Making Healthcare Safer IV

Prevention in Adults of Transmission of Infection With Multidrug-Resistant Organisms

Rapid Review

Structured Abstract

Objectives. This rapid review summarizes literature for patient safety practices intended to prevent and control the transmission of multidrug-resistant organisms (MDROs).

Methods. We followed rapid review processes of the Agency for Healthcare Research and Quality Evidence-based Practice Center Program. We searched PubMed to identify eligible systematic reviews from 2011 to May 2023 and primary studies published from 2011 to May 2023, supplemented by targeted gray literature searches. We included literature that addressed patient safety practices intending to prevent or control transmission of MDROs which were implemented in hospitals and nursing homes and that included clinical outcomes of infection or colonization with MDROs as well as unintended consequences such as mental health effects and noninfectious adverse healthcare-associated outcomes. The protocol for the review has been registered in PROSPERO (CRD42023444973).

Findings. Our search retrieved 714 citations, of which 42 articles were eligible for review. Systematic reviews, which were primarily of observational studies, included a wide variety of infection prevention and control (IPC) practices, including universal gloving, contact isolation precautions, adverse effects of patient isolation, patient and/or staff cohorting, room decontamination, patient decolonization, IPC practices specifically in nursing homes, features of organizational culture to facilitate implementation of IPC practices and the role of dedicated IPC staff. While systematic reviews were of good or fair quality, strength of evidence for the conclusions was always low or very low, due to reliance on observational studies. Decolonization strategies showed some benefit in certain populations, such as nursing home patients and patients discharging from acute care hospitalization. Universal gloving showed a small benefit in the intensive care unit. Contact isolation targeting patients colonized or infected with MDROs showed mixed effects in the literature and may be associated

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with mental health and noninfectious (e.g., falls and pressure ulcers) adverse effects when compared with standard precautions, though based on before/after studies in which such precautions were ceased. There was no significant evidence of benefit for patient cohorting (except possibly in outbreak settings), automated room decontamination or cleaning feedback protocols, and IPC practices in long-term settings. Infection rates may be improved when IPC practices are implemented in the context of certain logistical and staffing characteristics including a supportive organizational culture, though again strength of evidence was low. Dedicated infection prevention staff likely improve compliance with other patient safety practices, though there is little evidence of their downstream impact on rates of infection.

Conclusions. Selected infection prevention and control interventions had mixed evidence for reducing healthcare-associated infection and colonization by multidrug resistant organisms. Where these practices did show benefit, they often had evidence that applied only to certain subpopulations (such as intensive care unit patients), though overall strength of evidence was low.

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1. Background and Purpose

The Agency for Healthcare Research and Quality (AHRQ) Making Healthcare Safer (MHS) reports consolidate information for healthcare providers, health system administrators, researchers, and government agencies about practices that can improve patient safety across the healthcare system—from hospitals to primary care practices, long-term care facilities, and other healthcare settings. In spring 2023, AHRQ launched its fourth iteration of the MHS Report (MHS IV). Transmission-based Precautions as a patient safety practice (PSP) was identified as high priority for inclusion in the MHS IV reports using a modified Delphi technique by a Technical Expert Panel (TEP) that met in December 2022. The TEP included 15 experts in patient safety with representatives of governmental agencies, healthcare stakeholders, clinical specialists, experts in patient safety issues, and a patient/consumer perspective. See the MHS IV Prioritization Report for additional details.[1]

There have been concerted efforts to track and reduce the burden of healthcare-associated infections (HAIs) in the United States over the past several decades, with particular attention to infections attributable to medical procedures/devices as well as infections caused by certain multidrug-resistant organisms (MDROs). With these efforts, there has been a decrease in hospital-acquired infections and particularly procedure- and device-related infections, including surgical site infections, catheter-associated urinary tract infections, and central-line-associated bloodstream infections, as well as *Clostridioides difficile* (*C. difficile*) infection, though several of these trends have reversed in the short-term in context of the COVID-19 pandemic.[2,3] Meanwhile, the threat of antibiotic-resistant pathogens has seen more mixed progress; compared with the original 2013 Centers for Disease Control and Prevention (CDC) Antibiotic Resistance Threat Report, the 2019 report found a decrease in overall and hospital deaths from antibiotic-resistant organisms, with reductions in the burden of some MDROs including vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant *Pseudomonas*, but no change in carbapenem-resistant *Enterobacteriaceae* (CRE) and an increase in several other MDROs including ESBL-producing *Enterobacteriaceae* (ESBL-E) and *Candida auris*.[4] As with HAI rates, MDRO rates saw a significant setback with the COVID-19 pandemic; the 2022 CDC Special Report on COVID-19 Impact on Antimicrobial Resistance found substantial increases from 2019 to 2020 in rates of MRSA, VRE, ESBL-E, CRE, and MDR-*Pseudomonas*.[5] Given the success against device-associated HAIs and more mixed progress against MDROs, we framed our review of transmission-based precautions in context of prevention and control of HAIs by multidrug-resistant organisms.

1.1 Overview of the Patient Safety Practice

Several major categories of MDRO infection prevention practices are either addressed elsewhere or excluded from this edition of Making Healthcare Safer,

include those targeting invasive medical devices/procedures such as central-line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), ventilator associated pneumonia/events (VAP/VAE), surgical site infection (SSI), surveillance testing (will be discussed in a separate MHS IV chapter), as well as the broader practices of antimicrobial stewardship (which was discussed in Chapter IV of MHS III) and hand hygiene.

The remaining major category of patient safety practices targeting HAIs centers on reducing the transmission of multidrug-resistant organisms (MDROs) within a healthcare context, particularly within congregate care settings where patients and healthcare workers are in extended contact with each other—namely hospitals and nursing homes.

This review focuses on patient safety practices for reducing burden and transmission of MDROs and *C. difficile* within hospital and nursing home environments, including those centering around the patient microbiome (including decolonization but not MDRO surveillance testing, which is the focus of a separate MHS IV chapter), healthcare workers and the healthcare environment (barrier precautions and room decontamination), and patient distribution and staffing (patient isolation, patient/staff cohorting based on colonization status, and dedicated infection-control staffing). While *C. difficile* is not technically an MDRO, prevention of *C. difficile* transmission bears similarities to prevention of MDRO transmission in practice and intended outcome, therefore it is included in this chapter. We searched for literature surrounding VRE, MRSA, and *C. difficile*, and also included literature covering the multidrug-resistant *Enterobacterales* (including extended-spectrum beta-lactamase-producing [ESBL] *Enterobacterales* and CRE) as well as the rare but dangerous invasive yeast *Candida auris*. We excluded literature related to COVID-19 transmission-based precautions since this severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was primarily acquired by community spread (rather than hospital acquired) during the global pandemic and was met with widely varying infection control practices based on a shifting evidence base as well as logistical constraints of limited resources.

MHS I (2001) chapter 13 primarily focused on the use of barrier precautions in the prevention of HAIs with VRE and *C. difficile.* This report showed a significant reduction in incidence of these HAIs in association with barrier precautions, though multiple interventions were bundled together in many of the included studies and study designs were largely before-after cohort studies. MHS II (2013) chapter 7 included barrier isolation precautions while adding routine surveillance testing for healthcare-associated pathogens and distinction between use of isolation/barrier interventions based on colonization status with specific pathogens (so-called vertical interventions) or across certain hospital populations (such as all intensive care unit [ICU] patients) regardless of surveillance testing (so-called horizontal approach). MHS II again focused on VRE and *C. difficile*, with the addition of MRSA in recognition of the increasing incidence and high mortality of MRSA HAIs. The report found that while the size and quality of studies had improved since MHS I, most

