HL) independently reviewed full texts. If there were disagreements, these were first discussed between the two reviewers and if a consensus was not reached, a third reviewer was consulted. The guidelines included any controlled trials, cohort studies, interrupted time series (ITS) studies, case-control studies, diagnostic accuracy studies (DAS) and controlled before/after (CBA) studies. Due to the limited number of studies available, uncontrolled before/after (UBA) studies were included and described narratively. These were not used to make recommendations but were included to inform the Working Party of the additional evidence that existed. Similarly, data from mathematical model studies and excluded studies which provided additional evidence were included for each section but were not used when making recommendations. Results of study selection are available in Appendix 2.

7.4 Data extraction and quality assessment

Data collection and synthesis for these guidelines started before the NICE update for guideline methodology was published in 2018. Prior to this update, some studies were assessed using the quality assessment tools previously recommended. To ensure consistency, it was decided that the same checklists would be used for the remaining studies. For the type of studies where previous methodology did not recommend the specific checklists, they were assessed using the checklists recommended in the updated methodology. The quality checklists included:

Controlled trials (Randomised Controlled Trials (RCT) and non-Randomised Controlled Trials (n-RCT)): SIGN Methodology Checklist 2: Controlled Trials.

Cohort studies: SIGN Methodology Checklist 3: Cohort Studies.

Interrupted time series (ITS): Cochrane Effective Practice and Organisation of Care (EPOC) Risk of bias for interrupted time series studies.
 Case-controlled studies: SIGN Methodology Checklist 4: Case-control studies.
 Controlled before/after (CBA) studies: EPOC Risk of Bias (RoB) Tool (for studies with a control group).
 Uncontrolled before/after (UBA) studies: Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Quasi-Experimental Studies (non-randomized experimental studies).
 Diagnostic accuracy studies (DAS): SIGN Methodology Checklist 5: Studies of Diagnostic Accuracy

Studies were appraised independently by two reviewers (MS, AM, AB, GM, JW or HL) and any disagreements were resolved through discussion. Results of quality appraisal are available in Appendix 3.

Data were extracted by one reviewer and checked/corrected by another. For each question cluster the data from the included studies were extracted to create the tables of study description, data extraction and summary of findings tables (Appendix 4). The list of the studies rejected at full text stage with a reason for this decision, is included in the excluded study tables. Due to limited evidence, most of the data were described narratively. Where meta-analysis was possible, this was conducted in Review Manager 5.3 software for systematic reviews. This software only allows the entry for dichotomous data; it was not suitable for meta-analysis for decolonisation where a range of different decolonisation therapies were used. For this, the analyses were calculated manually, with sample proportion and confidence intervals [CI95%] obtained using the Wilson score interval (epitools.ausvet.com.au). For the therapies which showed a significant benefit, the risk ratios were calculated using MedCalc software (medcalc.net).

7.5 Rating of evidence and recommendations

For each outcome of the review question the certainty/confidence in the findings was established using considered judgment forms. The evidence was considered and judged using the following ratings: high, moderate, low, and very low, based on the characteristics of the studies included in evidence tables.

When writing recommendations, the Working Party considered the following:

- Who should act on these recommendations?
- What are the potential harms and benefits of the intervention and any unintended consequences?
- What is the efficacy and the effectiveness of each intervention?
- Is it possible to stop another intervention because it has been superseded by the new recommendation?
- What is the potential effect on health inequalities?

What is the cost-effectiveness of the intervention, including staff resources other economic concerns?

Can the recommended interventions be feasibly put into practice?

The wording of the evidence statements and the recommendations reflected the strength of the evidence and its classification. The following criteria were used:

‘offer’, ‘measure’, ‘advise’, ‘refer’, ‘use’ or similar wording was used if the Working Party believed that most practitioners/commissioners/service users would choose an intervention if they were presented with the same evidence: this usually means that the benefits outweigh harms, and that the intervention is cost-effective. This reflects a strong recommendation for the intervention. If there is a legal duty, or if not following a recommendation may have serious consequences, the word ‘must’ was used.

‘do not offer’ or similar wording was used if the Working Party believed that harms outweigh the benefits or if an intervention is not likely to be cost-effective. This reflects a strong recommendation against the intervention. If there is a legal duty, or if not following a recommendation may have serious consequences, the words ‘must not’ were used.

‘consider’ was used if the Working Party believed that the evidence did not support a strong recommendation, but that the intervention may be beneficial in some circumstances. This reflected a conditional recommendation for the intervention.

The ‘do not offer, unless...’ recommendation was made if the Working Party believed that the evidence did not support the strong recommendation, and that the intervention was likely not to be beneficial, but could be used in some circumstances, for instance if no other options were available. This reflected a conditional recommendation against the intervention.

7.6 Consultation process

Feedback on draft guidelines was received from the HIS Guideline Committee, and final changes made. These guidelines were then opened to consultation with relevant stakeholders (Supplementary Materials E). The draft report was available on the HIS website for four weeks. Views were invited on format, content, local applicability, patient acceptability, and recommendations. The Working Party reviewed stakeholder comments, and collectively agreed revisions.

8. Rationale for recommendations

8.1 What is the clinical and cost-effectiveness of universal versus targeted screening in minimising the transmission of MRSA?

While in certain instances screening is implemented for every patient entering the healthcare unit, it is not in the current UK NICE guidelines for healthcare facilities to implement universal screening. Screening is completed largely for some pre-operative patients or other high-risk

patients, such as those entering the intensive care unit (ICU). Despite this, there is disagreement in the literature about the clinical effectiveness of targeted screening in preventing the transmission of MRSA. Moreover, there is a debate about the cost-effectiveness of universal screening. The effectiveness of universal versus targeted screening was not assessed in previous MRSA guidelines,¹ although the recommendation endorsed the use of a targeted approach.

There was weak evidence of no benefit from one ITS³ which investigated the incidence of MRSA acquisition in all patients, excluding new-borns, admitted to hospital with the use of universal screening (n=61,782) as compared to targeted screening (n=76,273). The study found no significant difference in the incidence of MRSA acquisition in patients screened universally (47.5/100,000) as compared to those when a targeted approach was in use (41.8/100,000; p=0.923).

There was weak evidence of no benefit from one ITS study³ and one CBA study⁴ which investigated the incidence of MRSA infection in patients admitted to hospital with the use of universal screening as compared to targeted screening. One study³ of all patients, excluding new-borns, admitted to hospital found no significant difference in the incidence of MRSA bloodstream infection (BSI) in patients screened universally (1.8/1000pd (patient days) n=61,782), as compared to those when a targeted approach was in use (2.1/1000pd n=76,273; p value not reported). Another study⁴ of adult patients admitted to hospital for at least 24 hours with universal screening (n=61,782) compared to targeted screening (n=76,273) found that the rate of healthcare-associated MRSA infection (HCAI-MRSA) did not fall significantly (0.27% before versus 0.15% after the switch to universal screening), while the rate in the control hospital remained the same throughout the study period (0.10%, p=0.34).

There was weak evidence of no benefit from one CBA study⁴ which investigated the cost saving from a reduced incidence of healthcare-associated MRSA acquisition per each additional dollar spent on screening in adult patients admitted to hospital for at least 24 hours with the use of universal screening (n=3255) as compared to targeted screening (n=2037). The study found lower cost savings when screening patients universally (USD 0.50 saved) as compared to those when targeted approach was in use (USD 1.00 saved).

The Working Party considered the evidence and concluded that the universal screening strategy had no benefit over targeted screening. The clinical experience of the Working Party suggests that universal screening may be easier and more time-effective for staff as it removes the need to perform additional assessments to determine whether patients require such screening. When a targeted approach is used, careful consideration is needed to establish which patients should be considered at risk and that local risk factors are taken into account. The Working Party concluded that for screening to be effective, it needs to be linked to a specific action that either attempts to eradicate or suppress the MRSA in the patients (decolonisation) or minimises contact with MRSA colonised patients (isolation).

Recommendations

1.1 Targeted or universal patient MRSA screening must be performed and must be linked to a specific point of action such as decolonisation or isolation (or both).

1.2 Use at least a targeted approach but consider using universal screening as appropriate depending on local facilities.

1.3 If a targeted approach is used, define risk factors for MRSA carriage as appropriate for your area.

Good Practice points

GPP 1.1 Establish documented local protocols for how swabs should be taken. The swabs should include a minimum of two sites from the following: nose, perineum, device entry sites, wounds, urine, and sputum, as appropriate depending on clinical presentation.

8.2 What is the clinical and cost-effectiveness of repeat screening people who screen negative/positive on pre-admission/admission to prevent the transmission of MRSA?

If patients screen negative at admission, repeat screening can identify whether they acquired MRSA during their stay, so that appropriate actions can be taken. On the other hand, for those who screen positive, repeat screening can show whether an MRSA patient was successfully decolonised. It is currently unclear whether repeat MRSA screening is clinically and cost-effective and how the repeat screening should be performed. Effectiveness of repeat screening was not assessed in previous MRSA guidelines¹ and no recommendation was endorsed for its use.

No evidence was found from the studies published since 2004, which met the inclusion criteria for the study design, and which assessed the benefit of repeat screening for people who screened negative or positive on pre-admission/admission screening to prevent the transmission of MRSA.

The Working Party additionally considered the evidence from the excluded studies, which reported some benefit of repeat screening and, together with the clinical experience of the group members, suggested that repeat screening could be beneficial in some circumstances.

Recommendations

2.1 Do not perform repeat MRSA screening for patients who screen positive at admission unless the patient undergoes decolonisation therapy.

2.2 If the patient undergoes decolonisation therapy, consider repeat MRSA screening two to three days following the therapy, to determine whether decolonisation was successful or not. Do not delay a surgical procedure if the patient still tests positive.

2.3 Do not perform repeat MRSA screening routinely.

2.4 Consider re-screening patients who previously screened negative if there is a significant MRSA exposure risk (e.g. contact with a confirmed MRSA case) or where there is a locally-assessed risk of late acquisition.

8.3 What is the clinical and cost-effectiveness of rapid molecular diagnostics versus culture in screening to prevent the transmission of MRSA in hospital and non-acute care settings?

During the screening process for MRSA at a hospital or healthcare setting, a swab is taken from the patient and is usually analysed in conventional culture-based assays. This may include enrichment in broth, the use of selective media or chromogenic agar. While this process is straightforward and is considered the gold-standard diagnostic method, the turnaround time (TAT) for results can be more than 48 hours. This delay may result in the patient or healthcare staff transmitting MRSA to others or acquiring MRSA. Moreover, while waiting for results and trying to prevent patients from potentially transmitting MRSA, healthcare workers may need to implement preventative measures such as isolating patients, which are costly. To receive rapid results, rapid diagnostic techniques such as the polymerase chain reaction (PCR) method have been used for screening samples to establish the presence of MRSA in the swab. These molecular techniques may require the use of commercial tests and as a result, they tend to be costlier than culture, although laboratories may develop their own in-house methods. It is currently unknown whether molecular diagnostic techniques are beneficial in clinical practice in comparison to conventional culture methods, in terms of diagnostic accuracy, TAT, transmission rates and costs. Effectiveness of these methods of screening was not assessed in previous MRSA guidelines¹ and no recommendation was endorsed for their use.

There was strong evidence of similar diagnostic accuracy from the meta-analysis of 61 studies⁵⁻⁶⁵ which investigated the diagnostic accuracy of PCR versus culture screening (n=72,952 samples). The results of meta-analysis demonstrated that the overall sensitivity was 91.54% [CI95% 90.75-92.28], specificity was 97.00% [CI95% 96.86-97.12], positive predictive value was 70.03% [CI95% 69.11-70.94] and negative predictive value was 99.33% [CI95% 99.27-99.39]. The overall accuracy of PCR compared to culture results was 96.61% [CI95% 96.47-96.74]. There were an additional nine studies, which were not included in meta-analysis, either because they did not report data on the number of positive and negative values but reported sensitivity and specificity⁶⁶⁻⁷¹ or were identified later in the review process.⁷²⁻⁷⁴ All these studies reported results similar to those obtained from meta-analysis.

There was strong evidence of no benefit from the meta-analysis of three RCTs and one n-RCT^{33,71,75,76} which investigated the incidence of MRSA colonisation when using PCR screening (n=16,773) versus culture (n=17,754). The results of meta-analysis showed that the incidence of colonisation did not decrease significantly in the PCR group (n=268, 1.51%) when compared

to culture (n=324, 1.94%, OR=0.86 [CI95% 0.73-1.01]). These results are consistent with the results of studies which reported colonisation per 1000pd or 1000pd at risk, with one RCT⁷⁵ reporting significantly lower incidence in the PCR group (2.86 versus 4.10/1000pd, p=0.002) while four other studies reported non-significant differences (0.39 versus 0.35/1000pd, p=0.39,⁷⁷ 4.4. versus 4.9/1000pd at risk, p=0.27,³³ 2.57 versus 2.83/1000pd at risk, p=0.66,⁷⁶ 4.60 versus 5.39/1000pd at risk p value not reported⁷¹).

There was moderate evidence of no benefit from two RCTs^{33,76} which investigated the incidence of MRSA infection when using PCR screening versus culture. One study³³ found no difference in MRSA BSI in the group of patients where PCR was used (1/3553, 0.03%) compared to patients where culture was used (2/3335, 0.06%, p value not reported) and no difference in MRSA wound (included but not limited to surgical wound) infection (21/3335, 0.6% in PCR versus 22/3553, 0.7% in culture, p=0.77). Another study⁷⁶ found no significant difference in a rate of infection/1000pd in patients with PCR (5/1063, 4.06/1000pd) versus culture (2/1121, 1.57/1000pd, p=0.281).

There was strong evidence of benefit from 14 studies,^{10,15,27,33,38,42,45,53,59,62,71,75-77} which investigated the TAT of PCR and culture. There was a high degree of heterogeneity as to how TAT was reported across these studies, but they consistently showed significantly decreased TAT for PCR samples. The studies showed that the time from patient admission to results being available for PCR was under 24 hours^{33,71,76} and just over 24 hours for admission until isolation,^{62,76} while results for culture using the same TAT were 40.4 hours or longer.^{33,62,71,76} When TAT was defined as the time from the collection of the screening sample until results were available, it showed that these results could be available in less than two hours³⁸ and are typically available in under 24 hours for PCR.^{27,59,75} The results of culture were available after 28 hours at the earliest⁵⁹ and sometimes took more than two days.^{27,38,75} The studies which assessed TAT as the arrival of samples at the laboratory to results being available^{15,27,42,45,53,62} reported the shortest time for PCR at 1.8 hours and the average time as eight hours, while the shortest time for culture was 24 hours and the average time longer than 40 hours.

There was strong evidence of no benefit from eight studies^{10,15,33,56,62,76-78} investigating the cost of PCR versus culture. One UK study¹⁵ reported that the cost of one screen is approximately 2.5 times more when using PCR than culture (£4.29 versus £1.71, total cost £14,328.60 versus £5711.40 for a total sample of 3340). Another study¹⁰ estimated this cost to be higher: USD 6.71 and USD 7.52 (approx. £5.17 and £5.79) for culture (negative and positive result, respectively) and USD 25.50 (approx. £19.60) for PCR. This study, besides the cost of materials necessary for screening, considered the cost of staff required to process the samples (1.5-2min for culture and 5-9min for PCR per sample). Other studies reported 4-5 times higher screening costs compared to culture, although it is not possible to determine what was included in the estimation of the costs.^{56,78} Two studies did not report data on the cost of culture but reported that screening with PCR required an additional €4.961 (approx.

£4.27)⁷⁶ and €56.22/€69.62 (approx. £48.45/£59.99)⁶² depending on the assay. Three studies reported^{33,62,78} a potential cost saving when screening with PCR. One of these studies⁷⁸ of 232 participants reported that while the PCR screening cost itself was higher (additional CHF104,328.00, approx. £80,332.56 for universal screening and CHF11,988.00 approx. £9,230.76 for targeted screening), there is potential for reducing the costs of pre-emptive isolation by CHF38,528.00, approx. £29,666.56. Hence, while the net cost of universal isolation was still higher (CHF91,509.00, approx. £70,461.93), the targeted screening reduced the net costs by CHF14,186.00 (approx. £10,923.22). Another study,⁶² using targeted screening reported a reduction in the daily cost of isolation as €95.77 (approx. £73.74) and €125.43 (approx. £96.58) when using two PCR screening methods compared to culture. One study,³³ which used a universal screening approach reported that PCR screening reduced the number of inappropriately used isolation days from 399 to 277. While the authors did not report the cost analysis, they suggested that there was a potential to counterbalance the cost of PCR screening with the benefit from reducing the number of isolation days. Last study⁷⁷ reported that the total cost of screening with PCR was more expensive (CAN 3,656.92, approx. £2,281.92) than culture methods (CAN 2,937.06, approx. £1,832.73), although they did not report any information on how this cost was estimated.

Further evidence came from UBA studies, three of which reported a decrease in the incidence of MRSA acquisition when PCR screening was introduced,⁷⁹⁻⁸¹ and four of which reported a decrease in reducing TAT.^{11,79,81-83}

There was strong evidence from a total of 45 studies,^{5,7-11,13,14,16,17,19,22-24,27,29-32,35,37-41,43,45,47-51,53,57,58-61,62,64,65,67,69,72,73,78,84} which reported the occurrence of PCR inhibition rates. This is important because sometimes these can be mistaken for negative results. Overall, the inhibition rate was 2.98% [CI95% 2.80-3.17], although one study⁷³ which used a Point-of-Care Testing device, reported the inhibition rates as high as 8.1%.

The Working Party considered the evidence and concluded that diagnostic accuracy of PCR is similar to culture and there is a benefit in obtaining results in a shorter time. However, these benefits do not translate into clinical benefit of reducing the incidence of MRSA acquisition or infection and PCR screening may incur higher cost.

Recommendation

3.1 Use either PCR or traditional culture methods for MRSA screening as you consider appropriate depending on the local laboratory facilities.

Good practice point

GPP 3.1 If using PCR methods, maintain access to culture methodology for specific circumstances such as outbreak investigation or sensitivity testing, and to support molecular technologies.

8.4 What is the clinical and cost-effectiveness of screening staff to prevent the transmission of MRSA?

Members of staff in healthcare settings are not routinely screened for MRSA. Usually, they will undergo screening if an MRSA outbreak persists, staff are suspected to be carriers or when the source of the outbreak is unclear. MRSA can be traced back to staff if the strain of MRSA is the same as in patients. Screening under these three circumstances is the most common approach to staff screening, but there are some who argue that screening should be expanded, although the clinical and cost-effectiveness of this approach is not established. Our previous MRSA guidelines¹ did not recommend routine screening of staff, but the Working Party considered that it could be valuable under certain circumstances (e.g. when transmission of MRSA continues despite implementing preventative measures and epidemiological data suggest staff carriage).

No evidence was found in studies published since 2004 which met the inclusion criteria for the study design, and which assessed the benefit of performing staff screening on any patient-related outcomes.

There was weak evidence from one UBA study⁸⁵ which assessed the benefit of performing staff screening on the prevalence of staff MRSA carriage. The authors reported that a total of 27/566 (4.77%) of the staff were colonised with MRSA at their first screening, while 14/445 (3.15%) of staff were colonised at least once at subsequent screenings. While it is not possible to directly compare the before/after prevalence (some staff were screened more than once at subsequent screenings), the authors reported that 9/201 (4.48%) staff were colonised in 2005 and the prevalence from 2006-2008 was 12/207 (5.80%), 11/237 (4.64%) and 7/186 (3.76%) respectively. This suggests that overall, the prevalence did not change. The authors reported that for the staff who were screened more than once (n=221) and were given the decolonisation treatment following the positive screen, the colonisation rate dropped for this group from 5.88% to 2.71% (p=0.55) and the odds ratio of being colonised at second screen was 0.45 (CI95% not reported) compared to the first screen. It is not possible to determine whether the staff were subsequently recolonised at the follow-up screenings.

The Working Party considered the evidence from the excluded studies, which did not meet the inclusion criteria for study design and reported no benefit in routine staff screening, and together with the clinical experience of the Working Party members, concluded that staff screening is not beneficial except in certain circumstances described above.

Recommendations

4.1 Do not routinely screen staff for MRSA.

4.2 Consider screening staff for MRSA if there is an epidemiological reason for suspecting a staff member as a source of MRSA, e.g. if transmission continues on a unit despite active control measures, if epidemiological aspects of an outbreak are unusual, or if they suggest persistent MRSA carriage by staff.

Good practice points

GPP 4.1 Screen staff at the beginning of their shift to avoid mistaking transient carriage for persistent carriage. Appropriate sampling sites for staff screening include anterior nares and any areas of abnormal or broken skin.

GPP 4.2 For staff who test positive, consider additionally screening throat, hairline, and groin/perineum as these if positive, increase the risk of shedding into the environment and transmission.

GPP 4.3 If possible, involve the Occupational Health Team in the process of staff screening and management.

8.5 What approaches to the management of healthcare staff who are colonised with MRSA are most practical and effective at minimising the risk to patients?

If a member of staff tests positive for MRSA, the hospital is required to comply with appropriate governance to ensure that the risk of acquisition, and potentially infection, is minimised among the patients. This includes sending staff home, reducing their interaction with patients or treatment with topical antimicrobials. The cost-effectiveness and clinical benefit of these management strategies have not been established. Effectiveness of managing staff who screen positive for MRSA was not assessed in previous MRSA guidelines,¹ although the Working Party recommended developing local protocols which assess the individual staff member's risk of transmission to patients when agreeing their continuation or return to work. It was recommended that only staff members with colonised or infected hand lesions should be off work while receiving courses of decolonisation therapy, but this decision should be based on local risk assessments. To aid staffing resources, it was recommended to temporarily re-allocate staff carriers to low-risk tasks or to non-patient contact activities. The management of staff with nasal carriage was not included in previous guidelines.

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design and, which assessed the management of staff who tested positive for MRSA carriage.

