Effective Health Care Program

Comparative Effectiveness Review
Number 102

Screening for Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

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Screening for Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Prepared for:
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This report is based on research conducted by the Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2007-10058-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Technical Expert Panel*

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Screening for Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Structured Abstract

Objectives. To synthesize comparative studies that examined the benefits and harms of screening for methicillin-resistant *Staphylococcus aureus* (MRSA) carriage in the inpatient or outpatient setting.

Data sources. MEDLINE®, Embase®, the Cochrane Database of Systematic Reviews, the National Institute for Clinical Excellence, the National Guideline Clearinghouse, and the Health Technology Assessment Programme were searched from January 1990 to March 2012. A search of the gray literature included databases with regulatory information, clinical trial registries, abstracts and conference papers, grants and federally funded research, and information from manufacturers.

Review methods. We sought studies that compared MRSA screening strategies, including universal screening; screening of selected patient populations (surgery, intensive care unit, high risk); and no screening. Outcomes were MRSA acquisition; MRSA infection; morbidity (including complications of MRSA infection); mortality; adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors); and hospital resource utilization, such as length of stay. Data were abstracted by a team of reviewers and fact-checked by another team of reviewers. Study quality was assessed using the U.S. Preventive Services Task Force framework. Strength of the body of evidence was assessed according to the Agency for Healthcare Research and Quality "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."

Results. Forty-eight studies were abstracted for this review. Of these, only 1 was a randomized controlled trial; the other 47 studies utilized quasi-experimental study designs. Sixteen of the studies attempted to control for confounding and/or secular trends, and therefore had the potential to support causal inferences about the impact of MRSA screening on health outcomes and to contribute to the strength-of-evidence syntheses. This review found low strength of evidence that, compared with no screening, universal screening for MRSA carriage reduces healthcare-associated MRSA infection. For each of the other screening strategies evaluated, this review found insufficient evidence to determine the comparative effectiveness of screening on MRSA acquisition or infection.

Conclusions. There is low strength of evidence that universal screening of hospital patients decreases MRSA infection. However, there is insufficient evidence on other outcomes of universal MRSA screening, including morbidity, mortality, harms, and resource utilization. There is also insufficient evidence to support or refute the effectiveness of MRSA screening on any outcomes in other settings. The available literature consisted mainly of observational studies with insufficient controls for secular trends and confounding to support causal inference, particularly because other interventions were inconsistently bundled together with MRSA screening. Future research on MRSA screening should use design features and analytic strategies addressing secular trends and confounding. Designs should also permit assessment of effects of

specific bundles of screening and infection control interventions and address outcomes, including morbidity, mortality, harms, and resource utilization.

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Executive Summary

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) emerged as a clinically relevant human pathogen more than five decades ago.[1] The virulent bacterium was first detected in hospitals and other health care facilities where vulnerable hosts, frequent exposure to the selective pressure of intensive antimicrobial therapy, and the necessity for invasive procedures created a favorable environment for dissemination. MRSA emerged as an important cause of healthcare-associated infections, particularly central line–associated bloodstream infection, ventilator-associated pneumonia, and surgical site infection (SSI). Despite the adoption of infection-control measures, the incidence of MRSA infection at most U.S. hospitals steadily increased for many years,[2] but it is now decreasing.[3-6] Burton and colleagues[4] found a 49.6-percent decrease in the overall incidence of MRSA central line–associated bloodstream infection in U.S. intensive care units (ICUs) from 1997 to 2007. In a study of nine U.S. metropolitan areas, Kallen and colleagues[6] found a reduction in the incidence rate of hospital-onset invasive MRSA infections of 9.4 percent per year from 2005 to 2008 (95% confidence interval [CI], 14.7 to 3.8%; p=0.005).

While the decrease in the incidence of MRSA infection may be due to efforts to screen for MRSA carriage, it may also be due to secular trends (such as efforts to improve patient safety) and to confounders (such as efforts to improve the appropriate use of antibiotics and to decrease healthcare-associated infections in general, including catheter-associated bloodstream infection, ventilator-associated pneumonia, and SSI). Although not all studies concur, a number of analyses suggest that MRSA infections are associated with increased mortality and cost of care when compared with those due to strains that are susceptible to methicillin. Even the availability of newer pharmaceutical agents with specific activity against MRSA has not ameliorated the challenge of caring for patients with MRSA. The widespread use of these agents has been limited, in part due to toxicity, cost, and uncertainty as to optimal indications.[3]

The management and control of MRSA have been further complicated by dramatic changes in the epidemiology of transmission and infection observed over the past two decades. Specifically, *S. aureus* strains resistant to methicillin, once exclusively linked to hospital care, have increasingly been detected among patients in the community who lack conventional risk factors for MRSA infection.[5,7] Community-acquired MRSA has been linked to outbreaks of infection in hospitals and health care facilities.[8]

Conventional strategies for the control of MRSA (whether hospital or community associated) have focused on the prevention of spread from patient to patient (horizontal transmission). The effectiveness of hand hygiene in preventing the spread of MRSA has been demonstrated in observational studies in which hand hygiene promotion campaigns were associated with subsequent reductions in the incidence of MRSA among hospitalized patients.[9] While hand hygiene remains important in the effort to control MRSA transmission, the continued spread of the pathogen after its initial introduction in most facilities has prompted efforts to identify additional strategies. The use of contact isolation—including the donning of gowns and gloves when interacting with patients colonized or infected with MRSA and the assignment of such patients to single rooms or to a room with a group of affected patients—has been widely promoted and adopted. Such isolation precautions now are the centerpiece of most authoritative guidelines for MRSA control.[10] Despite the broad consensus associated with the use of contact isolation for MRSA prevention, the specific evidence in support of this practice remains limited and indirect.

Given the continued dissemination of MRSA at most U.S. hospitals, it is clear that these measures, as presently deployed, have been insufficient to check the spread of MRSA and other antibiotic-resistant pathogens.

A further limitation of these approaches—and, specifically, the use of isolation precautions—is the potential negative consequences of these measures. A series of studies have associated isolation precautions with worsened outcomes in terms of safety and patient satisfaction.[11] In addition, questions have been raised about specific performance measures, such as the frequency with which patients on isolation precautions are visited by treating physicians and the timely recording of vital signs. While the methodology employed in some of these studies has been questioned, no rigorous definitive analysis has been completed to exonerate isolation precautions.[12]

Based on the failure of conventional strategies (hand hygiene, barrier precautions, and isolation) to adequately control MRSA, more aggressive measures have been promoted in an effort to check the spread of this particularly virulent pathogen. In some European countries, an aggressive containment program identifies contacts of colonized and infected patients in an effort to intercede to prevent dissemination.[13] While such measures have not been widely adopted in most settings, some clinicians and scientists, and increasing numbers of public advocates and legislators have raised the call for more intensive efforts at MRSA control in the United States. Particular attention has been given to the potential value of active surveillance screening for MRSA. Because routine clinical cultures may identify as few as 18 percent of patients with asymptomatic carriage of antibiotic-resistant organisms such as MRSA, there exists a large reservoir of patients who are silent carriers of these organisms. These individuals may serve as a reservoir for further transmission. With active surveillance, microbiological samples are obtained from at-risk patients in the absence of signs or symptoms of infection in an effort to identify the underlying population of colonized individuals. By detecting the larger population of colonized individuals, conventional precautions, at the very least, can be implemented in a broader and more timely manner so as to interrupt horizontal transmission of MRSA. Detection of colonized patients also permits consideration of more aggressive interventions, including attempts at microbiological eradication or decolonization.

The specific evidence in support of active surveillance for MRSA has been promising, although a number of questions remain about the effectiveness of active surveillance for MRSA carriage and whether screening should be applied to all patient populations (universal screening) or to selected populations such as patients in the ICU or those undergoing surgical procedures (targeted screening). In addition, knowing which patients are colonized with MRSA is not expected to affect the frequency of spread if adherence to transmission-control strategies remains inadequate. Moreover, other efforts (such as attempts at decolonization or eradication, as well as programs to decrease healthcare-associated infections in general) may dramatically affect the impact of a MRSA-screening program. Therefore, trying to determine the impact of a screening program without detailed information about the deployment of decolonization measures is an important limitation to the available studies and has engendered considerable confusion among clinicians and policymakers.

Thus, a systematic review of the evidence is both justified and timely. The importance of gaining a better understanding of the evidence is also highlighted by the increasing demand for better control of MRSA and a higher standard for prevention of hospital-acquired infections in general.

Objective

The objective of this systematic review was to synthesize comparative studies that examined the benefits or harms of screening for MRSA carriage in the inpatient or outpatient settings. The review examined MRSA-screening strategies applied to all hospitalized or ambulatory patients (universal screening), as well as screening strategies applied to selected inpatient or outpatient populations (e.g., patients admitted to the ICU, patients admitted for a surgical procedure, or patients at high risk of MRSA colonization or infection), and compared them with no screening or with screening of selected patient populations (targeted screening). The review evaluated MRSA-screening strategies that included screening with or without isolation and with or without attempted eradication/decolonization. The patient population included all ambulatory patients (outpatients) and hospitalized patients (inpatients).

Key Questions

Key Question 1

Among ambulatory or hospitalized patients, what are the effects of a universal screening strategy for MRSA carriage (screen, isolate, eradicate/decolonize) when compared with no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

Key Question 2

Among ambulatory or hospitalized patients, what are the effects of a universal screening strategy for MRSA carriage (screen, isolate, eradicate/decolonize) when compared with screening of selected patient populations (targeted screening) on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

Key Question 3A

Among ambulatory or hospitalized patients, what are the effects of screening ICU patients for MRSA carriage (screen, isolate, eradicate/decolonize) when compared with no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and

nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

Key Question 3B

Among ambulatory or hospitalized patients, what are the effects of screening surgical patients for MRSA carriage (screen, isolate, eradicate/decolonize) when compared with no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

Key Question 3C

Among ambulatory or hospitalized patients, what are the effects of screening high-risk patients for MRSA carriage (screen, isolate, eradicate/decolonize) when compared with no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

Key Question 4

Among ambulatory or hospitalized patients, what are the effects of an expanded screening strategy for MRSA carriage (e.g., screen, isolate, eradicate/decolonize a broader group of patients, such as all patients admitted to the medical ward, the surgical ward, or the ICU) when compared with a limited screening strategy (e.g., screen, isolate, eradicate/decolonize a limited group of patients, such as patients admitted to the ICU) on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity [e.g., hypotension], antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization (e.g., length of stay)?

PICOTS (Population Intervention, Comparator, Outcome, Timing, and Setting) for the Key Questions

Population

All ambulatory patients (outpatients) and all hospitalized patients (inpatients). In addition, the following subpopulations were evaluated: (1) patients admitted to an ICU, (2) patients

undergoing surgical procedures, and (3) patients at high risk of MRSA colonization or infection (e.g., patients transferred from another health care facility, patients receiving hemodialysis).

Intervention

A MRSA screening strategy applied to all patients in a setting (universal screening) or applied to particular wards, units, or patients (targeted screening) that includes:

- MRSA screening using a testing modality (typically polymerase chain reaction [PCR]) with rapid turnaround (results available on the same day as the testing is performed) or
- MRSA screening using a testing modality with intermediate turnaround (results available next day to 2 days after testing performed) or
- MRSA screening using a testing modality (typically culture) with a longer turnaround time (results available more than 2 days after testing performed)

The screening strategy also may include:

- Isolation and/or
- Eradication/decolonization

Comparator

No screening or screening of selected patient populations (targeted screening).

Outcomes

Healthcare-associated MRSA acquisition; healthcare-associated MRSA infection; morbidity (including complications of MRSA infection); mortality; quality of care for noninfectious conditions; medical errors; adverse effects of screening and treatment, including allergic reactions, nonallergic toxicities, and resistance to antimicrobials; and hospital resource utilization such as length of stay.

Timing

Intervention through followup.

Settings

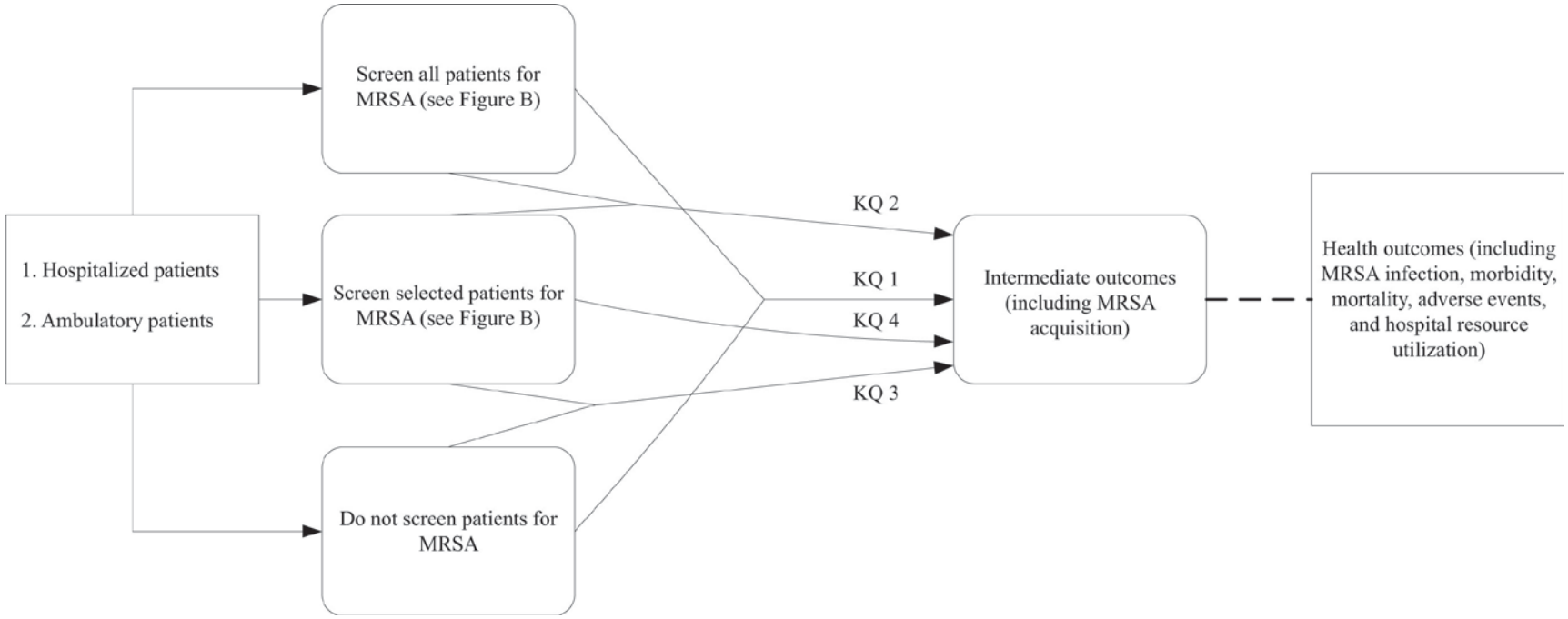
Inpatient (hospital wards and ICUs) and outpatient (ambulatory clinics, urgent care centers, and emergency departments).

A comprehensive review evaluating the benefits and harms of screening for MRSA carriage will identify areas of certainty and those that require additional prospective research.

Analytic Framework

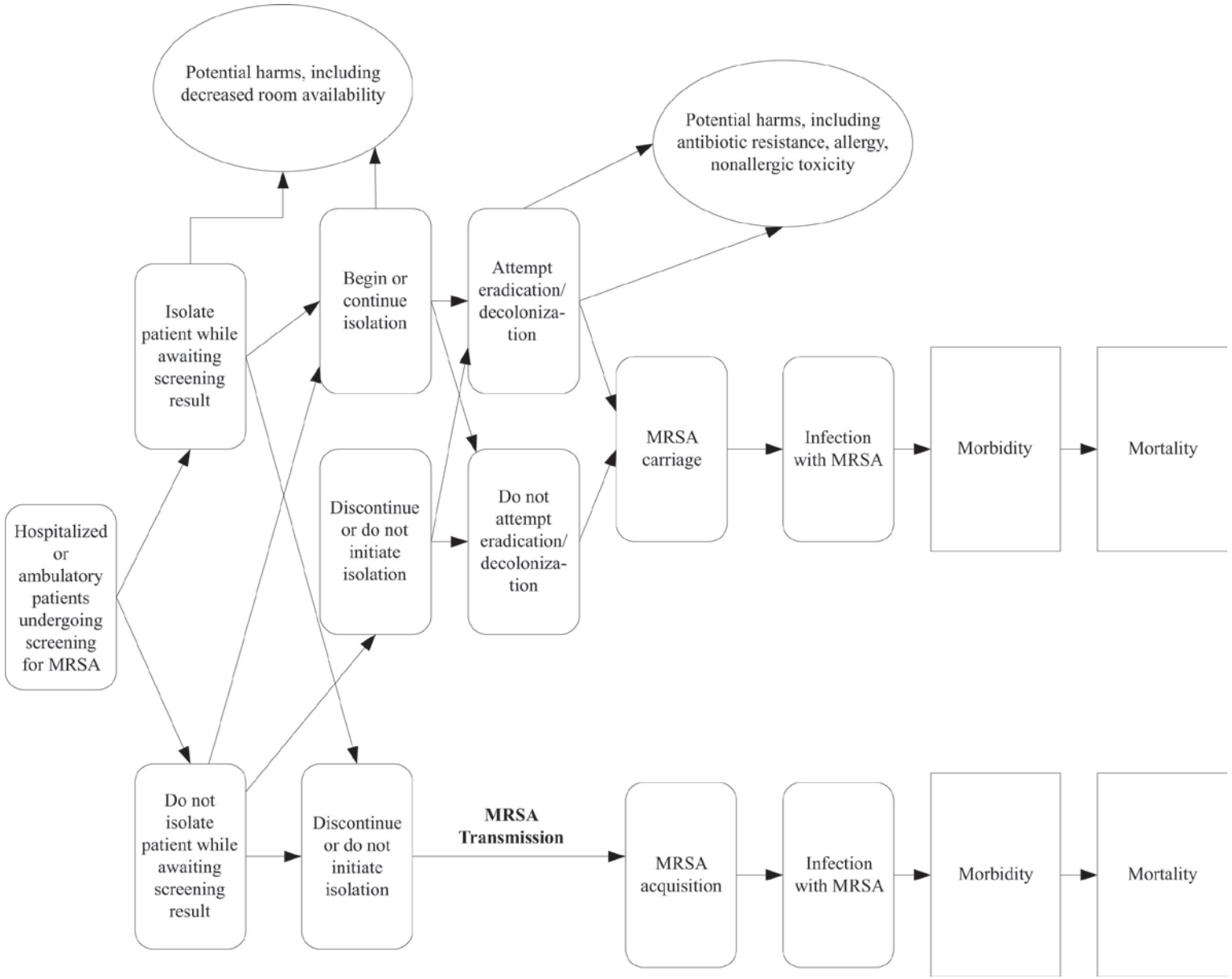
The analytic framework (Figure A) depicts the effects of screening for MRSA carriage on intermediate outcomes (including MRSA acquisition) and health outcomes (including MRSA infection, morbidity, and mortality). The detailed analytic framework (Figure B) depicts the effects of screening for MRSA carriage in detail. Once screened, patients may or may not be

Figure A. Analytic framework for MRSA screening



KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*

Figure B. Detailed analytic framework for MRSA screening



MRSA = methicillin-resistant *Staphylococcus aureus*

isolated while waiting for screening test results. Once the screening test results are received, patients who screen positive may be isolated; patients who screen negative are not. Eradication/decolonization may be attempted in patients who screen positive. Intermediate outcomes of MRSA screening, including MRSA transmission, are depicted in the figure. Health outcomes, including MRSA infection, morbidity, and mortality, are also depicted. Potential harms of screening include decreased room availability, decreased attention from health care personnel, antibiotic resistance, allergic reactions, and nonallergic toxicity.

Methods

Input From Stakeholders

This systematic review was developed by the Evidence-based Practice Center (EPC) with input from stakeholders. Stakeholders were broadly defined as anyone involved with making health care decisions, including patients, clinicians, professional and consumer organizations, and purchasers of health care. Individuals from various stakeholder groups were invited as Key Informants, Technical Experts, and/or Peer Reviewers to guide this systematic review.

Key Informants are end-users of research. A Key Informant panel highlighted the controversies surrounding MRSA screening and the challenges inherent in a review of this topic. The Key Questions were then posted on the Agency for Healthcare Research and Quality (AHRQ) Web site for public commentary. Input from the Key Informants panel and public were incorporated into the scope of the report and the analytic framework (Figures A and B).

The Technical Expert Panel reviewed the research protocol in two phases: (1) initial draft protocol; (2) revised protocol that incorporated the Panel's comments on the draft and findings of a preliminary literature search.

All potential Key Informants, Technical Experts, and Peer Reviewers were required to disclose any potential conflicts of interest in accordance with AHRQ policy. The AHRQ Task Order Officer and the EPC worked to balance, manage, or mitigate any potential conflicts of interest identified. Individuals who had conflicts of interest that precluded participation as informants, experts, or reviewers were able to submit comments through the public comment mechanism. Writing and editing the report were solely the responsibility of the EPC.

Data Sources and Selection

MEDLINE® was searched from January 1, 1990, through March 30, 2012, for randomized and nonrandomized comparative studies. Embase® was searched from January 1, 1990, to March 30, 2012, for randomized controlled trials (RCTs), nonrandomized comparative studies, and case series using similar search terms. The Cochrane Controlled Trials Register was searched without date restriction using the same search terms utilized for the MEDLINE and EMBASE searches. In addition, a search for systematic reviews was conducted in MEDLINE, the Cochrane Database of Systematic Reviews, and the Web sites of the National Institute for Clinical Excellence (United Kingdom), the National Guideline Clearinghouse, and the Health Technology Assessment Programme (United Kingdom). The gray literature was also searched, including databases with regulatory information, clinical trial registries, abstracts and conference papers, grants and federally funded research, and manufacturing information.

The titles and abstracts were screened for studies that looked at MRSA acquisition, MRSA infection, morbidity, mortality, harms of screening, and resource utilization when screening for

MRSA carriage compared with no screening or with limited screening. A single reviewer made the decision about full-text review. Citations marked as uncertain were reviewed by a second reviewer for consideration of full-text review. A third reviewer was consulted if necessary. We included RCTs and nonrandomized comparative studies.

Data Extraction and Quality Assessment

Data were abstracted by a team of reviewers and fact-checked by another reviewer. If there were disagreements, they were resolved through discussion among the review team. Categories of data elements were abstracted as follows: quality assessment (number of participants and flow of participants, treatment allocation methods, blinding, and independent outcome assessment); applicability and clinical diversity assessment (patient, diagnostic, and treatment characteristics); outcome assessment (primary and secondary outcomes, response criteria, followup frequency and duration, data analysis details).

Quality of included studies was assessed using the U.S. Preventive Services Task Force framework[14] based on the following criteria: assembly and maintenance of comparable groups; loss to followup; measurements (equal, reliable, and valid); clear definition of interventions; consideration of all important outcomes; and analysis (adjustment for potential confounders and intention-to-treat analysis). Three quality categories were used: good, fair, and poor. Quality of the abstracted studies was assessed by at least two independent reviewers, and the final quality rating was assigned by consensus adjudication.

Assessment of individual study quality was greatly informed by whether studies attempted to control for confounding and/or secular trends. Studies that used such analytic techniques are described as CCS studies, while those that did not are called non-CCS studies. Non-CCS studies used simple two-group statistical analyses. Observational studies that do not attempt to control for confounding and/or secular trends do not provide evidence that supports causal inference. The ratings of good, fair, and poor quality are reserved for CCS studies. Comments will be made in the main body of the report about results from non-CCS studies, but they are not included in strength of evidence (SOE) syntheses.

Data Synthesis and Analysis

Evidence was not suitable for quantitative synthesis via meta-analysis; therefore, a qualitative approach to synthesis was pursued.

The overall SOE grade was determined in compliance with the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews"[15] and is based on a system developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[16] This system explicitly addressed the following domains: risk of bias, consistency, directness, and precision. The grade of evidence strength was classified into the following four categories: high, moderate, low, and insufficient. Specific outcomes and comparisons were rated depending on the evidence found in the literature. The starting level of strength for a body of evidence differed according to whether it included RCTs or only observational evidence. Bodies of evidence from RCTs would start at high. If evidence was purely observational, the starting level of evidence would be low. However, high risk of bias due to study limitations or publication bias, or lack of consistency, precision, or directness may further decrease the SOE. If observational studies reported large effect sizes, presence of a dose-response association, or plausible confounding that would reduce the observed effect, the SOE could be raised. The grade

rating was made by independent reviewers, and disagreements were resolved by consensus adjudication.

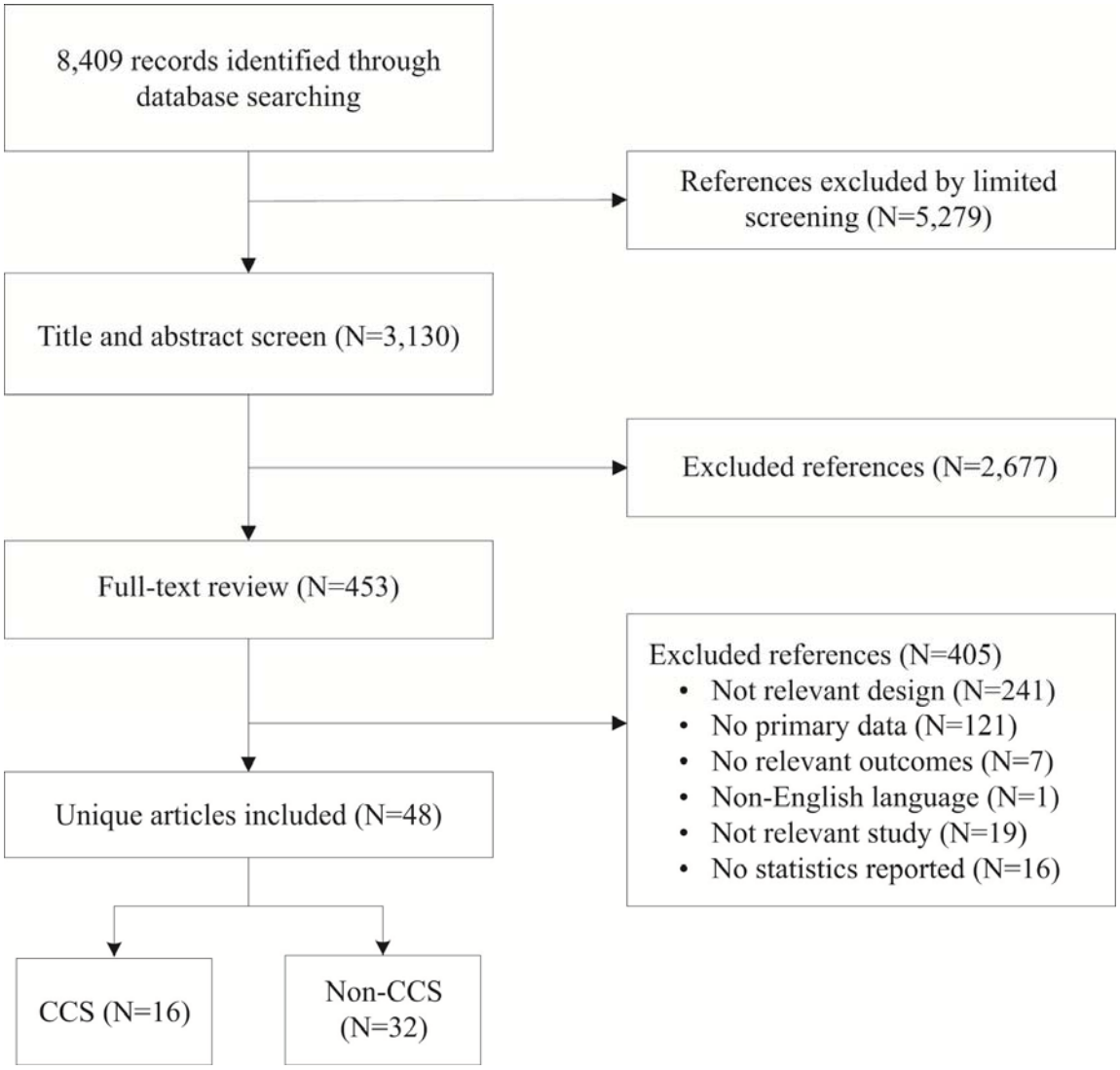
Results

Overview

Overall, 48 studies were abstracted for this review. (The complete list of references may be found in the full report.) Three studies reported outcomes that addressed Key Question 1, 2 studies reported outcomes that addressed Key Question 2, 14 studies reported outcomes that addressed Key Question 3A, 18 studies reported outcomes that addressed Key Question 3B, 8 studies reported outcomes that addressed Key Question 3C, and 10 studies reported outcomes that addressed Key Question 4. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is expected to impact healthcare-associated MRSA transmission and infection most proximately.

The 16 CCS studies[17-32] had the potential to support causal inferences about the impact of MRSA screening on health outcomes and therefore to contribute to the SOE analysis. Because screening for MRSA carriage in the hospital or ambulatory settings is expected to affect healthcare-associated MRSA acquisition, infection, morbidity, and mortality most proximately, healthcare-associated outcomes are the outcomes of interest. The 14 CCS studies[17,18,20,21,23-32] that reported a healthcare-associated outcome were included in the SOE analysis across all four Key Questions (Table A). Two of the CCS studies[19,22] did not report an outcome that was exclusively healthcare associated and therefore were excluded from the SOE analysis. The remaining 32 non-CCS studies performed simple two-group statistical analyses, which cannot support causal inferences; the non-CCS studies were therefore excluded from the SOE syntheses. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram (Figure C) depicts the flow of search screening and study selection.

Figure C. PRISMA diagram for identified published literature



CCS = studies controlling for confounding and/or secular trend; non-CCS = studies not controlling for confounding and/or secular trend; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Key Question 1: Universal Screening for MRSA Carriage Compared With No Screening

Three quasi-experimental CCS studies[17-19] described universal screening for MRSA carriage compared with no screening. The Robicsek et al. study[17] was judged to be of good quality; the Jain et al. study[18] and the Reilly et al. study[19] were judged to be of poor quality. However, the Reilly study did not contribute to the SOE assessment because it did not report an outcome that was exclusively healthcare associated.

Healthcare-Associated MRSA Acquisition

Only the Jain study[18] addressed this outcome. This study showed a statistically significant reduction in healthcare-associated MRSA acquisition in the ICU and non-ICU settings with

universal screening for MRSA. The risk of bias was judged to be high, as only one poor-quality observational study addressed this outcome. Because only one study[18] evaluated this outcome, the consistency was unknown. The outcome was indirect and findings were precise. Because the evidence base that addressed this outcome consisted of a single observational study, the starting level of SOE was low. SOE was lowered one level based on the high risk of bias. Therefore, the SOE that universal screening for MRSA carriage decreases healthcare-associated MRSA acquisition compared with no screening is insufficient.

Healthcare-Associated MRSA Infection

Both the Robicsek study[17] and the Jain study[18] addressed this outcome. Both studies found a statistically significant reduction in healthcare-associated MRSA infection with universal screening for MRSA compared with no screening, ranging from a reduction of 45 percent to 70 percent. Because the evidence base that addressed this outcome consisted of two quasi-experimental studies, the starting level for the SOE was low. The results were consistent, the outcome was direct, and the findings were precise. SOE was raised by one level based on the large effect size but lowered one level based on the high risk of bias. Therefore, the SOE that universal screening for MRSA carriage decreases healthcare-associated MRSA infection compared with no screening is low.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE is insufficient to assess the effect of universal screening for MRSA carriage compared with no screening on morbidity, mortality, harms, or resource utilization.

Key Question 2: Universal Screening for MRSA Carriage Compared With Screening of Selected Populations (Targeted Screening)

Two quasi-experimental CCS studies of good quality compared universal screening for MRSA carriage on hospital admission to screening of selected patient populations (targeted screening).[17,20]

Table A. Summary of outcome measures and strength of evidence

Key Question	Outcome	# of CCS Studies	Reference	Risk of Bias	Consistency	Directness	Precision	Overall Grade
KQ 1. Universal screening vs. no screening	MRSA acquisition	1 QEX	Jain, 2011[18]	High	Unknown	Indirect	Precise	Insufficient
	MRSA infection	2 QEX	Robicsek, 2008[17] Jain, 2011[18]	High	Consistent	Direct	Precise	Low SOE that MRSA screening is associated with lower rates of MRSA infection (Robicsek: -69.6%; 95% CI, -89.2 to -19.6%; Jain: -62% in ICU and -45% in non-ICU; both p<0.001)
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient
KQ 2. Universal screening vs. targeted screening	MRSA acquisition	0	No studies	NA	NA	NA	NA	Insufficient
	MRSA infection	2 QEX	Robicsek, 2008[17] Leonhardt, 2011[20]	Medium	Consistent	Direct	Imprecise	Insufficient
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient

Table A. Summary of outcome measures and strength of evidence (continued)

Key Question	Outcome	# of CCS Studies	Reference	Risk of Bias	Consistency	Directness	Precision	Overall Grade
KQ 3A. Screening of ICU at-risk patients vs. no screening	MRSA acquisition	1 RCT	Huskins, 2011[24]	Low	Inconsistent	Indirect	Imprecise	Insufficient
		3 QEX	Holzmann-Pazgal, 2011[23] Huang, 2006[21] Raineri, 2007[25]					
	MRSA infection	2 QEX	Robicsek, 2008[17] Muder, 2008[26]	High	Consistent	Direct	Imprecise	Insufficient
	MRSA bacteremia or bloodstream infection	2 QEX	Robicsek, 2008[17] Huang, 2006[21]	High	Consistent	Direct	Imprecise	Insufficient
	MRSA surgical site infection	1 QEX	Robicsek, 2008[17]	High	Unknown	Direct	Imprecise	Insufficient
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient
KQ 3B. Screening of surgical patients vs. no screening	MRSA acquisition	1 QEX-XR	Harbarth, 2008[27]	High	Inconsistent	Indirect	Imprecise	Insufficient
		1 QEX	Ellingson, 2011[28]					
	MRSA infection	1 QEX-XR	Harbarth, 2008[27]	High	Inconsistent	Direct	Imprecise	Insufficient
		1 QEX	Muder, 2008[26]					
	MRSA surgical site infection	1 QEX-XR	Harbarth, 2008[27]	High	Unknown	Direct	Imprecise	Insufficient
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient

Table A. Summary of outcome measures and strength of evidence (continued)

Key Question	Outcome	# of CCS Studies	Reference	Risk of Bias	Consistency	Directness	Precision	Overall Grade
KQ 3C. Screening of high-risk patients vs. no screening	MRSA acquisition	1 QEX	Rodriguez-Bano, 2010[31]	High	Unknown	Indirect	Imprecise	Insufficient
	MRSA infection	1 QEX	Harbarth, 2000[30]	High	Unknown	Direct	Precise	Insufficient
	MRSA bacteremia or bloodstream infection	2 QEX	Rodriguez-Bano, 2010[31] Chowers, 2009[29]	High	Consistent	Direct	Precise	Insufficient
	MRSA surgical site infection	1 QEX	Harbarth, 2000[30]	High	Unknown	Direct	Precise	Insufficient
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient
KQ 4. Expanded screening vs. limited screening	MRSA acquisition	2 QEX	Rodriguez-Bano, 2010[31] Ellingson, 2011[28]	High	Consistent	Indirect	Imprecise	Insufficient
	MRSA infection	1 QEX	Chaberny, 2008[32]	High	Unknown	Direct	Precise	Insufficient
	MRSA bacteremia	1 QEX	Rodriguez-Bano, 2010[31]	High	Unknown	Direct	Imprecise	Insufficient
	Morbidity, mortality, harms, resource utilization	0	No studies	NA	NA	NA	NA	Insufficient

CCS = studies that controlled for confounding and/or trend; CI = confidence interval; ICU = intensive care unit; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable; QEX = quasi-experimental; RCT = randomized controlled trial; SOE = strength of evidence; XR = crossover

Healthcare-Associated MRSA Acquisition

No studies addressed this outcome. Therefore, the SOE to evaluate the effect of universal screening for MRSA carriage compared with targeted screening on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection

Two quasi-experimental CCS studies found a reduction in healthcare-associated MRSA infection. Robicsek et al.[17] found that the rate of hospital-acquired MRSA infection declined by 52.4 percent (CI, 9.3 to 78.3%) in the universal screening group, while Leonhardt et al.[20] showed a 0.12-percent reduction in hospital-acquired infection with universal screening compared with targeted screening (p=0.23; difference in difference p=0.34). The risk of bias was judged to be medium, as two good-quality observational studies addressed this outcome.[17,20] The results were consistent, the outcome was direct, and the findings were imprecise. Because the evidence base for this outcome consisted of two observational studies, the starting level for the SOE was low. SOE was lowered by one level based on the medium risk of bias and by one level based on the imprecise results and is therefore insufficient. In summary, the SOE for change in healthcare-associated MRSA infection with universal screening compared with targeted screening for MRSA carriage is insufficient.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of universal screening for MRSA carriage compared with targeted screening on morbidity, mortality, harms, or resource utilization is judged to be insufficient.

Key Question 3A: MRSA Targeted Screening (ICU) Versus No Screening

Seven CCS studies[17,21-26] (one cluster RCT, six quasi-experimental studies) reported outcomes that addressed Key Question 3A, screening of ICU patients for MRSA carriage compared with no screening. The Huskins et al. study[24] was a good-quality cluster RCT. Of the six quasi-experimental studies, one was good quality,[17] one was fair quality,[22] and four were poor quality.[21,23,25,26] However, the fair-quality study[22] did not contribute to the SOE assessment because it did not report an outcome that was exclusively healthcare associated.

Healthcare-Associated MRSA Acquisition

Four CCS studies[21,23-25] (one cluster RCT, three quasi-experimental studies) evaluated this outcome. Although the three quasi-experimental studies[21,23,25] found statistically significant reductions in healthcare-associated colonization or infection, the good-quality cluster RCT[24] found a nonstatistically significant increase in healthcare-associated MRSA colonization or infection with targeted screening. Thus, the results were inconsistent. The outcome was indirect and the findings were imprecise. The evidence base included an RCT of good quality, so the starting level for the SOE was high. However, due to serious concerns about the lack of consistency, the SOE was reduced by two levels. The SOE was further reduced by one level due to lack of precision. In summary, the SOE to evaluate the effect of screening of ICU patients for MRSA carriage on MRSA acquisition is insufficient and lacks precision.

We conducted a sensitivity analysis in which we excluded the cluster RCT[24] from the SOE analysis because of criticisms of the lengthy turnaround time of its screening test and the failure to implement contact precautions and/or isolation while awaiting test results.[33,34] The three remaining quasi-experimental studies were of poor quality to address this outcome, which would still lead to insufficient SOE to evaluate the effect of screening of ICU patients for MRSA carriage on MRSA acquisition.

Healthcare-Associated MRSA Infection, Irrespective of Site

Two quasi-experimental CCS studies[17,26] (one good quality,[17] one poor quality[26]) evaluated this outcome. Both studies found a reduction in healthcare-associated MRSA infection with screening of ICU patients for MRSA carriage compared with no screening, although one of the studies did not find the difference to be statistically significant.[17] The risk of bias was judged as high, as the body of evidence that evaluated this outcome included only quasi-experimental studies, only one of which was of good quality. The results were consistent, the outcome was direct, and the findings were imprecise. Because the evidence base for this outcome includes only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias and the lack of precision. In summary, the SOE is insufficient to support or refute the statement that, compared with no screening, screening for MRSA carriage in ICU patients decreases healthcare-associated MRSA infection.

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

Two quasi-experimental CCS studies[17,21] evaluated this outcome. One good-quality study[17] found a reduction in the rate of acquired MRSA bloodstream infection with screening for MRSA in the ICU compared with no screening (absolute change in prevalence density, -0.15; 95% CI, -1.14 to 0.85); however, this reduction was not statistically significant. One poor-quality study[21] found a statistically significant reduction in the trend of incidence density of hospital-associated MRSA bloodstream infection in the ICU, non-ICU settings, and hospitalwide with screening for MRSA in the ICU. In addition, this study[21] found a statistically significant reduction in the trend of incidence of hospital-associated MRSA bloodstream infection hospitalwide with screening for MRSA in the ICU. The risk of bias was deemed to be high, as the body of evidence comprised quasi-experimental studies, only one of which was good quality.[17] The results were consistent and the outcome was direct. Because the individual studies did not consistently report statistically significant results, the findings were imprecise. Because the evidence base for this outcome includes only quasi-experimental studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias and the lack of precision. In summary, the SOE is insufficient to support or refute the statement that, compared with no screening, screening for MRSA carriage in ICU patients decreases healthcare-associated MRSA bacteremia or bloodstream infection.

Healthcare-Associated MRSA Surgical Site Infection

One good-quality quasi-experimental CCS study addressed this outcome.[17] It found a nonstatistically significant reduction in hospital-associated SSI with screening in the ICU compared with no screening (rate difference, -0.77; 95% CI, -1.85 to 0.30).[17] The risk of bias was deemed to be high, as the body of evidence consisted of only a single good-quality observational study. The consistency was unknown, the outcome was direct, and the findings were imprecise. Because the evidence base for this outcome included only one observational

study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening of ICU patients on healthcare-associated MRSA SSI is judged to be insufficient.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of screening of ICU patients for MRSA carriage on morbidity, mortality, harms, or resource utilization is judged to be insufficient.

Key Question 3B: MRSA Targeted Screening (Surgical Patients) Versus No Screening

Three CCS studies[26-28] described screening of surgical patients for MRSA compared with no screening. The Harbarth et al. study[27] was a prospective interventional cohort study with crossover design of good quality. The Muder et al. study[26] and the Ellingson et al. study[28] were quasi-experimental before/after studies of poor quality.

Healthcare-Associated MRSA Acquisition

Two CCS studies (one good quality,[27] one poor quality[28]) addressed this outcome. Neither study found statistically significant differences in MRSA acquisition with screening surgical patients (rate ratios from 0.78 to 1.1). With screening of surgical patients, the good-quality study found a nonstatistically significant increase in the rate ratio for MRSA acquisition,[27] while the Ellingson study[28] found nonstatistically significant reductions in the incidence rate ratio as well as in the trend in the incidence of MRSA colonization or infection. The risk of bias was deemed to be high because the body of evidence consisted of quasi-experimental studies, only one of which was good quality. The findings were inconsistent. The outcome was indirect, and the study findings were judged to be imprecise. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias, lack of consistency, and lack of precision. In summary, the SOE for the effect of screening of surgical patients on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection, Irrespective of Site

Two CCS studies (one good quality,[27] one poor quality[26]) reported the effect of screening for MRSA carriage in surgical wards on healthcare-associated infection. The good-quality study[27] found a nonstatistically significant increase in rates of MRSA infection with screening surgical patients (1.11/1,000 patient days vs. 0.91/1,000 patient days). However, the poor-quality study[26] found that MRSA infection steadily declined in the surgical ward (1.56/1,000 patient days pre, 0.63/1,000 patient days post; p=0.003). The risk of bias was judged to be high because the body of evidence that evaluated this outcome included only quasi-experimental studies, only one of which was of good quality.[27] The findings were inconsistent, a direct outcome was measured, and study findings were imprecise. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias, lack of consistency, and lack of precision. In summary, the SOE for the effect of screening for MRSA carriage in surgical patients on healthcare-associated MRSA infection is judged to be insufficient.

MRSA Surgical Site Infection

One good quality CCS study[27] reported on MRSA SSI. With screening in surgical patients, Harbarth and colleagues[27] found a nonstatistically significant increase in MRSA SSI (rate ratio, 1.2; 95% CI, 0.8 to 1.7). The risk of bias was judged to be high because the body of evidence that evaluated this outcome included only a quasi-experimental study.[27] With screening in surgical patients, Harbarth and colleagues[27] found no reduction in MRSA SSI; in fact, the rate was slightly higher, although not statistically significant. The consistency of the findings is unknown, the outcome is direct, and study findings were imprecise. Because the evidence base for this outcome included only one observational study, the starting level for the SOE was low. The SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening for MRSA carriage in surgical patients on MRSA SSI is judged to be insufficient.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of screening of surgical patients for MRSA carriage on morbidity, mortality, harms, or resource utilization is judged to be insufficient.

Key Question 3C: MRSA Targeted Screening (High-Risk Patients) Versus No Screening

Three CCS studies[29-31] described screening of high-risk patients for MRSA carriage compared with no screening. All of the studies employed a quasi-experimental study design and were of poor quality.

Healthcare-Associated MRSA Acquisition

One CCS study[31] evaluated this outcome. This study found a nonstatistically significant decrease in the incidence of MRSA acquisition (-0.065; 95% CI, -0.053 to 0.182). There was a statistically significant reduction in trend in incidence of MRSA acquisition (-0.045; 95% CI, -0.062 to -0.029). The risk of bias for the body of evidence was deemed to be high because only a single poor-quality quasi-experimental study[31] evaluated this outcome. The consistency was unknown, the outcome was indirect, and study findings were imprecise. Because the evidence base for this outcome consisted of only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening of high-risk patients on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection, Irrespective of Site

One[30] CCS study evaluated this outcome. This study showed a statistically significant reduction in healthcare-associated MRSA infection with screening of high-risk patients. The risk of bias for the body of evidence was deemed to be high because only one poor-quality quasi-experimental study addressed this outcome. The consistency was unknown, the outcome was direct, and study findings were precise. Because the evidence base for this outcome consisted of only one quasi-experimental study, the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening of high-risk patients on healthcare-associated MRSA infection is judged to be insufficient.