included studies again bundled multiple interventions, making it difficult to separate and compare impact of individual components. Studies showed mixed results in terms of incidence of colonization and/or infection with healthcare-associated pathogens. MHS III (2020) had chapters focusing in-depth on individual pathogens including *C. difficile* (chapter 4),[6] other multidrug resistant organisms (chapter 5),[7] and CRE (chapter 6).[8] These chapters included numerous types of patient safety practices relevant to their pathogens of focus, including several practices not directly relevant to the topic of our review (such as hand hygiene practices, antimicrobial stewardship, surveillance testing, and minimizing use of invasive devices/catheters). The chapter focusing on *C. difficile* included two PSPs directly relevant to this review, regarding environmental decontamination and multicomponent prevention interventions. In studies of environmental cleaning practices, they found that the addition of hydrogen peroxide or ultraviolet light decontamination to standard cleaning was associated with reductions in *C. difficile* infection (CDI) rates, though study quality was low and the sole randomized study found no significant difference in CDI rates with addition of UV to bleach cleaning.[6] In studies of multicomponent CDI prevention interventions variously composed of environmental cleaning, hand hygiene, isolation, antimicrobial stewardship, clinical and surveillance testing practices, they saw a consistent association between multicomponent interventions and reduced CDI rates.[6] The chapter focusing on other MDROs included two PSPs directly relevant to this review, namely environmental cleaning practices and chlorhexidine bathing. Clinical evidence was limited to guide choice of specific environmental cleaning agents for reducing MDROs.[7] They found high level of evidence supporting the use of chlorhexidine bathing for preventing MDRO acquisition and for decolonization of patients already affected by MDROs, particularly for Gram-positive bacteria such as MRSA and VRE and for infections related to invasive devices, though the majority of the literature addressed ICU patients.[7] The chapter addressing CRE primarily addressed use of contact isolation precautions to prevent CRE infection, and found evidence for contact isolation of patients infected or colonized by CRE, though the reviewed literature only studied contact isolation bundled together in combination with other PSPs.[8] Furthermore, they found little evidence to support use of active surveillance to identify colonized patients except in high-risk settings such as outbreaks, and limited evidence regarding duration of contact isolation and its discontinuation.[8] The conclusions from MHS I-III are listed in Table 1.

In the prioritization process, the Making Healthcare Safer IV TEP noted that the PSP was rated high priority. This topic was originally named "Transmission-based precautions" and was meant to include masks, gowns, decontamination, etc., for the prevention of hospital-acquired infections. During discussion the TEP recommended that this be broadened out to include aerosol transmission, in the context of the COVID-19 epidemic. However, a preliminary search of COVID-19 infection prevention studies yielded more than 13,000 titles, far in excess of what could be accomplished within the time and resources for Making Healthcare Safer IV. Thus, we returned the scope to

transmission-based precautions, in the context of MDRO infections, as was done in MHS II and III.

Table 1. Conclusions From Prior Editions of Making Healthcare Safer

Edition	Conclusions
Conclusion from MHS I	The majority of reviewed studies demonstrated a significant reduction in the incidence of VRE or *C. difficile* following barrier precaution interventions
	Context Is likely important in effectiveness
	Combined interventions might be more effective than single interventions
Conclusion from MHS II	Vertical interventions, such as active surveillance, has conflicting evidence of effectiveness
	Horizontal interventions, such as universal gloving, have been understudied
	Effectiveness likely varies depending on setting, endemic vs. outbreak, and ICU vs. general ward
	Multiple infection control measures, including hand hygiene and antimicrobial stewardship, are preferable to single interventions (such as contact precautions) alone.
Conclusion from MHS III	Screening and isolating asymptomatic carriers can prevent CDI transmission
	Studies support daily and/or discharge cleaning with chlorine-based agents for CDI-occupied rooms
	The addition of hydrogen peroxide decontamination or ultraviolet light decontamination to standard cleaning was associated with significant reductions in facility-level CDI rates
	Multicomponent interventions to prevent CDI were associated with significant decreases in CDI rates
	Chlorhexidine bathing for controlling MDROs is effective at reducing colonization, particularly by MDR gram-positive bacteria; evidence is mixed about its effective in reducing MDR-related infections
	Contact precautions have been shown to reduce transmission of CRE as part of infection control bundles

Notes: CDI = Clostridium difficile infection, ICU = Intensive Care Unit, MHS = Making Healthcare Safer, MDRO(s) = Multiple drug resistance Organisms, MDR = Multiple drug resistance, VRE = Vancomycin Resistant Enterococci

1.2 Purpose of the Rapid Review

The overall purpose of this review is to determine the effect of transmission-based precautions on preventing or mitigating the harms of MDRO infections in healthcare

settings. We will also consider costs, implementation, and unintended outcomes such as less patient-to-healthcare worker contact, increased depression, and anxiety.

1.3 Review Questions

(Note: For the scope of this review, these multidrug-resistant organism infections do not include CAUTI, CLABSI, and VAP, which are either discussed separately or excluded from MHS IV. Additionally, "healthcare settings" is defined as acute care hospital and nursing home settings, and does not include ambulatory care clinics, free-standing radiology centers, physical therapy offices, etc.)

1. What are the frequency and severity of healthcare-associated infections caused by multidrug resistant organisms?
2. What patient safety measures or indicators have been used to examine the frequency and severity of healthcare-associated infections caused by multidrug-resistant organisms?
3. What patient safety practices have been used to prevent or mitigate the harms of healthcare-associated infections caused by multidrug-resistant organisms and in what healthcare settings?
4. What is the reported rationale for using the patient safety practices to prevent or mitigate the harms of healthcare-associated infections caused by multidrug-resistant organisms?
5. What are the effectiveness and unintended effects of the patient safety practices and what new evidence has been published since the search was done for Making Healthcare Safer II (MHS II) and III (MHS III)?
6. What are the most common barriers and facilitators of implementing the patient safety practices?
7. What resources (e.g., cost, staff, time) are required for implementation?
8. What toolkits are available to support implementation of the patient safety practices?

2. Methods

We followed processes proposed by the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program.[9] The final protocol for this rapid review is posted on the AHRQ website at: https://www.ahrq.gov/research/findings/making-healthcare-safer/mhs4/index.html.

For this rapid review, strategic adjustments were made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. Adjustments included being as specific as possible about the questions, limiting the number of databases searched, modifying search strategies to focus on finding the most valuable studies (i.e., being flexible on sensitivity to increase the specificity of the search), and restricting the search to studies published recently (i.e., since 2011

when the search was done for the MHS II report) in English and performed in the United States. For this report, we screened all titles/abstracts and full-text articles by two independent reviewers. Conflicts were discussed and resolved during a team meeting.

We asked our content experts to answer Review Questions 1 and 2 by citing selected references that best answer the questions without conducting a systematic search for all evidence on the targeted harms and related patient safety measures or indicators. For Review Question 2, we focused on identifying relevant measures that are included in the Centers for Medicare & Medicaid Services (CMS) patient safety measures, AHRQ's Patient Safety Indicators, or the National Committee for Quality Assurance patient safety–related measures. We asked content experts to answer Review Questions 3 and 4 by citing selected references, including patient safety practices (PSPs) used and explanations of the rationale presented in the studies we found for Review Question 5. For Review Questions 6 and 7, we focused on the barriers, facilitators, and required resources reported in the studies we found for Review Question 5. For Review Question 8, we searched for publicly available patient safety toolkits developed by AHRQ or other organizations that could help to support implementation of the PSPs. To accomplish that task, we reviewed AHRQ's Patient Safety Network (PSNet) and AHRQ's listing of patient safety related toolkits and we included any toolkits mentioned in the studies we found for Review Question 5.[10,11]

2.1 Eligibility Criteria for Studies of Effectiveness

We searched for original studies and systematic reviews on Review Question 5 according to the inclusion and exclusion criteria presented in Table 2.

