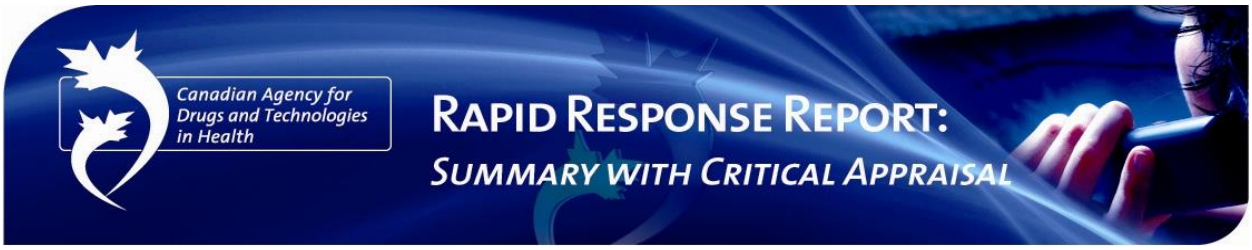


**TITLE: Universal Screening for Antibiotic-Resistant Organisms: A Review of the Clinical and Cost-Effectiveness**

**DATE:** 13 October 2015

## CONTEXT AND POLICY ISSUES

Antibiotic resistant organisms (AROs) are pathogens with resistance to common antibiotic agents and consequently are associated with higher risk of hospital-acquired infections (HAI).[1] Antibiotic resistant organisms can spread quickly as many colonized individuals may be asymptomatic. Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant enterococci (VRE) have been linked to healthcare settings more than other AROs.[2] Vancomycin-resistant enterococci (VRE) were first identified in the mid-1980s and an increasing trend of vancomycin-resistance has been observed in North America and Europe.[3-8] Methicillin-resistant *Staphylococcus aureus* rates have declined over the recent past but still exceed historical rates and remain a concern.[9-14] In response to rising MRSA mortality rates in the United Kingdom (UK) up to 2005,[15] the Department of Health followed-up with an initiative to reduce infection rates.[16] These kinds of measures may be reflected by the declining rates observed in some regions.

To prevent the risk of horizontal transmission of HAIs including infections due to AROs, various measures have been put forward. Approaches include, but are not limited to, restriction of antibiotic use and antimicrobial stewardship, education of staff, contact-isolation precautions (e.g., hand washing, personal protective equipment), rectal surveillance cultures, as well as routine screening.[17] It is well established that ARO-related infections can increase morbidity (e.g., infection-related complications), mortality, and healthcare costs.[18-26] These risks are of particular concern for vulnerable populations such as infants (especially pre-term and low birth weight infants), the elderly, and immunocompromised patients.
Screening is defined as a mode of identifying individuals at risk for colonization or currently colonized with AROs, that enables subsequent testing and intervention (e.g., contact precautions or decolonization).[1] Screening measures based on active clinical indicators may be insufficient for identifying asymptomatic carriers of MRSA who are a major ARO reservoirs.[27] As such, comprehensive surveillance measures such as universal screening have been proposed, which ensures sample testing in asymptomatic carriers without typical clinical indications for testing,[28] allowing earlier provision of intervention with the aim of reducing transmission and

infection.[11] In 2010, the Department of Health in England instituted universal screening of patients for MRSA at hospital admission in the place of targeted screening based on risk factors.[29,30] The alternative of screening high-risk patients at increased risk of ARO-related infection has been suggested. One international protocol advocates surveillance only in ICUs and not for other hospital admissions.[31] Many guidelines including those from the Society for Healthcare Epidemiology of America and the Association of Professionals in Infection Control and Epidemiology endorse the use of screening in 'appropriate circumstances'.[32] It is unclear whether all individuals or only high-risk individuals (e.g., surgical patients, intensive care unit [ICU] patients, patients admitted from nursing homes or other institutions, patients with a history of colonization etc.) derive more benefit from screening or whether other methods such as universal decolonization are more cost-effective.

Even with restriction to screening of specific clinical groups, such as surgery or ICU patients, the cost of universal screening of these patient groups may be unmanageable. The cost of maintaining an infection control program can vary depending on the extent of screening and add-on infection control measures.[33] Significant costs arise due to the requirement for contact and physical isolation, and other infection reduction responses.[34] It is estimated that 4.2% of patients hospitalized in Canada will become infected or colonized with MRSA, resulting in an estimated annual cost of $36.3 million CAD.[35,36] The estimated costs of VRE infection ($695,411 CAD) are substantially lower than those resulting from MRSA.[36] Over the 2010 to 2011 period, Vancouver Coastal Health, a health authority operating in Metro Vancouver, performed approximately 17 thousand screens (as per hospital admission screening algorithms) and spent $5.2 million CAD to isolate 612 cases of VRE. While colonization rates of VRE at Vancouver General Hospital increased from 2008/9 to 2012/13, infection rates remained stable, which led to the removal of VRE screening in 2013.[37] This example demonstrates that the cost-benefit of screening may vary depending on the ARO of interest. Screening requires major resources ranging from expanded laboratory capacity, staff training, and decolonization or isolation protocols; thus, it is necessary to monitor the necessity, feasibility and resource implications of implementation of screening programs.

CADTH has conducted several reviews on the effectiveness of various ARO screening strategies. A 2012 CADTH systematic review reported that based on limited observational evidence, weekly screening of high-risk units was associated with a reduction in VRE bacteremia versus no surveillance.[38] Several reports have been published on MRSA.[39-41] A 2009 Rapid Response summary with critical appraisal[40] reported that the evidence was inconclusive with regards to whether pre-operative MRSA screening was effective and that based on reviewed guidelines, pre-operative screening did not appear to be universally practiced or accepted. A 2011 Rapid Response summary of abstracts assessed the clinical evidence and guidelines regarding admission screening for MRSA.[39] The evidence presented suggested that screening of high-risk patients may reduce the risk of colonization and infection but that these conclusions were based on weak evidence and could not enable definitive recommendations.[39] A 2012 Rapid Response summary with critical appraisal[41] assessing the comparative effectiveness of targeted versus universal MRSA screening was unable to draw conclusions on the relative benefits of the respective approaches due to inconsistency in the evidence presented. Some studies suggested a benefit, while others observed no difference compared to standard infection control measures. Controlled studies trended towards no benefit, while the majority of studies reporting reduced infection and colonization rates were pre- and post-implementation studies. One 2014 Rapid Response summary of abstracts on the clinical effectiveness of carbapenemase-producing *Enterobacteriaceae* (CPE) (also referred to as carbapenem-resistant Enterobacteriaceae [CRE]) presented evidence that suggested that

screening of individuals admitted from health care facilities located in another country, or patients who had travelled abroad may be warranted.[42]

Considering the existing evidence, there is uncertainty regarding the effectiveness of active surveillance measures to detect AROs and whether screening has a greater impact when applied universally, to targeted at-risk populations, or whether there is a need for screening at all.[11] The cost of implementing screening programs may be offset by positive health gains, yet the cost-effectiveness of this approach has not been reviewed extensively.[43] This review will evaluate the comparative clinical and cost-effectiveness of these various approaches.

## RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of a universal screening strategy versus no screening for antibiotic resistant organisms?

2. What is the comparative clinical effectiveness of a universal screening strategy versus targeted screening of intensive care unit patients, surgical patients and other high risk patients for antibiotic resistant organisms?

3. What is the comparative clinical effectiveness of targeted screening versus no screening for antibiotic resistant organisms for intensive care unit patients, surgical patients, and other high risk patients?

4. What is the comparative cost-effectiveness of a universal screening strategy versus targeted screening or no screening for antibiotic resistant organisms?

## KEY FINDINGS

One review of systematic reviews and primary clinical studies, five primary clinical studies, and 15 economic evaluations were identified regarding the clinical and cost-effectiveness of various screening strategies for antibiotic resistant organisms. Taking into consideration issues with generalizability, difficulty interpreting the true effect of screening against the backdrop of a matrix of infection control measures, and substantial risk of confounding, the evidence suggests that from both clinical and cost perspectives having an MRSA screening program is likely beneficial compared to not having a screening program. Targeted screening may be preferred over universal screening due to more convincing evidence in support of clinical benefits and cost-savings, and reduced concern related to antibiotic resistance and downstream costs. Limited evidence was available in support of VRE screening programs and no evidence was identified regarding the clinical or cost-effectiveness of other screening programs for other AROs.

## METHODS

### Literature Search Methods

A focused literature search was conducted on key resources including Ovid Medline, PubMed, The Cochrane Library, ECRI, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between Jan 1, 2010 and Sep 14, 2015. A

supplemental broad search was conducted using methodological filters to limit retrieval to health technology assessments, systematic reviews, meta-analyses. This search was limited to documents published between Jan 1, 2013 and Sep 22, 2015.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

## Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. For questions on clinical effectiveness, only studies published from 2013 onward were considered for inclusion because of the availability of a comprehensive review[44] published in 2014 by the Institute of Health Economics (IHE) in Alberta, Canada with similar research questions and selection criteria. As the IHE review did not evaluate cost-effectiveness, search date inclusion range was expanded to 2010 onward for this question. A second reviewer screened these full-text articles for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

**Table 1:** Selection Criteria*

| | |
|---|---|
| **Population** | Q1, 2 and 4: Patients in hospital<br>Q3: High risk patients (e.g., intensive care unit patients, surgical patients, clinical populations at high risk of infection) |
| **Intervention**† | Q1, 2 and 4: Universal screening strategy<br>Q3 and Q4: Targeted screening |
| **Comparator** | Q1 and Q3: No screening<br>Q2: Targeted screening<br>Q4: No screening or targeted screening |
| **Outcomes** | Q1 to Q3: Clinical benefit (e.g., rate of ARO detection, rate of ARO transmission, rate of ARO-related infection);<br>Harms (e.g., morbidity, mortality, antibiotic resistance)<br>Q4: Cost-effectiveness outcomes (e.g., cost per infection /death prevented, cost per QALY, cost per infection detected) |
| **Study Designs** | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations |

*Note: antibiotic resistant organisms covered in this report will include Acinetobacter, CRE, MRSA, VRSA, VRE, ESBL-producing organisms

†Screening strategies executed in countries with developed market economies as defined by the Development Policy and Analysis Division of the United Nations' Department of Economic and Social Affairs will be included following the approach of the Institute of Health Economics (Alberta, Canada) report.[44,45] This includes, Australia, Canada, Japan, New Zealand, the United States, and European Counties

CRE = Carbapenem-resistant *Enterobacteriaceae*; ESBL = extended spectrum beta lactamase; MRSA = methicillin resistant *Staphylococcus aureus*; QALY = quality adjusted life year; VRSA = vancomycin resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *Enterococci*

## Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2010 for question four, and 2013 for questions one through three. Health technology assessment reports, systematic reviews (SR), and meta-analyses (MA) were excluded if there was incomplete reporting of methods or if they were superseded by a more recent and/or rigorous review, or an update. Randomized controlled trials (RCTs) and non-randomized studies were excluded if they were described within an included

SR. Economic studies that only reported direct costs and were not cost-effectiveness, cost-utility or cost-benefit analyses were also excluded. As previously mentioned, only studies conducted in countries with developed market economies as defined by the Development Policy and Analysis Division of the United Nations' Department of Economic and Social Affairs were included for review.[44,45]

### Critical Appraisal of Individual Studies

The included SRs were critically appraised using AMSTAR criteria,[46] and the methods used when conducting the literature search, study selection, quality assessment, data extraction and for summarizing the data were assessed. Primary clinical studies were critically appraised using Downs and Black checklist.[47] Reporting, external validity, internal validity in terms of bias and confounding, and power were assessed. Economic studies were assessed using the Drummond checklist.[48] Study design, data collection, analysis, and interpretation of results were evaluated. Summary scores were not calculated for the included studies; rather, strengths and limitations of each included study were described narratively.

## SUMMARY OF EVIDENCE

### Quantity of Research Available

A total of 614 citations were identified in the literature search. Following screening of titles and abstracts, 567 citations were excluded and 47 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search.[44,49] Of these 49 potentially relevant articles, 21 publications met the inclusion criteria and were included in this report. This was after exclusion of 28 studies; six studies due to an irrelevant or no comparator,[50-56] two studies due to an irrelevant intervention,[57,58] three studies due to irrelevant outcomes,[59-61] three publications that were review articles or letters to the editor,[2,62,63] six studies due to inclusion in the SR[44] included in this report,[16,64-68] five studies that reported only direct costs and not cost-effectiveness outcomes,[49,69-72] one study due to an irrelevant location,[73] and one duplicate report.[11] Appendix 1 describes the PRISMA flowchart of the study selection.

### Summary of Study Characteristics

Detailed study characteristics are presented in Appendix 2.

*Study Design*

One review of SRs,[44] five primary clinical studies,[30,51,74-76] and 15 economic evaluations[43,48,77-88] were identified regarding the clinical and cost-effectiveness of ARO screening strategies. The review of SRs[44] included a systematic search for SRs and a search (2003 to February 2014) for primary clinical studies. Seven systematic reviews and six primary clinical studies were included.[44]

The five primary clinical studies were all non-randomized studies of various design, including retrospective controlled before-and after studies,[30,51,76] one prospective cohort study,[74] and one cross-sectional study[75]

The economic evaluations included, three cost-benefit,[52,83,84] seven cost-effectiveness,[43,48,79,80,82,88,89] and five cost-utility analyses.[77,81,85-87] The evaluations were conducted from various perspectives including hospital or healthcare provider,[43,48,74,77-79,82-86,88,89] third-party payer,[77,85-87] decision-maker,[81] and societal.[87]

*Country of Origin*

The review of SRs[44] was conducted by authors in Alberta, Canada and included SR conducted by authors located in the United States (US), UK, Australia, and Canada. Locations of the primary studies reviewed were not reported.[44] The primary clinical studies were conducted in the US,[51,74] and UK.[30,75,76] The economic evaluations were primarily conducted from the US perspective.[43,48,77,78,80,83-87,89] Some studies were conducted from the perspective of other countries, including Switzerland,[71,88] the Netherlands,[79,82] Germany,[72] and the UK.[81]

*Patient Population*

In general, the patient populations included patients (either all patients or a targeted high-risk population) admitted to hospital, a specific hospital ward, or other healthcare settings. No restrictions were made based on sex, ethnicity, or socioeconomic status.