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

Two CCS studies[29,31] addressed this outcome. Both studies found statistically significant decreases in MRSA bacteremia. The risk of bias for the body of evidence was determined to be high, as two quasi-experimental studies of poor quality addressed this outcome. The study findings were consistent, the outcomes were direct, and study findings were precise. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening for MRSA carriage in high-risk patients compared with no screening on healthcare-associated MRSA bacteremia or bloodstream infection is judged to be insufficient.

MRSA Surgical Site Infection

One CCS study[30] addressed this outcome. The Harbarth[30] study showed a statistically significant reduction in MRSA SSI with screening of high-risk patients compared with no screening. The risk of bias for the body of evidence was deemed to be high because only a single poor-quality quasi-experimental study addressed this outcome. The consistency was unknown, the outcome was direct, and study findings were precise. Because the evidence base for this outcome consisted of only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening of high-risk patients on MRSA SSI is judged to be insufficient.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of screening of high-risk patients for MRSA carriage on morbidity, mortality, harms, or resource utilization is judged to be insufficient.

Key Question 4: Screening of a Broader Patient Population for MRSA Carriage (Expanded Screening) Compared With Screening of a Narrower Patient Population (Limited Screening)

Three CCS studies[28,31,32] described expanded screening for MRSA carriage compared with limited screening. The study by Rodriguez-Bano and colleagues[31] utilized an interrupted time series design, as did the study by Ellingson and colleagues.[28] The study by Chaberny and colleagues[32] utilized a before/after study design. All three studies were determined to be of poor quality.

Healthcare-Associated MRSA Acquisition

Two CCS studies[28,31] evaluated healthcare-associated MRSA infection or colonization. Although both studies found reductions in the incidence and trend of healthcare-associated MRSA colonization or infection with expanded screening, these reductions were not consistently statistically significant. The Rodriguez-Bano study[31] showed reductions in the incidence and trend of healthcare-associated MRSA infection or colonization with expanded screening compared with limited screening (change in trend, 0.047; 95% CI, 0.035 to 0.059; change in incidence, 0.077; 95% CI, -0.012 to 0.165). Although the reduction in trend was statistically significant, the reduction in incidence was not.[31] The Ellingson study[28] showed reductions in the incidence rate ratio for MRSA colonization or infection after the interventions (screening for MRSA carriage in the ICU: incidence rate ratio, 0.913; 95% CI, 0.356 to 2.343; screening for

MRSA carriage in all other acute care units: incidence rate ratio, 0.656; 95% CI, 0.440 to 0.979). The reduction was statistically significant for one intervention but not for the other. In addition, the Ellingson study[28] showed a reduction in the preintervention to postintervention trends (screening for MRSA carriage in the ICU: incidence rate ratio, 0.971; 95% CI, 0.938 to 1.004; screening for MRSA carriage in all other acute care units: incidence rate ratio, 0.998; 95% CI, 0.982 to 1.014).

The risk of bias for the body of evidence was determined to be high, as two quasi-experimental studies[28,31] of poor quality addressed this outcome. The study findings were consistent, the outcome was indirect, and study findings were imprecise. Because the evidence base for this outcome included only quasi-experimental studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of expanded screening for MRSA carriage compared with limited screening on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection, Irrespective of Site

One CCS study[32] addressed this outcome. With expanded screening, Chaberny et al.[32] found a reduction in the incidence density of healthcare-associated MRSA infection (change in level of -0.122; 95% CI, -0.204 to -0.040; p=0.004). In addition, Chaberny et al.[32] found a reduction in the monthly change in incidence density of healthcare-associated MRSA infection (change in slope, -0.008; 95% CI, -0.013 to -0.003; p=0.004). The risk of bias for the body of evidence was determined to be high because only one poor-quality quasi-experimental study addressed this outcome. The consistency was unknown, the outcome was direct, and study findings were precise. Because the evidence base for this outcome consisted of only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of expanded screening for MRSA carriage compared with limited screening on healthcare-associated MRSA infection is judged to be insufficient.

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

One CCS study[31] addressed this outcome. This study reported a reduction in hospital-acquired MRSA bacteremia with expanded screening compared with limited screening, but the CIs included the null (change in incidence: 0.002; 95% CI, -0.022 to 0.026; change in trend: 0.003; 95% CI, 0.000 to 0.006). The risk of bias was judged to be high because only one poor-quality quasi-experimental study addressed this outcome. The consistency was unknown, the outcome was direct, and study findings were imprecise. Because the evidence base for this outcome consisted of only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of expanded screening for MRSA carriage compared with limited screening on healthcare-associated MRSA bacteremia is judged to be insufficient.

Morbidity, Mortality, Harms, and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of expanded screening for MRSA carriage compared with limited screening on morbidity, mortality, harms, or resource utilization is judged to be insufficient.

Discussion

This review found a low strength of evidence to support the effectiveness of universal screening for MRSA carriage compared with no screening in reducing healthcare-associated MRSA infection. However, the available evidence is insufficient to reach a conclusion regarding the effectiveness of screening for MRSA carriage for any of the other comparisons and outcomes of interest evaluated.

The bulk of the available literature on the comparative effectiveness of screening for MRSA carriage consists of quasi-experimental studies, largely observational studies with a before/after study design. The sole cluster RCT[24] in this literature showed no favorable impact of screening, although concerns about the lengthy turnaround time of the screening modality used and the failure to implement barrier precautions, isolation, and/or decolonization while awaiting screening test results limit the applicability of this study's findings.

The use of observational studies to determine causal inference requires protection against bias and confounding through features of design, conduct, or analysis. For example, because the incidence of MRSA infection has been decreasing, studies that utilize a before/after study design without adequately controlling for secular trends are unable to distinguish between an effect due to the intervention and an effect due to the persistence of the secular trend itself. Similarly, because other interventions geared toward patient safety, quality improvement, or prevention of healthcare-associated infections may also decrease the incidence of MRSA infection, as may unmonitored efforts at decolonization/eradication or improvements to the physical plant that increase the availability of private hospital rooms, studies that utilize a before/after design and do not adequately control for these and other similar confounders cannot establish whether the effect seen is due to the intervention or to the confounding variable. Therefore, studies that performed simple statistical tests without adequate attempts to control for confounding and/or secular trends had to be excluded from the SOE analysis.

An important limitation of the available evidence regarding MRSA screening relates to heterogeneity in the nature of the interventions performed. By its nature, MRSA screening itself would not be expected to impact the frequency of subsequent transmission or infection. Rather, clinical outcomes are influenced by the application of additional infection-control interventions in response to the detection of colonization, including more rigorous hand hygiene, barrier precautions, environmental cleaning, and antimicrobial decolonization. That these interventions are often deployed as part of a "bundle" further limit the conclusions that can be drawn about the benefit attributable to screening compared with any other component of the intervention.

Many of the included studies provided insufficient information about the full scope of interventions deployed in conjunction with screening for MRSA carriage, especially those measures implemented in response to the new detection of MRSA colonization. For example, while decolonization for MRSA-positive patients may not have been recommended as part of the screening intervention, most studies did not address whether or not decolonization was specifically prohibited. As a result, the measured effect of the screening strategy may have been influenced by the application of uncontrolled and unmeasured interventions targeting MRSA colonization.

In addition, included studies often failed to examine the potential impact of other concurrent infection-prevention efforts on the measured impact of screening for MRSA carriage. Campaigns to reduce the frequency of vascular device infections, initiatives to improve hand hygiene, and interventions to promote an institutional culture of safety have been shown to influence the

frequency of many healthcare-associated infections, including those caused by MRSA. Therefore, the omission of this factor may be important.

Findings in Relationship to What Is Already Known

At least two previous systematic reviews have evaluated the impact of screening for MRSA carriage. McGinigle et al.[35] concluded that there were significant gaps in the evidence that precluded definitive recommendations about the effectiveness of screening for MRSA carriage. After meta-analysis, Tacconelli et al.[36] found a statistically significant reduction in the risk of MRSA bloodstream infection, but not SSI.

The conclusions of the present report are not substantially different from those reached in the previous systematic reviews, although there are some differences in the interpretation of the findings. In all three reports, the paucity of rigorous well-controlled studies employing uniform or even standardized microbiological and infection-control techniques serves as a critical limitation. The present review includes a much larger set of published studies for assessment. In addition, this Comparative Effectiveness Review utilized a more rigorous standard for assessment of study quality than did the prior reviews.

Guidelines and Public Policy

The 2006 Guidelines for the Management of Multidrug-Resistant Organisms in Healthcare Settings published by the Centers for Disease Control and Prevention (CDC) Healthcare Infection Control Practices Advisory Committee (HICPAC)[37] include active surveillance screening as a recommended control strategy for multidrug-resistant organisms (MDROs), including MRSA. This document recommends that such interventions be implemented when the frequency of MDRO infections has not decreased despite the use of more routine control measures.

The 2003 Society for Healthcare Epidemiology of America (SHEA) Guidelines for Preventing Nosocomial Transmission of Multidrug-Resistant Strains of *Staphylococcus Aureus* and *Enterococcus*[38] recommends that active surveillance cultures and contact precautions be implemented to prevent the spread of epidemiologically significant antibiotic-resistant pathogens. The guidelines further advise that these measures "should be implemented in all types of health care facilities throughout the system."

A subsequent SHEA position paper[39] stepped back from advocating mandatory screening, citing concerns about the importance of institutional risk assessment and possible unintended consequences of mandatory and widespread screening.

Overall, the strength of the available evidence and the findings of this review do not appear to readily support or refute the recommendations adopted by the CDC HICPAC or the SHEA Guidelines.

Applicability

The vast majority of included studies employed a quasi-experimental study design, largely an observational before/after design. The use of historical controls is subject to confounding due to epidemiological trends that contribute to variation in the incidence of infectious diseases over time. Even large studies conducted across multiple geographic sites and clinical settings can be influenced by these secular trends.[18] While such changes over time may reflect statistical variation alone, changes in disease incidence also may be due to outbreaks of infection, deviations and departures from best practice, the widespread dissemination of new prevention

practices, changes in antibiotic prescribing, seasonal influences, or even the application of other interventions that influence transmission or infection. Unless these epidemiologic trends are identified and accounted for, they may influence the perception of the effectiveness of screening for MRSA carriage.

Implications for Clinical and Policy Decisionmaking

Insufficient evidence is currently available to determine the comparative effectiveness of screening for MRSA carriage on MRSA transmission, MRSA infection, morbidity, mortality, harms, or resource utilization for most comparisons addressed in this review. However, compared with no screening, there is low SOE that universal screening for MRSA carriage decreases healthcare-associated MRSA infection. Unfortunately, we do not have a complete understanding of the health consequences to patients of MRSA screening and the resource utilization tradeoffs for institutions. The lack of evidence to compare the tradeoffs associated with various strategies of MRSA screening precludes conclusions that either support or refute the routine implementation of screening for MRSA carriage as part of organizational infection control in all settings.

Limitations of the Comparative Effectiveness Review Process

Determining the scope of the review posed an important challenge. The decision was made to be inclusive in considering the available literature, in which observational studies were overrepresented. In the same vein, contributors to this review were challenged to negotiate a rational and justifiable framework for presenting the many included observational studies. To this end, the decision was made to recognize the importance of the use of statistical methods to attempt to control for confounding and/or secular trends, as studies using these methods have the potential to support causal inferences about the impact of MRSA screening on health outcomes. The Results section highlights these studies, which also contributed to the SOE assessment.

Limitations of the Evidence Base, Research Gaps, and Future Research Opportunities

The available evidence is limited by inconsistency in the definition, application, and measurement of the interventions commonly bundled together with MRSA screening. Future studies that aim to contribute evidence on the benefits of screening for MRSA carriage must take a more controlled approach to the testing strategy utilized (e.g., PCR vs. culture), test turnaround time, management of patients before screening test results are known, transmission prevention strategy (e.g., contact precautions), and use of decolonization therapy. In addition, future research should quantify and account for the potential bias introduced by temporal trends, as well as the influence of concomitant infection prevention strategies and interventions.

Ideally, future studies will compare the effectiveness of screening strategies that employ different interventions, alone and in combination. In essence, this work will entail examining each element of an intervention bundle in order to accurately determine the benefit or harm that can be attributed to it. For example, it is possible that a single component of an intervention (such as the decolonization of patients found through screening to be MRSA positive) may independently produce a significant clinical benefit.

The cluster RCT is increasingly recognized as the optimal design for testing and evaluating the impact of infection-prevention strategies. In this approach, rather than randomizing

individual patients, wards or units are randomized to the intervention or control groups. This approach reduces the bias associated with even large multicenter observational studies. However, cluster RCTs may also face barriers to feasibility due to the large number of institutions needed to achieve balance after randomization. It is also imperative to improve the quality of quasi-experimental studies through: (1) more rigorous study design, (2) controlling for secular trends and confounders, and (3) reporting on the full range of clinically important outcomes.

Precise estimates of the comparative effectiveness of screening for MRSA carriage on morbidity and mortality are lacking. To allow meaningful assessment of these crucial health outcomes, future studies will need to enroll sufficient numbers of patients to be adequately powered to detect any effect. Thus, large multicenter trials will be needed.

Most importantly, to conclusively determine the comparative effectiveness of screening for MRSA carriage, the harms of screening compared with those of not screening or of screening selected patient populations must be clearly delineated. To attempt to measure the favorable impact of screening for MRSA carriage while ignoring its potential risks is to present incomplete and potentially misleading data.

Conclusions

There is low SOE that universal screening of hospital patients decreases MRSA infection. However, there is insufficient evidence on other outcomes of universal MRSA screening, including morbidity, mortality, harms, and resource utilization. There is also insufficient evidence to support or refute the effectiveness of MRSA screening on any outcomes in other settings. The available literature consisted mainly of observational studies with insufficient controls for secular trends and confounding to support causal inference, particularly because other inventions were inconsistently bundled together with MRSA screening. Future research on MRSA screening should use design features and analytic strategies addressing secular trends and confounding. Designs should also permit assessment of effects of specific bundles of screening and infection control interventions and address outcomes, including morbidity, mortality, harms, and resource utilization.

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Introduction

Background and Objectives for the Systematic Review

Methicillin-resistant *Staphylococcus aureus* (MRSA) first emerged as a clinically relevant human pathogen more than 5 decades ago.[1] The virulent bacterium was first detected in hospitals and other health care facilities where vulnerable hosts, frequent exposure to the selective pressure of intensive antimicrobial therapy, and the necessity for invasive procedures (which further compromise host defenses) created a favorable environment for dissemination. MRSA emerged as an important cause of health care–associated infections, particularly central line-associated bloodstream infection, ventilator-associated pneumonia, and surgical site infection (SSI). Despite the adoption of a number of measures to prevent spread, the incidence of MRSA infection at most U.S. hospitals steadily increased for many years[2] but is now decreasing.[3,4] Burton and colleagues found a 49.6 percent decrease in the overall incidence of MRSA central line-associated bloodstream infection in U.S. intensive care units (ICUs) from 1997-2007.[4] In a study of nine U.S. metropolitan areas, Kallen and colleagues[3] found a reduction in the incidence rate of hospital-onset invasive MRSA infections of 9.4 percent per year from 2005-2008 [95% confidence interval (CI): 14.7 to 3.8%; p=0.005]. While the decrease in the incidence of MRSA infection may be due to efforts to screen for MRSA carriage, it may also be due to secular trends (such as efforts to improve patient safety) and to confounders (such as efforts to improve the appropriate use of antibiotics and to decrease healthcare-associated infections in general, including catheter-associated bloodstream infection, ventilator-associated pneumonia and SSI).

Complicating matters, the management of MRSA infections remains a challenge for clinicians. Although not all studies concur, a number of analyses suggest that MRSA infections are associated with increased mortality and cost of care when compared with those due to strains that are susceptible to methicillin. A meta-analysis by Cosgrove and colleagues[5] identified a 2-fold increased risk of death associated with methicillin resistance. Engemann and colleagues[6] documented a significantly higher risk of poor outcomes and increased cost of managing patients with SSI due to MRSA when compared with patients infected with antibiotic-susceptible strains. Even the availability of newer pharmaceutical agents with specific activity against MRSA, including linezolid and daptomycin, has not lessened the challenge of caring for MRSA patients. The widespread use of these agents has been limited in part because of toxicity, cost, and uncertainty as to optimal indications.[7]

The management and control of MRSA has been further complicated by dramatic changes in the epidemiology of transmission and infection observed over the past 2 decades. Specifically, *S. aureus* strains resistant to methicillin, once exclusively linked to hospital care, have increasingly been detected among patients in the community who lack conventional risk factors for MRSA infection (such as prior antimicrobial therapy or invasive procedures).[8,9] These so-called community-associated MRSA (CA-MRSA) strains have demonstrated a predilection to affect specific populations. Clusters among schoolchildren and competitive athletes have been extensively described in both the scientific literature and the mass media.[7,10] CA-MRSA infection often manifests in characteristic clinical patterns—including aggressive skin and soft tissue infections (typically arising from an initial lesion often mistaken by patients and clinicians for a spider bite) and necrotizing pneumonia.[11] Extensive investigation has demonstrated a number of unique genetic and pathogenic features of CA-MRSA isolates that may provide insight into the epidemiology of these bacteria. CA-MRSA strains typically share a distinctive methicillin-resistance cassette that helps to explain the characteristic susceptibility of these

strains to non–beta-lactam antimicrobial agents such as clindamycin and trimethoprim/sulfamethoxazole.[12] In addition, CA-MRSA isolates commonly overexpress a particular set of virulence factors, including the Panton-Valentine leukocidin.[13] While the specific relationship between these features and the unique clinical and epidemiological characteristics of CA-MRSA remain to be elucidated, the importance of these strains continues to grow. CA-MRSA has increasingly been linked to outbreaks of infection in hospitals and health care facilities, and there is some evidence that these strains are now the dominant cause of staphylococcal disease in some settings.[14]

Strategies for the control of MRSA (whether health care or community-associated) have focused on the prevention of spread from patient to patient (horizontal transmission) as well as on the prevention of healthcare-associated infections more generally (e.g., catheter-associated blood stream infections and SSIs). It is generally acknowledged that environmental contamination and airborne transmission could plausibly play a minor role in transmission.[15,16] However, the majority of staphylococcal spread (and of MRSA) likely comes through a chain of transmission linking a colonized or infected patient and a previously unaffected patient by way of the hands or personal items of health-care workers. With this in mind, the most common tools used to prevent the spread of MRSA involve the disruption of these points of contact.

The effectiveness of hand hygiene in preventing the spread of MRSA has been demonstrated in quasi-experimental observational studies in which hand hygiene-promotion campaigns were associated with subsequent reductions in the incidence of MRSA among hospitalized patients. Pittet and colleagues[17] demonstrated a significant reduction in MRSA bloodstream infections in one robust investigation. The benefit of hand hygiene appears to be consistent, whether the use of soap and water or alcohol-based hand rubs is promoted.[18] The ease of adherence associated with the latter method suggests that this approach may be especially fruitful.

While hand hygiene remains important in the MRSA transmission-control efforts, the continued spread of the pathogen after initial introduction in most facilities has prompted efforts to identify more robust and effective strategies. The use of personal protective equipment—including the donning of gowns and gloves when interacting with patients colonized or infected with MRSA and the assignment of such patients to single rooms or to a room with a group of affected patients—has been widely promoted and adopted. Such isolation precautions now stand as the centerpiece in most authoritative guidelines regarding MRSA control.[19] Despite the broad consensus associated with the use of personal protective equipment for MRSA prevention, the specific evidence in support of this practice remains somewhat limited and indirect. Jernigan and colleagues[20] noted a significant decrease in the risk of MRSA transmission when isolation precautions were implemented in a pediatric unit. However, the fact that the study was conducted in the midst of a MRSA outbreak in the unit raises questions about the suitability of generalizing these findings to other circumstances, including settings in which MRSA is endemic. Moreover, a number of studies have examined the role of specific elements of isolation precautions (specifically, the use of gowns vs. gloves) with mixed results.[21]

Given the dissemination of MRSA at most U.S. hospitals despite these measures, it is clear that hand hygiene, barrier precautions and isolation, as presently deployed, have been insufficient to check the spread of MRSA and other antibiotic-resistant pathogens. Much of the blame for this underperformance can likely be attributed to the poor adoption of these measures at most health care facilities. When rigorously assessed, adherence to hand hygiene standards is especially disappointing; many hospitals report a compliance rate of less than 50 percent among health care workers. The situation with personal protective equipment use and adherence to

isolation precautions is difficult to assess, as compliance has been less commonly studied and reported. However, a recent report[22] found that despite the use of an electronic flag denoting the need for isolation precautions in the records of inpatients at an urban academic medical center, only 58 percent of such patients were placed in a private room and had appropriate signage posted on the door to the room. Other analyses of actual compliance with the donning of gowns and gloves have been similarly disappointing.

A further important limitation of these approaches—and specifically the use of isolation precautions—relates to the potential negative consequences of these measures. A series of studies have associated isolation precautions with worsened outcomes in terms of safety and patient satisfaction.[23] In addition, questions have been raised about specific performance measures, such as the frequency with which patients on isolation precautions are visited by treating physicians and the timely recording of vital signs. While the methodology employed in some of these studies has been questioned, no rigorous definitive analysis has been completed to exonerate isolation precautions.[24]

Based on the failure of conventional control strategies (hand hygiene, barrier precautions and isolation) to adequately control MRSA, more aggressive measures have been promoted in an effort to check the spread of this particularly virulent pathogen. In some European countries, an aggressive containment program colorfully referred to as "search and destroy," identifies contacts of colonized and infected patients in an effort to intercede to prevent dissemination.[25] While such measures have not been widely adopted in most settings, some clinicians, scientists, and increasing numbers of public advocates and legislators have raised the call for more intensive efforts at MRSA control in the U.S. Particular attention has been given to the potential value of active surveillance screening for MRSA. Because routine clinical cultures may identify as few as 18 percent of patients with asymptomatic carriage of antibiotic-resistant organisms such as MRSA, there exists a large reservoir of patients who are silent carriers of these organisms. These individuals may serve as a reservoir for further transmission. With active surveillance, microbiological samples are obtained from at-risk patients even in the absence of signs or symptoms of infection in an effort to identify the underlying population of colonized individuals. In most cases, this involves the collection of a nasal swab, as the nares have been identified as a common sanctuary site for MRSA in colonized individuals. At some centers, additional sites may be sampled, depending on the population under examination (e.g., the umbilicus of newborns; the sites of invasive devices or wounds). By detecting the larger population of colonized individuals, at the very least conventional precautions can be implemented in a broader and a more timely manner so as to interrupt horizontal transmission of MRSA. Detection of colonized patients also permits consideration of more aggressive interventions, including attempts at microbiological eradication or decolonization in order to prevent colonized individuals from becoming infected, as is discussed later.

The specific evidence in support of active surveillance for MRSA has been promising, although a number of questions remain regarding the suitability of this approach in some settings and populations. Some of the evidence for the effectiveness of active surveillance in controlling the spread of antibiotic-resistant organisms came from experience with vancomycin-resistant *Enterococcus* (VRE). In quasi-experimental studies, rectal screening for this pathogen was associated with decreased transmission at the level of individual units and wards,[26] whole hospitals,[27] and even across an entire region.[28] For MRSA, a number of studies have tested the hypothesis that identification of asymptomatic carriers can result in decreased MRSA transmission. Huang and colleagues[29] reported their experience of adding active surveillance

screening of patients in the ICU to an already comprehensive control strategy (including hand hygiene promotion) and a bundle of interventions to prevent central line-associated bloodstream infection. Only the addition of active surveillance resulted in a statistically significant decline in the incidence of MRSA bloodstream infections.[29] In perhaps the most widely cited report of active surveillance for MRSA, Robicsek and colleagues[30] described the impact of a staged implementation of screening, first among patients in an ICU and ultimately involving all patients admitted to a three-hospital health care system in the Chicago suburbs. With this approach, the prevalence and density of MRSA disease fell significantly among all patients. However, this is not to say that the experience with active surveillance has been universally effective. Harbarth and colleagues[31] found that active surveillance screening of surgical patients was not associated with a reduction in SSIs in a crossover-design study at a large Swiss center. Thus, questions remain not only about the effectiveness of active surveillance for MRSA carriage, but also about whether screening should be applied to all patient populations (universal screening) or to selected populations, such as patients in the ICU or those undergoing surgical procedures (targeted screening).

A number of methodological issues have been raised about many of the studies of active MRSA surveillance, including both those that support the practice and those that do not. These questions also reflect the methodological uncertainty about deploying the strategy in actual clinical practice. One key issue relates to the microbiological testing method applied. Early on, most surveillance programs relied on conventional culture methods. This approach, while reliable and familiar in the hands of most clinical laboratories, is plagued by the delayed availability of final results, in as much as culturing, subculturing, and formal susceptibility testing can require up to 5 to 6 days in some laboratories. Advances in culture methodology, including the use of chromogenic growth media, can shorten this waiting period, but still do not typically provide clinicians with information regarding the need for isolation precautions until a day or more after the samples are collected. Most recently, the advent of reliable and commercially available polymerase chain reaction (PCR) techniques offer the promise of rapid turnaround time for MRSA detection (often less than several hours). Farr has argued that without standardization and optimization to ensure rapid results from screening, comparisons regarding the relative effectiveness of active surveillance for MRSA are limited.[32] Some of the concerns about delayed screening results can be obviated by adopting a policy of early implementation of isolation precautions for all screened patients with the aim to discontinue these measures for those patients who test negative (irrespective of the assay employed). This so-called “guilty until proven innocent” approach, while sound from an epidemiological perspective, has presented logistical challenges at centers where the physical plant limits the availability of rooms and beds for such empirical isolation.

Determining the optimal approach once patients are identified as colonized with MRSA presents an even larger challenge to assessing the effectiveness of active MRSA surveillance. The impact of screening is likely to be exceptionally sensitive to the measures deployed once MRSA carriers are identified. As has been noted, adherence to basic prevention measures, such as hand hygiene and the use of personal protective equipment, is inconsistent in most settings in which compliance has been measured. Nonetheless, these very practices are considered central to the effectiveness of any active surveillance program. Simply stated, knowing which patients are colonized with MRSA should not be expected to affect the frequency of spread if adherence to transmission-control strategies remains inadequate. Surprisingly, even the most robust investigations of the effectiveness of active surveillance have not routinely described the

frequency of compliance with hand hygiene and use of personal protective equipment. Similarly, other more intensive measures may dramatically affect the impact of a MRSA-screening program. For example, efforts to decolonize or eradicate MRSA from carrier patients through the use of systemic or topical antimicrobial agents should have an important effect on the likelihood of transmission. This practice has been applied in a number of settings for both MRSA and staphylococcal disease in general.[33] The results have been mixed, depending on the population under study, and the risk for emerging antibiotic resistance as the result of such efforts remains a concern. With this in mind, to try to determine the impact of a screening program without detailed information about the deployment of decolonization measures is an important limitation to the available studies and has engendered considerable confusion among clinicians and policymakers.

In light of the promising, but limited, evidence in support of active MRSA surveillance and in consideration of the important methodological questions previously noted, a systematic review of the evidence appears to be both justified and timely. The importance of gaining a better understanding of the evidence is further highlighted by the increasing demand for better control of MRSA and a higher standard for prevention of hospital-acquired infections in general. Policymakers both within and outside of the U.S. health care system have heeded public concern surrounding these issues. The control of MRSA and other antibiotic-resistant bacteria has been highlighted as a likely target for pay-for-performance initiatives on the part of the U.S. Government and a number of private payers. The Joint Commission has highlighted the issue by identifying a National Patient Safety Goal regarding the control and prevention of antibiotic resistance. Perhaps most telling, some state jurisdictions in the U.S. have already mandated screening for MRSA. In some cases, these legislative mandates have been issued even in the face of direct opposition from clinical experts in the field.[34] It seems evident that the public and scientific debate regarding the merits and potential negative consequence of widespread MRSA screening will benefit from a systematic review of the available evidence.

Objective

The objective of this systematic review was to synthesize comparative studies that examined the benefits or harms of screening for MRSA carriage in the inpatient or outpatient settings. The review examined MRSA-screening strategies applied to all hospitalized or ambulatory patients (universal screening), as well as screening strategies applied to selected inpatient or outpatient populations (e.g., patients admitted to the ICU, patients admitted for a surgical procedure, or patients at high-risk of MRSA colonization or infection) and compared them to no screening or to screening of selected patient populations (targeted screening). The review evaluated MRSA-screening strategies that included screening with or without isolation and with or without attempted eradication/decolonization. The patient population included all ambulatory patients (outpatients) and hospitalized patients (inpatients).

Key Questions

Key Question 1

Among ambulatory or hospitalized patients, what are the effects of a universal screening strategy for MRSA carriage (screen, isolate, eradicate/decolonize) – when compared to no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

Key Question 2

Among ambulatory or hospitalized patients, what are the effects of a universal screening strategy for MRSA carriage (screen, isolate, eradicate/decolonize) – when compared to screening of selected patient populations (targeted screening) on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

Key Question 3A

Among ambulatory or hospitalized patients, what are the effects of screening ICU patients for MRSA carriage (screen, isolate, eradicate/decolonize) – when compared to no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

Key Question 3B

Among ambulatory or hospitalized patients, what are the effects of screening surgical patients for MRSA carriage (screen, isolate, eradicate/decolonize) – when compared to no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

Key Question 3C

Among ambulatory or hospitalized patients, what are the effects of screening high-risk patients for MRSA carriage (screen, isolate, eradicate/decolonize) – when compared to no screening on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

Key Question 4

Among ambulatory or hospitalized patients, what are the effects of an expanded screening strategy for MRSA carriage (e.g., screen, isolate, eradicate/decolonize a broader group of patients, such as patients admitted to the medical ward, the surgical ward or the ICU) – when compared to a limited screening strategy (e.g., screen, isolate, eradicate/decolonize a limited group of patients, such as patients admitted to the ICU) on:

- Intermediate outcomes such as MRSA transmission (as measured by new acquisition events)?
- Health outcomes such as the incidence of MRSA infection, morbidity (including complications of MRSA infection), mortality, adverse events (including allergic and nonallergic toxicity (e.g., hypotension), antimicrobial resistance, reduced quality of care, and medical errors), and hospital resource utilization such as length of stay?

PICOTS (Population, Intervention, Comparator, Outcome, Timing, and Setting) for the Key Questions

Patients

All ambulatory patients (outpatients) and all hospitalized patients (inpatients). In addition, the following subpopulations were evaluated: (1) patients admitted to an ICU; (2) patients undergoing surgical procedures; and (3) patients at high-risk of MRSA colonization or infection (e.g., patients transferred from another health care facility, patients receiving hemodialysis).

Intervention

A MRSA screening strategy applied to all patients in a setting (universal screening) or applied to particular wards, units or patients (targeted screening) that includes:

- 1. MRSA screening using a testing modality (typically PCR) with rapid turnaround (results available on the same day as the testing is performed) or
- 2. MRSA screening using a testing modality with intermediate turnaround (results available next day to 2 days after testing performed) or
- 3. MRSA screening using a testing modality (typically culture) with a longer turnaround time (results available greater than 2 days after testing performed)

And that may include:

- 1. Isolation and/or
- 2. Eradication/decolonization.

Comparator

No screening or screening of selected patient populations (targeted screening).

Outcomes

Healthcare-associated MRSA acquisition, health-care associated MRSA infection, morbidity (including complications of MRSA infection), mortality, harms including quality of care for noninfectious conditions, medical errors, adverse effects of screening and treatment including allergic reactions, nonallergic toxicities, and resistance to antimicrobials and hospital resource utilization such as length of stay. Outcome measures should specify whether they are exclusively healthcare-associated or whether they include community-associated outcomes. Healthcare-associated outcomes are most important for MRSA screening in the ambulatory and hospital settings.

Timing

Intervention through followup.

Settings

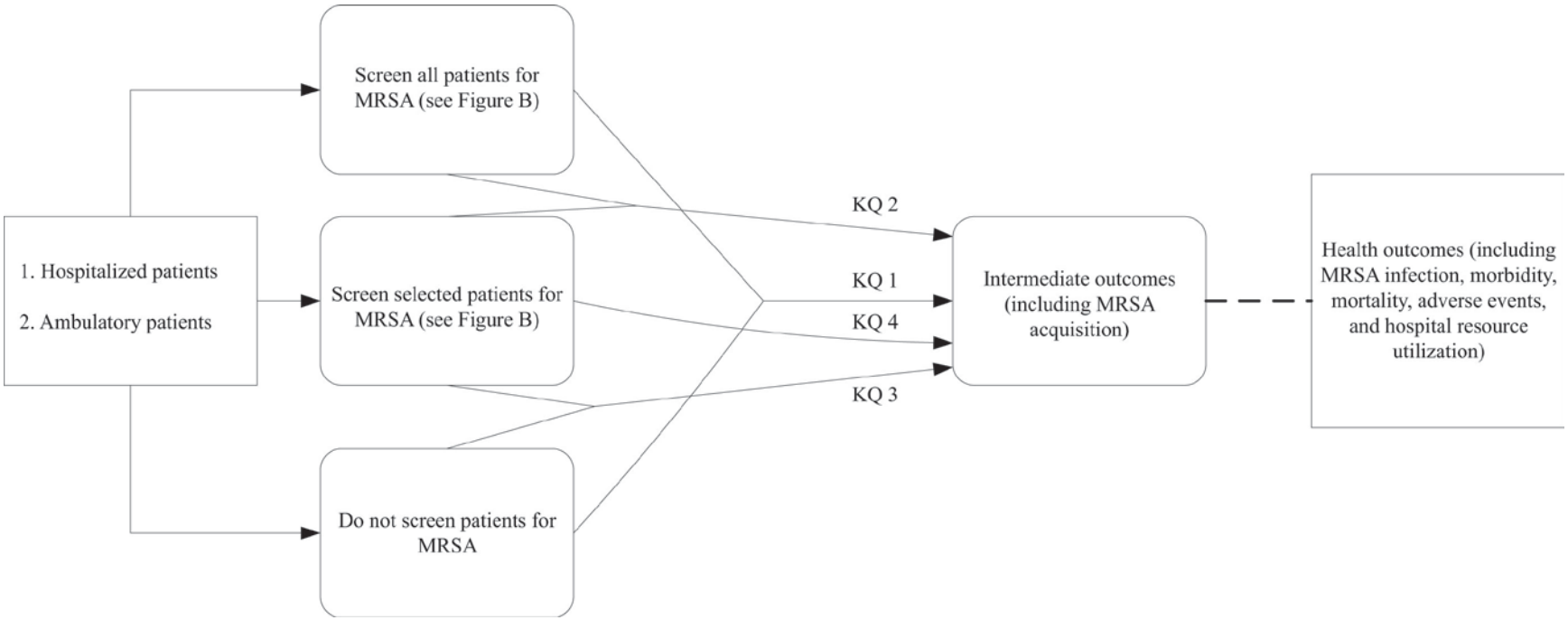
Inpatient (hospital wards and ICUs) and outpatient (ambulatory clinics, urgent care centers and emergency departments).

A comprehensive review evaluating the benefits and harms of screening for MRSA carriage will identify areas of certainty and those that require additional prospective research.

Analytic Framework

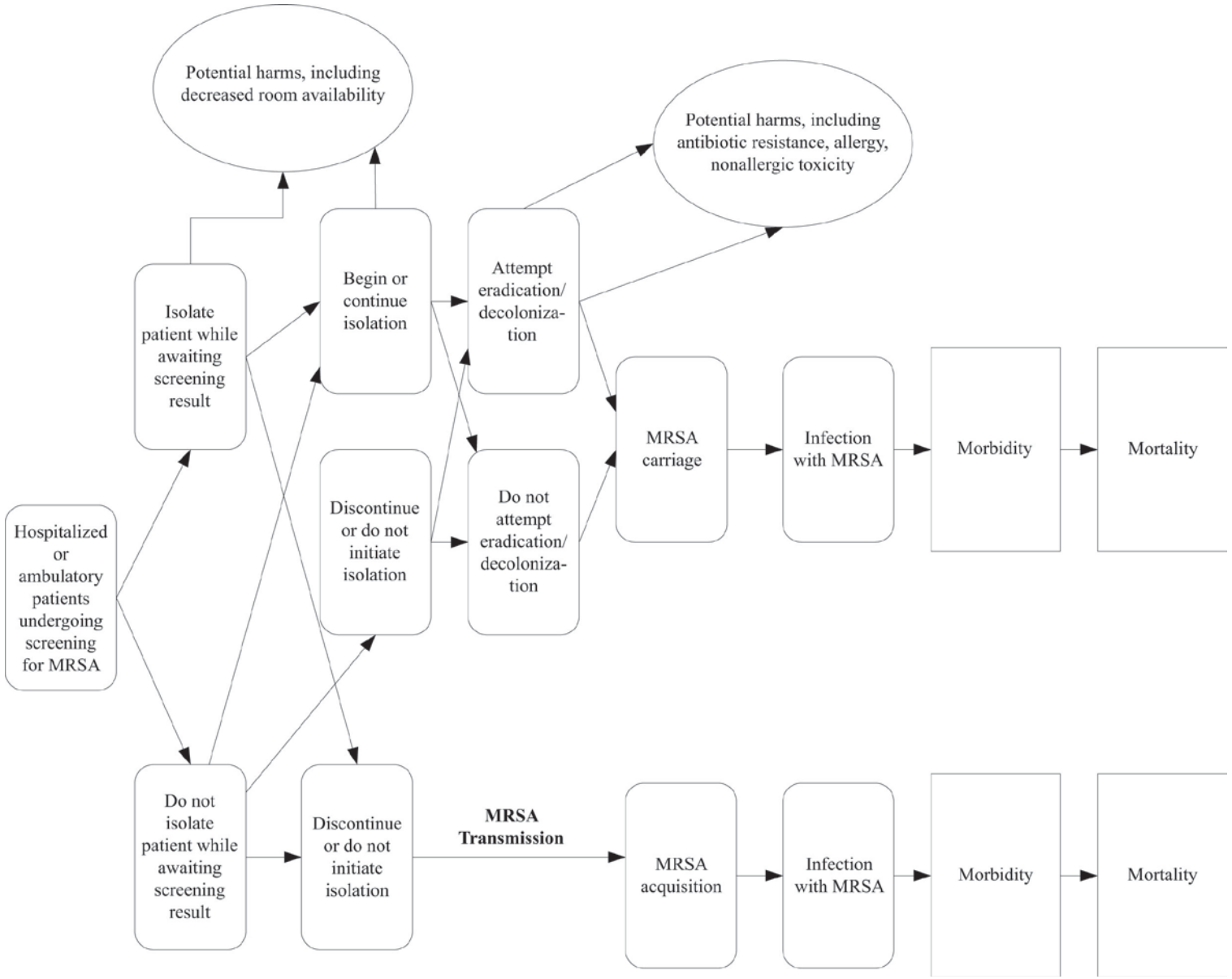
Figure 1 and Figure 2 depict the effects of MRSA screening on intermediate outcomes (including MRSA acquisition) and health outcomes (including infection, morbidity and mortality).

Figure 1. Analytic framework for MRSA screening



KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*

Figure 2. Detailed analytic framework for MRSA screening



KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; Test + = positive MRSA-screening test result; Test – = negative MRSA-screening test result

Methods

Methodological practices followed in this review were derived from the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews"[35] (hereafter referred to as the "Methods Guide") and its subsequent updates.

Topic Development and Refinement

Key questions were reviewed and refined as needed by the Evidence-based Practice Center (EPC) with input from Key Informants and the Technical Expert Panel (TEP) to assure that the questions were specific and explicit about what information was being reviewed. In addition, for Comparative Effectiveness reviews, the Key Questions were posted for public comment and finalized by the EPC after review of the comments.

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform health care decisions. The EPC solicited input from Key Informants when developing questions for systematic review or when identifying high priority research gaps and needed new research. Key Informants were not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Key Informants had to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals were invited to serve as Key Informants and those who presented without potential conflicts were retained. The AHRQ Task Order Officer and the EPC worked to balance, manage, or mitigate any potential conflicts of interest identified.

Literature Search Strategy

The databases listed below were searched for citations. The full search strings and strategies can be found in Appendix A. The search was limited to literature published from 1990 to the present because this is the evidence most applicable to current practice. The search was limited to the English-language literature because in past projects, our EPC has found the inclusion of non-English language literature did not yield sufficient high quality information to justify the resources required for translation.

- MEDLINE® (January 1, 1990, to March 30, 3012)
- Embase® (January 1, 1990, to March 30, 2012)
- Cochrane Controlled Trials Register (to March 2012)

To identify systematic reviews, we searched MEDLINE®, the Cochrane Database of Systematic Reviews, and the Web sites of the National Institute for Clinical Excellence, Guidelines.gov, and the Technology Assessment Programme of the National Health Service. We followed the AHRQ recommendations in its Methods Guide about inclusion of results from previously conducted meta-analyses and systematic reviews.[35] Our search strategy used the National Library of Medicine's Medical Subject Headings (MeSH®) keyword nomenclature developed for MEDLINE® and adapted for use in other databases. The searches were limited to

humans. We searched the Cochrane Controlled Trials Register using the same search teams utilized for the MEDLINE® and EMBASE® searches.

The TEP and individuals and organizations providing peer review were asked to inform the project team of any studies relevant to the Key Questions that were not included in the draft list of selected studies.

We searched indexed, electronically searchable conference abstracts by subject heading for the following conferences from the past 5 years: Interscience Conference on Antimicrobial Agents and Chemotherapy, Infectious Disease Society of America, Society for Healthcare Epidemiology of America, Association of Professionals in Infection Control and Epidemiology, American College of Physicians, Pediatric Infectious Diseases Society, European Society of Clinical Microbiology and Infectious Diseases, International Society of Infectious Diseases, Australasian Society of Infectious Diseases, International Sepsis Forum, and European Society of Intensive Care Medicine.

We reviewed Scientific Information Packets from the Scientific Resource Center and grey literature from the U.S. Food and Drug Administration Web site and ClinicalTrials.gov. We included those studies that have gone through a process equivalent to journal peer review.

In the course of this project, our EPC transitioned from EndNote® or ProCite® databases to use of Distiller SR®. Therefore, search results were initially stored in an EndNote9® database, subsequently transferred to Distiller SR®. In an initial screen of titles and abstracts, study selection criteria were applied by a single reviewer who marked each citation as: (1) eligible for review as a full-text article; 92) ineligible for full-text review; or (3) uncertain. Citations marked as uncertain were reviewed by a second reviewer and resolved by consensus opinion; and when necessary, discordant opinions will be resolved by a third reviewer. Throughout the title/abstract screening and study selection processes, reviewer training and quality control procedures were applied to achieve accuracy. Forms to facilitate title and abstract review were pilot tested during reviewer training.

Inclusion and Exclusion Criteria

We included randomized, controlled trials (RCTs) and nonrandomized, comparative studies (observational, case-control, and cohort studies) of populations, comparisons, interventions, and outcomes that were not adequately studied in controlled trials. We also used observational studies to assess comparative effectiveness in populations not well represented in RCTs. To classify observational study designs, we used the system developed by Briss and colleagues.[36] Studies were included that have these design characteristics and meet descriptions included under Population(s), Interventions, Comparators, Outcomes, Timing and Settings. Additionally, studies were excluded that: (1) did not describe any statistical analysis; or (2) report a relevant outcome only as a frequency without a denominator. Table 1 illustrates application of study selection criteria.

Table 1. Study selection criteria

Topic	Question	Exclude if
Language	Is article published in English?	not English
Publication Type	Does article report primary data?	no primary data (narrative reviews, commentaries, editorials, letters, news reports, etc.)
Species	Are the study participants human?	not human
Setting	Was study conducted among patients in ambulatory care or hospital settings?	if not patients in ambulatory health care or hospital settings (nursing homes); also apply if focus is not patients (e.g. health care workers)
Disease	Was MRSA the primary disease focus?	focus of study does not include or is not primarily centered on MRSA
Design	Was the design a comparison of MRSA screening vs. no screening or one screening method with another screening method?	the study is purely a comparison of culture vs. PCR or the study is not a RCT or QEX comparing either: • screening (by either culture or PCR) vs. no screening or • universal (all patients admitted to a hospital) vs. targeted screening or • more limited targeted screening vs. expanded targeted screening
Outcomes	Did the study report a relevant outcome?	no outcome is reported with a denominator or if one of these outcomes is not reported: • MRSA incidence or prevalence • morbidity • mortality • harms • MRSA acquisition/transmission, or • resource utilization
Statistical Analysis	Did the study report a statistical analysis?	no statistical analysis is reported, also sort into categories: 2-group tests vs. regression or time series analysis

MRSA = methicillin-resistant *Staphylococcus aureus*; PCR = polymerase chain reaction; QEX = quasi-experimental; RCT = randomized controlled trial

Study Selection

Final study selection criteria were applied to full-text articles to determine inclusion in the systematic review in the same manner as applied to title and abstract screening. Records of the reason for exclusion for each paper retrieved in full-text, but excluded from the review (Appendix B), were kept in the EndNote9® and Distiller SR® databases.

Search Strategies for Grey Literature

The EPC staff conducted a systematic search of the following grey literature sources to identify unpublished studies or studies published in journals that were not indexed in major bibliographic citation database in accordance with guidance from Effective Health Care Scientific Resource Center. The search strategies can be found in Appendix A.

1. Regulatory Information
    - U.S. Food and Drug Administration (www.FDA.gov)
2. Clinical Trial Registries
    - ClinicalTrials.gov
    - Current Controlled Trials
    - Clinical Study Results

- World Health Organization Clinical Trials

3. Abstracts and Conference Papers
    - Conference Papers Index
    - Scopus
    - Interscience Conference on Antimicrobial Agents and Chemotherapy
    - The Infectious Disease Society of America
    - The Society for Healthcare Epidemiology of America
    - The Association of Professionals in Infection Control and Epidemiology
    - The American College of Physicians
    - The Pediatric Infectious Diseases Society
    - The European Society of Clinical Microbiology and Infectious Diseases
    - The International Society of Infectious Diseases
    - The Australasian Society of Infectious Diseases
    - The International Sepsis Forum
    - The European Society of Intensive Care Medicine
4. Grants and Federally Funded Research
    - National Institute of Health Research Portfolio Online Reporting Tools (NIH RePORTER) (a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions)
    - Health Services Research Projects in Progress (HSRPROJ) (a database providing access to ongoing grants and contracts in health services research)
    - AHRQ Grants On-Line Database (AHRQ GOLD) (an online searchable database of AHRQ grants, working papers and Department of Health and Human Services recovery act projects)
5. Manufacturer database: Industry stakeholders were invited to submit the following types of information for possible inclusion as evidence:
    - A current product label;
    - Published RCTs and observational studies relevant to the clinical outcomes; and
    - Unpublished RCTs and observational studies relevant to the clinical outcomes.