Table 2. Inclusion and exclusion criteria

Study Parameter	Inclusion Criteria	Exclusion Criteria
Population	Adult patients (18+ years)	Pediatric patients (under 18 years)
Intervention	• Barrier precautions • Cohorting of patients and/or staff • Decolonization of patients • Decontamination of hospital environment ○ Room cleaning interventions in patient-care wards/ICUs • Dedicated staff	• Surveillance testing (topic of another MHS IV chapter) • Hand hygiene-only interventions • Education-only interventions • Respiratory precautions (droplet, airborne, negative pressure airflow) • Decontamination of surgical/procedural environment (operating rooms) • Decontamination of reusable medical equipment (surgical/procedural/endoscopic equipment)
Comparator	Usual care or alternative transmission-based precautions	N/A

Study Parameter	Inclusion Criteria	Exclusion Criteria

Outcome	• Clinical outcomes
	  ○ Surveillance testing patients' status for nosocomial pathogens
	  ○ Clinical healthcare-associated infection
	• Provider outcomes
	  ○ Changes in provider behavior such as room entry or physical examination
	• Cost
	• Unintended effects
	  ○ Patient mental health, social isolation, satisfaction
	  ○ Noninfectious adverse healthcare-associated outcomes (hospital-acquired pressure injuries, inpatient falls)
		• Clinical outcomes specifically for:
		  ○ Central-line associated bloodstream infection (CLABSI)
		  ○ Catheter-associated urinary tract infection (CAUTI)
		  ○ Ventilator-associated pneumonia or events (VAP/VAE)
		  ○ Surgical site infection (SSI)
		  ○ COVID-19 infection
		  ○ Tuberculosis infection

Timing	• Outcome occurring
	  ○ During index/current stay in hospital/nursing home
	  ○ Up to 12 months after discharge from index hospitalization/nursing home stay
		Outcome occurring prior to admission to hospital/nursing home study location
		Outcome occurring longer than a year after discharge from index hospital/nursing home

Setting	Inpatient acute-care hospitals and nursing home care settings in the United States	• Outpatient care settings • Outside of traditional healthcare settings • Prison settings • Site not in the United States
Type of studies	• Systematic reviews • Randomized trials • Non-randomized trials • Case control studies • Controlled before-after studies • Interrupted time series studies and repeated measures studies • Discontinuation studies • Studies published since 2011	• Not published in English • Not original research • Other study designs (e.g., uncontrolled before-after studies or cross-sectional studies)

2.2 Literature Searches for Studies of Effectiveness

We searched PubMed, and Cochrane, supplemented by a narrowly focused search for unpublished reports that are publicly available from governmental agencies, professional societies, or membership organizations with a strong interest in the topic, including the Centers for Disease Control and Prevention (CDC), AHRQ, the National Institutes of Health, National Quality Forum, and American Hospital Association. For details of the search strategy, see Appendix A.

2.3 Data Extraction (Selecting and Coding)

The title and abstract of each citation were screened by two independent team members based on predefined eligibility criteria (Table 1). Two independent members reviewed the full text of each remaining potentially eligible article to confirm eligibility and extract data. All conflicts were resolved in team meetings. At data extraction, one team member extracted the data and a second team member checked the accuracy of the extracted data.

We prioritized our efforts by extracting detailed information from the highest-quality studies. We sought to extract information from good- or fair-quality systematic reviews, randomized controlled trials (RCTs), nonrandomized controlled trials (NRCTs), and observational studies with a comparison group. We listed relevant pre-post studies with limited information in Appendix B, but we did not synthesize them in the text of the results section.

Reviewers extracted available information and organized it according to the review questions and included the author, publication year, study design, setting, sample size, intervention, and outcomes.

Where the literature varied between organizing MDRO prevention either by specific organism or by specific interventions, we favored literature which discussed specific interventions, though even for systematic reviews focusing on an individual intervention, it was rare for the literature to study interventions in isolation rather than as components of combinations of PSPs.

2.4 Risk of Bias (Quality) Assessment

For RCTs, we used the items in the Cochrane Collaboration's tool that cover the domains of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[12] For nonrandomized studies, we used specific items in the Risk of Bias in Nonrandomized Studies – Interventions (ROBINS-I) tool that assess bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported results. The risk of bias assessments focused on the main outcome of interest in each study.[13]

For recent eligible systematic reviews, the primary reviewer used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[14]

- Good – Recent relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.
- Fair – Recent relevant review that is not clearly biased but lacks comprehensive sources and search strategies.
- Poor – Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

2.5 Strategy for Data Synthesis

Selected data was compiled into evidence tables and synthesized narratively. We did not conduct a meta-analysis. For Review Question 5 about the effectiveness of PSPs, we recorded information about the context of each primary study and whether the effectiveness of the PSP differed across patient subgroups. We graded the strength of evidence for PSPs with more than one primary study of effectiveness using the methods outlined in the AHRQ Effective Health Care Program Methods Guide for Effectiveness and Comparative Effectiveness Reviews and focusing on key clinical outcomes such as infection rate and changes in provider behavior.[15] To assess the strength of evidence for included systematic reviews, we either used the strength (or certainty) of evidence recorded by the original authors of the systematic review, or if this was not available we assessed it ourselves considering how many original studies were included in the review, whether the included studies were RCTs or observational studies or a mix of both, whether the synthesis of evidence in the systematic review was meta-analytic or narrative, the size of the intervention effect, the heterogeneity of the results, what the authors of the systematic review stated as limitations of their review, and lastly how the authors of the systematic review described their conclusions.

3. Evidence Summary

3.1 Benefits and Harms

- This rapid review identified 42 relevant studies, of which we ultimately included 10 systematic reviews and 9 primary studies (including 5 randomized controlled trials) that described the effects of various PSPs targeting the healthcare-associated transmission of MDROs, including clinical outcomes of HAI and acquisition of MDROs.
- About half of the systematic reviews included at least some prospective randomized controlled trials, though the literature underlying the reviews was predominantly comprised of before-after studies or quasi-experimental studies.
- About half of the systematic reviews included meta-analyses; where they did, pooled risk ratios rarely excluded the null when all groups were included (i.e., outside of subgroup analyses).
- As a result, though the included systematic reviews were of good to fair quality, the strength of evidence for individual PSPs was generally low.
- The literature varied in whether PSPs were applied to specifically target patients known to be infected or colonized with MDROs, or applied universally to all patients within high-risk contexts such as ICUs or local outbreaks.
- The literature we reviewed primarily related to MRSA, VRE, and *C. difficile*, and to a lesser extent addressed highly resistant gram-negative bacteria such as CRE or ESBL Enterobacterales. No literature addressed the emerging threat of *Candida auris*.
- The literature we reviewed included diverse patient safety practices that can broadly be divided into the categories of barrier personal protective equipment/contact isolation; patient and/or staff cohorting; patient decolonization; disinfection of the hospital environment; and infection prevention/control in nursing home settings. The literature which we reviewed during our search period did not show strong evidence to support nor refute current standards within these categories of patient safety practices in terms of effects on infection or acquisition of MDROs, nor did we identify strong evidence in the period of our review for unintended adverse effects of the PSPs.
- Patient decolonization practices had the most consistent demonstration of benefit, and can reduce MDRO infections in certain populations (Moderate strength of evidence), with a systematic review of daily chlorhexidine bathing in ICU patients showing reduced MDRO acquisition, a large RCT showing reduced MRSA infections and associated hospitalizations with an intensive and prolonged post-discharge decolonization protocol for patients known to

carry MRSA, and a large RCT showing reduced risk of hospitalization for infection and for any cause in nursing homes where universal decolonization was implemented for the duration of nursing home stays.

- Universal gloving has a small effect in reducing MDRO infections, mostly in the ICU setting (Low strength of evidence). A meta-analysis of universal glove use (with 6 of 8 included studies in the ICU setting) showed a small reduction in HAI incidence, but this benefit was not seen when the analysis was restricted to only RCTs.
- Contact precautions showed mixed evidence in the endemic setting in terms of reducing MDRO infections (Low strength of evidence). A systematic review showed that when contact isolation was de-implemented by hospitals for those patients infected/colonized by MDROs, the rates of related infection did not change significantly. In contrast, a large cohort study of Veterans Affairs hospitals showed higher rates of MRSA infections in hospitals where surveillance testing and contact isolation was halted for patients infected and/or colonized with MRSA, compared to hospitals where these practices were continued. Another discontinuation study in a single hospital showed no difference of infections and fewer non-infectious adverse events such as falls and pressure ulcers after stopping routine contact isolation for patients infected/colonized by MRSA or VRE.
- A meta-analysis found more anxiety and depression in patients who were in infectious isolation than in patients who were not isolated (Low strength of evidence); effects on other mental health outcomes were nonsignificant.
- A systematic review found cohorting was perhaps helpful in the context of outbreaks but of unclear benefit in endemic situations (Low strength of evidence).
- Systematic reviews found no significant benefits for automatic room decontamination interventions compared to manual decontamination (Low strength of evidence).\
- Infection prevention and control practices in nursing home settings had insufficient evidence of bejnefits (outside of patient decolonization – see above) (Low strength of evidence).

3.2 Future Research Needs

- Much of the current literature studies infection prevention and control practices that are bundled together in multicomponent interventions, which limits the strength of evidence for any individual practice. Evidence reviewed in MHS II and MHS III supports the use of such multicomponent infection control bundles. Recognizing that this means that individual infection control PSPs should not be used in absence of other infection control practices, future prospective studies should ideally standardize all other infection control

practices across study arms aside from the intervention of interest, rather than implementing multiple practice changes at once.