The Working Party considered previous recommendations from MRSA guidelines and, together with the clinical experience of the members, suggested that staff who are identified

as MRSA positive may need a course of decolonisation therapy and sometimes may need to be excluded from clinical areas.

Recommendations

5.1 Consider excluding staff from work, reducing their interaction with patients, or offering decolonisation therapy as deemed appropriate.

5.2 Consider investigating the risk factors for staff MRSA carriage. Investigate staff members with persistent carriage in a multi-disciplinary setting to determine any associated factors.

Good practice points

GPP 5.1 For staff members with nasal carriage only: offer decolonisation therapy, exclusion is not required. For staff with infected lesion/skin rash: offer decolonisation therapy AND carry out a risk assessment to consider re-deploying them to low-risk areas or excluding them from work.

GPP 5.2 Develop local policies to guide the decision of when staff should be excluded from work and when they should return, taking into consideration the individual's risk of transmission to patients (e.g. a staff member colonised with MRSA who is working in an ICU or neonatal unit represents a greater potential risk to patients than a staff member with MRSA working in an outpatients' department).

8.6 What is the evidence that topical decolonisation therapy is clinically and cost-effective in minimising the transmission or eradication of MRSA? What is the evidence that the selected strategy for topical decolonisation results in resistance?

The most common topical decolonisation therapy offered to patients and staff is CHG and mupirocin, either as combination or alone. There is some disagreement in the literature over the clinical effectiveness of topical decolonisation in preventing MRSA colonisation or its eradication. It is generally acknowledged that complete eradication is not always possible, but a temporary suppression may be sufficient in some circumstances (e.g. prior to surgery). Moreover, there are risks that overuse of topical decolonisation therapies leads to resistance. This has led some healthcare facilities to implement other interventions such as putting patients in single rooms to prevent transmission to others. There is a need to understand clearly the clinical and cost-effectiveness as well as antimicrobial resistance risks of different decolonisation (defined here as a therapy which aims to eradicate or temporarily suppress the MRSA growth) therapies compared to the best standard of care, including those from no decolonisation therapy. Previous MRSA guidelines¹ recommended prophylactic use of mupirocin in conjunction with CHG for patients undergoing some operative procedures. This

was also recommended in outbreak situations. Throat decolonisation with systemic therapy was recommended only on the advice of the consultant microbiologist and was recommended in conjunction with nasal and skin decolonisation therapy with mupirocin and CHG. Skin decolonisation was recommended for pre-operative patients who were found positive for the carriage of MRSA. Skin decolonisation with 4% CHG wash, 7.5% povidone-iodine (PVP) or 2% triclosan was recommended.

Chlorhexidine (CHG)

There was strong evidence of benefit from twelve RCTs,⁸⁶⁻⁹⁸ four controlled trials,⁹⁹⁻¹⁰² eleven ITS studies,¹⁰³⁻¹¹³ two retrospective cohort studies^{114,115} and one CBA study¹¹⁶ which investigated the effectiveness of CHG washing on the prevalence of MRSA colonisation, incidence of MRSA acquisition, incidence of MRSA infection and the eradication of MRSA. The results of the meta-analyses showed that decolonisation therapy with CHG, either alone or in combination with another agent (PVP, polysporin or mupirocin), was consistently better than the comparison group (either no decolonisation or placebo) for all outcomes, except for incidence of MRSA acquisition when CHG was used alone. When CHG was used alone, the prevalence of MRSA was 2.1% in CHG group versus 25.5% in control group ($p<0.001$), the incidence of MRSA acquisition was 3.55% versus 3.04% ($p<0.0001$), the incidence of MRSA acquisition/1000pd was 2.35 versus 3.10, $p=0.051$, incidence of infection was 1.11% versus 1.49%, $p=0.0361$ and the incidence of infection per 1000pd was 0.22 versus 0.46, $p<0.0001$. When CHG was used alone or in combination with another therapy (PVP or mupirocin), the prevalence of MRSA was 5.3% versus 25.5%, $p<0.0001$, the incidence of MRSA acquisition was 1.57% versus 3.04%, $p<0.0001$, the incidence of acquisition per 1000pd was 0.89 versus 3.10, the incidence of infection was 1.11% versus 1.49%, $p=0.0361$, the incidence of infection per 1000pd was 0.08 versus 0.46, $p<0.0001$ and the rate of MRSA eradication was 60.5% versus 34.5%, $p<0.0001$, thus showing that CHG performs better when used in combination with nasal decolonisation therapy. The results remained significant when stratified by different types of setting (e.g. surgical, ICU, general ward) or when using a selective (only for MRSA positive patients) or universal (blanket) approaches, although there was large heterogeneity in the reported results between the individual studies. Additional evidence from the studies which provided data not compatible for entry into metanalysis, did not show a significant benefit of using CHG. One small ITS,¹¹² which used nasal mupirocin and 4% CHG wipes for patients colonised with MRSA in neonatal ICU did not report a significant decrease in the incidence of MRSA acquisition in the intervention period in comparison to pre-intervention (2.00 versus 2.38 events/1000pd, IRR=1.85 (incidence rate ratio) [CI95% 0.80–1.73], $p=NR$). An RCT⁹⁸ conducted in adult ICU patients with a treatment group receiving a daily 4% CHG wash and a control group receiving a daily soap and water wash reported no significant decrease in the incidence of HCAI-MRSA (2/226, 0.9% or 1.08/1000pd versus 6/223, 2.7% or 3.80/1000pd, RR=0.33, [CI95% 0.07-1.61], $p=0.1704$). Considering the small sample sizes, these two studies were likely underpowered, resulting in type I error. Further evidence came from eighteen UBA studies¹¹⁷⁻¹³⁴ which used CHG either in combination or alone. These other

studies showed heterogenous results with 11 studies reporting a benefit^{118,120-124,128,130-132,134} and seven reporting no significant change.^{117,119,125-127,129,133}

There was inconsistent evidence from two RCTs^{86,95} which assessed the effectiveness of CHG mouth rinse on the presence of MRSA in the oral cavity in patients admitted to ICUs. One study reported no effect of CHG on the presence of MRSA in dental plaque,⁸⁶ while another found a significantly lower prevalence of MRSA in both dental plaque (15.2 versus 37.3%, $p=0.006$) and oral mucosa (18.6 versus 39.7%, $p=0.011$).⁹⁵ The difference may be explained by the differences in CHG concentrations with 0.2% and 2% used, respectively. A small study assessing the effectiveness of CHG on the incidence of MRSA acquisition in patients with a peritoneal catheter found a benefit, although the sample size was too small to show a significant effect.⁹⁶

There was strong evidence from the meta-analysis of five studies^{97,102,105,108,132} and one narratively-described cross-sectional study¹³⁵ which investigated resistance to CHG. Meta-analysis showed a high proportion of isolates which were resistant to CHG in the group of patients with CHG bathing, although the rates were still high (27.7%) in the comparison group where CHG was not used. The use of CHG significantly increased the incidence of resistant isolates (OR=2.79 [CI95% 1.81-4.26], $p<0.0001$). There were not enough data to establish whether a universal approach to decolonisation carried a higher risk of developing resistance. One cross-sectional study,¹³⁵ which evaluated MRSA isolates obtained from the patients for resistance patterns, reported that those patients who were exposed to CHG were more likely to carry MRSA isolates with disinfectant resistance genes *qacA/B* and *qacC* than those who were not exposed (70.0% versus 43.4%, AOR=7.80 [CI95% 3.25-18.71], $p<0.001$ and AOR=0.18 [CI95% 0.04-0.94], $p=0.04$ respectively). Additionally, authors reported that a higher proportion of isolates obtained from patients previously exposed to CHG had a reduced susceptibility to CHG (minimum inhibitory concentration (MIC) levels ≥ 4 mg/L) than the isolates from patients with no exposure history AOR=3.15, [CI95% 1.14-8.74], $p=0.03$.

There was moderate evidence from fourteen studies,^{86,88-94,96,97,99,100,102,109,121} which reported adverse events associated with the use of CHG. These included rash,^{91,94,100} burning sensation,^{92,97} itching,^{92,94,97,100,109} redness,^{92,109} dryness,⁹² irritation,⁹⁷ fissures⁹⁷ and other not-specified skin reactions.⁹⁰ Three studies reported allergy to CHG^{88/89,96,102} and two reported discontinuation of CHG due to adverse events.^{97,100} Another three studies reported adverse events, but did not specify what they were.^{86,93,99} Despite the many studies reporting adverse events, meta-analysis showed that the overall rate of occurrence was low (0.15%) and not significantly different than the rate reported for studies which did not use skin decolonisation therapy or used a placebo (0.12%, OR=1.30 [CI95% 0.97-1.76], $p=0.0811$). The use of oral CHG was associated with a higher risk of adverse events (24% versus 0% in comparison group, OR=85.07 [CI95% 5.08-1424.00], $p=0.0020$) including burning sensation, unpleasant taste, dryness of the mouth and tenderness. These results are based on one

study⁹² which reported the side effects when 2% CHG was used. Another study⁸⁶ which used 0.2% CHG reported no adverse events.

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the cost-effectiveness of CHG bathing.

Mupirocin

There was strong evidence of benefit from the meta-analyses of ten RCTs,^{88/89,91-94,96,136-139} two control trials,^{140,141} three ITS,^{104,105,111} and two retrospective cohort studies,^{115,142} which investigated the effectiveness of nasal mupirocin on the prevalence of MRSA colonisation, incidence of MRSA acquisition, incidence of MRSA infection and eradication of MRSA. The results of the meta-analyses showed that mupirocin was not effective when used alone but was effective when used in combination with a skin decolonisation agent (e.g. CHG, triclosan or octenidine). When mupirocin was used alone, the prevalence of MRSA was 21.1% in the mupirocin group versus 25.5% in the control group ($p=0.1636$), the incidence of infection was 2.54% versus 1.49%, $p=0.1100$, and the eradication rate was 60.5% versus 34.5%, $p<0.0001$. When mupirocin was used alone or in combination with another therapy, the prevalence of MRSA was 15.5% versus 25.5%, $p=0.0001$, the incidence of MRSA acquisition was 1.12% versus 3.04%, $p<0.0001$, the incidence of acquisition per 1000pd was 0.62 versus 3.10, $p<0.0001$, the incidence of infection was 0.20% versus 1.49%, $p<0.001$, the incidence of infection per 1000pd was 0.02 versus 0.46, $p<0.0001$ and the rate of MRSA eradication was 63.2% versus 34.5%, $p<0.0001$. The two studies included a follow-up period (one month or longer) after successful decolonisation and reported that in a large proportion of patients, MRSA was redetected at follow-up.^{93,97} Both studies used mupirocin in combination with CHG, but this finding needs to be considered as a possible outcome for other protocols such as mupirocin alone or in combination with other agents. There was additional evidence from one small ITS,¹¹² which used nasal mupirocin and 4% CHG wipes for patients colonised with MRSA in a neonatal ICU and did not report a significant decrease in the incidence of MRSA acquisition in the intervention period in comparison to pre-intervention (2.00 versus 2.38 events/1000pd, IRR=1.85 [CI95% 0.80–1.73], $p=NR$). This study had a small sample size; thus, it was likely to be underpowered and at risk of type I error. Further evidence was obtained from thirteen UBA studies,^{119,121,122,123,124,126,130-132,134,143-146} which found similar results. Introduction of mupirocin itself was beneficial in one study¹⁴⁴ and not significantly reduced in another.¹⁴⁵ Application of mupirocin in combination with a skin decolonisation agent was beneficial in eight studies^{122,123,124,130-132,134,143} while three studies^{119,126,146} reported no significant benefit.

There was strong evidence of no relationship between mupirocin use and resistance from eight studies.^{92,93,97,105,132,138,141,147} Meta-analysis showed that the prevalence was slightly higher in the group where mupirocin alone was used as compared to the no mupirocin group

(13.27% versus 11.18%), although the difference was not significant (OR=1.21 [CI95% 0.64-2.29]).

There was moderate evidence from 12 studies,^{88/89,92-94,111,126,131,137,139,142} which reported adverse events associated with the use of mupirocin. The studies reported discomfort,^{88/89} burning sensation,⁹² itching,⁹² dryness,⁹² rhinorrhoea,⁹⁴ nasal irritation,⁹⁴ nose bleeds,¹³⁹ headaches,⁹⁴ congestion,⁹⁴ cough,⁹⁴ pharyngeal pain⁹⁴ and unspecified adverse events.^{92,93,111,126,131,137,138,142} Two studies reported that treatment had to be discontinued due to adverse events associated with mupirocin use in some patients^{94,138} and one study reported that 38% of the patients considered the treatment to be unpleasant, regardless of whether they experienced adverse events.⁹⁴ The results of meta-analysis showed that the use of mupirocin was associated with an over-six-times higher risk of experiencing adverse events when compared to a group that used no decolonisation or placebo (RR=6.44 [CI95% 4.85-8.54], p<0.0001). When comparing to nasal placebo only, the incidence of adverse events with mupirocin was significantly lower (RR=0.30 [CI95% 0.16-0.57], p=0.0002).

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the cost-effectiveness of mupirocin.

Octenidine

There was moderate evidence of benefit from one ITS,¹⁰⁴ one controlled trial¹⁴⁸ and one CBA study¹⁰¹ which investigated the effectiveness of skin decolonisation with octenidine on the incidence of MRSA acquisition and the incidence of MRSA infection. The results of the meta-analyses showed that octenidine alone or in combination with a nasal decolonisation agent was more effective when compared to no decolonisation or placebo. For octenidine alone, the incidence of MRSA acquisition was 2.96% in the octenidine group versus 3.04% in the control group (p=0.7361), and the incidence of infection was 0.81% versus 1.49%, p=0.001. When octenidine was used in combination with a nasal decolonisation agent, the incidence of MRSA acquisition/1000pd was 0.19 versus 3.10, p<0.001, and the incidence of infection per 1000pd was 0.01 versus 0.46, p<0.0001.

There was weak evidence of benefit from one CBA study¹⁰¹ and one ITS¹¹³ which investigated the effectiveness of nasal decolonisation with octenidine gel in combination with either CHG^{101,113} or octenidine wash.¹⁰¹ The CBA study¹⁰¹ reported that octenidine gel significantly reduced the MRSA prevalence rates as compared to the MRSA rates before decolonisation was in place (19.3% versus 38.5%, p=0.007 and 34.4% versus 48.1%, p=0.001 for octenidine wash and CHG wash, respectively) while the prevalence on the control ward where no decolonisation was in place remained the same (38.9% versus 43.4%, p=0.554). Another study,¹¹³ conducted in extended care facilities for stroke and trauma patients reported that the incidence of MRSA acquisition decreased from 7.0 to 4.4 events per 1000pd (p<0.0001).

There was weak evidence of resistance from one cross-sectional study,¹³⁵ which evaluated MRSA isolates obtained from patients. The study reported that those patients who were exposed to octenidine were more likely to carry MRSA isolates with disinfectant resistance genes *qacA/B* than those who were not exposed (AOR=11.79, [CI95% 5.14-27.04], $p<0.001$) but not more likely to carry the isolates with the *qacC* genes (AOR=0.55 [CI95% 0.23-1.31], $p=0.18$). The authors reported that a higher proportion of isolates obtained from patients previously exposed to octenidine had reduced susceptibility to octenidine (MIC levels ≥ 2 mg/L) than the isolates from patients with no exposure history AOR=0.27, [0.08-0.95], $p<0.01$.

There was moderate evidence from two studies^{101,148} which reported adverse events associated with the use of octenidine. One study which assessed adverse events when using octenidine soap reported no events in a sample of 5277 patients¹⁴⁸ while another assessing octenidine nasal gel reported one case (1/731, 0.14%) of adverse events (not specified) which resulted in discontinuation of use of the nasal gel in the affected patient.¹⁰¹

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the cost-effectiveness of octenidine.

Povidone-iodine (PVP)

There was weak evidence from one RCT,⁹⁴ which investigated the effectiveness of 5% PVP versus 2% nasal mupirocin alone and in combination with CHG wash on the incidence of deep surgical site infections (SSI) caused by MRSA in surgical patients (no denominator). The study reported a very low incidence of MRSA SSI and eradication of MRSA, with one case (0.12%) occurring in each group. There was further evidence from UBA studies, two of which reported a benefit of introducing PVP in combination with CHG when compared to CHG alone¹⁴⁹ or to no decolonisation protocol.¹²⁰ The remaining UBA study¹⁵⁰ reported no difference in clinical outcomes when mupirocin was replaced by PVP while reporting better patient experience in PVP group.

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the resistance of MRSA to PVP.

There was weak evidence from one RCT⁹⁴ which reported adverse events associated with the use of PVP. The study reported some adverse events including headache, rhinorrhoea, nasal irritation, congestion, cough and pharyngeal pain. These were less prevalent than those for mupirocin (1.78% versus 8.90%, $p<0.0001$). The authors reported that significantly fewer patients considered the treatment unpleasant (3.6% versus 38% in mupirocin group, $p<0.0001$), and concluded that this was possibly related to the fact that PVP was applied only twice on the day of the surgery as opposed to two applications for five days for the standard mupirocin treatment.

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the cost-effectiveness of PVP.

Other decolonisation therapies

There was weak evidence from nine other studies, which investigated the effectiveness of other agents on the prevalence of MRSA colonisation, the incidence of MRSA acquisition, the incidence of MRSA infection and the eradication of MRSA. The studies used a skin decolonisation regimen with 1% triclosan,^{138,151} 5% tea tree oil,¹⁵² polyhexanide cloths,¹⁵³ 3% hexachlorophene¹³⁹ as well as the nasal application of 30% medical grade honey ointment,¹³⁸ polyhexanide gel,¹⁵² polysporin triple ointment,⁹³ ofloxacin drops for eradication of MRSA in the ears,¹³⁶ gentamicin cream for peritoneal catheter exit sites¹⁴⁰ and alcohol-based nasal antiseptic.¹⁵⁴ One of these studies,¹⁵⁴ a UBA, suggested a potential benefit when using selective alcohol-based nasal antiseptic administered twice daily in addition to CHG bathing in place of extensively used contact precautions (CP) for all MRSA colonised patients. The authors reported that the incidence of MRSA BSI remained the same (data not reported) while they successfully reduced the number of isolation days by 88.33% ($p < 0.0001$) as well as a reduction in glove and gown use, which provided a saving of USD 430,604 (approx. £314,315) for the 10-month period in seven hospitals participating in the intervention. None of the therapies were reported to be effective.

The Working Party considered the evidence and concluded that high quality studies support the use of CHG and mupirocin, either used alone or in combination. Octenidine may be used as an alternative when CHG is not feasible. The effectiveness of alternative agents, including octenidine, PVP and triclosan needs to be adequately assessed. Concern remains about resistance associated with the use of CHG and mupirocin. Whilst the meta-analysis for mupirocin did not show that the risk of resistance increased with mupirocin use, the Working Party concluded that this most likely reflected the ecology of changing MRSA strains and not the evidence that the resistance is not resultant from the excessive use.

Recommendations

6.1 Use mupirocin for nasal decolonisation, either selectively (i.e., for those who are colonised) or universally (i.e., for all high-risk patients).

6.2 Use chlorhexidine, either selectively or universally, for body decolonisation to reduce MRSA carriage.

6.3 Consider alternatives (e.g. octenidine) where mupirocin and chlorhexidine are not feasible.

6.4 Monitor the emergence of resistance, especially to mupirocin and chlorhexidine, if used extensively.

Good Practice Points

GPP 6.1 Follow manufacturers' guidance when using decolonisation products.

GPP 6.2 For skin decolonisation, if 4% chlorhexidine wash is used, moisten the skin, apply the wash, and leave for 1-3min before rinsing off; if 2% chlorhexidine wipes are used, do not rinse off.

GPP 6.3 For skin decolonisation, pay special attention to known carriage sites such as the axilla, groin, and perineal area.

GPP 6.4 After each bath and wash, provide clean clothing, bedding, and towels.

GPP 6.5 Consider using chlorhexidine in neonates only if there is no alternative and there is no broken skin present (for evidence on CHG safety in neonates, see Appendix 5).

GPP 6.6 Make healthcare workers and patients aware that decolonisation therapy does not necessarily result in complete eradication but that achieving temporary suppression is sufficient in many circumstances.

8.7 What is the clinical and cost-effectiveness of environmental screening/sampling in minimising the transmission of MRSA?

MRSA resists desiccation and can survive in hospital dust for up to a year. It is found throughout the hospital environment, particularly around patients known to be colonised or infected with the bacterium. Environmental contamination with MRSA may contribute to transmission when healthcare workers contaminate their hands or gloves by touching contaminated surfaces, or when patients come into direct contact with contaminated surfaces. There is little understanding of whether environmental screening/sampling has a beneficial effect on environmental MRSA contamination or clinical outcomes. Previous MRSA guidelines did not assess this outcome and did not provide any recommendation.

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design, and which assessed the benefit of environmental screening/sampling on the prevalence of MRSA colonisation or the incidence of MRSA acquisition.

There was weak evidence from one stepped wedge trial¹⁵⁵ which assessed the effectiveness of the cleaning/disinfection bundle on the rates of BSI in hospitals with ICUs. The bundle consisted of training and providing advice on the use of cleaning/disinfection agents and the feedback to staff after cleaning and disinfection. The study reported a beneficial improvement in overall cleanness, but no effects on MRSA BSI (n=22, 0.17/10,000pd versus n=66, 0.19/10,000pd, p=0.7674). Further evidence came from one UBA study¹⁵⁶ which reported an

intervention where the environmental services staff received training, following which audits were periodically conducted. General cleanness was assessed using adenosine triphosphate (ATP) bioluminescence assay and results were fed back to the staff. The authors reported that no changes were observed in the incidence of MRSA acquisition in the pre- and post-intervention periods (n= 171 acquisitions versus=178 respectively, p value not reported).

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design, and which assessed the cost-effectiveness of environmental screening/sampling.