These sources were searched using sensitive searches similar to the searches in bibliographic databases, except for the following:

- Regulatory information: The FDA website was searched for 510(k) decision summary documents related to devices used for diagnosis of MRSA- Xpert MRSA SA/SSTI®, XPert MRSA SA/BC®, XPert MRSA®, GeneOhm® MRSA assay and BBL ChromAgar MRSA.
- For clinical registries, NIH RePORTER, HSRPROJ, and AHRQ GOLD searches were limited to completed studies only.
- For abstracts and conferences, studies published prior to 2006 were excluded.

Data Extraction and Data Management

Data Elements

Using Distiller SR® software, the following data elements from the intervention studies were abstracted, or recorded as "not reported" (see Appendixes C, D, and E). The data elements to be abstracted were defined in consultation with the TEP and included the following:

- Quality Assessment:
  - Number of participants and flow of participants through steps of study
  - Treatment allocation methods (including concealment)
  - Use of blinding
  - Prospective vs. retrospective
  - Use of independent outcome assessor
- Assessment of Applicability & Clinical Diversity:
  - Patient characteristics, including
    - Age
    - Sex
    - Race/ethnicity
    - Disease and type
    - Disease duration
    - Other prognostic characteristics (e.g., comorbidities and other potential confounders and/or effect modifiers)
    - Setting
      - Outpatient
      - Inpatient
  - Diagnostic and Treatment Characteristics, including
    - Type of assay used to screen for MRSA and its turnaround time
    - Decision-making for diagnosis and/or treatment
    - Antibiotic usage
    - Other treatment modalities
    - Duration of observation
- Outcome Assessment:
  - Identified primary outcome
  - Identified secondary outcomes
  - Response criteria
  - Followup frequency and duration
  - Data analysis details:
    - Statistical analyses (statistical test/estimation results)
      - Test used
      - Summary measures
      - Sample variability measures
      - Precision of estimate
      - p values
    - Regression modeling techniques
    - Model type
    - Candidate predictors and methods for identifying candidates
    - Univariate analysis results

- Selected predictors and methods for selecting predictors
- Testing of assumptions
- Inclusion of interaction terms
- Multivariable model results
- Discrimination or validation methods and results
- Calibration or "goodness-of-fit" results

Evidence Tables

Templates for evidence tables were created in Microsoft Excel® and Microsoft Word® after data were downloaded from Distiller SR®. Forms to facilitate data abstraction were pilot tested during implementation of quality control to achieve accuracy. One reviewer performed primary abstraction of all data elements into the evidence/abstraction tables, and a second reviewer reviewed the articles and evidence tables for accuracy (see Appendix F, Data Abstraction Tables). Disagreements were resolved by discussion, and if necessary, by consultation with a third reviewer. When small differences occurred in quantitative estimates of data from published figures, the values were obtained by averaging the estimates of the two reviewers.

Quality Assessment of Individual Studies

Definition of Ratings Based on Criteria

In adherence with the Methods Guide,[35] the general approach to grading individual comparative studies was that used by the U.S. Preventive Services Task Force.[37] This approach is relevant to both RCTs and nonrandomized comparative interventions studies. Assessment of the quality of included nonrandomized comparative intervention studies by this approach was informed by a selection of items proposed by Deeks et al.,[38] as shown in Appendix G. Assessment of individual study quality was greatly informed by whether studies attempted to control for confounding and/or secular trends. Studies that used such analytic techniques are described as "CCS studies," while those that did not are called "non-CCS" studies. Non-CCS studies used simple two-group statistical analyses. Observational studies that do not attempt to control for confounding and/or secular trends do not provide evidence that supports causal inference and according to U.S. Preventive Services Task Force approach were considered fatally flawed and therefore of poor quality. The quality of the abstracted studies and the body of evidence was assessed by two independent reviewers. Discordant quality assessments were resolved with input from a third reviewer, if necessary.

- The quality of studies was assessed on the basis of the following criteria:
    - Initial assembly of comparable groups: adequate randomization, including concealment and whether potential confounders (e.g., other concomitant care) were distributed equally among groups
    - Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination)
    - Important differential loss to followup or overall high loss to followup
    - Measurements: equal, reliable, and valid (includes masking of outcome assessment)
    - Clear definition of interventions
    - All important outcomes considered

    - Analysis: adjustment for potential confounders, intention-to-treat analysis
- The rating of intervention studies encompasses the three quality categories described here.
    - *Good:* Meets all criteria; comparable groups are assembled initially and maintained throughout the study (followup at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention is given to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.
    - *Fair:* Studies graded as "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: In general, comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with followup; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is done for RCTs.
    - *Poor:* Studies graded as "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study or comparability was not documented; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Non-CCS studies would therefore be fatally flawed, while CCS studies may also be rated as poor. For RCTs, intention-to-treat analysis is lacking.

Appropriate analysis is a key aspect of study quality ratings. Among CCS studies, ratings emphasized whether investigators attempted an appropriate analysis which tested for trend, addressed autocorrelation and adjusted for at least one confounder. Studies that reported baseline group characteristics, considered and analyzed at least one healthcare-associated outcome, and conducted appropriate analysis (tested for trend, addressed autocorrelation, and included at least one confounder in the analysis) were rated "good." Studies that met the criteria for good quality except that they did not report a healthcare-associated outcome were rated "fair." Studies that failed to report baseline group characteristics and/or to conduct appropriate analysis were rated "poor." The Results chapter synthesizes the strength of evidence (SOE) for CCS studies that presented at least one healthcare-associated outcome; but CCS studies that did not report at least one healthcare-associated outcome and non-CCS studies are only commented on in the text, and not included in the SOE syntheses.

Data Synthesis

Because of the heterogeneity of the data, this evidence review did not perform formal data synthesis through meta-analysis. If a meta-analysis could have been performed, subgroup and sensitivity analyses would have been based on assessment of clinical diversity in available studies. Anticipated subgroups included patients at high risk for MRSA, including those with end-stage renal disease and those residing in long-term care facilities. The Methods Guide[35] and the paper by Owens and colleagues[39] were used to rate the strength of the overall body of evidence.

Assessment of Applicability

Applicability of findings in this review was assessed within the EPICOT framework (Evidence, Population, Intervention, Comparison, Outcome, Timestamp). Selected studies were assessed for relevance against target populations, interventions of interest, and outcomes of interest.

Grading the Body of Evidence for Each Key Question

The system used for rating the strength of the overall body of evidence was developed by the AHRQ for its Methods Guide,[35,39] based on a system developed by the Grading of Recommendations Assessment, Development and Evaluation Working Group.[40] This system explicitly addresses the following domains: risk of bias, consistency, directness, and precision. Additional domains such as strength of association, publication bias, coherence, dose-response relationship, and residual confounding were assessed when appropriate.

Table 2 describes criteria for selecting different levels within each of the four required domains.

Table 2. Strength of evidence rating domains

Domain	Level	Criteria
Risk of bias	General	Degree to which studies have high likelihood of protection against bias; derived from assessment of the risk of bias in individual studies; incorporates both study design and conduct; grading this domain requires assessment of aggregate quality of studies within each major study design and integration into overall risk of bias score; limitations of design for reducing bias in addressing a Key Question should be taken into account. If studies differ substantially in risk of bias, may give greater weight to those studies with low risk of bias.
	Low	At least 1 good quality RCT.
	Medium	At least: 1 fair quality RCT; or 1 good quality observational study and 1 additional study of good or fair quality.
	High	Does not meet minimum requirements for low or medium.
Consistency	General	Degree to which studies are similar in effect sizes; degree to which studies have same direction of effect (even in presence of statistical heterogeneity).
	Consistent	Effect sizes have same direction.
	Inconsistent	Effect sizes are in different directions.
	Unknown	Single study evidence base.
Directness	General	A single direct link between intervention and health outcome; intervention and comparator(s) compared head-to-head within a study.
	Direct	Direct head-to-head comparison of interventions within a study or assesses a health outcome.
	Indirect	Not a direct head-to-head comparison of interventions within a study or assesses an intermediate outcome.
Precision	General	Degree of certainty surrounding an effect estimate.
	Precise	Uncertainty around an effect compatible with only one of these: clinically important superiority, inferiority or noninferiority. In absence of meta-analysis, individual studies consistently report precise and/or statistically significant results.
	Imprecise	Uncertainty around an effect compatible with both clinically important superiority and inferiority. In absence of meta-analysis, individual studies do not consistently report precise and/or statistically significant results.

RCT = randomized controlled trial

The grade of evidence strength is classified into four categories as shown in Table 3. Rules for the starting SOE and factors that would raise or lower the strength are also described in the Table 3.

Table 3. Strength of evidence categories and rules

Strength of Evidence/Rules	Criteria
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient	Evidence is either unavailable or does not permit estimation of an effect.
Starting level of strength, RCT evidence	High
Starting level of strength, observational evidence	Low
Raise strength	Among observational studies, raise strength by one level if a large effect size is observed, presence of dose-response association or plausible confounding that would decrease the observed effect. A very large effect size could raise strength by two levels.
Reduce strength	Reduce strength by one level is there is serious concern in an area such as: high risk of bias, inconsistent findings; consistency unknown; evidence is indirect; results are imprecise or presence of publication bias. Very serious concern in an area would reduce strength by two levels.

The process of grading a body of evidence can be illustrated with examples. A body of evidence represented by a single RCT rated as good in quality and multiple poor quality observational studies would have a starting strength of high. The risk of bias domain in this instance would be rated as low. If the RCT and observational studies reported results with opposite directions of effect, an inconsistent pattern for the consistency domain, the strength would be reduced by two levels. Assume that studies perform direct head-to-head comparisons of an intervention and comparator and report on an important health outcome, leading to a rating of direct on the directness domain. In the absence of meta-analysis, the pattern of opposite effect directions would render the aggregate results imprecise on the precision domain, reducing strength by at least one level. The path through all domains would take the strength from moderate through three reductions to a final strength of insufficient.

Another purely observational body of evidence that included one good quality study and multiple poor quality studies would have a starting SOE of low. If the body consists of one good quality study and one poor quality study, the risk of bias domain would be rated as high, reducing strength by at least one level. If results are rated consistent, direct, and precise, the starting level of low and the high risk of bias reduction would lead to a final strength of insufficient. However, a large effect could raise the strength to low. In another example, a medium risk of bias would exist if there is a good quality study and at least one other good or fair study. If there were consistent results, direct evidence and precise effect estimates, the strength could be raised above low if there is a large effect, a clear dose-response association or plausible confounding that would reduce the observed effect.

Peer Review, Public Commentary, and Technical Expert Panel

Peer reviewers were invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. Peer review comments on the preliminary draft of the report were considered by the EPC in preparation of the final draft of the report. Peer reviewers did not participate in the writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments will be documented and published three months after the publication of the evidence report.

Potential reviewers had to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Invited peer reviewers could not have any financial conflict of interest greater than $10,000. Peer reviewers who disclosed potential business or professional conflicts of interest were able to submit comments on draft reports through the public comment mechanism.

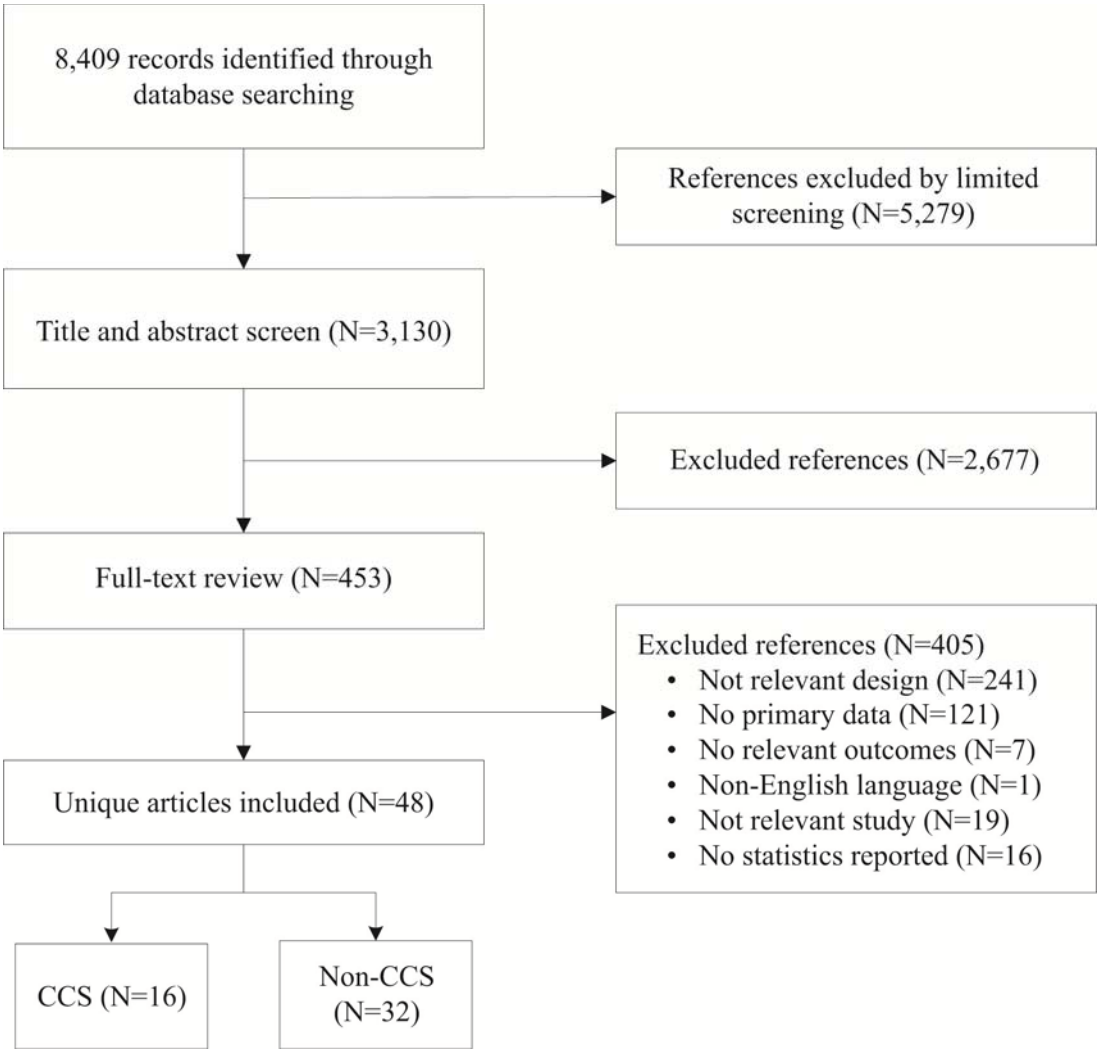
A TEP was formed to provide consultation on the development of the protocol and evidence tables for the review. Ad hoc clinical questions were also addressed to the TEP.

Results

Literature Search

Of the 8409 records identified through the literature search, we limited screening to those references that contained the terms “screen* OR surveil*” in title or abstract. Of the 5279 references that did not contain the key textwords, none met eligibility criteria. Of the remaining 3130 records, 3082 were excluded at various stages of screening and 48 records were included. Of these 48 studies, 16 studies attempted to control for confounding and/or secular trends (CCS studies) and 32 studies did not attempt to control for confounding and/or secular trends (non-CCS studies). The PRISMA diagram (Figure 3) depicts the flow of search screening and study selection.

Figure 3. PRISMA diagram for identified published literature



CCS = studies controlling for confounding and/or secular trend; non-CCS = studies not controlling for confounding and/or secular trend

Grey Literature Search

We evaluated the results of the grey literature search with results summarized in Figure 4.

- **Regulatory information:** The search yielded 49 studies from the 510(k) summaries obtained for MRSA; the assays included Xpert MRSA SA/SSTI, XPert MRSA SA/BC, XPert MRSA, GeneOhm MRSA assay and BBL ChromAgar MRSA. All 49 citations were excluded—28 were duplicates and 21 met one or more exclusion criterion. No new studies were identified from this source.
- **Clinical trial registries:** Citations for published articles linked to trials registered at ClinicalTrials.gov were included. The search yielded 168 clinical trials, of which, 167 were excluded during the title and abstract screen—86 were duplicate (literature citations already included in the reference database) and 81 met one or more exclusion criterion (e.g., did not compare MRSA screening versus an alternative or noncomparative trial). One reference was reviewed in full-text and was excluded according to the study protocol.
- **Abstracts and conference papers:** The search yielded 1,113 citations, of which, 1085 were excluded during the title and abstract screen—22 references were duplicate and 1063 met one or more exclusion criterion. Twenty-eight references were reviewed by a third team member in full-text and all were excluded according to the study protocol.
- **Grants and federally funded research:** The search yielded 15 citations and all 15 were excluded—3 were duplicates and 13 met one or more exclusion criterion.
- **Manufacturer database:** In response to requests, scientific information packets were received from CEPHEID. The submissions consisted of descriptive text supported by 15 citations. No abstracts or unpublished data were provided by the company. Of the 15 references, 13 were excluded during abstract and title screen—9 were duplicate and 4 met one or more exclusion criterion. The remaining two references were evidence reports—one from the Canadian Agency for Drugs and Technologies in Health (CADTH) and one from ECRI Institute. Further, the CADTH report was cross-referenced to another relevant CADTH report and hence was included in the full-text review. The full-text review of these three evidence reports yielded 80 references. Of these, all 80 were excluded—48 were duplicates and 32 met one or more exclusion criterion.

Overview of Studies Included in the Present Review

Overall, 48 studies were abstracted for this review. They are summarized in Table 4. Three studies[30,41,42] evaluated universal screening for MRSA carriage compared to no screening (Key Question 1), two studies[30,43] evaluated universal screening for MRSA carriage compared to screening of selected patient populations (targeted screening) (Key Question 2), 14 studies[29,30,44-55] evaluated screening for MRSA carriage in ICU patients compared to no screening (Key Question 3A), 18 studies[31,55-69,74,81] evaluated screening for MRSA carriage in surgical patients compared to no screening (Key Question 3B), eight studies[70-77] evaluated screening for MRSA carriage in high-risk populations compared to no screening (Key Question 3C), and 10 studies[56,72,78-85] evaluated screening of limited populations for MRSA carriage compared to screening of expanded populations (Key Question 4).

Of the 48 studies abstracted for this review, 16 were CCS studies.[29-31,41-47,55,56,70-72,78] Controlling for secular trends is important because the incidence of MRSA infection has been decreasing in recent years. Therefore, studies that do not adequately control for secular trends

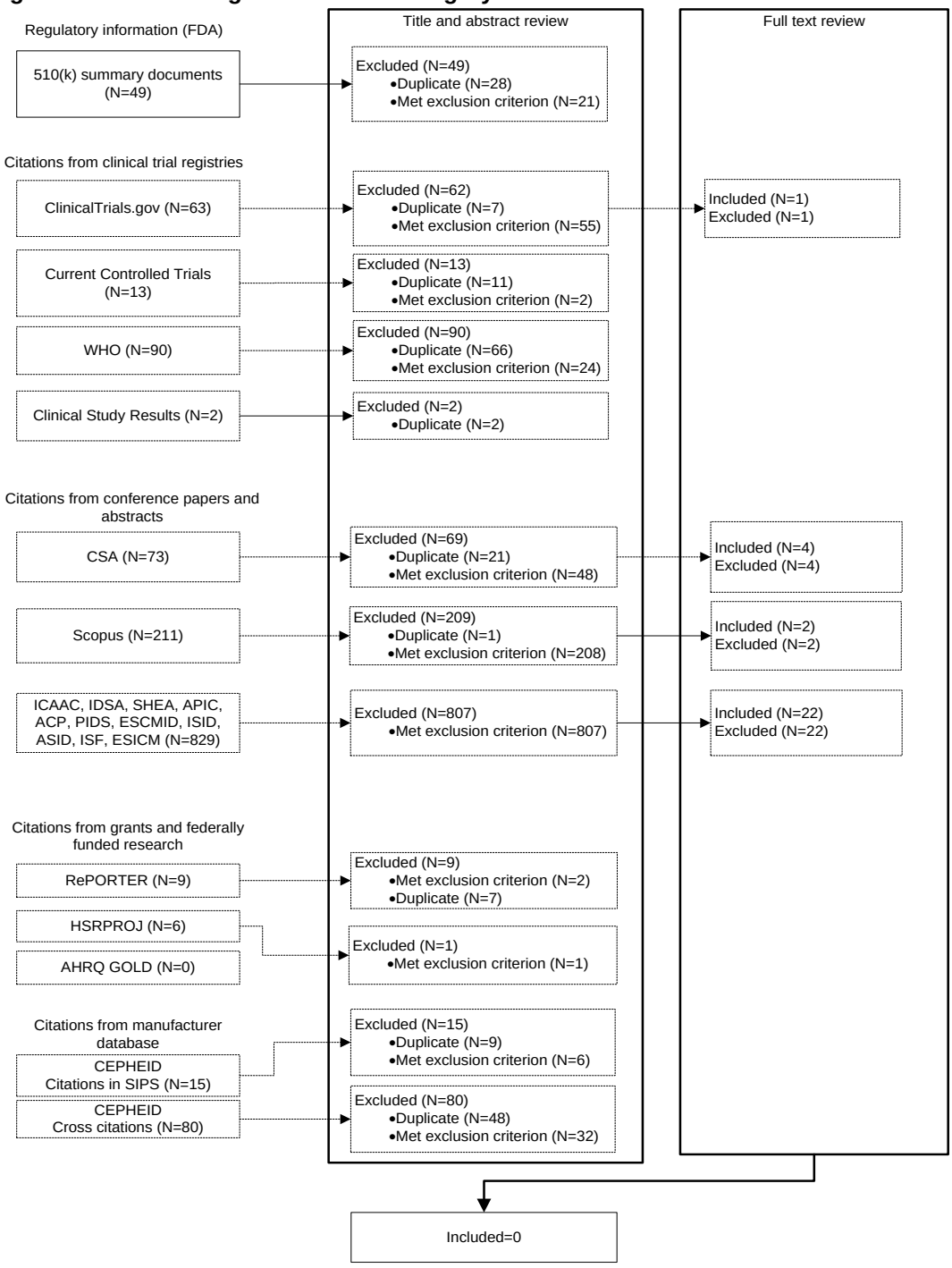
may show a decrease in the incidence of MRSA infection with screening, though that decrease may actually be attributable to a secular trend. Similarly, interventions designed to decrease healthcare-associated infection more generally (e.g., interventions to reduce SSIs or catheter-associated bloodstream infections) may also reduce MRSA infection. Studies that fail to control for these confounders may show a decrease in the incidence of MRSA infection with screening, though that decrease may actually be attributable to a confounder, rather than to screening. As a result, only the studies that adequately controlled for confounders and/or secular trends had the potential to support causal inferences about the impact of MRSA screening on health outcomes. Therefore, only these studies had the potential to be included in the SOE syntheses. The remaining 32 non-CCS studies performed simple two-group statistical analyses which cannot support causal inferences; the non-CCS studies were, therefore, excluded from the SOE syntheses.

The quality of the CCS studies was subsequently rated as good, fair, or poor. Studies that reported baseline group characteristics, considered and analyzed at least one healthcare-associated outcome, and conducted appropriate analysis (tested for trend, addressed autocorrelation, and included at least one confounder in the analysis) were rated "good." Studies that met the criteria for good quality except that they did not report a healthcare-associated outcome were rated "fair." Studies that failed to report baseline group characteristics and/or to conduct appropriate analysis were rated "poor."

Of the 16 CCS studies, 14[29-31,41,43,45-47,55,56,70-72,78] reported on a healthcare-associated outcome. Because screening for MRSA carriage in the hospital or ambulatory settings is most proximately expected to affect healthcare-associated MRSA acquisition, infection, morbidity and mortality, health-care associated outcomes are the outcomes of interest. The 14 studies[29-31,41,43,45-47,55,56,70-72,78] that reported a healthcare-associated outcome were included in the SOE analysis across all four Key Questions. Two of the CCS studies[42,44] did not report an outcome that was exclusively health care-associated and therefore, were excluded from the SOE analysis.

For each Key Question, the results chapter is organized as follows: overview of the literature, results of CCS studies, results of non-CCS studies, SOE assessment and comments on pattern of results for non-CCS studies.

Figure 4. PRISMA diagram for identified grey literature



ACP = American College of Physicians; AHRQ = Agency for Healthcare Research and Policy; APIC = Association of Professionals in Infection Control and Epidemiology; ASID = Australasian Society of Infectious Diseases; CSA = http://www.csa.com; ESCMID = European Society of Clinical Microbiology and Infectious Diseases; ESICM = European Society of Intensive Care Medicine; FDA = Food and Drug Administration; GOLD = Grants On-Line Database; HSRPROJ = Health Services Research Projects in Progress; ICAAC = Interscience Conference on Antimicrobial Agents and Chemotherapy; IDSA = Infectious Disease Society of America; ISF = International Sepsis Forum; ISID = International Society of Infectious Diseases; PIDS = Pediatric Infectious Diseases Society; RePORTER = Research Portfolio Online Reporting Tools; SHEA = Society for Healthcare Epidemiology of America; WHO = World Health Organization

Table 4. Overview of abstracted studies

A. CCS, Good Quality, used in SOE synthesis

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Harbarth, et al., 2008[31]	QEX-CG, X-OVER				•			•	•	•			
Huskins, et al., 2011[46]	RCT			•				•					
Leonhardt, et al., 2011[43]	QEX-CG		•						•				
Robicsek, et al., 2008[30]	QEX-BA	•	•	•					•	•			

B. CCS, Fair quality, not used in SOE synthesis

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Gould, et al., 2007[44]	QEX-ITS			•							•		

C. CCS, Poor quality, used in SOE synthesis

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Chaberny, et al., 2008[78]	QEX-BA						•		•		•		
Chowers, et al., 2009[70]	QEX-ITS					•				•			
Ellingson, et al., 2011[56]	QEX-ITS				•			•		•			
Harbarth, et al., 2000[71]	QEX-BA					•			•	•			
Holzmann-Pazgal, et al., 2011[45]	QEX-BA			•				•					
Huang, et al., 2006[29]	QEX-ITS			•				•		•			
Jain, et al., 2011[41]	QEX-BA	•						•	•	•			
Muder, et al.,2008[55]	QEX-BA			•	•				•				
Raineri, et al., 2007[47]	QEX-BA			•				•					
Rodriguez-Bano, et al.,2010[72]	QEX-ITS					•	•	•		•			

Table 4. Overview of abstracted studies (continued)

D. CCS, Poor quality, not used in SOE synthesis

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Reilly, et al., 2012[42]	QEX-BA	•										•	

E. Non-CCS, not used in SOE synthesis

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Blumberg and Klugman, 1994[48]	QEX-BA			•									•
Bowler, et al., 2010[73]	QEX-BA					•			•				
Boyce, et al., 2004[49]	QEX-BA			•					•				
Clancy, et al., 2006[50]	QEX-BA			•					•				
Chen, et al., 2012[69]	QEX-BA				•					•			
de la Cal, et al., 2004[51]	QEX-BA			•				•		•			
Enoch, et al., 2011[85]	QEX-BA						•				•		
Eveillard, et al., 2006[79]	QEX-BA						•	•					
Girou, et al., 2000[80]	QEX-BA						•	•					
Jog, et al., 2008[58]	QEX-BA				•					•			
Kelly, et al., 2012[68]	QEX-BA				•							•	
Keshtgar, et al., 2008[74]	QEX-BA					•				•			
Kim DH, et al., 2010[59]	QEX-BA				•					•			
Kurup, et al., 2010[52]	QEX-BA			•					•				
Lipke and Hyott 2010[60]	QEX-BA				•					•			
Malde, et al., 2006[61]	QEX-BA				•					•			
Nixon, et al., 2006[62]	QEX-BA				•					•			
Pan, et al., 2005[75]	QEX-BA					•				•			

Table 4. Overview of abstracted studies (continued)

E. Non-CCS, not used in SOE synthesis (continued)

Author, Year	Design	KQ1	KQ2	KQ3A	KQ3B	KQ3C	KQ4	HCA Acq	HCA Inf	HCA Site Inf	HCA /Imp Acq	HCA/ Imp Inf	HCA/ Imp Site Inf
Pofahl, et al., 2009[63]	QEX-BA				•					•			
Salaripour, et al.,2006[76]	QEX-BA					•		•					
Sankar, et al., 2005[57]	QEX-BA				•				•				
Schelenz, et al., 2005[81]	QEX-BA						•	•					
Simmons 2011[53]	QEX-BA			•					•				
Sott, et al., 2001[64]	QEX-BA				•					•			
Souweine, et al., 2000[54]	QEX-BA			•							•		
Supriya, et al., 2009[65]	QEX-BA				•					•			
Thomas, et al., 2007[66]	QEX-BA				•					•			
Thompson, et al., 2009[82]	QEX-BA						•	•		•			
Trautmann, et al., 2007[83]	QEX-BA						•	•		•			
Walsh, et al., 2011[67]	QEX-BA				•					•			
Wernitz, et al., 2005[77]	QEX-BA					•			•	•			
West, et al., 2006[84]	QEX-BA						•		•				

Acq = acquisition; BA= before after; CCS = attempted to control for confounding and/or secular trends; CG = control group; HCA = healthcare-associated; Imp = imported; Inf = infection; ITS = interrupted time series; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; QEX = quasi-experimental; RCT = randomized controlled trial; SOE = strength of evidence; X-over = cross over

Key Question 1. Universal Screening for MRSA Carriage Compared With No Screening

Overview

This section describes the literature that evaluates universal screening for MRSA carriage compared with no screening. After an overview of the literature, the results are described for each outcome: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. The emphasis in this chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. The study that did not report healthcare-associated outcomes is discussed in the results section below. However, because this study did not report a healthcare-associated outcome, it did not contribute to the SOE analysis. The outcome data from this study is presented in Appendix F. Table 5 summarizes the studies reviewed for Key Question 1 that presented healthcare-associated outcomes.

Table 5. KQ1: Healthcare-associated MRSA acquisition and infection

Outcome	Study	Quality	Statistical Result	Synthesis
HCA acquisition	Jain et al., 2011[41]	Poor	SS ↓	SOE = insufficient
HCA infection	Robicsek et al., 2008[30]	Good	SS ↓	SOE = low
	Jain et al., 2011[41]	Poor	SS ↓	

HCA = healthcare-associated; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; SOE = strength of evidence; SS = statistically significant

Three CCS studies[30,41,42] compared universal screening for MRSA carriage to no screening. All three studies used quasi-experimental study designs. Table 6 displays key elements in rating of study quality. Only the Robicsek study[30] reported baseline characteristics and met the required elements for appropriate analysis of results; it was judged to be of good quality. The Jain study[41] was judged to be of poor quality as it had limitations in the reporting of baseline characteristics and analysis of results. Although Jain[41] reported baseline characteristics for the intervention period, baseline data from the control period were not reported, precluding comparison between periods. Appropriate analysis was not accomplished because no adjustment for confounders was reported. The Reilly study[42] was judged to be of poor quality because it did not report any baseline group characteristics and did not meet any of the elements required for appropriate analysis of results. Another concern with the Reilly study[42] is that it did not report whether its infection outcome was exclusively health care-associated. As a result, community-acquired cases may have been included.

Table 6. KQ1: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Robicsek et al., 2008[30]	Sex, ethnicity, long term care residence, history hospital admission, admission-discontinuation details, medical condition	segmented Poisson regression, D-W test	Y	Tested for	Y (admitting hospital)	Y	Good
Jain et al., 2011[41]	Reported for intervention period but not control period	Poisson regression, D-W test	Y	Tested for	NR	N	Poor
Reilly et al., 2012[42]	NR	Poisson regression, before vs. after introduction of MRSA screening	NR	NR	NR	N	Poor

CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; KQ = Key question; MRSA = methicillin-resistant *Staphylococcus aureus*; N = no; NR= not reported; Y = yes
*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

All three studies were conducted in multihospital organizations of acute care hospitals. The Jain study[41] occurred in Veterans Affairs hospitals, the Robicsek study[30] occurred in academic and community hospitals and the Reilly study[42] occurred in acute hospitals including a tertiary referral hospital, district general hospital and island hospital. All three studies had a large number of subjects. The Robicsek study[30] specified the sample size for the intervention group (n=73,464) and for the control group (39,521). The Jain study[41] specified the sample size for the intervention group (n=1,934,598), but not for the control group, as did the Reilly study[42] (intervention group n=81,438, control group n=unspecified).

For two of the studies[30,41], the interventions included at least one intervention in addition to universal screening for MRSA carriage. For the Robicsek study,[30] the intervention was nasal surveillance for MRSA colonization on the first day of hospitalization for all patients, as well as decolonization (with intranasal antimicrobials and topical antimicrobial washes) for those patients who tested positive for MRSA.[30] For the Jain study[41], the intervention was a MRSA bundle including surveillance for nasal colonization with MRSA for all patients within 24 hours of admission to the hospital, all patients not already known to be colonized or infected with MRSA transferred from one unit to another within the hospital, and all patients not already known to be colonized or infected with MRSA on discharge from the hospital; contact precautions for patients colonized or infected with MRSA; hand hygiene; and an institutional culture change wherein infection control became the responsibility of everyone who had patient contact.[41] One of the studies utilized PCR to screen patients for MRSA[30] and one[41] utilized either culture or PCR to screen patients for MRSA carriage. For the Reilly study,[42] the intervention was surveillance of all patients on admission for MRSA carriage, except psychiatric, obstetric and pediatric admissions. Those patients who were found to be colonized with MRSA underwent isolation and decolonization. The Robicsek study utilized PCR to screen patients for MRSA[30]

and the Jain study[41] utilized either culture or PCR to screen patients for MRSA carriage. For all three studies, the control condition consisted of no screening.

The primary outcome for the Robicsek[30] and Jain[41] studies was the rate of healthcare-associated MRSA infection. For the Robicsek study,[30] the primary outcome was the aggregate healthcare-associated rate of MRSA infection in the hospital. For the Jain study,[41] the primary outcome was the rate of healthcare-associated MRSA infections. The primary outcomes for the Reilly study[42] were the rates of MRSA colonization, infection and bacteremia.

The infection control practices differed for MRSA-positive patients during the intervention and control periods. None of the studies recommended actions for patients awaiting test results for the intervention or control groups. However, all three studies recommended more intensive actions for MRSA-positive patients in the intervention group than for MRSA-positive patients in the control group. In the Robicsek study,[30] the MRSA-positive intervention group received isolation or cohorting, barrier precautions, dedicated equipment for staff use, and decolonization (with intranasal antimicrobials and topical antimicrobial washes). For its MRSA-positive control group, the Robicsek study[30] recommended isolation or cohorting, barrier precautions, and dedicated equipment for staff use, but no decolonization. For its MRSA-positive intervention group, the Jain study[41] recommended contact precautions, hand washing, and repeat assays while it did not recommend any action for its MRSA-positive control group. For its MRSA-positive intervention group, the Reilly study[42] recommended isolation and decolonization while it did not recommend any action for its MRSA-positive control group. Only the Robicsek study[30] described the turnaround time for testing (0.67 day).

Results by Outcome

The Jain study[41] reported on healthcare-associated MRSA acquisition and healthcare-associated MRSA infection. The Robicsek study[30] reported on healthcare-associated MRSA infection. The Reilly study reported on MRSA infection, but did not specify that this outcome was exclusively health care-associated, suggesting that the reported results might also include community associated infections. Therefore, the Reilly study[42] did not contribute to the SOE assessment for universal screening for MRSA carriage compared to no screening. Outcomes data for this study is presented in the Appendix F.

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is health care-associated, rather than imported. Only one poor quality quasi-experimental study[41] addressed this outcome. This study by Jain et al.,[41] defined healthcare-associated MRSA colonization or infection as a positive sample for MRSA obtained more than 48 hours after admission from a patient not previously known to be colonized or infected with MRSA. Patients not known to be colonized or infected with MRSA who were readmitted to the hospital within 48 hours after discharge and were found to be positive at the time of readmission were also considered to have a transmission event. With universal screening for MRSA, this study showed a statistically significant reduction in healthcare-associated MRSA in the ICU (-17 percent relative risk reduction) and in non-ICU settings (-21 percent relative risk reduction).

Strength of Evidence

Overall, compared to no screening, the SOE was assessed as insufficient that universal screening for MRSA carriage decreases healthcare-associated MRSA acquisition based on the positive findings from a single, quasi-experimental before/after study.[41] The risk of bias was judged to be high as only one poor quality observational study addressed this outcome. Because only one study[41] evaluated this outcome, the consistency of the results was unknown. The study addressed healthcare-associated MRSA acquisition, an intermediate and therefore, indirect outcome. The effect was judged to be precise, given the statistically significant reduction in health care-associate MRSA acquisition seen in this study. Because the evidence base that addressed this outcome consisted of a single observational study, the starting level of SOE was low. SOE was lowered level based on the high risk of bias. Therefore, compared to no screening, the SOE is insufficient that universal screening for MRSA carriage decreases healthcare-associated MRSA acquisition.

Healthcare-Associated MRSA Infection

One good quality quasi-experimental study[30] by Robicsek and one poor quality quasi-experimental study[41] by Jain addressed healthcare-associated MRSA infection overall. In their definition of hospital-acquired infection, both studies included infection that had occurred more than two days after admission. The Robicsek study[30] defined infection as the sum total of all bloodstream infections (positive blood culture in the absence of a positive clinical culture from another site), respiratory tract infections (positive respiratory culture, compatible chest radiograph and decision to treat), urinary tract infections (positive urine culture and decision to treat or growth of more than 100,000 colony-forming units/mL plus at least 50 leukocytes per high-power field), and SSIs (positive culture of a surgical site). Infections were considered hospital-associated if they occurred more than two days after admission and within 30 days of discharge. The Jain study[41] defined healthcare-associated MRSA infection according the Center for Disease Control and Prevention's (CDC's) National Healthcare Safety Network guidelines with three modifications: (1) the diagnosis of MRSA infection required a positive culture; (2) a positive culture was considered to be imported if it was obtained within 48 hours after admission; (3) a positive clinical culture obtained from a patient in whom infection was not present or incubating at the time of admission as defined by National Healthcare Safety Network guidelines criteria was considered to be health care-associated if it was obtained more than 48 hours after admission.

Compared to no screening, both studies found a statistically significant reduction in healthcare-associated MRSA infection with universal screening for MRSA. For the good quality study,[30] the change in the rate of MRSA infection from a Poisson regression model was -69.6 percent with broad confidence intervals (95% CI: -89.2 to -19.6). For the poor quality study,[41] the relative reduction in the rate of MRSA infection was -62 percent in ICU settings and -45 percent in non-ICU settings. The p value for trend in both settings was <0.001.[41]

Strength of Evidence

Overall, compared to no screening, the SOE was judged to be low that universal screening for MRSA carriage decreases healthcare-associated MRSA infection. Two quasi-experimental studies[30,41] reported this outcome; the Jain study was a before/after design judged to be of poor quality[41] and the Robicsek study was an interrupted time series design[30] judged to be of good quality. The risk of bias for the body of evidence was judged as high, as only quasi-experimental

studies addressed this outcome, only one of which[30] was good quality. Because both studies found a reduction in healthcare-associated MRSA infection with screening, the results were consistent. The results were also direct because healthcare-associated MRSA infection is a health outcome. The effect was judged to be precise, given the statistically significant reduction in healthcare-associated MRSA infection seen in these studies. Because the evidence base that addressed this outcome consisted of two quasi-experimental studies, the starting level of SOE was low. SOE was raised by one level based on the large effect size, though lowered one level based on the high risk of bias. Therefore, compared to no screening, the SOE is low that universal screening for MRSA carriage decreases healthcare-associated MRSA infection.

Morbidity, Mortality, Harms and Resource Utilization

Results

No studies addressed these outcomes.

Strength of Evidence

Because no studies addressed these outcomes, compared to no screening, the SOE is insufficient to assess the effect of universal screening for MRSA carriage on morbidity, mortality, harms or resource utilization.

Summary Strength of Evidence Across Key Question 1

A summary of the main syntheses for this question is given in Table 7.

Table 7. Strength of evidence for studies comparing universal screening versus no screening

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Universal screening vs. No screening	MRSA Acquisition	1 QEX (N=1,934,598) Jain 2011[41]	High	Unknown	Indirect	Precise	Insufficient
	MRSA Infection	2 QEX (N= 112,985) Robicsek 2008[30] (N=1,934,598) Jain 2011[41]	High	Consistent	Direct	Precise	Low*

QEX = quasi-experimental; MRSA = methicillin-resistant *Staphylococcus aureus*

[§]Studies that controlled for confounding and/or trend.

*Optional domain for effect magnitude invoked, raising strength of evidence by one level due to large effect size.

Key Question 2. Universal Screening for MRSA Carriage Compared With Screening of Selected Patient Populations (Targeted Screening)

Overview

This section describes the literature that evaluates universal screening for MRSA carriage compared to screening of selected patient populations (targeted screening). After an overview of the literature, the body of evidence is described for each outcome measure: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. The emphasis in this

chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. Table 8 summarizes the studies reviewed for Key Question 2.

Table 8. KQ2: Healthcare-associated MRSA infection

Outcome	Study	Quality	Statistical Result	Synthesis
HCA infection	Robicsek et al.[30]	Good	SS ↓	SOE=insufficient
	Leonhardt et al.[43]	Good	NSS↓	

HCA = health care associated; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; NSS = not statistically significant; SOE = strength of evidence; SS = statistically significant

Two quasi-experimental studies compared universal screening for MRSA carriage on hospital admission to screening of selected patient populations (targeted screening).[30,43] Leonhardt and colleagues (n=15,049) was a case-control study[43] and the study by Robicsek and colleagues[30] (n=77,856) was a limited time series design; both studies were judged to be good quality. Both studies presented baseline characteristics (Table 9) for intervention and control groups and conducted appropriate analyses (tested for trend, addressed autocorrelation and controlled for at least one confounder). Both studies reported on an important outcome, healthcare-associated MRSA infection.

Table 9. KQ2: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Robicsek et al., 2008[30]	Sex, ethnicity, long term care residence, history hospital admission, admission-discontinuation details, medical condition	Segmented Poisson regression, D-W test	Y	Tested for	Y (admitting hospital)	Y	Good
Leonhardt et al., 2011[43]	Age, sex, race, case mix	Difference in difference analysis	Y	Tested for	Y (ICP)	Y	Good

CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; ICP = infection control practices; KQ = Key question; MRSA = methicillin-resistant *Staphylococcus aureus*; Y = yes
*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

As its comparison group, the Robicsek study[30] evaluated screening of patients admitted to the ICU. The Leonhardt study[43] evaluated screening of high-risk patients, including those admitted to the ICU as its comparison group. In its high-risk group, this study also included patients with a history of MRSA infection or colonization, those with a history of prior hospitalization including transfers within the past 6 months, patients from long-term care facilities and correctional institutes, patients receiving hemodialysis and selected orthopedic and cardiothoracic surgery patients.

The Robicsek study[30] conducted followup for MRSA disease for 180 days after discharge, though patients in the intervention group were followed for less than 180 days if they were

discharged in the final 180 days of the study period. The Leonhardt study[43] did not specify the duration of followup.

Both studies utilized PCR to screen for MRSA carriage. Turnaround times for screening results were reported by the Robicsek study,[30] but not by the Leonhardt study.[43] The Robicsek study[30] found the turnaround time to be 2.5 days for the control period and 0.67 day for the intervention period.

The Robicsek study[30] cited the aggregate hospital-associated MRSA infection rate as its primary outcome. This study included several secondary outcomes including rates of healthcare-associated MRSA and methicillin-sensitive *Staphylococcus aureus* bacteremia, rates of aggregate MRSA infections occurring up to 180 days after discharge, and adherence to MRSA surveillance. The Leonhardt study[43] cited the clinical effectiveness and the cost benefit of universal screening versus targeted screening for MRSA as its primary outcome.

The infection control practices used to care for MRSA-positive patients differed between intervention and control group patients for the Robicsek study[30] but were the same for the Leonhardt study.[43] For MRSA-positive patients in the intervention group, Robicsek et al.[30] utilized contact isolation and decolonization (with nasal antimicrobials and topical antimicrobial washes). However, MRSA-positive patients in the control group received contact isolation without decolonization. For MRSA-positive patients in both intervention and control groups, Leonhardt et al.,[43] utilized contact isolation and when appropriate, perioperative decolonization and antibiotic prophylaxis.

The infection control practices used to care for patients while waiting for screening test results were the same for intervention and control group patients for both studies. Robicsek et al.,[30] utilized no interventions during this time period. Leonhardt et al.,[43] recommended contact isolation for patients previously known to be MRSA positive.

Results by Outcome

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is health care-associated, rather than imported.

Results

No studies addressed this outcome.

Strength of Evidence

No studies addressed this outcome. Therefore, the SOE to evaluate the effect of universal screening for MRSA carriage compared to targeted screening on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection

Results

Although both studies showed a reduction in hospital-acquired MRSA infection with universal screening for MRSA carriage compared to targeted screening, only the Robicsek study showed a statistically significant reduction. Using a segmented Poisson regression, Robicsek et al.,[30] found that the rate of hospital-acquired MRSA infection declined by 52.4 percent (CI: 9.3

to 78.3 percent) in the universal screening group compared to the targeted screening group. Leonhardt et al.,[43] showed a 0.12 percent reduction in hospital-acquired infection with universal screening compared to targeted screening, a result that is close to a null effect. However, this reduction was not statistically significant (p=0.23), nor was the difference in difference (p=0.34).