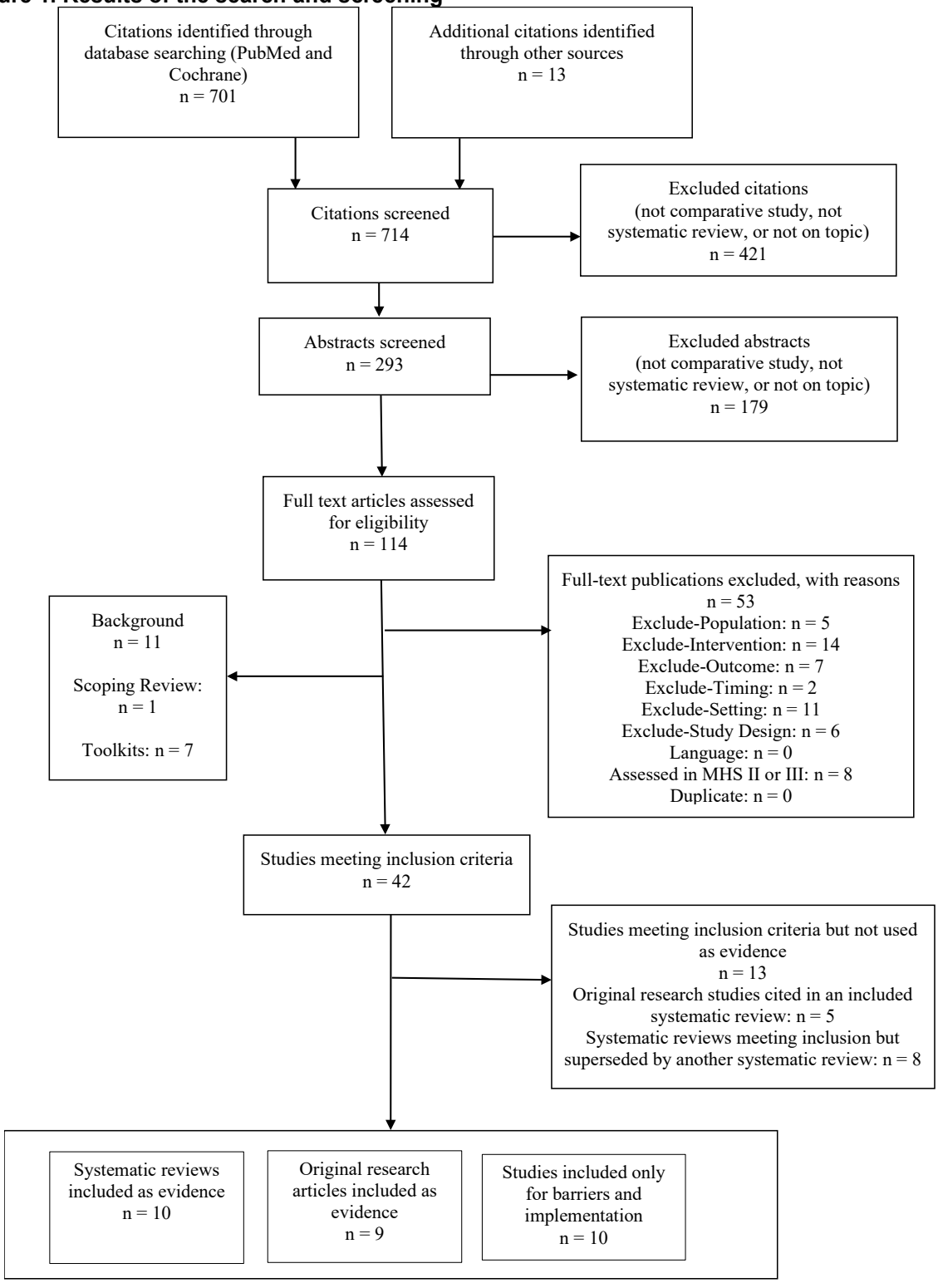
- The literature appears to be limited for the most dangerous, extremely drug-resistant organisms such as carbapenem-resistant bacteria and *Candida auris*. This is likely in part due to their relative rarity compared with more common drug-resistant pathogens such as MRSA and *C. difficile*, but it may also reflect the less robust systems for tracking and reporting these pathogens compared to the mandated, ubiquitous reporting standards dictated by CMS for MRSA bacteremia and *C. difficile* infection. More research is needed.

4. Evidence Base

4.1 Number of Studies

Our search retrieved 714 unique titles and abstracts from which we reviewed 114 full-text articles for eligibility (Figure 1). We found 42 studies that met our eligibility criteria.[16-57] A listing of studies excluded during full-text review is included in Appendix B, List of Excluded Studies, and information abstracted from each included study is provided in Table 2.

Figure 1. Results of the search and screening



4.2 Findings for Review Questions

4.2.1 Review Question 1. What Are the Frequency and Severity of Healthcare-associated Infections Caused by Multidrug-Resistant Organisms?

The most comprehensive estimates of U.S. burden of drug-resistant organisms come from the CDC's periodic Antibiotic Resistance Threat Reports, the most recent full version of which was published in 2019.[4] In the 2019 AR Threat Report, the CDC described a total estimated annual burden of 2.8 million infections from antibiotic-resistant bacteria resulting in 35,000 deaths, as well as an additional 223,900 hospitalizations for *C. difficile* infection with 12,800 deaths. While specific estimates are not made of the proportion of this burden which affects patients in acute care hospitals or nursing home settings, the data primarily comes from hospital lab data and medical records and so inherently reflect hospital-associated infections; the data do not capture non-hospitalized patients for most pathogens included in the report. The subsequent 2022 Special Report of COVID-19 Impact on Antimicrobial Resistance provides the most recent estimates of burden of individual MDR pathogens in the US, many of which have increased in context of the COVID-19 pandemic, though overall estimates of total MDRO infections are not updated from the 2019 report due to limitations in reporting system data from COVID-19.[5] As of the 2022 Special Report, MRSA causes an estimated 279,300 infections and 9,800 deaths annually in the US. Carbapenem-resistant Enterobacterales cause 12,700 infections and 1,100 deaths per year, while ESBL-producing Enterobacterales cause 197,500 cases and 9,300 deaths per year.

4.2.2 Review Question 2. What Patient Safety Measures or Indicators Have Been Used To Examine the Frequency and Severity of Healthcare-Associated Infections Caused by Multidrug-Resistant Organisms?

The National Healthcare Safety Network (NHSN) is the most robust system to track HAI, as CMS requires reporting of certain infection data to NHSN depending on the type of healthcare facility. Acute care hospitals have the most rigorous reporting requirements, including CLABSI, CAUTI, SSI following colon surgery or hysterectomy, and positive clinical lab tests for bloodstream MRSA and *C. difficile*.[58] Rates of MRSA and *C. difficile* lab events are available for public review at the facility level via the Hospital Compare tool available at medicare.gov/care-compare . Aside from the inherent MDRO data in the MRSA and *C. difficile* reporting, other NHSN HAI reports are to include culprit pathogen data including antimicrobial susceptibility whenever available, though this is not always reported;

for example, carbapenem susceptibility was reported with approximately three-quarters of *Enterobacterales* infections captured by NHSN used in the CDC's 2018-2021 HAI Pathogens and Antimicrobial Resistance Report.[59] NHSN reporting does not capture MDROs causing other non-reportable types of infections (for example, MRSA cellulitis unrelated to a central line or surgical site, or ESBL *E.coli* urinary tract infection without an indwelling catheter). Skilled nursing facilities are not currently required to report any infection prevention/control data to NHSN, aside from staff vaccination rates against influenza and COVID-19. The CDC has attempted to build more robust reporting mechanisms to track MDRO infections in the US since the first 2013 Antibiotic Resistance Threat Report, including the establishment in 2016 of the establishment of the Antimicrobial Resistance Lab Network.[60] Other reporting systems of possible relevance included the National Notifiable Disease Surveillance System[61] and the Emerging Infection Program.[62]

4.2.3 Review Question 3. What Patient Safety Practices Have Been Used To Prevent or Mitigate the Harms of Healthcare-Associated Infections Caused by Multidrug-Resistant Organisms and in What Healthcare Settings?