The review of SRs[44] included patients of any age admitted to hospital or other healthcare settings (e.g., long-term care). The individual SRs included patients in acute care or ICU settings, deemed at high risk for ARO colonization or infection (e.g., previously known infection or colonization), and all types of surgical patients or specific surgical populations (e.g., orthopedic surgery).

The primary clinical studies included all admitted hospital patients,[30,51,75,76] and infants admitted to neonatal ICUs.[74]

The economic studies included all admitted hospital patients,[78-80,82-84,87,89] lung and heart transplant patients,[77] patients admitted to ICU,[81] orthopedic surgery patients,[48,86] cardiac surgery patients,[85] all surgical patients,[88] and patients admitted to Veteran's Health Administration facilities in the US.[43]

*Interventions and Comparators*

*Screening Technology*

A variety of screening assays were used with the majority of studies assessing screening protocols that used PCR (rapid screening) or chromogenic agar culture (conventional screening).

*Follow-Up Interventions*

The review of SRs[44] included ARO screening strategies that may or may not include surveillance, isolation and eradication/decolonization. The primary studies included screening strategies combined with barrier and isolation precautions.[51,74] In some cases only screening in isolation was considered or the matrix of infection control measures was unclear.[30,75,76]

The economic studies considered follow-up interventions. Several studies assumed subsequent decolonization for positive screens.[43,48,77,85,86] Two studies considered both isolation precautions and decolonization.[81,88] Several studies considered isolation and/or contact precautions.[78-80,82,84,87,89] One study reported unspecified infection control measures as the follow-up.[83]

*Types of Comparisons*

For the clinical evidence, there was a mix of comparisons. One publication explored all comparisons of universal, targeted, and no screening.[44] Some studies only compared universal to targeted screening (details in Appendix 2).[30,51,75,76] One study only compared targeted screening to no screening.[74]

For the economic evidence, two studies compared both universal and targeted screening to no screening.[80,82] Three studies compared universal to targeted screening.[79,83,89] Seven studies compared targeted screening to no screening.[48,77,81,84-86,88] Finally, three studies compared universal screening to no screening.[43,78,87]

*ARO Species of Interest*

The review of SRs[44] assessed evidence on screening for MRSA and methicillin-sensitive *Staphylococcus aureus* (MSSA, not an ARO), VRE, and extended spectrum beta lactamase (ESBL)producing organisms. The majority of the primary studies included (both clinical and cost-effectiveness studies) assessed screening for MRSA, while two studies assessed screening for both MRSA and MSSA.[48,77] None of the evidence assessed CRE or vancomycin-resistant *Staphylococcus aureus* screening programs.

*Outcomes*

The review of SRs[44] aimed to assess both effectiveness and safety outcomes associated with various screening approaches. Ultimately, the included studies reported on colonization and infection rates (including local infections, surgical site infections, and bloodstream infections), and rates of ARO positive admission. No studies reported on the safety of ARO screening. Proposed safety outcomes included antimicrobial resistance, medical errors, reduced quality of care and allergic and non-allergic toxicity. Most of these outcomes would not be direct impacts of screening but of the subsequent intervention approach informed by screening.

Similarly the primary clinical studies[30,51,74-76] reported on MRSA infection rate and detection rate, and one study reported on mortality.[51]

The economic studies reported on outcomes including cost benefit outcomes (e.g., cost of screening per cost savings of infections avoided),[78,82,84] cost per quality adjusted life year (QALY),[77,81,85-87] and cost-effectiveness outcomes (e.g., cost per infection avoided,[79,80,82,88,89] cost per reduction in septic revision rate,[48] and cost per infection and deaths avoided[43]). Further details on key model assumptions of the economic studies are presented in Appendix 2.

**Summary of Critical Appraisal**

Study strengths and limitations are presented in detail in Appendix 3.

## CLINICAL EVIDENCE

### Systematic Reviews

The review of SRs and primary studies[44] did not include a pre-published protocol and the a priori nature of the objectives was unclear. There was a lack of duplicate study selection and data abstraction, increasing the risk of biased reporting and accidental omissions. The review included a comprehensive literature search for SRs on multiple databases and a thorough grey literature search. The search date for primary studies was restricted to the time period between 2003 and February 2014 under the assumption that most trials would be included in the retrieved SRs, however, there remains the possibility that older relevant studies were not captured in this review. Publications were limited to English language documents and it was unclear whether unpublished literature was considered, though most of the included SRs did not discuss unpublished literature. A detailed list of included and excluded studies was provided and characteristics of included studies were provided. The scientific quality of each category of study type was assessed using an appropriate tool, and these considerations were carried forward and discussed in the formulation of conclusions. No pooling of results was conducted and publication bias was not assessed for the overall review or by any individual SR. Funding sources were disclosed and while the main affiliations of reviewers and contributors was stated, potential conflict of interest was unclear.

### Primary Clinical Studies

#### Reporting

A study hypothesis, aim or objective was clearly stated by all but one study.[74] All studies[30,51,74-76] described outcomes clearly prior to reporting of results, provided a description of the intervention, and reported main results with clarity. All but one study[75] provided a clear description of patient level characteristics. Three studies[30,75,76] did not report the distribution of potential confounders. Some studies reported estimates of random variability and actual probability values,[51,74] but not all.[30,75,76] This was acceptable in the case of some studies as no direct comparisons were made between groups. One study provided outcomes for limited adverse events (i.e., mortality),[74] but in general there was underreporting and lack of consideration for direct and indirect adverse events. Losses to follow-up were not considered by any study. While the retrospective use of databases may reduce the risk of patient drop-outs it would not account for patients who were scheduled for screening but left the hospital prior to testing or those without follow-up screens or lost results due to human or analytical error.

#### External Validity

While the patients included in analysis were generally representative of the institutions they were admitted to, generalizability to other institutions is limited, especially under circumstances where there are differences in overall infection control protocols, prevalence of the AROs of interest, screening technologies, and even physical layout of the facility. There were no concerns that participating patients were different from those who were recruited. The context of the study setting in terms of staff and facilities was considered to be representative of the facilities or specific wards where the studies took place.

*Internal Validity – Bias*

None of the studies attempted blinding of study subjects or outcome assessors. As the outcomes were objective this was likely not a major concern. However, performance bias cannot be ruled out, especially with regards to outcome assessors. In addition, the level of compliance with the screening protocol at the respective institutions was not discussed with the exception of one study[74] that reported 100% compliance. In the case of imperfect adherence to the assessed screening strategies the clinical effectiveness of screening may be underestimated. Whether all analyses were pre-planned was unclear in all cases. No studies adjusted for length of follow-up; therefore, in the event that insufficient follow-up time was allotted to detect all cases of infection, effectiveness of screening could be underestimated. Basic statistical tests were used to assess outcomes for all studies and were deemed appropriate. The main outcome measures were valid in all cases but none of the screening technologies have perfect diagnostic accuracy,[59] therefore, the risk of incorrect screening results is of relevance.

*Internal Validity – Confounding*

In the case of the before-and-after studies[30,51,76] and the prospective cohort study,[74] patients in comparison groups were not recruited during the same time period; therefore, difference in patient care and background infection control strategies during those time periods cannot be ruled out as contributing to any observed effects. Patients in the comparison groups were recruited from the same hospital populations. None of the studies randomized subjects to the comparative screening protocols so potential selection bias, especially in relation to judgement of eligibility for screening in the case of targeted screening protocols, may be an issue. Some studies used regression analysis to assess factors that could influence the risk of infection[51,74] but no studies assessed factors such as diagnostic accuracy of the screening technology, which could potentially affect the results of screening. No studies adjusted for losses to follow-up.

*Power*

None of the studies reported a sample size calculation, though the studies were primarily database studies examining large numbers of patients.

*ECONOMIC EVIDENCE*

*Study design*

All studies explicitly stated a research question or objective and provided an explanation of the economic importance of the work. The viewpoints (or perspectives) or the analysis were clearly stated or apparent in all but two cases.[48,83] None of the studies provided a clear rationale for choosing comparators. In some cases it was clear that the comparator was an alternate screening strategy proposed by either a guideline or mandated by a government health body. The comparators or alternative programs were clearly described in all but one case.[81] Most of the studies stated the form of economic evaluation clearly or via description of outcomes[43,48,77,78,80-83,86,86-89] with the exception of two studies.[79,84] The form of economic evaluation was justified in relation to the research questions in all cases, but justification was not provided for the choice of analysis approach with the exception of one study.[82]

*Data collection*

All studies provided sources of effectiveness estimates, though in many cases this included either clinical opinion or assumptions. Most studies were simulated models, but the studies that used their own primary data[48,77,78,80,83,88] all provided information about the design and results of the base study. For studies that used effect estimates from alternate sources, all but one[82] study failed to describe the method of synthesis or pooling. One study[80] failed to described the primary outcome measure explicitly. Of the cost-utility analyses[77,81,85-87] all described the method of valuing benefits. The remainder of the studies did not consider value in the effectiveness outcome and thus could not provide information about the allocative efficiency of the intervention. In addition, none of the studies assessed productivity changes. Quantities and costs were not clearly separated in all but five studies,[48,81,82,84,89] but the methods of estimating costs could be discerned in most cases.[48,78,79,81-89] Currency and price data was recorded in most cases[77-80,82,85-88] but not all[43,48,81,83,84,89] (though based on the location of conduct they could be assumed). Information about adjustment for inflation was only provided by several studies.[43,78,89] Details about the model used was provided by all studies. Explicit justification for the choice of model used was not provided.

*Analysis and Interpretation*

Seven studies[43,78,80,82,83,86,88] stated the time horizon of the model. Six studies stated a discount rate[78,79,82,85-87] but did not provide justification for the choice of rate. None of the studies without discount rates gave justification for the omission. All but one study[82] provided information on their approach to sensitivity analysis. Justification was provided for the choice of variables used in sensitivity analysis by only a few studies,[43,48,78,85-87] but the ranges over which variables were varied were at least referenced or discussed briefly by most studies.[43,48,77-81,85,88,89] Relevant alternatives were compared in all cases. Incremental analysis was reported in all cases though results were reported both aggregated and disaggregated by only some studies.[43,79-82,82,84,85,88] All studies provided an answer to the study question, though clarity of reporting varied, and the conclusions followed the data as reported and considered limitations.

**Summary of Findings**

Detailed study findings are presented in Appendix 4.

Overall, evidence is limited and inconsistent preventing definitive conclusions regarding the comparative effectiveness of the assessed screening strategies. Further, the complex matrix of interventions assessed clouds what the isolated or relative effect of screening would be independent of other infection control measures.

*CLINICAL EVIDENCE*

*What is the comparative clinical effectiveness of a **universal screening** strategy versus **no screening** for antibiotic resistant organisms?*

Evidence to support this question was available from the review of SRs.[44] Two SRs within the review assessed this comparison. One SR concluded that due to methodological flaws and the multi-component nature of the interventions tested it was not possible to draw conclusions on the effectiveness of universal screening in tertiary or long-term care patients. The other SR

reported that there was limited evidence to suggest that universal screening of hospital patients reduces MRSA infection.[11]

What is the comparative clinical effectiveness of a **universal screening** strategy versus **targeted screening** of intensive care unit patients, surgical patients and other high risk patients for antibiotic resistant organisms?

Evidence to support this question was available from the review of SRs,[44] and four primary clinical studies.[30,51,75,76] Overall, there is some evidence that the use of a universal screening strategy may reduce the risk of infection, though this was not observed by all studies. Targeted strategies may result in fewer cases of MRSA colonization being identified. However, an observed increase in mupirocin resistance suggests that the benefit derived from reduction in infection rate would need to outweigh the resource and feasibility demands, and potential risks associated with screening everyone.

One SR and two primary studies included in the review of SRs[44] reported on this comparison. The SR[11] reported that there was insufficient evidence to support universal versus targeted screening. One retrospective cohort study[90] comparing targeted and universal screening in all patients admitted to medical, surgical, pediatric and maternity services reported that based on multivariate analysis, universal screening was associated with a significant reduction in the prevalence density of MRSA bacteremia and incidence of hospital acquired MRSA bacteremia, as well as a significant reduction in 30-day mortality. One interrupted time series[16] conducted in multiple hospitals that compared screening in high-risk patients (e.g., surgery, MRSA positive patients, oncology, admitted from high-risk setting) versus universal screening in all hospital patients reported that there was a statistically significant reduction in MRSA bacteremia and numerical reduction in hospital acquired MRSA bacteremia with the introduction of universal screening. In addition, the percentage of mupirocin resistance increased numerically.

The four primary clinical studies identified[30,51,75,76] had varied results. Most of the evidence came from before and after studies that assessed the impact of introducing universal screening on rate of detection or rate of infection. There was evidence from one study that the rate of infection was not affected with the introduction of universal screening,[76] and evidence from one study of increased rates of infection, despite an observed reduction in hospital acquired MRSA in analysis that excluded patients with a history of MRSA infection or colonization.[51] It was also reported that using targeted approaches to screening versus universal screening may reduce the ability to capture all cases of MRSA.[30,75,76] The degree of omission varied by study and may depend on the specific type of screening and facility.

*What is the comparative clinical effectiveness of **targeted screening** versus **no screening** for antibiotic resistant organisms for intensive care unit patients, surgical patients, and other high risk patients?*

Evidence to support his question was available from the review of SRs,[44] and one primary clinical study.[74]

Six SRs and three primary studies from the review of SRs[44] reported on this comparison. One SR reported that there was insufficient evidence to support targeted screening versus no screening.[11] One SR reported a potential reduction in surgical site infections and wound complications in orthopedic surgery patients.[64] One SR reported that in high-risk acute care patients (patients with previous MRSA or elective orthopedic and cardiac surgery patients) the

interventions used in the primary studies assessed were too embedded within a broader infection control strategy to draw conclusions regarding their effectiveness.[91] One SR reported that in acute care settings in European hospitals the studies were of too poor quality and low generalizability to draw conclusions on the effectiveness of targeted screening.[92] One SR conducted by CADTH reported that based on limited observational evidence, lower VRE bacteremia rates were associated with active surveillance of high-risk patients (hematology, oncology and transplant patients, ICU wards).[38] The final SR reported that in surgical ICU patients, poor quality evidence may support the use of active surveillance but quality of the evidence prevents recommendations regarding this intervention.[93] The additional three primary studies (one randomized controlled trial and two retrospective cohort studies) reported conflicting results. One cluster RCT conducted in ICU patients, reported that screening reduced the rate of MRSA positive cultures.[94] One retrospective cohort study also reported a reduction in MRSA positive cultures in orthopedic hospitals that instituted screening compared to those who did not conduct preadmission screening.[68] The other retrospective cohort study reported no difference in the rate of hospital acquired MRSA infection during screening of ICU patients versus no screening.