The Working Party considered the evidence and, together with clinical experience of the Working Party members, concluded that there is currently insufficient evidence to support the routine use of screening/sampling of equipment. However, it was recognised that there may be circumstances (e.g. outbreaks) where this may be beneficial.

Recommendations

7.1 Do not screen/sample the environment routinely.

7.2 Consider using environmental screening/sampling as part of targeted investigation of an outbreak.

8.8 What are the most effective cleaning/disinfection agents and technologies for reducing environmental contamination in the near patient environment and minimising transmission of MRSA?

There is evidence supporting the role of cleaning and disinfection in hospitals as an important intervention in the control of MRSA. Unfortunately, it often constitutes part of an overall IPC package in response to an outbreak and its importance as a stand-alone activity remains undetermined. There are a variety of cleaning and disinfection agents and technologies available for reducing environmental contamination but guidance regarding the best approaches is limited and the policies vary considerably between hospitals. Disinfection agents include alcohols (e.g. isopropyl, ethyl alcohol, methylated spirit), quaternary ammonium compounds (QAC) (e.g. alkyl dimethyl benzyl ammonium chloride, alkyl dimethyl ethyl benzyl, ammonium chloride), phenolics (e.g. benzyl-4-chlorophenol, amylphenol, phenyl phenol) and sodium hypochlorite (e.g. sodium dichloroisocyanurate). It is not known which agents are efficient for decontamination (decontamination relates to a process where microbial contamination is removed to render the environment or an item safe; please see the glossary). Previous guidelines recommended that cleaning regimens and products should be in accordance with local policy, and that they should include products able to remove organic material.¹ Additionally, new approaches have been proposed, including room decontamination with ultraviolet (UV) irradiation or hydrogen peroxide vapour (HPV) systems or the use of antimicrobial surfaces, but their effectiveness in preventing MRSA acquisition and infection was not discussed by the previous guidelines.¹

There was moderate evidence for benefit from two controlled trials^{157,158} and one ITS¹⁵⁹ which investigated the effectiveness of HPV on hospital cleanness. All studies reported that using HPV in addition to the standard cleaning and disinfection regimen (i.e., what was used in the hospital before an intervention was introduced) resulted in a significantly lower number of sites contaminated with MRSA. One study¹⁵⁷ in particular showed that the terminal cleaning (this term is used to describe a process of thorough cleaning and disinfection; please refer to glossary in Supplementary Materials file) with standard sanitiser (details not reported) resulted in 66.1% of sites still being contaminated with MRSA as opposed to 1.2% when HPV was added to post-manual cleaning and disinfection (OR=0.02 [CI95% 0.00-0.13], $p<0.0001$). Another trial¹⁵⁸ which assessed the number of rooms contaminated with MRSA found a lower rate of contamination in rooms where HPV was used in conjunction with manual cleaning and disinfection with QAC, concentration not reported), although the difference was not significant (2.02% versus 3.80%, OR=0.53 [CI95% 0.21-1.31], $p=0.1708$) compared to the rooms terminally cleaned with QAC only. The last study¹⁵⁹ showed a significantly lower proportion of sites contaminated with MRSA (6.2% versus 7.2%, OR=0.86 [CI95% 0.79-0.94], $p=0.0008$). This translated to a significant reduction of MRSA acquisition (186 versus 334 cases, $p<0.0001$) and a small, non-significant decrease in MRSA BSI (0.11 versus 0.16 cases/1000pd, $p=0.58$). Further evidence came from one UBA study¹⁶⁰ which reported that significantly fewer sites were contaminated with MRSA following the use of HPV when compared to a standard cleaning/disinfection with QAC (concentration not reported) and 0.5% sodium hypochlorite (0.06% versus 2.14%, OR=0.03 [CI95% 0.01-0.11], $p<0.0001$).

There was inconsistent evidence of the benefit from one RCT,¹⁶¹⁻¹⁶³ one controlled trial,¹⁶⁴ one ITS¹⁶⁵ and two CBA studies^{166,167} which assessed the effectiveness of UV devices on the colony counts and the reduction of MRSA contamination^{163,164} and MRSA acquisition rates.^{161,162,165-167} One RCT, which was described in three separate articles¹⁶¹⁻¹⁶³ reported that MRSA acquisition and infection rates were not affected using UV-C light devices. This was regardless of whether the outcomes were assessed on the whole hospital population¹⁶² ($n=259$, 0.31% in QAC + UV-C light arm, $n=242$, 0.29% hypochlorite + UV-C arm versus $n=204$, 0.27% in QAC arm) or just patients in rooms previously occupied by MRSA carriers¹⁶¹ ($n=54$, 1.6% in QAC + UV-C light arm, $n=89$, 2.3% hypochlorite + UV-C arm versus $n=73$, 2.1% in QAC arm). These studies showed that UV-C light may be used as a part of an IPC strategy due to their benefits in controlling bacteria other than MRSA. The authors collected environmental samples and published the data in a separate article.¹⁶³ The mean number of colony forming units (cfu) in rooms and bathrooms was 8.52 in the QAC group, 4.34 in hypochlorite group and 0.11 and 0.85 for QAC and hypochlorite with UV-C groups, respectively (significance not reported). Another controlled trial¹⁶⁴ reported that the colony counts and the reduction of MRSA contamination from baseline did not improve following the introduction of the UV-C light system (99.4% versus 91.1% hypochlorite (1:10) alone). This study reported a high variation in colony counts in the manual cleaning/disinfection arm, which was attributed to inconsistencies in cleaning and disinfection by the personnel. Two low-quality CBA

studies^{166,167} conducted in ICUs and one ITS¹⁶⁵ showed the benefit of adding pulsed-xenon UV (PX-UV) device to standard cleaning and disinfection with either QAC (concentration not reported),¹⁶⁶ hypochlorite (concentration not reported),¹⁶⁷ or standard cleaning and disinfection (details not reported).¹⁶⁵ The first CBA study¹⁶⁶ reported that the incidence of MRSA acquisition in the intervention ICUs decreased from 3.56 to 2.21 events per 1000pd (IRR=0.556 [CI95% 0.309–0.999], $p=0.0497$) following the use of PX-UV device, while it significantly increased from 0.33 to 0.38 events per 1000pd (IRR=10.967 [CI95% 7.061–17.033], $p<0.0001$) in other hospital wards. The second study¹⁶⁷ reported a decrease from 14.02 to 9.5 MRSA acquisitions per 10,000pd (IRR=0.71 [CI95% 0.57-0.88], $p<0.002$) in the intervention ICUs using a PX-UV device, while reporting that the neighbouring high care units and the general wards did not experience a decrease in MRSA acquisitions (IRR=0.85 [CI95% 0.65-1.12], $p=0.283$ and IRR=1.14 [CI95% 0.62-2.12], $p=0.663$ respectively). Finally, one ITS¹⁶⁵ reported a benefit of adding a UV-C device to standard cleaning and disinfection (not described) in general acute wards. The device resulted in the incidence of HCAI-MRSA decreasing from 0.7% (91/12,747 or 1.42/1000pd) to 0.5% (61/13,177, RR=0.65 [CI95% 0.47-0.70], $p=0.0087$ or 0.98/1000pd), which in ITS analysis corresponded to a 30.79% reduction, $p=0.02$. The authors reported annual savings of USD 1,219,878 (approx. £889,474) mostly due to a decreased length of stay (LOS). Further evidence came from two UBA studies which used UV-C devices and found no effect on MRSA colonisation¹⁶⁸ or infection.¹⁶⁹

There was weak evidence of no benefit from one controlled study with crossover¹⁷⁰ and RCT¹⁷¹ which assessed the effectiveness of adding copper fittings to high-touch surfaces to prevent MRSA transmission. One study¹⁷¹ reported no difference in the incidence of MRSA infections in patients admitted to isolation rooms with copper surfaces (2/36) as compared to standard surfaces (3/34, OR=0.63 [CI95% 0.10-.4.00], $p=0.6240$). Another study¹⁷⁰ reported that adding copper fixtures did not result in a decrease in the number of sites being contaminated with MRSA (2.3% versus 3.7% for the sites without copper, OR=0.621, [CI95% 0.306-1.262], $p=0.217$). Both studies concluded that copper surfaces can be used as a part of an IPC strategy due to their benefits in controlling bacteria other than MRSA.

There was weak evidence of benefit from one RCT of acceptable quality¹⁷² and low-quality controlled trial¹⁷³ which assessed the effectiveness of antimicrobial curtains. The RCT¹⁷² compared the MRSA contamination (no patient outcomes) of standard curtains and antimicrobial curtains impregnated with halamine (BioSmart®) with or without hypochlorite spray twice weekly. The authors described that halamine curtains can be 're-charged' with hypochlorite, during which process amine polymers impregnated into the fabric are able to bind the chlorine ions, which in turn provide an antimicrobial benefit. The study reported no decrease in the number of curtains contaminated with MRSA when comparing the halamine and standard curtains (7/14, 50% versus 7/13, 53.8%, not significant). There was no decrease when comparing the standard curtains to curtains pre-sprayed in halamine with the hypochlorite group (7/13, 53.8% versus 6/14 (42.9%, not significant). The number of contaminated curtains after spraying reduced from six (42.9%) to one (7.1%, significance not

reported). Another study, which was a low-quality controlled trial¹⁷³ compared two different types of antimicrobial curtain (impregnated with either silver, or QAC combined with polyorganosiloxane) to a standard curtain. There was a significant decrease in the number of curtains contaminated when comparing curtains impregnated with QAC and polyorganosiloxane (3/580, 0.5%) and a standard curtain (204/507 (40.2%), RR=0.02 [CI95% 0.00-0.04], $p<0.0001$, a difference of 39.7% [CI95% 34.8–44.0%], but no decrease in the number of curtains contaminated with MRSA when comparing silver impregnated (137/267, 51.3%) and the standard curtain (204/507 (40.2%), RR=1.28 [CI95% 1.09-1.49], $p=0.0025$).

There was weak evidence from one UBA study¹⁷⁴ assessing the effectiveness of titanium dioxide-based photocatalyst reactive to visible light, which was painted to the walls and high-touch surfaces in medical ICU rooms. The authors reported a significant decrease in the number of MRSA acquisitions by patients (4/280, 1.4% or 2.57/1000pd) from the pre-intervention period (15/341, 4.4% or 9.30/1000pd, $p=0.01$; IRR=0.26 [CI95% 0.06–0.81]).

There was inconsistent evidence of benefit reported by one RCT^{161/162}, three controlled trials¹⁷⁵⁻¹⁷⁷ and two ITS^{178,179} studies investigating different types of cleaning and disinfection agents. One ITS,¹⁷⁸ which replaced hypochloric acid (concentration 1000ppm) with chlorine dioxide (concentration 275 ppm) reported a significant change in MRSA acquisition per 100 bed days/month at 12 months from the start of the intervention. Another ITS¹⁷⁹ reported that switching from cleaning with detergent wipes followed by alcohol wipes (details on ingredients and concentration not reported) to one wipe system (containing <0.5% benzalkonium chloride, <0.5% didecyl dimethyl ammonium chloride and <0.10% polyhexamethylene biguanide) in a general hospital setting, resulted in the reduction of the incidence of MRSA acquisition from 26.8 per 100,000pd to 9.4 per 100,000pd ($p<0.0001$). The authors reported that there was no significant difference in the incidence of MRSA BSI between the pre- and post-intervention periods (1.8 and 0.2 per 100,000pd respectively, p value not reported). One controlled trial¹⁷⁶ reported beneficial effects of 10% bleach (not specified, presumably hypochlorite) compared to Biomist® (QAC in 58.6% alcohol), with the proportion of sites contaminated with MRSA in Biomist® group reported as 5/23 (21.7%), while there were no contaminated sites in the bleach group (0/40, 0%, $p=0.0007$). Other controlled trials did not report any difference in cleaning and disinfection or clinical outcomes when using a disinfectant with QAC (0.25% QAC, referred to as ammonium arm) versus bleach arm (1:10 hypochlorite wipes),^{161/162} or QAC (concentration not reported) versus 0.5% hydrogen peroxide wipes¹⁷⁵ or when comparing QAC (concentration not reported), 10% hypochlorite, hydrogen peroxide with peracetic acid (concentration not reported) or standard detergent (i.e., what was previously used in practice, details not reported) to each other.¹⁷⁷ Further evidence came from two UBA studies. One study¹⁸⁰ reported no change in environmental contamination after switching from standard detergent (details not reported) to sodium hypochlorite with 1000ppm chlorine (13.2% versus 10.1%, OR=1.31 [CI95% 0.70-2.46], $p=0.4021$). Another study¹⁸¹ used JUC® spray, a polymeric surfactant containing QAC (concentration not reported), which was sprayed on the surfaces following the cleaning. The

study found that none of the bed units (0/18, 0.0%) were contaminated with MRSA following the treatment. This was in contrast to 4/18 (22.2%) of sites cleaned with hypochlorite, concentration not reported (OR=0.11 [CI95% 0.01-2.21], p=0.1501). The study was too small to draw inferences, but authors concluded that JUC® spray may be beneficial in controlling staphylococcal load for up to four hours following its application.

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design, and which investigated the cost-effectiveness of different cleaning and disinfection agents or hands-free devices.

The Working Party considered the data above and, together with clinical experience of the Working Party members, concluded that there is no evidence that antimicrobial surfaces can control MRSA. Some new technologies can be used as a part of wider IPC strategy to eliminate the inconsistencies associated with manual cleaning and disinfection, while HPV/UV-C/PX-UV may be beneficial as a part of terminal cleaning. The Working Party considered that the disinfection agents have similar efficacy against MRSA.

Recommendations

8.1 Continue using currently utilised products approved for use in healthcare.

8.2 Consider hydrogen peroxide vapour (HPV) or ultraviolet (UV-C, PX-UV) devices as an adjunct to terminal cleaning as a part of a wider IPC strategy.

8.9 What is the evidence that local surveillance and feedback to staff is effective in minimising the transmission of MRSA?

Surveillance plays two roles with respect to IPC: it allows detection of infected/colonised individuals necessary for their removal from the general population, and it allows quantification of control success. Many hospitals have introduced surveillance systems to monitor MRSA cases. This surveillance can be used to assess the infection risk of people in hospital and inform the response. Since the last guidelines were published, mandatory national surveillance of MRSA cases has been set up in many countries, with hospitals being required to report infections to public health bodies (for example, in England, acute trusts are required to report all cases of BSI). This not only allows monitoring on a hospital level, but also allows the hospitals to compare their data to other facilities and to the national average.

There was moderate evidence from one RCT¹⁸² and two ITS^{183,184} studies which assessed the effectiveness of hospital surveillance on the incidence of MRSA BSI or MRSA acquisition.

One study,¹⁸² which recruited three units in participating hospitals and randomly assigned one unit into each intervention, used statistical process control charts (SPC) to monitor and feedback the MRSA acquisition rates to the staff on participating units. The authors reported

a decrease in the average MRSA acquisition rates in the units which used either SPC charts alone or SPC charts with Pareto charts, which promoted IPC improvements on the units in comparison to the wards which did not use the charts. For the SPC group, the authors reported that the MRSA rate was stable during the baseline period with a possible increase in acquisition as observed from the last six points on the chart before the intervention was introduced. A monthly average of 48 cases was observed during the baseline period, which fell to 30 cases per month post-intervention. For SPC + Pareto charts, continuous post-intervention improvements were observed with the average MRSA acquisition reduced from 50 to 26 cases per month. Lastly, the control arm experienced a slight pre-intervention reduction and a more significant post-intervention reduction from an average of 49 cases to 36 per month. This decrease was not sustained, and in the last six out of seven points shown on SPC charts, an increase in the number of MRSA acquisitions was observed. One ITS¹⁸³ showed a marked reduction in BSI in ICU as well as other hospital patients even though the surveillance was limited to ICU only. The authors did not report a p value, but the prevalence rate was 1.6/1000pd in ICU and 0.6/1000pd in hospital. These rates are substantially lower than those predicted by ITS analysis which would have been 4.1/1000pd and 1.4/1000pd, respectively, if surveillance was not in place. The authors did not report any information about the interventions which were introduced following the surveillance. The last ITS study,¹⁸⁴ which used SPC charts to feed the data back to staff to drive the improvement across the hospital, reported that the incidence of MRSA acquisition across the hospital decreased from 3.0 [CI95% 2.8-3.2] to 1.7 [CI95% 1.6-1.8] events per 100 patient admissions ($p < 0.001$). The decrease was also observed in ICUs (9.3 [CI95% 7.5-11.2] versus 6.7 [CI95% 5.2-8.5], $p = 0.047$). The authors reported that a significant decrease was observed in hospital MRSA BSI (0.45 [CI95% 0.38-0.52] pre-intervention versus 0.27 [CI95% 0.24-0.32] per 100 patient admissions, $p = 0.02$ post-intervention) as well as in ICU central line-associated MRSA BSI (CLABSI) (2.0 [CI95% 1.3-3.0] versus 1.1 [CI95% 0.7-1.7] per 100 device days, $p = 0.018$ for pre- and post-intervention respectively).

Further evidence of the benefit came from a total of eight UBA studies.¹⁸⁵⁻¹⁹² Two of these studies reported a decreased prevalence of MRSA colonised patients in their hospitals.^{186,187} One study,¹⁸⁵ which reported a very low baseline prevalence of MRSA demonstrated that five years after the start of a mandatory surveillance of MRSA BSI cases, the prevalence of MRSA did not decrease significantly in their hospital (4.3% versus 12.2%, $p = 0.317$) when comparing all MRSA isolates. A significant change was observed when only non-BSI isolates were included (3.5% versus 8.6%, $p < 0.001$). While the rate of MRSA BSI remained unchanged throughout the five years (data not reported, $p = 0.555$), the rate of non-BSI isolates decreased each quarter by 0.47-1.61 cases/1000 patient episodes, which was significant ($p = 0.007$). The authors concluded that since the rate of MRSA BSI was very low in their setting, surveillance of non-BSI cases may be more beneficial. Furthermore, of the UBA studies which reported incidence of MRSA infection, four reported that the incidence of MRSA BSI declined following the introduction of surveillance,^{187,190-192} two reported no benefit^{185,189} and, one reported the benefit on some but not all units in the hospital.¹⁸⁸

The Working Party considered the evidence from the included studies and together with the evidence from previous guidelines and the clinical experience of the Working Party members, concluded that hospital surveillance must remain a component of any strategy to prevent and control MRSA infections.

Recommendation

9.1 Undertake surveillance routinely as part of the hospital's infection prevention and control strategy and to comply with mandatory national requirements.

8.10 What is the evidence that local and/or national surveillance for MRSA is effective in driving service/ system improvement?

Beyond the hospital-wide surveillance system further extensive surveillance of MRSA cases may be performed at unit level. Previous MRSA guidelines concluded that surveillance must be undertaken routinely as part of the hospital's IPC programme and that it must be a recognised element of the clinical governance process. Thus, there should be clear arrangements identifying those responsible for acting on the results in individual hospital directorates. This question was not assessed in our previous MRSA guidelines and no recommendation was made.

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design, and which assessed the effectiveness of local versus national surveillance for MRSA in driving service or system improvement.

Other sources of evidence were considered. One excluded study,¹⁹³ which did not meet the criteria for this review, reviewed the data of the mandatory surveillance of MRSA in England. Since 2001 when mandatory surveillance was introduced, all acute trusts reported the data quarterly. This data was publicly published, and the feedback was given to the trusts. Additionally, the trusts were given a target to reduce their MRSA BSI rates by 50% by 2008 and all trusts not meeting their trajectories were audited. The overall rate of BSI in England decreased by 56% between 2004 and 2008 and further decreased by 50% from 2008 to 2011, reaching 1.8 cases per 100,000pd. The authors reported that mandatory surveillance and feedback from the surveillance drove the implementation of interventions which ultimately contributed to reduced incidence of MRSA BSI.

Data on MRSA BSI surveillance for England, Scotland, Wales and Northern Ireland as well as all European Union countries are available (<https://www.gov.uk/government/statistics/mrsa-bis-annual-data>; <https://ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/report>).

The Working Party considered the evidence from the above study, and together with the evidence from previous guidelines and the clinical experience of the Working Party members, concluded that recommendation cannot be made based on current knowledge.

Recommendation

10.1 No recommendation

Good Practice Point

GPP 10.1 Consider using local surveillance of MRSA acquisition (colonisation and infection) as a component of local strategies to prevent and control MRSA and to drive improvement where needed.

8.11 To what extent are contact precautions effective in minimising the transmission of MRSA? To what extent does the isolation or cohorting of patients minimise the transmission of MRSA and what are the costs?

Staphylococcus aureus is a commensal organism of human skin occupying body sites such as nose, axilla, and groin. Patients with MRSA are commonly colonised at these body sites and the organism may contaminate their immediate environment.¹⁹⁴ Transmission of MRSA in healthcare settings occurs when *Staphylococcus aureus* is acquired on the hands of staff and then transferred to other patients, surfaces or equipment.¹⁹⁵ Hand hygiene with either soap and water or alcohol hand rub removes microorganisms including MRSA from hands, and interrupts transmission.¹⁹⁶ Standard precautions¹⁹⁷ and recommendations from the WHO Hand Hygiene guidelines¹⁹⁶ require that staff wash their hands before and after direct contact with the patient and their immediate environment, and any susceptible site on the patient. Standard precautions are therefore essential to prevent transmission of MRSA to other patients and protect susceptible sites on the patient from infection.¹⁹⁶

The previous MRSA guidelines¹ found consistent weaknesses in studies reporting the use of screening and isolation interventions for the prevention of MRSA because many reports describe the simultaneous implementation of multiple interventions, making it difficult to draw clear conclusions about the effect of any intervention independently. They concluded that there was some acceptable evidence that screening and isolation of patients contribute to reductions in MRSA outbreak and endemic situations. The recommendations in the previous guidelines were therefore that 'a standard approach to isolation precautions should be adopted in accordance with the general principles of IPC, rather than introducing specific guidance for the management of MRSA that may lead to differing standards.' The guidelines recommended that patients were managed in accordance with the type of setting, the resources available locally (e.g. numbers of isolation rooms), and the risk that they pose to others or that is posed to them.