There are widely varying patient safety practices which have been used to prevent or mitigate harms of HAIs caused by multidrug-resistant organisms. These can be broadly divided into practices which directly address the interaction of patients, healthcare workers, and the healthcare environment, in addition to practices which indirectly address those interactions and seek to improve or facilitate direct safety practices. Direct interventions include the universal standard precaution of regular hand hygiene (not addressed in our review as evidence and utilization of this practice is widely accepted), use of personal protective equipment (PPE, typically in combination in context of standardized isolation precautions), distribution of patients and/or staff (patient flow and cohorting), decontamination of the healthcare environment (cleaning of hospital rooms and equipment), antimicrobial interventions for patients who have infections (antibiotic stewardship, addressed in another chapter of MHS IV) or are colonized (decolonization) with MDROs. There are also indirect patient safety practices which seek to improve performance or utilization of these direct measures, including education and training for healthcare workers and/or patients, tracking of patient colonization or infections with MDROs (for risk-stratification and guidance of application of direct practices, especially surveillance testing for asymptomatic MDRO colonization/carriage, which is addressed in another chapter of MHS IV), monitoring and review of adherence or success of direct measures (auditing and feedback), and overall supervision or support of these patient safety practices (dedicated infection prevention and control staff). Many of these practices apply across the spectrum of patient care settings, but our area of focus is on the acute

care hospital and nursing home settings where there are frequent and sustained interactions between patients, healthcare workers, and the healthcare environment.

4.2.4 Review Question 4. What Is the Reported Rationale for Using the Patient Safety Practices To Prevent or Mitigate the Harms of Healthcare-Associated Infections Caused by Multidrug-Resistant Organisms?

Many of the patient safety practices are intended to directly prevent the transmission of multidrug-resistant organisms via direct touch from people or surfaces carrying MDROs (colonized or infected patients/staff, or surfaces and objects contaminated by those people) to people or surfaces which do not already carry MDROs (at-risk patients/staff, or clean/uncontaminated objects or surfaces). This includes hand hygiene (removal of MDROs contaminating the hands of healthcare workers) and barrier-type PPE such as gloves and/or gowns, which directly separate healthcare worker skin and clothing from patient skin, body fluids, clothing, and the patient's room environment. The rationale for patient decolonization practices is to reduce or eliminate MDROs in the patient microbiome, typically using topical antimicrobial agents or antiseptics which are not widely used to treat clinical infection and are therefore unlikely to breed resistance to the antibiotics used in clinical treatment of infections. Decontamination of the healthcare environment seeks to kill MDROs harbored on surfaces and objects shared by multiple patients and healthcare workers in order to prevent the transmission of MDROs when that surface is later touched by another at-risk patient or healthcare worker. Safety practices related to patient flow and distribution are thought to limit or avoid altogether the interaction of at-risk patients/staff with those patients known to be colonized with MDROs; for example, patients known to be colonized with an MDRO might be cohorted together in a shared room or unit, as they are not at risk of acquiring the MDRO in question from each other, while at-risk patients who are not known to be infected or colonized with the MDRO of interest are admitted preferentially to a different room or unit. Contact isolation precautions as defined by the CDC include components of patient flow/cohorting, use of PPE (gloves and gowns), and appropriate room cleaning/environmental decontamination.[63]

The rationales for antibiotic stewardship safety practices are fundamentally different and address in vivo evolution of MDROs under selective pressure from antibiotics, but we will defer further discussion to our colleagues who are focusing on antibiotic stewardship in a separate chapter of MHS IV.

The rationale for surveillance testing is to identify patients colonized with a given MDRO in order to guide patient cohorting as well as to select patients for targeted application of isolation precautions/PPE use, decolonization, additional decontamination/room cleaning, with intent to achieve more efficient or cost-effective selective application of those practices; while knowledge of infection or

colonization status is relevant to the PSPs of our focus, surveillance testing as a PSP itself is addressed in another chapter of MHS IV.

The common rationale for many of the patient safety practices that indirectly affect MDRO transmission is to improve the utilization or performance of the direct PSPs discussed above. This includes education, training, monitoring/auditing, and feedback practices that often focus on correct or consistent hand hygiene, PPE use, or environmental cleaning. This same rationale applies to the practice of designating specific healthcare staff who are dedicated experts in infection prevention and control practices, whose work often supports educational, monitoring/auditing, and feedback practices, which in turn seeks to continuously improve quality and adherence to direct infection prevention and control patient safety practices.

4.2.5 Review Question 5. What Are the Effectiveness and Unintended Effects of the Patient Safety Practices and What New Evidence Has Been Published Since the Search Was Done for Making Health Care Safer II (MHS II) and III (MHS III)?

We identified 10 good- or fair-quality systematic reviews about interventions of interest,[17,18,22,25,35,37,48,50,53,56] and an additional 9 original research studies.[20,28,36,41,44-46,51,52] We excluded 8 systematic reviews that otherwise met eligibility criteria because they were superseded by a more recent or more relevant systematic review,[16,21,23,26,30,32,39,40] We also excluded 5 original research studies because they were included in a systematic review that we include[24,29,33,38,42] We next discuss the specific interventions covered in the included studies. Results will be presented in the following order: first we will discuss specific interventions, then we will discuss adverse effects of isolation, and finally we will shift to review the literature surrounding infection prevention and control practices in nursing home settings.

4.2.5.1 Universal Gloving

Universal gloving refers to the use of disposable gloves when caring for all patients in a given setting regardless of infection or colonization status, such as all patients admitted to a given facility or ward. Our literature search identified one new systemic review about the effectiveness of universal gloving on HAIs.[22] This review, which we judged to be good quality, searched through July 2018 and identified 8 eligible studies, 4 of which were randomized controlled trials and 4 were controlled before-and-after studies. Five studies focused on MRSA and VRE (with one of these also including carbepenem-resistant *Klebsiella*, and another study also including CAUTI), and the remaining 3 studies assessed all HAIs. Four studies were of universal gloving as a sole intervention—2 studies focused on universal

gloving and gowning, 1 study added modified contact precautions, and the last study focused on universal gloving as part of a bundle. Six of the eight studies were done in ICUs. Three studies were in pediatric populations. Random effects pooled analyses of all 8 studies yielded an incidence rate ratio of 0.89, 95% confidence interval (CI) 0.72, 1.10, with an I2 statistic of 59%. Stratified analyses by study design, intervention type (universal gloving alone or as part of multiple interventions), pathogen, or ward yielded random effects pooled incidence rate ratios of between 0.75 and 1.01, with 95% CIs that either slightly included or slightly excluded the null. The strongest observed effect was reduction of infections in pediatric ICUs (pooled incidence rate ratio = 0.75; 95% CI 0.65, 0.87). The authors concluded that "universal gloving was associated with reduced incidence of HAIs. However, the results were not statistically significant when only RCTs were pooled." We assessed the strength of evidence from this review as Low that universal gloving reduced HAIs.

Our search did not identify any new original research articles related to universal gloving for prevention and control of MDROs.

4.2.5.2. Contact Precautions

Our search identified a single original research article which addressed contact isolation.[20] Bessesen and colleagues performed a nonrandomized head-to-head trial comparing different isolation strategies for hospitalized adults known or found to be infected or colonized with MRSA, with one strategy employed at each of two VA hospitals. One hospital (hospital A) observed contact isolation for MRSA-positive patients with use of gown and gloves for all encounters, while the other hospital (hospital B) observed upgraded standard precautions for MRSA-positive patients including gloves for all encounters with addition of a gown only if anticipating contact with blood, body fluids, secretions, or excretions. Surveillance MRSA nares testing varied slightly between hospitals during the study period, with both using PCR screening at admission, but hospital A used surveillance cultures at transfer, death, discharge, and weekly, while hospital B used PCR at transfer, death, and discharge but not weekly. During the 4-year study, the authors saw no difference in MRSA acquisition (159 events in 100,559 patient-days with incidence density of 1.58 per 1,000 patient-days at hospital A, versus 145 events in 92,741 patient-days with incidence density of 1.56 per 1,000 patient-days at hospital B, p=0.98) nor in MRSA hospital-acquired infection (incidence density of 0.19 per 1,000 patient-days at hospital A versus 0.16 per 1,000 patient-days at hospital B, p=0.78), in the context of similar prevalence of MRSA infection or colonization at admission (11.9% at hospital A, 12.7% at hospital B). Gown costs were estimated from total consumption and a standard unit price, resulting in annual gown costs of $183,609 at hospital A and $25,812 at hospital B.