The additional primary clinical study identified[74] reported that in infants admitted to a NICU, rates of infection and length of hospital stay were not different between the screening and no screening periods. There was one death during the surveillance period (attributable to MRSA) and no deaths during the non-screening period.[74]

*ECONOMIC EVIDENCE*

*What is the comparative cost-effectiveness of a **universal screening** strategy versus **targeted screening** or **no screening** for antibiotic resistant organisms?*

*Universal or Targeted Screening versus Each Other and No Screening*

*A) Cost-Effectiveness Studies*

Two studies reported on the cost-effectiveness of universal or targeted screening versus no screening from a hospital perspective.[82] One study, conducted in the Netherlands[82] reported that universal screening was associated with an incremental cost-effectiveness ratio (ICER) of $131 000 USD per infection prevented versus targeted screening. In sensitivity analyses, reduced prevalence of MRSA and use of PCR versus chromogenic agar screening technology increased the ICER. Universal screening was economically dominated by targeted screening.[82] Further, average cost-effectiveness ratios were calculated for universal (range = $5700 to $21 100 USD) and targeted screening (range = $4100 to $12 500 USD) versus no screening, with the upper value representing a high risk setting.[82] One study conducted in the US[80] reported that universal screening had an ICER of $14 955 USD per MRSA hospital acquired infection prevented versus no screening. It was also reported that universal screening had an ICER of $49 749 USD per MRSA hospital acquired infection prevented versus targeted screening.[80] Targeted screening was a dominant strategy over universal and no screening across most ranges for costs, rate of infection reduction, and length of stay in the ICU.[80] The probability of cost-effectiveness was reduced with increased costs of screening as well as with reduced efficacy of infection prevention.[80]

*Universal Screening versus Targeted Screening*

*A) Cost-Effectiveness*

Three studies[79,80,89] reported on the cost-effectiveness of universal versus targeted screening. One study[79] conducted in the Netherlands that compared universal screening to three different targeted screening protocols concluded that the approach of screening only previously documented carriers and subsequent isolation was the most cost-effective at a range of efficacy estimates. Universal screening was associated with the highest costs for a range of efficacy estimates.[79] At 25% assumed efficacy of isolation, only screening of previously documented carriers or these patients plus ICU patients was expected to be cost-saving within 10 years.[79] Another study, conducted in the US[80] from the hospital perspective, reported that universal screening was associated with reduced MRSA colonizations but increased costs, producing an ICER of $49 748 USD per infection prevention versus targeted screening. The targeted strategy dominated over no screening and it was reported that the targeted strategy was cost-effective versus universal screening.[80] The third study, conducted in the US from a hospital administrator perspective, screening of all patients compared with only high-risk patients resulted in a greater reduction in the number of MRSA colonizations and infections but at increased, offsetting cost.[89]

*B) Cost-Benefit*

One study conducted from the US hospital perspective reported on the cost-benefit of universal versus targeted screening.[83] The study suggested that the extra costs associated with universal screening versus targeted screening of high risk patients were not offset by the costs recovered due to avoided infections.[83]

*Universal Screening versus No Screening*

*A) Cost-Effectiveness*

One study reported on the cost-effectiveness of universal versus no screening.[43] The study, conducted in the US[43] from a health-care provider perspective reported that compared to no screening, universal screening and subsequent decolonization was dominant (less expensive and reduced more infection and deaths) than not screening. Even with no subsequent decolonization and only contact isolation precautions, universal screening was economically dominant. In sensitivity analysis, only very low risk of infection in non-carriers and benefit of decolonization, and cost of infection ($2768 USD) resulted in universal screening plus decolonization not being the dominant strategy.[43]

*B) Cost Utility*

One study[87] reported on the cost utility of universal versus no screening. The study,[87] reported from societal and third-party payer perspectives in the US, that universal screening was economically dominant over no screening assuming a basic reproductive rate of 1.5 or greater and an MRSA prevalence of 15%. Universal screening remained cost-effective at a reproductive rate of 0.25 or higher and MRSA prevalence of 1% or greater in sensitivity analyses.[87] When accounting for pre-identified MRSA carriers, screening resulted in an ICER of $10 863 USD per QALY, which reduced with increased MRSA prevalence and basic reproductive rate and lower rate of pre-identified MRSA carriers.

*C) Cost-Benefit*

One study reported on the cost-benefit of universal versus no screening from the US hospital perspective.[78] The costs of universal screening and subsequent contact precautions outweighed the reduced costs of preventing MRSA-related infection.[78]

*Targeted Screening versus No Screening*

*A) Cost-Effectiveness*

Two studies reported on the cost-effectiveness of targeted versus no screening.[48,88] One study conducted in the US from a healthcare provider perspective[48] reported that assuming a 10% reduction in rate of surgical revision and an average cost of septic revision less than $70 thousand USD it would be cost-saving to forego screening, but if costs increased above $70 thousand USD the screening program would result in cost savings.[48] For spine surgery patients, using the same criteria for revision rates, the cost of treating a spine surgery would need to be less than $30 thousand USD for the screening program to not be cost saving.[48] Overall, due to the great costs of septic revisions, the reduction achieved by screening of these patients would only need to be modest (10%) to be cost saving.[48] The other study, conducted in Switzerland from the hospital perspective,[88] reported that targeted screening in surgical patients, was more costly than not screening but resulted in reduced infection, producing an ICER of 30 784 Swiss Francs. Similarly, targeted screening of only high-risk surgical patients resulted in higher costs and reduced infection probability versus no screening.[88] Costs avoided by infection reduction did not offset the costs of implementing screening strategies and it is unlikely that screening is cost-effective versus no screening, especially in areas with low rates of infection. Prevalence of colonization on admission, probability of cross-transmission, efficacy of decolonization and contact precautions, and cost of infection and screening influenced the cost-effectiveness in sensitivity analysis.[88]

*B) Cost Utility*

Four studies[77,81,85,86] reported on the cost utility of targeted versus no screening. One study, conducted in the UK from a decision-maker perspective[81] reported that for patients admitted to the ICU, screening of patients and subsequent decolonization had a 30% chance of being cost-effective at a willingness to pay (WTP) threshold of £30 000 per QALY. This strategy had the highest net monetary benefit at WTP thresholds over £5 000 per QALY.[81] Universal screening without decolonization (replaced with isolation) was unlikely to be cost-effective at a WTP threshold of £20 000 or £30 000.[81] It should be noted that the strategy of universal decolonization was also investigated and deemed the most cost-effective strategy but concern over antibiotic resistance was expressed.[81] One US study[86] reported that screening of orthopedic surgery patients was economically dominant over no screening from the hospital and third-party payer perspective and remained cost-effective even at lower MRSA colonization prevalence and lower decolonization success rates.[86] Another US study[85] reported that in cardiac surgery patients, assuming that an ICER of $20 000 USD/QALY or less was strongly cost-effective, targeted screening was strongly cost-effective or economically dominant at a wide-margin of decolonization success rates and MRSA colonization rates tested in sensitivity analyses from both the hospital and third-party payer perspectives. A third US study[77] reported that screening in lung and heart-transplant recipients screening and subsequent decolonization was economically dominant compared to no screening from both third-party and hospital

perspectives, including when colonization rates, probability of infection, and efficacy of decolonization were varied in sensitivity analyses.

*C) Cost-Benefit*

One study conducted from a US healthcare provider perspective reported on the cost-benefit of targeted versus no screening.[84] Targeted screening of ICU patients resulted in cost-savings to the hospital. Despite increased costs of screening, the costs saved due to averted infections offset the investment.[84]

**Limitations**

In addition to the aforementioned critical appraisal points (Appendix 3) there was concern regarding generalizability of the results, issues with assessing complex interventions, and reporting deficiencies relevant to both the clinical and economic evidence.

*Clinical Evidence*

*Generalizability*

The results from studies conducted in one region or time period may have limited generalizability to others on the basis of differences in MRSA prevalence and incidence of infection, which can vary with geography, and over time.[95]

There was an apparent bias towards conduct and publication of studies on MRSA. While this is an important and relevant ARO in healthcare settings, there are many other AROs of interest and results from these studies cannot be applied to inform the clinical effectiveness of screening strategies for other organisms. The clinical evidence presented only provides information on screening for MRSA, VRE, and extended-spectrum beta lactamase-producing *Enterobacteriaceae* (ESBL-E). The effectiveness data only relates to the AROs assessed and does not necessarily speak to overall infection reduction. For instance, if an MRSA screening strategy was implemented and effective at a hypothetical institution but the concern was another ARO, the costs and clinical harms of an infection outbreak with a different organism could negate or dilute any benefit of an MRSA strategy.

The type of screening technology that is implemented (PCR versus chromogenic agar culture) may influence the accuracy and timeliness with which ARO cases are identified.[59] As culture techniques take longer to process than PCR, a case may have time to infect more individuals prior to isolation or decolonization. Screening using PCR may be more clinically effective than chromogenic agar.[96] As such, a study that considered only PCR screening may not be relevant to institutions that only have culture techniques available.

Lastly, findings on the utility of MRSA screening in different high-risk populations have shown variable results. Background infection control measures, MRSA prevalence and risk, general population characteristics, and potential adverse outcomes may differ significantly across clinical populations; therefore, results on specific groups of patients should not be assumed to apply to other clinical populations.[86,97,98] Similarly, results on broad categories of high-risk patients such as all orthopedic surgery patients, or all surgical patients may not be directly applicable to specific high-risk groups (e.g., vascular or spinal surgery) given the potential variability in efficacy of decolonization, and infection risk.

*Complex Interventions*

Screening is not conducted in isolation and the background infection control measures instituted at various facilities and in various jurisdictions may vary greatly. This issue was discussed extensively within the IHE report.[44] Five of the SRs included mentioned difficulty in formulating conclusions regarding the effectiveness of screening due to the multiple components included in infection control interventions as well as due to limitations of the study design of included studies.[44] The authors expressed concern regarding the difficulty faced in attempting to tease out the specific effect of screening separate from the matrix effect of an infection prevention protocol. When infection control practices include multiple interventions it may not be possible to evaluate the relative effects of different classes of approaches (e.g., screening, contact precautions, decolonization).[99] As screening relies on diagnostic accuracy and timeliness of the various technologies and the effectiveness of subsequent interventions such as contact precautions, isolation or quarantine, and decolonization to derive clinical benefit, the effectiveness of these combined strategies and transparency regarding reporting of the strategies applied are important considerations.

Many of the included studies failed to report details of their entire infection protocols. This is a limitation for both the primary studies and for comparing results across studies and contexts. Application of research results on individual components of these strategies outside of the matrix in which they were studied should be approached with caution. For example, if a screening strategy was investigated in the context of assumed subsequent decolonization, applying screening in a setting where decolonization is not available may not be advisable.

*Confounding*

Some potential confounders that were not considered by most of the studies were time to reporting of screening results, sensitivity and specificity of the screening technologies (e.g., PCR available faster and with higher sensitivity,[100] but at higher cost[72] than culture methods), compliance of the facility with the screening protocol (e.g., were all eligible subjects screened) and the prevalence of AROs in the source community studied. Level of compliance would have the potential to influence the results substantially. For instance, if basic measures such as hand hygiene and contact isolation are not followed as per protocol, this could hypothetically influence the perceived effectiveness of screening. Baseline infection control measures and the level of compliance achieved may vary across facilities and jurisdictions, which could affect the success of a screening program.

*Reporting Deficiencies*

In general there was limited adverse event reporting – some issues such as morbidity and mortality, psychosocial risks of isolation,[44] antibiotic resistance associated with decolonization post-screening, and indirect adverse effects of false screening results (e.g., unnecessary exposure to decolonization agents) were not considered. In particular, widespread use of decolonization may pose risks of emergent resistance against common agents in use.[101,102] Presence of resistance may reduce the effectiveness of decolonization treatment and thus the effectiveness of screening.[103,104] For clinical effectiveness studies, it may be of interest to determine what the effect on relevant morbidity outcomes and mortality would be as the effect on detection of MRSA colonization or rate of infection does not give a direct measure of clinical benefit.

*Economic Evidence*

Some of the limitations of the clinical evidence, especially generalizability issues, may apply to the economic evidence as well.

The economic evaluations did not comprehensively account for downstream costs resulting from the information gained from screening. While decolonization or contact isolation procedures informed by screening were accounted for by some studies, relevant costs including additional hygiene measures, screening of contacts, increased demands on staff, and follow-up screening of infected and colonized patients[72] were not considered.

None of the economic evaluations were conducted from a Canadian perspective. In order to apply these results to the Canadian context, consideration of the relevance of model inputs to Canadian healthcare settings, discount rates, necessary, adjustments for inflation, currency conversion, WTP thresholds and the study populations assessed would need to occur. Unless the economic evidence was reoriented to reflect the Canadian setting, the results presented may have limited generalizability.

As a general comment, the majority of the models presented are simulations based on external data and although based on the best available evidence, may not reflect what would occur in real-life. This is particularly true of studies that may have relied on expert or clinical opinion in the formulation of estimates, and those that used data from alternate jurisdictions or populations, or data of limited quality, to inform their effect estimates and costs.

## CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

This report reviewed evidence regarding the clinical and cost-effectiveness of various screening protocols for AROs.