The definitions of hospital-acquired infection differed between the two studies. One study[43] defined an infection as hospital acquired if it occurred on or after day 4 of hospitalization. The other study[30] defined an infection as hospital acquired if it occurred more than 48 hours after admission and 30 days or less after discharge.

Strength of Evidence

The SOE to evaluate the effect of universal screening for MRSA carriage compared to targeted screening on healthcare-associated MRSA infection was judged to be insufficient. The risk of bias was judged to be medium as two good quality observational studies addressed this outcome.[30,43] With universal screening, both studies[30,43] found a reduction in healthcare-associated MRSA infection. Using a segmented Poisson regression, Robicsek et al.,[30] found that the rate of hospital-acquired MRSA infection declined by 52.4 percent (CI: 9.3 to 78.3 percent) in the universal screening group compared to the targeted screening group. Leonhardt et al.,[43] showed a 0.12 percent reduction in hospital-acquired infection with universal screening compared to targeted screening. However, this reduction was not statistically significant (p=0.23), nor was the difference in difference (p=0.34). Therefore, the results were consistent, because both studies showed a reduction in infection with screening. The studies evaluated MRSA infection, a health outcome. Therefore, the outcome was direct. Because the individual studies did not consistently report statistically significant results, the findings were imprecise. Because the evidence base for this outcome consisted of two observational studies, the starting level for the SOE was low. SOE was lowered by one level based on the medium risk of bias and by one level based on the imprecise results and is therefore, insufficient. In summary, the SOE is insufficient to support or refute that, compared to targeted screening, universal screening for MRSA carriage decreases healthcare-associated MRSA infection.

Morbidity, Mortality, Harms, and Resource Utilization

Results

No studies addressed these outcomes.

Strength of Evidence

Because no studies addressed these outcomes, the SOE to evaluate the effect of universal screening for MRSA carriage compared to targeted screening on morbidity, mortality, harms or resource utilization is judged to be insufficient.

Summary Strength of Evidence Across Key Question 2

A summary of the main syntheses for this question follows in Table 10.

Table 10. Strength of evidence for studies comparing universal screening versus screening in selected patient population

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Universal Vs Screening of Selected Patients	MRSA Acquisition	No studies	NA	NA	NA	NA	Insufficient
	MRSA Infection	2 QEX (N=92,905) (Robicsek 2008,[30] Leonhardt 2011[43])	Medium	Consistent	Direct	Imprecise	Insufficient

MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable; QEX = quasi-experimental
[§]Studies that controlled for confounding and/or trend.

Key Question 3A. Screening of ICU Patients for MRSA Carriage Compared With No Screening

Overview

This section describes the literature that evaluates screening of ICU patients for MRSA carriage compared to no screening. After an overview of the literature, the results are described for each outcome: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. Within the category of MRSA infection, we also included results for MRSA bacteremia or bloodstream infection and for MRSA SSI, as some studies present these outcomes rather than the broader outcome of MRSA infection irrespective of site. The emphasis in this chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. Studies that did not report healthcare-associated outcomes are discussed in the results section below. However, because these studies did not report a healthcare-associated outcome, they did not contribute to the SOE analyses. The outcomes data from these studies is presented in the Appendix F. In addition, SOE syntheses presented here include only CCS studies. Because studies that use simple two-group statistical analyses cannot support causal inferences, the non-CCS studies were excluded from the SOE analysis. Following the SOE syntheses, we comment on the pattern of results seen in non-CCS studies. Table 11 summarizes the studies reviewed for Key Question 3A and Table 12 details the study quality ratings. Note that Table 11 does not include the studies by Gould,[44] Blumberg[48] and Souweine et al.,[54] because they did not report outcomes that were exclusively health-care associated.

Table 11. KQ3A: Healthcare-associated MRSA acquisition, infection, bacteremia, or surgical-site infection

Outcome	Study	Quality	Statistical Result	Synthesis
HCA acquisition	Huskins et al., 2011[46]	Good	NSS ↑	SOE=insufficient
	Huang et al., 2006[29]	Poor	SS ↓	Comment: Results more favorable than the good quality Huskins study, however causal inference is not possible.
	Raineri et al., 2007[47]	Poor	SS ↓	
	Holzmann-Pazgal et al., 2011[45]	Poor	SS ↓	
	de la Cal et al., 2004[51]	Non-CCS	SS ↓	
HCA infection	Robicsek et al., 2008[30]	Good	NSS ↓	SOE=insufficient
	Muder et al., 2008 [55]	Poor	SS ↓	Comment: Results more consistently favorable than Robicsek, however causal inference is not possible.
	Clancy et al., 2006[50]	Non-CCS	SS ↓[a]/ NSS↓[b]	
	Boyce et al.,2004[49]	Non-CCS	SS ↓	
	Kurup et al.,2010[52]	Non-CCS	NSS ↓	
	Simmons et al.,2011[53]	Non-CCS	SS ↓	
HCA bacteremia/ blood stream infection	Robicsek et al.,2008[30]	Good	NSS ↓	SOE=insufficient
	Huang et al.,2006[29]	Poor	SS ↓	Comment: Results more consistently favorable than Robicsek, however causal inference is not possible.
	de la Cal et al.,2004[51]	Non-CCS	SS ↓	
HCA surgical site infection	Robicsek et al.,2008[30]	Good	NSS ↓	SOE=insufficient

CCS = study attempted to control for confounding and/or secular trends; HCA = healthcare-associated; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; NSS = not statistically significant; SOE = strength of evidence; SS = statistically significant

[a]Reduction in hospital-acquired MRSA infection in the surgical ICU as well as in the pooled analysis of the surgical ICU, medical ICU, and wards with screening for MRSA in the ICU was statistical significant.

[b]Reduction in hospital-acquired MRSA infection in the medical ICU or the wards was not statistically significant.

Table 12. KQ3A: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Gould et al., 2007[44]	Age, sex, APACHE II, ICU deaths, length of stay	Segmented regression, D-W test	Y (also MSSA)	Accounted for	Y (number patients admitted to ICU)	Y	Fair
Huang et al., 2006[29]	NR	Segmented regression, D-W test	Y (also MSSA)	Adjusted for	NR	N	Poor
Raineri et al., 2007[47]	Patient-days, age, length of stay, sex, SAPS II	Segmented regression, D-W test	Y	Tested for	NR	N	Poor
Robicsek et al., 2008[30]	Sex, ethnicity, long term care residence, history hospital admission, admission-discontinuation details, medical condition	Segmented regression, D-W test	Y	Tested for	Y (admitting hospital)	Y	Good
Holzmann-Pazgal et al., 2011[45]	NR	Multivariable linear regression during int per only	N(inter-vention period only)	Tested for	hand hygiene compliance	N	Poor
Huskins et al., 2011[46]	ICU length of stay, prehospital-ization residence, history hospital admission, age, sex, nonoperative primary diagnosis, APACHE III, MODS, hx MRSA/VRE colonization/ infection past year	ANCOVA adjusted for BL incidence, multivariable Cox proportional hazards model regression	Y	Tested for	Y (multiple ICU-level and pt- level variables)	Y	Good
Muder et al., 2008[55]	NR	Segmented Poisson regression	Y	NR	NR	N	Poor

ANCOVA = analysis of covariance; APACHE = Acute Physiology and Chronic Health Evaluation; BL = baseline; CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; Hx = history; ICU = intensive care unit; KQ = Key Question; MODS = Multiple Organ Dysfunction Score; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus;* N = no; NR = not reported; Pt = patient; SAPS = Simplified Acute Physiology Score; VRE = vancomycin-resistant *Enterococcus*; Y = yes
*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

Fourteen studies described screening of ICU patients for MRSA carriage compared to no screening. Seven were CCS studies[29,30,44-47,55] and seven[48-54] were non-CCS studies. Of the CCS studies, the Robicsek[30] and Huskins[46] studies were judged to be of good quality overall because they presented baseline characteristics for intervention and control groups, conducted appropriate analyses (tested for trend, addressed autocorrelation and controlled for at least one confounder) and reported on an important (healthcare-associated) outcome. The Gould[44] study was judged to be of fair quality because it did not report on an outcome that was exclusively health care-associated, suggesting that its outcomes may have included both community-acquired and healthcare-associated cases. The Huang,[29] Muder,[55] Raineri[47] and Holzmann-Pazgal[45] studies were judged to be of poor quality. The Huang study[29] was rated as poor quality because it did not report baseline group characteristics and whether the analysis controlled for confounders. The Muder study[55] was rated as poor quality because it did not report baseline group characteristics, addressing autocorrelation, and whether its analysis controlled for confounders. The Raineri study[47] was rated as poor quality because it did not report adjusting for any confounders. The Holzmann-Pazgal study[45] was rated as poor quality because though it controlled for the confounding influence of hand hygiene compliance and for trend during the intervention period, it did not address trend during the pre-intervention period.

Of the good quality studies, Huskins[46] was a cluster RCT and Robicsek[30] utilized a before/after quasi-experimental design. The Gould study, a study of fair quality, utilized a quasi-experimental interrupted time series design.[44] Of the poor quality studies, all four utilized a quasi-experimental study design. The Huang study[29] utilized an interrupted time series design and the other three studies[45,47,55] utilized a before/after design. All seven non-CCS studies[48-54] utilized a before/after design.

In terms of sample size, both good quality studies[30,46] specified the sample size for the intervention group and for the control group. Among the good quality studies, the range in sample size for the intervention group was 1,615–39,521; the range in sample size for the control group was 2,441–40,392. The total sample size for the good quality studies[30,46] was 83,969. For the fair quality study, the sample size for the control group was 1,232, the sample size for the intervention group was 1,421, and the total sample size was 2,653.[44,45] Of the poor quality studies, two[45,47] specified the sample size and two[29,55] did not. Among the poor quality studies, the range in sample size for the intervention group was 2367-3311; the range in sample size for the control group was 667-730. The total sample size for the poor quality studies was 7,075. For the good, fair and poor quality studies combined, the total sample size was 86,622.

Of the non-CCS studies, two of seven specified the sample size for the intervention group and for the control group.[48,51] Four non-CCS studies[49,50,52,53] specified the sample size only for the intervention group. One[54] of the non-CCS studies did not specify the sample size for any group. Of the non-CCS studies, the range in sample size for the intervention group was 351–2,605; the range in sample size for the control group was 140–2,315. For the non-CCS studies, the total sample size including patients in both the intervention and control groups was at least 9,369.

All 14 studies evaluated patients in the ICU. The Holzmann-Pazgal study[45] focused its intervention on the pediatric ICU. The Blumberg study[48] also evaluated patients in a pediatric oncology unit.

The MRSA screening interventions could be divided into two general categories: multicomponent MRSA screening interventions or MRSA screening alone. The interventions in both good quality studies[30,46] consisted of MRSA screening alone. The fair quality study[44]

consisted of a multicomponent intervention including surveillance cultures of the nares, throat, axillae, and groin on admission to the ICU, decolonization for all patients (with intranasal antimicrobials and topical antimicrobials), isolation, decolonization for MRSA-positive patients, and barrier nursing for MRSA-positive patients. Of the poor quality studies, two[29,47] were multicomponent interventions and one[45] consisted of screening for MRSA carriage alone. The intervention from Huang and colleagues[29] included four sequential interventions: (1) a campaign to increase sterile barrier precautions during central venous catheter placement; (2) the hospital wide institution of alcohol-based hand rubs; (3) a hand hygiene campaign; and (4) nasal surveillance for MRSA in all ICU patients on admission and weekly throughout the ICU stay. The intervention from Muder and colleagues[55] included four components: (1) the use of standard precautions (especially hand hygiene) before and after contact with patients and their environment; (2) contact precautions for all patients infected or colonized with MRSA; (3) active surveillance cultures to identify patients colonized with MRSA; and (4) an industrial systems-engineering approach to facilitate delivery of the infection control program. The intervention from Raineri et al.,[47] included two interventions. The first intervention included active surveillance for MRSA (a nasal swab on admission to the ICU and every 3 days throughout the ICU stay), contact precautions (gloves and hand hygiene, with gowns and masks reserved for procedures at risk for MRSA transmission), decolonization of carriers (with intranasal antimicrobials and topical antimicrobials), repeat testing after treatment, and additional treatment for those patients who continued to test positive. Staff education was provided throughout the intervention. The second intervention included all of the components of the first intervention, as well as the movement of the ICU to a new ward where isolation or cohorting could be performed.

Of the non-CCS studies, three[48,51,54] were multicomponent interventions, and four[49,50,52,53] consisted of screening for MRSA carriage alone. One[51] of the non-CCS studies included two interventions. For the study by de la Cal et al.,[51] the first intervention consisted of surveillance samples from the nose, throat, rectum, tracheostomy and pressure sores, on admission to the ICU and weekly throughout the ICU stay. Enteral vancomycin was administered to MRSA positive patients. The second intervention also included surveillance samples from the nose, throat, rectum, tracheostomy, and pressure sores, on admission to the ICU and weekly throughout the ICU stay. In addition, all patients expected to require mechanical ventilation for three or more days received enteral vancomycin and selective digestive decontamination with oral and intravenous antibiotics. In addition, vancomycin paste was administered topically to the oropharynx, tracheostomy site, and pressure sores 4 times a day. Vancomycin solution was administered via nasogastric tube 4 times a day. Patients were washed with a topical antimicrobial solution twice a week.

The Souweine study[54] used an intervention that included surveillance cultures (on admission to the ICU, weekly throughout the ICU stay, and at discharge from the ICU), isolation procedures (handwashing, gown and gloves, cleansing patients), attempted eradication of MRSA nasal carriage with mupirocin, and staff education. The Blumberg study[48] also utilized a multicomponent intervention. This intervention included screening of staff at study onset and six months later, screening of patients at study onset followed by sampling of new patients three times a week, decolonization and repeat assays.

Of the good quality studies, the Robicsek study[30] utilized PCR to screen patients for MRSA and the Huskins study[46] utilized culture. The fair quality study utilized culture to screen patients for MRSA.[44] Of the poor quality studies, all four[29,45,47,55] utilized culture to screen patients for

MRSA. Of the non-CCS studies, five studies[48-51,54] utilized culture to screen patients for MRSA, one[53] utilized PCR to screen patients for MRSA, and one[52] utilized culture to screen some patients for MRSA and PCR to screen other patients for MRSA. For all of the studies, the control condition consisted of no screening.

The primary outcomes for the majority of the studies included healthcare-associated MRSA acquisition (either colonization, infection or both colonization and infection). There were several distinctive primary outcomes of interest. For the Huskins study,[46] the primary outcome was the ICU-level incidence of new events of colonization or infection with MRSA or VRE. The inclusion of VRE was unusual among the 13 studies. Almost all of the studies focused on outcomes that were documented in the ICU. However, for the Robicsek study,[30] the primary outcome was the aggregate rate of MRSA infection in the hospital and for the Simmons study,[53] the primary outcomes were the ICU-acquired MRSA rate, and the hospital-wide MRSA rate. The Blumberg study[48] included the identification and treatment of MRSA-positive staff and patients as a primary outcome of interest. For the Huang study,[29] the primary outcome was rates of MRSA bacteremia.

Of the studies of fair or good quality, the Huskins study[46] and the Gould study[44] recommended actions for patients in the intervention group before test results were known, but no actions for patients in the control group before test results were known. The Huskins study[46] recommended universal gloving and contact precautions for those patients infected or colonized with MRSA or VRE during the prior year. The Gould study[44] recommended topical and intranasal antimicrobials while awaiting test results. In contrast, the Robicsek study[30] recommended no action for patients in either the intervention group or the control group before test results were known. The Muder study[55] recommended contact precautions for those with a prior history of MRSA infection or colonization. None of the other poor quality studies[29,45,47] recommended action before test results were known for patients in the intervention group or the control group.

The majority of non-CCS studies (four of seven) took no action before test results were known for patients in the intervention group or the control group. Two of the non-CCS studies recommended actions for patients in the intervention group while awaiting test results. The Souweine study[54] recommended isolation for patients transferred from another ICU while awaiting test results. For the first half of the intervention period, the Kurup study[52] recommended no action for patients while awaiting test results; in the second half of the intervention period however, this study recommended topical antimicrobial washes for patients while awaiting test results.

Once a patient was found to be MRSA-positive, all of the good quality[30,46] and fair quality studies[44] recommended the same action for these patients in the intervention group as for those in the control group. All of these studies[30,44,46] recommended isolation and barrier precautions. In addition, the Robicsek study[30] recommended dedicated equipment for staff use. Of the poor quality studies, only one[45] recommended the same action for MRSA-positive patients in the intervention group as in the control group. The Holzmann-Pazgal study[45] recommended isolation and barrier precautions for MRSA-positive patients in both the intervention and control groups. In contrast, three[29,47,55] of the poor quality studies recommended different actions for MRSA-positive patients in the intervention and control groups. Huang et al.,[29] recommended contact precautions for MRSA-positive patients in the intervention group and no action for MRSA-positive patients in the control group. Raineri et al.,[47] recommended contact precautions (hand hygiene and gloves; gowns and masks when performing procedures at risk for MRSA

transmission), intranasal and topical antimicrobials, and repeat assays for MRSA-positive patients in the first and second intervention groups. In addition, this study[47] recommended isolation and cohorting for MRSA-positive patients in the second intervention group. No action was recommended for MRSA-positive patients in the control group.[47] Muder et al.,[55] recommended contact precautions for MRSA-positive patients in the intervention group, but did not specify an action for MRSA-positive patients in the control group.

Only one[49] of the seven non-CCS studies recommended exactly the same action for MRSA-positive patients in the intervention group as in the control group. Boyce et al.,[49] recommended contact precautions for MRSA-positive patients in both the intervention and control groups. Two of the non-CCS studies[50,53] recommended similar actions for MRSA-positive patients in the intervention and control groups. The Clancy study[50] recommended isolation or cohorting, barrier precautions, handwashing compliance checks, contact isolation compliance checks, and repeat assays for MRSA-positive patients in the intervention group. Isolation or cohorting and barrier precautions were recommended for MRSA-positive patients in the control group.[50] In another non-CCS study, Simmons and colleagues[53] recommended contact isolation, potential decolonization (with intrasnasal antimicrobials), and repeat assays for MRSA-positive patients in the intervention group. Contact isolation, potential decolonization (type unspecified), and repeat assays were recommended for MRSA-positive patients in the control group. Four[48,51,52,54] of the seven non-CCS studies recommended different interventions for MRSA-positive patients in the intervention group than in the control group. de la Cal et al.,[51] recommended isolation or cohorting, barrier precautions, topical antimicrobials, oral or intravenous antimicrobials, and hand washing for MRSA-positive patients in the intervention group. Isolation or cohorting, barrier precautions and hand washing were recommended for MRSA-positive patients in the control group.[51]

Souweine et al.,[54] recommended isolation or cohorting, barrier precautions, intranasal antimicrobials, topical antimicrobial washes, hand washing, and repeat assays for MRSA-positive patients in the intervention group. In addition, all soiled articles, moist body substances, and waste were wrapped in double bags before removal from patient rooms.[54] No interventions were recommended for MRSA-positive patients in the control group.[54] Blumberg et al.,[48] recommended isolation or cohorting for patients admitted to the ICU (not for those admitted to the pediatric oncology unit), barrier precautions, intranasal antimicrobials, topical antimicrobial washes, and alcohol-based hand rubs for MRSA-positive patients in the intervention group. In addition, cohort nursing was attempted for MRSA-positive patients in the intervention group.[48] No interventions were recommended for MRSA-positive patients in the control group.[48] Kurup et al.,[52] recommended isolation or cohorting, topical antimicrobial washes, and repeat assays for MRSA-positive patients in the intervention group. No interventions were recommended for MRSA-positive patients in the control group.[52]

Of the studies of good, fair or poor quality, five of the seven reported test turnaround time.[29,30,45,46,55] The Robicsek study described the turnaround time as 2.5 days[30] and the Huskins study as 5.2 days ± 1.4 days.[46] The Huang study,[29] the Muder study[55] and the Holzmann-Pazgal study[45] described test turnaround time as two days. The Simmons study[53] (a non-CCS study) reported test turnaround time as 12 hours.

Results by Outcome

The Huskins study,[46] the Huang study,[29] the Raineri study,[47] and the Holzmann-Pazgal study[45] reported on healthcare-associated MRSA acquisition. The Robicsek study[30] reported on

healthcare-associated MRSA infection regardless of site, as did the Muder study.[55] The Robicsek study[30] also reported on healthcare-associated MRSA bacteremia or bloodstream infection, as did the Huang study.[29] In addition, the Robicsek study[30] reported on MRSA SSI. The Gould study[44] reported on MRSA infection, but did not specify that this outcome was exclusively health care-associated, suggesting that the reported results might also include community associated infections. Therefore, the Gould study[44] did not contribute to the SOE assessment for screening of ICU patients for MRSA carriage compared to no screening. Outcomes data for this study is presented in the Appendix F.

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is health care-associated, rather than imported. One good quality study,[46] three poor quality studies,[29,45,47] and one non-CCS study[51] addressed this outcome. The Huskins study,[46] a good quality study, was a cluster RCT and the poor quality studies[29,45,47] and the non-CCS study[51] utilized quasi-experimental designs.

The definitions of hospital-associated infection differed from study to study. The Huskins study[46] defined hospital-associated as a positive-MRSA sample 2 or more days after admission to the ICU in a patient whose ICU length of stay was at least 3 days with no history of colonization or infection in the prior year, no positive clinical culture within two days after admission to the ICU, and a negative surveillance culture within 2 days of admission to the ICU. The Huang study[29] defined hospital-associated infection as a first-ever MRSA-positive sample more than 2 days after admission if not previously hospitalized at that institution within the prior year, or at any time during the hospital admission if hospitalized at that institution in the prior year. The Raineri study[47] defined ICU-associated as a MRSA-positive isolate identified at least 48 hours after admission in patients with no previous MRSA isolate documented and at least one negative screen from the ICU. The Holzmann-Pazgal study[45] defined hospital-acquired as the initial isolation of MRSA in any specimen obtained more than 48 hours after admission. The non-CCS study[51] defined colonization or infection as hospital-associated if the MRSA-positive sample was obtained more than 72 hours after admission.

Compared to no screening, the good quality study[46] found a nonstatistically significant increase in healthcare-associated MRSA colonization or infection with screening for MRSA carriage in the ICU. However, the poor quality studies[29,45,47] found a statistically significant reduction in hospital-acquired MRSA colonization or infection with screening for MRSA carriage in the ICU, as did the non-CCS study.[51]

Strength of Evidence

The SOE to evaluate the effect of screening for MRSA carriage in ICU patients compared to no screening on healthcare-associated MRSA acquisition was determined to be insufficient. Of the four CCS-studies[29,45-47] that evaluated this outcome, the Huskins study was a good quality, cluster RCT,[46] while the Huang study,[29] the Holzmann-Pazgal study[45] and the Raineri study[47] were quasi-experimental before/after studies of poor quality. For the group of studies, the risk of bias was deemed to be low because of the good quality RCT that addressed this outcome. With targeted screening, the Huskins RCT[46] found a nonstatistically significant increase in healthcare-associated MRSA colonization or infection. However, the Huang,[29] Raineri,[47] and Holzmann-Pazgal[45] studies found statistically significant reductions in healthcare-associated colonization or infection. Because the estimates of effect have different directions, the results were inconsistent.

The studies addressed healthcare-associated MRSA acquisition, an intermediate and therefore, indirect outcome. Because the individual studies did not consistently report statistically significant results, the findings were imprecise. The evidence base included a RCT of good quality, so the starting level for the SOE was high. However, the lack of consistency and lack of precision raised serious concerns. With targeted screening, the RCT[46] found a nonstatistically significant increase in healthcare-associated MRSA colonization or infection, while the quasi-experimental studies[29,45,47] found statistically significant reductions in healthcare-associated colonization or infection. Due to the very serious concern related to uncertainty about the direction of effect (opposite direction of effect with the RCT and the quasi-experimental studies), the SOE was reduced by two levels. The SOE was further reduced by one level due to lack of precision, another serious concern. In summary, the SOE to evaluate the effect of screening of ICU patients for MRSA carriage on MRSA acquisition is insufficient.

The cluster RCT[46] was criticized in the literature because of lengthy turnaround time of the screening test used in the study and the failure to implement contact precautions and/or isolation while awaiting test results.[86] Therefore, we conducted a sensitivity analysis, excluding the cluster RCT[46] from the SOE analysis. Because the evidence base for this outcome would then include only observational studies, the starting level for the SOE would be low. SOE would be lowered by the high risk of bias (because of only three observational studies of poor quality in the evidence base). Therefore, even if the Huskins trial[46] was excluded from the studies that evaluated this outcome, the SOE to evaluate the effect of screening of ICU patients for MRSA carriage on MRSA acquisition would remain insufficient.

Comment, Non-CCS Studies

One non-CCS study[51] evaluated the impact of screening for MRSA carriage in the ICU on healthcare-associated MRSA transmission. The non-CCS study by de la Cal and colleagues[51] found a statistically significant reduction in hospital-acquired MRSA colonization or infection with screening of ICU patients for MRSA carriage.

Healthcare-Associated MRSA Infection, Irrespective of Site

One good quality study,[30] one poor quality study[55] and four[49,50,52,53] non-CCS studies addressed this outcome. The definitions of hospital-associated MRSA infections were diverse. The Robicsek study[30] defined infection as the sum total of all bloodstream infections (positive blood culture in the absence of a positive clinical culture from another site), respiratory tract infections (positive respiratory culture, compatible chest radiograph and decision to treat), urinary tract infections (positive urine culture and decision to treat or growth of more than 100,000 colony-forming units/mL plus at least 50 leukocytes per high-power field), and SSIs (positive culture of a surgical site). Infections were considered to be hospital associated if they occurred more than 2 days after admission and within 30 days of discharge. The Muder study[55] used the CDC definition of healthcare-associated infection. The Clancy study[50] defined hospital-associated infection as the first clinical specimen (ordered to evaluate for infection) positive for MRSA more than 72 hours after admission. The Simmons study[53] defined hospital-associated MRSA rates using the National Nosocomial Infection Surveillance system. The study by Boyce and colleagues[49] utilized CDC criteria to define hospital-associated infection. Patients were considered to have a hospital-associated MRSA infection if the infection began more than 3 days after admission to the ICU in a patient with no prior history of MRSA. The Kurup study[52] utilized CDC criteria to define infection. Patients were considered to have a hospital-associated

MRSA infection if the first MRSA isolate from any source was recovered more than 24 hours after ICU admission in a patient with no known prior history of MRSA.[52]

Compared to no screening, the good quality study[30] found a reduction in hospital-acquired MRSA infection with screening of ICU patients for MRSA carriage (rate difference -1.46 [95% CI: -3.43 to 0.51]); however, this reduction was not statistically significant. The poor quality study[55] found a statistically significant reduction in the rate of healthcare-associated infection with screening of ICU patients for MRSA carriage (rate 5.45/1000 patient-days prior to the intervention, 1.35/1000 patient-days following the intervention, a 75 percent reduction, p=0.001). In addition, compared to no screening, one[52] of the non-CCS studies found no statistically significant reduction in hospital-acquired MRSA infection with screening of ICU patients for MRSA carriage. However, two[49,53] of the non-CCS studies found a statistically significant reduction in hospital-acquired MRSA infection with screening of ICU patients for MRSA carriage. In addition, compared to no screening, one[50] of the non-CCS studies found a statistically significant reduction in hospital-acquired MRSA infection in the surgical ICU, as well as in the pooled analysis of the surgical ICU, medical ICU, and wards with screening for MRSA in the ICU. However, this same study[50] found no statistically significant reduction in hospital-acquired MRSA infection in the medical ICU or the wards.[50]

Strength of Evidence

The SOE to evaluate the effect of screening for MRSA carriage in ICU patients compared to no screening on healthcare-associated MRSA infection was determined to be insufficient. Two CCS studies[30,55] addressed this outcome. The Muder study[55] utilized a before/after design and was judged to be of poor quality because it did not report baseline characteristics, addressing autocorrelation, and whether its analysis controlled for confounders. The Robicsek study[30] was an interrupted time series design judged to be of good quality. The risk of bias was judged as high, as the body of evidence that evaluated this outcome included only quasi-experimental studies, only one of which was of good quality. With screening, the Robicsek study[30] found a reduction in healthcare-associated MRSA infection (rate difference -1.46; 95% CI: -3.43 to 0.51); however, this reduction was not statistically significant. With segmented Poisson regression, the change in the rate of healthcare-associated infection was -36.2 percent (95% CI: -65.4 to 9.8). The Muder study[55] found a statistically significant reduction in healthcare-associated MRSA infection with screening (rate 5.45/1000 patient-days prior to the intervention, 1.35/1000 patient-days following the intervention, a 75 percent reduction, p=0.001). Therefore, the results were consistent, because both studies showed a reduction in infection with screening. The studies evaluated MRSA infection, a health outcome. Therefore, the outcome was direct. Because the individual studies did not consistently report statistically significant results, the findings were imprecise. Because the evidence base for this outcome includes only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias and the lack of precision. In summary, the SOE is insufficient to support or refute that, compared to no screening, screening for MRSA carriage in ICU patients decreases healthcare-associated MRSA infection.

Comment, Non-CCS Studies

Four non-CCS studies evaluated the impact of screening for MRSA carriage in the ICU on healthcare-associated MRSA infection, regardless of site.[49,50,52,53] Compared to no screening, all of these studies demonstrated a reduction in healthcare-associated MRSA infection with

screening of ICU patients for MRSA carriage. For two[49,53] of these studies, the reduction was statistically significant, while for one[52] of the studies it was not. For another[50] of the non-CCS studies, the reduction was statistically significant in some settings, but not in others.

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

One good quality study,[30] one poor quality study,[29] and one non-CCS study[51] addressed this outcome. The good quality study[30] by Robicsek, which also reported MRSA infection irrespective of site, defined bloodstream infection as a positive blood culture in the absence of a positive clinical culture from another site. Infections were considered to be hospital associated if they occurred more than 2 days after admission and within 30 days of discharge. The poor quality study[29] defined hospital-associated cases as those with a first-ever MRSA-positive blood culture more than 2 days after admission if not previously hospitalized at that institution within the prior year, or at any time during the hospital admission if hospitalized at that institution in the prior year. The non-CCS study[51] used the term "positive diagnostic sample" rather than infection to avoid bias in the definition of some infections (e.g., ventilator-associated pneumonia). Diagnostic samples (those performed for reasons other than surveillance) were considered hospital associated if the sample was obtained more than 72 hours after admission.

The good quality study[30] found no statistically significant reduction in the rate of acquired MRSA bloodstream infection with screening for MRSA in the ICU compared to no screening for MRSA (absolute change in prevalence density -0.18 (95% CI: -0.99 to 0.62). Compared to no screening for MRSA, the poor quality study[29] found a statistically significant reduction in the trend of the hospital-associated incidence density of MRSA bloodstream infection in the ICU, non-ICU settings, and hospital wide with screening for MRSA in the ICU. In addition, this study[29] found a statistically significant reduction in the trend of the hospital-associated incidence of MRSA bloodstream infection hospital wide with screening for MRSA in the ICU. The non-CCS study[51] found a statistically significant reduction in the rate of acquired MRSA bacteremia (including bloodstream infection) with screening for MRSA in the ICU compared to no screening for MRSA.

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in ICU patients compared to no screening on healthcare-associated MRSA bacteremia or bloodstream infection was judged to be insufficient. Two CCS studies addressed this outcome; the Robicsek study was a limited time series design[30] of good quality and the Huang study was a before/after study[29] of poor quality because it did not report baseline group characteristics and whether its analysis controlled for confounders. The risk of bias was deemed to be high as the body of evidence was comprised of quasi-experimental studies, only one of which was good quality[30]. Because both studies showed a reduction in MRSA bacteremia or bloodstream infection with screening, the results were consistent. The studies evaluated healthcare-associated MRSA bacteremia or bloodstream infection, which are health outcomes. Therefore, the outcome was direct. Because the individual studies did not consistently report statistically significant results, the findings were imprecise. Because the evidence base for this outcome includes only quasi-experimental studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias and the lack of precision. In summary, the SOE is insufficient to support or refute that compared to no screening, screening for MRSA carriage in ICU patients decreases healthcare-associated MRSA bacteremia or bloodstream infection.

Comment, Non-CCS Studies

One non-CCS study[51] evaluated the impact of screening for MRSA carriage in the ICU on healthcare-associated MRSA bacteremia or bloodstream infection. Compared to no screening, this study[51] found a statistically significant reduction in the rate of acquired MRSA bacteremia (including bloodstream infection) with screening for MRSA in the ICU.

Healthcare-Associated MRSA Surgical Site Infection

One good quality study[30] addressed this outcome. The Robicsek study found a reduction in hospital-associated SSIs with screening in the ICU compared to no screening; however, this reduction was not statistically significant.[30] With screening, the study found no statistically significant reduction in healthcare-associated MRSA infection (rate difference -0.77; 95% CI: -1.85 to 0.30).

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in ICU patients compared to no screening on healthcare-associated MRSA SSI was judged to be insufficient. One CCS study addressed this outcome; it was a limited time series design of good quality.[30] The risk of bias was deemed to be high as the body of evidence consisted of only a single good quality observational study.[30] Because only one study addressed this outcome, the consistency was unknown. The study evaluated SSI, a health outcome. Therefore, the outcome was direct. Because the study did not report statistically significant results, the findings were imprecise. Because the evidence base for this outcome included only one observational study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening of ICU patients on healthcare-associated MRSA SSI is judged to be insufficient.

Morbidity, Mortality, Harms and Resource Utilization

Results

No studies addressed these outcomes.

Strength of Evidence for Screening of ICU Patients for MRSA Carriage on Morbidity, Mortality, Harms and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of screening of ICU patients for MRSA carriage on morbidity, mortality, harms or resource utilization is judged to be insufficient.

Summary Strength of Evidence Across Key Question 3A

A summary of the main syntheses for this question follows in Table 13.

Table 13. Strength of evidence for studies comparing screening of ICU patients versus no screening

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Screening of ICU Risk Pts Vs No Screening	MRSA Acquisition	1 RCT (N=4,056) (Huskins 2011[46]) 3 QEX (N=3097) (Holzmann-Pazgal 2011[45]) (N=Unclear) (Huang 2006[29]) (N=21,754; 166,877[‡]) (Raineri 2007[47])	Low	Inconsistent	Indirect	Imprecise	Insufficient
	MRSA Infection	2 QEX (N=Unclear) (Robicsek 200830) (N=Unknown) Muder 2008[55]	High	Consistent	Direct	Imprecise	Insufficient
	MRSA Bacteremia or Blood Stream Infection	2 QEX (N=Unclear) (Robicsek 2008[30]) (N=Unclear) (Huang 2006[29])	High	Consistent	Direct	Imprecise	Insufficient
	MRSA Surgical Site Infection	1 QEX (N=Unclear) (Robicsek 2008[30])	High	Unknown	Direct	Imprecise	Insufficient

ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable; QEX = quasi-experimental; RCT = randomized controlled trial

[§]Studies that controlled for confounding and/or trend.

[‡] Patient days.

Key Question 3B. Screening of Surgical Patients for MRSA Carriage Compared With No Screening

Overview

This section describes the literature that evaluates screening surgical patients for MRSA carriage compared to no screening. After an overview of the literature, the results are described for each outcome measure: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. Within the category of MRSA infection, we also included results for MRSA SSI, as some studies present this outcome rather than the broader outcome of MRSA infection, irrespective of site. The emphasis in this chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. SOE syntheses presented here include only CCS studies. Because studies that use simple two-group statistical analyses cannot support causal inferences, the non-CCS studies were excluded from the SOE analysis. Following each SOE synthesis, we comment on the results seen in non-CCS studies. Table 14 summarizes the

studies reviewed for Key Question 3B. The study quality details for CCS studies are shown in Table 15.

Table 14. KQ3B: Healthcare-associated MRSA acquisition, infection, or surgical site infection

Outcome	Study	Quality	Statistical Result	Synthesis
HCA acquisition	Harbarth et al., 2008[31]	Good	NSS ↑	SOE = insufficient
	Ellingson et al., 2011[56]	Poor	NSS ↓	
HCA infection	Harbarth et al., 2008[31]	Good	NSS ↑	SOE = insufficient
	Muder et al., 2008[55]	Poor	SS ↓	
	Kelly et al., 2012[68]	Non-CCS	NSS ↓	
	Sankar et al., 2008[57]	Non-CCS	SS ↓	
HCA surgical site infection	Harbarth et al., 2008[31]	Good	NSS ↑	SOE = insufficient Comment: Results from non-CCS studies more consistently favorable than CCS studies, however causal inference is not possible
	Chen et al., 2012[69]	Non-CCS	NSS ↓	
	Jog et al., 2008[58]	Non-CCS	SS ↓	
	Keshtgar et al., 2007[74]	Non-CCS	SS ↓	
	Kim et al., 2010[59]	Non-CCS	SS ↓	
	Lipke et al., 2010[60]	Non-CCS	NSS ↓	
	Malde et al., 2006[61]	Non-CCS	SS ↓	
	Nixon et al., 2006[62]	Non-CCS	SS ↓/NSS ↓[a]	
	Pofahl et al., 2009[63]	Non-CCS	SS ↓NSS ↓[b]	
	Schelenz et al., 2005[81]	Non-CCS	NSS ↓	
	Sott et al., 2001[64]	Non-CCS	NSS ↓	
	Supriya et al., 2009[65]	Non-CCS	SS ↓	
	Thomas et al., 2007[66]	Non-CCS	SS ↓	
	Walsh et al., 2011[67]	Non-CCS	SS ↓	

CCS = studies controlling for confounding and/or secular trend; non-CCS = studies not controlling for confounding and/or secular trend; HCA = Healthcare-associated; KQ = Key Question; NSS = not statistically significant; SOE = strength of evidence; SS = statistically significant

[a]The reduction in rate was statistically significant for patients admitted emergently, though not for patients admitted electively and screened prior to admission.

[b]The reduction in rate was statistically significant for patients who underwent joint replacement, though not for patients undergoing other surgical procedures.

Eighteen studies described screening surgical patients for MRSA compared to no screening. Three[31,55,56] were CCS studies; 15 were non-CCS studies. The Harbarth study[31] was a prospective, interventional cohort study with crossover design. This study[31] was judged to be of good quality overall because it presented baseline characteristics for the intervention and control groups, conducted appropriate analyses (tested for trend, addressed autocorrelation and controlled for at least one confounder) and reported on an important (healthcare-associated) outcome. The Muder study[55] was a quasi-experimental before/after study design. This study[55] was judged to be of poor quality, as it did not report baseline group characteristics, addressing autocorrelation, and whether its analysis controlled for confounders. The Ellingson study[56] was a quasi-experimental study with an interrupted time series design. This study[56] was determined to be of poor quality as it did not report baseline group characteristics or whether its analysis controlled for confounders. Of the 14 non-CCS studies, all employed a quasi-experimental before/after study design.

Table 15. KQ3B: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Harbarth et al., 2008[31]	Pt-days, direct admissions, surgical procedures, length of stay, antibiotics, ABHRs	Poisson regression, ANCOVA	Y	Accounted for	Y (Colonization pressure, ABHRs, antibiotic selection pressure)	Y	Good
Muder et al., 2008[55]	NR	Segmented Poisson regression	Y	NR	NR	N	Poor
Ellingson et al., 2001[56]	NR	Interrupted time series analysis with Poisson model	Y	Tested for	NR	N	Poor

ABHR = alcohol-based hand rubs; ANCOVA = analysis of covariance; CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; ICP = infection control practices; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; N = no; NR = not reported; Pt = patient; Y = yes
*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

All 18 studies evaluated patients undergoing a surgical procedure. There was considerable variation in the type of surgical patient targeted for screening. Five studies[31,55,60,63,74] included patients across a broad range of surgeries. Six studies[57,59,62,64,68,69] focused on orthopedic surgery patients (including spine surgery) and three studies[58,67,81] focused on cardiothoracic surgery patients. Three studies included very specific surgical patient populations (e.g., vascular,[61] head and neck cancer,[65] percutaneous endoscopic gastrostomy placement[66]) One study[56] evaluated patients admitted to a surgical ward, but did not describe the type(s) of surgical patients included. The 18 studies were all conducted in Europe or the U.S. (one Swiss study, seven U.S. studies, and ten U.K./Ireland studies).

The MRSA screening protocol varied among studies, as did the infection control practices that accompanied screening. In terms of the MRSA screening protocol, five studies[31,58,59,63,74] utilized PCR to screen for MRSA and nine studies utilized culture.[55,56,61,62,64-67,69] Four studies did not specify whether PCR or culture was utilized to screen for MRSA.[57,60,68,81] While waiting for screening test results, two studies[55,63] utilized contact isolation for at least some patients. Four studies[58,62,67,74] initiated MRSA eradication by topical antimicrobial wash and/or intranasal antibiotics. When bed availability allowed, one study[68] isolated high-risk populations (e.g., health care workers, nursing home residents and those known to be previously colonized or infected with MRSA) while waiting for screening results. Eleven studies did not describe the initiation of special procedures while waiting for screening results. Ten studies[57,60- 64,67- 69,74] screened at least some patients prior to hospitalization, so MRSA status was known prior to hospitalization. Once patients were found to be MRSA positive, studies varied in the number of interventions applied. The most intensive combination included four elements (contact isolation, intranasal antibiotics, topical antimicrobials, and adjustment in systemic antibiotics) at the time of surgery for four studies.[31,59,62,81] Seven studies[58,61,63,64,66,67,74] used a protocol with intranasal antibiotics, topical antimicrobials, and adjustment in systemic antibiotics, but did not describe contact isolation procedures. The study by Kelly[68] used intranasal antimicrobials and/or topical

antimicrobials, isolation and repeat swabs. The remaining six studies used two or fewer procedures in various combinations.

The control arms of each of the sixteen studies included no systematic screening for MRSA. However, the infection control practices of the control groups did vary considerably especially in cases where an individual with MRSA was identified during routine care. In the study by Harbarth et al.,[31] control period patients found to have MRSA were treated just as they were in the intervention periods with a combination of isolation, intranasal antibiotics, topical antimicrobial wash, and adjusted use of systemic antibiotic prophylaxis. In the study by Nixon,[62] again, intranasal antibiotics and topic antimicrobial wash were used. Walsh and colleagues[67] isolated patients with MRSA and adjusted the use of systemic antibiotic prophylaxis. Three other studies[58,63,65] described isolating or cohorting patients found to have MRSA during control periods. Most studies provided very little specific information about routine care for patients without MRSA during control periods.

Study durations were divided into control periods and intervention periods of varying lengths. Seven studies had observation periods of two years or more.[31,55,56,61,66-68] Two studies[62-65] had observation periods less than 1 year. The remaining nine studies[57-60,63,66,69,74,81] had observation periods of 1 to 2 years. Six studies[58-60,63,67,81] identified MRSA SSI rates as the primary endpoint of interest. Three studies[31,65,66] used broader MRSA endpoints such as MRSA infection rates. Ellingson et al.,[56] Sankar et al.,[57] Kelly et al.,[68] and Nixon et al.,[62] identified the incidence of MRSA colonization or infection as the primary endpoint. Malde et al.,[61] identified wound infection, major limb amputation and death as primary endpoints. Sott et al.,[64] identified postoperative sepsis associated with MRSA as the primary endpoint. Muder et al.,[55] identified the effectiveness of an industrial systems-engineering approach to a MRSA prevention program as its primary endpoint. Keshtgar et al.,[74] described the rate of MRSA SSI and bacteremia as the primary endpoints. Chen et al,[69] identified the prevalence of MRSA colonization and the rate of MRSA SSI as the primary endpoints.

Results by Outcome

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is health care-associated, rather than imported.

Results

Two CCS studies addressed this outcome. The study by Harbarth et al.,[31] a good quality study with a crossover design, specifically evaluated the incidence of nosocomial MRSA acquisition which included both new infection and colonization. With screening of surgical patients, Harbarth et al.,[31] found an increase in the rate ratio for MRSA acquisition to 1.1, but the confidence intervals were wide and not statistically significant (95% CI: 0.8-1.4). The study by Ellingson et al,[56] a poor quality study with an interrupted time series design evaluated the incidence of MRSA colonization and infection. With screening of surgical patients, Ellingson et al.,[56] found the intervention resulted in an incidence rate ratio of 0.775, but the confidence intervals were wide and not statistically significant (0.371-1.617). Ellingson et al.,[56] also found a reduction in the trend in the incidence of MRSA colonization or infection (incidence rate ratio 0.958), but the confidence intervals were not statistically significant (0.909-1.009).

Strength of Evidence

The SOE for the effect of screening surgical patients for MRSA carriage compared to no screening on healthcare-associated MRSA acquisition was judged to be insufficient. Two CCS studies addressed this outcome; the Harbarth study was a good quality quasi-experimental study[31] with a crossover design and the Ellingson study[56] was a poor quality study with an interrupted time series design. The Ellingson study[56] was determined to be of poor quality as it did not report baseline group characteristics or whether its analysis controlled for confounders. The risk of bias was deemed to be high because the body of evidence consisted of quasi-experimental studies, only one of which was good quality. The findings were inconsistent, because one study[31] found an increase in MRSA acquisition with screening and the other[56] found a reduction. Thus, the direction of effect differed between the two studies. The studies addressed healthcare-associated MRSA acquisition, an intermediate and therefore, indirect outcome. The study findings were judged to be imprecise because the individual studies did not consistently report statistically significant results. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias, lack of consistency and lack of precision. In summary, the SOE for the effect of screening of surgical patients on healthcare-associated MRSA acquisition is judged to be insufficient.