4.2.5.2.1. Studies of Discontinuation of Contact Precautions

Our literature search identified 1 recent systematic review and meta-analysis of studies that assess the effect of discontinuing contact precautions[37] along with 1 newer study not included in that systematic review.[41] An additional study, assessing the effect of contact precautions on MRSA and VRE infections but not meeting some eligibility criteria for this review,[64] was also identified and is briefly mentioned. Finally, an additional original study was published after the date of our original search but identified during peer review.[28]

The systematic review,[37] which we judged to be of good quality, searched through August 2019 and identified 17 studies meeting eligibility criteria, of which 12 studies provided data for the meta-analytic synthesis. Eligible studies had to evaluate the discontinuation of routine use of contact precautions for patients infected or colonized with multidrug-resistant organisms. Two studies were about device-associated HAI rates, and the other 15 studies targeted hospitalwide MRSA or VRE or both. The studies evaluated discontinuation of routine contact isolation for patients infected or colonized with VRE in two studies, with MRSA in six studies (one of which continued to isolate infected but not colonized patients), with either MRSA or VRE in eight studies, with either MRSA or ESBL-E in one study, and with MRSA, VRE, or ESBL-E in one study. All but two studies were from the United States, and 15 of the 17 studies were quasi-experimental pre-post assessments. Ten of the studies reported compliance with an alternative intervention after discontinuation of contact precautions, such as hand hygiene, bare-below-the-elbows, or chlorhexidine bathing. About half of studies continued active microbial surveillance. In a pooled analysis of data from 11 studies, there was no statistically significant difference in MRSA infection rates (random effects risk ratio = 0.84 in favor of stopping contact precautions, 95% CI 0.71, 1.01) with negligible heterogeneity and no evidence of publication bias. A pooled analysis of data from 7 studies showed a statistically significant difference in VRE infection rates favoring stopping contact precautions (random effects risk ratio = 0.81; 95% CI 0.71, 0.94), again with negligible heterogeneity and no evidence of publication bias. These data fall short of proof that contact precautions are ineffective, but neither do they support a conclusion that contact precautions are effective. Additional research is needed. We assessed the strength of evidence from this review as Low.

An additional study,[41] reporting outcomes not included in the above systematic review (but whose data on MRSA and VRE infections are included in the above meta-analytic results), was identified. In this study, reportable noninfectious adverse events that can be influenced by provider contact time were defined as postoperative respiratory failure, hemorrhage/hematoma, thrombosis, wound dehiscence, pressure ulcers, and falls/trauma. Comparing rates prior to and after discontinuation of routine contact precautions, there was no change in the rate of infectious adverse events (CLABSI, *C. difficile* infection, postoperative sepsis, CAUTI, and VAP) whereas the rate of noninfectious adverse events decreased a statistically significant 19 percent. The authors speculate that contact precautions

may have been a barrier to healthcare provider access to inpatients and this contributed to higher non-infectious adverse event rates with use of routine contact isolation.

Finally, a recently published large prospective cohort study compared differences in hospital-acquired MRSA infection in all 123 Veterans Affairs acute-care hospitals nationally, after each facility was given the policy choice to discontinue use of any combination of active surveillance testing for MRSA (AS), contact isolation for patients colonized with MRSA (CPC), and contact isolation for patients infected with MRSA (CPI) (in context of the COVID-19 pandemic, in consideration of need to conserve isolation supplies).[28] Over the 24-month study period and a total of 5,225,174 patient-days, higher facilitywide rates of MRSA HAI were observed when all three of these practices were discontinued (0.22 MRSA HAI per 1000 patient-days with no AS or CPC or CPI), compared to continued use of any combination (or all) of these practices (between 0.09 to 0.12 MRSA HAI per 1000 patient-days depending on which practices were continued; $p<0.05$ for any combination when compared to no AS or CPC or CPI). Discontinuing all three practices (no AS or CPC or CPI) also showed higher rates of MRSA HAI compared to continuing all three practices (AS+CPC+CPI) in ICU patients (0.65 vs 0.20 MRSA HAI per 1000 patient-days; $p<0.001$) and non-ICU patients (0.12 vs 0.07 MRSA HAI per 1000 patient-days; $p=0.01$). Again comparing between discontinuing all practices (no AS or CPC or CPI) to continuing all practices (AS+CPC+CPI), rates of MRSA bloodstream infections were higher facility-wide (0.09 vs 0.03 per 1000 patient-days, $p<0.001$), in ICU patients (0.26 vs 0.06 per 1000 patient-days, $p<0.001$), and non-ICU patients (0.05 vs 0.02 per 1000 patient-days, $p=0.01$). There was no change in the relationship between combination of practices used and rate of MRSA HAI after accounting for facility complexity and current COVID-19 rates using a negative binomial regression model.

Overall, we conclude that the evidence is mixed for routine use of contact precautions for reducing MDRO infections in the endemic setting, and strength of evidence is Low.

4.2.5.3. Cohorting

Our literature search identified one new systematic review about the effect of cohorting patients to reduce the incidence of *C. difficile* infections and other multidrug-resistant organisms.[17] Cohorting was defined as the practice of grouping together patients who are colonized or infected with the same organism to confine their care to one area, to prevent contact with other susceptible patients. This review, which we judged to be of good quality, searched through November 2019 and identified 87 eligible studies. There were no randomized trials, with 49 studies being retrospective and 35 studies being controlled before-and-after studies. Most studies (74%) were performed in the setting of an outbreak. About 25 percent of

studies were about MRSA, 25 percent were about CRE or ESBL-E, about 20 percent were about VRE, and 7 percent were about *C. difficile.* Sixty percent of studies cohorted both patients and staff. The synthesis of results was narrative. In general studies reported decreased rates of infection after implementing cohorting, although this was not always the case, and the cohorting was usually implemented along with other infection control practices simultaneously rather than as a single intervention. The authors concluded that cohorting "may be a reasonable strategy as part of multimodal approach to curtailing MDRO outbreaks," which we assessed the strength of evidence from this review as Low. They added "whether it is an effective strategy in endemic situations is unknown," a conclusion for which we assessed the strength of evidence as Very Low.

Our search did not identify any new original research articles related to patient cohorting for prevention and control of MDROs.

4.2.5.4. Environmental Decontamination

In a journal article derived from work for Making Healthcare Safer III, Schoyer and colleagues examined the evidence regarding environmental cleaning strategies on reducing *C. difficile* infection rates.[53] This review, which we judged of fair quality, conducted a search through 2018 and identified 12 eligible studies, using four categories of disinfecting agents: bleach-based, hydrogen peroxide, UV light, and one study of launderable bed covers. All studies were before-and-after studies. The synthesis was narrative. The authors concluded that facility-level infection rates significantly decreased with environmental cleaning and decontamination interventions, but that study designs were weak. Although the authors did not formally judge the certainty of evidence, their narrative description indicates it could be no higher than Low certainty evidence.

Our literature search identified one recent systematic review about the effects of environmental decontamination.[25] This review searched through March 2020 to find studies of automated technologies using either hydrogen peroxide or UV light on cleaning and disinfecting hospital surfaces. This review, which was judged to be good quality, identified 43 eligible studies. About half of studies used peroxide and the other half used UV light, although all studies in the setting of an outbreak used peroxide. Almost all studies were before-and-after studies. There was one cluster randomized trial, and 4 controlled studies. Pathogens were a mix of organisms including MRSA (37% of studies), VRE (33% of studies), *C. difficile*, (63% of studies) CRE, MDRO in general, and other organisms. The synthesis of results was narrative. The authors discussed in detail a number of methodologic and analytic problems with studies, including the use of historical controls, the problem of confounders, the role of industry in funding studies, and how data were analyzed. While the authors concluded that there were clear benefits from non-touch devices in vitro, the authors concluded that there was insufficient evidence of benefit with automated room cleaning technologies over-and-above traditional manual cleaning

practices, which they recognized as already established as effective. We assessed the strength of evidence for their conclusions from this review as Low.

Our search identified one original research article addressing environmental decontamination,[51] as well as another original research article which used antimicrobial materials to address room contamination,[52] Details are in the evidence table (Table 2).