The comparative clinical effectiveness of various screening protocols for AROs was assessed by one review of SRs,[44] and five primary clinical studies.[30,51,74-76] There was limited evidence suggesting reduced MRSA infection rates with **universal screening** versus **no screening**, but the complex multi-intervention context of screening prevented confidence in this conclusion.[11,44] The evidence regarding **universal screening** versus **targeted screening** was mixed. Evidence from one SR was inconclusive,[11] and the evidence from multiple primary clinical studies was conflicting with some showing associations of universal screening with reduced infection and mortality,[16,90] and others showing no change or an increase.[11,30,44,51,75,76] It is apparent that fewer cases of MRSA would be detected with targeted screening, but the relative impact of those omissions on clinical outcomes is unclear.[30,75,76] Further, observed increases in antibiotic resistance[16] along with the lack of clarity concerning clinical effectiveness, suggests that caution should be taken in consideration of universal protocols. The most evidence was available regarding **targeted screening** versus **no screening**.[44,74] There was still concern regarding clouding of the results by the complex nature of the matrix of delivery of screening interventions. Some SR evidence suggested reduced infection and wound complications in orthopedic surgery patients, and reduced VRE bacteremia in high-risk patients,[44,64] but confidence in other SR evidence was insufficient to make conclusions about other high-risk populations.[11,44] There was further support for effectiveness in orthopedic patients,[68] conflicting evidence regarding ICU patients, and no evidence to support effectiveness in NICU patients[74] from primary studies.[44]

The cost-effectiveness of various screening protocols for AROs was evaluated by 15 economic evaluations.[43,48,77-89] Depending on the WTP threshold, **universal screening** is likely to be cost effective over **no screening**,[80,82] and some studies demonstrated that it was economically dominant in terms of cost per prevention of infections and deaths, as well as cost per QALYs gained.[43,87] However, **targeted screening** was economically dominant over **universal screening** in most of the scenarios tested. Alternatively, reported ICERs suggested very high costs per benefit for universal screening that were unlikely to be cost-effective, and recovered costs due to infections avoided were unlikely to offset the costs of screening.[79,80,82,83,89] **Targeted screening** was also cost-effective compared to **no screening** in terms of reduced revision for orthopedic surgery patients,[48] and cost per QALYs gained for ICU patients when paired with decolonization.[81] Further, it was economically dominant or cost-effective in cardiac and orthopedic surgery patients, and heart and lung transplant patients.[77,85,86] In addition, the costs saved by averting infection in ICU patients offset the costs of screening in one study.[84] Targeted screening was unlikely to be cost-effective in general surgical patients in one study.[88]

Overall, **universal screening** is likely more effective than **no screening** from a clinical and cost perspective. In addition, it might enable identification of more ARO cases; however, given the concern regarding antibiotic resistance, the high costs of implementing such approaches, and substantial inconsistency present in the evidence base, consideration of targeted screening approaches may be warranted. **Targeted screening** approaches were generally preferred to **universal screening** approaches from a cost-perspective, particularly in several high-risk populations (e.g., orthopedic surgery, vascular surgery, ICU patients, documented MRSA carriers). Further, there was clinical evidence to support the use of **targeted screening** over **no screening** in some high-risk populations (i.e., orthopedic surgery patients), and evidence that targeted screening is cost-effective versus no screening in many high-risk populations.

Given the identified limitations, as well as the inconsistency and lack of firm conclusions discussed by previous evidence syntheses and CADTH reviews.[36,38,40-42,44] Further research is needed to understand the true effect of screening strategies outside of the context of other infection control measures, the relative effects of different strategies in certain high-risk populations, and to orient the economic evidence to a more interpretable Canadian context. Focusing research studies more directly on homogenous high-risk populations with an emphasis on accounting for matrix confounding of background infection control measures and context on screening interventions may provide valuable information to inform implementation of screening protocols.

In conclusion, the evidence-base for ARO screening strategies has several important limitations, including challenges in interpreting complex interventions, limited generalizability, and the threat of potential confounders. All evidence considered, the clinical and cost-effectiveness data suggest that having any screening strategy over no strategy is likely beneficial, and that targeted strategies may be more beneficial over universal strategies, given the more definitive clinical evidence-base, and demonstration of cost-effectiveness.

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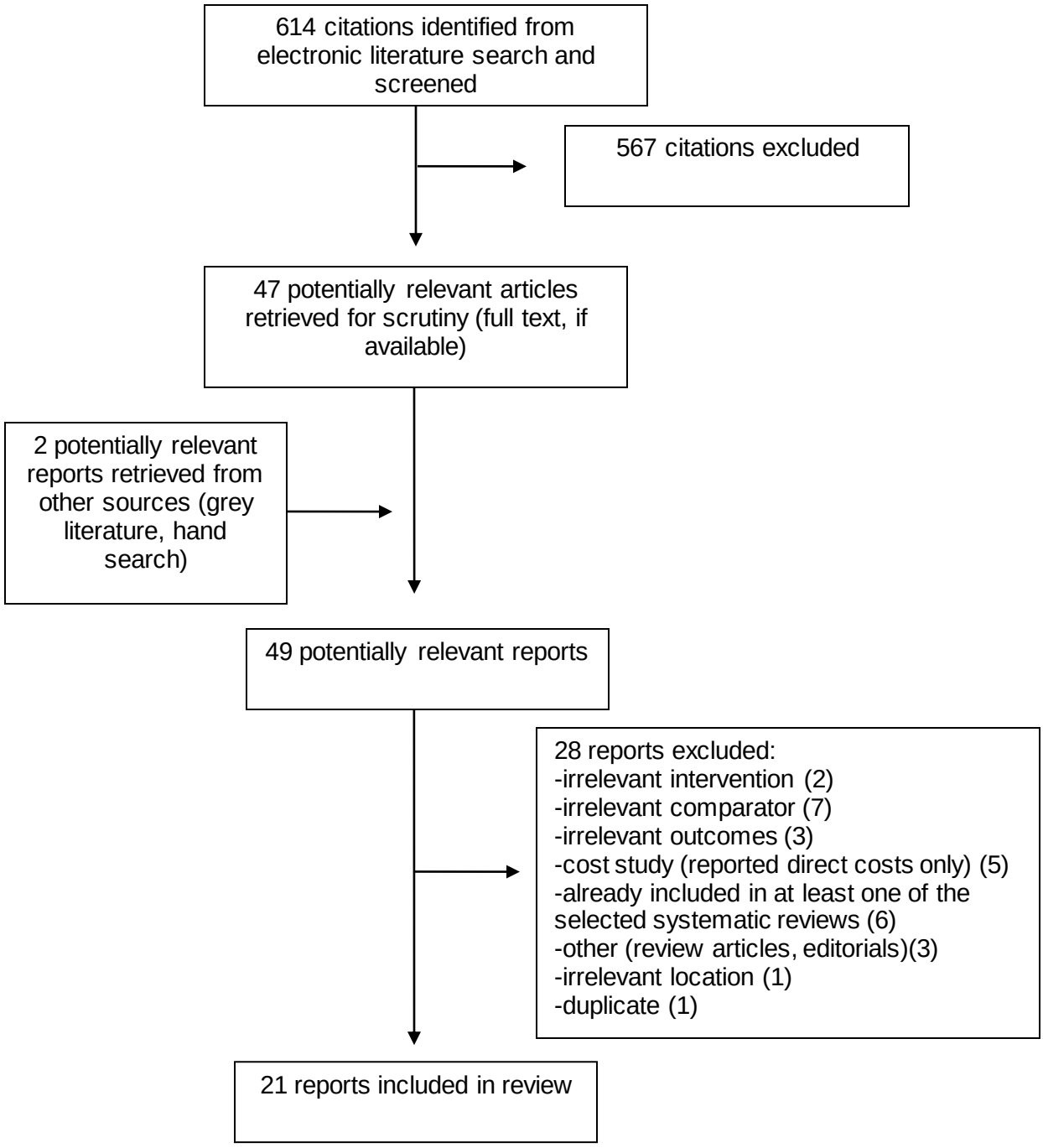
**APPENDIX 1: Selection of Included Studies**



## APPENDIX 2: Characteristics of Included Publications

**Table A1:** Characteristics of Included Reviews of Systematic Reviews

| First Author, Publication Year, Country, Search Dates | Types and numbers of primary studies included | Population Characteristics | AROs | Intervention | Comparator(s) | Clinical Outcomes; Length of Follow-Up |
|---|---|---|---|---|---|---|
| Bond, 2014[44] Institute of Health Economics, Alberta, Canada,<br><br>2003 to February 2014 for primary studies, conception of databases to February 2014 for systematic reviews | n = 7 systematic reviews,<br><br>n = 6 primary studies (n = 1 cluster randomized study, n = 5 quasi-experimental designs)* | Patients of any age admitted to hospital | Acinetobacter, CRE, MRSA, VRSA, VRE, ESBL-producing organisms | Any ARO universal screening strategy | Targeted ARO screening,<br><br>No screening | Clinical effectiveness,<br><br>Safety;<br><br>Length of follow-up unclear |

*This review also reported on five clinical practice guidelines,[44] but as these reports were out of scope the results will not be discussed
ARO = antibiotic resistant organism; CRE = Carbapenem-resistant *Enterobacteriaceae*; ESBL = extended spectrum beta lactamase; MRSA = methicillin resistant *Staphylococcus aureus*; VRSA = vancomycin resistant *Staphylococcus aureus*; VRE= vancomycin-resistant *Enterococci*;

**Table A2**: Characteristics of Included Primary Clinical Studies

| First Author, Publication Year, Country, Study Name | Study Design | Patient Characteristics | AROs | Intervention(s);Screening Technology | Comparator(s) | Clinical Outcomes |
|---|---|---|---|---|---|---|
| Jennings, 2014[51] US | Retrospective controlled before-and-after study (identified by authors as cohort) | All admitted inpatients at a single hospital, n = 72 312;<br><br>Subgroup = surgical patients | MRSA | Universal screening for MRSA (2010 to 2011), n = 36244 (n = 16740 surgical patients);<br><br>Nasal swab with PCR | Targeted screening (patients with history of MRSA, previously hospitalized in the last year, transferred from extended care, presence of open wounds, admitted to ICU or on current hemodialysis) (2007 to 2998), n = 36068 (n = 15044 surgical patients) | MRSA infection rate, mortality |

**Table A2**: Characteristics of Included Primary Clinical Studies

| First Author, Publication Year, Country, Study Name | Study Design | Patient Characteristics | AROs | Intervention(s);Screening Technology | Comparator(s) | Clinical Outcomes |
|---|---|---|---|---|---|---|
| Kaushick, 2014[74] US | Prospective cohort study | Youth patients in the neonatal intensive care unit (urban, inner city, tertiary care hospital), n = 3088 | MRSA | Targeted screening of MRSA (April 2006 to March 2008);<br><br>Single nasal swab with PCR | No screening (April 2008 to April 2010) *enrolled retrospectively* | Rate of MRSA blood stream infection |
| Otter, 2014[30] UK | Retrospective controlled before-and-after study | Patients admitted to two hospital locations, n = 28 892 | MRSA | Universal screening for MRSA;<br><br>Method of detection unclear | Targeted screening of high –risk individuals for MRSA | Proportion of MRSA cases detected |
| Fuller, 2013[75] UK | Cross sectional survey | Patients admitted to an hospital during a single week, n = 790 | MRSA | Universal screening;<br><br>Chromogenic agar or PCR | CLAS;<br><br>Screen only high-risk<br><br>Screen high risk + CLAS for low risk | Proportion of MRSA cases |
| Collins, 2011[76] UK | Retrospective controlled before-and-after study | All patients residing in hospital for more than 48 hours, n = 11 895 | MRSA | Universal active surveillance cultures for MRSA;<br><br>Chromogenic culture method (sites: nose throat and perineum, and additional specimens in those with open wounds) | Targeted screening of only high and medium risk groups* | MRSA cases detected |

*Critical care, elderly care, medicine, renal, surgery, urology, admissions, cancer services, cardiology, hematology, infectious diseases, neurology, orthopedics)
CLAS = checklist activated screening; MRSA = methicillin resistant *Staphylococcus aureus*; PCR = polymerase chain reaction; UK = United Kingdom;