Healthcare-Associated MRSA Infection, Irrespective of Site

Four studies reported the effect of MRSA screening in surgical wards on healthcare-associated MRSA infection. The Harbarth and Muder[31,55] studies were CCS studies, while the Sankar and Kelly studies[57,68] were non-CCS studies.

For the Harbarth study,[31] infection was defined as hospital-acquired if it occurred more than 48 hours after admission and less than 72 hours after discharge from the surgical service. This endpoint was assessed among patients with previously known or newly identified MRSA carriage. With screening of surgical patients, Harbarth and colleagues[31] found no reduction in the rate of acquired MRSA infection. In fact, the rate of MRSA infection was slightly higher in the intervention group than in the control group (1.11/1000 patient days vs. 0.91/1000 patient days) but was not statistically significant.[31] This analysis adjusted for colonization pressure, antibiotic selection pressure, use of alcohol-based hand rubs, temporal trends, and clustering.

For the Muder study,[55] healthcare-associated MRSA infection was based on CDC definitions. Using a segmented Poisson regression, Muder and colleagues[55] found that MRSA infection steadily declined in the surgical ward (1.56/1000 patient days pre, 0.63/1000 patient days post, p=0.003).

Sankar et al.,[57] did label MRSA outcomes as hospital-acquired infection but did not provide a specific definition. Sankar et al.,[57] reported that the proportion of patients with MRSA infection declined from 2.4 percent (4/164) to 0.0 percent (0/231) in an unadjusted analysis. Kelly et al.,[68] defined MRSA infection according to the CDC guidelines for the prevention of SSIs. With screening for MRSA, Kelly et al.,[68] reported a reduction in MRSA infection from 0.49 percent prior to the intervention to 0.35 percent after the intervention. However, this reduction was not statistically significant (p=0.108).

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in surgical patients compared to no screening on healthcare-associated MRSA infection was judged to be insufficient. Two CCS

studies addressed this outcome; the Harbarth study[31] was a prospective, interventional cohort study with crossover design of good quality and the Muder study[55] was a before/after study of poor quality. The Muder study[55] was determined to be of poor quality because it did not report baseline group characteristics, addressing autocorrelation, and whether its analysis controlled for confounders. The risk of bias was judged to be high because the body of evidence that evaluated this outcome included only quasi-experimental studies, only one of which was of good quality[31]. With screening in surgical patients, Harbarth and colleagues found no reduction in MRSA infection. On the contrary, the rate was slightly higher, though not statistically significant.[31] On the other hand, the Muder study[55] found a statistically significant reduction in MRSA SSI. The findings were inconsistent, because one study[31] found an increase in MRSA acquisition with screening and the other[56] found a reduction. Thus, the direction of effect differed between the two studies. Both studies[31,55] evaluated healthcare-associated MRSA infection, a health outcome and therefore, a direct outcome measure. The study findings were judged to be imprecise because the individual studies did not consistently report statistically significant results. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias, lack of consistency and lack of precision. In summary, the SOE for the effect of screening for MRSA carriage in surgical patients on healthcare-associated MRSA infection is judged to be insufficient.

Comments, Non-CCS Studies

Two non-CCS studies[57,68] evaluated the impact of screening for MRSA carriage in surgical patients on healthcare-associated MRSA infection. Compared to no screening, these studies[57,68] found a statistically significant reduction in the rate of healthcare-associated MRSA infection with screening for MRSA in surgical patients.

MRSA Surgical Site Infection

Fourteen of 18 surgical ward studies reported on MRSA SSI. For three studies, SSI due to MRSA was attributed to surgery if it was documented within 30 days following the surgical procedure.[31,59,67] In addition, the Walsh study[67] attributed the SSI to surgery if the sternum or deep-organ space was involved within one year of surgery. These three studies also defined MRSA acquisition with some specificity. The Harbarth study,[31] a good quality study, found no difference in the rate of MRSA SSI after adjustment for covariates. With screening in surgical patients, Harbarth and colleagues[31] found an increase in MRSA SSI which was not statistically significant (rate ratio 1.2; 95% CI: 0.8-1.7). On the other hand, Kim and colleagues[59] and Walsh and colleagues,[67] both non-CCS studies, found significant reductions in the proportion of surgical patients experiencing MRSA SSI.

The remaining non-CCS surgical ward studies, that addressed MRSA SSI varied in their specific definition of a MRSA SSI. Four of the studies mentioned criteria for identifying MRSA SSI such as the Nosocomial Infection Surveillance System criteria.[58,60,63,64] Six studies[61,62,65,66,69,81] required both signs of an infected wound and a positive wound swab for MRSA to identify a MRSA SSI. The Keshtgar study[74] relied on its hospital wound team to identify SSI through observation, questioning of staff, examination of medical records, and contact with patients by phone or mail.

For all of the non-CCS, the point estimates for MRSA SSI rates were lower in screening periods in comparison to control periods. In seven studies[58,59,61,65-67,74] these differences in rates were statistically significant. For four studies,[60,63,69,81] the reductions were not statistically

significant. For the Nixon study,[62] the reduction in rate was statistically significant for patients admitted emergently, though not for patients admitted electively and screened prior to admission. In the Pofahl study,[63] the reduction in rate was statistically significant for patients who underwent joint replacement, though not for patients undergoing other surgical procedures.

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in surgical patients compared to no screening on MRSA SSI was judged to be insufficient. One CCS studies addressed this outcome; the Harbarth study[31] was a prospective, interventional cohort study with crossover design of good quality. The risk of bias was judged to be high because the body of evidence that evaluated this outcome included only quasi-experimental study. With screening in surgical patients, Harbarth and colleagues found no reduction in MRSA SSI; in fact the rate was slightly higher, though not statistically significant.[31] The consistency of the findings is unknown, because only one study addressed this outcome. The study evaluated MRSA SSI, a health outcome and therefore, a direct outcome measure. The study findings were judged to be imprecise because the individual study did not report statistically significant results. Because the evidence base for this outcome included only one observational study, the starting level for the SOE was low. The SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening for MRSA carriage in surgical patients on MRSA SSI is judged to be insufficient.

Comment, Non-CCS Studies

Thirteen non-CCS studies evaluated the impact of screening for MRSA carriage in surgical patients on healthcare-associated MRSA infection. Compared to no screening, all of the non-CCS studies found a reduction in the rate of MRSA SSI with screening for MRSA carriage in surgical patients. For seven of these studies, the reduction was statistically significant.[58,59,61,65-67,74] For one study[62] the reduction was statistically significant for one outcome, but not for another; and for five studies,[60,63,64,69,81] the reduction was not statistically significant.

Morbidity

No CCS studies evaluated the impact of screening for MRSA carriage in surgical patients on morbidity. However, one non-CCS quasi-experimental study formally evaluated MRSA morbidity. Malde and colleagues[61] were specifically interested in major limb amputations among patients who were found to have MRSA colonization or infection. From the Malde study,[61] amputation rates declined significantly from 27.8 percent to 9.0 percent for patients with elective admissions. For patients with emergency admissions, the rate of amputation did decline from 50.0 percent to 38.8 percent, but this was not statistically significant.

Strength of Evidence

Because no CCS studies addressed this outcome, the SOE to evaluate the effect of screening for MRSA carriage in surgical patients on morbidity is judged to be insufficient.

Comment, Non-CCS Studies

One non-CCS study addressed this outcome. With screening, Malde and colleagues[61] found a statistically significant reduction in amputation rates from 27.8 percent to 9.0 percent for patients admitted electively. For patients with emergency admissions, the rate of amputation declined from 50.0 percent to 38.8 percent, but this was not statistically significant.[61]

Mortality

Results

No CCS studies evaluated the impact of screening for MRSA carriage in surgical patients on mortality. However, one non-CCS quasi-experimental study reported on mortality rates among patients with MRSA colonization or infection.

In the study by Malde and colleagues[61] for both elective and emergency admissions, mortality rates for patients with MRSA declined with screening.[61] However, these reductions were not statistically significant.

Strength of Evidence

Because no CCS studies addressed this outcome, the SOE to evaluate the effect of screening for MRSA carriage in surgical patients on mortality is judged to be insufficient.

Comment, Non-CCS Studies

One non-CCS study[61] addressed this outcome. With screening, Malde and colleagues[61] found reductions in mortality for patients admitted electively or emergently. However, these reductions were not statistically significant.[61]

Harms

Results

No studies addressed this outcome.

Strength of Evidence for Screening of Surgical Patients for MRSA Carriage on Harms

Because no studies addressed this outcome, the SOE to evaluate the effect of screening of surgical patients for MRSA carriage on harms is judged to be insufficient.

Resource Utilization

Results

No CCS studies evaluated the impact of screening for MRSA carriage in surgical patients on resource utilization. However, one non-CCS quasi-experimental study reported the impact of screening surgical patients for MRSA carriage on resource utilization. Sankar and colleagues[57] found that with screening, the mean length of hospital stay declined by almost one day. In unadjusted analysis, this result was found to be statistically significant.[57]

Strength of Evidence

Because no CCS studies addressed this outcome, the SOE to evaluate the effect of screening for MRSA carriage in surgical patients on resource utilization is judged to be insufficient.

Comments, Non-CCS Studies

One non-CCS study[57] addressed this outcome. With screening, Sankar and colleagues[57] found a reduction in the mean length of hospital stay of almost one day. In unadjusted analysis, this result was found to be statistically significant.[57]

Summary Strength of Evidence Across Key Question 3B

A summary of the main syntheses for this question follows in Table 16.

Table 16. Strength of evidence for studies comparing screening of surgical patients versus no screening

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Screening of Surgical Pts Vs No Screening	MRSA Acquisition	1 QEX -crossover design (N=21,754) (Harbarth 2008[31]) 1 QEX (N=Unclear) (Ellingson 2011[56]	High	Inconsistent	Indirect	Imprecise	Insufficient
	MRSA infection	1 QEX -crossover design (N=21,754) (Harbarth 2008[31]) 1 QEX (N=21,449[‡]) (Muder 2008[55])	High	Inconsistent	Direct	Imprecise	Insufficient
	MRSA Surgical Site Infection	1 QEX - crossover design (N=21,754) (Harbarth 2008[31])	High	Unknown	Direct	Imprecise	Insufficient

MRSA = methicillin-resistant *Staphylococcus aureus*; QEX = quasi-experimental
[§]Studies that controlled for confounding and/or trend.
[‡] Patient days.

Key Question 3C. Screening of High-Risk Patients for MRSA Carriage Compared With No Screening

Overview

This section describes the literature that evaluates screening of high-risk patients for MRSA carriage compared to no screening. Studies defined high risk based on the patient population (e.g., transferred from a nursing home or other health care facility) or the ward (e.g., high prevalence of MRSA transmission or infection). After an overview of the literature, the results are described for each outcome measure: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. Within the category of MRSA infection, we also included results for MRSA bacteremia or bloodstream infection and for MRSA SSI, as some studies present these outcomes rather than the broader outcome of MRSA infection irrespective of site. The emphasis in this chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. SOE syntheses presented here include only CCS studies. Because studies that use simple two-group statistical analyses cannot support causal inferences, the non-CCS studies were excluded from the SOE analysis. Following the SOE syntheses, we comment on the pattern of results seen in non-CCS studies. Table 17 summarizes the studies reviewed for Key Question 3C. Table 18 shows study quality details for CCS studies.

Table 17. KQ3C: Healthcare-associated MRSA acquisition, infection, bacteremia, or surgical site infection

Outcome	Study	Quality	Statistical Result	Synthesis
HCA acquisition	Rodriguez-Bano et al., 2010[72]	Poor	NSS ↓	SOE = insufficient Comment: Causal inference is not possible based on non-CCS studies
	Salaripour et al., 2006[76]	Non-CCS	SS ↓	
HCA infection	Harbarth et al., 2000[71]	Poor	SS ↓	SOE = insufficient
	Bowler et al., 2010[73]	Non-CCS	SS ↓	
	Wernitz et al., 2005[77]	Non-CCS	SS ↓	
HCA bacteremia/ blood stream infection	Rodriguez-Bano et al., 2010[72]	Poor	SS ↓	SOE = insufficient Comment: Causal inference is not possible based on non-CCS studies
	Chowers et al., 2009[70]	Poor	SS ↓	
	Wernitz et al., 2005[77]	Non-CCS	SS ↓	
	Pan et al., 2005[75]	Non-CCS	SS ↓	
HCA surgical site infection	Harbarth et al., 2000[71]	Poor	SS ↓	SOE = insufficient Comment: Causal inference is not possible based on non-CCS studies
	Keshtgar et al., 2008[74]	Non-CCS	SS ↓	

HCA = healthcare-associated; KQ = Key Question; non-CCS = studies not controlling for confounding and/or secular trend; NSS = not statistically significant; SOE = strength of evidence; SS = statistically significant

Eight studies described screening of high-risk patients for MRSA carriage compared to no screening. Three were CCS studies[70-72] and five[73-77] were non-CCS studies. Of the CCS studies, all of the studies were of poor quality.[70-72] The Rodriguez-Bano[72] study was determined to be of poor quality because it did not perform an appropriate analysis (it performed indirect control of confounders rather than statistical adjustment within the segmented regression analysis). The study by Chowers et al.[70] was judged to be of poor quality as it did not report baseline group characteristics or whether its analysis controlled for confounders. The Harbarth study[71] was also determined to be of poor quality as it did not report baseline group characteristics, addressing autocorrelation, or whether its analysis controlled for confounders.

All eight studies employed a quasi-experimental study design. The study by Rodriguez-Bano and colleagues, which was of poor quality[72] utilized an interrupted times series design, as did the study by Chowers and colleagues,[70] another poor quality study. The other studies utilized a before/after study design. In terms of clinical setting, all eight studies evaluated hospitalized patients. Four of the studies took place in teaching hospitals, two in community hospitals, and one in a regional referral hospital.

Table 18. KQ3C: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Harbarth et al., 2000[71]	NR	Poisson regression	N	NR	NR	N	Poor
Chowers et al., 2009[70]	NR	Poisson regression	Y	Tested for	NR	N	Poor
Rodriguez-Bano et al., 2010[72]	Age, number diagnoses, antibiotics	segmented regression, D-W test	Y	Tested for	N (indirect control)	N	Poor

CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; KQ = Key question; MRSA = methicillin-resistant *Staphylococcus aureus*; N = No; NR = not reported; Y = yes
*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

"Screening of high-risk patients" was defined differently across studies. The study by Rodriguez-Bano and colleagues[72] evaluated the screening of patients on high-risk wards as well as high-risk patients. High-risk wards were defined based on clinical epidemiology. High-risk patients were those who were readmitted or who were admitted from long-term care facilities or other hospitals. The Harbarth[71] study also evaluated the screening of patients on high-risk wards as well as high-risk patients. High-risk patients were patients known to have been previously colonized or infected with MRSA or roommates of patients found to be MRSA-positive; high-risk wards were those with the highest rate of MRSA colonization or infection. The study by Chowers and colleagues[70] evaluated screening of high-risk patients, defined as patients hospitalized during the prior month, receiving hemodialysis, previously known to be MRSA-positive, or transferred from another ward in the hospital, a long-term care facility or another hospital. Of the non-CCS studies, the study by Keshtgar[74] evaluated screening of patients on high-risk wards; the studies by Salaripour,[76] Wernitz,[77] and Bowler[73] evaluated screening of high-risk patients; and the study by Pan[75] evaluated screening of patients on high-risk wards as well as high-risk patients. The studies varied in their execution of the MRSA screening protocol and the infection control practices that accompanied screening. Seven studies utilized culture to screen patients for MRSA. The Keshtgar study[74] utilized PCR to screen patients for MRSA. The Chowers study[70] first utilized culture and then utilized PCR to screen patients for MRSA.

The study by Rodriguez-Bano and colleagues[72] included MRSA bacteremia as a primary outcome. The other studies reported diverse primary endpoints ranging from nosocomial MRSA[76] to MRSA bloodstream infection.[75]

Of the CCS studies, studies by Rodriguez-Bano and colleagues[72] and by Chowers and colleagues[70] reported test turnaround time. For the Rodriguez-Bano study,[72] the reported turnaround time was described as 37 to 51 hours after culture was performed. The Chowers study[70] reported turnaround time as 2 to 4 days after culture was performed and 24 hours after PCR was performed. Of the non-CCS studies, one reported test turnaround time and four did not. The Keshtgar study[74] noted the time from sample collection to receipt in lab was 13.7 hours (9.78-15.1), from receipt in the lab to obtaining the result 21.8 hours (21.0-22.5), and from obtaining result to calling the service with the result 1.03 hours (0.83-1.41).

The Pan study[75] reported the compliance rate for contact precautions (203/370 patients or 55 percent overall, 62 percent for those known to be MRSA positive during the hospitalization). None of the other seven studies reported the compliance rate for contact precautions.

Beyond MRSA screening, the intervention protocols varied considerably in their infection control practices. For one of its interventions, the study by Rodriguez-Bano and colleagues[72] took no specific action for patients awaiting test results in the intervention group or control group. For the other of its interventions, this study[72] recommended that patients in the intervention group who were readmitted and were previously colonized with MRSA were preemptively isolated before the results of screening tests were available. The study did not specify any such actions for patients in the control group. Of the other two CCS studies, one[70] took no specific action for patients awaiting test results in the intervention or control groups. The exception was the study by Harbarth et al.[71] The Harbarth study[71] recommended preemptive isolation of patients previously known to be colonized or infected with MRSA for the intervention group, but not for the control group. For the five non-CCS studies, three studies[73,75,76] took no specific action for patients awaiting test results in the intervention or control groups. The exceptions were the studies by Wernitz et al.[77] and Keshtgar et al.[74] The Wernitz study[77] recommended isolation, barrier precautions and topical antimicrobial wash for all potential MRSA carriers pending screening test results. The same protocol was applicable to control group patients awaiting test results. The Keshtgar study[74] recommended intranasal antimicrobials and topical antimicrobial washes for patients who required emergency surgery before the screening test results were available.

Once a patient was found to be MRSA-positive, the Rodriguez-Bano study[72] recommended different actions for MRSA-positive patients in the intervention group in comparison to the control group. In this study,[72] MRSA-positive patients in the intervention group received contact precautions and decolonization (intranasal antimicrobials, topical antimicrobial washes) as well as dedicated patient care equipment and disinfection of surfaces and devices. MRSA-positive patients in the control group also received contact precautions, dedicated patient care equipment and disinfection of surfaces and devices, but did not receive decolonization. One of the non-CCS studies, the Wernitz study[77] recommended the same action for MRSA-positive patients in the intervention group and in the control group. For the Harbarth,[71] Chowers,[70] Salaripour,[76] and Pan studies,[75] steps were taken to isolate and decolonize MRSA-positive patients in the intervention group but no interventions were recommended for MRSA-positive patients in the control group. For the Bowler[73] and Keshtgar studies,[74] decolonization was recommended for MRSA-positive patients in the intervention group, but not for MRSA-positive patients in the control group.

The control arms of each of the eight studies included no systematic screening for MRSA. However, the infection control practices of the control groups did vary especially in cases where an individual with MRSA was identified during routine care. As mentioned above, the Wernitz study[77] decolonized patients in the control group who were found to be MRSA positive.

Results by Outcome

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is healthcare-associated, rather than imported. Two studies[72,76] evaluated healthcare-associated MRSA infection or colonization as an outcome. One[72] was a CCS study and one[76] was a non-CCS study. The Rodriguez-Bano study, a CCS study, was determined to be of poor quality[72] because it used indirect control of confounders rather that statistical adjustment within the segmented regression analysis. Definition of this healthcare-associated MRSA acquisition differed between the studies. The Rodriguez-Bano study[72] defined

cases as health care-associated if the first sample yielding MRSA was obtained more than 3 calendar days after hospital admission or if the first sample yielding MRSA was obtained from an ambulatory patient with an identified association with recent health care delivery. Cases were excluded as nonincident if a positive clinical culture result could be identified anywhere in the laboratory information system (including long-term care and outpatient settings) within the prior year. The Salaripour study[76] defined cases as health care-associated if a positive culture result was obtained more than 72 hours after admission.

In terms of findings, for the Rodriguez-Bano study,[72] the reported change in incidence of MRSA acquisition from a segmented regression analysis was -0.065 with confidence intervals that included zero (change in incidence after second intervention -0.053 to 0.182). Considering the baseline rate of 0.55/1000 patient days, this change in incidence rate would be equivalent to a relative risk reduction of -11.8 percent. The reported change in trend in incidence of MRSA acquisition was -0.045 (95% CI: -0.062 to -0.029; $p<0.001$).[72] In univariate analysis, compared to no screening, both interventions showed a reduction in MRSA colonization or infection, though this reduction was not statistically significant.[72] The Salaripour study[76] also found a statistically significant reduction in healthcare-associated MRSA infection with targeted screening (-0.18 per 1000 patient-days, a 30 percent reduction).

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in high-risk patients compared to no screening on healthcare-associated MRSA acquisition was judged to be insufficient. One CCS study[72] addressed this outcome. This study, by Rodriguez-Bano and colleagues, was an interrupted time series design of poor quality.[72] The study was judged to be of poor quality because it did not conduct an appropriate analysis, using indirect control of confounders rather that statistical adjustment within its segmented regression analysis. The risk of bias for the body of evidence was deemed to be high because only a single poor quality quasi-experimental study[72] evaluated this outcome. As only one study[72] evaluated this outcome, the consistency of the findings was unknown. The study addressed healthcare-associated MRSA acquisition, an intermediate and therefore, indirect outcome. The study findings[72] were judged to be imprecise because the study reported statistically significant findings for trend, though nonstatistically significant findings for rate. Because the evidence base for this outcome included only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of screening of high-risk patients on healthcare-associated MRSA acquisition is judged to be insufficient.

Comment, Non-CCS Study

One non-CCS study[76] addressed this outcome. With screening of high-risk patients, the Salaripour study[76] demonstrated a statistically significant reduction in healthcare-associated MRSA colonization or infection.

Healthcare-Associated MRSA Infection, Irrespective of Site

Results

Three studies[71,73,77] evaluated the impact of screening for MRSA carriage in high-risk patients on healthcare-associated MRSA infection. One[71] was a CCS study and two[73,77] were non-CCS studies. All three studies defined healthcare-associated MRSA infection as clinical

signs of infection 48 hours or more after admission, with MRSA isolated as the causative pathogen. All studies showed a statistically significant reduction in healthcare-associated MRSA infection with screening of high-risk patients compared to no screening.

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in high-risk patients compared to no screening on healthcare-associated MRSA infection was judged to be insufficient. One CCS study[71] addressed this outcome. This study, by Harbarth and colleagues,[71] utilized a before/after design and was judged to be of poor quality as it did not report baseline group characteristics, addressing autocorrelation, or whether its analysis controlled for confounders. The risk of bias for the body of evidence was deemed to be high because only one poor quality quasi-experimental study addressed this outcome. As only one study evaluated this outcome, the consistency of the findings was unknown. This study evaluated healthcare-associated MRSA infection, a health outcome and therefore, a direct outcome measure. The study findings were judged to be precise because they were statistically significant. Because the evidence base for this outcome included only one quasi-experimental study, the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening of high-risk patients on healthcare-associated MRSA infection is judged to be insufficient.

Comment, Non-CCS Studies

Two non-CCS studies evaluated this outcome.[73] Compared to no screening, both studies showed a statistically significant reduction in healthcare-associated MRSA infection with screening of high-risk patients.[73,77]

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

Four studies addressed the impact of screening on rates of healthcare-associated MRSA bacteremia or bloodstream infection. Two were CCS studies[70,72] and two were non-CCS studies[75,77]. Of the CCS studies, both the Rodriguez-Bano study[72] and the Chowers study[70] were determined to be of poor quality. The Rodriguez-Bano study[72] measured MRSA bacteremia and defined cases as health care-associated if the first sample yielding MRSA was obtained more than 3 calendar days after hospital admission or if the first sample yielding MRSA was obtained from an ambulatory patient with an identified association with recent health care delivery. The Wernitz[77] and Pan[75] studies defined cases as health care-associated if a positive, clinical MRSA culture result was obtained at least 48 hours after admission. The Chowers study[70] defined bacteremia as health care-associated if a positive blood culture result was obtained from blood drawn 48 hours or more after admission, or from blood drawn at admission from any patient who had been admitted to the study hospital during the prior year.

With segmented regression analysis, the study by Rodriguez-Bano and colleagues[72] reported that the change in incidence of MRSA bacteremia was -0.051 after the intervention (95% CI: -0.083 to -0.020, p=0.002). The change in trend in MRSA bacteremia was -0.006 after the second intervention (95% CI: -0.10 to -0.01, p=0.01). In univariate analysis, compared to no screening, both interventions showed a reduction in MRSA bacteremia, though this reduction was not statistically significant. The Chowers study[70] found a reduction in the average number of bacteremia cases per 1,000 patient-days by a factor of 0.55 with one component of the intervention (95% CI: 0.36–0.83). With another component of the intervention, there was a reduction in the average number of bacteremia cases per 1,000 patient-days by a factor of 0.27

(95% CI: 0.14–0.58). The Wernitz[77] and Pan[75] studies also showed a statistically significant reduction in healthcare-associated MRSA bloodstream infection with screening of high-risk patients compared to no screening.

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in high-risk patients compared to no screening on healthcare-associated MRSA bacteremia or bloodstream infection was judged to be insufficient. Two CCS studies addressed this outcome. The study by Rodriguez-Bano et al.,[72] utilized a limited time series design and was judged to be of poor quality because it used indirect control of confounders rather that statistical adjustment within the segmented regression analysis. The study by Chowers et al.,[70] also utilized a limited time series design and was judged to be of poor quality as it did not report baseline group characteristics or whether its analysis controlled for confounders. The risk of bias for the body of evidence was determined to be high as two quasi-experimental studies[70,72] of poor quality addressed this outcome. The study findings were consistent, because both studies[70, 72] showed a reduction in MRSA bacteremia or bloodstream infection with screening. The studies[70,72] evaluated MRSA bacteremia or MRSA bloodstream infection, which are health outcomes and therefore, direct outcome measures. The study findings were judged to be precise because the individual studies consistently reported statistically significant results. Because the evidence base for this outcome included only observational studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening for MRSA carriage in high-risk patients compared to no screening on healthcare-associated MRSA bacteremia or bloodstream infection is judged to be insufficient.

Comment, Non-CCS Studies

Two non-CCS studies evaluated this outcome.[75,77] Compared to no screening, both studies showed a statistically significant reduction in healthcare-associated MRSA infection with screening of high-risk patients.[75,77]

MRSA Surgical Site Infection

Two studies addressed this outcome. One was a CCS study[71] and one[74] was a non-CCS study. Both the Harbarth[71] and Keshtgar[74] studies showed a statistically significant reduction in healthcare-associated MRSA SSI with screening of high-risk patients compared to no screening.

Strength of Evidence

The SOE for the effect of screening for MRSA carriage in high-risk patients compared to no screening on MRSA SSI was judged to be insufficient. One CCS study[71] addressed this outcome. This study, by Harbarth and colleagues,[71] utilized a before/after design and was judged to be of poor quality as it did not report baseline group characteristics, addressing autocorrelation, or whether its analysis controlled for confounders. The risk of bias for the body of evidence was deemed to be high because only a single poor quality quasi-experimental study[71] addressed this outcome. As only one study[71] evaluated this outcome, the consistency of the findings was unknown. The study[71] evaluated MRSA SSI, a health outcome and therefore, a direct outcome measure. The study findings were judged to be precise because the individual study that addressed this question reported a statistically significant result. Because the evidence base for this outcome included only one quasi-experimental study, the starting level for the SOE was low.

SOE was lowered by the high risk of bias. In summary, the SOE for the effect of screening of high-risk patients on MRSA SSI is judged to be insufficient.

Comment, Non-CCS Studies

One non-CCS study[74] addressed this outcome. The Keshtgar[74] study showed a statistically significant reduction in MRSA SSI with screening of high-risk patients compared to no screening.

Morbidity, Mortality, Harms and Resource Utilization

Results

No studies addressed these outcomes.

Strength of Evidence for Screening of High-Risk Patients for MRSA Carriage on Morbidity, Mortality, Harms and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of screening of high-risk patients for MRSA carriage on morbidity, mortality, harms or resource utilization is judged to be insufficient.

Summary Strength of Evidence Across Key Question 3C

A summary of the main syntheses for this question follows in Table 19.

Table 19. Strength of evidence for studies comparing screening of high risk patients versus no screening

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Screening of High Risk Pts Vs No Screening	MRSA Acquisition	1 QEX (N=Unclear) (Rodriguez-Bano 2010[72])	High	Unknown	Indirect	Imprecise	Insufficient
	MRSA Infection	1 QEX (N=506,012) (Harbarth 2000[71])	High	Unknown	Direct	Precise	Insufficient
	MRSA Bacteremia/ Blood Stream Infection	2 QEX (N=Unclear) (Rodriguez-Bano 2010[72]) (N=377,945; 1,535,806[‡]) (Chowers 2009[70])	High	Consistent	Direct	Precise	Insufficient
	MRSA Surgical Site Infection	1 QEX (N=506,012) (Harbarth 2000[71])	High	Unknown	Direct	Precise	Insufficient

MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable; QEX = quasi-experimental
[§]Studies that controlled for confounding and/or trend.
[‡] Patient days.

Key Question 4. Screening of a Broader Patient Population for MRSA Carriage (Expanded Screening) Compared With Screening of a Narrower Patient Population (Limited Screening)

Overview

This section describes the literature that evaluates expanded screening for MRSA carriage compared to limited screening. Studies described in this section conducted MRSA surveillance for a limited patient population or number of wards (e.g., screening of all patients admitted to the ICU) at baseline and then expanded MRSA surveillance to a larger population or number of wards (e.g., screening of all patients admitted to acute care units). These studies compared outcomes during the expanded screening period to those during the limited screening period. After an overview of the literature, the results are described for each outcome measure: MRSA acquisition, MRSA infection, morbidity, mortality, harms, and resource utilization. Within the category of MRSA infection, we also included results for MRSA bacteremia or bloodstream infection, as some studies present these outcomes rather than the broader outcome of MRSA infection irrespective of site. The emphasis in this chapter is on outcomes describing healthcare-associated events. Healthcare-associated outcomes are the primary outcomes of interest because screening for MRSA carriage in health care facilities is most proximately expected to impact healthcare-associated MRSA transmission and infection. SOE syntheses presented here include only CCS studies. Because studies that use simple two-group statistical analyses cannot support causal inferences, the non-CCS studies were excluded from the SOE analysis. We present the SOE assessment for MRSA acquisition, MRSA infection (considering studies that addressed either MRSA infection regardless of site together with those that addressed MRSA bacteremia or bloodstream infection), morbidity, mortality, harms and resource utilization. Following the SOE syntheses, we comment on the pattern of results seen in non-CCS studies. Table 20 summarizes the studies reviewed for Key Question 4. Note that Table 20 does not include the Enoch study[85] because it did not report outcomes that were exclusively health-care associated. Table 21 shows the study quality details for CCS studies.

Table 20. KQ4: Healthcare-associated MRSA acquisition, infection, or bacteremia

Outcome	Study	Quality	Statistical Result	Synthesis
HCA acquisition	Rodriguez-Bano et al., 2010[72]	Poor	Incidence NSS ↓ Trend SS ↓	SOE=insufficient Comment: Causal inference is not possible based on non-CCS studies
	Ellingson et al., 2011[56]	Poor	Incidence SS ↓[a] Incidence NSS↓[b] Trend NSS ↓	
	Eveillard et al., 2006[79]	Non-CCS	SS ↓	
	Girou et al., 2000[80]	Non-CCS	NSS ↓	
	Schelenz et al., 2005[81]	Non-CCS	SS ↓	
	Thompson et al., 2009[82]	Non-CCS	SS ↓	
	Trautmann et al., 2007[83]	Non-CCS	SS ↓	
HCA infection	Chaberny et al., 2008[78]	Poor	SS ↓	SOE=insufficient Comment: Causal inference is not possible based on non-CCS studies
	West et al., 2006[84]	Non-CCS	NSS ↓	
HCA bacteremia/ blood stream infection	Rodriguez-Bano et al., 2010[72]	Poor	Incidence NSS ↓ Trend NSS ↓	SOE=insufficient Comment: Causal inference is not possible based on non-CCS studies
	Thompson et al., 2009[82]	Non-CCS	SS ↓	
	Trautmann et al., 2007[83]	Non-CCS	SS ↓	

HCA = health care associated; KQ = Key Question; non-CCS = studies not controlling for confounding and/or secular trend; NSS = non statistically significant; SOE = strength of evidence; SS = statistically significant

[a]The reduction was statistically significant following the third intervention.

[b]The reduction was not statistically significant following the second intervention.

Ten studies[56,72,78-85] described limited screening for MRSA carriage compared to expanded screening. The studies by Chaberny[78], Ellingson,[56] and Rodriguez-Bano[72] were CCS studies; the remaining seven[79-85] were non-CCS studies. All ten[56,72,78-85] studies employed a quasi-experimental study design.

The study by Rodriguez-Bano and colleagues[72] utilized an interrupted time series design as did the study by Ellingson and colleagues.[56] The eight other studies utilized a before/after study design. The study by Rodriguez-Bano[72] and colleagues was judged to be of poor quality[72] because it controlled for confounders indirectly, rather than employing statistical adjustment within the segmented regression analysis. The study by Ellingson and colleagues[56] was determined to be of poor quality because it did not report baseline group characteristics or whether its analysis controlled for confounders. The study by Chaberny and colleagues[78] was determined to be of poor quality because it did not report whether its analysis controlled for confounders.

Table 21. KQ4: Study quality details for CCS studies

Author, Year	Reported Baseline Characteristics	Analytic Technique	Test for Trend (1)	Addressed Auto-Correlation (2)	Adjusted for at Least 1 Confounder (3)	Appropriate Analysis of Results*	Quality
Chaberny et al., 2008[78]	Pt-days, length of stay	Segmented regression of ITS	Y	Tested for	NR	N	Poor
Rodriguez-Bano, et al., 2010[72]	Age, number diagnoses, antibiotics	Segmented regression, D-W test	Y	Tested for	N (indirect control)	Y	Poor
Ellingson, et al., 2011[56]	NR	Interrupted time series analysis with Poisson model	Y	Tested for	NR	N	Poor

CCS = attempted to control for confounding and/or secular trends; D-W = Durbin-Watson test for autocorrelation; ITS = interrupted time-series; KQ = Key Question; MRSA = methicillin-resistant *Staphylococcus aureus*; N = no; NR = not reported; Pt = patient; Y = yes

*The study was judged to meet appropriate analysis if all 3 elements (1, 2, 3) were present.

All ten studies evaluated hospitalized adult patients. All of the CCS studies[56,72,78] took place in more than one area of the hospital, as did one of the non-CCS studies.[85] Three[82-84] of the non-CCS studies took place in the ICU. One of the non-CCS studies was conducted on the cardiothoracic ward,[81] one on the internal medicine ward,[79] and one on the dermatology ward.[80]

The exact composition of the expanded MRSA screening intervention varied across the studies. Eight studies utilized culture to screen patients for MRSA. The study by Schelenz and colleagues[81] did not specify whether screening was performed with culture or PCR. The study by Enoch and colleagues[85] initially utilized culture to screen for MRSA, then introduced screening with PCR. For the study by Rodriguez-Bano and colleagues,[72] the intervention was active surveillance for MRSA and decolonization in patients and health care workers in wards with documented MRSA transmission, and surveillance of all patients admitted from other hospitals or from long-term care facilities and all readmitted patients previously colonized with MRSA. For the study by Chaberny and colleagues,[78] the intervention was screening of readmitted patients as well as roommates of patients with MRSA plus screening of all admitted patients on surgical wards and ICUs. For the study by Ellingson and colleagues,[56] the intervention consisted of systems and behavior change strategies to promote adherence to the infection control protocol, enhanced emphasis on hand hygiene and environmental disinfection, and surveillance testing of the anterior nares and open wounds within 48 hours after admission. The intervention was begun in the surgical ward, then in the surgical ICU and ultimately, in all acute care units of the hospital. For two of the non-CCS studies, the intervention was screening of all patients admitted to a single ward. The study by Eveillard and colleagues[79] screened all patients admitted to the internal medicine service. The study by Girou and colleagues[80] screened all patients admitted to the dermatology ward within 48-72 hours of admission.

Two of the non-CCS studies included screening of high-risk patients as well as those admitted to the ICU. The study by West and colleagues[84] defined high risk patients as those transferred from another hospital, admitted from long-term care facilities, readmitted within 30 days after discharge, or admitted to a nephrology service. The study by Trautmann and colleagues[83] defined high-risk patients as (1) patients with chronic open wounds or pressure sores; (2) patients transferred from secondary or tertiary acute care hospitals; (3) bed-bound

patients from chronic care facilities; (4) patients with insulin-dependent diabetes mellitus; and (5) patients with chronic renal failure on dialysis. In addition to screening, the Trautmann study[83] included additional interventions including a written standard detailing hygienic precautions for MRSA, acquisition of long-sleeved isolation gowns, acquisition of carts to facilitate the use of separate supplies for MRSA patients, isolation signs, enhanced documentation of MRSA cases, feedback and staff training, and flagging of electronic charts for patients with MRSA. For the study by Thompson and colleagues,[82] the intervention was screening all admissions to the ICU, daily antimicrobial washes for all patients regardless of MRSA status, scrubs for medical staff, computer keyboards with a wipeable surface, and standardized care of vascular lines.

For the study by Schelenz and colleagues,[81] the intervention included multiple components: (1) preadmission, admission, and weekly screening for all admitted ward patients; (2) decolonization (intranasal antimicrobials, topical antimicrobials) for patients found to be MRSA positive; (3) admission of patients from high-risk units (ICUs, other hospitals), only after MRSA status known; (4) audit plus feedback; (5) education and support; (6) closure of operating rooms to facilitate repairs; (7) alcohol hand rub; (8) isolation on admission for patients known to be colonized with MRSA; (9) decolonization (intranasal antimicrobials, topical antimicrobials) of both MRSA carriers and those with pending screening test results 24 hours before surgery; (10) isolation and barrier precautions for MRSA-positive patients; (11) designated nurses for MRSA-positive patients; (12) a nursing care pathway for MRSA; (13) use of clippers to prepare the skin in the operating room; (14) preoperative skin disinfection with a rapidly drying solution; (15) improvements in environmental cleaning; (16) alterative in IV antibiotic prophylaxis; and (17) recovery in the operating room when possible, rather than admission to the ICU. The study by Enoch and colleagues[85] also included multiple interventions including screening (first of patients with central venous catheters, then elective screening, then emergency screening along with seven-day testing), decolonization (all patients admitted to the ICU of high dependency unit regardless of test result), prosthetic device care, input from an infection control team, and enhanced environmental cleaning and space for isolation.

An important feature of this group of studies was that limited screening was already occurring at baseline, so it is important to understand the nature of screening during control periods. For the Rodriguez-Bano study[72] the control condition consisted of active surveillance for MRSA and decolonization in patients and health care workers in wards with documented MRSA transmission. The Chaberny study[78] screened readmitted patients as well as roommates of patients with MRSA. For the Ellingson study, an interrupted time series design, the control condition was patients in the surgical ward and subsequently patients in the surgical ICU. For five of the non-CCS studies, the control condition consisted of screening high-risk patients. The Eveillard study[79] screened patients with a history of MRSA carriage, hospitalization, or institutionalization within the prior year, intra- or inter-hospital transfers, and patients with chronic skin lesions. The Girou study[80] screened patients transferred from other wards, with a history of prior hospitalization in the past 3 years, with chronic wounds, or with a disease with denuded skin. The Trautmann study[83] screened (1) patients with chronic open wounds or pressure sores; (2) patients transferred from secondary or tertiary acute care hospitals; (3) bed-bound patients from chronic care facilities; (4) patients with insulin-dependent diabetes mellitus; and (5) patients with chronic renal failure on dialysis. The Thompson study[82] screened high-risk patients, but did not define this population group. For the West study,[84] the control condition was screening upon admission to the ICU and weekly thereafter. The Enoch study[85] screened patients

considered to be high risk by national guidelines. For the Schelenz study,[81] the control condition was pre-admission, admission, and weekly MRSA screening.

While all ten studies evaluated similar MRSA outcomes, the primary outcome of interest varied. For the Rodriguez-Bano study,[72] the primary outcome was rates of MRSA colonization or infection and rates of bacteremia. For the Ellingson study,[56] the primary outcome was the clinical incidence of MRSA colonization or infection. For the Chaberny and West studies,[78,84] the primary outcome was incidence of nosocomial MRSA infection. For the Eveillard study[79], the primary outcomes were the prevalence of MRSA carriage on admission, the efficiency of the selective screening program and the effectiveness of the screening program on controlling MRSA transmission. For the Girou study,[80] the primary outcomes were the number of patients without risk factors found to screen positive for MRSA, the rate of acquired MRSA, and the rate of imported MRSA. For the Thompson study,[82] the primary outcome was to detect long-term trends in the prevalence of MRSA in admissions, MRSA acquisition and bacteremia rates within the ICU, and to determine the effect of the three interventions. For the Trautmann study,[83] the primary outcome was the nosocomial MRSA transmission. For the Schelenz study,[81] the primary outcomes were rates of MRSA acquisition and infection. For the Enoch study,[85] the primary outcome was the use of bacteremia compared with clinical isolates to determine the effectiveness of the interventions.

Infection control practices varied in the background of these studies. In terms of actions taken while awaiting test results, the study by Rodriguez-Bano and colleagues,[72] a poor quality study, recommended actions for patients in the intervention group while awaiting test results. This study[72] recommended preemptive isolation for readmitted patients previously colonized with MRSA. However, preemptive isolation or decolonization for patients was not recommended for patients in the control group while awaiting test results. The studies by Chaberny and colleagues[78] and Ellingson and colleagues,[56] both poor quality studies, did not report actions while waiting for screening test results. Similarly, the study by Enoch and colleagues,[85] a non-CCS study, did not report actions for patients awaiting test results in the intervention group or in the control group. Five of the non-CCS studies utilized the same action for patients in the intervention group awaiting test results as for patients in the control group awaiting test results. The West study[84] recommended preemptive isolation and barrier precautions for patients found to have MRSA colonization or infection on a prior admission. The Girou study[80] recommended isolation and barrier precautions for patients at high risk of MRSA acquisition. Four studies[78,79,82,83] recommended no interventions while awaiting screening test results. The Schelenz study[81] utilized different actions for patients in the intervention group awaiting tests results as for patients in the control group awaiting test results. No interventions were recommended for patients in the control group while awaiting screening results. In the intervention group, patients were not admitted to the ward until their MRSA status was known. In addition, presumptive decolonization was recommended for patients in the intervention group whose test results were not available 24 hours prior to surgery.

Once a patient was found to have a MRSA positive screening test, practices were similar for patients in the intervention and control groups. The Rodriguez-Bano study[72] utilized similar interventions for MRSA-positive patients in the intervention and control groups. Action consisted of isolation (including barrier precautions), decolonization (intranasal and topical antimicrobials) and follow up nasal swabs for both the groups. Hand hygiene was recommended for the care of MRSA-positive patients in both groups, but alcohol hand rubs were available only during the intervention period. In the Ellingson study,[56] MRSA-positive patients in the

intervention and control groups received contact precautions and unspecified hand hygiene. Similarly, the Chaberny study[78] utilized the same interventions for MRSA-positive patients in the intervention group and in the control group, as did four of the non-CCS studies.[79,80,82,84] Two[81,83] of the non-CCS studies utilized similar interventions for MRSA-positive patients in the intervention group and in the control group. For one of these studies, MRSA-positive patients in the intervention group were isolated, but those in the control group were isolated only if an isolation room was available.

Results by Outcome

Healthcare-Associated MRSA Acquisition

Healthcare-associated MRSA acquisition is measured by MRSA colonization or by MRSA colonization or infection that is health care-associated, rather than imported. Seven studies evaluated healthcare-associated MRSA infection or colonization as an outcome. The studies by Rodriguez-Bano and colleagues[72] and Ellingson and colleagues[56] were the CCS studies, while the studies by Eveillard and colleagues,[79] Trautmann and colleagues,[83] Thompson and colleagues,[82] Girou and colleagues,[80] and Schelenz and colleagues[81] were non-CCS studies. The Rodriguez-Bano study, an interrupted time series design, was determined to be of poor quality[72] because it controlled for confounders indirectly, rather than employing statistical adjustment within the segmented regression analysis. The study by Ellingson and colleagues,[56] an interrupted time series design, was determined to be of poor quality because it did not report baseline group characteristics or whether its analysis controlled for confounders.

The study by Rodriguez-Bano and colleagues, a poor quality study[72] defined cases as health care-associated if the first sample yielding MRSA was obtained more than 3 calendar days after hospital admission or if the first sample yielding MRSA was obtained from an ambulatory patient with an identified association with recent health care delivery. The study by Ellingson and colleagues[56] defined cases as health care-associated if a positive, clinical MRSA culture result was obtained at least 48 hours after admission to an acute care unit or if the patient was transferred, within 48 hours after transfer to another unit.

The Eveillard and Trautmann studies[79,83] defined colonization or infection as health care-associated if patients were identified as MRSA positive two or more days after admission. The Thompson study[82] defined colonization or infection as health care-associated if growth of MRSA was noted five or more days after admission to the ICU in patients who initially screened negative for MRSA. The Girou study[80] defined colonization or infection as health care-associated if the first MRSA isolate from any source was recovered more than 72 hours after admission. The Schelenz study[81] defined MRSA acquisition as the isolation of MRSA from any site more than 72 hours after admission to the ward in patients who had no previous history of MRSA colonization or infection. MRSA infections were defined as the isolation of MRSA from blood culture or surgical wound sites that had evidence of clinical infection.