Since then, the US guideline for isolation precautions has been published¹⁹⁸ which recommended the use of CP for the management of patients with some multidrug-resistant organisms (MDRO), although not specifically MRSA. This guidance recommends that, to contain pathogens, staff don PPE on room entry and discard it on exit, and more specifically that gloves and gowns should be worn when touching patients' intact skin or surfaces in close proximity to the patient. The recommendations are based on a theoretical rationale rather than epidemiological evidence that the use of PPE in this way prevents transmission of MDRO.¹⁹⁸ These guidelines recommended that room cleaning and disinfection is prioritised for patients on CP. The use of CP for the management of patients with MDRO is now widespread but in the UK setting plastic aprons are used in place of gowns. Evidence for the efficacy of CP in reducing transmission of MRSA is uncertain as there are limited acceptable studies that compare CP versus the absence of CP independently.

There was inconsistent evidence from two cluster RCT^{199,200} and three ITS²⁰¹⁻²⁰³ studies which investigated the effectiveness of CP on MRSA acquisition and infection. One study,¹⁹⁹ which used active surveillance combined with CP for MRSA positive patients and universal gloving until patients were confirmed as MRSA negative, reported no significant difference in the incidence of new MRSA acquisitions. This study used CP in both groups, with one arm extending the application of CP (universal gloving) to a broader set of potential carriers in combination with enhanced surveillance and screening. Another study²⁰⁰ compared universal gloving for all patient contacts with CP (gloves/gowns) for patients known to be MRSA positive. Universal gloving was associated with a significant decrease in new MRSA acquisitions (-2.98 risk difference between intervention and control group; $p=0.46$) but the effect of CP versus no CP was not tested. One ITS²⁰¹ found no difference in MRSA acquisition in MRSA colonised or infected patients placed in a single room or nurse cohorted patients as compared to patients with no single room or cohorting. Standard precautions were used with all patients, but this included elements of CP (aprons for all patient contact, gloves for all devices and washing patients). Another ITS²⁰² found a 60% reduction in MRSA acquisition associated with rapid screening, CP and isolation, compared to no isolation and standard precautions (adjusted HR=0.39, [CI95% 0.24-0.62]; $p<0.001$; segmented regression change in slope $p<0.001$). This study was sensitive to bias as a stricter screening method was used during the intervention period, the separate effect of single room and CP were not distinguished, and the study was conducted in an ICU where MRSA was endemic, and decolonisation was not a routine practice. One very low-quality ITS²⁰³ in an acute hospital found a decrease in MRSA device-associated infection rates associated with discontinuing CP for known MRSA positives, but other practice changes were introduced at the same time.

There was moderate evidence of a negative effect of CP on the patient experience and mental wellbeing from five qualitative studies.²⁰⁴⁻²⁰⁷ These studies focused specifically on the impact of isolation for MRSA colonisation or infection. These studies concluded that isolation had an impact on patient experience and resulted in increased anxiety and low mood.²⁰³⁻²⁰⁷ Additionally, in a study of 57 Dutch MRSA colonised patients,²⁰⁸ it was reported that a

substantial proportion of MRSA carriers reported stigma due to MRSA, and stigma was associated with poor mental health. These studies were all small scale, in different populations and for varying durations of isolation. They reported mixed findings but suggested that isolation should be of as short a duration as possible to avoid anxiety and potential depression.

No evidence was found from the studies published since 2004 meeting the inclusion criteria for the study design, which assessed the cost-effectiveness of CP.

Additional evidence was obtained from national guidelines¹⁹⁷ and seven UBA studies^{154,209-214} which attempted to discontinue CP in hospitals (including ICU and general wards). In one of these studies a nurse cohorting area was associated with a significant decrease in MRSA transmission.²⁰⁹ Another study²¹⁰ found no effect of including gowns as part of CP on risk of MRSA transmission. The remaining studies^{154,211-214} found no difference in the rate of MRSA acquisition associated with discontinuation of CP for known MRSA patients.

The Working Party considered the evidence from the included studies together with the evidence from previous guidelines and the clinical experience of the Working Party members, and concluded that the decision to isolate or cohort patients colonised with MRSA should be based on risk assessment and patient experience. Currently there is little evidence that CP are necessary, but the Working Party acknowledged that they are widely used in health and care settings and that some facilities may decide to continue with this practice.

Recommendations

11.1 Use standard infection prevention and control precautions in the care of all patients to minimise the risk of MRSA transmission.

11.2 For patients known to be colonised/infected with MRSA, consider using contact precautions for direct contact with the patient or their immediate environment. If contact precautions are used, gloves and aprons must be changed between care procedures and hand hygiene must be performed after glove removal.

11.3 Consider placing patients colonised or infected with MRSA in a single room. The decision to use a single room should be based on a risk assessment that considers the risk of transmission associated with the patient's condition and the extent of colonisation or infection (e.g. sputum, exfoliating skin condition, large open wounds) and the risk of transmission to other patients in the specific care setting e.g. in burns units.

11.4 Where isolation is deemed necessary, isolate patients for the shortest possible time to minimise feelings of stigma, loneliness, and low mood.

11.5 Provide clear information to patients about the need for the use of protective equipment to reduce feelings of stigma.

11.6 Be consistent in the use of protective equipment to ensure that patients have confidence in the decision to place them in isolation.

Good Practice Points

GPP 11.1 Advise visitors about the need and available facilities for hand hygiene.

GPP 11.2 Where applicable, advise visitors about the use gloves and aprons.

GPP 11.3 When considering the need to isolate a patient with MRSA in a single room, other demands on single-room use may take priority and alternative strategies such as nurse cohorting may be appropriate.

GPP 11.4 If isolation or cohorting of MRSA patients is not possible, use decolonisation therapy to temporarily suppress MRSA and prevent transmission to other patients.

GPP 11.5 Prioritise room cleaning and disinfection for MRSA patients placed in isolation or on contact precautions.

8.12 What is the evidence that the transfer of patients who are colonised or infected with MRSA between wards/ other care settings contributes to the transmission of MRSA?

Patients who are colonised or infected with MRSA have the potential to transmit MRSA to other patients in the same clinical area. Frequent movement of patients within a single healthcare setting or movement between related healthcare settings has the potential to increase the transmission of MRSA within the healthcare population and between different care settings such as a hospice or residential home. The evidence is currently lacking in establishing the effect of intra- and inter- hospital transfers of patients with MRSA on the rate of new acquisition of MRSA. Evidence for the impact that transferring patients between different units has on the transmission of MRSA can be derived from studies that have used genotyping of isolates to track the transmission of MRSA between patients. In this way, epidemiological links can be established to provide evidence for the extent to which the transfer of patients within and between healthcare facilities contributes to the transmission of infection. Previous MRSA guidelines recommended that patient transfers should be kept to a minimum.

There was moderate evidence from two cross-sectional surveys^{215,216} one prospective cohort study²¹⁷ and one surveillance study²¹⁸ which investigated the effect of patient transfer on MRSA transmission. One study²¹⁵ using whole genome sequencing (WGS) to investigate the origins of 685 MRSA isolates identified in a 13-month period from a total of 610 patients in a single healthcare network comprising of three hospitals, outpatients and community settings, found that 41% (248/610) of MRSA patients were linked in a total to 90 transmission clusters (defined as at least two patients), most of which (68%, 61/90) involved multiple settings. Of these clusters, 42 (38%) involved different settings within one hospital and 30% (n=27) involved more than one hospital. One transmission cluster involved 32 patients between all three. Complex patterns of frequent hospital stays resulted in 81% (26/32) of the MRSA patients who were identified having had multiple contacts with one another during ward stays at any hospital but no outpatient contact, and had shared a GP (general practitioner) or residential area, suggesting that MRSA was transmitted on the wards and spread to other settings as a result of transfers. Another study²¹⁶ used a social network approach by analysing Hospital Episode Statistics (HES) data in England from April 2006 to March 2007 to determine how movements between healthcare institutions, which were derived from patient admissions, affected the incidence of BSI. The MRSA incidence rate for a hospital (adjusted for cluster-specific mean MRSA BSI rates) was found to be contingent on the number of patients it shared with other hospitals within its cluster. The incidence of MRSA BSI increased as the interconnectedness of the hospitals surveyed increased, with strongly connected hospitals in large clusters found to have significantly higher MRSA BSI rates than less connected hospitals. Another study²¹⁷ obtained genotypes and matched the MRSA screening results from admission and discharge from all patients previously admitted to 36 general specialty wards at two Scottish hospitals. The prevalence of MRSA in discharge screens was 2.9% [CI95% 2.43-3.34] and in the set of 2724 patients with paired screens, the odds ratio of acquiring MRSA was 2.64 for patients who stayed on four or more wards compared to those who stayed in three or less. In the last study,²¹⁸ surveillance cultures were obtained from 584 residents admitted to nursing facilities within one healthcare network, representing approximately half of the residents who were admitted to these facilities during the study period. Surveillance cultures were obtained at admission together with data on healthcare contact and antimicrobial use. WGS was performed and the analysis focused on isolates which appeared genetically similar. The gene flow in these facilities was estimated based on single nucleotide variants using Wright's F statistic. A total of 89/117 (76%) MRSA isolates belonged to ST5 or closely related isolates. The authors observed a positive correlation between patient sharing between hospitals and nursing facilities and concluded that the burden of antibiotic resistant organisms (including MRSA) was endemic in their healthcare network and driven by patient sharing in these institutions.

There was moderate evidence from five epidemiological investigations of outbreaks,²¹⁹⁻²²³ which assessed the effect of patient transfers on transmission of MRSA. These studies involved specific outbreak clones, which facilitated investigation of transmission events, and

provided data on the role of hospital transfers. One study²²² reported an outbreak of an unusual New York/Japan epidemic MRSA clone in Western Australia in 22 patients and two healthcare workers who acquired the MRSA. Transfers between another acute hospital (n=3 patients), a community hospital (n=4 patients) and regional care facility (n=3 patients) illustrated how patients acted as vectors and contributed to the transmission of infection. Another study²¹⁹ reported transmission of four new cases of a Pantone-Valentine leucocidin (PVL) MRSA strain from a patient transferred from another hospital, while another study²²⁰ identified MRSA transmission to 13 patients and nine healthcare workers from patients transferred from another hospital. One outbreak investigation²²³ identified that transfer of patients between neonatal and paediatric ICU was a key factor in the transmission of MRSA with a total of 13 patients in paediatric ICU and 14 patients in neonatal ICU acquiring the same MRSA strain. In another outbreak investigation,²²¹ a total of 16 cases of MRSA transmission occurred from a baby, which was transferred from another hospital.

There was moderate evidence from eleven risk factor studies²²⁴⁻²³⁴ which investigated the risk of MRSA acquisition related to transfers between healthcare settings. The studies found that admissions from other acute settings^{224,225,227,229} and long-term settings²²⁴⁻²²⁹ were significant risk factors for detection of MRSA on admission. In a logistic regression model analysis of 81,000 admissions to acute care in Scotland,²³¹ admission 'not from home' was a significant risk factor for MRSA colonisation on admission (OR=3.025 [CI95% 2.685-3.407] and the risk of colonisation increased with the frequency of previous admissions (four or more previous admissions OR=2.484 [CI95% 2.111-2.923]. Although there was a higher incidence of MRSA acquisition for patients who stayed in more wards, this was not statistically significant (OR=1.91 [CI95% 0.97-3.98], p=0.061). Another multivariate analysis of 12,072 admissions (399 with MRSA) to a university hospital in Switzerland²²⁶ found patients who were admitted as an inter-hospital transfer had an odds ratio of 2.4 [CI95% 1.3-4.4] for MRSA carriage. Another Swiss study²³³ of 1621 patients admitted to a geriatric unit, identified an increased risk of MRSA on admission screening associated with intra-hospital transfer (adjusted OR=2.5; [CI95% 1.2-5.3] p=0.02) and hospitalisation within the last 2 years (adjusted OR=2.7 [CI95% 1.1-6.0], p=0.03) and in a small case-control study of 187 admissions to surgical wards of a limited resource hospital in Indonesia, transfer from another hospital was associated with an increased risk of MRSA carriage (OR=7.7 [CI95% 1.2-9.1]).²³² One case-control study,²³⁴ which investigated risk factors for MRSA acquisition in a neonatal ICU identified bed transfer as a potential risk factor, but this was insignificant in the multivariate analysis (43/67, 64% versus 103/201 (51%), OR=1.83 [CI95% 0.97-3.49], p=0.06).

Further cross-sectional studies investigated prevalence and reasons for MRSA acquisition. These studies reported higher prevalence of MRSA in patients previously exposed to another ward,²³⁵ another hospital,²³⁶ or a long-term facility.²³⁷ Another cross-sectional study²³⁸ compared the incidence of MRSA acquisition for the patients who stayed in two, three or four and more wards to the patients who were in one ward during their hospital stay. When the groups of multiple wards were combined, there was a higher incidence of MRSA acquisition

than for patients who stayed in one ward, although this was not significant (OR=1.91 [CI95% 0.97-3.98], p=0.061). When the groups were compared separately, the risk increased with the number of wards the patients stayed in, although this was still not significant. Lastly, one case-control study²³⁹ which investigated the incidence of MRSA infection reported no increased risk in patients transferred to another hospital when compared to those who remained in one hospital throughout their stay.

The Working Party considered the above evidence and the recommendations from previous guidelines and concluded that evidence suggests that patient transfers contribute to transmission of MRSA.

Recommendations

12.1 Do not transfer patients between wards, units, hospitals, or other clinical settings unless it is clinically necessary.

12.2 Inform the receiving ward/unit/care home and the ambulance/transport service that the patient is colonised/infected with MRSA.

Good Practice Point

GPP 12.1 MRSA colonisation is not a barrier to discharging patients to another health care setting, their home or residential care.

8.13 What role does shared equipment have in the transmission of MRSA and how should shared equipment be decontaminated?

One of the risks for transmitting MRSA to patients within healthcare premises or long-term care facilities is the use of improperly cleaned and disinfected medical equipment. When equipment is shared and not cleaned in between patient use, transmission of organisms such as MRSA can occur. Examples of equipment that may be shared between patients include venepuncture tourniquets, stethoscopes, ultrasound transducers, thermometers, blood pressure cuffs, dermatoscopes, pulse oximeters, hoists, hand-held devices, and keyboards. Such equipment needs to be decontaminated after each patient use. Decontamination is the use of physical or chemical means (e.g. alcohol/detergent wipes/sprays, chlorine tablets) to remove, inactivate or destroy pathogens on an item to prevent transmission of infectious agents and render the item safe for use on other patients. Previous MRSA guidelines recommended that patient shared equipment should either be suitable for decontamination or should be single-patient use and discarded as clinical waste after use.

There was weak evidence of potential risk of MRSA transmission from eight studies²³⁹⁻²⁴⁶ which evaluated microbial contamination of shared equipment. One experiment²³⁹ involved

the contamination of stethoscope diaphragms with a known inoculum of MRSA. These were then a) pressed directly onto selective agar and b) onto a pig skin surface and then selective agar. The number of MRSA transferred directly to the agar was approximately 2 Log₁₀, with 1 to 1.5 Log₁₀ fewer transferred by indirect transfer. Following simulated auscultation on 57 patients colonised with MRSA, stethoscopes were pressed onto selective agar and the same procedure was conducted with a sterile gloved hand for comparison. The stethoscope was less likely to transfer MRSA from the patients' skin to agar than gloved hands (11/57 (19%) versus 15/57 (26%); $p=0.05$), with a mean of 5.9 (+/-8.6) versus 14.3 (+/-11.4) ($p=0.01$) acquired and transferred by stethoscopes compared to gloved hands. Wiping the diaphragm with 70% isopropyl alcohol, 70% ethanol, or sterile water, removed 100%, 100% and 94% of the MRSA respectively. Although this study provides evidence that MRSA are potentially transferred by stethoscopes, the number of organisms transferred is lower than would be transferred on hands. A 10-second wipe with alcohol removed all MRSA from the stethoscope and even wiping with water removed over 90% of the contamination. A similar study²⁴⁵ tested a stethoscope disinfection UV device in comparison to wiping the diaphragm with 70% alcohol during examinations of MRSA patients (six skin locations around heart and abdomen for 5-sec contact each). The authors reported that 17/45 (38%) of stethoscopes were contaminated with MRSA, and that after using the UV device, the number reduced to four (9%) ($p<0.01$). The mean number of colonies fell from 4.00 to 0.08 colony forming units (cfu, $p=0.45$). In the 70% isopropyl alcohol pad group, a total of 7/20 (35%) stethoscopes were initially contaminated and cleaning with the pad removed microorganisms from all (0.0%) ($p<0.01$). The sample size was too small to make any inferences between the UV and the alcohol group.

Another study²⁴⁰ cultured the handles of 300 wall-mounted and portable digital thermometers in an acute and long-term care hospital; 8% were contaminated with one or more pathogens, although only 1% of these pathogens were MRSA. To test the risk of cross-contamination from contaminated thermometer handles, six handles on digital thermometers in portable units were inoculated with a DNA marker (generated from a mosaic virus) and an additional fluorescent marker was applied to assess if the thermometer handles were cleaned. The handles were checked at day one and two (acute setting) and 14 (long-term care setting) to assess if the fluorescent marker had been removed. High-touch surfaces (e.g. bed rails, call buttons), other portable equipment and ward areas (e.g. nursing stations) and patient hands (acute setting) were sampled for the presence of the DNA marker on day one and two 2 (acute) and day 14 (long-term care). In the long-term care area, the DNA marker was detected on high-touch surfaces in 21% of 14 rooms sampled and 80% (4/5) of shared portable equipment not previously inoculated with the marker. In the acute setting, the marker was detected in 33% (2/6) of rooms and on the hands of one of six patients. None of the fluorescent markers were removed by day two (acute setting) or 14 (long-term care setting). This study provides evidence that reusable patient equipment does become contaminated with pathogens, although the frequency of contamination with MRSA was very low. If thermometer handles are contaminated, the model suggested there was a risk of

transfer to both the patient and other sites in the care environment. Although not possible to generalise, in the study sites, this shared equipment did not appear to be cleaned.

Four studies evaluated methods of decontamination of shared equipment to minimise the risk of transmission of MRSA. Two used UV light-based devices and one a hydrogen peroxide cabinet. All studies were laboratory-based experiments, and the findings are difficult to apply to a clinical setting. In one study,²⁴¹ an UV-C cabinet designed to deliver large amounts of UV-C radiation for the disinfection of individual pieces of clinical equipment up to approximately 1m³ in size, was evaluated against known pathogens. Eight items were tested (blood pressure gauge and cuff, patient call button, infusion pump, tympanic thermometer, oximeter base unit, keyboard, TV remote control). They were inoculated at nine sample points with a known concentration of test organisms (including a clinical MRSA isolate) and exposed to UV-C for two 30-second doses of 1590 L/m². Additional tests were conducted using bovine serum albumen to represent soiling with organic matter and performance was compared with wiping with an antimicrobial wipe. The cabinet cycle consistently reduced the number of organisms by at least 4.7 Log₁₀ or below 10 cfu on 80% of sample sites but contamination persisted on other sites. The authors reported that efficacy was not affected by organic soil and that a thorough cleaning (4 strokes) with a wipe achieved similar Log₁₀ reductions as the cabinet for some items. The authors concluded the cabinet could provide a means of rapidly decontaminating patient-related equipment but that these laboratory-based findings might not be replicated in use. Another study²⁴² involved testing the efficacy of a portable, hand-held UV irradiation device (Sterilray) designed to be held over surfaces while emitting UV-C radiation. In the laboratory, a known concentration of MRSA was inoculated onto a plastic surface and at 100mJ/cm² the UV device reduced MRSA cfu by 5.4 Log₁₀. A range of surfaces in 27 rooms where a patient was MRSA positive (call light, bedside table, telephone, bed rail) were tested, by culturing before and after the use of the UV-device. A total of 106 sites were cultured and the number positive after use of the device was reduced from 46% to 27% (p=0.007). The less effective reduction associated with in-use items may reflect the effect of organic contamination on the efficacy of the method.

The efficacy of a cabinet that uses 35% hydrogen peroxide mist to disinfect ultrasound transducers in an automated seven-minute cycle was evaluated in simulated use tests in the laboratory.²⁴³ Standardised carrier tests included MRSA inoculated onto a hard plastic surface in combination with organic challenge (5% v/v horse serum). The process successfully eliminated MRSA from 20 carriers. In another study,²⁴⁴ decontamination of ultrasonographic probes inoculated with a known concentration of MRSA was evaluated using a three-step decontamination process (1. cleaning with a dry towel, 2. saline moistened towel, 3. QAC germicidal wipe) or by germicidal wipe alone. In surveillance cultures from probes used in the emergency department taken prior to the experiment, only one of 164 cultures recovered MRSA and only 1.2% of the probes were contaminated by clinically significant pathogens. In the 3-step decontamination process, MRSA was not eliminated after wiping with the towel

but the germicidal wipe in both the 3-step and single step process, eliminated 100% and 90% of MRSA, respectively.

Finally, one study²⁴⁶ described an outbreak investigation involving MRSA and meticillin-sensitive *Staphylococcus aureus* (MSSA) strains. Using the data from clinical isolates, environmental sampling and patient records, together with WGS analysis which helped to identify the clusters, the authors were able to trace the outbreak to contaminated anaesthesia equipment, which following disinfection of an operating room and equipment, was not a source of further cases.

Recommendations

13.1 Clean and disinfect shared pieces of equipment used in the delivery of patient care after each use, utilising products as specified in a local protocol.

Good Practice Points

GPP 13.1 Make all healthcare workers aware of the importance of maintaining a clean and safe care environment for patients. Every healthcare worker needs to know their specific responsibilities for cleaning and decontaminating the clinical environment and the equipment used in patient care.