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| McKinnell, 2015[78] US | Cost-benefit analysis,<br><br>Hospital perspective | Hospital-wide universal screening for MRSA and contact precautions for MRSA carriers;<br><br>No screening | All admissions to a hospital in the US | MRSA | Not stated but likely duration of hospitalization | MRSA colonization prevalence was 7.3% for nares and 9.5% for the total body. | Cost of screening per cost savings of infection prevented |
| Clancy, 2014[77] US | Cost-utility analysis (decision-analytic model),<br><br>Hospital and third-party payer perspectives | Targeted screening and subsequent decolonization,<br><br>No screening | Lung and heart-lung transplant recipients at a hospital in Pittsburgh, US (median age 59 years) | MRSA and MSSA | Not stated but assumed to be up to 90 days post-transplant | SA infections occurred within 90 days of lung transplantation.<br><br>The life expectancy for all patients post-transplant was 5 years. | Cost per QALY |
| Gurieva, 2013[79] The Netherlands | Cost-effectiveness analysis,<br><br>Hospital perspective | Universal screening;<br><br>Targeted screening of previous MRSA carriers,<br><br>Targeted screening of previous MRSA carriers and ICU admissions,<br><br>Targeted screening of previous MRSA carriers and patients hospitalized within the past year | Patients admitted to 3 hospitals in the Netherlands | MRSA | 10 years | For the comparator, the endemic prevalence of MRSA was 5% hospital-wide and 20% in ICUs.<br><br>The transmission risk between ICUs and non-ICU wards was 3:1. | Cost per MRSA infection prevented |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | | *Positive screen followed up with isolation precautions* | | | | | |
| Kang, 2012[80] US | Cost-effectiveness analysis (decision-tree),<br><br>Hospital perspective | Universal screening or targeted screening (ICU admissions);<br><br>Targeted Screening;<br><br>No screening<br><br>*Positive screens followed up with isolation and contact precautions* | Patients admitted to an academic hospital in the US | MRSA | Duration of hospitalization | There were no cases, in which an MRSA-colonized patient was transferred from a non-ICU ward to an ICU ward.<br><br>The MRSA HAI rate in non-ICR wards was 33% of the rate in the ICU.<br><br>The incremental cost of an MRSA HAI was equivalent to that of a general HAI. | Cost per MRSA infection prevented |
| Hubben, 2011[82] The Netherlands | Cost-effectiveness analysis (discrete event simulation model),<br><br>Hospital perspective | Universal screening or targeted screening (of high risk patients who had a 10x higher probability of being admitted to hospital than normal patients) with subsequent isolation/contact precautions and room cleaning;<br><br>No screening | Patients admitted to a single hospital in the Netherlands | MRSA | Not stated but likely duration of hospitalization | The transmission rate in ICUs was 3 times higher compared to other wards.<br><br>Infected patients had the same infectiousness and discharge probabilities as MRSA carriers.<br><br>Single-room isolation reduced the risk of transmission by 80%. | Cost per MRSA infection avoided |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| Leonhardt, 2011[83] US | Cost-benefit analysis (piggy back study),<br><br>Hospital perspective | Universal screening;<br><br>Targeted screening of high risk patients (positive history of MRSA infection or colonization; prior hospitalization, including transfers, within 6 months; admission to the ICU; patients from long-term care facilities and correctional institutes; patients receiving dialysis; and selected orthopedic and cardiothoracic surgery patients.)<br><br>*Positive screens followed up with unspecified infection control measures* | Patients admitted to 2 community hospitals, n = 15049: | MRSA | Not stated but likely duration of hospitalization | The two hospitals* were equivalent.<br><br>Patients in the two hospitals use private rooms, not requiring isolation for MRSA carriers.<br><br>*One was designated the control hospital (with only targeted screening throughout the study duration). The other was designated the intervention hospital (with targeted screening for the first part of the study duration and universal screening for the remainder of the study duration). | Incremental benefit to cost ratio |
| Nyman, 2011[84] US | Cost-benefit analysis; Markov model,<br><br>Healthcare provider perspective | Targeted MRSA screening of ICU patients at a single institution (standard culture, chromogenic agar or PCR) and subsequent isolation | Patients admitted to a single hospital | MRSA | Lifetime | Starting probabilities assumed to be 5.15% colonized and 2.75% infected | Cost of screening per cost reduction due to infection reduction (presented as net savings per |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | (Veteran's affairs`) | precautions;<br><br>No intervention (screening) | | | | | hospital admission) |
| Olchanski, 2011[89] US | Cost-effectiveness analysis; Decision-analytic model,<br><br>Hospital administrator perspective | Universal MRSA screening (PCR, culture with selective media or culture with nonselective media);<br><br>Targeted screening of:<br><br>A) ICU patients only,<br><br>B) All high-risk patients (re-admitted to hospital, transferred from another medical facility, prior MRSA infection, frequent contact with any medical facility or admitted to the ICU),<br><br>C) Patients with a history of MRSA colonization or infection<br><br>*Positive screens* | Patients admitted to a single teaching hospital | MRSA | 1 month and 12 months (extrapolated) | Rate of MRSA colonization proportional to the number of MRSA carriers in the hospital population,<br><br>Patients assigned to individual isolation precautions not sources of transmission,<br><br>Cost-relevance over the past 5-10 years (no adjustment for inflation),<br><br>Number of patients assumed constant and 100% hospital occupancy,<br><br>Division of hospital into floors wards and units within which MRSA colonization or infection transfer | Cost per infection prevented (only presented disaggregated, not as ICER) |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | | *followed up with isolation precautions* | | | | can occur but not between,<br><br>MRSA transmission rate is consistent across wards,<br><br>No change in prevalence of MRSA in hospital population, proportion of patients admitted who are colonized reflects inpatient prevalence, and proportion of transmissions resulting in active infections constant and higher in ICU setting,<br><br>Compliance with screening program assumed | |
| Robotham, 2011[81] UK | Cost-utility analysis (dynamic transmission model),<br><br>Healthcare | Targeted screening of all patients on admission and weekly thereafter,<br><br>No screening (clinical cultures only), | Patients admitted to an ICU | MRSA | Not stated; time dependent model used | Assumed all clinical cultures were taken using the same technology as for screening,<br><br>Isolation was | Cost per QALY,<br><br>NMB |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | decision-maker perspective | Targeted screening upon admission and weekly of high risk patients<br><br>**All combined with isolation or decolonization with mupirocin or chlorhexidine washing (a total of 12 strategies compared for screening and isolation, and 9 for screening and decolonization)*<br><br>Screening technologies: conventional culture, chromogenic agar, PCR | | | | application of contact precautions rather than physical separation | |
| Slover, 2011[48] US | Cost-effectiveness analysis (Markov model),<br><br>Healthcare provider perspective | Targeted screening of all patients upon admission (and subsequent decolonization depending on result of test),<br><br>No screening | All patients enrolled in a preadmission testing program for hip or knee arthroplasty, or spinal fusion (orthopedic surgery) at a single institution | MRSA and MSSA | Not stated | Event probability rates and costs of testing and treatment for infection were based on the primary study while costs of surgery were derived from other research | Cost per reduction in septic revision rate |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| Lee, 2010[85] US | Cost-utility analysis (Monte Carlo decision-analytic model),<br><br>Third-party payer and hospital perspectives | Targeted screening (with single anterior nares culture) and subsequent decolonization,<br><br>No screening | Otherwise healthy cardiac surgery patients (aged 65) admitted for surgery | MRSA | Not stated – likely the peri-operative period of the patients cardiac surgical procedure | Assumed baseline QALY of patients to be 0.84 | Cost per QALY |
| Lee, 2010[86] US | Cost-utility analysis (Stochastic decision analytic computer simulation model),<br><br>Third-party payer and hospital perspectives | Targeted universal MRSA screening (anterior nares or 2 body site swabs) and subsequent decolonization;<br><br>No screening or decolonization | Orthopedic surgery patients (median age 65 years) being admitted for surgery | MRSA | Not stated – likely the duration of the health condition | Assumed WTP threshold of $50 000 dollars per QALY and threshold of $20 000 dollars per QALY to suggest strong economic support | Cost per QALY |
| Lee, 2010[87] US | Cost-utility analysis (Stochastic computer simulation model – dynamic transmission),<br><br>Societal and | Universal MRSA screening (single nares specimen surveillance culture) with subsequent respiratory droplet isolation precautions;<br><br>No screening | All adult general medical patients admitted to hospital (median age, 40 years) | MRSA | Not stated – likely the duration of illness (up to one week in most cases) | Patients with positive screens placed under isolation precautions could not transmit MRSA to other hospital patients,<br><br>Probability of colonization with | Cost per QALY |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | third-party payer perspectives | | | | | MRSA based on MRSA prevalence | |
| Murthy, 2010[88] Switzerland | Cost-effectiveness analysis (decision analytic Markov model),<br><br>Hospital perspective | Targeted universal MRSA screening (PCR screening) with subsequent decolonization (nasal mupirocin and chlorhexidine washing), contact precautions and physical isolation<br><br>Targeted screening for risk factors (hospitalization or antibiotic use) combined with pre-emptive isolation and contact precautions pending chromogenic agar results.<br><br>No screening | Surgical patients | MRSA | Period of hospitalization | Rate of cross-transmission from carriers to non-carriers assumed to be 20% in base case analysis | Cost per MRSA infection avoided |
| Nelson, 2010[43] US | Cost-effectiveness analysis (decision-analytic model),<br><br>Veteran's | Universal surveillance (nasal swab, PCR screening) plus subsequent decolonization (mupirocin or chlorhexidine | All patients admitted to a Veteran's Health Administration facility | MRSA | Duration of inpatient stay | Patients known to be colonized with MRSA were not assumed to be isolated<br><br>Author's assumption used in the case of | Cost per MRSA infection and deaths avoided |

**Table A3:** Characteristics of Included Cost Studies

| First author, Publication Year, Country | Type of Analysis, Perspective | Intervention; Comparator | Study Population | AROs | Time Horizon | Main Assumptions | Outcome |
|---|---|---|---|---|---|---|---|
| | Health Administration (Healthcare provider) perspective | bathing);<br><br>Universal screening and subsequent contact precautions;<br><br>No screening | | | | indirect benefit of decolonization | |

ICER = incremental cost-effectiveness ratio; ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; MRSA HAI = hospital-acquired methicillin-resistant *Staphylococcus aureus* infection; NMB = net monetary benefit; PCR = polymerase chain reaction; QALY = quality adjusted life years; SA = *Staphylococcus aureus*; UK = United Kingdom; US = United States

## APPENDIX 3: Critical Appraisal of Included Publications

**Table A4:** Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[46]

| Strengths | Limitations |
|---|---|
| Bond, 2013[44] | |
| *AMSTAR*<br>• Comprehensive literature search on multiple databases conducted; grey literature search conducted and reported in detail<br>• List of included and excluded studies provided<br>• Characteristics of included studies listed<br>• Scientific quality of included SRs assessed using AMSTAR criteria; primary studies assessed using the Cochrane risk of bias tool (for randomized studies) or the Ottawa-Newcastle Checklist (for observational studies)<br>• Only narrative synthesis was conducted therefore the nature of methods used to combine study findings, and assessment of publication bias was not conducted<br>• Funding sources disclosed | *AMSTAR*<br>• No review protocol published and a priori nature of objectives unclear<br>• Single author involved in study selection and data abstraction<br>• Date (2003 to 2014, only for primary publications*) and language (English) of publications were limited<br>• Unclear whether unpublished literature was considered<br>• Affiliations of authors and contributors stated but conflict of interest unclear<br>*Other*<br>• AMSTAR ratings for the individual SRs ranged from meeting 3 to 9 of the 11 criteria; therefore, some of the reviews included are likely of poor quality<br>• All reviews only reported results narratively and there was high heterogeneity in regards to study design of included studies |

*Assumed that SRs identified would include most studies prior to these search dates
SR = systematic review

**Table A5:** Strengths and Limitations of Primary Clinical Studies using Downs and Black[47]

| Strengths | Limitations |
|---|---|
| Jennings, 2014[51] | |
| *Reporting*<br>• Hypothesis, outcomes, patient characteristics, interventions, potential confounders, and main findings clearly described<br>• Estimates of random variability reported<br>• Actual probability values reported<br>*External Validity*<br>• Participants representative of patients treated within the single medical/trauma center<br>• Database study; therefore, no perceived differences in those who participated versus those who were recruited<br>• Context of study in terms of staff and facilities representative of the broader hospital setting<br>*Internal Validity – Bias*<br>• Statistical tests for main outcome | *Reporting*<br>• Adverse events resulting from intervention not reported<br>• Losses to follow-up not reported<br><br>*External Validity*<br>• Patients not necessarily representative of other similarly sized medical institutions given potential differences in the context of care (e.g., infection control measures)<br>*Internal Validity – Bias*<br>• No blinding of participants or outcome assessors<br>• Whether all analyses were pre-planned was unclear<br>• No adjustment for length of follow-up<br>• Compliance of institution with screening protocols unavailable<br>• Outcome dependent on PCR screen which does not have perfect diagnostic accuracy<br>*Internal Validity – Confounding* |

**Table A5:** Strengths and Limitations of Primary Clinical Studies using Downs and Black[47]

| Strengths | Limitations |
|---|---|
| appropriate<br>• Main outcome measures valid<br>*Internal Validity – Confounding*<br>• All patients were recruited from the same hospital population | • Before and after cohorts not recruited during the same time period<br>• No randomization of study subjects<br>• Regression analysis only conducted on risk factors for infection, not with regards to screening<br>• No mention of accounting for losses to follow-up<br>*Power*<br>• Sample size calculation not disclosed |
| Kaushik, 2014[74] | |
| *Reporting*<br>• Main outcome, patient characteristics, intervention, distribution of potential confounders, main findings clearly described<br>• Estimates of random variability provided<br>• Limited adverse events reported<br>• Actual probability values reported<br>*External Validity*<br>• Patients representative of all infants admitted to the NICU at the single institution<br>• No difference in attempted recruits and patients – all infants included in analysis<br>• Context of study in terms of staff and facilities representative of the NICU unit<br>*Internal Validity – Bias*<br>• Statistical tests for main outcome appropriate<br>• 100% compliance with screening reported<br>• Main outcome measures valid<br>*Internal Validity – Confounding*<br>• All patients were recruited from the same NICU population | *Reporting*<br>• Hypothesis or aim not explicitly stated<br>• Losses to follow up not disclosed<br>*External Validity*<br>• Patients not necessarily representative of other similarly sized NICUs given potential difference in context of care (e.g., infection control measures)<br>*Internal Validity – Bias*<br>• No blinding of participants or outcome assessors<br>• Whether all analyses were pre-planned was unclear<br>• No adjustment for length of follow-up<br>• Outcome dependent on PCR screen which does not have perfect diagnostic accuracy<br>*Internal Validity – Confounding*<br>• Before and after cohorts not recruited during the same time period<br>• No randomization of study subjects<br>• Regression analysis only conducted on risk factors for infection, not with regards to screening<br>• No mention of accounting for losses to follow-up<br>*Power*<br>• Sample size calculation not disclosed |
| Otter, 2014[30] | |
| *Reporting*<br>• Objective, outcomes, patient characteristics, intervention, and main findings clearly described<br>*External Validity*<br>• Subjects representative of patients admitted to the two hospitals studied<br>• Database study; therefore, no perceived differences in those who participated versus those who were recruited<br>• Context of study in terms of staff and facilities representative of the two hospitals<br>*Internal Validity – Bias*<br>• Statistical tests for main outcome appropriate | *Reporting*<br>• Distribution of potential confounders not described<br>• Estimates of random variability not provided<br>• Adverse events not reported<br>• Losses to follow up not disclosed<br>• No probability values reported<br>*External Validity*<br>• Patients not necessarily representative of other similarly sized hospital settings given potential differences in context of care (e.g., infection control measures)<br>*Internal Validity – Bias*<br>• No blinding of participants or outcome assessors<br>• Whether all analyses were pre-planned was unclear<br>• No adjustment for length of follow-up<br>• Level of compliance with screening protocols unclear |

**Table A5:** Strengths and Limitations of Primary Clinical Studies using Downs and Black[47]

| Strengths | Limitations |
|---|---|
| • Main outcome measures valid<br>*Internal Validity – Confounding*<br>• All patients recruited from the same hospital trust | *Internal Validity – Confounding*<br>• Same group of patients acted as own comparator group (recruited over a single time period)<br>• No randomization of study subjects<br>• No adjustment for potential confounders<br>• No mention of accounting for losses to follow-up<br>*Power*<br>• Sample size calculation not disclosed; however, authors mentioned that the sample size was 'limited' |
| Fuller, 2013[75] | |
| *Reporting*<br>• Study aims, main outcomes, interventions and main findings clearly described<br>*External Validity*<br>• Patients representative of all English NHS acute trust patients screened during a single week<br>• Database study; therefore, no perceived differences in those who participated versus those who were recruited<br>• Context of study in terms of staff and facilities representative of English NHS acute trusts<br>*Internal Validity – Bias*<br>• Statistical tests for main outcome appropriate<br>• Main outcome measures valid<br>*Internal Validity – Confounding*<br>• All patients recruited from the same hospital network | *Reporting*<br>• Patient level characteristics not reported<br>• Potential confounders not described<br>• Estimates of random variability and probability values not reported<br>• Adverse events not reported<br>• Losses to follow-up not disclosed<br>*External Validity*<br>• Patients not necessarily representative of those treated in other hospital networks, given potential differences in context of care (e.g., infection control measures)<br>*Internal Validity – Bias*<br>• No blinding of study subjects or outcome assessors<br>• Whether all analyses were pre-planned was unclear<br>• No adjustment for length of follow-up<br>• Level of compliance with screening protocols unclear<br>*Internal Validity – Confounding*<br>• Same group of patients acted as own comparator group (recruited over a single time period)<br>• No randomization of study subjects<br>• No adjustment for potential confounders<br>• No mention of accounting for losses to follow-up<br>*Power*<br>• Sample size calculation not disclosed |
| Collins, 2011[76] | |
| *Reporting*<br>• Study aims, main outcomes, patient characteristics, interventions and main findings clearly described<br>*External Validity*<br>• Subjects representative of patients admitted to the single multi-site hospital<br>• Database study; therefore, no perceived differences in those who participated versus those who were recruited<br>• Context of study in terms of staff and facilities representative of the single hospital | *Reporting*<br>• Distribution of confounders not described<br>• Estimates of random variability and probability values not reported<br>• Adverse events not reported<br>• Losses to follow-up not disclosed<br>*External Validity*<br>• Patients not necessarily representative of those treated at other hospitals, given potential differences in context of care (e.g., infection control measures)<br>*Internal Validity – Bias*<br>• No blinding of study subjects or outcome assessors<br>• Whether all analyses were pre-planned was unclear |