The Rodriguez-Bano study[72] showed reductions in the incidence and trend of healthcare-associated MRSA infection or colonization with expanded screening compared to limited screening. Though the reduction in trend was statistically significant (change in trend after the third intervention 0.047; 95% CI: 0.035 to 0.059, $p<0.001$), the reduction in incidence was not (change in incidence after the third intervention 0.077 [NSS; 95% CI: -0.012 to 0.165]).[72] Of note, for the calculation of incidences of MRSA colonization or infection, only patients who had MRSA isolated from clinical samples were included because active surveillance was not

performed uniformly throughout the study periods. The Ellingson study[56] showed reductions in the incidence rate ratio for MRSA colonization or infection after the second intervention (screening for MRSA carriage in the ICU, incidence rate ratio 0.913, 95% CI: 0.356 to 2.343) and after the third intervention (screening for MRSA carriage in all other acute care units, incidence rate ratio 0.656, 95% CI: 0.440 to 0.979). In addition, the Ellingson study[56] showed reduction in the pre- to post-intervention trends (screening for MRSA carriage in the ICU, incidence rate ratio 0.971, 95% CI: 0.938 to 1.004) and after the third intervention (screening for MRSA carriage in all other acute care units, incidence rate ratio 0.998, 95% CI: 0.982 to 1.014). All five of the non-CCS studies showed a reduction in hospital-acquired MRSA infection with expanded targeted screening compared to limited targeted screening. The studies by Eveillard, Thompson, Trautmann, and Schelenz[79,81-83] showed a statistically significant reduction and the study by Girou[80] did not.

Strength of Evidence

The SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA acquisition was determined to be insufficient. Two CCS studies addressed this outcome. The study by Rodriguez-Bano et al.,[72] utilized a limited time series design and was judged to be of poor quality because it used indirect control of confounders rather than statistical adjustment within the segmented regression analysis. The study by Ellingson et al.,[56] also utilized a limited time series design, and was judged to be of poor quality as it did not report baseline group characteristics or whether its analysis controlled for confounders. The risk of bias for the body of evidence was determined to be high as two quasi-experimental studies[56,72] of poor quality addressed this outcome. The study findings were consistent, because both studies found a reduction in healthcare-associated MRSA acquisition with screening. The studies addressed healthcare-associated MRSA acquisition, an intermediate and therefore, indirect outcome. The study findings were judged to be imprecise because the individual studies did not consistently report statistically significant results. Because the evidence base for this outcome included only quasi-experimental studies, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA acquisition is judged to be insufficient.

Comments, Non-CCS Studies

Five non-CCS studies addressed this outcome.[79-83] With expanded screening compared to limited screening, all five studies showed a reduction in MRSA infection. The reduction was statistically significant for four of the non-CCS studies,[79,81-83] though not for one[80] of the non-CCS studies.

Healthcare-Associated MRSA Infection, Irrespective of Site

Two studies[78,84] addressed this outcome. The study by Chaberny and colleagues[78] was a CCS-study while the study by West and colleagues[84] was a non-CCS study. The study by Chaberny and colleagues[78] was determined to be of poor quality because it did not report whether its analysis controlled for confounders. Both studies defined hospital-acquired infection as an infection detected at least 72 hours after admission. Chaberny et al.,[78] showed a statistically significant reduction in hospital-acquired MRSA infection (based on the change in level and slope of the incidence density) with expanded screening compared to limited screening. West et

al.,[84] showed a reduction in hospital-acquired MRSA infection with expanded screening compared to limited screening; however, this reduction was not statistically significant.

Strength of Evidence

The SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA infection irrespective of site was determined to be insufficient. One CCS study addressed this outcome. The study by Chaberny et al.,[78] utilized a before/after study design and was judged to be of poor quality as it did not report whether its analysis controlled for confounders. The risk of bias for the body of evidence was determined to be high because only one poor quality quasi-experimental study addressed this outcome. With expanded screening, Chaberny et al.,[78] found a reduction in the incidence density of healthcare-associated MRSA infection (change in level -0.122, 95% CI: -0.204 to -0.040, p=0.004). In addition, Chaberny et al.,[78] found a reduction in the monthly change in incidence density of healthcare-associated MRSA infection (change in slope -0.008, 95% CI: -0.013 to -0.003, p=0.004). The consistency of the findings was unknown, because only one study addressed this outcome. This study evaluated MRSA infection, a health outcome and therefore, a direct outcome measure. The study findings were judged to be precise, because the single study that addressed this outcome found statistically significant results. Because the evidence base for this outcome included only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias. In summary, the SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA infection is judged to be insufficient.

Healthcare-Associated MRSA Bacteremia or Bloodstream Infection

Three studies addressed this outcome. The study by Rodriguez-Bano and colleagues[72] was a CCS study, while the studies by Thompson and colleagues[82] and by Trautmann and colleagues[83] were non-CCS studies. The study by Rodriguez-Bano and colleagues was determined to be of poor quality[72] because it controlled for confounders indirectly, rather than employing statistical adjustment within the segmented regression analysis. The Rodriguez-Bano study[72] defined bacteremia as health care-associated if the first sample yielding MRSA had been obtained more than 3 calendar days after hospital admission or if the first sample yielding MRSA had been obtained from an ambulatory patient who had an identified association with recent health care delivery. The Thompson study[82] defined bacteremia as ICU-acquired if the first positive blood culture occurred on or after the fifth day in the ICU. Patients who grew MRSA from other sites prior to or after the elucidation of MRSA from the blood were included. The Trautmann study[83] defined septicemia as hospital-acquired if it was identified two or more days after admission. The CDC definition was used to define septicemia.

The Rodriguez-Bano study[72] reported a reduction in hospital-acquired MRSA bacteremia with expanded targeted screening compared to limited targeted screening, but the confidence intervals included the null (change in incidence after the third intervention 0.002, 95% CI: -0.022 to 0.026; change in trend after the third intervention 0.003, 95% CI: 0.000 to 0.006). The Trautmann study[83] showed a statistically significant reduction in hospital-acquired MRSA intravenous catheter-associated septicemia with expanded targeted screening compared to limited targeted screening. The Thompson study[82] showed a statistically significant reduction in hospital-acquired MRSA bacteremia with expanded targeted screening compared to limited targeted screening.

Strength of Evidence

The SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA bacteremia was judged to be insufficient. One CCS study addressed this outcome. The study by Rodriguez-Bano et al.,[72] utilized a limited time series design and was judged to be of poor quality because it used indirect control of confounders rather that statistical adjustment within the segmented regression analysis. The risk of bias was judged to be high because only one poor quality quasi-experimental study addressed this outcome. The Rodriguez-Bano[72] study reported a reduction in hospital-acquired MRSA bacteremia with expanded targeted screening compared to limited targeted screening, but the confidence intervals included the null (change in incidence after the third intervention 0.002, 95% CI: -0.022 to 0.026; change in trend after the third intervention 0.003, 95% CI: 0.000 to 0.006). The consistency of the findings was unknown, because only one study addressed this outcome. This study investigated MRSA bacteremia, a health outcome and therefore, a direct outcome. The study findings were judged to be imprecise because the study did not report statistically significant results. Because the evidence base for this outcome included only one quasi-experimental study, the starting level for the SOE was low. SOE was lowered by the high risk of bias and lack of precision. In summary, the SOE for the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA bacteremia is judged to be insufficient.

Comment, Non-CCS Studies

Two studies that did not use statistical methods to attempt to control for confounders and/or secular trends (non-CCS studies) addressed this outcome.[82-83] Both of the studies[82,83] evaluated the effect of expanded screening for MRSA carriage compared to limited screening on healthcare-associated MRSA bacteremia or bloodstream infection, a proxy for healthcare-associated MRSA infection.

With expanded screening, both studies showed a reduction in healthcare-associated MRSA infection. For one of the studies,[83] the reduction was statistically significant, while for one of the studies, it was not.[82]

Morbidity, Mortality, Harms and Resource Utilization

No studies addressed these outcomes.

Strength of Evidence for Expanded Screening for MRSA Carriage Compared to Limited Screening on Morbidity, Mortality, Harms and Resource Utilization

Because no studies addressed these outcomes, the SOE to evaluate the effect of expanded screening for MRSA carriage compared to limited screening on morbidity, mortality, harms or resource utilization is judged to be insufficient.

Summary Strength of Evidence Across Key Question 4

A summary of the main syntheses for this question follows in Table 22.

Table 22. Strength of evidence for studies comparing expanded screening versus limited screening

Strategies Compared	Outcome	No of Studies[§]	Risk of Bias	Consistency	Directness	Precision	Overall Grade
Expanded Screening vs. Limited Screening	MRSA Acquisition	2 QEX (N=Unclear) (Rodriguez-Bano 2010[72]) (N=Unclear) (Ellingson 2011[56])	High	Consistent	Indirect	Imprecise	Insufficient
	MRSA Infection	1 QEX (N=219,124; 1,987,676[‡]) (Chaberny 2008[78])	High	Unknown	Direct	Precise	Insufficient
	MRSA Bacteremia	1 QEX (N=Unclear) (Rodriguez-Bano 2010[72])	High	Unknown	Direct	Imprecise	Insufficient

MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable; QEX = quasi-experimental
[§]Studies that controlled for confounding and/or trend.
[‡] Patient days.

Discussion

Key Findings and Strength of Evidence

Summary of Results

This review found a low strength of evidence to support the effectiveness of universal screening for MRSA carriage compared to no screening in reducing healthcare-associated MRSA infection. However, the available evidence is insufficient to reach a conclusion regarding the effectiveness of screening for MRSA carriage for all of the other comparisons and outcomes of interest evaluated. The bulk of the available literature on the comparative effectiveness of screening for MRSA carriage consists of quasi-experimental studies, largely observational studies with a before/after study design. The sole cluster RCT[46] in this literature showed no favorable impact of screening, though concerns about the lengthy turnaround time of the screening modality used and the failure to implement barrier precautions, isolation and/or decolonization while awaiting screening test results limit the applicability of this study's findings. The use of observational studies to determine causal inference requires protection against bias and confounding through features of design, conduct or analysis. For example, because the incidence of MRSA infection has been decreasing, studies that utilize a before/after study design without adequately controlling for secular trends are unable to distinguish between an effect due to the intervention and an effect due to the persistence of the secular trend itself. Similarly, because other interventions geared toward patient safety, quality improvement or prevention of healthcare-associated infections may also decrease the incidence of MRSA infection, as may unmonitored efforts at decolonization/eradication or improvements to the physical plant that increase the availability of private hospital rooms, studies that utilize a before/after design and do not adequately control for these and other similar confounders cannot establish whether the effect seen is due to the intervention or to the confounding variable. Therefore, studies that performed simple statistical tests without attempts to control for confounding and/or secular trends were excluded from the SOE analysis.

An important limitation of the available evidence regarding MRSA screening relates to heterogeneity in the nature of the interventions performed. By its nature, MRSA screening itself would not be expected to impact the frequency of subsequent transmission or infection. Rather, clinical outcomes are influenced by the application of additional infection control interventions in response to the detection of colonization, including more rigorous hand hygiene, barrier precautions, environmental cleaning, and antimicrobial decolonization. That these interventions are often deployed as part of a "bundle" further limit the conclusions that can be drawn about the attributable benefit of screening compared to any other component of the intervention.

Many of the included studies provided insufficient information about the full scope of interventions deployed in conjunction with screening for MRSA carriage, especially those measures implemented in response to the new detection of MRSA colonization. For example, while decolonization for MRSA-positive patients may not have been recommended as part of the screening intervention, most studies did not address whether or not decolonization was specifically prohibited. As a result, the measured effect of the screening strategy may have been influenced by the application of uncontrolled and unmeasured interventions targeting MRSA colonization.

In addition, included studies often failed to examine the potential impact of other concurrent infection-prevention efforts on the measured impact of screening for MRSA carriage. Campaigns to reduce the frequency of vascular device infections, initiatives to improve hand hygiene, and interventions to promote an institutional culture of safety have been shown to influence the frequency of many healthcare-associated infections, including those caused by MRSA. Therefore, their omission may be important.

Based on the most important and distinctive subgroups of evaluations of MRSA screening strategies, the review is organized to examine the clinical effectiveness of MRSA screening under the following circumstances: (1) universal screening compared to no screening, (2) universal screening compared to screening of selected patient populations, (3a) screening of ICU patients compared to no screening, (3b) screening of surgical patients compared to no screening, (3c) screening of other high-risk patients compared to no screening and (4) screening of a broader population (expanded screening) compared to screening of a limited population (limited screening). This discussion specifically addresses the outcomes of MRSA screening strategies in studies that attempted to control for confounders and/or secular trends (CCS studies). When studies that did not attempt to control for confounders and/or secular trends addressed an outcome, we provided our comments on such studies.

MRSA Transmission

By design, the most immediate effect of MRSA screening strategies should be to interrupt the transmission of MRSA between patients, irrespective of the clinical setting under investigation. The impact of MRSA screening on the frequency of transmission can be estimated through examination of the acquisition of MRSA colonization (often considered in conjunction with the incidence of new infection) among patients not previously affected. Based on the CCS studies included in this review, there was insufficient evidence to reach a conclusion on the effect of any screening strategy (universal screening vs. no screening, universal screening vs. screening of selected patient populations, screening of ICU patients vs. no screening, screening of surgical patients vs. no screening, screening of high-risk patients vs. no screening, screening of limited patient populations vs. screening of expanded patient populations) on MRSA transmission.

Incidence of MRSA Infection

Reduction in the incidence of MRSA infection is the primary anticipated clinical benefit of intensive strategies for MRSA control, and specifically screening. Based on the findings of this review, there was low SOE in support of universal vs. no screening for MRSA carriage. However, we found insufficient evidence to determine the impact of MRSA screening on the incidence of MRSA infection for all of the other comparisons examined (universal screening vs. screening of selected patient populations, screening of ICU patients vs. no screening, screening of surgical patients vs. no screening, screening of high-risk patients vs. no screening, screening of limited patient populations vs. screening of expanded patient populations).

Morbidity and Mortality

Ideally, MRSA screening and other infection prevention strategies will meaningfully impact consequences of infection such as overall patient morbidity and mortality. Unfortunately, comprehensive review of the available literature identified only one study (and none that attempted to control for confounders and/or secular trends) that specifically addressed the issue

of whether MRSA screening impacts patient morbidity (including complications of MRSA infection) or mortality compared to no screening or to limited screening. As a result, there is insufficient evidence to reach a conclusion.

Potential Harms

In assessing the comparative effectiveness of any intervention, whether diagnostic, therapeutic or screening, it is essential to assess the potential harms of the intervention compared to the harms of not performing the intervention. Unfortunately, none of the studies that attempted to control for confounders and/or secular trends addressed the harms of screening compared to the harms of not screening or the harms of screening compared to the harms of screening selected patient populations. As a result, there is insufficient evidence to reach a conclusion.

Hospital Resource Utilization

Hospital resource utilization is an increasingly important element of any intervention that is considered for widespread adoption. MRSA screening programs could offer both the anticipated benefit of reduced consumption of some resources (for example, reduced length of hospital stay). However, the potential benefits must be weighed against the possibility that screening and subsequent infection prevention interventions could also be associated with additional costs. In this review, no study that attempted to control for confounders and/or secular trends was identified that systematically examined the impact of screening compared to no screening or to limited screening on resource utilization. As a result, the evidence is insufficient to support a conclusion regarding the comparative impact of screening on resource utilization.

Strength of Evidence

Overall, this review found a low SOE to support the effectiveness of universal screening for MRSA carriage compared to no screening for the outcome of healthcare-associated MRSA infection. However, this review found insufficient evidence available to reach a conclusion regarding the effectiveness of screening for MRSA carriage for all of the other comparisons and outcomes of interest evaluated. Given the observational nature of many of the studies included in this review, a higher quality rating was assigned to those reports that endeavored to control for the risk of bias and confounding through the use of advanced statistical measures. Because the incidence of MRSA infection has been decreasing, studies that utilize a before/after study design without adequately controlling for secular trends are unable to distinguish between an effect due to the intervention and an effect due to the persistence of the secular trend. Similarly, because interventions geared toward patient safety, quality improvement or prevention of healthcare-associated infections (such as catheter-associated bloodstream infections or SSIs) may also decrease the incidence of MRSA infection, as may unmonitored efforts at decolonization/eradication or improvements to the physical plant that increase the availability of private hospital rooms, studies that utilize a before/after design and do not adequately control for these and other confounders are unable to determine whether the effect seen is due to the intervention or to the confounding variable. The use of observational studies to determine causal inference requires protection against bias and confounding through features of design, conduct or analysis. Therefore, studies that performed simple statistical tests without attempts to control for confounding and/or secular trends were excluded from the SOE analysis. Unfortunately, these studies comprised the bulk of the available literature on screening for MRSA carriage. The one RCT[46] (a design that minimizes the risk of bias) to examine the impact of MRSA surveillance

failed to show a favorable impact of screening, though concerns about the lengthy turnaround time of the screening modality used and the failure to implement barrier precautions, isolation and/or decolonization while awaiting screening test results limit the applicability of this study's findings.

Publication bias is a consideration in weighing the potential impact of a new strategy or technique in infection prevention and clinical quality improvement. There is considerable experience with screening for MRSA in hospitals as these strategies are routinely and commonly used for hospital based performance improvement. However, the published literature represents data which is generated as part of clinical trials in assessing the effectiveness of such screening strategies. This published data is only a fraction of the total experience and therefore, may be biased in important ways. However, examination of meeting abstracts and other grey literature did not support publication bias.

As was acknowledged by the authors of many of the reports assessed as part of this review, substantial limitations exist that preclude the opportunity to reach important conclusions about the overall effect and utility of MRSA screening. Many of these limitations are detailed specifically later in this discussion. Foremost among these considerations is the ability to adequately control for bias and confounding owing to omissions in design features and statistical analysis of observational studies. In addition, only one non-CCS study assessed the morbidity and mortality associated with MRSA screening compared to no screening or to limited screening. No studies evaluated the potential harms and resource utilization associated with MRSA screening compared to no screening or to limited screening.

Findings in Relationship to What Is Already Known

Systematic Reviews

At least two previous systematic reviews have been undertaken in order to assess the impact of MRSA screening in a variety of settings.[87,88] A 2008 systematic review[87] identified 16 observational studies and four economic analyses. The authors reported that none of the assessed studies was graded as good quality. The authors concluded that there were significant gaps in the evidence that precluded definitive recommendations about the effectiveness of MRSA screening.

Tacconelli et al.[88] reviewed nine intervention studies and one cluster randomized crossover trial in 2009. This meta-analysis of studies reporting the same outcome measures revealed a statistically significant reduction in the risk of MRSA bloodstream infections but not SSIs.

While some the conclusions of the present report are not substantially different than those reached in the previous systematic reviews, there are some differences in the interpretation of the findings. In all three reports, the paucity of rigorous, well-controlled studies employing standardized microbiological and infection control techniques serves as a critical limitation. In the present review, a much larger set of published studies is included for assessment. This is largely a function of the large number of studies and reports that have been published since the time that the previous two reports were completed. This is also an indicator of the intense activity in this field over the past several years, itself indicative of the proliferation of MRSA screening in the U.S. and elsewhere. Also distinguishing the present study is the more rigorous grading of the available evidence which may have contributed to the different conclusions reached in the systematic reviews.

Guidelines and Public Policy

Though the evidence-based reviews have reached similar conclusions, authoritative bodies have expressed diverse opinions and recommendations. The 2006 Guidelines for the Management of Multidrug-Resistant Organisms in Healthcare Settings published by the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC)[89] include active surveillance screening as a recommended intensified control strategy for multidrug resistant organisms (MDRO), including MRSA. The document recommends that such interventions should be implemented when the frequency of MDRO infections are not decreasing despite the use of more routine control measures.

The 2003 Society for Healthcare Epidemiology of America Guidelines for Preventing Nosocomial Transmission of Multidrug-Resistant Strains of *Staphylococcus aureus* and *Enterococcus*[90] take a more affirmative stand regarding the deployment of MRSA screening. The authors recommend that active surveillance cultures and contact precautions be implemented to prevent the spread of epidemiologically significant antibiotic-resistant pathogens. The guidelines further advise that these measures "should be implemented in all types of healthcare facilities throughout the system."

On the basis of such strong conclusions articulated by authoritative bodies, MRSA screening has been accepted by many key stakeholders as an established standard of care. In a number of U.S. jurisdictions, the practice has been mandated through legislative and regulatory rules, beginning in 2008. A subsequent SHEA position paper,[34] stepped back from advocating for mandatory screening, citing concerns about the importance of institutional risk assessment and possible unintended consequences of mandatory and widespread screening.

Based on the conclusions reached in the current review of specific Key Questions regarding MRSA screening, the applicability of these findings and the strength of the available evidence do not appear to readily support or refute the recommendations adopted by the CDC HICPAC[89] or in the earlier SHEA Guidelines. That MRSA screening has been adopted as a mandatory practice through legislative action in some jurisdictions is also not easily supported or refuted by the findings of the present review.

Applicability

Ultimately, the value of published evidence regarding MRSA screening or indeed any clinical intervention is largely determined by the applicability of these data to a wider range of populations in diverse settings. Applicability assessment depends on a body of evidence sufficient to permit conclusions about the comparative outcomes of MRSA screening strategies. This body of evidence does not reach a level of sufficiency; therefore, comments will be limited to relevance to the PICOTS (population, intervention, comparator, outcomes, timing, setting) elements rather than applicability.[40] The PICOTS format provides a practical and useful structure to this exercise and is employed in the subsections that follow.[40]

Population and Settings

The question of which patient populations may benefit most from MRSA screening remains controversial and is reflected in the diversity of clinical contexts in which screening has been evaluated to date. In a number of studies, the impact of screening when applied to groups of clinically or geographically well-defined populations has been examined. Prominent among these are the ICU and surgery inpatient populations. The application of findings from the ICU

and surgery patients to other patient populations is questionable. Specifically, ICU and surgery patients are at especially high risk for healthcare-associated infection as a result of distinctive aspects of their condition and management. For example, patients in both groups frequently undergo compromise of the integument barrier (e.g., insertion of vascular access devices, other invasive procedures) that increases their likelihood of clinically significant infection caused by colonizing strains of bacteria. Therefore, these groups may be especially likely to derive benefit from interventions that reduce the risk of acquisition or colonization with virulent pathogens such as MRSA.

Perhaps in recognition of this potential bias, a number of studies reviewed here examined the impact of MRSA screening in more clinically heterogeneous patient populations, encompassing a broader range of risk for subsequent deep infection. When high-risk patients are identified among this more diverse pool, the same questions arise regarding the applicability to less vulnerable patients.

The potential benefit and harms of MRSA screening have not yet been systematically evaluated in a number of special populations. Specifically, this review did not identify published studies that attempted to control for confounders and/or secular trends that specifically examined the comparative effectiveness of screening for MRSA carriage among children, pregnant women or elderly individuals (except in those cases where advanced age was identified as a specific indicator of high risk). An evaluation of the favorable and unfavorable experience with MRSA screening in such groups is essential.

Interventions

The first fundamental barrier to widespread applicability of the findings of any MRSA screening program relates to technical variation in the screening methodology itself. Given the limited evidence base, the present review did not allow for a more rigorous and systematic comparison of the relative performance of various laboratory methods or reporting standards. That said, these differences have been widely identified as important potential confounders affecting the evaluation of the performance of an MRSA screening program. One key element relates to the timing with which microbiologic assay results are returned and made available to treating clinicians. Presumably, a delay in reporting these results (such as might be associated with a culture-based lab approach) could limit the potential impact of screening in that the benefit in reduced transmission derived from the implementation of barrier precautions would itself be delayed. Such a delay, or for that matter variability in the performance sensitivity of one laboratory method versus another, could impact the effectiveness of a screening program and the resultant applicability.

Another important limitation to the applicability of the available evidence regarding MRSA screening relates to heterogeneity in the nature of the interventions performed. By its nature, MRSA screening itself (that is to say, the act of detecting MRSA through microbiologic techniques) would not be expected to impact the frequency of subsequent transmission or infection. Rather, it is the application of additional infection control interventions in response to the detection of colonization, including more rigorous hand hygiene and strict barrier precautions, environmental cleaning and even antimicrobial decolonization, that will influence clinical outcomes. That these interventions are often deployed as part of a “bundle” can further limit the conclusions that can be drawn about the attributable benefit of screening versus any of the other interventions.

A number of the studies examined as part of this review offered insufficient information to the reader regarding the full scope of interventions deployed in conjunction with MRSA screening, and specifically those measures implemented in response to the new detection of MRSA colonization. While the application of barrier precautions (the donning of gowns and gloves when caring for MRSA-positive patients) was frequently cited, most reports did not completely control for other practice standards that may have changed in light of new positive screening tests. For example, while decolonization may not have been recommended as part of an MRSA screening intervention, available studies do not, for the most part, address whether or not the use of products such as intranasal mupirocin was specifically prohibited. As a result, the reader cannot be certain that the measured effect was not influenced by the application of such uncontrolled and unmeasured interventions targeting MRSA. In addition, the studies examined as part of this review frequently excluded mention of the assessment of compliance to the specified interventions, leaving readers uncertain as to whether the failure to impact clinical outcomes can be attributed to a lack of effect or poor execution on the part of practitioners.

The heterogeneity in describing interventions was further compounded by a failure in the majority of reviewed reports to explicitly examine the potential impact of other concurrent interventions targeting different outcomes apart from MRSA that could have affected the measured impact of MRSA screening itself. These include but are not limited to campaigns to reduce the frequency of vascular device infections, hand hygiene improvement initiatives and even interventions meant to promote an institutional culture of safety. In that such measures have been shown to potentially influence the frequency of a diversity of healthcare-associated infections (including those caused by MRSA), their omission may be important.

Comparisons

The majority of studies included in this review are of an observational nature and employ a relatively straightforward before/after design. While this approach is generally appreciated to be of limited rigor, the application of historical controls (pre-intervention) may be especially problematic in the assessment of interventions to prevent the dissemination of infectious pathogens in closed populations (such as hospital inpatients). More specifically, studies conducted in this environment and in this manner are subject to confounding owing to epidemiological trends and phenomena that contribute to typical variations in the incidence of infectious diseases over time. In this context, the smaller the population, the greater the variability that may be encountered. While such changes over time may reflect statistical variation alone, changes in disease incidence may also be due to clusters of infection (which in turn might be attributable to new and more virulent strains of pathogens such as MRSA), deviations and departures from best practice or even the application of other interventions that might influence transmission or infection.

Larger before/after studies, even when conducted across multiple geographic sites and clinical settings, could also be influenced by larger secular trends in the incidence of contagious diseases.[41] These broader changes in infectious diseases epidemiology may be attributed to diverse influences including the more widespread dissemination of new prevention practices, changes in antibiotic prescribing, seasonal influences or other unknown factors. That there have been changes in the incidence of some specific MRSA infections over the past decade has been well documented. Unless these macro-trends in epidemiology are identified and accounted for, it is possible that such phenomena could be attributed to the influence of interventions such as MRSA screening.

Where specific populations have been screened (e.g., high risk, surgical patients, etc.) also introduces a challenge to applicability. This is especially the case when decision rules are applied in order to identify individuals at high risk for MRSA carriage and/or infection. While some risk factors for MRSA disease have been well characterized across diverse populations (e.g., prior antibiotic receipt or frequent contact with the health care system), other factors may be more institution- or population-specific, again limiting the applicability of some of these studies.

Outcomes

The challenge of identifying specific direct health outcomes (such as morbidity and mortality) affected by MRSA screening again limits the applicability of the available evidence and is discussed in greater detail later. In general however, it can be noted that the value of transmission or new acquisition as a surrogate for more meaningful clinical outcomes is limited. Acquisition of new colonization represents just one step in the continuum of a patient progressing through the following states: 1) uncolonized to 2) colonized to 3) infected to 4) complications including death. To the extent that there is variation between individual patients, patient types, clinical settings and institutions in terms of the risk of progressing from colonized to overtly infected and from infected to morbidity and mortality will impact the applicability of the results based on just consideration of acquisition. Similarly, one must anticipate that even in the rare studies in which more meaningful outcomes are reported (including mortality), variation in clinical practices and management between patients, providers and organizations could serve to blunt or exaggerate the benefit attributed to MRSA screening itself.

More detailed analysis of the effect of MRSA screening on specific types of infection (such as vascular access device related bloodstream infections and SSI), whether considered as a primary outcome or examined on a post hoc basis, offers at least the opportunity to more clearly estimate the applicability of study findings. However, this opportunity is contingent on an examination and quantification of the impact of other variables related to both the risk of and interventions to prevent such infections in the study population. Unfortunately, such analysis was not available among the studies included in the present review.

Implications for Clinical and Policy Decisionmaking

Based on the relatively limited strength of the evidence base and its uncertain applicability, evidence gaps limit the implications that can be drawn for clinical practice and policy decision-making. Further, decision-making is influenced by the complex context regarding the deployment of a resource intensive strategy such as MRSA screening. Factors that contribute to this complexity are outlined in the following sections which consider the circumstances surrounding decision-making at the level of an individual hospital and the wider community.

Clinical (Hospital-Based) Decisionmaking

Clinical and administrative leaders make decisions about the deployment of hospital-based infection prevention strategies based on a number of factors. First among these is the clinical impact of the particular infection or pathogen that is to be targeted (as determined by the size of the population affected and the severity of associated disease). In this context, infections that occur frequently and that are associated with substantial morbidity and mortality are generally targeted as a high priority for intervention. Ideally, an important next step is to critically examine the performance of those prevention strategies that have already been deployed. In addition to

pursuing rigorous surveillance data to accurately measure the impact on outcomes, hospital decision makers strive to determine whether the effectiveness of these strategies is in any way limited, such as by poor compliance with best practices or inadequate resource allocation. The next step is to determine the likely impact of the strategy under consideration. This assessment, which is aligned most closely with the type of systematic examination of the available evidence included in this review, compels hospital leadership to identify best practices that are most applicable to the problem and the local environment. A critical element of this review was to ascertain the potential unintended consequences and harms of the intervention so as to best assess the impact and to try to mitigate risk. Finally, economic considerations must be evaluated. In general, resources applied to infection prevention are limited and must be allocated efficiently so as to minimize risk of infection to the greatest number of patients.

According to accreditation standards adopted at most U.S. hospitals, the process described in the preceding paragraph should be undertaken on a periodic basis by a multidisciplinary group as part of formal infection control risk assessment. This exercise, which may be undertaken in a semi-quantitative fashion employing standardized tools, is intended to ensure that infection prevention resources are allocated in the most rational manner.

Based on examination of the available evidence as summarized in this review, it appears that insufficient information is currently available to support or refute the routine implementation of MRSA screening by local infection prevention experts and hospital leaders as part of organizational infection control risk assessment in all settings. Fundamental limitations (discussed in the following section) regarding the impact of MRSA screening on diverse populations and a variety of outcomes are most critical. Decision-making is further hindered by a near complete absence of systematic evidence regarding the potential harms of MRSA screening. However, even in the absence of these data, hospital leaders may feel compelled to make a determination regarding the appropriateness of MRSA screening based on the other factors described at the beginning of this section. More specifically, if MRSA infection is affecting a large number of patients and the resultant infections are severe and even life threatening, infection prevention experts and hospital leadership may feel the potential benefits of screening outweigh the risks, even in light of the limited available evidence to deploy a screening program. This may especially be the case if other interventions, when maximally deployed and supported, have been unable to check the spread of infection. In essence, this advice mirrors that offered in the CDC HICPAC guidelines previously cited.

Policy Decisionmaking

The challenges of applying the available evidence base are further compounded when decision making about MRSA screening is considered as a matter of public policy (such as in accreditation standards or legislative mandates). In this context, limitations of the applicability of the available evidence (see previous section) are especially important. One of the key arguments that has been raised against the application of broad policy mandates compelling the implementation of MRSA screening relates to the value of institutional risk assessment in determining the most appropriate control strategies for MRSA and indeed all infectious threats. In this setting, understanding the precise needs and values of the institution and then reviewing the available evidence to determine the extent to which the experience reported in the literature can be applied is essential.

Limitations of the Comparative Effectiveness Review Process

There were a number of questions and potential limitations that arose during the clinical effectiveness review process. One unexpected challenge related to intense research and policy activity surrounding MRSA screening in the time during which the review was conducted. Ongoing surveillance of the available literature as well as close scrutiny of meeting abstracts and the grey literature was undertaken to mitigate the risk that important new studies would be omitted.

Another important challenge came when determining the scope of the review. In general, the decision was made to be inclusive in considering the available literature, in which observational studies make up the bulk of the literature.

In the same vein, contributors to this review were challenged to negotiate a rational and justifiable framework for grading the SOE of the many observational reports included in the assessment. To this end, the decision was made to recognize the importance of more advanced statistical methods in attempting to control for confounding inherent in this study approach.[91-93] As a result, those reports that employed regression analysis or time series analysis were assigned a higher level of quality than other reports. A more detailed discussion of the review of the SOE is provided elsewhere in this report.

Limitations of the Evidence Base, Research Gaps and Future Research Opportunities

As has been noted, there are numerous limitations to the available evidence base that ultimately compromise the applicability of these findings to clinical and policy decision-making. In this section, these limitations are more clearly articulated and then important gaps in the available evidence are identified as targets for future research. In undertaking the comprehensive needs assessment, the PICOTS structure is once again adapted. Finally, specific concerns related to study design and analytical methods are outlined, again in the hopes of encouraging improved standards in future research.

Populations and Settings

There is an inherent tension when selecting patient populations and clinical settings for the application of MRSA screening. Larger and more diverse patient groups (such as those that might be captured in a universal screening algorithm) offer the greatest opportunity to detect benefits and harms as measured by meaningful clinical outcomes (including morbidity and mortality). At the same time, the impact of screening on such heterogeneous groups may be biased by uncontrolled confounders or diluted by the inclusion of patients at varying degree of risk for MRSA acquisition or subsequent infection.

Ideally, future studies could target larger more homogeneous patient populations. This approach will permit the detection of even rare outcomes while simultaneously extending the applicability of the findings to similar large populations and patient groups. Moreover, by restricting inclusion so as to control for confounding that arises in heterogeneous patient populations, the opportunity to detect true biological predictors of benefit or harm are maximized. Realistically, this degree of scale will only be achieved through large multicenter

trials, as is noted at the end of this section. In the future, widespread use of electronic medical records may provide predictors of benefits or harms.

Another concern regarding the patient populations included in the available evidence base relates to the study of special populations. While the risk of MRSA infection varies in some of these groups, it is essential that the potential positive and negative impact of MRSA screening on unique groups such as children and pregnant women be explored.

Interventions

As has been noted, there are severe limitations in the available evidence that can be attributed to pronounced inconsistency in defining, applying and measuring the various interventions that are bundled as part of MRSA screening. As a result, future studies that aim to contribute evidence on the benefits of screening for MRSA carriage must take a more controlled approach to the application of specific laboratory measures (e.g., PCR versus culture), test turnaround time, the management of patients while awaiting test results, transmission prevention strategies (e.g., contact precautions), and the use of decolonization therapy and environmental control. In addition, more precise accounting is required in order to best understand and quantify the potential bias introduced by secular and local epidemiologic trends and the influence of concomitant infection prevention strategies and interventions. This last point is especially important as infection prevention strategies (including MRSA screening) are typically deployed in sequence or concurrently. In this manner, it is essential to document the context in which screening was implemented so as to best understand the impact of the intervention. Important considerations could include prior MDRO control programs and an assessment of the culture of safety at the study sites.

In terms of addressing these shortcomings, it is unrealistic to believe that a standardized and uniform approach can be recommended and applied to all future studies of MRSA screening. Lacking such a standard, a maximally transparent approach to reporting such details is absolutely critical. During study design and budgeting, extreme caution should be applied to ensure that early methodological decisions (such as the selection of a testing modality with a lengthy turnaround time) do not undermine the applicability and strength of the findings that might ultimately be generated.

Ideally, additional studies can be undertaken that will effectively compare the impact of screening strategies employing a variety of specific interventions and approaches. In essence, this work will entail examining each element of an intervention bundle in order to accurately determine the attributable benefit or harm for each component of the bundle. It may be the case, for example, that a component such as decolonization for incidentally discovered cases of MRSA may independently produce a significant clinical benefit.

Comparisons

Clinically meaningful and methodologically sound comparisons serve as the cornerstones that support the SOE and applicability of applied clinical research. This is especially true when reporting the findings of observational studies. If there is one key shortcoming in the available evidence for MRSA screening, it relates to fundamental issues of study design and specifically the overreliance on before/after studies.

As has been noted elsewhere in this discussion, the before/after design allows for the introduction of considerable unmeasured bias into even large observational epidemiologic

studies. In this regard, even the large multicenter examinations of the impact of MRSA screening, when executed as a simple before/after design, may be seen as severely flawed.

Increasingly, it is recognized that the optimal design for testing and evaluating the impact of a novel infection prevention strategy is the cluster-RCT. With this approach, an individual unit (such as a single ICU) is randomized to either an intervention or control arm. However, cluster RCTs may also face barriers to feasibility due to the large number of institutions needed to achieve balance after randomization. It is also imperative to improve the quality of quasi-experimental studies through: (1) more rigorous study design; (2) controlling for secular trends and confounders; and (3) reporting on the full range of clinically important outcomes.

Outcomes

Deficiencies in the evidence base regarding specific outcomes can be addressed in alignment with the outcomes of interest that served as the original basis for much of this review. For any future research comparing MRSA screening strategies, it is critical that these clinically significant outcomes be precisely defined and collected.

In terms of the incidence of MRSA infection, we found that many comparative studies of screening for MRSA carriage reported on healthcare-associated MRSA infection. However, the definition of MRSA infection varied among studies. For future research in this field, it is imperative that case definitions are precise and specific. Ideally these will be adjusted to harmonize with existing case definitions from the CDC and elsewhere.

Precise estimates of the impact of MRSA screening on morbidity and mortality remain lacking in the extant literature that evaluates the comparative effectiveness of screening for MRSA carriage. To allow more meaningful assessment of these crucial health outcomes, future studies will need to enroll sufficient numbers of patients to be adequately powered to detect the effect of screening for MRSA carriage compared to no screening or to screening of selected patient populations on morbidity and mortality. Once again, this purpose will be best served in all likelihood through the establishment of multicenter studies.

So long as more comprehensive studies of morbidity and mortality remain elusive, the use of MRSA acquisition and transmission as a surrogate to measure the impact of screening will persist. That said, the rigor with which this outcome is tested should be enhanced. Specifically, there is the opportunity to apply more standardized approaches to the collection of surveillance specimens to detect new colonization events. Moreover, the confounding that could be introduced by failing to examine the frequency with which various patient populations proceed from colonization to infection can be mitigated through more careful analysis.

If there is a singular deficiency in determining the applicability of the results of MRSA screening studies it is directly linked to the failure to measure the unintended harms that can come with even a well-intentioned screening program compared with the harms of not screening or of screening selected patient populations. Among the numerous potential harms that have been associated with MRSA screening and related interventions are: social isolation and increased risk of safety events associated with contact precautions, inappropriate use of mupirocin, increased risk of inappropriate systemic antibiotic use, delays in patient flow and hospital discharge, and stigma associated with colonization or infection. To attempt to measure the favorable impact of MRSA screening while ignoring the potential risks is to present incomplete and potentially misleading data.

Conclusions

There is low SOE that universal screening of hospital patients decreases MRSA infection. However, there is insufficient evidence on other outcomes of universal MRSA screening, including morbidity, mortality, harms and resource utilization. There is also insufficient evidence to support or refute the effectiveness of MRSA screening on any outcomes in other settings. The available literature consisted mainly of observational studies with insufficient controls for secular trends and confounding to support causal inference, particularly because other inventions were inconsistently bundled together with MRSA screening. Future research on MRSA screening should use design features and analytic strategies addressing secular trends and confounding. Designs should also permit assessment of effects of specific bundles of screening and infection control interventions and address outcomes including morbidity, mortality, harms and resource utilization.

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Abbreviations

Abd	abdominal
ACP	American College of Physicians
AHRQ	Agency for Healthcare Research and Policy
ANOVA	analysis of variance
ANCOVA	analysis of covariance
APIC	Association of Professionals in Infection Control and Epidemiology
BA	before/after
BICP	background infection control practices
BP	barrier precautions
BPCC	barrier precautions compliance checks
BSI	bloodstream infections
C	control
CADTH	Canadian Agency for Drugs and Technologies in Health
CA-MRSA	community-acquired MRSA
CCS	studies attempted to control for confounding/secular trends
CDC	Centers for Disease Control and Prevention
CG	control group
CHKGL	checklist/guidelines
CI	confidence interval
Coh	cohorting
EPC	Evidence-based Practice Center
EPICOT	Evidence, Population, Intervention, Comparison, Outcome, Timestamp
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ESICM	European Society of Intensive Care Medicine
FDA	U.S. Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HICPAC	Healthcare Infection Control Practices Advisory Committee
HCA	health care-associated
HCW	health care worker
HH	hand hygiene
HW	handwashing
ICAAC	Interscience Conference on Antimicrobial Agents and Chemotherapy
ICP	infection control practices
ICPW	infection control practices while waiting for MRSA test results
ICU	intensive care unit
INAM	intranasal antimicrobial
Int	intervention
IRR	incidence rate ratio
ISDA	Infectious Disease Society of America
ISF	International Sepsis Forum
ISID	International Society of Infectious Diseases
Iso	isolation

ITS	interrupted time series
IV	intravenous
IVAB	intravenous antibiotics
KI	Key Informants
KQ	Key Question
MDRO	multi-drug resistant organism
MeSH®	Medical Subject Headings®
MICU	medical intensive care unit
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-sensitive *Staphylococcus aureus*
NA	not applicable
N/n	no; number
NG	nasogastric
NHS	National Health Service
NHSN	National Healthcare Safety Network
non-CCS	studies did not attempt to control for confounding/secular trends
NR	not reported
NSS	not statistically significant
PCR	polymerase chain reaction
PEG	percutaneous endoscopic gastrostomy
PICU	pediatric intensive care unit
PICOTS	patient(s), intervention(s), comparator(s), outcome(s), timing, setting(s)
PIDS	Pediatric Infectious Diseases Society
PO	oral/by mouth
POAB	oral antibiotics
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QEX	quasi-experimental
RCT	randomized, controlled trial
RR	relative risk
SHEA	Society for Healthcare Epidemiology of America
SICU	surgical intensive care unit
SIR	standardized infection ratio
SOE	strength of evidence
SS	statistically significant
SSI	surgical site infection
TAMW	topical antimicrobial washes
TEP	Technical Expert Panel
Test +	positive MRSA screening test result
Test -	negative MRSA screening test result
TOO	Task Order Officer
U.S.	United States
U	unclear/unknown
UK	United Kingdom
Unspec	unspecified

USPSTF	U.S. Preventive Services Task Force
VRE	vancomycin-resistant *Enterococcus*
WHO	World Health Organization
X-over	crossover
Y	yes

Appendix A. Search Strategies

The following electronic databases were searched for citations.

- MEDLINE® (January 1, 1990, to September 1, 2011)
- EMBASE® (January 1, 1990, to September 1, 2011)
- Cochrane Controlled Trials Register (to September 1, 2011)

The MEDLINE® search resulted in 4746 unique citations. The EMBASE® search resulted in 3199 citations. The Cochrane search resulted in no new citations.

PubMed Search

8/24/10 – yield 4746

Search updated 9/1/11 for 8/24/10 to 9/1/11

"Methicillin-Resistant Staphylococcus aureus"[Mesh]
OR ("Methicillin Resistance"[Mesh] AND "Staphylococcus aureus"[Mesh])
OR "methicillin-resistant staphylococcus aureus" OR MRSA
AND
"prevention and control "[Subheading] OR "Mass Screening"[Mesh] OR screening OR screened OR screen OR surveillance OR diagnosis
AND
randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR "clinical trial" OR ((singl* OR doubl* OR trebl* OR tripl*) AND (mask* OR blind*)) OR placebos [mh] OR placebo* OR random* OR research design [mh:noexp] OR follow-up studies [mh] OR prospective studies [mh] OR prospectiv* OR volunteer*) OR "Comparative Study "[Publication Type] OR "Evaluation Studies "[Publication Type] OR control OR controlled OR controls

EMBASE Search

10/18/10 – yield 3199

Search updated 9/1/11 for 10/18/10 to 9/1/11

'methicillin-resistant staphylococcus aureus'/exp OR ('methicillin resistance'/exp AND 'staphylococcus aureus'/exp) OR MRSA AND [humans]/lim
AND
'prevention and control'/exp OR 'mass screening'/exp OR 'screening'/exp OR screened OR screen OR surveillance OR 'diagnosis'/exp AND [humans]/lim
AND
'randomized controlled trial'/exp OR 'randomised controlled trial'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR (singl* OR doubl* OR trebl* OR tripl* AND (mask* OR blind*)) OR placebo* OR random* OR 'follow-up study'/exp OR 'prospective study'/exp OR

prospectiv* OR volunteer* OR 'comparative study'/exp OR 'evaluation study' OR 'control'/exp OR controlled OR controls AND [humans]/lim

Cochrane Search

10/18/10

Search updated 9/1/11 – search last 12 months – no unique records found

"methicillin-resistant staphylococcus aureus" OR (“Methicillin Resistant" AND "Staphylococcus aureus")
AND
Screening OR Diagnosis OR surveillance

Search Strategy for Gray Literature

Regulatory Information

FDA

Source: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm
Date searched: 6/21/2011
Search strategy: 510(k) summary documents for the following were searched on FDA@devices
Xpert MRSA SA/SSTI
XPert MRSA SA/BC)
XPert MRSA
GeneOhm MRSA assay
BBL ChromAgar MRSA
Records: 49

Clinical Trial Registries

NIH Database

Source: http://clinicaltrials.gov/
Date searched: 6/17/2011
Search strategy: Keyword + [ALL-FIELDS] AND "COMPLETED" [OVERALL-STATUS]
Key words: “MRSA Screen” “MRSA Screening” “MRSA surveillance” “MRSA active surveillance” “MRSA intervention” “MRSA prevention”
Records: 63

BioMed Central

Source: http://www.controlled-trials.com/mrct/
Date searched: 6/13/2011
Search strategy: “MRSA” for completed trials
Records:13

PhRMA

Source: http://www.clinicalstudyresults.org/home/
Date searched: 6/20/2011
Search strategy: Search String = "MRSA" for completed trials
Records: 2

WHO International Clinical Trials Registry Platform Search Portal

Source: http://apps.who.int/trialsearch/
Date searched: 6/20/2011
Search strategy: Search String = "MRSA" in the Title for ALL recruitment status trials
Records: 90

Conference Papers and Abstracts

Cambridge Scientific Abstracts

Source: http://www.csa.com/factsheets/cpi-set-c.php
Date searched: 6/28/2011
Search strategy: search string "MRSA"
Records:73

Scopus

Source: http://www.scopus.com/home.url
Date searched:6/29/2011
Search strategy: search string "MRSA"
Records:211

Specific Conferences and Association Meetings

Source:

1. ICAAC (Interscience Conference on Antimicrobial Agents and Chemotherapy)
2. The Infectious Disease Society of America
3. The Society for Healthcare Epidemiology of America
4. The Association of Professionals in Infection Control and Epidemiology
5. The American College of Physicians
6. The Pediatric Infectious Diseases Society
7. The European Society of Clinical Microbiology and Infectious Diseases
8. The International Society of Infectious Diseases
9. The Australasian Society of Infectious Diseases
10. The International Sepsis Forum
11. The European Society of Intensive Care Medicine

Date searched: 6/21/2011
Search strategy: KW: "MRSA"
Records:829

Government Documents

RePORTER

Source: http://projectreporter.nih.gov/reporter.cfm
Date searched: 6/20/2011
Search strategy: key word “MRSA” OR “methicillin-resistant”
Records:9

HSRPROJ

Source: http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm
Date searched: 6/15/2011
Search strategy: key word “MRSA” OR “methicillin-resistant”
Records:6

AHRQ GOLD

Source: http://gold.ahrq.gov/projectsearch/
Date searched: 6/15/2011
Search strategy: key word “MRSA” OR “methicillin-resistant”
Records: 0

Manufacturer Database

Source: CEPHEID
Date posted: 8/3/11
Date searched: 6/29/2011
Search strategy: Not applicable
Records: 95

Appendix B. Excluded Studies

Excluded: Foreign Language

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Excluded: No Primary Data

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Excluded: Does Not Meet Criteria During Quality Control: Review

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Appendix C. MRSA Abstract and Title Screening Form

1. Is article published in English? Exclude if not English.

- ◉ Yes
- ☐ No
- ☐ Uncertain

2. Does article report primary data? Exclude if no primary data (narrative reviews, commentaries, editorials, letters, news reports, etc...)