GPP 13.2 Introduce policies for staff, patients, and visitors to clean their hands before and after they use the shared equipment.

8.14 What information do patients and relatives require in relation to screening, decolonisation and management to minimise anxiety and improve the patient experience? What information do patient's, families and primary/ home care professionals need when a patient is discharged home?

Opinion polls have demonstrated that the fear of developing MRSA is the single greatest concern of people who need to go into hospital for treatment. MRSA has received considerable media coverage, which has helped to shape public awareness. Unfortunately, most of the reporting has been negative and alarmist, so patients due for hospital admission are often anxious about the risk of MRSA infection. Much of the anxiety that patients with MRSA feel stems from the fact that they are not fully or appropriately informed. Lay people do not appear to access credible sources of information, or, if they do access them, are unable to understand their messages. Organisations that provide patient-focused information about MRSA are generic in scope, so that specific information may take time and effort to locate.

There was moderate evidence from a retrospective matched cohort study,²⁴⁷ one retrospective case-control study,²⁴⁸ one survey,²⁴⁹ and five qualitative studies,²⁵⁰⁻²⁵⁴ all undertaken in North America, which investigated the quality of care and other adverse

outcomes potentially associated with isolation for MRSA colonisation or infection. One survey, which evaluated the use of CP in patients with MRSA,²⁴⁹ indicated that patients who were subject to isolation for MRSA were as satisfied with their care as patients who were not isolated. The authors reported that, in this hospital, an infection preventionist made frequent visits to patients placed on CP so that they would be reassured. In a retrospective case control study²⁴⁸ in a tertiary care setting, the authors reported that non-isolated patients had a slightly shorter hospital stay of 6.0 versus 7.0 days but isolated patients received significantly fewer bedside visits ($p=0.01$) and showed a tendency toward more preventable complications ($p=0.06$). Isolated patients had less documented care and less bedside visits from medical staff, which could hamper the therapeutic relationship. In a retrospective matched cohort study²⁴⁷ to examine the effect of isolation precautions on hospital related outcomes and the cost of care, the authors reported no significant differences in 30-day emergency department visits, formal complaints, or inpatient mortality rates between the cohorts. Similar to patients with respiratory illness, patients isolated for MRSA stayed 30% longer (LOS 11.9 days versus 9.1 days [CI95%: 1.22-1.39]), were hospitalised 13% longer than expected, (LOS/ELOS [estimated LOS], 1.3 versus 1.2; [CI95%: 1.07-1.20]) and had 43% higher costs of care (direct cost, CAD 11,009 versus CAD 7670 [CI95% 1.33-1.54]) compared to matched controls.

Five qualitative studies included findings that related to the patient experience of isolation.²⁵⁰⁻²⁵⁴ The studies suggested that patients had a poor understanding of the reason for their isolation and were confused about the need and variation in the use of protective equipment (gloves, aprons, gowns). This confusion led to feelings of anger and frustration toward healthcare staff and the healthcare institution. Isolation in a side room was perceived to have both positive and negative aspects; positives were greater freedom from routine, greater privacy and solitude, and the perception that visitors were given greater freedom. The negative characteristics were a lack of attention from staff and feeling lonely and stigmatised. Isolation also indicated to some the severity (or not) of the condition.

Recommendations

14.1 Make patients aware of the reasons for MRSA screening and decolonisation.

14.2 Inform patients of their screening result as soon as it is available.

14.3 For patients who are identified as MRSA positive, provide consistent and appropriate information about:

The difference between colonisation and infection

The microorganism

How MRSA is acquired and transmitted

How MRSA is treated

The reasons for contact precautions or isolation.

14.4 On discharge provide consistent and appropriate information about:

The risks to household members, friends, and family.

The implications for future health and health care.

Persons who need to be notified about their MRSA colonisation status.

If applicable, instructions on decolonisation regimen with the information that the results may not be permanent.

14.5 Provide information in a format and language that the patient and their family is able to understand.

Good Practice Points

GPP 14.1 Use patient leaflets provided in the Supplementary Materials of this guideline.

GPP 14.2 Inform patients about the possibility of re-colonisation and the importance of changing linen, towels, and clothes daily.

8.15 What needs to be considered by healthcare professionals when a person who is colonised or infected with MRSA dies?

MRSA colonisation or infection in a deceased person is not a risk, but can cause concern amongst funeral directors with some even refusing to take the body. There is negligible risk to mortuary staff or funeral directors provided that standard IPC precautions are employed. An approach to address this problem should include staff training and education. IPC guidelines for funeral directors do exist for many hospital trusts but there is inconsistency in the contents of such guidelines as well as in their implementation. Consistent guidance on what needs to be considered by healthcare professionals when a person who is colonised or infected with MRSA dies, would facilitate the deceased's family obtaining funeral services and protect the involved personnel to minimise the risks of transmission of MRSA. Our previous MRSA guidelines recommended that the IPC precautions for handling deceased patients should be the same as those used in life.

No evidence was found in the studies published since 2004 which met the inclusion criteria for the study design, and which investigated the handling of deceased patients who were colonised or infected with MRSA.

Recommendation

15.1 Follow national guidance for managing infection risks when handling the deceased.

9. Further research

Research recommendations:

- 1598 **RR 1.1** Studies showing cost-effectiveness and practicality of performing targeted versus
1599 universal screening.
- 1600 **RR 1.2** Validation studies for targeted screening tools.
- 1601 **RR 3.1** Further studies assessing the clinical and cost-effectiveness of molecular diagnostic
1602 methods.
- 1603 **RR 3.2** Studies that describe the real-life, clinically relevant TAT (i.e., the time between when
1604 the patient should be screened, and when the test results are available to the clinician).
- 1605 **RR 4.1** Well-described reports discussing staff implicated in outbreaks.
- 1606 **RR 6.1** Rigorous comparative studies assessing the effectiveness of alternatives to mupirocin
1607 and chlorhexidine.
- 1608 **RR 7.1** Studies which show whether environmental sampling and feedback to cleaning staff
1609 has a role in reducing MRSA transmission.
- 1610 **RR 8.1** Studies that assess the effectiveness of antimicrobial surfaces and touch-free devices
1611 on the environmental contamination with MRSA as well as MRSA transmission.
- 1612 **General research recommendation** Studies conducted in health and social care settings other
1613 than the acute hospital sector.
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10. References

1. Coia J.E., Duckworth G.J., Edwards D.I., Farrington M., Fry C., Humphreys H. et al. Guidelines for the control and prevention of meticillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities. *J Hosp Infect*, 2006; 63(Suppl 1):S1-44.
2. Brown N.M., Goodman A.L., Horner C., Jenkins A., Brown E.M. Treatment of meticillin-resistant *Staphylococcus aureus* (MRSA): updated guidelines from the UK. *JAC-Antimicrob Resist*, 2021; 3:dlaa114
3. Roth V.R., Longpre T., Taljaard M., Coyle D., Suh K. N., Muldoon K.A., et al. Universal versus Risk Factor Screening for Meticillin-resistant *Staphylococcus aureus* in a Large Multicenter Tertiary Care Facility in Canada. *Infect Control Hosp Epidemiol*, 2016; 37(1):41-48.
4. Leonhardt K.K., Yakusheva O., Phelan D., Reeths A., Hosterman T., Bonin D. et al. Clinical effectiveness and cost benefit of universal versus targeted meticillin-resistant *Staphylococcus aureus* screening upon admission in hospitals. *Infect Control Hosp Epidemiol*, 2011; 32(8):797-803
5. Al Zobydi A., Jayapal V., Alkhanjaf A., Al-Dashel Y.A.Y., Divakaran M.P. Rapid detection of Meticillin-resistant *Staphylococcus Aureus* MRSA in nose, groin, and axilla swabs by the BD GeneOhm MRSA Achromopeptidase assay and comparison with culture. *Saudi Med J*, 2013; 34(6):597-603.
6. Arcenas S., Spadoni S., Mohammad A., Kiechle F., Walker K., Fader R.C. et al. Multicenter evaluation of the LightCycler MRSA advanced test, the Xpert MRSA assay, and MRSASelect directly plated culture with simulated workflow comparison for the detection of Meticillin-resistant *Staphylococcus Aureus* in nasal swabs. *J Mol Diagnostics*, 2012; 14(4):367-375.
7. Aydiner A., Lüsebrink J., Schildgen, V., Winterfeld I., Knüver O., Schwarz K. et al. Comparison of two commercial PCR methods for Meticillin-resistant *Staphylococcus Aureus* (MRSA) screening in a tertiary care hospital. *PLoS One*, 2012; 7:e43935.
8. Bischof, L. J., Lapsley, L., Fontecchio, K. Jacosalem D., Young C., Hankerd R. et al. Comparison of chromogenic media to BD GeneOhm Meticillin-resistant *Staphylococcus Aureus* (MRSA) PCR for detection of MRSA in nasal swabs. *J Clin Microbiol*, 2009; 47(7):2281-2283.
9. Bishop E. J., Grabsch E. A., Ballard S. A., Mayall B., Xie S., Martin R. et al. Concurrent analysis of nose and groin swab specimens by the IDI-MRSA PCR assay is comparable to analysis by individual-specimen PCR and routine culture assays for detection of colonization by Meticillin-resistant *Staphylococcus Aureus*. *J Clin Microbiol*, 2006; 44(8):2904-2908.
10. Boyce J.M., Havill N.L. Comparison of BD GeneOhm Meticillin-resistant *Staphylococcus Aureus* (MRSA) PCR versus the Chromagar MRSA assay for screening patients for the presence of MRSA strains. *J Clin Microbiol*, 2008; 46(1):350-351.
11. Creamer E., Dolan A., Sherlock O., Thomas T., Walsh J., Moore J. et al. The effect of rapid screening for Meticillin-resistant *Staphylococcus Aureus* (MRSA) on the

- 1660 identification and earlier isolation of MRSA-positive patients. *Infect Control Hosp*
1661 *Epidemiol*, 2010; 31(4):374-381.
- 1662 12. Daeschlein G., Assadian O., Daxboeck F., Kramer A. Multiplex PCR-Elisa for direct
1663 detection of MRSA in nasal swabs advantageous for rapid identification of non-MRSA
1664 carriers. *Eur J Clin Microbiol Infect Dis*, 2006; 25(5):328-330.
- 1665 13. Dalla Valle C., Pasca M. R., De Vitis D., Marzani F.C., Emmi V., Marone P. Control of
1666 MRSA infection and colonisation in an intensive care unit by GeneOhm MRSA assay
1667 and culture methods. *BMC Infect Dis*, 2009; 9:137.
- 1668 14. Dalpke A.H., Hofko M., Zimmermann S. Comparison of the BD Max Meticillin-
1669 resistant *Staphylococcus Aureus* (MRSA) assay and the BD GeneOhm MRSA
1670 Achromopeptidase assay with direct- and enriched-culture techniques using clinical
1671 specimens for detection of MRSA. *J Clin Microbiol*, 2012; 50 (10):3365-3367.
- 1672 15. Danial J., Noel M., Templeton K.E., Cameron F., Mathewson F., Smith M. et al. Real-
1673 time evaluation of an optimized real-time PCR assay versus Brilliance Chromogenic
1674 MRSA agar for the detection of Meticillin-Resistant *Staphylococcus Aureus* from
1675 clinical specimens. *J Med Microbiol*, 2011; 60(3):323-328.
- 1676 16. De San N., Denis O., Gasasira M.-F., De Mendonça R., Nonhoff C., Struelens M.J.
1677 Controlled evaluation of the IDI-MRSA assay for detection of colonization by
1678 Meticillin-resistant *Staphylococcus Aureus* in diverse mucocutaneous specimens. *J*
1679 *Clin Microbiol*, 2007; 45(4):1098-1101.
- 1680 17. Drews S.J., Willey B.M., Kreiswirth N., Wang M., Ianes T., Mitchell J. et al. Verification
1681 of the IDI-MRSA assay for detecting Meticillin-resistant *Staphylococcus Aureus* in
1682 diverse specimen types in a core clinical laboratory setting. *J Clin Microbiol*, 2006;
1683 44(10):3794-3796.
- 1684 18. Eigner U., Veldenzer A., Fahr A.M., Holfelder M. Retrospective evaluation of a PCR
1685 based assay for the direct detection of Meticillin-resistant *Staphylococcus Aureus* in
1686 clinical specimen. *Clin Lab*, 2012; 58(11-12):1319-1321.
- 1687 19. Eigner U., Veldenzer A., Holfelder M. Validation of the Fluorotype® MRSA assay for
1688 the rapid identification of Meticillin-resistant *Staphylococcus Aureus* directly from
1689 patient material. *J Microbiol Methods*, 2014; 107:71-73.
- 1690 20. Elias J., Heuschmann P.U., Schmitt C., Eckhardt F., Boehm H., Maier S. et al.
1691 Prevalence dependent calibration of a predictive model for nasal carriage of
1692 Meticillin-resistant *Staphylococcus Aureus*. *BMC Infect Dis*, 2013; 13:111.
- 1693 21. Francis, S. T., Rawal, S., Roberts, H., Riley P., Planche T., Kennea N.L. Detection of
1694 Meticillin-Resistant *Staphylococcus Aureus* (MRSA) colonization in newborn infants
1695 using real-time Polymerase Chain Reaction (PCR). *Acta Paediatr*, 2010; 99(11):1691-
1696 1694.
- 1697 22. Ghebremedhin B., König B., König W. BD GeneOhm-MRSA assay for detection of
1698 Meticillin-resistant *Staphylococcus Aureus* directly in nasal and non-nasal swab
1699 specimens from haematologic patients. *Eur J Microbiol Immunol*, 2011; 1(4):297-
1700 301.

23. Gray J., Patwardhan S.C., Martin W. Meticillin-Resistant *Staphylococcus Aureus* screening in obstetrics: A Review. *J Hosp Infect*, 2010; 75(2):89-92.
24. Hassan H., Shorman M. Evaluation of the BD GeneOhm MRSA And VanR assays as a rapid screening tool for detection of Meticillin-resistant *Staphylococcus Aureus* and Vancomycin-Resistant Enterococci in a tertiary hospital in Saudi Arabia. *Int J Microbiol*, 2011; 861514.
25. Ho T.-H., Huang Y.-C., Lin T.-Y. Evaluation of the BD GeneOhm StaphSR assay for detection of *Staphylococcus Aureus* in patients in intensive care units. *J Microbiol Immunol Infect*, 2011; 44(4):310-315.
26. Holfelder M., Eigner U., Turnwald A.M., Witte W., Weizenegger M., Fahr A. Direct Detection Of Meticillin-resistant *Staphylococcus Aureus* In Clinical Specimens By A Nucleic Acid-Based HybriDisation Assay. *Clin Microbiol Infect*, 2006; 12(12):1163-1167.
27. Hombach M., Pfyffer G.E., Roos M., Lucke K. Detection of Meticillin-resistant *Staphylococcus Aureus* (MRSA) in specimens from various body sites: performance characteristics of the BD GeneOhm MRSA assay, the Xpert MRSA assay, and broth-enriched culture in an area with a low prevalence of MRSA infections. *J Clin Microbiol*, 2010; 48(11):3882-3887.
28. Hope W.W., Morton A.P., Looke D.F.M., Schooneveldt J.M., Nimmo G.R. A PCR method for the identification of meticillin-resistant *Staphylococcus aureus* (MRSA) from screening swabs. *Pathology*, 2004; 36(3):265–268
29. Hos N. J., Wiegel P., Fischer J., Plum G. Comparative evaluation of two fully-automated real-time PCR methods for MRSA admission screening in a tertiary-care hospital. *Eur J Clin Microbiol Infect Dis*, 2016; 35(9):1475-1478.
30. Huh H.J., Kim E.S., Chae S.L. Meticillin-resistant *Staphylococcus aureus* in nasal surveillance swabs at an intensive care unit: an evaluation of the LightCycler MRSA advanced test. *Ann Lab Med*, 2012;32(6):407-412.
31. Huletsky A., Lebel, P., Picard, F. J., Bernier M., Gagnon M., Boucher N et al. Identification of Meticillin-resistant *Staphylococcus Aureus* carriage in less than 1 hour during a hospital surveillance program. *Clin Infect Dis*, 2005; 40(7):976-981.
32. Izumikawa K., Yamamoto Y., Yanagihara K., Kiya T., Matsuda J., Morinaga Y. et al. Active surveillance of Meticillin-resistant *Staphylococcus Aureus* with the BD GeneOhm MRSA™ Assay in a respiratory ward in Nagasaki, Japan. *Jpn J Infect Dis*, 2012; 65(1):33-36.
33. Jeyaratnam D., Whitty C.J.M., Phillips K., Liu D., Orezzi C., Ajoku U. et al. Impact of rapid screening tests on acquisition of Meticillin Resistant *Staphylococcus Aureus*: cluster randomised crossover trial. *BMJ Clin Res*, 2008; 336(7650):927-930.
34. Jog S., Cunningham R., Cooper S., Wallis M., Marchbank A., Vasco-Knight P. et al. Impact of preoperative screening for Meticillin-Resistant *Staphylococcus Aureus* by real-time Polymerase Chain Reaction in patients undergoing cardiac surgery. *J Hosp Infect*, 2008; 69(2):124-130.

- 1742 35. Kerremans J. J., Maaskant J., Verbrugh H. A., van Leeuwen W.B., Vos M.C. Detection
1743 of Meticillin-resistant *Staphylococcus Aureus* in a low-prevalence setting by
1744 Polymerase Chain Reaction with a selective enrichment broth. *Diagn Microbiol Infect*
1745 *Dis*, 2008; 61(4):396-401.
- 1746 36. Kim M.H., Lee W.I., Kang S.Y. Detection of Meticillin-resistant *Staphylococcus Aureus*
1747 in healthcare workers using real-time Polymerase Chain Reaction. *Yonsei Med J*,
1748 2013; 54(5):1282-1284.
- 1749 37. Kleinschmidt S., Lidstone C., Henderson B., Faoagali J. Comparison of the BD
1750 GeneOhm MRSA assay, broth enrichment culture and ChromID MRSA for detection
1751 of Meticillin-resistant *Staphylococcus Aureus* from inter-hospital intensive care
1752 transfer patients. *Healthcare Infect*, 2009; 14(3):89-93.
- 1753 38. Laurent C., Bogaerts P., Schoevaerdt D., Denis O., Deplano A., Swine C. et al.
1754 Evaluation of the Xpert MRSA assay for rapid detection of Meticillin-resistant
1755 *Staphylococcus Aureus* from nares swabs of geriatric hospitalized patients and
1756 failure to detect a specific *scmec* type IV variant. *Eur J Clin Microbiol Infect Dis*,
1757 2010; 29(8):995-1002.
- 1758 39. Lee S., Park Y.-J., Park K.-G., Jekarl D.W., Chae H., Yoo J.-K. et al. Comparative
1759 evaluation of three Chromogenic media combined with broth enrichment and the
1760 real-time PCR-based Xpert MRSA assay for screening of Meticillin-resistant
1761 *Staphylococcus Aureus* in nasal swabs. *Ann Lab Med*, 2013; 33(4):255-260.
- 1762 40. Lucke K., Hombach M., Hug M., Pfyffer G.E. Rapid detection of Meticillin-resistant
1763 *Staphylococcus Aureus* (MRSA) in diverse clinical specimens by the BD GeneOhm
1764 MRSA assay and comparison with culture. *J Clin Microbiol*, 2010; 48(3):981-984.
- 1765 41. Mehta M.S., Paule S.M., Hacek D.M., Thomson R.B., Kaul K.L., Peterson L.R.
1766 Optimization of a Laboratory-Developed Test Utilizing Roche Analyte-Specific
1767 Reagents for Detection of *Staphylococcus aureus*, Meticillin-resistant *S. aureus*, and
1768 Vancomycin-Resistant *Enterococcus* Species. *J Clin Microbiol*, 2008; 46(7):2377-2380
- 1769 42. Molan A., Nulsen M. Thomas, G. Meticillin-resistant *Staphylococcus Aureus* (MRSA):
1770 isolation from nasal and throat swabs transported in liquid or semisolid media;
1771 identification by PCR compared with culture. *N Z J Med Lab Sci*, 2013; 67(1):8-16.
- 1772 43. Oberdorfer K., Pohl S., Frey M., Heeg K., Wendt C. Evaluation of a single-locus real-
1773 time polymerase chain reaction as a screening test for specific detection of
1774 meticillin-resistant *Staphylococcus aureus* in ICU. *Eur J Clin Microbiol Infect Dis*,
1775 2006; 25(10):657-663
- 1776 44. Ornskov D., Kolmos B., Bendix Horn, P., Nederby Nielsen J., Brandslund I.,
1777 Schouenborg P. Screening for Meticillin-resistant *Staphylococcus Aureus* in clinical
1778 swabs using a high-throughput real-time PCR-based method. *Clin Microbiol Infect*,
1779 2008; 14(1):22-28.
- 1780 45. Parcell B.J., Phillips G. Use of Xpert® MRSA PCR point-of-care testing beyond the
1781 laboratory. *J Hosp Infect*, 2014; 87(2):119-121.