**Table A5:** Strengths and Limitations of Primary Clinical Studies using Downs and Black[47]

| Strengths | Limitations |
|---|---|
| *Internal Validity – Bias*<br>• Statistical tests for main outcome appropriate<br>• Main outcome measures valid<br>*Internal Validity – Confounding*<br>• All patients recruited from the same hospital | • No adjustment for length of follow-up<br>• Level of compliance with screening protocols unclear<br>*Internal Validity – Confounding*<br>• Same group of patients acted as own comparator group (recruited over a single time period)<br>• No randomization of study subjects<br>• No adjustment for potential confounders<br>• No mention of accounting for losses to follow-up<br>*Power*<br>• Sample size calculation not disclosed |

PCR = polymerase chain reaction; NICU = neonatal intensive care unit

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| McKinnell, 2015[78] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of research question stated<br>• Viewpoints of analysis (hospital) stated<br>• Form of economic evaluation stated and fit with research questions<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Details of design and results of base study presented<br>• Primary outcome clearly stated<br>• Methods for estimating quantities and costs described<br>• Currency and price data recorded<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>• Time horizon stated<br>• Discount rate stated<br>• Approach to sensitivity analysis (one-way, two-way and probabilistic) given<br>• References provided for choice of variables and ranges for sensitivity analysis<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Answer to the study question provided<br>• Conclusions follow data as reported and consider limitations<br><br>*Other*<br>• The mathematical model incorporated complexities, including diagnostic accuracy (i.e., sensitivity, specificity) and multiple screening sites (i.e., nares, oropharynx) and screening technologies (i.e., culture, PCR). | *Study Design*<br>• Rationale for choosing alternative programmed not stated<br>• No justification given for form of economic evaluation<br>*Data Collection*<br>• Details of method of synthesis or pooling of estimates unclear<br>• Value and productivity not considered in analysis<br>• Quantities not reported separately from costs<br>• No justification for choice of model and key parameters provided<br>*Analysis and Interpretation of Results*<br>• No justification provided for discount rate<br>• Results not reported disaggregated<br><br>*Other*<br>• The study used surrogate data for the US from the literature, instead of real data, for the mathematical model. The literature search strategy for identifying the surrogate data was not described.<br>• Study findings may not be generalizable to other settings such as those in Canada and may be different from real-life settings.<br>• The study did not include in the cost analysis the costs of MRSA infection treatment (e.g., antibiotics). Therefore, the cost estimates may not have been comprehensive. |

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| Clancy, 2014[77] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of research question stated<br>• Viewpoints of analysis (hospital and third-party payer) clearly stated<br>• Alternatives well described<br>• Type of economic evaluation used is stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Details of base cohort study provided<br>• Primary outcome clearly stated<br>• Methods to value benefits cited and details of subjects form whom valuations obtained reported<br>• Currency and price data recorded (2012 USD)<br>• Details of model design provided<br>*Analysis and Interpretation of Results*<br>• Discount rate (3%) disclosed<br>• Approach to sensitivity analysis (one way, two way, three way and probabilistic) disclosed<br>• Relevant alternative compared<br>• Incremental analysis reported<br>• Answer to study question provided and conclusions follow the data as reported considering limitations<br>*Other*<br>• The cost analysis was comprehensive, identifying all costs related to screening for MRSA, contact precautions, infection treatment, and infections averted. | *Study Design*<br>• Rationale for alternative program not provided<br>• Choice for type of economic evaluation not justified<br>*Data Collection*<br>• Some effectiveness estimates based on expert opinion – otherwise based on direct clinical experience or cited existing literature<br>• Method of synthesis or pooling of estimates not clear<br>• Productivity changes not reported<br>• Quantities not reported separate from costs<br>• Methods for estimation of quantities and costs not described<br>• Choice of model not justified by authors<br>*Analysis and Interpretation of Results*<br>• Time horizon not explicitly stated but assumed duration of length of stay up to 90 days post lung-transplant<br>• No justification provided for choice of discount rate<br>• Choice of sensitivity analysis variables not justified by authors<br>• Major outcomes not reported disaggregated<br>*Other*<br>• The study used data from a single hospital in the US. Therefore, the study findings may not be generalizable to the Canadian setting<br>• The study used surrogate data from the literature or expert opinion for the mathematical model when real data were not available. The literature search strategy for identifying the surrogate data was not described. |
| Gurieva, 2013[79] | |
| *Study Design*<br>• Objective clearly stated<br>• Economic importance of research question stated<br>• Viewpoints of analysis (hospital) clearly stated<br>• Alternative clearly described<br>*Data Collection*<br>• Sources of effectiveness estimates stated<br>• Primary outcome measures clearly stated<br>• Methods for estimation of costs described<br>• Currency was recorded in 2010 Euros<br>• Details of model provided | *Study Design*<br>• Viewpoint not justified by author<br>• Rationale for alternative programs compared not provided<br>• Form of economic evaluation not explicitly stated or justified by author<br>*Data Collection*<br>• Methods of synthesis or pooling for combined estimates unclear<br>• Value and productivity not considered in analysis |

| **Table A6:** Strengths and Limitations of Economic Studies using Drummond[105] | |
|---|---|
| **Strengths** | **Limitations** |
| *Analysis and Interpretation of Results*<br>• Inflation rate (3%) disclosed<br>• Uncertainty of stochastic data considered, credibility intervals provided<br>• Approach to sensitivity analysis (one-way) given<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Results presented disaggregated<br>• Answer to study question given<br>• Conclusions follow data as reported and are accompanied by limitations<br><br>*Other*<br>• The mathematical model incorporated complexities, including diagnostic accuracy (i.e., sensitivity, specificity) | • Quantities not reported separately from unit costs<br>• Methods for estimation of quantities not described<br>• Justification for choice of model not provided<br>*Analysis and Interpretation of Results*<br>• Time horizon not disclosed<br>• Discount rate not justified by authors<br>• Justification for variables varied in sensitivity analysis not provided<br><br>*Other*<br>• The study used data from hospitals in the Netherlands. Therefore, the study findings may not be generalizable to other settings such as those in Canada.<br>• The study used surrogate data from the literature for the mathematical model when real data were not available. The literature search strategy for identifying the surrogate data was not described. Therefore, the study findings may be different from real-life settings. |
| Kang, 2012[80] | |
| *Study Design*<br>• Research question is stated<br>• Economic importance of question is stated<br>• Viewpoint (hospital) of analysis stated<br>• Rationale for alternative screening protocols provided<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Primary outcome measure clearly stated<br>• Currency reported as 2009 US dollars<br>• Details of model used provided<br>*Analysis and Interpretation of Results*<br>• Time horizon stated as duration of hospitalization<br>• Approach to sensitivity analysis (one way and probablistic) stated<br>• Ranges for sensitivity analysis justified through cited literature<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Results reported aggregated and disaggregated<br>• Answer to study question provided<br>• Conclusions follow data as reported and consider limitations | *Study Design*<br>• Viewpoint not justified by author<br>• Choice of form of economic evaluation not justified by author<br>*Data Collection*<br>• Details of methods of synthesis or pooling not disclosed<br>• Value and productivity not considered in analysis<br>• Quantities and costs not reported separately<br>• No adjustment for inflation<br>• Choice of model not justified by author<br>*Analysis and Interpretation of Results*<br>• Discount rate not stated and no justification provided<br>• No justification provided for choice of variables for<br>• sensitivity analysis<br><br>*Other*<br>• The study used surrogate data from the literature or expert opinion for the mathematical model. Therefore, the study findings may be different from real-life settings. |

| **Table A6:** Strengths and Limitations of Economic Studies using Drummond[105] | |
|---|---|
| **Strengths** | **Limitations** |
| *Other*<br>• The literature search strategy for identifying surrogate data from the literature for the mathematical model was described. | • Authors reported that some of the key input parameters were not derived from reliable data and relied on clinical expertise<br>• Modeling method did not consider long-term outcomes or mortality |
| Hubben, 2011[82] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Economic importance of research question stated<br>• Viewpoint of analysis (healthcare provider) clearly stated<br>• Alternative programs clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Details of methods of synthesis or pooling provided<br>• Primary outcome measure clearly stated<br>• Quantities reported separately from costs<br>• Methods of estimating quantities and costs described<br>• Currency reported as 2007 USD<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>• Time horizon stated (15 years)<br>• Discount rate stated (3%)<br>• Approach to sensitivity analysis (one way and probablistic) given<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Results reported aggregated and disaggregated<br>• Answer to study question provided<br>• Conclusions follow data as reported and consider limitations<br><br>Other<br>• The mathematical model incorporated complexities, including diagnostic accuracy (i.e., sensitivity, specificity), multiple screening technologies (i.e., PCR, chromogenic media), different prevalence settings (i.e., high, medium), and multiple hospitals (i.e., simulated hospital inpatients modeled to have been admitted to one of three hospitals). | *Study Design*<br>• Justification for viewpoint not provided, but authors stated that more data is needed to conduct analysis from the societal perspective<br>• Rationale for alternatives not provided<br>• Choice of form of economic evaluation not justified by authors<br>*Data Collection*<br>• Details of design of effectiveness study not provided but stated to be based on data from a single medical centre<br>• Value and productivity not considered in analysis<br>• Price adjustments for inflation not disclosed<br>• No justification provided for choice of model<br>*Analysis and Interpretation of Results*<br>• Justification for discount rate not provided<br>• No justification provided for choice of variables in sensitivity analysis or ranges<br><br>*Other*<br>• The study did not include the savings from averting MRSA HAIs (e.g., shorter hospital stay, averted treatment costs) in the cost analysis. Therefore, the cost estimates may not have been accurate. |
| Leonhardt, 2011[83] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of research question stated<br>• Alternative being compared described<br>• Form of economic evaluation stated | *Study Design*<br>• Viewpoint not clearly stated but implied that it is a hospital viewpoint<br>• No rationale provided for choosing alternative programs<br>• No justification given for form of economic |

| **Table A6:** Strengths and Limitations of Economic Studies using Drummond[105] | |
|---|---|
| **Strengths** | **Limitations** |
| *Data Collection*<br>• Source of effectiveness estimates stated as primary case-control study<br>• Details, design and results of effectiveness study given<br>• Primary outcome measure stated<br>• Methods of estimating quantities and costs described<br>• Details of model given<br>*Analysis and Interpretation of Results*<br>• Time horizon (hospital stay) stated<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Major outcomes presented aggregated and disaggregated<br>• Answer to study question provided<br>• Conclusions follow data as reported and consider limitations<br><br>*Other*<br>• The study used real data, when available, from two hospitals in the US and also adjusted for case-mix, providing actual, as opposed to theoretical, evidence.<br>• The study design involving two hospitals (i.e., one with the intervention, the other without) and two measurements at each hospital (i.e., pre- and post-intervention) offered a methodological strength, controlling for factors such as seasonality. | evaluation<br>*Data Collection*<br>• Value and productivity not considered in analysis<br>• Quantities and costs not reported separately<br>• Currency not reported but implied USD as stated in results<br>• No adjustment for inflation stated<br>• No justification provided for choice of model<br>*Analysis and Interpretation of Results*<br>• No discount rate stated<br>• No sensitivity analysis conducted<br><br>*Other*<br>• The study used data from hospitals in the US, that routinely use private rooms for patients. Therefore, the study findings may not be generalizable to the Canadian setting<br>• The study did not include the costs of MRSA infection treatment (e.g., antibiotics) in the cost analysis. Therefore, the cost estimates may not have been accurate. |
| Nyman, 2011[64] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Economic importance of research question is stated<br>• Viewpoint of analysis (hospital) clearly stated<br>• Alternatives being compared clearly described<br>*Data Collection*<br>• Source of effectiveness estimates provided<br>• Primary outcome measures clearly stated<br>• Quantities reported separately from costs<br>• Methods for estimating quantities and costs provided<br>• Details of the model used provided<br>*Analysis and Interpretation of Results*<br>• Approach to sensitivity analysis (one way) given<br>• Relevant alternatives compared<br>• Outcomes presented disaggregated and aggregated<br>• Answer to the study question given<br>• Conclusions follow data as reported and | *Study Design*<br>• No justification provided for viewpoint<br>• No justification provided for alternative programs<br>• Form of economic evaluation not explicitly stated and justification not provided<br>*Data Collection*<br>• Details of methods of synthesis or pooling of estimates unclear<br>• Value and productivity not considered in analysis<br>• Information on currency not provided<br>• No justification provided for choice of model<br>*Analysis and Interpretation of Results*<br>• Time horizon not explicitly stated (assumed to be lifetime)<br>• Discount rate not reported or justified<br>• Choice of variables and ranges over which variables varied for sensitivity analysis not justified by author |

| **Table A6:** Strengths and Limitations of Economic Studies using Drummond[105] | |
|---|---|
| **Strengths** | **Limitations** |
| accompanied by relevant limitations | • Reported that incremental cost effectiveness analysis was not possible |
| Olchanski, 2011[89] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Economic importance of research question stated<br>• Viewpoint of analysis (hospital administrator) clearly stated<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Primary outcome clearly stated<br>• Quantities and costs reported separately<br>• Methods for estimating quantities and costs described<br>• Stated no adjustment for inflation (based on assumption that costs have remained relatively constant over the past decade)<br>• Details of model used provided<br>*Analysis and Interpretation of Results*<br>• Approach to sensitivity analysis provided (probabilistic)<br>• References provided for ranges applied for sensitivity analysis<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Answer to the study question given<br>• Conclusions follow data as reported and consider limitations | *Study Design*<br>• No justification given for choice of viewpoint<br>• No rationale given for choice of alternate programs<br>• No justification given for type of economic evaluation used<br>*Data Collection*<br>• Methods of synthesis or pooling of estimates not provided<br>• Value and productivity not considered in analysis<br>• Currency not explicitly stated (assumed to be USD, year unclear)<br>• No justification given for choice of model<br>*Analysis and Interpretation of Results*<br>• Time horizon not explicitly stated – assumed to be 30 days based on results<br>• Discount rate not stated<br>• No justification provided for choice of variables in sensitivity analysis<br>• Major results only reported disaggregated |
| Robotham, 2011[81] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Economic importance of question stated<br>• Viewpoint of analysis (decision-maker) clearly stated<br>• Alternatives clearly described<br>• Form of economic evaluation stated and fits research questions<br>• Primary outcome clearly stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Method to value benefits stated and reference provided<br>• Quantities and costs reported separately<br>• Method for estimation of quantities and costs described<br>• Details of model given<br>*Analysis and Interpretation of Results*<br>• Approach to sensitivity analysis (probabilistic) | *Study Design*<br>• No rationale given for alternative programs<br>• No justification given for choice of type of economic evaluation<br>*Data Collection*<br>• Methods of synthesis or pooling of estimates not provided<br>• Productivity not considered in analysis<br>• Currency not explicitly stated (assumed to be £)<br>• Adjustment for inflation or conversion unclear<br>• Justification for choice of model not provided<br>*Analysis and Interpretation of Results*<br>• Time horizon not stated<br>• Discount rate not stated<br>• No justification given for choice of variables for sensitivity analysis |