- ☐ Yes
- ☐ No
- ☐ Uncertain

3. Are the study participants human? Exclude if non human participants.

- ☐ Yes
- ☐ No
- ☐ Uncertain

4. Was study conducted among patients in ambulatory care or hospital settings? Exclude if not patients in ambulatory health care or hospital settings (nursing homes); also apply if focus is not patients (e.g. health care workers).

- ☐ Yes
- ☐ No
- ☐ Uncertain

5. Was MRSA the primary disease focus? Exclude if focus of study does not include or is not primarily centered on MRSA.

- ☐ Yes
- ☐ No
- ☐ Uncertain

6. Was the design a comparison of MRSA screening vs no screening or one screening method with another screening method? Exclude if the study is not a randomized controlled trial (RCT) or quasi-experimental study (QEX) comparing either screening (by either culture or PCR) vs no screening OR more limited screening vs expanded screening (NDE, see more detailed description of included and excluded study designs below); should also mark for retrieval.

- ☐ Yes
- ☐ No
- ☐ Uncertain

Appendix D. MRSA Full-Text Screening Form

1. Is article published in English? Exclude if not English.

- ☐ Yes
- ☉ No
- ☐ Uncertain

2. Does article report primary data? Exclude if no primary data (narrative reviews, commentaries, editorials, letters, news reports, etc...)

- ☐ Yes
- ☐ No
- ☐ Uncertain

3. Are the study participants human? Exclude if non human participants.

- ☐ Yes
- ☐ No
- ☐ Uncertain

4. Was study conducted among patients in ambulatory care or hospital settings? Exclude if not patients in ambulatory health care or hospital settings (nursing homes); also apply if focus is not patients (e.g. health care workers).

- ☐ Yes
- ☐ No
- ☐ Uncertain

5. Was MRSA the primary disease focus? Exclude if focus of study does not include or is not primarily centered on MRSA.

- ☐ Yes
- ☐ No
- ☐ Uncertain

6. Was the design a comparison of MRSA screening vs no screening or one screening method with another screening method? Exclude if the study is not a randomized controlled trial (RCT) or quasi-experimental study (QEX) comparing either screening (by either culture or PCR) vs no screening OR more limited screening vs expanded screening (NDE, see more detailed description of included and excluded study designs below); should also mark for retrieval.

- ☐ Yes
- ☐ No, compared different forms of MRSA screening
- ☐ No, irrelevant study
- ☐ Uncertain

7. Did the study report a relevant outcome? Exclude if: no outcome is reported with a denominator or if one of these outcomes is not reported: MRSA incidence or prevalence, morbidity, mortality, harms, or resource utilization.

- ☐ Yes

☐ No

☐ Uncertain

8. Did the study report a statistical analysis? Exclude if: no statistical analysis is reported, also sort into categories: 2-group tests vs regression or time series analysis. If you answer 'Yes', please enter 1 for two-group test and 2 for time-series or regression analysis in the adjacent text box.

☐ Yes

☐ No

☐ Uncertain

9. Additional Comments:

10. Quality control: After QC review, should article be included?

☐ Yes

☐ No

☐ Uncertain

11. QC comments

Appendix E. MRSA Data Abstraction Form Elements

Study Characteristics

1. First Author (last name, first name)
2. Year
3. Country
4. Study Design
    a. RCT
    b. ITS
    c. QEX-BA
    d. QEX-CG
    e. X-OVER
5. Intervention N:
    a. Rate:
    b. Proportion:
    c. Both:
6. Indicate the units for the Intervention N:
    a. Person-Time
    b. Individuals
    c. Other
7. Control N:
    a. Rate:
    b. Proportion:
    c. Both:
8. Indicate the units for the Control N:
    a. Person-time
    b. Individuals
    c. Other:
9. Intervention(s) (including assay type)
10. Control Intervention(s) (including assay type)
11. Setting
12. Study duration
13. Pre-defined endpoints
14. Inclusion Criteria
15. Exclusion Criteria
16. Participant Characteristics of Intervention Group
17. Participant Characteristics of Control Group
18. Colonization Pressure Intervention Group
19. Colonization Pressure Control Group
20. Turnaround Time
21. Duration of Follow-Up Intervention Group
22. Duration of Follow-Up Control Group
23. Source of Funding and Disclosed Author-Industry Relationships

Outcomes

1. Study Description of Outcome (how did article label the outcome?)
2. Study Definition of Numerator of Outcome
3. Study Definition of Denominator of Outcome
4. Indicate how the outcome measure is reported and specify units if rate (e.g., per 1000 patient-days)
    a. Rate:
    b. Proportion
    c. Both:
    d. Other:
5. If the outcome is a rate indicate the units
    a. per 100 patient days
    b. per 1000 patient days
    c. per 10,000 patient days
    d. per 100 admissions

    e. per 1000 admissions
    f. per 10,000 admissions
    g. Other:
6. Frequency of Outcome in Intervention Group:
7. Frequency of Outcome in Control Group:
8. Difference [Screening-Control (95% CI)]
9. Difference Metric:
    a. Rate Ratio:
    b. Risk Ratio:
    c. Rate Difference:
    d. Risk Difference:
10. Analysis (e.g., Regression, Name of Statistical Test)
11. Univariate Analysis Results (variable1 (p value); ...)
12. Multivariate Analysis Results (variable1 (p value); ...)
13. Were covariates included in multivariate models based on univariate analysis p values?
    a. Yes
    b. No
    c. Uncertain
14. Describe decisions for building final multivariate model.

Study Quality

1. Initial assembly of comparable groups
    a. Yes
    b. No
    c. Uncertain
2. Maintenance of comparable groups (includes attrition, crossovers, adherence, and contamination)
    a. Yes
    b. No
    c. Uncertain
3. Avoidance of important differential loss to followup or overall high loss to followup.
    a. Yes
    b. No
    c. Uncertain
4. Measurements reliable, valid, equal (includes masking of outcome assessment)
    a. Yes
    b. No
    c. Uncertain
5. Interventions comparable/ clearly defined
    a. Yes
    b. No
    c. Uncertain
6. All important outcomes considered
    a. Yes
    b. No
    c. Uncertain
7. Appropriate analysis of results (adjustment for potential confounders and intention-to-treat analysis)
    a. Yes
    b. No
    c. Uncertain
8. Funding/ sponsorship source acknowledged
    a. Yes
    b. No
    c. Uncertain
9. Overall Rating
    a. Good
    b. Fair
    c. Poor
10. Were baseline prognostic characteristics clearly described and groups shown to be comparable?
    a. Yes
    b. No
    c. Uncertain
11. Were interventions clearly specified?

a. Yes
b. No

12. Were participants in treatment groups recruited in the same time period?
    a. Yes
    b. No
    c. Uncertain
13. Was there an attempt by investigators to allocate participants to treatment groups in an attempt to minimize bias?
    a. Yes
    b. No
14. Were concurrent/concomitant treatments clearly specified and given equally to treatment groups?
    a. Yes
    b. No
15. Were outcome measures clearly valid, reliable, and equally applied to treatment groups?
    a. Yes
    b. No
16. Were outcome assessors blinded?
    a. Yes
    b. No
    c. Uncertain
17. Was the length of follow-up adequate? (median/mean, range of follow-up)
    a. Yes
    b. No
18. Was attrition below an overall high level (<20%)?
    a. Yes
    b. No
    c. Uncertain
19. Was the difference in attrition between treatment groups below a high level (<15%)?
    a. Yes
    b. No
    c. Uncertain
20. Did the analysis of outcome data incorporate a method for handling confounders such as statistical adjustment?
    a. Yes
    b. No
21. Did the study design use a separate control group?
    a. Yes
    b. No
22. Did the statistical analysis use regression or time series modeling?
    a. Yes
    b. No

Appendix F. Data Abstraction Tables

Appendix Table F1. Characteristics of studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Chaberny et al., 2008,[1] Germany	QEX-BA	Expanded Vs Limited Screening	C + Int: (219,124 admissions; 1,987,676 patient-days)	Limited screening of high risk (roommates and known readmitted patients) using culture: 01/01/02 - 06/30/04	Expanded screening of high risk patients plus major surgical wards and ICUs using culture: (07/01/04 - 12/31/04)	Hospital	Primary: incidence of nosocomial MRSA infections for the entire hospital.
Chowers et al., 2009,[2] Israel	QEX-ITS	Screening of High Risk Pts Vs No Screening	C + Int: (n=377,945; 1,535,806 patient days)	No screening: 11/01 - 07/03	Screening using culture of high risk patients in periods 1 and 2, using PCR in periods 3 and 4: 7/03-12/07	Community hospital	Primary: nosocomial MRSA bacteremia rates Secondary: number of MRSA-positive carriers per number of screened patients
Ellingson et al., 2011,[3] USA	QEX-ITS	Screening of High Risk Pts Vs No Screening	NR	No screening: 10/99-10/01	Screening using culture in surgical ward, surgical ward plus SICU, surgical ward plus SICU plus all remaining acute care wards: 10/01-05/08	Veterans Affairs acute care hospital	Clinical incidence of MRSA colonization or infection. Secondary outcomes included clinical incidence of MSSA colonization /infection, quarterly incidence of MRSA bloodstream infection, monthly proportion of all clinically incident *S. aureus* isolates that were resistant to methicillin.
Gould et al., 2007,[4] UK	QEX-ITS	Screening of ICU Risk Pts Vs No Screening	C: (n=1232) Int: (n=1421)	No screening:	Screening at time of ICU admission by culture: 05/01 - 04/03	Mixed MICU/SICU	Acquisition and spread of MRSA in the ICU.

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Harbarth et al., 2008,[5] Switzerland	QEX-CG, X-OVER	Screening of Surgical Pts Vs No Screening	C: (83,120 patient days ; 10,910 admissions) Int: (83,757 patients days; 10,844 admissions)	Standard IC alone: Period 1 ((10/04 - 06/05): Urology, transplant & abd. surgery wards Period 2 (09/05 - 05/06):Orthopedic, neurosurgery, plastic surgery, cardio, & thoracic surgery wards	Standard IC plus screening in surgical wards using PCR Int 1: (10/04-06/05) Orthopedic, Neurosurgery, plastic surgery, cardiovascular, & thoracic surgery wards Int 2 (09/05-05/06): Urology, transplant, & abd. surgery wards	Abdominal surgery, orthopedics, urology, neurosurg, cardiovasc surgery, thoracic surgery, plastic surgery, and solid organ transplantation wards.	Primary: nosocomial MRSA infection rates; Secondary: MRSA SSI rates; MRSA colonization infection rates
Harbarth et al., 2000,[6] Switzerland	QEX-BA	Screening of High Risk Pts Vs No Screening	C + Int: (50,6012 admissions)	No screening: 01/89 - 12/92	Screening in high risk wards using culture: 01/93 - 12/97	Primary and tertiary care teaching hospital	Reservoir of MRSA patients and rate of MRSA bacteremia
Holzmann-Pazgal et al., 2011,[7] USA	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n= 730) Int: (n=2367)	No screening: 1/06-12/06	Screening in PICU by culture: 1/07-12/09	PICU	Incidence of MRSA transmission and nosocomial MRSA acquisition in the PICU
Huang et al., 2006,[8] USA	QEX-ITS	Screening of ICU Risk Pts Vs No Screening	NR	No screening: 01/96 - 07/02	Screening culture (on admission ICU and weekly through ICU stay): 09/03 - 12/04	ICU	MRSA bacteremia
Huskins et al., 2011,[9] USA	RCT	Screening of ICU Risk Pts Vs No Screening	C: (n=1615) Int: (n= 2441)	No screening: 3/06-8/06	Screening in ICU by culture: 3/06 - 8/06	Adult ICUs: MICU/SICU	ICU-level incidence of new events of colonization or infection with MRSA or VRE. Secondary ICU-level outcomes were the incidences of colonization or infection with MRSA and VRE calculated separately as well as several processes of care measures.

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Jain et al., 2011,[10] USA	QEX-BA	Universal Vs No Screening	Int: 1,934,598	No screening: 10/05-9/07	MRSA bundle including universal screening using culture or PCR: 10/07-6/10	Veterans Affairs hospitals	Health care-associated MRSA infections
Leonhardt et al., 2011,[11] USA	QEX-CG (Case Control)	Universal Vs Screening of Selected Pts	C: (n= 5931) Int: (n=9118)	Screening in high risk patients using PCR: 04/09 - 12/09	Universal screening using PCR: 04/09 - 12/09	Community hospital	Hospital-acquired MRSA infection; MRSA prevalence on admission
Muder et al., 2008,[12] USA	QEX-BA	Screening of Surgical Pts Vs No Screening Screening of ICU Pts Vs No Screening	C (year 2002): (9,796 person-time Int (year 2006): (11,653 person-time)	No screening: Surgical ward: (09/00 - 10/01); Surgical ICU: (09/02 - 10/03)	Standard precautions emphasizing hand hygiene, contact precautions, active surveillance cultures, and a systems-engineering approach to infection control: Surgical ward (10/01 - 09/26/06) Surgical ICU (10/03 - 09/26/06)	Surgical ward Surgical ICU	MRSA transmission and infection rates
Raineri et al., 2007,[13] Italy	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=667; 5,456 patient-days) Int1: (n=1995 total admissions to the ICU; 13669 patient-days) Int2: (n=1316 total admissions; 8310 patient days)	No screening: 01/96 - 12/31/97	Screening by culture in ICU: 01/01/98 - 2005	MICU/SICU	MRSA infections diagnosed in ICU and acquisition of MRSA during ICU stay

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Reilly et al., 2012,[14] Scotland	QEX: Before/after	Universal screening vs no screening	81,438	No screening, duration 18 months prior to the intervention	Universal screening (screening of all admissions except psychiatric, obstetric and pediatric admissions), 8/08-7/09	Three National Health Service boards including six acute hospitals	Colonization prevalence, infection incidence and infection incidence indicators (first clinical isolates from routine laboratory data)
Robicsek et al., 2008,[15] USA	QEX-BA	Universal Vs No Screening	C: (n= 39,521) Int: (n=73,464)	No screening: 8/03-8/04	Universal screening using PCR: 9/05-9/07	3-hospital organiza-tion	Primary: Aggregate hospital-associated MRSA Infection rate; Secondary: Rate of health care-associated MRSA and MSSA bacteremia, rates of aggregate MRSA infection occurring up to 180 days after discharge, adherence to MRSA surveillance.
		Universal Vs Screening of Selected Pts	C: (4392 ICU admissions) Int: (n=73,464)	Screening in ICU using PCR: 9/04-8/05	Universal screening using PCR + routine therapy for colonization: 9/01/05 - 4/30/07	ICU	
		Screening of ICU Risk Pts Vs No Screening	C: (n=39,521) Int: (n=40392)	No screening: 08/03 - 08/04	Screening in ICU by PCR: 09/04 - 08/05	ICU	

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Rodriguez-Bano et al., 2010,[16] Spain	QEX-ITS	Screening of High Risk Pts Vs No Screening	NR	No screening: Period A 1/95-12/96 Period B 1/9712/-98	Period C: Screening using culture in patients + HCW in wards with suspected MRSA transmission and screening of roommates of patients with MRSA colonization in wards without active screening : 01/99 - 12/00 Period D: In addition to period C intervention, active screening in readmitted patients previously colonized with MRSA and patients admitted from other health care facilities: 1/01-12/08	Tertiary teaching hospital	Rates of MRSA colonization or infection and rates of MRSA bacteremia
	QEX-ITS	Expanded Vs Limited Screening	NR	Limited in high risk units using culture: period C 1/99-12/00	Expanded screening of high risk units OR high risk units plus high risk patients via culture: Period D 01/01-12/08	Tertiary referral hospital	

Abd: Abdominal; BA: Before after; C: Control; CG: Control group; HCW: Health care workers; IC: Infection control; ICU: Intensive care unit; Int: Intervention; ITS: Interrupted time series; MICU: Medical intensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* MSSA: Methicillin-sensitive *Staphylococcus aureus;* N: No; NR: Not reported; PCR: Polymerase chain reaction; PICU: Pediatric intensive care unit; QEX: Quasi-experimental; RCT: Randomized controlled trial; SICU: Surgical intensive care unit; SSI: Surgical site infection; X-over: Cross over; Y: Yes

Appendix Table F2. Characteristics of studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Blumberg, et al., 1994,[17] South Africa	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=2315) Int: (n=2605)	No screening: 1 year	Screening in ICU and pediatric oncology unit using culture: 1 year	ICU (MICU, SICU, PICU and pediatric oncology)	Identification and treatment of MRSA-positive staff and patients as well as to isolate MRSA-positive patients in the ICU and pediatric oncology units.
Bowler et al., 2010,[18] USA	QEX-BA	Screening of High Risk Pts Vs No Screening	NR	No screening: 07/05 - 06/06	Screening of high risk patients using culture: 07/06 - 06/08	Regional-referral Hospital.	Prevalence and nosocomial transmission of MRSA
Boyce et al., 2004,[19] USA	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=not specified) Int: (n=523)	No screening: Beginning 5 months before spring of 2003	Screening at time of SICU admission by culture: Beginning in spring 2003 and continue 5 months after that.	SICU	Number of health care-associated MRSA infections acquired in the SICU
Chen et al., 2012,[20] US	QEX-BA	Screening of surgical patients vs no screening	1002	No screening (patients who received preoperative clearance from their primary care physicians)	Screening of surgical patients who received preoperative testing within the study hospital	Hospital	Prevalence of MRSA colonization; impact of the intervention on early wound complications
Clancy et al., 2006,[21] USA	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=not specified) Int: (n=1890)	01/02 - 03/03	Screening at time of MICU or SICU admission by culture: 04/03 - 06/04	MICU/SICU	Primary: Incidence of MRSA infection; Secondary: Percentage of ICU patients colonized or infected with MRSA on admission, mean number of census-days after admission that a clinical specimen was positive for MRSA in patients who developed nosocomial infections

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
de la Cal et al., 2004,[22] Spain	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=140) Int1: (n=258) Int2: (n=401)	No screening: 07/96 - 04/97	Screening at time of MICU /SICU admission or those expected to be on ventilation > 3 days using culture: 05/97 - 09/97	Adult MICU/SICU	Incidence of ICU-acquired MRSA colonization or infection
Enoch et al., 2011,[23] UK	QEX-BA	Expanded screening vs limited screening		Limited screening	Expanded screening	Hospital	The measurement of bacteremia vs clinical isolates to determine the effectiveness of the interventions
Eveillard et al., 2006,[24] France	QEX-BA	Expanded Vs Limited Screening	C: Int: (n=455)	Limited screening of selected high risk patients using culture: 04/02 - 09/02	Expanded screening of patients admitted to internal medicine ward using culture: 04/03 - 09/03	Internal medicine ward in a teaching hospital	Prevalence of MRSA carriage on admission
Girou et al., 2000,[25] France	QEX-BA	Expanded Vs Limited Screening	C: (n= 370) Int: (n=359)	Limited screening of high risk patients admitted to dermatology ward using culture: 09/96 - 05/97	Expanded screening of patients admitted to dermatology ward using culture: 05/97 - 12/97	Dermatology ward (including 2 ICU beds)	Number of patients with MRSA + screening sample in intervention period without risk factors, Rate of acquired MRSA, Rate of imported MRSA
Jog et al., 2008,[26] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n= 697) Int: (n=765)	No screening: 10/04-09/05	Screening in cardiac surgery unit using PCR: 10/05-09/06	Cardiac surgery and general ward in a teaching hospital	SSIs in patients undergoing cardiac surgery. MRSA rates were measured as well.

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Kelly et al., 2012,[27] Ireland	QEX: BA	Screening of surgical patiens vs no screening	12259	No screening	Pre-operative assessment clinic in which all patients presenting for elective surgery underwent routine screening for MRSA. Admissions to the trauma ward were swabbed within one hour of admission.	Hospital	MRSA infection and colonization
Keshtgar et al., 2008,[28] UK	QEX-BA	Screening of High Risk Pts Vs No Screening	C: (1,469,399 person-time) Int: (221,027 person time)	No screening: 01/00-12/05	Screening of critical care, elective and emergency surgery wards using PCR: 01/06 - 12/06	Teaching hospital; critical care, routine and emergency surgical wards.	Rate of MRSA wound infection and bacteremia
Kim et al., 2010,[29] USA	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n= 5293) Int: (n=7019)	No screening: 10/05 - 07/06	Screening at preadmission in patients undergoing elective orthopedic surgery using PCR: 07/06 - 09/07	Orthopedic surgery ward	MRSA SSI rate
Kurup et al., 2010,[30] Singapore	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n=not specified) Int: (n=653)	No screening: 07/06 - 06/07	MICU screening using culture and SICU screening using PCR: 07/07 - 06/08	MICU, SICU	MRSA infection rates in the MICU and SICU

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Lipke et al., 2010,[31] USA	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=NR) Int: (n=5570)	No screening: 02/05 - 01/06	Screening in patients undergoing selected surgical procedures at preadmission using culture: 02/06 - 01/07	Community hospital	MRSA SSI rate
Malde et al., 2006,[32] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=6555) Int: (n=4141)	No screening: 01/96 - 12/00	Screening for elective and emergency surgery vascular admissions using culture Emergency admissions 01/01 - 12/04 Elective admissions 01/01 - 12/04	Vascular ward in university hospital	Primary outcomes: Wound infection, Major limb amputation, Mortality. Secondary outcomes: MRSA infection, Colonization or Infection with MRSA
Nixon et al., 2006,[33] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=2341) Int: (n=3253)	No screening: 01/03 - 05/03	Screening in orthopedic surgery elective patient pre-admission or before transfer using culture: Elective 1/04 - 05/04 Trauma 01/04 - 05/04	Orthopedic ward in a university hospital	MRSA SSI incidence, MRSA Colonization, Morbidity and Mortality of MRSA patients (colonized and infected)
Pan et al., 2005,[34] Italy	QEX-BA	Screening of High Risk Pts Vs No Screening	NR	No screening: 01/96 - 06/97	Screening of high risk patients and wards using culture: 01/00 - 12/01	Community hospital	Incidence rate of MRSA bloodstream infection

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Pofahl et al., 2009,[35] USA	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n= 8469) Int: (n=5094)	No screening: 01/04 - 02/07	Screening in surgical patients using PCR: (02/15/07 - 07/01/08)	Surgical ward in a tertiary care hospital	MRSA SSI rate
Salaripour et al., 2006,[36] Canada	QEX-BA	Screening of High Risk Pts Vs No Screening	NR	No screening: 02/00 - 02/01	Screening of high risk patients using culture: 03/01 – 2005	Hospital	Rate of Nosocomial MRSA
Sankar et al., 2005,[37] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=164) Int: (n=231)	No screening: 10/00 - 04/01	Screening at preadmission in patients undergoing elective total joint arthroplasty using culture: 04/01 - 10/01	Elective orthopedic ward	Post-operative MRSA infection; length of hospital stay
Schelenz et al., 2005,[38] UK	QEX-BA	Expanded Vs Limited Screening	C: (n= 1075) Int: (n=1075)	Limited screening: likely to have used culture: Started 16 months before August 2000	Expanded screening: Started September 2000 and continued for 16 months.	Cardiothoracic surgical ward	MRSA acquisition and infection rates
Simmons et al., 2011,[39] USA	QEX-BA	Screening of ICU Risk Pts Vs No Screening	Not specified	No screening: 01/07 - 06/08	ICU screening using PCR: 07/08 - 12/09	ICU	ICU-acquired MRSA rate, Hospital-wide MRSA rate
Sott et al., 2001,[40] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=113) Int: (n=123)	No screening: Year 2005 (12 months)	Screening at preadmission in patients undergoing elective primary total hip replacement using culture: Year 2006 (12 months)	Orthopedic unit	MRSA post-operative sepsis
Souweine et al., 2000,[41] France	QEX-BA	Screening of ICU Risk Pts Vs No Screening	C: (n= 233) Int: (n=351)	No screening: 05/94 - 04/95	Screening on ICU admission using culture: 05/95 - 04/96	MICU/SICU	Patients infected or colonized by MRSA in the ICU

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
Supriya et al., 2009,[42] Scotland	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n= 84) Int: (n=31)	No screening: 02/06 - 02/07	Screening at preadmission in head and neck cancer surgery patients using culture: 07/07 - 01/08	Tertiary referral center	MRSA infection rates
Thomas et al., 2007,[43] UK	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n=101) Int: (n=47)	No screening: 01/02 - 09/04	Screening for all patients referred for PEG insertion using culture: 10/04 - 08/06	Endoscopy unit in a hospital	Peristomal MRSA Infection
Thompson et al., 2009,[44] UK	QEX-BA	Expanded Vs Limited Screening	C: Int: (n=914)	Limited screening of high risk patients in ICU using culture: 01/01 - 11/06	Expanded screening of all ICUs using culture: 12/06 - 06/08	ICU	Prevalence of MRSA in admissions and its acquisition and bacteremia rates within ICU
Trautmann et al., 2007,[45] Germany	QEX-BA	Expanded Vs Limited Screening	NR	Limited screening of high risk patients using culture: 01/02 - 12/02	Expanded screening of high risk patients plus SICU using culture: dates NR	Surgical ICU	NR
Walsh et al., 2011,[46] USA	QEX-BA	Screening of Surgical Pts Vs No Screening	C: (n= 2766) Int: (n=2496)	No screening: 01/04 - 01/07	Screening at pre-admission of patients undergoing elective cardiothoracic surgery using culture: 02/07 - 01/31/10	Cardiothoracic surgery ward and ICU in a community hospital	MRSA SSI rate
Wernitz et al., 2005,[47] Germany	QEX-BA	Screening of High Risk Pts Vs No Screening	C: (n= 36,118) Int: (n=36,962)	No screening: 09/99 - 03/01	Screening of high risk patients using culture: 05/01 - 11/02	Acute care university teaching hospital:	Frequency of hospital-acquired MRSA infection

Author, Year, Country	Design	MRSA Strategy	N	Control (strategy, duration)	Intervention (strategy, duration)	Study Setting	End Points
West et al., 2006,[48] USA	QEX-BA	Expanded Vs Limited Screening	C: Int: (n=7,712)	Limited screening on ICU admission using culture: 09/01 - 06/02	Expanded screening of ICU admission plus those at high risk admitted to general wards using culture: 07/02 - 10/03	Tertiary care facility + suburban hospital ICU in a community hospital	Rate of nosocomial MRSA infection.

BA: Before after; C: Control; CG: Control group; IC: Infection control; ICU: Intensive care unit; Int: Intervention; MICU: Medical intensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No; NR: Not reported; PCR: Polymerase chain reaction; PEG: Percutaneous endoscopic gastrostomy; PICU: Pediatric intensive care unit; QEX: Quasi-experimental; SICU: Surgical intensive care unit; SSI: Surgical site infection

Appendix Table F3. Infection control practices in studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Chaberny et al., 2008,[1] Germany	Expanded Vs Limited Screening	None	Isol/coh, BP, HW, Alcohol-based hand rubs, INAM, TAMW	Audit and feedback	None	Isol/coh, BP, INAM, TAMW, HW, Alcohol-based hand rubs	Audit and feedback
Chowers et al., 2009,[2] Israel	Screening of High Risk Pts Vs No Screening	None	None	Contact isolation, roommates screened for MRSA	None	Contact isolation, eradication	Monitoring to ensure compliance with screening and contact isolation (periods 2 and 4 only).
Ellingson et al., 2011,[3] USA	Screening of High Risk Pts Vs No Screening	None	None	None	None	Contact precautions, Unspec HH,	Unspec HH, Decontaminate spaces, systems and behavior change strategies to promote adherence to the behavior change protocol.
Gould et al., 2007,[4] UK	Screening of ICU Risk Pts Vs No Screening	Isol/coh, BP	None	None	Isol/coh, BP	INAM, TAMW	None

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Harbarth et al., 2000,[6] Switzerland	Screening of High Risk Pts Vs No Screening	None	None	None	Isol/coh of patients previously known to be colonized or infected with MRSA	Isol/coh, INAM, TAMW, IVAB (only for those with MRSA infection), surveillance cultures	HH education program. Computer alerts, Alcohol-based hand rubs, Surveillance cultures of roommates and outbreak investigations, when possible.
Harbarth et al., 2008,[5] Switzerland	Screening of ICU Risk Pts Vs No Screening	None	Period 1 & 2: Isol/coh, BP, INAM, TAMW, Other- Adjustment of antibiotic prophylaxis	Period 1 & 2: Other- standard hand hygiene	Period 1 & 2: None	Period 1 & 2: Isol/coh, BP, INAM, TAMW, Computer alerts, Antibiotic route unspecified	Period 1: Other- standard hand hygiene Period 2: Other- Antibiotics route unspecified, Alcohol-based hand rubs
Holzmann-Pazgal et al., 2011,[7] USA	Screening of ICU Risk Pts Vs No Screening	Isol/coh, BP	None	None	Isol/coh, BP	None	HWCC
Huang et al., 2006,[8] USA	Screening of ICU Risk Pts Vs No Screening	None	None	Campaign for sterile central venous catheter placement, alcohol-based hand rubs, hand hygiene campaign	Contact precautions	None	Campaign for sterile central venous catheter placement, alcohol-based hand rubs, hand hygiene campaign

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Huskins et al., 2011,[9] USA	Screening of ICU Risk Pts Vs No Screening	Iso/coh, BP	None	Reinforcement of IC practices, unspecified HH	Iso/coh, BP	Universal gloving. Contact precautions for those patients infected or colonized with MRSA or VRE during the prior year.	Visual aids/signage, Reinforcement of IC practices, report on providers' use of universal gloving, unspecified HH
Jain et al., 2011,[10] USA	Universal Vs No Screening	None	None	None	None	Contact precautions, HW, Repeat assays	Culture change campaign
Leonhardt et al., 2011,[11] USA	Universal Vs Screening of Selected Pts	Isol/coh, BP (only for patients known to be MRSA positive)	Isol/coh, BP, BPCC, perioperative decolonization and antibiotic prophylaxis when appropriate	Isol/coh, BP	Isol/coh, BP (only for patients known to be MRSA positive)	Isol/coh, BP, BPCC, perioperative decolonization and antibiotic prophylaxis when appropriate	Reinforcement of ICP
Muder et al., 2008,[12] USA	Screening of Surgical Pts Vs No Screening Screening of ICU Pts Vs No Screening	None	None	None	Standard precautions not known to be colonized or infected with MRSA. Contact precautions for those with a history of MRSA colonization or infection in the prior two years.	Contact precautions.	None

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Raineri et al., 2007,[13] Italy	Screening of ICU Risk Pts Vs No Screening	None	None	None	Intervention 1: Contact precautions (hand hygiene and gloves, when performing procedures at risk for MRSA transmission, gowns and masks). INAM, TAMW, repeat assays. Intervention 2: Same as intervention 1 plus Iso/Coh	None	Staff education.
Reilly et al., 2012,[14] Scotland	Universal screening vs no screening					Isolation and decolonization	Hand hygiene campaigns and audits, mandatory surveillance, cleaning monitoring, antimicrobial stewardship programs, and routine infection control teams locally.
Robicsek et al., 2008, [15] USA	Screening of ICU Risk Pts Vs No Screening	Isol/coh, BP, dedicated equipment for staff use	None	None	Isol/coh, BP, dedicated equipment for staff use,	None	None
Robicsek et al., 2008,[15] USA	Universal Vs No Screening	None	Isol/coh, BP, dedicated equipment for staff use	None	None	Isol/coh, BP, dedicated equipment for staff use. INAM, TAMW.	Physician and nursing education. Monitored adherence and provided feedback.

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Robicsek et al., 2008,[15] USA	Universal Vs Screening of Selected Pts	None	Isolation, BP, dedicated equipment for staff use	None	None	Isol/coh, BP, dedicated equipment for staff use. INAM, TAMW.	Physician and nursing education. Monitored adherence and provided feedback.
Rodriguez-Bano et al., 2010,[16] Spain	Screening of High Risk Pts Vs No Screening	None	Period A: None Period B: Contact precautions, dedicated patient care equipment, disinfection of surfaces and devices	Unspec HH, strict cleaning policy	Period C: None Period D: Preemptive isolation of readmitted patients previously colonized with MRSA	Contact precautions, decolonization (INAM, TAMW), dedicated patient care equipment, disinfection of surfaces and devices	Unspec HH, strict cleaning policy, alcohol hand rubs

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Rodriguez-Bano et al., 2010,[16] Spain	Expanded Vs Limited Screening	None	Isol/coh, BP, BPCC, Unspec HHDecolonization (INAM, TAMW) for patients without open wounds, respiratory tract colonization, mechanical ventilation, NG tube, urinary tract colonization in presence of urinary catheter, high-level mupirocin resistance. Follow up nasal swabs after 1 week to check for decolonization.	None	Preemptive isolation for readmitted patients previously colonized with MRSA	Isol/coh, BP, BPCC, Unspec HH, alcohol hand rubs, Decolonization (INAM, TAMW) for patients without open wounds, respiratory tract colonization, mechanical ventilation, NG tube, urinary tract colonization in presence of urinary catheter, high-level mupirocin resistance. Follow up nasal swabs after 1 week to check for decolonization.	Alcohol hand hygiene education

BICP: Background infection control practices; BP: Barrier precautions; CHKGL: Checklist/Guidelines; Coh: Cohorting; HH: hand hygiene; HWCC: hand hygiene compliance checks; ICP: Infection control practices; ICPW: Infection control practices while waiting for MRSA results; ICU: Intensive care unit; INAM: Intransal antimicrobial; Iso: isolation; IV: Intravenous; IVAB: Intravenous antibiotics; MICU: Medical intensive care unit; MRSA: Methicillin resistant infection control practices; NG: Nasogastric; OR: Operation room; PO: Oral; POAB: Oral antibiotics; TAMW: Topical antimicrobial wash; Unpsec: Unspecified; VRE: Vancomycin resistant enterococcus

Appendix Table F4. Infection control practices in studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Blumberg, et al., 1994,[17] South Africa	Screening of ICU Risk Pts Vs No Screening	None	None	None	Isol/coh (only for patients admitted to ICU, not for those admitted to pediatric oncology unit), BP, INAM, TAMW, alcohol-based hand rubs. Attempt to perform cohort nursing. Repeat assays.	None	None
Bowler et al., 2010,[18] USA	Screening of High Risk Pts Vs No Screening	None	None	None	None	INAM, TAMW, POAB, Repeat assays, screening of household contacts	None
Boyce et al., 2004,[19] USA	Screening of ICU Risk Pts Vs No Screening	None	None	None	Contact precautions	None	None
Chen et al., 2012,[20] US	Screening of surgical patients vs no screening				Screening performed prior to hospitalization	Intranasal antimicrobials; topical antimicrobials	

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Clancy et al., 2006,[21] USA	Screening of ICU Risk Pts Vs No Screening	Isol/coh, BP,	None	BP	Isol/coh, BP, HWCC, contact isolation compliance checks, repeat assays	None	New MICU with 24 private rooms (prior unit with only 1 private room). Two new general medical and surgical floors, each with 22 private rooms (previously no private rooms). Increased availability of alcohol hand foam dispensers.
de la Cal et al., 2004,[22] Spain	Screening of ICU Risk Pts Vs No Screening	Isol/coh, BP, HW	None	BP, HW, Decontaminate spaces,	Interventions 1 and 2: Isol/coh, BP, TAMW, PO/IVAB, HW, PO antibiotics.	None	Intervention 1: BP, HW, Decontaminate spaces, Intervention 2: Same as intervention 1 plus oral antibiotics (for high risk patients), selective digestive decontamination with PO and IVAB, topical antibiotics, TAMW.

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Enoch, 2011, UK	Expanded screening vs limited screening	Decolonization until screen negative		Daily review of MRSA patients. Annual deep clean of clinical areas. Board provided with monthly review.		Opening of new isolation ward. Octenisan used to replace Aquasept for decolonization. Beginning in 4/09, decolonization of all pts admitted to ICU/HDU, irrespective of result. New inf control matron & secretary posts appointed. Wkly review of +ve pts by multi-disciplinary team (consultant microbiologist, inf control nurse, antibiotic pharmacist and ward matron) Peripheral cannula access nurse appointed. New inf control nurse appointed (one whole-time equivalent). Enhanced information provided of MRSA status on discharge from acute trust to community regarding ongoing Rx, monitoring and risk of recurrence	Antibiotic audit program. Care bundles introduced (adapted from Saving Lives). Central lines, peripheral lines, urinary catheters. Competencies for asepsis introduced Chloraprep for catheter insertion introduced. Peripheral cannula access team created in Sept 2009. Close liaison between matrons/ facilities and cleaning contractor. Enhanced deep clean activities. Enhanced education Chlorclean introduced for environmental cleaning of contaminated bed spaces/ isolation facilities. New inf control matron and secretary posts appointed. Weekly review of positive patients by multi-disciplinary team (

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Eveillard et al., 2006,[24] France	Expanded Vs Limited Screening	None	Isol/coh, BP	None	None	Isol/coh, BP	None
Girou et al., 2000,[25] France	Expanded Vs Limited Screening	Isol/coh, BP, HW (for patients at high risk of MRSA acquisition only)	Isol/coh, BP, HW, repeat assays	None	Isol/coh, BP, HW (for patients at high risk of MRSA acquisition only)	Isol/coh, BP, HW, repeat assays.	None.
Jog et al., 2008,[26] UK	Screening of Surgical Pts Vs No Screening	None	Isol/coh, Computer alerts, Antibiotics Route Unspecified	Decontaminate spaces, Other- Ward audits on IC practices and education	INAM, Other- topical triclosan 2%	Isol/coh, INAM, IVAB, Computer alerts, Other- topical triclosan 2%	Unspec HH, Decontaminate spaces, Other- Ward audits on IC practices and education

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Kelly et al., 2012,[27] Ireland	Screening of surgical patients vs no screening				Where bed numbers allowed, patients from high risk populations (e.g., health care workers, nursing home residents and those known to be previously colonized or infected with MRSA) were nursed in isolation until results were available.	Intranasal antimicrobials and/or chlorhexidine bodywash. Repeat swabs. Isolation.	Patients in the same room of a ward in which a MRSA patient had been staying were repeat swabbed and isolated if positive. Nursing and medical staff began wearing disposable aprons and gloves for all MRSA patient interactions. Alcohol hand rub containers were installed outside each ward room. The charge nurse was responsible for ensuring adherence to infection control standards.
Keshtgar et al., 2008,[28] UK	Screening of High Risk Pts Vs No Screening	None	None	None	INAM, TAMW for patients who required emergency surgery before results returned	INAM, TAMW , IVAB (if antibiotic prophylaxis required)	None

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Kim et al., 2010,[29] USA	Screening of Surgical Pts Vs No Screening	None	None	None	None	Isol/coh, INAM, TAMW, IVAB, Repeat assays, Other- personalized education and instruction on the eradication by telephone	None
Kurup et al., 2010,[30] Singapore	Screening of ICU Risk Pts Vs No Screening	None	None	None	Isol/coh, TAMW, Repeat assays	None for the 1st half of the intervention period TAMW for the 2nd half of the intervention period	Staff education. HH campaign. HWCC.
Lipke et al., 2010,[31] USA	Screening of Surgical Pts Vs No Screening	None	None	None	None	INAM, TAMW, Other- Education booklet: Living with MRSA, which included facts, treatment and prevention related to MRSA infections	Other- The nurses had a pre-intervention in-service program that ensured that they understood nursing practice changes, change antiseptic cloth before surgery
Malde et al., 2006,[32] UK	Screening of ICU Risk Pts Vs No Screening	None	None	None	Isol/coh, BP, Unspec HH	None Isol/coh, BP, INAM, TAMW, PO/IVAB, MW, Unspec HH, Repeat assays, Delayed admission	HW

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Nixon et al., 2006,[33] UK		Elective: None Trauma:	Elective: Isol/coh, BP, INAM, TAMW, HW Trauma:	Elective: None Trauma:	Elective: Other- delayed admission; Trauma: TAMW, Antibiotic route unspecified	Elective: TAMW, Delayed admission, Antibiotic route unspecified, Other- beds are "ring-fenced" Trauma: Isol/coh, BP, TAMW, IVAB, Repeat assays, Delayed admission	Elective and Trauma: Decontaminate spaces, Other- staff education program, Environmental cleaning guideline, Alcohol-based hand rubs
Pan et al., 2005,[34] Italy	Screening of High Risk Pts Vs No Screening	None	None	None	None	Isol/coh, BP, INAM, TAMW, HW, Other- Colonized wounds were treated with TAM cream	None
Pofahl et al., 2009,[35] USA	Screening of Surgical Pts Vs No Screening	Isol/coh	Isol/coh	None	None	INAM, TAMW	None
Salaripour et al., 2006,[36] Canada	Screening of High Risk Pts Vs No Screening	None	None	None	None	Contact precautions, TAMW, PO/IVAB,, Decontaminate spaces, Signs, Computer alerts, patient and family education. Provided housekeeping with list of rooms of patients under precautions.	Revamp policies for contact precautions, environmental cleaning and transport. Calls to clinical units to remind them to culture high-risk patients. Education of staff. Hand hygiene campaign.
Sankar et al., 2005,[37] UK	Screening of ICU Risk Pts Vs No Screening	None	IVAB	IVAB	None	INAM, TAMW, IVAB, Repeat assays, Delayed admission	Other- IV antibiotics

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Schelenz et al., 2005,[38] UK	Expanded Vs Limited Screening	None	INAM, TAM, Iso (if isolation room available), BP	None	Decolonization (INAM, TAM) of patients with pending screening test results 24 hours before surgery. Admission of patients from high-risk units (ICUs, other hospitals), only after MRSA status known.	INAM, TAM, Iso, BP, alcohol hand rub,	Audit + feedback. Education. Closure of operating rooms to facilitate repairs. Designated nurses for MRSA + patients. Nursing care pathway for MRSA. Use of clippers to prepare the skin in the OR. Pre-operative skin disinfection with a rapidly drying solution. Improvements in environmental cleaning. Alternative in IV antibiotic prophylaxis. Recovery in the OR when possible, rather than admission to the ICU.

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Simmons et al., 2011,[39] USA	Screening of ICU Risk Pts Vs No Screening	Contact isolation, decolonization (type unspecified), Repeat assays	None	None	Contact isolation, decolonization (INAM) an option, Repeat assays	None	Nurses given compliance reports for swab collection and initiation of isolation precautions
Sott et al., 2001,[40] UK	Screening of Surgical Pts Vs No Screening	None	None	None	None	INAM, TAMW, Antibiotic route unspecified, Other- patient counseled by nurse	Other- standard antibiotic prophylaxis
Souweine et al., 2000,[41] France		None	None	None	Isol/coh, BP, INAM, TAMW, HW, Repeat assays, Other- All soiled articles, moist body substances, and waste were wrapped in double bags before removal from rooms	Isol/coh (for patients transferred from another ICU)	Other- imipenem as empiric antibiotic treatment is discouraged; prompt discharge of patients is mandatory, Reinforcement of IC practices
Supriya et al., 2009,[42] Scotland	Screening of Surgical Pts Vs No Screening	None	Isol/coh	None	Isol/coh	Isol/coh, CHKGL, Repeat assays	Repeat assays
Thomas et al., 2007,[43] UK	Screening of ICU Risk Pts Vs No Screening	None	None	None	None	INAM, TAMW, IVAB, Delayed admission, Antibiotic route unspecified	Other- Prophylaxis: Antibiotic Rout Unspecified

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Thompson et al., 2009,[44] UK	Expanded Vs Limited Screening	None.	Isol/coh, BP, Unspec HH, Decontaminate spaces, TAM, INAM Other- Bed curtains replaced and unused items disposed of	Unspec HH, daily cleaning of each bed space. Campaigns to improve practice.	None	Isol/coh, BP, INAM, TAMW, Unspec HH, Other- bed curtains replaced and unused items disposed of.	TAMW, Unspec HH, HWCC, Other- OR scrubs for medical staff and computer keyboards with wipeable surface introduced. Standardized central line care and care to prevent ventilator-associated pneumonia.