- 1782 46. Pasanen T., Korkeila M., Mero S., Tarkka E., Piiparinen H., Vuopio-Varkila J. A
 1783 Selective Broth Enrichment Combined With Real-Time Nuc-Meca-PCR In The
 1784 Exclusion Of MRSA. *APMIS*, 2010; 118(1):74-80.
- 1785 47. Patel P., Robicsec A., Grayes A., Schora D.M., Peterson K.E., Wright M.O., et al.
 1786 Evaluation of Multiple Real-Time PCR Tests on Nasal Samples in a Large MRSA
 1787 Surveillance Program. *Am J Clin Pathol*, 2015; 143(5):652-658
- 1788 48. Patel P.A., Ledebor N.A., Ginocchio C.C., Condon S., Bouchard S., Qin P. et al.
 1789 Performance of the BD GeneOhm MRSA Achromopeptidase assay for real-time PCR
 1790 detection of Meticillin-resistant *Staphylococcus Aureus* in nasal specimens. *J Clin*
 1791 *Microbiol*, 2011; 49(6):2266-2268.
- 1792 49. Patel P.A., Schora D.M., Peterson K., Grayes A., Boehm S., Peterson L.R. Performance
 1793 of the Cepheid Xpert® SA nasal complete PCR assay compared to culture for
 1794 detection of MeticillinSensitive And Meticillin-resistant *Staphylococcus Aureus*
 1795 colonization. *Diagn Microbiol Infect Dis*, 2014; 80(1):32-34.
- 1796 50. Paule S.M., Hacek D.M., Kufner B., Truchon K., Thomson R.B., Kaul K.L. et al.
 1797 Performance of the BD GeneOhm Meticillin-resistant *Staphylococcus Aureus* test
 1798 before and during high-volume clinical use. *J Clin Microbiol*, 2007; 45(9):2993-2998.
- 1799 51. Peterson L.R., Liesenfeld O., Woods C.W., Allen S.D., Pombo D., Patel P.A. et al.
 1800 Multicenter evaluation of the LightCycler Meticillin-resistant *Staphylococcus Aureus*
 1801 (MRSA) advanced test as a rapid method for detection of MRSA in nasal surveillance
 1802 swabs. *J Clin Microbiol*, 2010; 48(5):1661-1666.
- 1803 52. Podzorski R.P., Li H., Han J., Tang Y.-W. MVPlex assay for direct detection of
 1804 Meticillin-resistant *Staphylococcus Aureus* in naris and other swab specimens. *J Clin*
 1805 *Microbiol*, 2008; 46(9):3107-3109.
- 1806 53. Roisin S., Laurent C., Nonhoff C., Deplano A., Hallin M., Byl B. et al. Positive Predictive
 1807 Value of the Xpert MRSA assay diagnostic for universal patient screening at hospital
 1808 admission: influence of the local ecology. *Eur J Clin Microbiol Infect Dis*, 2012;
 1809 31(5):873-880.
- 1810 54. Sarda V., Molloy A., Kadkol S.H., Janda W.M., Hershow R., McGuinn M. Active
 1811 surveillance for Meticillin-resistant *Staphylococcus Aureus* in the neonatal intensive
 1812 care unit. *Infect Control Hosp Epidemiol*, 2009; 30(9):854-860.
- 1813 55. Schuenck R.P., Lourenco M.C.S., Iório, N.L.P., Ferreira A.L.P., Nouér S.A., Santos
 1814 K.R.N. Improved and rapid detection of Meticillin-resistant *Staphylococcus Aureus*
 1815 nasal carriage using selective broth and multiplex PCR. *Res Microbiol*, 2006;
 1816 157(10):971-975.
- 1817 56. Schulz M., Nonnenmacher C., Mutters R. Cost-effectiveness of rapid MRSA screening
 1818 in surgical patients. *Eur J Clin Microbiol Infect Dis*, 2009; 28(11):1291-1296.
- 1819 57. Seki M., Takahashi H., Yamamoto N., Hamaguchi S., Ojima M., Hirose T. et al.
 1820 Polymerase Chain Reaction-based active surveillance of MRSA in emergency
 1821 department patients. *Infect Drug Resist*, 2015; 8:113-118.
- 1822 58. Smith M.H., Hodgson J., Eltringham I.J. Evaluation of the BD GeneOhm assay using
 1823 the Rotor-Gene 6000 platform for rapid detection of Meticillin-resistant

- 1824 Staphylococcus Aureus from pooled screening swabs. J Clin Microbiol, 2010;
1825 48(12):4559-4562.
- 1826 59. Snyder J.W., Munier G.K., Johnson C.L. Comparison of the BD GeneOhm Meticillin-
1827 resistant Staphylococcus Aureus (MRSA) PCR assay to culture by use of BBL
1828 Chromagar MRSA for detection of MRSA in nasal surveillance cultures from intensive
1829 care unit patients. J Clin Microbiol, 2010; 48(4):1305-1309.
- 1830 60. Svent-Kucina N., Pirs M., Mueller-Premru M., Cvitkovic-Spik V., Kofol R., Seme K.
1831 One-year experience with modified BD GeneOhm MRSA assay for detection of
1832 Meticillin-resistant Staphylococcus Aureus from pooled nasal, skin, and throat
1833 samples. Diagn Microbiol Infect Dis, 2009; 63(2):132-139.
- 1834 61. Taguchi H., Ohta S., Yukioka T., Matsumoto T., Ishikawa H. Prevalence of Meticillin-
1835 resistant Staphylococcus Aureus based on culture and PCR in inpatients at a tertiary
1836 care center in Tokyo, Japan. J Infect Chemother, 2012; 18(5):630-636.
- 1837 62. Wassenberg M.W.M., Kluytmans J.A.J.W., Box A.T.A., Bosboom R.W., Buiting A.G.M.,
1838 van Elzakker E.M.P. et al. Rapid screening of meticillin-resistant Staphylococcus
1839 aureus using PCR and chromogenic agar: a prospective study to evaluate costs and
1840 effects. Clin Microbiol Infect, 2010; 16(12): 1754-1761
- 1841 63. Yam W.C., Siu G.K.H., Ho P.L., Ng T.K., Que T.L., Yip K.T. et al. Evaluation of the
1842 LightCycler meticillin-resistant Staphylococcus aureus (MRSA) advanced test for
1843 detection of MRSA nasal colonization. J Clin Microbiol, 2013; 51(9): 2869–2874
- 1844 64. Yarbrough M.L., Warren D. K., Allen K., Burkholder D., Daum R., Donskey C. et al.
1845 Multicenter Evaluation of the Xpert MRSA NxG Assay for Detection of Meticillin-
1846 resistant Staphylococcus aureus in Nasal Swabs. J Clin Microbiol, 2018;
1847 56(1):e01381-17
- 1848 65. Zhang S., Drews S., Tomassi J., Katz K.C. Comparison of Two Versions of the IDI-MRSA
1849 Assay Using Charcoal Swabs for Prospective Nasal and Nonnasal Surveillance
1850 Samples. J Clin Microbiol, 2007; 45(7): 2278–2280
- 1851 66. Elshabrawy W.O., Zaki M.E., Kamel M.F. Genetic and phenotypic study of Meticillin-
1852 resistant Staphylococcus Aureus among patients and health care workers in
1853 Mansoura University Hospital, Egypt. Iran J Microbiol, 2017; 9(2):82-88.
- 1854 67. Rajan L., Smyth E., Humphreys H. Screening for MRSA in ICU Patients. How does PCR
1855 compare with culture? J Infect, 2007; 55(4):353-357.
- 1856 68. Silbert S., Kubasek C., Galambo F., Vendrone E., Widen R. Evaluation of BD Max
1857 StaphSR and BD Max MRSA XT assays using eswab-collected specimens. J Clin
1858 Microbiol, 2015; 53(8):2525-2529.
- 1859 69. Wolk D.M., Marx J.L., Dominguez L., Driscoll D., Schiffman R.B. Comparison of
1860 MRSASelect agar, CHROMagar Meticillin-resistant Staphylococcus aureus (MRSA)
1861 Medium, and Xpert MRSA PCR for detection of MRSA in Nares: diagnostic accuracy
1862 for surveillance samples with various bacterial densities. J Clin Microbiol, 2009;
1863 47(12):3933-6
- 1864 70. Wolk D.M., Picton E., Johnson D., Davis T., Pancholi P., Ginocchio C.C. et al.
1865 Multicenter evaluation of the Cepheid Xpert meticillin-resistant Staphylococcus

- aureus (MRSA) test as a rapid screening method for detection of MRSA in nares. *J Clin Microbiol*, 2009; 47(3):758–764
71. Wu P.J., Jeyaratnam D., Tosas O., Cooper B.S., French G.L. Point-of-care universal screening for meticillin-resistant *Staphylococcus aureus*: a cluster-randomized cross-over trial. *J Hosp Infect*, 2017; 95(3):245-252
72. Bulliard E., Grandbastien B., Senn L., Greub G., Blanc D.S. Evaluation of three consecutive versions of a commercial rapid PCR test to screen for meticillin-resistant *Staphylococcus aureus*. *Clin Microbiol Infect*. 2019; 25(11):1430.e1-1430.e4.
73. Dewar S., Vass D., MacKenzie F.M., Parcell B.J. Point-of-care testing by healthcare workers for detection of meticillin-resistant *Staphylococcus aureus*, *Clostridioides difficile*, and norovirus. *J Hosp Infect*. 2019; 103(4):447-453.
74. von Allmen N., Gorzelniak K., Liesenfeld O., Njoya M., Duncan J., Marlowe E.M. et al. Liquid and Dry Swabs for Culture- and PCR-Based Detection of Colonization with Meticillin-resistant *Staphylococcus aureus* during Admission Screening. *Eur J Microbiol Immunol (Bp)*, 2019; 9(4):131–137.
75. Hardy K., Price C., Szczepura A., Gossain S., Davies R., Stallard N. et al. Reduction in the rate of meticillin-resistant *Staphylococcus aureus* acquisition in surgical wards by rapid screening for colonization: a prospective, cross-over study. *Clin Microbiol Infect*, 2010; 16(4):333–339
76. Roisin S., Laurent C., Denis O., Dramaix M., Nonhoff C., Hallin M. et al. Impact of rapid molecular screening at hospital admission on nosocomial transmission of Meticillin-resistant *Staphylococcus Aureus*: cluster randomised trial. *PLoS One*, 2014; 9(5):e96310.
77. Conterno L.O., Shymanski J., Ramotar K., Toye B., van Walraven C., Coyle D. et al. Real-time Polymerase Chain Reaction detection of Meticillin-resistant *Staphylococcus Aureus*: impact on nosocomial transmission and costs. *Infect Control Hosp Epidemiol*, 2007; 28(10):1134-1141.
78. Bühlmann M., Bögli-Stuber K., Droz S., Mühlemann K. Rapid screening for carriage of Meticillin-resistant *Staphylococcus Aureus* by PCR and associated costs. *J Clin Microbiol*, 2008; 46(7):2151-2154.
79. Aldeyab M.A., Kearney M.P., Hughes C.M., Scott M.G., Tunney M.M., Gilpin D.F. et al. Can the use of a rapid Polymerase Chain Screening method decrease the incidence of nosocomial Meticillin-Resistant *Staphylococcus Aureus*? *J Hosp Infect*, 2009; 71(1):22-28.
80. Cunningham R., Jenks P., Northwood J., Wallis M., Ferguson S., Hunt S. Effect on MRSA transmission of rapid PCR testing of patients admitted to critical care. *J Hosp Infect*, 2007; 65(1):24-28.
81. Hallak G., Neuner B., Schefold J.C., Gorzelniak K., Rapsch B., Pfülleret R. al. Preemptive isolation precautions of patients at high risk for Meticillin-resistant *Staphylococcus Aureus* in combination with ultrarapid Polymerase Chain Reaction Screening as an effective tool for infection control. *Infect Control Hosp Epidemiol*, 2016; 37(12):1489-1491.
82. Harbarth S., Masuet-Aumatell C., Schrenzel J., Francois P., Akakpo C., Renzi G. et al. Evaluation of rapid screening and pre-emptive contact isolation for detecting and

- controlling Meticillin-resistant Staphylococcus Aureus in critical care: an
interventional cohort study. Crit Care, 2006; 10(1):R25.
83. Floré K., Van den Abeele A.-M., Verschraegen G. Speed of molecular detection
techniques for Meticillin-resistant Staphylococcus Aureus admission screening in an
acute care hospital. J Hosp Infect, 2010; 75(2):103-106.
84. Tsang S.T.J., McHugh M.P., Guerendiain D., Gwynne P.J., Boyd J., Simpson A.H.R.W.
et al. Underestimation of Staphylococcus aureus (MRSA and MSSA) carriage
associated with standard culturing techniques: one third of carriers, missed. Bone
Joint Res, 2018; 7(1):79-84
85. Edmundson S.P., Hirpara K.M., Bennett D. The effectiveness of meticillin-resistant
Staphylococcus aureus colonisation screening in asymptomatic healthcare workers in
an Irish orthopaedic unit. Eur J Clin Microbiol Infect Dis, 2011; 30(9): 1063-1066
86. Berry P.M., Davidson J., Masters K., Rolls K., Ollerton R. Effects of three approaches
to standardized oral hygiene to reduce bacterial colonization and ventilator
associated pneumonia in mechanically ventilated patients: a randomised control
trial. Int J Nurs Stud, 2011; 48(6):681-688
87. Boonyasiri A., Thaisiam P., Permpikul C., Judaeng T., Suiwongsa B., Apiradeewajeset
N. et al. Effectiveness of chlorhexidine cloths for the prevention of multidrug
resistant bacterial colonization and hospital-acquired infections in intensive care unit
patients: a randomized trial in Thailand. Infect Control Hosp Epidemiol 2016;
37(3):245-53
88. Camus C., Bellissant E., Seville V., Perrotin D., Garo B., Legras A. et al. Prevention of
acquired infections in intubated patients with the combination of two
decontamination regimens. Crit Care Med, 2005; 33(2):307-3014
89. Camus C., Seville V., Legras A., Garo B., Renault A., Le Corre P. et al.
Mupirocin/chlorhexidine to prevent meticillin-resistant Staphylococcus aureus
infections: post hoc analysis of a placebo-controlled, randomized trial using
mupirocin/chlorhexidine and polymyxin/tobramycin for the prevention of acquired
infections in intubated patients. Infection, 2014; 42(3):493-502
90. Climo M.W., Yokoe D.S., Warren D.K., Perl T.M., Bolon M.B., Herwaldt L.A. et al.
Effect of daily chlorhexidine bathing on hospital-acquired infection. New Eng J Med,
2013; 368(6):533-542
91. Huang S.S., Septimus E., Kleinman K., Moody J., Hickok J., Avery T.R., et al. Targeted
versus universal decolonization to prevent ICU infection. New Eng J Med, 2013;
368(24):2255-2265
92. Kline S.E., Neaton J.D., Lynfield R., Ferrieri P., Kulasingam S., Dittes K. et al.
Randomized controlled trial of a self-administered five-day antiseptic bundle versus
usual disinfectant soap showers for preoperative eradication of Staphylococcus
aureus colonization. Infect Control Hosp Epidemiol, 2018; 39(9):1049-57
93. O'Grady S., Hirji Z., Pejcic-Karapetrovic B., Fung S., Dedier H., Takata-Shewchuk J. et
al. A double-blind, randomized, controlled trial of topical polysporin triple compound
versus topical mupirocin for the eradication of colonization with meticillin-resistant
Staphylococcus aureus in a complex continuing care population. Can J Infect Dis Med
Microbiol, 2009; 20(3):e49–e55.

- 1954 94. Phillips M., Rosenberg A., Shopsis B., Cuff G., Skeete F., Foti A. et al. Preventing
1955 surgical site infections: a randomized, open-label trial of nasal mupirocin ointment
1956 and nasal povidone iodine solution. *Infect Control Hosp Epidemiol*, 2014; 35(7):826–
1957 832
- 1958 95. Tuon F.F., Gavrilko O., de Almeida S., Sumi E.R., Alberto T., Rocha J.L. et al.
1959 Prospective randomised controlled study evaluating early modification of oral
1960 microbiota following admission to the intensive care unit and oral hygiene with
1961 chlorhexidine. *J Glob Antimicrob Resist*, 2017; 8:159-163
- 1962 96. Wang H.H., Hung S.Y., Chang, M.Y., Lee Y.C., Lin H.F., Lin T.M. et al. Bacterial
1963 colonization patterns in daily chlorhexidine care at the exit site in peritoneal dialysis
1964 patients - A prospective, randomized controlled trial. *PLoS One*, 2017;
1965 12(10):e0184859
- 1966 97. Wendt C., Schinke S., Württemberger M., Oberdorfer K., Bock-Hensley O., von Baum
1967 H. Value of whole-body washing with chlorhexidine for the eradication of meticillin-
1968 resistant *Staphylococcus aureus*: a randomized, placebo-controlled, double-blind
1969 clinical trial. *Infect Control Hosp Epidemiol*, 2007; 28(9):1036-1043
- 1970 98. Pallotto C., Fiorio M., de Angelis V., Ripoli A., Franciosi E., Quondam Girolamo L. et
1971 al. Daily bathing with 4% chlorhexidine gluconate in intensive care settings: a
1972 randomized controlled trial. *Clin Microbiol Infect*, 2019; 25(6):705-710.
- 1973 99. Amirov C.M., Binns M.A., Jacob L.E., Candon H.L. Impact of chlorhexidine bathing on
1974 meticillin-resistant *Staphylococcus aureus* incidence in an endemic chronic care
1975 setting: A randomized controlled trial. *Am J Infect Control*, 2017; 45(3):298-300
- 1976 100. Bleasdale S.C., Trick W.E, Gonzalez I.M., Lyles R.D., Hayden M.K., Weinstein
1977 R.A. Effectiveness of chlorhexidine bathing to reduce catheter-associated BSI in
1978 medical intensive care unit patients. *Arch Intern Med*, 2007; 167(19):2073-2079
- 1979 101. Chow A., Hon P.Y., Tin G., Zhang W., Poh B.F., Ang B. Intranasal octenidine
1980 and universal antiseptic bathing reduce meticillin-resistant *Staphylococcus aureus*
1981 (MRSA) prevalence in extended care facilities. *Epidemiol Infect*, 2018; 146(16):2036-
1982 2041
- 1983 102. Lowe C.F., Lloyd-Smith E., Sidhu B., Ritchie G., Sharma A., Jang W. et al.
1984 Reduction in hospital-associated meticillin-resistant *Staphylococcus aureus* and
1985 vancomycin-resistant *Enterococcus* with daily chlorhexidine gluconate bathing for
1986 medical inpatients. *Am J Infect Control*, 2017; 45(3):255-259
- 1987 103. Batra R., Cooper B.S., Whiteley C., Patel A.K., Wyncoll D., Edgeworth J.D.
1988 Efficacy and limitation of a chlorhexidine-based decolonization strategy in preventing
1989 transmission of meticillin-resistant *Staphylococcus aureus* in an intensive care unit.
1990 *Clin Infect Dis*, 2010; 50(2):210-217
- 1991 104. Bradley C.W., Wilkinson M.A.C., Garvey M.I. The Effect of Universal
1992 Decolonization With Screening in Critical Care to Reduce MRSA Across an Entire
1993 Hospital. *Infect Control Hosp Epidemiol*, 2017; 38(4):430-435
- 1994 105. Cho O.-H., Baek E.H., Bak, M.H., Suh Y.S., Park K.H., Kim S. et al. The effect of
1995 targeted decolonization on meticillin-resistant *Staphylococcus aureus* colonization or
1996 infection in a surgical intensive care unit. *Am J Infect Control*, 2016; 44(5):533-538
- 1997 106. Dicks K.V., Lofgren E., Lewis S.S., Moehring R.W., Sexton D.J., Anderson D.J. A
1998 Multicenter Pragmatic Interrupted Time Series Analysis of Chlorhexidine Gluconate

- 1999 Bathing in Community Hospital Intensive Care Units. *Infect Control Hosp Epidemiol*,
2000 2016; 37(7):791-797
- 2001 107. Kengen R., Thoonen E., Daveson K., Loong B., Rodgers H., Beckingham W. et
2002 al. Chlorhexidine washing in intensive care does not reduce BSI, blood culture
2003 contamination and drug-resistant microorganism acquisition: an interrupted time
2004 series analysis. *Crit Care Resusc*, 2018; 20(3):231-40
- 2005 108. Kim J.S., Chung Y.K., Lee S.S., Lee J.A., Kim H.S., Park E.Y. et al. Effect of daily
2006 chlorhexidine bathing on the acquisition of meticillin-resistant *Staphylococcus*
2007 *aureus* in a medical intensive care unit with meticillin-resistant *S aureus* endemicity.
2008 *Am J Infect Control*, 2016; 44(12):1520-1525
- 2009 109. Munoz-Price L.S., Hota B., Stemer A., Weinstein R.A. Prevention of BSI by Use
2010 of Daily Chlorhexidine Baths for Patients at a Long-Term Acute Care Hospital. *Infect*
2011 *Control Hosp Epidemiol*, 2009; 30(11):1031-1035
- 2012 110. Rupp M.E., Cavalieri R.J., Lyden E., Kucera J., Martin M.A., Fitzgerald T. et al.
2013 Effect of Hospital-Wide Chlorhexidine Patient Bathing on Healthcare-Associated
2014 Infections. *Infect Control Hosp Epidemiol*, 2012; 33(11):1094-1100
- 2015 111. Schweizer M.L., Chiang H.Y., Septimus E., Moody J., Braun B., Hafner J. et al.
2016 Association of a bundled intervention with surgical site infections among patients
2017 undergoing cardiac hip or knee surgery. *JAMA*, 2015; 313(21):2162-2171
- 2018 112. Bozzella M. J., Soghier L., Harris T., Zell L., Short B.L., Song X. Impact of
2019 decolonization on meticillin-resistant *Staphylococcus aureus* transmission and
2020 infection in a neonatal intensive care unit. *Infect Control Hosp Epidemiol*. 2019;
2021 40(10): 1123-1127.
- 2022 113. Chow A., Wong J., Zhang W., Poh B.-F., Ang B. Intranasal octenidine and
2023 universal chlorhexidine bathing can reduce meticillin-resistant *Staphylococcus*
2024 *aureus* acquisition in an extended care facility in Singapore. *J Hosp Infect*. 2020;
2025 105(4): 628-631.
- 2026 114. Colling K., Statz C., Glover J., Banton K., Beilman G. Pre-operative antiseptic
2027 shower and bath policy decreases the rate of *S. aureus* and meticillin-resistant *S.*
2028 *aureus* surgical site infections in patients undergoing joint arthroplasty. *Surg Infect*
2029 (Larchmt), 2015; 16(2):124-32
- 2030 115. Malcolm T.L., Robinson L.D., Klika A.K., Ramanathan d., Higuera C.A., Murray
2031 T.G. Predictors of *Staphylococcus aureus* Colonization and Results after
2032 Decolonization. *Interdiscip Perspect Infect Dis*, 2016; 2016:4367156.
- 2033 116. Viray M.A., Morley J.C., Coopersmith C.M., Kollef M.H., Fraser V.J., Warren
2034 D.K. et al. Daily bathing with chlorhexidine-based soap and the prevention of
2035 *Staphylococcus aureus* transmission and infection. *Infect Control Hosp Epidemiol*,
2036 2014; 35(3):243-250
- 2037 117. Chan A.K., Ammanuel S.G., Chan A.Y., Oh T., Skrehot H.C., Edwards C.S. et al.
2038 Chlorhexidine Showers Are Associated with a Reduction in Surgical Site Infection
2039 Following Spine Surgery: An Analysis of 4266 Consecutive Surgeries. *Neurosurgery*.
2040 2020; 85(6):817–826.