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| given<br>• References provided for ranges for sensitivity analysis<br>• Relevant alternatives are compared<br>• Incremental analysis reported<br>• Outcomes presented disaggregated and aggregated<br>• Answer to study question given<br>• Conclusions follow data as reported and are accompanied by appropriate caveats | |
| Slover, 2011[48] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Viewpoint of analysis<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates provided<br>• Details and design of effectiveness study given<br>• Outcome clearly stated<br>• Quantities reported separately from costs<br>• Methods for estimation of quantities and costs described<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>• Approach to sensitivity analysis (2-way) stated<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Answer to the study question given<br>• Conclusions follow data as reported and consider limitations | *Study Design*<br>• Economic importance of research questions not explicitly stated<br>• Viewpoint of analysis not explicitly stated (did disclose that only direct costs were considered)<br>• No rationale provided for viewpoint<br>• No rationale provided for alternate programs<br>• Form of economic evaluation fits with research questions<br>• No justification provided for form of economic evaluation<br>*Data Collection*<br>• Value and productivity not considered in analysis<br>• Currency not explicitly stated (assumed to be USD during year of cohort study)<br>• No mention of adjustment for inflation<br>• No justification provided for choice of model<br>*Analysis and Interpretation of Results*<br>• Time horizon not stated<br>• Discount rate not stated<br>• Reference provided for range and choice of variables in sensitivity analysis<br>• Main results only reported disaggregated |
| Lee, 2010[85] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of question stated<br>• Viewpoint of analysis stated<br>• Limited description of rationale for alternative programs provided<br>• Alternatives clearly described<br>• Form of economic evaluation stated and fits research questions<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Methods to value benefits stated | *Study Design*<br>• No justification provided for form of economic evaluation<br>*Data Collection*<br>• Method of synthesis or pooling for estimates unclear<br>• Information about patients from which valuations were obtained not provided<br>• Productivity not considered in analysis<br>• Quantities and costs not reported separately<br>• No adjustments made for inflation<br>• No justification provided for choice of model |

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| • Method for estimating quantities and costs described<br>• Currency data provided<br>• Details of model given<br>*Analysis and Interpretation of Results*<br>• Discount rate (3%) applied<br>• Approach to sensitivity analysis given<br>• Choice of variables and ranges for sensitivity analysis justified<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Results presented aggregated and disaggregated<br>• Answer to study question given<br>• Conclusions follow data as reported and consider limitations | and key parameters<br>*Analysis and Interpretation of Results*<br>• Time horizon not stated explicitly but assumed to be hospital stay<br>• No justification provided for choice of discount rate |
| Lee, 2010[86] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of question stated<br>• Viewpoints stated<br>• Alternatives clearly described<br>• Form of economic evaluation stated and fits research questions<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Methods used to value benefits stated<br>• Methods of estimating quantities and costs described<br>• Currency data provided<br>• Details of model given<br>*Analysis and Interpretation of Results*<br>• Time horizon stated<br>• Discount rate (3%) applied<br>• Approach to sensitivity analysis given<br>• Choice of variables for sensitivity analysis justified<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Answer to study question given<br>• Conclusions follow data as reported and consider limitations | *Study Design*<br>• Rationale for choosing alternatives not provided<br>• No justification given for form of economic evaluation<br>*Data Collection*<br>• Methods of synthesis or pooling of estimates unclear<br>• Primary outcome not explicitly stated but implied<br>• Details of subjects valuations derived from unclear<br>• Productivity not considered in analysis<br>• No adjustments made for inflation<br>• Quantities not reported separately form costs<br>• No justification provided for choice of model or key parameters<br>*Analysis and Interpretation of Results*<br>• No justification provided for choice of discount rate<br>• No justification provided for ranges used in sensitivity analysis<br>• No disaggregated results reported |
| Lee, 2010[87] | |
| *Study Design*<br>• Research question stated<br>• Economic importance of question stated<br>• Viewpoint of analysis stated<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Methods to value benefits stated | *Study Design*<br>• Rationale for choosing alternatives unclear<br>• No justification provided for choice of form of economic evaluation<br>*Data Collection*<br>• Primary outcome not explicitly stated but clear based on results<br>• Details of subjects valuations derived from unclear |

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| • Methods for estimating quantities and costs described<br>• Currency data recorded<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>*Other*<br>• Discount rate (3%) applied<br>• Approach to sensitivity analysis provided<br>• Choice of variables for sensitivity analysis justified<br>• Relative alternatives compared<br>• Incremental analysis reported<br>• Answer to study question given<br>• Conclusions follow data s presented and consider limitations | • Productivity not considered in analysis<br>• Quantities not reported separately from costs<br>• No adjustment made for inflation<br>• Justification not provided for choice of model and key parameters<br>*Analysis and Interpretation of Results*<br>• Time horizon not explicitly stated but assumed to be length of hospital stay<br>• Justification not provided for choice of discount rate<br>• No justification provided for ranges for sensitivity analysis<br>• Disaggregated results not presented<br>*Other*<br>• Influence of decolonization on economic value not assessed<br>• Results only reflective of single nares specimen surveillance, not other screening technologies |
| Murthy, 2010[88] | |
| *Study Design*<br>• Research aims clearly stated<br>• Economic importance of research question stated<br>• Viewpoint of analysis (hospital administrator) clearly stated<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates stated<br>• Details and design of effectiveness study given<br>• Outcome clearly stated<br>• Method of estimating quantities and costs described<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>• Time horizon declared as period of hospitalization<br>• Currency (CHF) declared<br>• Approach for sensitivity analysis (univariate) given<br>• References provided for ranges for sensitivity analysis<br>• Relevant alternatives are compared<br>• Incremental analysis reported<br>• Outcomes presented disaggregated and aggregated<br>• Answer to the study question given<br>• Conclusions follow the data as reported and include limitations | *Study Design*<br>• Rationale for viewpoint not stated<br>• Rationale for alternative programs not stated<br>• Form of economic evaluation fist research questions<br>• No justification for form of economic evaluation provided<br>*Data Collection*<br>• Value and productivity not considered in analysis<br>• Quantities and costs not recorded separately<br>• No adjustment for inflation reported<br>• No justification provided for choice of model<br>*Analysis and Interpretation of Results*<br>• No discount rate stated<br>• No justification provided for choice of sensitivity analysis variables |

**Table A6:** Strengths and Limitations of Economic Studies using Drummond[105]

| Strengths | Limitations |
|---|---|
| Nelson, 2010[43] | |
| *Study Design*<br>• Research objectives clearly stated<br>• Economic importance of research question stated<br>• Viewpoint of analysis (healthcare provider Veterans Health Administration)<br>• Alternatives clearly described<br>• Form of economic evaluation stated<br>*Data Collection*<br>• Source of effectiveness estimates provided<br>• Primary outcome clearly stated<br>• Quantities and costs not reported separately<br>• Details of model provided<br>*Analysis and Interpretation of Results*<br>• Time horizon stated (length of inpatient hospital stay)<br>• Approach to sensitivity analysis (one-way, and two-way) given<br>• Justification provided for choice of variables and ranges for sensitivity analysis<br>• Relevant alternatives compared<br>• Incremental analysis reported<br>• Outcomes presented disaggregated and aggregated<br>• Answer to study question given<br>• Conclusions follow data as reported and limitations considered | *Study Design*<br>• No justification provided for viewpoint<br>• Rationale for alternative programs not stated<br>• Form of economic evaluation fits with research questions<br>• No justification provided for form of economic evaluation<br>*Data Collection*<br>• Methods of synthesis or pooling of estimates not stated<br>• Value and productivity not considered in analysis<br>• Currency not stated but assumed to be USD<br>• Adjustment for inflation not stated<br>• No justification provided for choice of model<br>• Discount rate not stated |

CHF = Swiss Franc; PCR = polymerase chain reaction; USD = United States dollars

## APPENDIX 4: Main Study Findings and Author's Conclusions

**Table A7:** Summary of Findings of Included Systematic Reviews

| Main Study Findings | Author's Conclusions |
|---|---|
| Bond, 2013[44] | |
| *SRs* | • There is little high-quality evidence to support the use of screening of patients (universal or targeted) for the reduction of healthcare acquired ARO incidence, infection, mortality or morbidity<br>• Well-designed prospective studies that can discern individual effects of respective infection measures, including screening, are needed |
| • Seven SRs of varying quality (moderate to high) that reported narrative summaries of study results published between 2006 and 2013 and based on MRSA or VRE screening, or both, in patients of various backgrounds (general hospitalized patients, orthopedic surgery patients, high-risk patients, ICU patients, pediatric patients in acute care) were included.<br>• Regardless of the comparison made (i.e., universal to targeted screening, universal to no screening, targeted to no screening) ARO screening has only a small (as determined by retrospective studies) or no effect (based on higher quality quasi-experimental studies and randomized controlled trials) on ARO-related outcomes such as colonization and infection rates<br>• The direct effect of screening on ARO-related outcomes was hard to discern due to the matrix delivery of various infection prevention strategies in tandem with screening protocols<br>• No information was available on adverse outcomes associated with screening<br>• No evidence was available on ESBL-producing organisms or CPO | |
| *Primary Clinical Studies* | |
| • Six primary studies, not included in the seven aforementioned SRs based on MRSA or ESBL-E screening<br>• No results were available on universal versus no screening<br>• One cluster randomized study reported that over short term follow-up targeted screening and isolation and targeted screening and targeted decolonization are less effective than no screening plus universal decolonization in reducing MRSA colonization and infection rates in ICU patients<br>• Similar to the issues with the SRs, as screening was 'bundled' as an intervention with other infection control strategies it is difficult to draw conclusions regarding the direct effectiveness of screening | |

ARO = antibiotic resistant organism; ESBL-E = extended-spectrum β-lactamase producing *Enterobacteriaceae*; ICU = intensive care unit; MRSA = methicillin resistant *Staphylococcus aureus;* SR = systematic review; VRE = vancomycin resistant *Enterococci*

| Table A8: Summary of Findings of Included Primary Clinical Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| Jennings, 2014[51] | |
| • MRSA infection rate = 1.3% before and 3.2% after universal screening<br>• MRSA infection rate in surgical group = 1.4% before and 2.3% after<br>• Rates of HA-MRSA decreased over time in all patients (1.2 versus 0.87) and surgical patients (1.4 versus 1.0)<br>• Multivariate models suggested that African American race, increased length of stay were positively associated with HA-MRSA, whereas female sex and being in the after cohort was negatively associated with HA-MRSA – this was consistent when only the after cohort was analyzed<br>• MRSA colonization was associated positively with African American race, and increased age, and negatively with female sex, Hispanic race, and being in the surgical group<br>• HA-MRSA infection was associated with a higher mortality in the total patient population and before and after subgroups though there was no difference in the rate of mortality before and after in the total or surgical group population | • MRSA infection rates increased over the after institution of a screening program for the entire patient population and patients in the surgical group<br>• When patients with a history of infection were excluded the overall rate of HA-MRSA decreased with the introduction of the screening program<br>• Study suggests that screening is associated with a reduced rate of HA-MRSA |
| Kaushik, 2014[74] | |
| • Rate of infection was similar before and after institution of screening ([3.8/1000] versus [5.3/1000], p = 0.73), all incidents of infection occurred in MRSA colonized patients<br>• 1 MRSA associated death post-surveillance and 0 pre-surveillance, similar impact of MRSA on morality<br>• Length of hospital stay, days until the development of MRSA were not different between pre and post surveillance groups | • While the rate of infection was similar, the authors suggest that since all infections occurred in MRSA colonized patients, screening may still be an appropriate strategy in the NICU setting |
| Otter, 2014[30] | |
| • If the previous targeted screening protocol versus the universal screening protocol was used, 24% of patients would have been screened which would have identified 55% of all MRSA cases | • Targeted screening may miss a substantial proportion of MRSA carriers that would be identified by universal screening |
| Fuller, 2013[75] | |
| • The percentage of MRSA positives that would be identified with CLAS and CLAS in low risk and screening all high risk is approximately 20% lower (81 and 82%), and the percentage for only screening high-risk specialty admissions is substantially lower (8.5%)<br>• The number of patients needed to screen to identify a single new positive case were high | • Universal MRSA screening may not be the optimal strategy as the increased resources required result in a very low yield of newly detected cases of MRSA colonization<br>• The ability to treat all cases optimally (e.g., contact isolation) is limited<br>• Checklist activated screening reduces the number of laboratory tests substantially while |

| **Table A8:** Summary of Findings of Included Primary Clinical Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| (n = 97 for emergency admissions in acute trusts, n = 462 for day-case admissions in acute trusts)<br>• CLAS would identify 80% of all MRSA positive patients detected by universal screening and reduce the rate of screening by 50%, whereas screening high-risk specialty admissions would only detect 10% of MRSA positive patients and reduce screening by 90% | still identifying a large proportion of MRSA cases<br>• While high risk targeted screening results in a low yield of MRSA colonized cases, the difficulties involved in implementing checklist activated screening may make this a more feasible option and may still capture the patients with the highest potential excess clinical risks and costs due to MRSA infection. |
| Collins, 2011[76] | |
| • Rates of MRSA infection remained 'relatively constant' throughout the phases of screening<br>• Based on data from a single surveillance month, n = 7 MRSA positive patients (detected with the universal screening protocol) would not have been detected with the targeted screening protocol | • The search and destroy strategy of screening high and medium risk groups was able to detect the majority of MRSA colonized patients; therefore, screening low risk or all (universal) patient groups may be unnecessary |