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
Trautmann et al., 2007,[45] Germany	Expanded Vs Limited Screening	None	Isol/coh, BP (short/long sleeved gowns), INAM, TAMW, Decontaminate spaces. Oral rinses for some.	None	None	Isol/coh, BP (long sleeved gowns), INAM, TAMW, Decontaminate spaces, Oral rinses for some, written MRSA standard. Signs, Alcohol-based hand rubs, MRSA "carts" were placed outside MRSA patient room which supplied separate supplies for MRSA patients like reusable stethoscopes and blood pressure cuffs. Hand disinfectant, gloves, gowns and masks were also on the cart. Electronic flagging of patient charts.	Surveillance, feedback and staff training also implemented.
Walsh et al., 2011,[46] USA	Screening of Surgical Pts Vs No Screening	None	Isol/coh, HW, Antibiotics Route Unspecified	TAMW, IVAB, Other- Glucose control	None	INAM, Repeat assays, Antibiotic route unspecified	Repeat assays, Other- Intranasal antimicrobial
Wernitz et al., 2005,[47] Germany	Screening of High Risk Pts Vs No Screening	Isol/coh, BP, TAMW	Isol/coh, BP, INAM, TAMW, PO/IVAB (if necessary for clinical indications) HH, Repeat assays	None	Isol/coh, BP, TAMW (all for potential MRSA carriers only)	Isol/coh, BP, INAM, TAMW, PO/IVAB (if necessary for clinical indications) , Unspec HH ,Repeat assays	None

Author, Year, Country	MRSA Strategy	Control- ICP for MRSA+	Control-ICPW	Control- BICP	Intervention- ICP for MRSA+	Intervention- ICPW	Intervention- BICP
West et al., 2006,[48] USA	Expanded Vs Limited Screening	Isol/coh, BP for patients with MRSA coloniza-tion or infection on previous admission	Isol/coh, BP, HW, Decontaminate spaces, Alcohol-based hand rubs	None	Isol/coh, BP for patients found to have MRSA colonization or infection on previous admission	Isol/coh, BP, HW, Decontaminate spaces, Alcohol-based hand rubs	None

BICP: Background infection control practices; BP: Barrier precautions; CHKGL: Checklist/Guidelines; Coh: Cohorting; HH: hand hygiene; HWCC: hand hygiene compliance checks; ICP: Infection control practices; ICPW: Infection control practices while waiting for MRSA results; ICU: Intensive care unit; INAM: Intransal antimicrobial; Iso: isolation; IV: Intravenous; IVAB: Intravenous antibiotics; MICU: Medical intensive care unit; MRSA: Methicillin resistant infection control practices; NG: Nasogastric; OR: Operation room; PO: Oral; POAB: Oral antibiotics; TAMW: Topical antimicrobial wash; Unpsec: Unspecified; VRE: Vancomycin resistant enterococcus

Appendix Table F5. Health care-associated MRSA colonization or infection: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Ellingson et al., 2011,[3] USA	Screening of High Risk Pts Vs No Screening	2.40 per 1000 patient days at risk	1.88 per 1000 patient days at risk	IRR; non-intensive care surgical unit: 0.782 (95% CI 0.683-0.922); Percent change: -21.8 (95% CI -33.7 to -8.8) Poisson			Interrupted time series Immediate intervention impact: Incidence rate ratio 0.964 (95% CI 0.714-1.300), percent change (-3.6 (-29.6 to 30.0), NSS Change in pre- to post-intervention trends: IRR 0.968 (95% CI 0.948-0.988); percent change -3.2 (-5.2 to -1.2). p<0 .01.Persistence of trend in postintervention period: IRR 0.989 (95% CI 0.985-0.992); percent change -1.1 (-1.5 to -0.8),p<0 .01.
	Screening of Surgical Patients vs No Screening		Incidence rate ratio 0.775 (95% CI 0.371-1.617) Trend in the incidence of MRSA colonization or infection 0.958 (95% CI 0.909-1.009).				

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
	Expanded screening vs limited screening	After the second intervention (screening for MRSA-carriage in the ICU), incidence rate ratio 0.913, 95% CI: 0.356 to 2.343. After the second intervention (screening for MRSA-carriage in the ICU), trend in incidence rate ratio 0.971, 95% CI: 0.938 to 1.004.	After the third intervention (screening for MRSA-carriage in all other acute care units), incidence rate ratio 0.656, 95% CI: 0.440 to 0.979. After the third intervention (screening for MRSA-carriage in all other acute care units), trend in incidence rate ratio 0.998, 95% CI: 0.982 to 1.014.				
Harbarth et al., 2008,[5] Switzerland	Screening of Surgical Pts Vs No Screening	Pooled results : 1.59 per 1000 patient days	Pooled results : 1.69 per 1000 patient days		1.1 (95% CI 0.8-1.4)	Chi-square, Fisher's exact, test, Wilcoxon rank sum test	Poisson regression with GEE approach Number of patients with nosocomial MRSA acquisition: control periods 132; intervention periods 142 Adjusted for monthly number of admitted patients with previously known MRSA carriage, study month, monthly use of alcohol-based hand rubs, and antibiotic selection pressure

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
							exerted by antibiotics without activity against MRSA
Holzmann-Pazgal et al., 2011,[7] USA	Screening of ICU Risk Pts Vs No Screening	6.88 (2006) Per 1000 patient days	2.40 (2008) Per 1000 patient days	p=0.001		Chi-Square, Fisher's exact test,	Linear trend analysis using a general linear model, Multivariate linear regression, Corrgram autocorrelation of the MRSA acquisition rate was used to evaluate for seasonal variation Trend analysis and linear regression only conducted during intervention period.
Huang et al., 2006,[8] USA	Screening of ICU Risk Pts Vs No Screening	43 cases per 1000 patients at risk	23 cases per 1000 patients at risk	p<0.001			Time series, segmented regression
Huskins et al., 2011,[9] USA	Screening of ICU Risk Pts Vs No Screening	13.5 +/- 2.1 Mean +/- SE ICU level incidence per 1000 patient days at risk adjusted for baseline incidence	16.0 +/- 1.8 Mean +/- SE ICU level incidence per 1000 patient days at risk adjusted for baseline incidence	=0.39			An ICU-level analysis-of-covariance model with adjustment for baseline incidence and with the use of an F-test, with a two-sided P value of 0.05.
Jain et al., 2011,[10] USA	Universal Vs No Screening	ICUs 10/07: 3.02 Per 1000 patient days	ICUs 6/10: 2.50 Per 1000 patient days	p<0.001 for trend	-17%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
		Non-ICU 10/07: 2.54 Per 1000 patient days	Non-ICU 6/10: 2.00 Per 1000 patient days	p<0.001 for trend	-21%		
Rodriguez-Bano et al., 2010,[16] Spain	Expanded Vs Limited Screening	After intervention 2: 0.28 per 1000 patient days (95% CI: 0.17-0.40)	After intervention 3: 0.07 per 1000 patient days (95% CI 0.06-0.08)				Results of segmented regression analysis: b6 (change in incidence after 3rd

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
							intervention)=0.077 (-0.012 to 0.165)(p=0.04). Change in trend after 3rd intervention: b7=0.047 (0.035–0.059)(p<0.001).
Rodriguez-Bano et al., 2010,[16] Spain	Screening of High Risk Pts Vs No Screening	0.55 per 1000 patient days (95% CI: 0.48-0.61)	After intervention 2: 0.28 per 1000 patient days (95% CI: 0.17-0.40) After intervention 3: 0.07 per 1000 patient days (95% CI 0.06-0.08)	Not statistically significant.		Fisher exact test.	Segmented regression: Change in incidence after 2nd intervention: -0.065 (95% CI -0.053 to 0.182), P=0.2: Change in trend after 2nd intervention: -0.045 (95% CI -0.062 to -0.029), P<.001

C: Control; CI: Confidence interval; Diff: Difference; GEE: Generalized estimating equation; I: Intervention; IRR: Incidence Rate Ratio; MRSA: Methicillin-resistant *Staphylococcus aureus;* NSS: Not statistically significant; Y: Yes

Appendix Table F6. Health care-associated or acquired MRSA infection or colonization: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate analysis
Chaberny et al., 2008,[1] Germany	Expanded Vs Limited Screening						Segmented regression analysis of interrupted time series, incidence density of MRSA-positive patients per 1000 pd in the whole hospital: Slope before intervention 0.0340 (95% CI .026 to 0.042), p<0.001 Change in level after intervention: Not significant Change in slope after intervention: -0.015 (95% CI -0.032 to 0.001), p 0.002
Raineri et al., 2007,[13] Italy	Screening of ICU Risk Pts Vs No Screening	3.5 (2.1-5.4) per 1000 patient days	1: 1.7 (1.1-2.5) per 1000 patient days	p=0.0023		Chi square, Fisher's exact test, Kruskal-Wallis analysis of variance	Segmented regression Significant rate level reduction after intervention 1:β_2: -3.9, 95% CI -6.31 to -1.40, p=0.003 Significant trend change after intervention 1: β_3: -0.7, 95% CI -1.22 to -0.24, p=0.005

C: Control; CI: Confidence interval; Diff: Difference; I: Intervention; ICU: Intensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* pd: patient days; Y: Yes;

Appendix Table F7. Health care-associated MRSA infection: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Chaberny et al., 2008,[1] Germany	Expanded Vs Limited Screening						Segmented regression of interrupted time series, incidence density of nosocomial MRSA infected patients: slope before intervention 0.006 (0.003-0.009), P<0.000, change in level after intervention -0.122 (-0.204 to -0.040), p=0.004. Change in slope after intervention -0.008 (-0.013 to -0.003), p=0.004.
Harbarth et al., 2008,[5] Switzerland	Screening of Surgical Pts Vs No Screening	0.91 per 1000 patient days	1.11 per 1000 patient days		1.2 (95% CI 0.9-1.7)	Chi-square, Fisher's exact test, Wilcoxon rank sum test, Poisson regression with GEE approach	Number of patients with any type of nosocomial MRSA infection, No. (%): control periods 76(.7); intervention periods 93(.9)Total No. of MRSA infections (patients may have had multiple sites of infection): control periods 88; intervention periods 103
Harbarth et al., 2000,[6] Switzerland	Screening of High Risk Pts Vs No Screening	2.25 per 10000 patient days	0.87 per 10000 patient days	p<0.001			Poisson regression
Jain et al., 2011,[10] USA	Universal Vs No Screening	ICUs: 10/07: 1.64 per 1000 patient days	ICUs: 06/10: 0.62 Per 1000 patient days	p<0.001 for trend	-62%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
	Universal Vs No Screening	Non-ICUs: 10/07: 0.47 Per 1000 patient days	Non-ICUs: 6/10: 0.26 Per 1000 patient days	p<0.001 for trend	-45%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
Leonhardt et al., 2011,[11] USA	Universal Vs Screening of Selected Pts	Baseline period: 0.1% Intervention period: 0.1%;	Baseline period: 0.27% Intervention period: 0.15%	p=0.95; p=0.23;	Difference over time in control: 0.0% ; Difference over time in intervention: -0.12%,		Difference-in-differences analysis. Standard errors were tested for autocorrelation with the Durbin-Watson statistic Difference-in-Difference: -0.12, p=0.34

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Muder et al., 2008,[12] USA	Screening of Surgical Pts Vs No Screening	Unit A: 1.56 per 1000 patient days	Unit A: 0.63 per 1000 patient days	p=0.003	-60%		Segmented Poisson Regression
		Unit B: 5.45 per 1000 patient days	Unit B: 1.35 per 1000 patient days	p=0.001	-75%		Segmented Poisson Regression
Muder et al., 2008,[12] USA	Screening of Surgical Pts Vs No Screening Screening of ICU patients vs no screening	1.56/1000 patient-days 5.45/1000 patient-days	0.63/1000 patient-days 1.35/1000 patient-days	P=0.003 P=0.001	60% reduction 75% reduction		Segmented Poisson regression
Robicsek et al., 2008,[15] USA	Universal Vs Screening of Selected Pts	3.88 per 10000 patient days (95% CI 3.18 to 4.69)	7.45 per 10000 patient days (95% CI 6.13 to 8.96)				Segmented Poisson regression Change 52.4% (CI -78.3% to -9.3%), p<0.05, adjusted prevalence density ratio 0.48 (0.22 to 0.91), p<0.05, time parameter estimate of regression line before intervention 1.00 (95% CI: 0.94 to 1.07), p>0.05, time parameter estimate of regression line during intervention 0.95 (95% CI: 0.89 to 1.02), p>0.05.
Robicsek et al., 2008, [15] USA	Screening of Surgical Pts Vs No Screening	8.91 per 10000 pt days (95% CI 7.56-10.43)	7.45 per 10000 pt days (95% CI 6.13 to 8.96)	p=0.149	-1.46 (95% CI -3.43 to 0.51)		Segmented Poisson regression Change: -36.2% (95% CI: -65.4% to 9.8%), p>0.05, adjusted prevalence density ratio 0.64 (95% CI: 0.35 to 1.10), p>0.05, time parameter estimate of regression line before intervention 1.00 (95% CI: 0.94 to 1.07), p>0.05, time parameter estimate of regression line during intervention 1.04 (95% CI: 0.95 to 1.12), p>0.05.

C: Control; CI: Confidence Interval; Diff: Difference; GEE: Generalized estimating equation; I: Intervention; ICU: Intensive Care Unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* Y: Yes

Appendix Table F8. MRSA infection: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate analysis
Chaberny et al., 2008,[1] Germany	Expanded Vs Limited Screening						Segmented regression analysis of interrupted time series, incidence density of MRSA-positive patients per 1000 pd in the whole hospital: Slope before intervention 0.0340 (95% CI .026 to 0.042), p<0.001 Change in level after intervention: Not significant Change in slope after intervention: -0.015 (95% CI -0.032 to 0.001), p 0.002
Raineri et al., 2007,[13] Italy	Screening of ICU Risk Pts Vs No Screening	3.5 (2.1-5.4) per 1000 patient days	1: 1.7 (1.1-2.5) per 1000 patient days	p=0.0023		Chi square, Fisher's exact test, Kruskal-Wallis analysis of variance	Segmented regression Significant rate level reduction after intervention 1:β_2: -3.9, 95% CI -6.31 to -1.40, p=0.003 Significant trend change after intervention 1: β_3: -0.7, 95% CI -1.22 to -0.24, p=0.005
Reilly et al., 2012,[14] Scotland	Targeted screening vs no screening			P=0.0209	Incidence of MRSA infection decreased during the year of the intervention		Poisson regression revealed a 37% decrease in first non-screening clinical isolates of MRSA for two NHS boards (95% CI: 28.6-44.7%) and 11.7% (95% CI 1.2-21.1%) for the other NHS board.

C: Control; CI: Confidence interval; Diff: Difference; I: Intervention; ICU: Intensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* Y: Yes

Appendix Table F9. Health care-associated MRSA bacteremia or BSI: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Chowers et al., 2009,[2] Israel	Screening of High Risk Pts Vs No Screening	0.171000 patient days	Screening alone: 0.09 1000 patient days Screening + monitoring: 0.15 1000 patient days Screening with PCR: 0.11 1000 patient days Screening with PCR + monitoring: 0.046 1000 patient days	p=0.59 (compared with preinter-vention period) p=0.13 (compared with preinter-vention period) p=0.02 (compared with preinter-vention period)			
Ellingson et al., 2011,[3] USA	Screening of High Risk Pts Vs No Screening			p=.02	54% decrease in MRSA BSI incidence per 1,000 patient-days in the postinterve n-tion period		Interrupted time series

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Huang et al., 2006,[8] USA	Screening of ICU Risk Pts Vs No Screening	2.8 per 1000 patient days	0.7 per 1000 patient days		-2.1		BSI control calculated via time series model projection based on secular trends prior to screening. Interrupted time series design. Segmented regression models. The Durbin-Watson statistic was used to adjust for serial autocorrelation. Hospital-associated incidence density: Annual trend prior to any intervention: 0.4, p<0.001, Change in trend in the ICU following routine MRSA surveillance: -1.6, p=0.007
		0.5 per 1000 patient days	0.3 per 1000 patient days		-0.2		Hospital-associated incidence density: Annual trend prior to any intervention: 0.02, p=0.08, Change in trend in non-ICU settings following routine MRSA surveillance: -0.3, p=0.008
		0.9 per 1000 patient days	0.3 per 1000 patient days		-0.6		Hospital-associated incidence density: Annual trend prior to any intervention: 0.07, p=0.001, Change in trend hospital wide following routine MRSA surveillance: -0.5, p=0.002
Jain et al., 2011,[10] USA	Universal Vs No Screening	ICU: Not device-associated 10-12/07: 0.14 Per 1000 patient days	ICU: Not device-associated 4-6/10: 0.03 Per 1000 patient days	p<0.001 for trend	-79%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
		Non-ICU 10-12/07: 0.12 Per 1000 patient days	Non-ICU 4-6/10: 0.05 Per 1000 patient days	p=0.11	-58%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
		ICU: Device associated 10-12/07: 0.16 Per 1000 patient days	ICU: Device associated 4-6/10: 0.06 Per 1000 patient days	p<0.001 for trend	-62%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
		ICU: Associated with central venous catheters 10.07: 0.46 Per 1000 patient days	ICU: Associated with central venous catheters 6/10: 0.31 Per 1000 patient days	p<0.001 for trend	-33%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
		Non-ICU 10-12/07: 0.12 Per 1000 patient days	Non-ICU 4-6/10: 0.05 Per 1000 patient days	p=0.11	-58%	Student's t-test, ANOVA with Duncan's multiple comparisons method	Poisson regression. Durbin-Watson statistic
Robicsek et al., 2008,[15] USA	Universal Vs No Screening	1.45 (95% CI, 0.94-2.13) Per 10000 patient days	0.44 (95% CI, 0.22-0.76) Per 10000 patient days	p<0.001	-1.01 (95% CI, -1.63 to -0.39)		Segmented regression
Robicsek et al., 2008, [15] USA	Screening of ICU Risk Pts Vs No Screening	1.45 per 10000 patient days (95% CI 0.94-2.13)	1.26 per 10000 patient days (95% CI 0.76-1.97)		-0.18 (-0.99 to 0.62) p 0.66	Segmented regression	
Rodriguez-Bano et al., 2010,[16] Spain	Screening of High Risk Pts Vs No Screening	Control 0.10 per 1000 patient days (0.08-1.13)	After intervention 2: 0.04 per 1000 patient days (95% CI 0.03-0.05) After Intervention 3: 0.02 per 1000 patient days (0.0-0.3)	Not Significant		Fischer	Segmented regression analysis: Change in incidence after 2nd intervention: -0.051 (-0.083 to -0.020), P=0.002 Change in trend after 2nd intervention: -0.006 (-0.010 to -0.01), P=0.01

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Rodriguez-Bano et al., 2010,[16] Spain	Expanded Vs Limited Screening	After intervention 2: 0.04 per 1000 patient days (95% CI 0.03-0.05)	After Intervention 3: 0.02 per 1000 patient days (0.0-0.3)				Results of segmented regression analysis: b6 (change in incidence after 3rd intervention)=0.0002 (-0.022 to 0.026), p=0.8. Change in trend after 3rd intervention: b7=0.003 (0.000–0.006), p=0.05.

BSI: Blood stream infection; C: Control; CI: Confidence interval; Diff: Difference; I: Intervention; ICU: Intensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* PCR: Polymerase chain reaction; Y: Yes

Appendix Table F10. Health care-associated or acquired MRSA bacteremia or BSI: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Gould et al., 2007,[4] UK	Screening of ICU Risk Pts Vs No Screening						Segmented regression Preintervention slope -0.05 (95% CI -0.18 to 0.08), p 0.428 Post-intervention slope 0.03 (95% CI -0.10 to 0.16), p 0.645 Change in slope 0.08 (-0.10 to 0.27), p 0.376 Change in level -1.32 (95% CI -3.88 to 1.23), p 0.302
Raineri et al., 2007,[13] Italy	Screening of ICU Risk Pts Vs No Screening	1.65 Per 1000 patient days (95% CI 0.8-3.1)	Intervention 1: 0.29 Per 1000 patient days (95% CI 0.08-0.75) Intervention 2: 0.6 Per 1000 patient days (95% CI 0.2-1.4)	p=0.02		Chi-square for trend. Fisher's exact test. Kruskal-Wallis analysis of variance for continuous variables between periods.	

C: Control; CI: Confidence interval; Diff: Difference; I: Intervention; ICU: InAppendix Table F10. health care-associated or acquired MRSA bacteremia or BSI: studies that used statistical methods to attempt to control for confounding or secular trendstensive care unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* Y: Yes

Appendix Table F11. Healthcare associated MRSA surgical site infections: studies that used statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Harbarth et al., 2008,[5] Switzerland	Screening of Surgical Pts Vs No Screening	0.99 per 100 procedures	1.14 per 100 procedures	Number of surgical site MRSA infection: control periods 60; intervention periods 70	Rate Ratio: 1.2 (95% CI 9.8-1.7)	Chi-square, Fisher's exact test, Wilcoxon rank sum test	Poisson regression with GEE approach Analysis adjusted for monthly number of admitted patients with previously known MRSA carriage, study month, monthly use of alcohol-based hand rubs, and antibiotic selection pressure exerted by antibiotics without activity against MRSA
Harbarth et al., 2000,[6] Switzerland	Screening of High Risk Pts Vs No Screening	0.75 per 10000 patient-days	0.27 per 10000 patient-days	p<0.001			Poisson regression
Muder et al., 2008,[12] USA	Screening of Surgical Pts Vs No Screening Screening of ICU Patients Vs No Screening	1.91% for the facility for the overall intervention periods	1.91% for the facility for the overall intervention periods	p=0.60 for chi-square test for trend.			
Robicsek et al., 2008,[15] USA	Universal Vs No Screening	2.83 (95% CI 2.10 to 3.75)	1.63 (95% CI 1.19 to 2.18)	p=0.008	-1.20 (95% CI -2.07 to -0.34)		Segmented regression
Robicsek et al., 2008, [15] USA	Screening of ICU Risk Pts Vs No Screening	2.83 (95% CI 2.10 to 3.75)	2.06 (95% CI 1.40-2.93)	p=0.165	-0.77 (95% CI -1.85 to 0.30)	Segmented regression	

C: Control; CI: Confidence Interval; Diff: Difference; I: Intervention; ICU: Intensive Care Unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* Y: Yes

Appendix Table F12. Health care-associated MRSA colonization or infection: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
de la Cal et al., 2004,[22] Spain	Screening of ICU Risk Pts Vs No Screening	Intervention 1: 31/100 patients 14.82/1000 patient-days Intervention 2: 31/100 patients 14.82/1000 patient-days	Intervention 1: 14/100 patients 7.92/1000 patient days Intervention 2: 2/100 patients 1.30 per 1000 patient days	p<0.01, p<0.006 p<0.001, p<0.001		Chi square, Fisher exact test	
Salaripour et al., 2006,[36] Canada	Screening of High Risk Pts Vs No Screening	0.61 per 1000 patient days	0.43 per 1000 patient days	Rates each year from 2001-2005 were significantly lower than the target (p<0.01) and significantly lower than the internal benchmark rate of 0.61 in 2000 (p<0.001).			
Eveillard et al., 2006,[24] France	Expanded Vs Limited Screening	1.13 per 1000 patient days	0.14 per 1000 patient days		RR= 8.1 (95% CI 1.06-64.5) p<0.02	Chi square or Fisher's exact test	
Thompson et al., 2009,[44] UK	Expanded Vs Limited Screening	19.6 Per 1000 bed-days (95% CI 16.5-22.7)	11.8 per 1000 bed-days (95% CI 7.3-16.3)		Rates of acquisition of MRSA from the fifth day in ICU in those initially negative comparing intervention to control chi-square p=.016	Chi-square	

Trautmann et al., 2007,[45] Germany	Expanded Vs Limited Screening	MICU (incidence density per 1000 patient days) 12.2 MICU (incidence density per 1000 patient days) 5.8	SICU (incidence density Per 1000 patient days) 8.3 (2005) 7.5 (2006) MICU (incidence density Per 1000 patient days) 3.3 (2005) 1.7 (2006)		P<0.05 P<0.05	Chi-square	
Girou et al., 2000,[25] France	Expanded Vs Limited Screening	2.9%	2.4%		P=0.68	Chi-square, Fisher's exact test or ANOVA	
Schelenz et al., 2005,[38] UK	Expanded Vs Limited Screening	4.0%	1.5%		RR=2.41 (95% CI: 1.32-4.42) p=0.003	Relative risk, chi square	

C: Control; CI: Confidence interval; Diff: Difference; I: Intervention; ICU: Intensive care unit; MICU: Medical care intensive unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No; RR: Relative risk; SICU: Surgical care intensive unit

Appendix Table F13. Health care-associated or acquired MRSA infection or colonization: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate analysis
Enoch et al., 2011,[23] UK	Expanded screening vs limited screening	8.6/1000 patient episodes (clinical isolates excluding bacteremia)	3.5/1000 patient episodes (clinical isolates excluding bacteremia)	<0.001	Annual decrease of between 0.47 and 1.61 cases/1000 patient episodes (p=0.007).	Chi-square	
Souweine et al., 2000,[41] France	Screening of ICU Risk Pts Vs No Screening	12 (5.2%)	6 (1.7%)	p 0.018		Chi square or Fisher's exact test	

C: Control; Diff: Difference; I: Intervention; ICU: Intensive care unit; N: No

Appendix Table F14. Healthcare-associated MRSA infection: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Bowler et al., 2010,[18] USA	Screening of High Risk Pts Vs No Screening	0.64 per 10000 patient days	0.32 per 1000 patient days	p<0.01		Student's t test	
Boyce et al., 2004,[19] USA	Screening of Surgical Pts Vs No Screening	2.2%	0.7%	p=0.033		Chi-square	
Clancy et al., 2006,[21] USA	Screening of Surgical Pts Vs No Screening	SICU : 9.1 per 1000 patient days	SICU : 4.7 per 1000 patient days	p<0.002		Paired Student's t test	
		MICU: 4.0 per 1000 patient days	MICU : 3.3 per 1000 patient days	p=0.62		Paired Student's t test	
		Wards: 0.53 per 1000 patient days	Wards : 0.32 per 1000 patient days	p=0.17	1	Paired Student's t test	
		Pooled: 4.5 per 1000 patient days	Pooled : 2.8 per 1000 patient days	p<0.01		Paired Student's t test	
Kurup et al., 2010,[30] Singapore	Screening of Surgical Pts Vs No Screening	2.7 per 1000 patient days	2.4 per 1000 patient days	p=0.48	-0.3	Student t-test	
Sankar et al., 2005,[37] UK	Screening of Surgical Pts Vs No Screening	2.4%	0%	p<0.05	-2.4%	Fisher exact test, unpaired Student's t test	
Simmons et al., 2011,[39] USA	Screening of Surgical Pts Vs No Screening	Hospital-wide rates: 0.8 per 1000 patient days	Hospital-wide rates: 0.38 per 1000 patient days	p=0.0003		Nonparametric Wilcoxon test	
		ICU Rates : 3.19 per 1000 patient days	ICU Rates : 1.66 per 1000 patient days	p=0.005		Nonparametric Wilcoxon test	
Wernitz et al.,	Screening of	48/119	38/205				Standardized infection ratio: 0.52

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
2005,[47] Germany	High Risk Pts Vs No Screening						(38/73.2), 95% CI: 0.37-0.71. (Calculated by dividing the number of observed patients with health care-associated MRSA infection in the screening period by the expected number of patients with health care-associated MRSA infection calculated from nosocomial infection rates during the control period.
West et al., 2006,[48] USA	Expanded Vs Limited Screening	Hospital 1: Tertiary Care: 0.76 per 1000 patient days	Hospital 1: Tertiary Care: 0.46 per 1000 patient days	p=0.05		Wilcoxon rank sum test	
		Hospital 2: Suburban: 0.72 per 1000 patient days	Hospital 2: Suburban: 0.57 per 1000 patient days	p=0.35		Wilcoxon rank sum test	

C: Control; CI: Confidence Interval; Diff: Difference; I: Intervention; ICU: Intensive Care Unit; MICU: Medical Intensive Care Unit; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No; SICU: Surgical Intensive Care Unit

Appendix Table F15. MRSA infection: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate analysis
Kelly et al., 2012,[27] Ireland		Infection rate 0.49%	Infection rate 0.35%	P=0.108		Binomial comparison	
Souweine et al., 2000,[41] France	Screening of ICU Risk Pts Vs No Screening	12 (5.2%)	6 (1.7%)	p 0.018		Chi square or Fisher's exact test	

C: Control; Diff: Difference; I: Intervention; ICU: Intensive care unit; N: No

Appendix Table F16. Health care-associated MRSA bacteremia or BSI: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
de la Cal et al., 2004,[22] Spain	Screening of ICU Risk Pts Vs No Screening	3.7 per 1000 patient days	0.9 per 1000 patient days	p<0.01		Chi square, Fisher exact test	
Pan et al., 2005,[34] Italy	Screening of High Risk Pts Vs No Screening	0.64 Per 1000 admissions Primary MRSA BSI 0.12	0.37 Per 1000 admissions Primary MRSA BSI 0.03	RR 0.57. 95% CI 0.35 to 0.92, P=0.0003 RR 0.29 95% CI 0.08-1.09, p=0.06		Chi-square or Fisher's exact test	
Thompson et al., 2009,[44] UK	Expanded Vs Limited Screening	3.7 (95% CI 2.6-4.8) % of those acquiring MRSA >/= 5 days after admission with subsequent MRSA bacteremia: 18.7 (12.2-25.2)	0.4 (95% CI 0-2.9) % of those acquiring MRSA >/= 5 days after admission with subsequent MRSA bacteremia: 3.8 (0-11.1)	Chi-square p=0.009 Not statistically significant			
Trautmann et al., 2007,[45] Germany	Expanded Vs Limited Screening	Incidence per 1000 device days of device-associated MRSA infections: Septicemia 0.4	Incidence per 1000 device days of IV catheter-associated septicemia 0	p<.0125 Incidence density test			
Wernitz et al., 2005,[47] Germany	Screening of High Risk Pts Vs No Screening	13/119	7/205	Standardized infection ratio: 0.35 (7/20.1), 95% CI: 0.14-0.71.			

C: Control; Diff: Difference; I: Intervention; ICU: Intensive care unit; N: No

Appendix Table F17. Health care-associated or acquired MRSA bacteremia or BSI: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Blumberg, et al., 1994,[17] South Africa	Screening of ICU Risk Pts Vs No Screening	Pediatric oncology ward 12/924 blood cultures performed = 1.3%	Pediatric oncology ward In intervention year: 0/1026 blood cultures performed = 0%	p=0.000123 p=0.06 compared with pre-treatment period		Two-tailed Fisher's exact test	
		ICU 14/1391 blood cultures performed = 1%	ICU In year following intervention year: 3/815 blood cultures performed 4/1579 blood cultures performed = 0.25% In year following intervention year: 10/1934 blood cultures performed = 0.5% 82/18784 blood cultures performed = 0.44%	p=0.016 p not specified p=0.047		Two-tailed Fisher's exact test	
		Non-targeted areas of the hospital 62/20068 blood cultures performed = 0.3%	Non-targeted areas of the hospital In year following intervention year: 112/18977 blood cultures performed = 0.59%	p=0.00004 compared with pre-treatment period		Two-tailed Fisher's exact test	
Enoch et al., 2011,[23] UK	Expanded screening vs limited screening			0.555	No significant change in the annual MRSA bacteremia rate/patient episode	Chi square	

C: Control; Diff: Difference; I: Intervention; ICU: Intensive care unit; N: No

Appendix Table F18. MRSA BSI (not clearly acquired): studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Schelenz et al., 2005,[38] UK	Expanded vs Limited Screening	1.1% (12/1075)	0.2% (2/956)		RR 5.34 (95% CI 1.20-23.78); p 0.014	RR 5.34 (95% CI 1.20-23.78); p 0.014	

BSI: Blood stream infection; CI: Confidence interval; C: Control; Diff: Difference; I: Intervention; ICU: Intensive care unit; N: No; RR: Relative Risk

Appendix Table F19. Healthcare associated MRSA surgical site infection: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Chen et al., 2012,[20] US	Screening of surgical patients vs no screening	5/17	1/17	Those tested and treated for MRSA showed a trend toward fewer MRSA wound complications (p=0.118)		Fisher's exact test	
Jog et al., 2008,[26] UK	Screening of Surgical Pts Vs No Screening	1.15%	0.26%	Relative risk reduction: 0.77, 95% CI: (0.056-0.95), p<0.05	0.89%	Chi square, Koopman's likelihood-based approximation for relative risk	
Keshtgar et al., 2008,[28] UK	Screening of High Risk Pts Vs No Screening	1.44 per 1000 patient-days	1.25 per 1000 patient-days	p=0.021		Fisher's exact test	1.44 per 1000 patient-days
Kim et al., 2010,[29] USA	Screening of Surgical Pts Vs No Screening	0.19%	0.06%	p=0.0315	-0.13%	Chi square, Fisher exact test	
Lipke et al., 2010,[31] USA	Screening of Surgical Pts Vs No Screening	0.73%	0.16%	p=0.0538	0.57%	Fisher exact test	
Malde et al., 2006,[32] UK	Screening of Surgical Pts Vs No Screening	Elective surgery: 55.6%	Elective surgery: 22.4%	p=0.002 for trend	33.2%	Chi square	
		Emergency surgery: 62.5%	Emergency surgery: 43.8%	p=0.042 for trend	18.7%	Chi square	
Nixon et al., 2006,[33] UK	Screening of Surgical Pts Vs No Screening	Trauma: 1.57%	Trauma:0.69%	p=0.035 for trend	0.88%	Chi square	
		Admissions: 0.56%	Admissions: 0.17%	p=0.06 for trend	0.39%	Chi square	

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Pofahl et al., 2009,[35] USA	Screening of Surgical Pts Vs No Screening	0.23% per 100 procedures	0.09% per 100 procedures		0.14%	Chi-Square with Yate's continuity correction	Overall SSI, Non-significant p-value; Hysterectomy: Control= ~0.11 Intervention= ~0.08, Non-significant p-value; Orthopedics: Control= 0.30 Intervention= 0.00, p-value=0.04; Cardiac: Control= ~0.24 Intervention= ~0.19, Non-significant p-value;
Schelenz et al., 2005,[38] UK	Expanded Vs Limited Screening	Sternal wound: 2.6% (28/1075) Leg wound: 1.5% (16/1075)	Sternal wound 1.4% (13/956) Leg wound 0.7% (7/956)	RR 1.92 (95% CI 1.00-3.68), p 0.057 RR 2.03 (95% CI 0.84-4.92), p 0.141			
Supriya et al., 2009,[42] Scotland	Screening of Surgical Pts Vs No Screening	28.57%	9.68%	p= 0.034	18.89%	Chi square	
Thomas et al., 2007,[43] UK	Screening of Surgical Pts Vs No Screening	19%	2%		17%	Chi square with Yates correction	MRSA PEG site infections by year for the control period: 12% (5 of 42) in 2002 20% (7 of 35) in 2003 29% (7 of 24) in 2004; an overall infection rate of 19%. Intervention period vs. overall rate chi-square= 5.16, P < 0.025; intervention period vs. 2004 chi-square= 6.76, P < 0.01; intervention period vs. 2003 chi-square= 4.35, P < 0.05

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test	Multivariate Analysis
Walsh et al., 2011,[46] USA	Screening of Surgical Pts Vs No Screening	1.16%	0.08%	RR= 0.069; (95% CI: 0.016-0.286); P< 0.001)	1.08%	Chi square and relative risk reduction	

C: Control; CI: Confidence Interval; Diff: Difference; I: Intervention; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No; PEG: percutaneous endoscopic gastrostomy; RR: Relative risk; SSI: Surgical Site Infection

Appendix Table F20. MRSA related morbidity: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test
Malde et al., 2006,[32] UK	Screening of Surgical Pts Versus No Screening	Elective Admissions: Major limb amputation among MRSA positive (colonized and infected) in elective admissions 27.8%	Elective Admissions: Major limb amputation among MRSA positive (colonized and infected) in elective admissions 9.0%	p=0.026	18.8%	Chi square
		Emergency Admissions: Major limb amputation among MRSA positive (colonized and infected) in elective admissions 50.0%	Emergency Admissions: Major limb amputation among MRSA positive (colonized and infected) in elective admissions 38.8%	p=0.26	11.2%	Chi square

C: Control; Diff: Difference; I: Intervention; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No

Appendix Table F21. MRSA related mortality: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test
Malde et al., 2006,[32] UK	Screening of Surgical Pts Versus No Screening	Elective Admissions 16.7%	Elective Admissions 9.0%	p>0.05	7.7%	Chi square
		Emergency Admissions 25.0%	Emergency Admissions 12.4%	p=0.067	12.6%	Chi square

C: Control; Diff: Difference; I: Intervention; MRSA: Methicillin-resistant *Staphylococcus aureus;* N: No

Appendix Table F22. MRSA resource utilization: studies that did not use statistical methods to attempt to control for confounding or secular trends

Author, Year, Country	MRSA Strategy	Control	Intervention	p value	Diff (I-C)	Statistical Test
Sankar et al., 2005,[20] UK	Screening of Surgical Pts Vs No Screening	10.43 days (SD 4.2 days, range 5-29 days)	9.47 days (SD 2.6 days, range 5-26 days)	p <0.05	0.96 days	Fisher's exact test, unpaired Student's t test

C: Control; Diff: Difference; I: Intervention; MRSA: Methicillin-resistant *Staphylococcus aureus;* SD: standard deviation; N: No

Appendix Table F23. USPSTF study quality ratings

Study	MRSA Strategy	Assembled CG	Maintained CG	Minimal follow up loss	Measurements equal, valid & reliable	Interventions clearly defined	Important outcomes	Appropriate analysis of results	Funding Acknowledged	Overall USPSTF rating	Separate control group
Blumberg, et al., 1994[17]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	N	N	Y	Poor	N
Bowler et al., 2010[18]	Screening of High Risk Pts Vs No Screening	U	U	U	Y	Y	Y	N	Y	Poor	N
Boyce et al., 2004[19]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	N	Poor	N
Chaberny et al., 2008[1]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	Y	Poor	Y
Chen et al., 2012[20]	Screening surgical patients vs no screening	Y	U	U	Y	Y	Y	N	N	Poor	Y
Chowers et al., 2009[2]	Screening of High Risk Pts Vs No Screening	U	U	U	Y	N	Y	N	N	Poor	N
Clancy et al., 2006[21]	Screening of ICU Risk Pts Vs No Screening	Y	N	U	Y	Y	Y	N	Y	Poor	N
de la Cal et al., 2004[22]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Ellingson et al., 2011[3]	Screening of High Risk Pts Vs No Screening	U	U	U	U	Y	N	N	N	Poor	N
Enoch et al., 2011[23]	Expanded targeted screening vs limited targeted screening	U	U	U	Y	Y	N	U	Y	Poor	N
Eveillard et al., 2006[24]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Girou et al., 2000[25]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Gould et al., 2007[4]	Screening of ICU Risk Pts Vs No Screening	Y	U	U	Y	Y	U	Y	Y	Fair	N
Harbarth et al., 2000[6]	Screening of High Risk Pts Vs No Screening	U	U	U	N	N	Y	N	Y	Poor	N
Harbarth et al., 2008[5]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	Y	Y	Good	Y
Holzmann-Pazgal et al., 2011[7]	Screening of ICU Risk Pts Vs No Screening	N	U	U	U	Y	Y	N	N	Poor	N
Huang et al., 2006[8]	Screening of ICU Risk Pts Vs No Screening	U	U	U	Y	Y	U	N	Y	Poor	N
Huskins et al., 2011[9]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	Y	Y	Good	Y
Jain et al., 2011[10]	Universal Vs No Screening	U	U	U	N	Y	Y	N	Y	Poor	N

Study	MRSA Strategy	Assembled CG	Maintained CG	Minimal follow up loss	Measurements equal, valid & reliable	Interventions clearly defined	Important outcomes	Appropriate analysis of results	Funding Acknowledged	Overall USPSTF rating	Separate control group
Jog et al., 2008[26]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Kelly et al., 2012,[27]	Screening of surgical patients vs no screening	U	U	U	Y	Y	U	N	N	Poor	N
Keshtgar et al., 2008[28]	Screening of High Risk Pts Vs No Screening	U	U	U	Y	Y	Y	N	Y	Poor	N
Kim et al., 2010[29]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Kurup et al., 2010,[30]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Leonhardt et al., 2011[11]	Universal Vs Screening of Selected Pts	Y	U	U	U	Y	Y	Y	Y	Good	Y
Lipke et al., 2010[31]	Screening of Surgical Pts Vs No Screening	Y	Y	U	U	Y	Y	N	N	Poor	N
Malde et al., 2006[32]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Muder et al., 2008[12]	Screening of Surgical Pts Vs No Screening	U	U	U	Y	Y	N	N	N	Poor	N
Muder et al., 2008[12]	Screening of ICU patients vs no screening	U	U	U	Y	Y	Y	N	N	Poor	N
Nixon et al., 2006[33]	Screening of Surgical Pts Vs No Screening	Y	Y	Y	Y	Y	Y	N	N	Poor	N
Pan et al., 2005[34]	Screening of High Risk Pts Vs No Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Pofahl et al., 2009[35]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	N	Poor	N
Raineri et al., 2007[13]	Screening of ICU Risk Pts Vs No Screening	N	N	U	U	Y	U	N	Y	Poor	N
Reilly et al., 2012[14]	Universal screening vs no screening	U	U	U	U	U	U	U	Y	Poor	N
Robicsek et al., 2008[15]	Universal Vs No Screening	Y	U	Y	Y	Y	Y	Y	Y	Good	N
Robicsek et al., 2008[15]	Universal Vs Screening of Selected Pts	Y	U	Y	Y	Y	Y	Y	Y	Good	Y
Robicsek et al., 2008[15]	Screening of ICU Risk Pts Vs No Screening	Y	U	Y	Y	Y	Y	Y	Y	Good	N
Rodriguez-Bano et al., 2010[16]	Screening of High Risk Pts Vs No Screening	N	U	U	Y	Y	N	Y	Y	Fair	N
Rodriguez-Bano et al., 2010[16]	Expanded Vs Limited Screening	N	U	U	Y	Y	N	Y	Y	Fair	N

Study	MRSA Strategy	Assembled CG	Maintained CG	Minimal follow up loss	Measurements equal, valid & reliable	Interventions clearly defined	Important outcomes	Appropriate analysis of results	Funding Acknowledged	Overall USPSTF rating	Separate control group
Salaripour et al., 2006[36]	Screening of High Risk Pts Vs No Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Sankar et al., 2005[37]	Screening of Surgical Pts Vs No Screening	Y	Y	U	U	Y	Y	N	N	Poor	N
Schelenz et al., 2005[38]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Simmons et al., 2011[39]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	N	N	N	Poor	N
Sott et al., 2001[40]	Screening of Surgical Pts Vs No Screening	Y	Y	U	U	Y	Y	N	N	Poor	N
Souweine et al., 2000[41]	Screening of ICU Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	Y	Poor	N
Supriya et al., 2009[42]	Screening of Surgical Pts Vs No Screening	Y	Y	U	U	Y	N	N	Y	Poor	N
Thomas et al., 2007[43]	Screening of Surgical Pts Vs No Screening	Y	Y	U	U	Y	Y	N	Y	Poor	N
Thompson et al., 2009[44]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	Y	Poor	N
Trautmann et al., 2007[45]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	N	Poor	N
Walsh et al., 2011[46]	Screening of Surgical Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	N	Poor	N
Wernitz et al., 2005[47]	Screening of High Risk Pts Vs No Screening	Y	Y	U	Y	Y	Y	N	N	Poor	N
West et al., 2006[48]	Expanded Vs Limited Screening	U	U	U	Y	Y	Y	N	N	Poor	N

CG: comparable groups; ICU: Intensive Care Unit; N:No; U: Unknown; USPSTF: United States Preventive Services Task Force; Y: Yes

Appendix F Reference Citations

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Appendix G. Deeks' Criteria To Assess Quality of Nonrandomized Comparative Studies

The quality of included nonrandomized comparative intervention studies was also assessed based on a selection of items proposed by Deeks et al.,[*] to inform the approach used by the U.S. Preventive Services Task Force,[†] as follows:

- Was sample definition and selection prospective or retrospective?
- Were inclusion/exclusion criteria clearly described?
- Were participants selected to be representative?
- Was there an attempt to balance groups by design?
- Were baseline prognostic characteristics clearly described and groups shown to be comparable?
- Were interventions clearly specified?
- Were participants in treatment groups recruited in the same time period?
- Was there an attempt by investigators to allocate participants to treatment groups in an attempt to minimize bias?
- Were concurrent/concomitant treatments clearly specified and given equally to treatment groups?
- Were outcome measures clearly valid, reliable and equally applied to treatment groups?
- Were outcome assessors blinded?
- Was the length of follow-up adequate?
- Was attrition below an overall high level (less than 20 percent)?
- Was the difference in attrition between treatment groups below a high level (less than 15 percent)?
- Did the analysis of outcome data incorporate a method for handling confounders such as statistical adjustment?

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