Ray and colleagues performed a randomized controlled trial[51] in 15 acute care hospitals (1 additional hospital assigned to the intervention arm dropped out after randomization but before the study began) which compared usual care with a fluorescent-marker-based monitoring and feedback protocol for environmental services staff performing hospital room cleaning, with an emphasis on rooms used for *C. difficile* isolation. Room cleaning was performed using bleach wipes at all hospitals. In the intervention arm, a fluorescent marker was used to assess cleaning of several high-touch surfaces in *C. difficile* isolation rooms (daily and post-discharge cleaning) and in non-*C. difficile* rooms (post-discharge cleaning only). The intervention arm showed a marked decrease in post-discharge high-touch surface *C. difficile* culture rates between baseline and intervention periods in *C. difficile* rooms, but room surface cultures after cleaning did not correlate with rates of *C. difficile* infection nor translate into overall changes in *C. difficile* infection rates.

Salgado and colleagues performed a small randomized controlled trial[52] in three ICUs, comparing copper vs standard materials for several high-touch surfaces in patient rooms, predicated on the antimicrobial properties of copper as a strategy for environmental self-decontamination. Patients were enrolled at ICU admission and followed until hospital discharge. The primary outcome was a composite of any hospital acquired infection or acquisition of MRSA or VRE colonization, which occurred in 7.1% of patients (21 of 294) in the intervention arm vs 12.8% (41 of 320) in the control arm (p=0.02). The secondary outcome of hospital-acquired infection alone occurred in 3.4% (10 of 294) of patients in the intervention arm versus 8.1% (26 of 320) in the control arm (p=0.013), though rates were not standardized to patient-days and sample size was small.

Overall, we conclude that certain environmental decontamination practices may reduce MDRO infections, but strength of evidence is Low.

4.2.5.5. Patient Decolonization

Our literature search identified three systematic reviews of use of chlorhexidine wipes or baths to reduce hospital-acquired infections.[18, 35, 48] The most recent of these, which we judged to be of good quality, searched through 2014 for studies of daily chlorhexidine bathing in the ICU.[35] The search yielded 15 eligible studies, of which 3 were RCTs. Although primarily focused on the outcomes of CLABSI, CAUTI, and VAP, the review did find one RCT and seven controlled before-and-after studies that measured MRSA acquisition and a pooled analysis resulted in a fixed effects risk ratio of 0.78 (95% CI 0.68, 0.91) favoring chlorhexidine bathing.

The I2 statistic was 12 percent. A pooled analysis of one RCT and four controlled before-and-after studies that measured VRE acquisition showed a random effects pooled risk ratio of 0.56 (95% CI 0.31, 0.99) favoring chlorhexidine bathing. The I2 statistic was 67 percent. The authors concluded that their data "suggest that daily chlorhexidine bathing can significantly reduce healthcare associated infections in ICUs." We assessed the strength of evidence of this conclusion as Low. Their conclusion was consistent with the conclusions of the two older reviews,[18, 48] that also assessed use in long term care and obstetric contexts in addition to the ICU.

Our search identified two original research articles addressing decolonization[36,45] and a third study published after our search date was identified during peer review.[46]

Huang and colleagues performed a randomized controlled trial[35] in 24 centers (17 acute care hospitals, 7 nursing homes) comparing post-discharge patient hygiene education alone (n=1,063) to patient education plus a 6-month decolonization regimen (n=1,058), for adult patients who tested positive for MRSA during the recruitment hospitalization. The post-discharge decolonization protocol comprised daily bathing or showering with 4 percent chlorhexidine, twice-daily chlorhexidine mouthwash, and twice-daily nasal mupirocin which were completed for 5-day periods, repeating twice per month for the 6 months after discharge from enrollment hospitalization. Over 1 year of followup, the decolonization arm showed 30 percent lower risk of the primary outcome of MRSA infection according to CDC criteria (HR 0.70; 95% CI, 0.52 to 0.96, P=0.03), corresponding to MRSA infection rate of 0.098 per participant-year in the decolonization arm versus 0.139 per participant-year in the education-only arm. The investigators also reported a 29 percent lower risk of the secondary outcome of hospitalization due to CDC-defined MRSA infection (HR 0.71; 95% CI, 0.51 to 0.99). There were 17% fewer clinically-judged infections due to any pathogen in the decolonization arm (HR 0.83; 95% CI, 0.70 to 0.99) resulting in fewer hospitalizations due to any infection in the decolonization arm (HR 0.76; 95% CI, 0.62 to 0.93), though the difference in any-cause infection did not reach statistical significance when using CDC criteria for infection (HR 0.84; 95% CI, 0.70 to 1.01). Because only 65 percent of the intervention arm were fully adherent to this intensive decolonization protocol, results were analyzed both per protocol as well as as-treated based on level of adherence, but we did not include any as-treated analyses as incomplete adherence would be expected in real clinical practice with an outpatient multicomponent protocol lasting 6 months after discharge.

Mehta and colleagues performed a controlled before-and-after study[45] in a single orthopedic hospital which compared rates of MRSA prevalence density before and after implementation of a protocol of universal preoperative decolonization prescribed at outpatient preoperative visits, along with in-hospital perioperative antibiotic choice guided by preoperative MRSA nares screening in patients undergoing elective arthroplasty or spine fusion. Decolonization comprised twice-daily nasal mupirocin for 5 days before surgery and preoperative

chlorhexidine bathing (chlorhexidine shower the night before surgery initially, later modified to chlorhexidine wipes night before and morning of surgery). The authors report a reduction of the prevalence density of unique clinical MRSA culture results (excluding any surveillance testing as well as serial positive cultures of infected patients) in their orthopedic hospital from 1.23 per 1,000 patient-days before implementation (79 positive cultures, 64,327 patient-days, over a 21-month period) versus 0.83 per 1,000 patient-days in the implementation period (53 positive cultures, 63,860 patient-days, over 20-month period) (p=0.026). Comparison was made over the same time period to their affiliated nearby university hospital where the decolonization protocol was not implemented; no difference was seen in MRSA prevalence density in the university hospital comparing the baseline period to the implementation period (1.27 vs 1.24 per 1000 patient-days, p=0.787). However, the authors could not conclude that the decrease seen with the decolonization protocol could be entirely attributed to mupirocin decolonization alone, as there were several other interventions included in this protocol. MRSA nares cultures obtained at outpatient preoperative visits were also used to determine choice of perioperative antibiotic prophylaxis at time of surgery (vancomycin for MRSA-positive, cefazolin for MRSA-negative patients unless allergic in which case clindamycin was used). Also, patients who did not adhere to the preadmission mupirocin decolonization protocol and grew any *Staph aureus* (MRSA or MSSA) on their preoperative nares surveillance cultures were prescribed the 5-day nasal mupirocin course postoperatively during hospitalization, and the subset whose cultures grew MRSA were also placed in isolation precautions upon hospitalization (isolation precautions were not specified but presumably referred to contact precautions).

Finally, a recent cluster-randomized controlled trial compared routine bathing to chlorhexidine bathing plus nasal povidone-iodine in nursing home patients.[46] Twenty-eight nursing homes were randomized to either routine care or decolonization protocol comprising chlorhexidine for all routine bathing/showering plus nasal povidone-iodine used twice daily for 5-day periods (at admission and repeating every two weeks throughout duration of nursing home stay), and all nursing homes were observed during 18-month baseline period which was then compared to the 18-month intervention period, altogether accounting for 3,109,607 patient-days. When comparing rates of hospital transfer due to infection between the intervention to baseline periods, the nursing homes in the control arm saw no difference (risk ratio 1.00, 95% CI 0.96-1.04) while the decolonization arm saw a reduced risk ratio of 0.83 (95% CI 0.79-0.88), resulting in a difference in risk ratio of 16.6% (95% CI 11.0-21.8). Similarly, there was a difference in risk ratio of 14.6% (95% CI 9.7-19.2) favoring decolonization over routine care in terms of risk of hospitalization due to any cause when comparing intervention to baseline period.

Overall, we conclude that patient decolonization can reduce MDRO infection in certain populations (Moderate strength of evidence).