CLAS = checklist activated screening; HA = hospital acquired; MRSA = methicillin resistant *Staphylococcus aureus;* NICU = neonatal intensive care unit

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| McKinnell, 2015[78] | |
| • Under baseline conditions, the costs of universal MRSA screening and contact precautions outweighed the projected benefits generated by preventing MRSA-related infections, resulting in economic costs of $104,000 per 10,000 admissions (95% CI, $83,000-$126,000).<br>• Cost savings occurred only when the mathematical model used estimates at the extremes of the key parameters. Non-nares MRSA screening and PCR-based testing resulted in modest savings from more MRSA infections averted but substantial economic costs of screening. | • Universal MRSA screening, although providing potential benefit in preventing MRSA infections, is relatively costly and may be economically burdensome for a hospital.<br>• The results were sensitive to:<br>- The impact of MRSA invasive disease, suggesting that there are likely subpopulations for which MRSA screening and contact precautions may result in cost savings for the hospital.<br>- The efficacy of the MRSA intervention, suggesting that more efficacious strategies with greater projected benefits may be cost-neural or even cost-saving. |
| Clancy, 2014[77] | |
| • SA screening and decolonization was economically dominant for all scenarios tested, providing more cost savings and health benefits compared to no screening. Savings per case averted ranged from $73,567 to $133,157 (from a hospital perspective) and $10,748 to $16,723 (from a third party perspective) in 2012 $US, varying positively with the probability of colonization, infection, and decolonization efficacy. | The results support routine SA screening and decolonization of lung and heart-lung transplant patients. |

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| Gurieva, 2013[79] | |
| • The costs of intervention measures per infection averted were lowest for MRSA screening and isolation of carriers in previously-documented carriers only, ranging from €632 to €8,447 for isolation efficacy levels of 100% and 10%, respectively, in 2010 €. Universal screening was associated with the highest costs per infection averted, ranging from €19,918 to €164,093 for isolation efficacy levels of 100% and 10%, respectively, in 2010 €.<br>• With the baseline isolation efficacy level of 25%, only two strategies (i.e., MRSA screening and isolation of carriers in previously-documented carriers only or in previously-documented carriers and ICU admissions) was expected to be cost-saving within 10 years. Whether a strategy will be cost-saving critically depended on the isolation efficacy levels and the costs per infection averted. | MRSA screening and isolation of carriers in previously-documented carriers only or in previously-documented carriers and ICU admissions are the most cost-saving strategies, with fastest return of investment. When administered universally or to previously-documented carriers and frequent patients, the intervention may never be cost-saving. |
| Kang, 2012[80] | |
| • Under baseline conditions, targeted MRSA screening was a dominant strategy, preventing 59 MRSA HAIs and costing $282,770 less compared to no screening. Universal screening was associated with an ICER of $14,955 per MRSA HAI prevented compared to no screening. Compared to targeted screening, universal screening would prevent an additional 34 MRSA HAIs but cost nearly $1.7 million more, with an ICER of $49,749 per MRSA HAI prevented.<br>• In univariate sensitivity analyses, targeted screening for MRSA was a dominant strategy across most parameter ranges. However, the probability of targeted screening being cost-effective decreased as:<br>  ○ The incremental cost of an MRSA HAI increased.<br>  ○ The rate of reduction in the MRSA HAI rate attributable to the intervention decreased.<br>  ○ The mean length of stay in the ICU increased.<br>• Probabilistic sensitivity analysis demonstrated that targeted screening was the most cost-effective when willingness-to-pay to prevent an MRSA HAI was less than $71,300. | Targeted MRSA screening is cost-saving, compared to no screening, and cost-effective, compared to universal screening. Therefore, targeted screening is the most cost-effective strategy in an academic hospital setting with a high prevalence of or high costs associated with an MRSA HAI. |
| Hubben, 2011[82] | |
| • When MRSA screening using PCR, as opposed to the chromogenic media-based test, in the high prevalence setting, universal screening cost an additional $6.1M and averted an additional 46 infections, compared to targeted screening, resulting in an ICER of $131,000 per infection | Targeted MRSA screening was more cost-saving than universal screening in both high and medium prevalence settings and regardless of which of the two test methods is used. |

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| averted. The ICER increased with the medium prevalence setting (vs. high) and with the chromogenic media-based test (vs. PCR).<br>• MRSA screening would be less effective and more costly if neighboring hospitals did not screen. | |
| Leonhardt, 2011[83] | |
| • For every $1 spent on universal versus targeted screening for MRSA, only $0.50 was recovered in avoided costs of MRSA HAIs.<br>• Compared with targeted MRSA screening, universal screening increased the rate of detection of MRSA upon hospital admission but did not significantly reduce the rate of MRSA HAIs. | Universal MRSA screening compared to targeted screening was associated with higher costs of care and was not cost-beneficial. |
| Nyman, 2011[84] | |
| • $484 dollars saved per admission with universal standard culture test ($483 and $476 per admission with chromogenic agar and PCR tests) | Screening of ICU patients results in a net cost savings to the hospital |
| Olchanski, 2011[89] | |
| • Universal screening compared to screening of high risk patients is associated with reduced number of MRSA colonizations but an increased program cost due to the cost of isolating patients<br>• Screening only ICU patients decreases program costs relative to only screening high risk patients but increases infection rates<br>• Cost savings of not screening completely offset by the large infection-related costs | The additional costs that occur with universal screening offset potential savings of infection reduction compared to targeted screening of high risk patients |
| Robotham, 2011[81] | |
| • Screening combined with decolonization using chlorhexidine had a 30% chance of being cost-effective at a WTP threshold of £30 thousand pounds per QALY and was the most cost-effective strategy with the exception of universal decolonization<br>• Screening and decolonization (when universal decolonization wasn't considered) had the highest net monetary benefit of all strategies considered at WTP thresholds over £50 thousand pounds per QALY<br>• Screening without subsequent decolonization (isolation of patients used instead) was unlikely to be cost effective at WTP thresholds of £20 or £30 thousand pounds per QALY | • Universal decolonization was deemed to be cost-saving in the ICU setting but concerns were expressed regarding the risk of antibiotic resistance; therefore, the next best strategy was deemed to be screening and subsequent decolonization<br>• Considering the risk of antibiotic resistance, combining universal screening with decolonization of identified cases may represent good value for money |
| Slover, 2011[48] | |
| • For joint arthroplasty, assuming a 10% reduction in rate of revision and an average cost of septic revision less than $70 thousand dollars it would be cost-saving to forego screening; however, if costs of revision increase above $70 thousand the screening program would be cost saving | • Due to the large cost of treating infection and of revision surgery after the procedures in question, the cost of implementing a screening program would be recouped with the reduction in infection<br>• Universal screening and subsequent decolonization for orthopedic surgery |

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| • For the spine population, the screening program is more likely to be cost saving due to a higher infection rate and higher cost of treating infection – given a 10% reduction in revision rate, the cost of treating a spine surgery must be less than $30 thousand for the screening program to not be cost saving<br>• If the cost of treating an infected hip or knee arthroplasty is $15000 then the screening program needs to reduce revision rates by 35% to be cost saving | patients requires only a modest reduction in the rate of surgical site infection to be cost saving |
| Lee, 2010[85] | |
| From the third-party payer perspective:<br>• Universal MRSA screening of cardiac surgery patients was 'strongly' cost-effective (defined as < $20000/QALY) or dominant for a wide margin of decolonization success rates and MRSA colonization rates<br>• Universal screening was cost-effective approximately 50% of the time when MRSA prevalence was 10% and the WTP threshold was $50,000 whereas with increasing MRSA prevalence, screening became the optimal choice the majority of the time at WTP thresholds lower than $50000<br>From the hospital perspective:<br>• Considering opportunity costs of lost bed days, universal screening was economically dominant even at low MRSA colonization prevalence and low decolonization success rates<br>• Rather than economically dominant, screening was still strongly cost-effective when colonization prevalence was <2.5% and decolonization was< 50% effective<br>• When two rather than one location for screening was introduced (higher execution costs), screening was highly cost effective at MRSA colonization prevalence as low as 1% and 25% decolonization success rates, at rates higher than 1% prevalence and 50% success of decolonization, screening was a dominant strategy | From both third-party payer and hospital perspectives:<br>• In cardiac surgery patients, universal preoperative screening is a cost-effective strategy for MRSA prevention<br>• Depending on the prevalence of MRSA colonization and the level of decolonization success, a screening strategy may even be cost-saving (dominant economically) |
| Lee, 2010[86] | |
| From the third-party payer perspective:<br>• MRSA screening was either 'strongly' cost-effective or economically dominant with varied decolonization success rates and MRSA prevalence rates<br>• When only anterior nares swabs were used (lowest cost) MRSA screening was economically dominant when decolonization was at least 50% successful | From both the third-party payer and hospital perspectives, MRSA screening and subsequent decolonization of orthopedic surgery patients was primarily economically dominant over no screening but became transitioned to being cost-effective (rather than dominant) at lower MRSA colonization prevalence and lower decolonization success probabilities from the |

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| and MRSA colonization prevalence was at least 2.5%<br>• When a second body site was sampled (higher cost) MRSA screening remained primarily economically dominant at a variety of MRSA colonization prevalences and a decolonization success rate of at least 75%; or when MRSA colonization prevalence was at least 5% and decolonization was at least 25% successful<br>• Assuming a decolonization success probability of 25% and MRSA colonization prevalence of 10% with a WTP threshold set at $50000 dollars, MRSA is cost-effective approximately 65% of the time<br>  ○ As MRSA colonization rates increase the probability of screening being cost-effective is achieved at lower willingness to pay thresholds<br><br>From the hospital perspective:<br>• Universal MRSA screening and subsequent decolonization of culture-positive patients was economically dominants for all scenarios wherein the MRSA colonization prevalence was at least 1% and the decolonization success probability was at least 25% at costs of decolonization up to 200$ | payer perspective. |
| Lee, 2010[87] | |
| Baseline model:<br>• Universal MRSA screening was economically dominant when the basic reproductive rate was 1.5 or greater and MRSA prevalence was 15% or greater, and when the reproductive rate was 2.5 or greater and the MRSA prevalence was 5% or greater.<br>• Universal MRSA screening was cost-effective when the reproductive rate was 0.25 or higher and the prevalence was 1% or greater<br>• MRSA infection resulted in a mean increase of 5.1 days in patient length of stay and each lost bed-day corresponded to over $1.4 million in revenue lost<br>• Acceptability curves depicted that at MRSA colonization prevalence of 1% screening is cost effective for more than 50% of patients<br><br>Model accounting for Pre-identified MRSA carriers:<br>• Screening was a cost-effective strategy throughout the range of scenarios tested – when the MRSA colonization prevalence was as low as 1% and the basic reproductive rate was as low as 0.25, and 33% of carriers were identified and under contact precautions, the ICER was $10863 per QALY – with increasing prevalence the ICER reduced | Universal MRSA screening of adult general medical patients for MRSA may be cost effective at a wide range of MRSA prevalences and MRSA transmission dynamics |

| **Table A9:** Summary of Findings of Included Cost Studies | |
|---|---|
| **Main Study Findings** | **Author's Conclusions** |
| accordingly eventually reaching economic dominance, similarly an increased basic reproductive rate and a reduced proportion of pre-identified MRSA carriers moved the ICER in this direction | |
| Murthy, 2010[88] | |
| • Compared to no screening, universal screening with PCR was more costly but resulted in a lower infection rate, ICER = CHF 30 784 per infection prevented<br>• Compared to no screening, targeted screening for risk factors also resulted in higher costs and a lower infection probability<br>• Compared to universal screening with PCR the targeted screening for risk factors was more costly and less effective (dominated by universal screening)<br>*Sensitivity Analysis:*<br>• Prevalence of colonization on admission was a predictor of cost-effectiveness in that when it decreases the cost-effectiveness of PCR universal screening is reduced and vice-versa<br>• Reduced probability of cross-transmission, reduced efficacy of decolonization and contact precautions, and increased cost of infection and rapid screening negatively influenced the cost effectiveness<br>• Reducing turnaround time and increased decolonization efficacy improved cost-effectiveness | • At the single centre, cost avoided by a reduction in MRSA infection did not wholly offset the costs associated with implementing either universal or targeted screening protocols.<br>• Universal rapid screening or targeted screening was unlikely to be cost-effective in the context of the research centre due to low rates of MRSAS infection and other well-developed infection control procedures |
| Nelson, 2010[43] | |
| • Compared to universal screening alone or no screening, universal screening plus subsequent decolonization was associated with lower average costs and more infection and deaths avoided (economically dominant)<br>• Compared to no screening, universal screening alone was also economically dominant<br>• In threshold analysis, only risk of hospital acquired MRSA infection in non-carriers (0%), direct benefit of decolonization (1%) and cost of hospital acquired MRSA infection ($2768) had values that resulted in universal screening plus decolonization not being the dominant strategy (being replaced by universal screening in the case of decolonization benefit, and by no screening in the other two cases) | Universal screening plus decolonization was an economically dominant strategy over universal screening alone or no screening in terms of the costs per prevention of infections and infection associated deaths |

CHF = Swiss Franc; HAI = hospital-acquired infection; ICER = incremental cost-effectiveness ratio; ICU = intensive care unit; MRSA = methicillin resistant *Staphylococcus aureus;* PCR = polymerase chain reaction; QALY = quality adjusted life years; WTP = willingness-to-pay