118. Armellino D., Woltmann J., Parmentier D., Musa N., Eichorn A., Silverman R. et al. Modifying the risk: once-a-day bathing "at risk" patients in the intensive care unit with chlorhexidine gluconate. *Am J Infect Control*, 2014; 42(5):571-573
119. Baratz M.D., Hallmark R., Odum S.M., Springer B.D. Twenty Percent of Patients May Remain Colonized With Meticillin-resistant *Staphylococcus aureus* Despite a Decolonization Protocol in Patients Undergoing Elective Total Joint Arthroplasty. *Clin Orthop Relat Res*, 2015; 473(7):2283-2290
120. Bebko S.P., Green D.M., Awad S.S. Effect of a preoperative decontamination protocol on surgical site infections in patients undergoing elective orthopaedic surgery with hardware implantation. *JAMA Surg* 2015; 150(5):390-395
121. Climo M.W., Sepkowitz K.A., Zuccotti G., Fraser V.J., Warren D.K., Perl T.M., et al. The effect of daily bathing with chlorhexidine on the acquisition of meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and healthcare-associated BSI: results of a quasi-experimental multicenter trial. *Crit Care Med*, 2009; 37(6):1858-1865
122. Fraser T.G., Fatica C., Scarpelli M., Arroliga A.C., Guzman J., Shrestha N.K. et al. Decrease in *Staphylococcus aureus* colonization and hospital-acquired infection in a medical intensive care unit after institution of an active surveillance and decolonization program. *Infect Control Hosp Epidemiol*, 2010; 31(8):779-783
123. Hacek D.M., Robb W.J., Paule S.M., Kudrna J.C., Stamos V.P., Peterson L.R. *Staphylococcus aureus* nasal decolonization in joint replacement surgery reduces infection. *Clin Orthop Relat Res*, 2008; 466(6):1349–1355
124. Johnson A.T., Nygaard R.M., Cohen E.M., Fey R.M., Wagner A.L. The Impact of a Universal Decolonization Protocol on Hospital-Acquired Meticillin-resistant *Staphylococcus aureus* in a Burn Population. *J Burn Care Res*, 2016; 37(6):525-530
125. Kassakian S.Z., Mermel L.A., Jefferson J.A., Parenteau S.L., Machan J.T. Impact of chlorhexidine bathing on hospital-acquired infections among general medical patients. *Infect Control Hosp Epidemiol*, 2011; 32(3):238-243
126. Kohler P., Sommerstein R., Schonrath F., Ajdler-Schäffler E., Anagnostopoulos A., Tschirky S. et al. Effect of perioperative mupirocin and antiseptic body wash on infection rate and causative pathogens in patients undergoing cardiac surgery. *Am J Infect Control*, 2015; 43(7):33-38
127. Musuuza J.S., Sethi A.K., Roberts T.J., Safdar N. Implementation of daily chlorhexidine bathing to reduce colonization by multidrug-resistant organisms in a critical care unit. *Am J Infect Control*, 2017; 45(9):1014-1017
128. Petlin A., Schallom M., Prentice D., Sona C., Mantia P., McMullen K. et al. Chlorhexidine gluconate bathing to reduce meticillin-resistant *Staphylococcus aureus* acquisition. *Crit Care Nurse*, 2014; 34(5):17-25
129. Popovich K.J., Hota B., Hayes R., Weinstein R.A., Hayden M.K. Effectiveness of routine patient cleansing with chlorhexidine gluconate for infection prevention in the medical intensive care unit. *Infect Control Hosp Epidemiol*, 2009; 30(10):959-963

130. Rao N., Cannella B.A., Crossett L.S., Yates A.J., McGough R.L., Hamilton C.W. Preoperative screening/decolonization for *Staphylococcus aureus* to prevent orthopaedic surgical site infection: prospective cohort study with 2-year follow-up. *J Arthroplasty*, 2011; 26(8):1501-1507
131. Richer S.L., Wenig B.L. The efficacy of preoperative screening and the treatment of methicillin-resistant *Staphylococcus aureus* in an otolaryngology surgical practice. *Otolaryngol Head Neck Surg*, 2009; 140(1):29-32
132. Ridenour G., Lampen R., Federspiel J., Kritchevsky S., Wong E., Climo M. Selective use of intranasal mupirocin and chlorhexidine bathing and the incidence of methicillin-resistant *Staphylococcus aureus* colonization and infection among intensive care unit patients. *Infect Control Hosp Epidemiol*, 2007; 28(10):1155-1161
133. Seyman D., Oztoprak N., Berk H., Kizilates F., Emek M. Weekly chlorhexidine douche: Does it reduce healthcare-associated BSI? *Scand J Infect Dis*, 2014; 46(10):697-703
134. Thompson P., Houston S. Decreasing methicillin-resistant *Staphylococcus aureus* surgical site infections with chlorhexidine and mupirocin. *Am J Infect Control*, 2013; 41(7):629-33
135. Htun H. L., Hon P.Y., Holden M.T.G., Ang B., Chow A. Chlorhexidine and octenidine use, carriage of *qac* genes, and reduced antiseptic susceptibility in methicillin-resistant *Staphylococcus aureus* isolates from a healthcare network. *Clin Microbiol Infect*, 2019; 25(9):1154.
136. Furukawa M., Minekawa A., Haruyama T., Narui Y., Sugita G., Sugita R. Clinical effectiveness of ototopical application of mupirocin ointment in methicillin-resistant *Staphylococcus aureus* otorrhea. *Otol Neurotol*, 2008; 29(5):676-8
137. Gordon R.J., Chez N., Jia H., Zeller B., Sobieszczyk M., Brennan C. et al. The NOSE study (nasal ointment for *Staphylococcus aureus* eradication): a randomized controlled trial of monthly mupirocin in HIV-infected individuals. *J Acquir Immune Defic Syndr*, 2010; 55(4):466-472
138. Poovelikunnel T.T., Gethin G., Solanki D., McFadden E., Codd M., Humphreys H. Randomized controlled trial of honey versus mupirocin to decolonize patients with nasal colonization of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect*, 2018; 98(2):141-148
139. Weintrob A., Bebu I., Agan B., Diem A., Johnson E., Lalani T. et al. Randomized, Double-Blind, Placebo-Controlled Study on Decolonization Procedures for Methicillin-resistant *Staphylococcus aureus* (MRSA) among HIV-Infected Adults. *PLoS One*, 2015; 10(5):e0128071
140. Chu K.H., Choy W.Y., Cheung C.C., Fung K.S., Tang H.L., Lee W. et al. A prospective study of the efficacy of local application of gentamicin versus mupirocin in the prevention of peritoneal dialysis catheter-related infections. *Perit Dial Int*, 2008; 28(5):505-508.

- 2122 141. Huang Y.C., Lien R.I., Lin T.Y. Effect of mupirocin decolonization on
2123 subsequent meticillin-resistant *Staphylococcus aureus* infection in infants in
2124 neonatal intensive care units. *Pediatr Infect Dis J*, 2015; 34(3):241-245
- 2125 142. Unemura Y., Ishida Y., Suzuki Y., Yanaga K. Impact of prophylactic mupirocin
2126 for radical esophagectomy. *J Infect Chemother*, 2006; 12(5):257-263
- 2127 143. Gray D., Foster K., Cruz A., Kane G., Toomey M., Bay C. et al. Universal
2128 decolonization with hypochlorous solution in a burn intensive care unit in a tertiary
2129 care community hospital. *Am J Infect Control*, 2016; 44(9):1044-1046
- 2130 144. Huang Y.C., Lien R.I., Su L.H., Chou Y.H., Lin T.Y. Successful control of
2131 meticillin-resistant *Staphylococcus aureus* in endemic neonatal intensive care units –
2132 a 7-year campaign I. *PLoS One*, 2011; 6(8):e23001
- 2133 145. Mori N., Hitomi S., Nakajima J., Okuzumi K., Murakami A., Kimura S.
2134 Unselective use of intranasal mupirocin ointment for controlling propagation of
2135 meticillin-resistant *Staphylococcus aureus* in a thoracic surgery ward. *J Infect*
2136 *Chemother*, 2005; 11(5):231-233
- 2137 146. Kim J. J., Blevins M.W., Brooks D.J., Stehle J.R., McLouth C.J., Viviano J.P.
2138 Successful control of a meticillin-resistant *Staphylococcus aureus* outbreak in a burn
2139 intensive care unit by addition of universal decolonization with intranasal mupirocin
2140 to basic infection prevention measures. *Am J Infect Control*. 2019; 47(6):661-665.
- 2141 147. Caffrey A.R., Quilliam B.J., LaPlante K.L. Risk factors associated with
2142 mupirocin resistance in meticillin-resistant *Staphylococcus aureus*. *J Hosp Infect*,
2143 2010; 76(3):206-210
- 2144 148. Harris P.N.A., Le B.D., Tambyah P., Hsu L.Y., Pada S., Archuleta S. et al.
2145 Antiseptic body washes for reducing the transmission of meticillin-resistant
2146 *Staphylococcus aureus*: A cluster crossover study. *Open Forum Infect Dis*, 2015;
2147 2(2):ofv051
- 2148 149. Urias D.S., Varghese M., Simunich T., Morrissey S., Dumire R. Preoperative
2149 decolonization to reduce infections in urgent lower extremity repairs. *Eur J Trauma*
2150 *Emerg Surg*, 2018; 44(55):787-93
- 2151 150. Torres E.G., Lindmeir-Snell J.M., Langan J.W., Burnikel B.G. Is Preoperative
2152 Nasal Povidone-Iodine as Efficient and Cost-Effective as Standard Meticillin-resistant
2153 *Staphylococcus aureus* Screening Protocol in Total Joint Arthroplasty? *J Arthroplasty*,
2154 2016; 31(1):215–218
- 2155 151. Urbancic, K.F., Mårtensson J., Glassford N., Eyeington C., Robbins R., Ward
2156 P.B. et al. Impact of unit-wide chlorhexidine bathing in intensive care on BSI and
2157 drug-resistant organism acquisition. *Crit Care Resusc*, 2018; 20(2):109-116
- 2158 152. Blackwood B., Thompson G., McMullan R., Stevenson M, Riley T.V., Alderdice
2159 F.A. et al. Tea tree oil (5%) body wash versus standard care (Johnson's Baby
2160 Softwash) to prevent colonization with meticillin-resistant *Staphylococcus aureus* in
2161 critically ill adults: a randomized controlled trial. *J Antimicrob Chemother*, 2013;
2162 68(5):1193-9

- 2163 153. Landelle C., von Dach E., Haustein T., Agostinho A., Renzi G., Renzoni A.
2164 Randomized, placebo-controlled, double-blind clinical trial to evaluate the efficacy of
2165 polyhexanide for topical decolonization of MRSA carriers. *J. Antimicrob Chemother*,
2166 2016; 71(2):531-538
- 2167 154. Christie J., Wright D., Liebowitz J., Stefanacci P. Can a nasal and skin
2168 decolonization protocol safely replace contact precautions for MRSA-colonized
2169 patients? *Am J Infect Control*. 2020; 48(8):922-924
- 2170 155. Mitchell B.G., Hall L., White, N., Barnett A.G., Halton K., Paterson D.L. et al. An
2171 environmental cleaning bundle and health-care-associated infections in hospitals
2172 (REACH): a multicentre, randomised trial. *Lancet Infect Dis*, 2019; 19(4):410-418
- 2173 156. Hung I. C., Chang H-Y., Cheng A., Chen M.W., Chen A.C., Ting L. et al.
2174 Implementation of human factors engineering approach to improve environmental
2175 cleaning and disinfection in a medical center. *Antimicrob Resist Infect Control*, 2020;
2176 9(1):17
- 2177 157. French G.L., Otter J.A., Shannon K.P., Adams N.M.T., Watling D., Parks M.J.
2178 Tackling contamination of the hospital environment by meticillin-resistant
2179 *Staphylococcus aureus* (MRSA): a comparison between conventional terminal
2180 cleaning and hydrogen peroxide vapour decontamination. *J Hosp Infect*, 2004;
2181 57(1):31-37
- 2182 158. Passaretti C.L., Otter J.A., Reich N.G., Myers J., Shepard J., Ross T. et al. An
2183 evaluation of environmental decontamination with hydrogen peroxide vapor for
2184 reducing the risk of patient acquisition of multidrug-resistant organisms. *Clin Infect*
2185 *Dis*, 2013; 56(1):27-35
- 2186 159. Mitchell, B.G., Digney, W., Locket, P. Dancer S.J. Controlling meticillin-
2187 resistant *Staphylococcus aureus* (MRSA) in a hospital and the role of hydrogen
2188 peroxide decontamination: an interrupted time series analysis. *BMJ Open*, 2014;
2189 4(4):e004522
- 2190 160. Manian F.A., Griesenauer S., Senkel D., Setzer J.M., Doll S.A., Perry A.M. et al.
2191 Isolation of *Acinetobacter baumannii* complex and meticillin-resistant
2192 *Staphylococcus aureus* from hospital rooms following terminal cleaning and
2193 disinfection: can we do better? *Infect Control Hosp Epidemiol*, 2011; 32(7):667-672
- 2194 161. Anderson D.J., Chen L.F., Weber D.J., Moehring R.W., Lewis S.S., Triplett P.F.
2195 et al. Enhanced terminal room disinfection and acquisition and infection caused by
2196 multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced
2197 Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover
2198 study. *Lancet*, 2017; 389(10071):805-814
- 2199 162. Anderson D.J., Moehring R.W., Weber D.J., Lewis S.S., Chen L.F., Schwab J.C.
2200 et al. Effectiveness of targeted enhanced terminal room disinfection on hospital-
2201 wide acquisition and infection with multidrug-resistant organisms and *Clostridium*
2202 *difficile*: a secondary analysis of a multicentre cluster randomised controlled trial
2203 with crossover design (BETR Disinfection). *Lancet Infect Dis*, 2018; 18(8):845-53

163. Rutala W. A., Kanamori H., Gergen M.F., Knelson L.P., Sickbert-Bennett E.E., Chen L.F. et al. Enhanced disinfection leads to reduction of microbial contamination and a decrease in patient colonization and infection. *Infect Control Hospital Epidemiol*, 2018; 39(9):1118-1121.
164. Jinadatha C., Quezada R., Huber T.W., Williams J.B., Zeber J.E., Copeland L.A. Evaluation of a pulsed-xenon ultraviolet room disinfection device for impact on contamination levels of methicillin-resistant *Staphylococcus aureus*. *BMC Infect Dis*, 2014; 14:187
165. Raggi R., Archuleta K., Haag C.W., Tang W. Clinical, operational, and financial impact of an ultraviolet-C terminal disinfection intervention at a community hospital. *Am J Infect Control*, 2018; 46(11):1224-1229.
166. Kitagawa H., Mori M., Kawano R., Hara T., Kashiwaga S., Hayashi Y. et al. Combining pulsed xenon ultraviolet disinfection with terminal manual cleaning helps reduce the acquisition rate of methicillin-resistant *Staphylococcus aureus*. *Am J Infect Control*. 2021; 49(8):1048-1051
167. Morikane K., Suzuki S., Yoshioka J., Yakuwa J., Nakane M., Nemoto K. Clinical and microbiological effect of pulsed xenon ultraviolet disinfection to reduce multidrug-resistant organisms in the intensive care unit in a Japanese hospital: a before–after study. *BMC Infect Dis*. 2020; 20:82.
168. Haas J.P., Menz J., Dusza S., Montecalvo M.A. Implementation and impact of ultraviolet environmental disinfection in an acute care setting. *Am J Infect Control*, 2014; 42(6):586-90
169. Vianna P.G., Dale C.R., Simmons S., Stibich M., Licitra C.M. Impact of pulsed xenon ultraviolet light on hospital-acquired infection rates in a community hospital. *Am J Infect Control*, 2016; 44(3):299-303
170. Karpanen T.J., Casey A.L., Lambert P.A., Cookson B.D., Nightingale P., Miruszenko L. et al. The antimicrobial efficacy of copper alloy furnishing in the clinical environment: a crossover study. *Infect Control Hosp Epidemiol*, 2012; 33(1):3-9
171. Salgado C.D., Sepkowitz K.A., John J.F., Cantey J.R., Attaway H.H., Freeman K.D. et al. Copper surfaces reduce the rate of healthcare-acquired infections in the intensive care unit. *Infect Control Hosp Epidemiol*, 2013; 34(5):479-486
172. Wilson G., Jackson V., Boyken L., Puig-Asensio M., Marra A.R., Perencevich E. et al. A randomized control trial evaluating efficacy of antimicrobial impregnated hospital privacy curtains in an intensive care setting. *Am J Infect Control*, 2020; 48(8):862-868.
173. Luk S., Chow V.C.Y., Yu K.C.H., Hsu E.K., Tsang N.C., Chuang V.W.M. et al. Effectiveness of antimicrobial hospital curtains on reducing bacterial contamination- A multicenter study. *Infect Control Hospital Epidemiol*, 2018; 40(2):164-170.
174. Kim M.H., Lee S.G., Kim K.S., Heo Y.J., Oh J.E., Jeong S.J. Environmental disinfection with photocatalyst as an adjunctive measure to control transmission of

- 2245 met icillin-resistant Staphylococcus aureus: a prospective cohort study in a high-
2246 incidence setting. BMC Infect Dis, 2018; 18(1):610.
- 2247 175. Boyce J.M., Guercia K.A., Sullivan L., Havill N.L., Fekieta R., Kozakiewicz J. et
2248 al. Prospective cluster controlled crossover trial to compare the impact of an
2249 improved hydrogen peroxide disinfectant and a quaternary ammonium-based
2250 disinfectant on surface contamination and health care outcomes. Am J Infect
2251 Control, 2017; 45(9):1006-1010
- 2252 176. Jury L.A., Cadnum J.L., Jennings-Sanders A., Eckstein E.C., Curtis S.C., Donskey
2253 J. Evaluation of an alcohol-based power sanitizing system for decontamination of
2254 hospital rooms of patients with met icillin-resistant Staphylococcus aureus carriage.
2255 Am J Infect Control, 2010; 38(3):234-236
- 2256 177. Zeber J.E., Coppin J.D., Villamaria F.C., Williams M.D., Copeland L.A,
2257 Chatterjee P. et al. Use of ultraviolet irradiation in addition to commonly used
2258 hospital disinfectants or cleaners further reduces the bioburden on high-touch
2259 surfaces. Open Forum Infect Dis, 2019; 17(6):ofz529.
- 2260 178. Conlon-Bingham G., Aldeyab M., Kearney M.P., Scott M.G., Baldwin N.,
2261 McElnay J.C. Reduction in the incidence of hospital-acquired MRSA following the
2262 introduction of a chlorine dioxide 275 ppm-based disinfecting agent in a district
2263 general hospital. Eur J Hosp Pharm, 2016; 23(1):28-32
- 2264 179. Garvey M.I., Wilkinson M.A.C., Bradley C.W., Holden K.L., Holden E. Wiping
2265 out MRSA: Effect of introducing a universal disinfection wipe in a large UK teaching
2266 hospital. Antimicrob Resist Infect Control, 2018; 7(1):155
- 2267 180. Patel S.S., Pevalin D.J., Prosser R., Couchman A. Comparison of detergent-
2268 based cleaning, disinfectant-based cleaning, and detergent-based cleaning after
2269 enhanced domestic staff training within a source isolation facility. Br J Infect Control,
2270 2007; 8(3):20-25
- 2271 181. Yuen J.W.M., Chung T.W.K., Loke A.Y. Met icillin-resistant Staphylococcus
2272 aureus (MRSA) contamination in bedside surfaces of a hospital ward and the
2273 potential effectiveness of enhanced disinfection with an antimicrobial polymer
2274 surfactant. Int J Environ Res Public Health, 2015; 12(3):3026-3041
- 2275 182. Curran E., Harper P., Loveday H., Gilmour H., Jones S., Benneyan J., et al.
2276 Results of a multicentre randomised controlled trial of statistical process control
2277 charts and structured diagnostic tools to reduce ward-acquired met icillin-resistant
2278 Staphylococcus aureus: the CHART Project. J Hosp Infect, 2008; 70(2):127-35.
- 2279 183. Huang S.S., Yokoe D.S., Hinrichsen V.L., Spurchise L.S., Datta R., Miroshnik I.
2280 et al. Impact of routine intensive care unit surveillance cultures and resultant barrier
2281 precautions on hospital-wide met icillin-resistant Staphylococcus aureus bacteremia.
2282 Clin Infect Dis, 2006; 43(8):971-8
- 2283 184. Harrington G., Watson K., Bailey M., Land G., Borrell S., Houston L. et al.
2284 Reduction in hospitalwide incidence of infection or colonization with met icillin-
2285 resistant Staphylococcus aureus with use of antimicrobial hand-hygiene gel and
2286 statistical process control charts. Infect Control Hosp Epidemiol, 2007; 28(7):837-844

- 2287 185. Enoch D.A., Cargill J.S., Sismey A., Karas J.A. MRSA surveillance in a UK district
2288 hospital: measuring clinical isolates with MRSA is more useful than measuring MRSA
2289 BSI. *J Hosp Infect*, 2011; 79(4):287-91
- 2290 186. Gastmeier P., Schwab F., Chaberny I., Geffers C. Individual units rather than
2291 entire hospital as the basis for improvement: the example of two Meticillin-resistant
2292 *Staphylococcus aureus* cohort studies. *Antimicrob Resist Infect Control*, 2012; 1(1):8
- 2293 187. Karas J.A., Enoch D.A., Eagle H.J., Emery M.M. et al. Random meticillin-
2294 resistant *Staphylococcus aureus* carrier surveillance at a district hospital and the
2295 impact of interventions to reduce endemic carriage. *J Hosp Infect*, 2009; 71(4):327-
2296 32
- 2297 188. Pan A., Carnevale G., Catenazzi P., Colombini P., Crema L., Dolcetti L. et al.
2298 Trends in meticillin-resistant *Staphylococcus aureus* (MRSA) BSI: effect of the MRSA
2299 “search and isolate” strategy in a hospital in Italy with hyperendemic MRSA. *Infect*
2300 *Control Hosp Epidemiol*, 2005; 26(2):127-133
- 2301 189. Robicsek A., Beaumont J., Paule S., Hacek D.M., Thomson R.B., Kaul K.L. et al.
2302 Universal surveillance for meticillin-resistant *Staphylococcus aureus* in 3 affiliated
2303 hospitals. *Ann Intern Med*, 2008; 148(6):409-18
- 2304 190. Shitrit P., Gottesman B.S., Katzir M., Kilman A., Ben-Nissan Y., Chowers M.
2305 Active surveillance for meticillin-resistant *Staphylococcus aureus* (MRSA) decreases
2306 the incidence of MRSA bacteremia. *Infect Control Hosp Epidemiol*, 2006;
2307 27(10):1004-8
- 2308 191. Walter J., Haller S., Blank H., Eckmanns T., Sin M.A., Hermes J. Incidence of
2309 invasive meticillin-resistant *Staphylococcus aureus* infections in Germany, 2010 to
2310 2014. *Euro Surveill*, 2015; 20(46):no pagination.
- 2311 192. West T.E., Guerry C., Hiott M., Morrow N., Ward K., Salgado C.D. Effect of
2312 targeted surveillance for control of meticillin-resistant *Staphylococcus aureus* in a
2313 community hospital system. *Infect Control Hosp Epidemiol*, 2006; 27(3):233-238
- 2314 193. Johnson A.P., Davies J., Guy R., Abernethy J., Sheridan E., Pearson A. et al.
2315 Mandatory surveillance of meticillin-resistant *Staphylococcus aureus* (MRSA) BSI in
2316 England: the first 10 years. *J Antimicrob Chemother*, 2012; 67(4):802-809
- 2317 194. Cimolai N. MRSA and the environment: implications for comprehensive
2318 control measures. *Eur J Clin Microbiol Infect Dis*, 2008; 27(7):481-493
- 2319 195. Marimuthu K, Pittet D, Harbarth S. The effect of improved hand hygiene on
2320 nosocomial MRSA control. *Antimicrob Resist Infect Control*, 2014; 3:34.
- 2321 196. World Health Organisation. WHO Guidelines on Hand Hygiene in Health Care:
2322 First Global Patient Safety Challenge Clean Care Is Safer Care. Geneva: World Health
2323 Organization; 2009.
- 2324 197. Loveday H.L., Wilson J.A., Pratt R.J., Golsorkhi M., Tingle A., Bak A. et al.
2325 Epic3: national evidence-based guidelines for preventing healthcare-associated
2326 infections in NHS hospitals in England. *J Hosp Infect*, 2014; 86(Suppl 1):S1-70

198. Siegel J.D., Rhinehart E., Jackson M., Chiarello L., Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control*, 2007; 35(10 Suppl 2):S165-193.
199. Huskins C.W., Huckabee C.M., O'Grady N., Murray P., Kopetskie H., Zimmer L. et al. Intervention to reduce transmission of resistant bacteria in intensive care. *N Engl J Med*, 2011; 364(15):1407-18
200. Harris A.D., Pineles L., Belton B., Johnson J.K., Shardell M., Loeb M. et al. Universal Glove and Gown Use and Acquisition of Antibiotic resistant bacteria in the ICU: A Randomized Trial. *JAMA*, 2013; 310(15):1571-80
201. Cepeda J.A., Whitehouse T., Cooper B., Hails J., Jones K., Kwaku F. Isolation of patients in single rooms or cohorts to reduce spread of MRSA in intensive-care units: prospective two-centre study. *Lancet*, 2005; 365(9456):295–304
202. Marshall C., Richards M., McBryde E. Do Active Surveillance and Contact Precautions Reduce MRSA Acquisition? A Prospective Interrupted Time Series. *PLoS One*, 2013; 8(3):e58112.
203. Bearman G., Abbas S., Masroor N., Sanogo K., Vanhoozer G., Cooper K. et al. Impact of Discontinuing Contact Precautions for Meticillin-resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococcus*: An Interrupted Time Series Analysis. *Infect Control Hosp Epidemiol*, 2018; 39(6):676-682
204. Catalano G., Houston S.H., Catalano M.C., Butera A.S., Jennings S.M., Hakala S.M. et al. Anxiety and depression in hospitalized patients in resistant organism isolation. *South Med J*, 2003; 96(2):141-5
205. Kennedy P., Hamilton L.R. Psychological impact of the management of meticillin-resistant *Staphylococcus aureus* (MRSA) in patients with spinal cord injury. *Spinal Cord*, 1997; 35(9):617-9
206. Tarzi S., Kennedy P., Stone S., Evans S. Meticillin-resistant *Staphylococcus aureus*: psychological impact of hospitalization and isolation in an older adult population. *J Hosp Infect*, 2001; 49(4):250-254
207. Wassenberg M.W., Severs D., Bonten M.J. Psychological impact of short-term isolation measures in hospitalised patients. *J Hosp Infect*, 2010; 75(2):124-127
208. Rump B., De Boer M., Reis R., Wassenberg M., Van Steenberghe J. Signs of stigma and poor mental health among carriers of MRSA. *J Hosp Infect*, 2017; 95(3):268-274
209. Curran E.T., Hamilton K., Monaghan A., McGinlay M., Thakker B. Use of a temporary cohort ward as part of an intervention to reduce the incidence of meticillin-resistant *Staphylococcus aureus* in a vascular surgery ward. *J Hosp Infect*, 2006; 63(4):374-379.
210. Bessesen M.T., Lopez K., Guerin K., Hendrickson K., Williams S., O'Connor-Wright S., Granger D. et al. Comparison of control strategies for methicillin-resistant *Staphylococcus aureus*. *Am J Infect Control*, 2013; (11):1048-1052.
211. Carey D., Price K., Neal S., Compton C., Ash C., Bryan N. et al. The impact of discontinuing contact precautions for multidrug resistant organisms at a less than 400-bed level II teaching hospital and a community hospital: A 3-month pilot study. *Am J Infect Control*, 2020; 48(3):333-336

- 2371 212. Renaudin L., Llorens M., Goetz C., Gette S., Citro V., Poulain S. et al. Impact of
2372 Discontinuing Contact Precautions for MRSA and ESBLE in an Intensive Care Unit: A
2373 Prospective Noninferiority Before and After Study. *Infect Control Hosp Epidemiol*,
2374 2017; 38(11):1342-1350.
- 2375 213. Gandra S., Barysaukas C.M., Mack D.A., Barton B., Finberg R., Ellison R.T.
2376 Impact of contact precautions on falls, pressure ulcers and transmission of MRSA and
2377 VRE in hospitalized patients. *J Hosp Infect*, 2014; 88(3):170-176.
- 2378 214. Rupp M.E., Fitzgerald T., Hayes K., Van Schooneveld T., Hewlett A., Clevenger
2379 R. et al. Effect of Cessation of Contact Isolation for Endemic Methicillin-Resistant
2380 *Staphylococcus aureus* and Vancomycin-Resistant Enterococci. *Infect Control Hosp*
2381 *Epidemiol*, 2017; 38(8):1005-1007.
- 2382 215. Auguet O.T., Stabler R.A., Betley J., Preston M.D., Dhaliwal M., Gaunt M. et al.
2383 Frequent Undetected Ward-Based Meticillin-resistant *Staphylococcus aureus*
2384 Transmission Linked to Patient Sharing Between Hospitals. *Clin Infect Dis*, 2018;
2385 5;66(6):840-848.
- 2386 216. Donker T., Wallinga J., Slack R., Grundmann H. Hospital Networks and the
2387 Dispersal of Hospital-Acquired Pathogens by Patient Transfer. *PLoS One*, 2012;
2388 7(4):e35002
- 2389 217. van Velzen E.V.H., Reilly J.S., Kavanagh K., Leanord A., Edwards G.F.S., Girvan
2390 E.K. et al. A Retrospective Cohort Study into Acquisition of MRSA and Associated Risk
2391 Factors after Implementation of Universal Screening in Scottish Hospitals. *Infect*
2392 *Control Hosp Epidemiol*, 2011; 32(9):889-896
- 2393 218. Wang J., Foxman B., Pirani A., Lapp Z., Mody L., Snitkin E.S. Application of
2394 combined genomic and transfer analyses to identify factors mediating regional
2395 spread of antibiotic-resistant bacterial lineages. *Clin Infect Dis*, 2020; 71(10):E642-
2396 E649
- 2397 219. Garvey M.I., Bradley C.W., Holden K.L., Oppenheim B. Outbreak of clonal
2398 complex 22 Panton–Valentine leucocidin-positive methicillin-resistant *Staphylococcus*
2399 *aureus*. *J Infect Prevent*, 2017; 18(5):224–230
- 2400 220. van Rijen M.M., Bosch T., Heck M.E., Kluytmans J.A.J.W. Methicillin-resistant
2401 *Staphylococcus aureus* epidemiology and transmission in a Dutch hospital. *Hosp*
2402 *Infect*, 2009; 72(4):299-306
- 2403 221. Coombs G.W., van Gessel H., Pearson C.J., Godsell M.-R., O'Brien F.G.,
2404 Christiansen K.J. Controlling a Multicenter Outbreak Involving the New York/Japan
2405 Methicillin-resistant *Staphylococcus aureus* Clone. *Infect Control Hosp Epidemiol*,
2406 2007; 28(7):845-52.
- 2407 222. Laroyer C., Lehours P., Tristan A., Boyer F., Marie V., Elleau C. et al. Outbreak
2408 in newborns of methicillin-resistant *Staphylococcus aureus* related to the sequence
2409 type 5 Geraldine clone. *Am J Infect Control*, 2016; 44(2016):e9-e11
- 2410 223. Barnes S.L., Harris A.D., Golden B.L., Wasil E.A., Furuno J.P. Contribution of
2411 interfacility patient movement to overall methicillin-resistant *Staphylococcus aureus*
2412 prevalence levels. *Infect Control Hosp Epidemiol*, 2011; 32(11):1073-1078.

224. Casas I., Sopena N., Esteve M., Quesada M.D., Andrés I., Matas L. et al. Prevalence of and risk factors for meticillin-resistant *Staphylococcus aureus* carriage at hospital admission. *Infect Control Hosp Epidemiol*, 2007; 28(11):1314–1317
225. Fukuda M., Tanaka H., Kajiwara Y., Sugimura T., Oda E., Suenaga H. et al. High-risk populations for nasal carriage of meticillin-resistant *Staphylococcus aureus*. *J Infect Chemother*, 2004; 10(3):189-91.
226. Haley C.C., Mittal D., Laviolette A., Jannapureddy S., Parvez N., Haley R.W. Meticillin-resistant *Staphylococcus aureus* infection or colonization present at hospital admission: multivariable risk factor screening to increase efficiency of surveillance culturing. *J Clin Microbiol*, 2007; 45(9):3031-3038
227. Harbarth S., Sax H., Fankhauser-Rodriguez C., Schrenzel J., Agostinho A., Pittet D. Evaluating the probability of previously unknown carriage of MRSA at hospital admission. *Am J Med*, 2006; 119(3):275.e15-23.
228. Lucet J.C., Grenet K., Armand-Lefevre L., Harnal M.H., Bouvet E., Regnier B. et al. High prevalence of carriage of meticillin-resistant *Staphylococcus aureus* at hospital admission in elderly patients: implications for infection control strategies. *Infect Control Hosp Epidemiol*, 2009; 26(2):21-6.
229. Minhas P., Perl T.M., Carroll K.C., John S.W., Shangraw K.A., Fellerman D. et al. Risk factors for positive admission surveillance cultures for meticillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci in a neurocritical care unit. *Crit Care Med*, 2011; 39(10):2322-2329
230. Reilly J.S., Stewart S., Christie P., Allardice G., Smith A., Masterton R. et al. Universal screening for meticillin-resistant *Staphylococcus aureus*: interim results from the NHS Scotland pathfinder project. *J Hosp Infect*, 2010; 74(1):35-41.
231. Reilly J.S., Stewart S., Christie P., Allardice G., Stari T., Matheson A. et al. Universal screening for meticillin-resistant *Staphylococcus aureus* in acute care: risk factors and outcome from a multicentre study. *J Hosp Infect*, 2012; 80(1):31-35.
232. Santosaningsih D., Santoso S., Verbrugh H.A., Severin J.A. Risk Factors for Meticillin-resistant *Staphylococcus aureus* Carriage among Patients at Admission to the Surgical Ward in a Resource-Limited Hospital in Indonesia. *Am J Trop Med Hyg*, 2017; 97(5):1310-1312.
233. Sax H., Harbarth S., Gavazzi G., Henry N., Schrenzel J., Rohner P. et al. Prevalence and prediction of previously unknown MRSA carriage on admission to a geriatric hospital. *Age Ageing*, 2005; 34(5):456–462
234. Washam M.C., Ankrum A., Haberman B.E., Staat M.A., Haslam D.B. Risk factors for staphylococcus aureus acquisition in the neonatal intensive care unit: A matched case-case-control study. *Infect Control Hosp Epidemiol*, 2018; 39(1):46-52.
235. Callejo-Torre F., Bouza J.M., Astigarraga O.P., Coma Del Corral M.J., Martínez M.P., Alvarez-Lerma F. et al. Risk factors for meticillin-resistant *Staphylococcus aureus* colonisation or infection in intensive care units and their reliability for predicting MRSA on ICU admission. *Infez Med*, 2016; 24(3):201-209.
236. Muralidhar B., Anwar S.M., Handa A.I., Peto T.E.A., Bowler I.C.J.W. Prevalence of MRSA in emergency and elective patients admitted to a vascular surgical unit: implications for antibiotic prophylaxis. *Eur J Vasc Endovasc Surg*, 2006; 32(4):402-407.

- 2458 237. Rao G., Michalczyk P., Nayeem N., Walker G., Wigmore L. Prevalence and risk
2459 factors for meticillin-resistant *Staphylococcus aureus* in adult emergency admissions
2460 a case for screening all patients? *J Hosp Infect*, 2007; 66(1):15-21
- 2461 238. Yamakawa K., Tasaki O., Fukuyama M., Kitayama J., Matsuda H., Nakamori Y.
2462 et al. Assessment of risk factors related to healthcare-associated meticillin-resistant
2463 *Staphylococcus aureus* infection at patient admission to an intensive care unit in
2464 Japan. *BMC Infect Dis*, 2011; 11:303
- 2465 239. Vajravelu R., Guerrero D., Jury L., Donskey C. Evaluation of Stethoscopes as
2466 Vectors of *Clostridium difficile* and Meticillin-resistant *Staphylococcus aureus*. *Infect*
2467 *Control Hosp Epidemiol*, 2012; 33(1):96-98.
- 2468 240. John A., Alhmidi H., Cadnum J., Jencson A.L., Gestrich S., Donskey C.J.
2469 Evaluation of the potential for electronic thermometers to contribute to spread of
2470 healthcare-associated pathogens. *Am J Infect Control*, 2018; 46(6):708-710.
- 2471 241. Moore G., Ali S., Cloutman-Green E.A., Bradley C.R., Wilkinson M.A.C., Hartley
2472 J.C. et al. Use of UV-C radiation to disinfect non-critical patient care items: a
2473 laboratory assessment of the Nanoclave Cabinet. *BMC Infect Dis*, 2012; 12:174
- 2474 242. Nerandzic M.M., Cadnum J.L., Eckart J.E., Donskey C.J. Evaluation of a hand-
2475 held far-ultraviolet radiation device for decontamination of *Clostridium difficile* and
2476 other healthcare-associated pathogens. *BMC Infect Dis*, 2012; 12:120
- 2477 243. Vickery K., Gorgis V.Z., Burdach, J., Patel D. Evaluation of an automated high-
2478 level disinfection technology for ultrasound transducers. *J Infect Public Health*, 2014;
2479 7(2):153-160
- 2480 244. Frazee B.W., Fahimi J., Lambert L., Nagdev A. Emergency department
2481 ultrasonographic probe contamination and experimental model of probe
2482 disinfection. *Ann Emerg Med*, 2011; 58(1):56-63
- 2483 245. Faulx G.R., Emig E.L., Alhmidi H., Ng-Wong Y.K., Mana T.S.C., Cadnum J.L. et
2484 al. Efficacy of a wearable ultraviolet-C light device for semiautomated
2485 decontamination of stethoscopes between each use. *Infect Control Hosp Epidemiol*,
2486 2020; 41(2):244-246.
- 2487 246. Ochoa S.A., Cruz-Córdova A., Mancilla-Rojano J., Escalona-Venegas G.,
2488 Esteban-Kenel V., Franco-Hernández I. et al. Control of Meticillin-resistant
2489 *Staphylococcus aureus* Strains Associated With a Hospital Outbreak Involving
2490 Contamination From Anesthesia Equipment Using UV-C. *Front Microbiol*, 2020;
2491 11:600093.
- 2492 247. Masse V., Valiquette L., Boukhoudmi S., Bonenfant F., Talab Y., Carvalho J.C.
2493 et al. Impact of meticillin-resistant *Staphylococcus aureus* contact isolation units on
2494 medical care. *PLoS One*, 2013; 8(2):e57057.
- 2495 248. Tran K., Bell C., Stall N., Tomlinson G., McGeer A., Morris A. et al. The Effect
2496 of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site,
2497 Retrospective, Propensity Score-Matched Cohort Study. *J Gen Intern Med*, 2017;
2498 32(3):262-268
- 2499 249. Livorsi D.J., Kundu M.G., Batteiger B., Kresse A.B. The Effect of Contact
2500 Precautions for MRSA on Patient Satisfaction Scores. *J Hosp Infect*, 2015; 90(3):263–
2501 266

- 2502 250. Newton J.T., Constable D., Senior V. Patients' perceptions of meticillin-
2503 resistant *Staphylococcus aureus* and source isolation: a qualitative analysis of
2504 source-isolated patients. *J Hosp Infect*, 2001; 48(4):275-80.
- 2505 251. Skyman E., Sjöström H., Hellström L. Patients' experiences of being infected
2506 with MRSA at a hospital and subsequently source isolated. *Scand J Caring Sci*, 2010;
2507 24(1):101-107.
- 2508 252. Lindberg M., Carlsson M., Högman M., Skytt B. Suffering from meticillin-
2509 resistant *Staphylococcus aureus*: experiences and understandings of colonisation. *J*
2510 *Hosp Infect*, 2009; 73(3):271-277.
- 2511 253. Webber K.L., Macpherson S., Meagher A., Hutchinson S., Lewis B. The impact
2512 of strict isolation on MRSA positive patients: an action-based study undertaken in a
2513 rehabilitation center. *Rehabil Nurs*, 2012; 37(1):43-50.
- 2514 254. Burnett E., Lee K., Rushmer R., Ellis M., Noble M., Davey P. Healthcare-
2515 associated infection and the patient experience: a qualitative study using patient
2516 interviews. *J Hosp Infect*, 2010; 74(1):42-7.

2517

Abbreviations

2518	AOR – adjusted odds ratio
2519	ATP – adenosine triphosphate
2520	BSI – bloodstream infection
2521	CBA – controlled before/after (study)
2522	cfu – colony forming units
2523	CHG – chlorhexidine gluconate
2524	CI – confidence intervals
2525	CLABSI – central line-associated bloodstream infection
2526	CP – contact precautions
2527	DAS – diagnostic accuracy study
2528	ELOS – estimated length of stay
2529	GP – general practitioner
2530	HCAI – healthcare-associated infection
2531	HES – Hospital Episode Statistics
2532	HPV – hydrogen peroxide vapour
2533	HR – hazard ratio
2534	ICU – intensive care unit
2535	IPC – infection prevention and control
2536	IRR – incidence rate ratio
2537	ITS – interrupted time series (study)
2538	LOS – length of stay
2539	MDRO – multidrug-resistant organism
2540	MIC – minimum inhibitory concentration
2541	MRSA – Meticilin-resistant <i>Staphylococcus aureus</i>
2542	MSSA – Meticilin-sensitive <i>Staphylococcus aureus</i>
2543	NICE – National Institute for Health and Care Excellence
2544	NR – not reported
2545	OR – odds ratio
2546	PCR – polymerase chain reaction
2547	pd – patient days
2548	

2549	PICO – Population-Intervention-Comparator-Outcome (framework)
2550	PPE – personal protective equipment
2551	PVL – Panton-Valentine leucocidin
2552	PVP – povidone-iodine
2553	PX-UV – pulsed-xenon ultraviolet
2554	QAC – quaternary ammonium compound
2555	RCT – randomised controlled trial (RCT)
2556	RR – risk ratio
2557	SIGN – Scottish Intercollegiate Guidelines Network
2558	SPC – statistical process control (chart)
2559	SSI – surgical site infections
2560	TAT – turnaround time
2561	UBA – uncontrolled before/after (study)
2562	UV-C – ultraviolet-C
2563	WGS – whole genome sequencing
2564	