4.2.5.6. Adverse Effects of Isolation

Our literature search identified one newer review on the adverse effects of isolation.[50] This review, which we judged to be fair quality, searched through 2018 for studies assessing the psychological or nonpsychological outcomes in adult patients who are in infectious isolation. The search identified 26 studies meeting eligibility criteria. Fourteen of these studies were performed in the United States, three were performed in Canada, and one study came from both countries. Most studies did not list the infection for which patients were being isolated, but of those that did, 5 studies were about patients in isolation for MRSA and 1 study was about patients in isolation for MDRO. The synthesis was both meta-analytic for the outcome of anxiety and depression, and narrative for all other outcomes. Eight studies reporting anxiety outcomes that were pooled using a random effects model yielded a standardized mean difference of 1.45 (95% CI 0.56, 2.34) favoring higher anxiety when isolated. There was significant heterogeneity (I2=96%). Similarly, for depression, the random effects pooled estimate of 8 studies yielded a standardized mean difference of 1.28 (95% CI 0.47, 2.09), meaning more depression when isolated. Again, there was significant heterogeneity (I2=96%). For the remaining psychological outcomes, such as confusion, worry, and sadness, the authors note that "infective isolation precautions make little difference to psychological outcomes, [but] where it does make a difference this is primarily negative". Similarly for non-infectious outcomes like falls, pressure ulcer, "any adverse event", the authors conclude "there was a trend" for more "errors" to occur in those who are isolated. They concluded that "there are a number of apparently negative aspects to contact precautions." We assessed the strength of evidence from this review as Low for their conclusions.

Our search did not identify any new original research articles related to adverse effects of isolation precautions used for prevention and control of MDROs, aside from the study by Martin and colleagues, discussed in section 4.2.5.2.1, which showed a statistically-significant 19% decrease of non-infectious adverse events (including falls, pressure ulcers, hemorrhage, thrombosis, and post-operative respiratory failure, and wound dehiscence) after halting routine use of isolation precautions for MRSA and VRE.[41] Overall, we conclude that noninfectious, nonpsychological adverse events may be higher in patients in infective isolation compared to patients who are not isolated, but strength of evidence is Low.

4.2.5.7. Infection Prevention and Control Practices in Nursing Home Settings

Our literature search identified one newer systematic review of infection control approaches for MDRO in long term care facilities.[56] This review, which we judged to be of good quality, searched through 2020 and focused on MRSA, VRE, multidrug-resistant gram negative bacteria including ESBL *Enterobacterales* and

CRE, and *C. difficile*. The search identified 19 studies meeting their inclusion criteria of which 11 contributed data to their main analysis: 5 were randomized trials, one was a controlled before-and-after study, and 5 were uncontrolled before-and-after studies. Interventions were classified into 8 categories and then whether they were horizontal or vertical, with horizontal interventions being administrative engagement, education, environmental cleaning, hand hygiene, performance improvement, and source control. Decolonization of colonized subjects was classified as a vertical intervention. The authors pooled analysis of data from 11 studies reporting on MRSA infections showed no statistically significant effect of infection prevention and control practice (for example, for interventions of long duration, the pooled random effects relative risk reduction was 0.81, 95% CI of 0.60, 1.10). Subgroup and sensitivity analyses in general also showed no statistically significant effect, one exception being active surveillance and decolonization in one subgroup of studies (pooled random effects RR = 0.34, 95% CI 0.22, 0.53). The authors concluded that there were no statistically significant beneficial effects from infection prevention and control practices on MRSA infection rates in long-term care facilities, highlighting the need for more research. While the authors did not formally assess the certainty of evidence of their conclusion, they do say the "evidence was overall low in quality," and we assessed the strength of evidence for their conclusion about infection control practices and MRSA rates as Low.

Our search identified one new original research article addressing prevention and control of MDROs in long-term care facilities.[44] We discussed a separate randomized controlled trial of patient decolonization in nursing homes in section 4.2.5.5 Patient Decolonization, above.

McConeghy and colleagues performed a randomized pair-matched controlled trial in 10 nursing homes comparing usual care to implementation of a multimodal bundle of infection prevention and control interventions, including staff education, provision of handwashing and cleaning products, and auditing and feedback using a dashboard reporting clinical infection rates as well as surveillance cultures from high-touch surfaces. Primary outcomes were related to staff satisfaction and hand hygiene compliance which are not relevant to our review, but relevant secondary outcomes included any infection, lower respiratory infection, antibiotic starts, and hospitalization. The authors report statistically significant reductions in absolute rates of total infections (2.9 +/- 1.3 in intervention facilities vs 4.1 +/- 2.2 in control facilities, p=0.03) and lower respiratory infections (0.8 +/- 0.6 in intervention facilities vs 1.5 +/- 1.2 in control facilities, p=0.01), though these reductions did not reach significance in difference-in-difference analysis. Antibiotic starts and hospitalization did not show statistically significant differences between intervention and control arms.

Overall, we conclude that infection prevention and control practices in long term care facilities (outside of patient decolonization, as described above) have not

to date found effects on rates of MDRO infections in the endemic setting, but strength of evidence was Low.

Table 3. Evidence table for included original research studies

Author, Year	Study Design	Setting	Sample Size	Intervention	Outcome
Bessesen et al, 2013[20]	Non-randomized head-to-head	2 acute care hospitals (one per arm)	193,300 patient-days across both sites	Contact isolation (gloves + gown for all room entry) vs upgraded standard precautions (gloves for room entry, + gown for contact with body fluids) for patients infected/colonized with MRSA	No difference in incidence density of MRSA acquisition (1.58 vs 1.56 per 1000 patient-days, p=0.98) or MRSA hospital-acquired infection (0.19 vs 0.16 per 1000 patient-days, p=0.78). Annual gown costs higher with contact isolation strategy ($183,609 vs $25,812)
Evans et al, 2023[28]	Prospective cohort analysis of non-randomized discontinuation of study practices	123 acute care hospitals (all Veterans Affairs hospitals)	5,225,174 patient-days	Optional discontinuation of any combination of MRSA active surveillance testing (AS), contact precautions for patients colonized with MSRA (CPC), and/or contact precautions for patients infected with MRSA (CPI)	Higher hospital-wide MRSA HAI rate when all three practices were discontinued (no AS or CPC or CPI) compared to continuing any combination of these practices (0.22 vs. 0.09-0.12 MRSA HAI per 1000 patient-days, p<0.05). Discontinuing all three practices (no AS or CPC or CPI) showed higher rates of MRSA HAI compared to continuing all three practices (AS+CPC+CPI) both in ICU patients (0.65 vs 0.20 MRSA HAI per 1000 patient-days, p<0.001) and non-ICU patients (0.12 vs 0.07 MRSA HAI per 1000 patient-days, p=0.01).

Author, Year	Study Design	Setting	Sample Size	Intervention	Outcome
Huang et al, 2019[36]	Randomized controlled trial	24 centers (17 acute care hospitals, 7 nursing homes)	2121 patients	Post-discharge hygiene education alone vs patient education plus decolonization protocol (chlorhexidine mouthwash and bathing; nasal mupirocin) repeated in 5-day courses twice per month for 6 months	Over one year follow-up, decolonization arm had 30% lower risk of CDC-defined MRSA infection (HR 0.70; 95% CI, 0.52 to 0.96); 29% lower risk of hospitalization for MRSA infection (HR 0.71; 95% CI 0.51 to 0.99); 17% lower risk of any clinically-judged infection (HR 0.83; 95% CI, 0.70 to 0.99; not significant when using CDC criteria); 24% lower risk of hospitalization for any infection (HR 0.76; 95% CI, 0.62 to 0.93)
Martin et al, 2018[41]	Discontinuation study (before/after)	Single acute care hospital	50,268 patient-days	De-implementation of routine use of contact isolation precautions for patients infected or colonized with MRSA and/or VRE	Noninfectious adverse events (postoperative respiratory failure, hemorrhage/hematoma, thrombosis, wound dehiscence, pressure ulcers, falls/trauma) decreased by 19% (12.3 to 10.0 per 1000 admissions, p=0.022) [Infectious outcomes were included in a relevant systematic review.]
McConeghy et al, 2017[44]	Randomized controlled trial	10 nursing homes (5 per arm, pair-matched)	861 patients at baseline	Multi-component infection prevention/ control bundle with staff education, sanitation supplies, and auditing/ feedback dashboard for infection rates and high-touch surface cultures, vs usual care	Total infections 2.9 vs 4.1 per 1000 patient-days (p=0.03), lower respiratory infections 0.8 vs 1.5 per 1000 patient-days (p=0.01); neither reached significance in difference-in-difference analysis. No difference in antibiotic starts or hospitalization.
Mehta et al, 2013[45]	Controlled before-after study	Single orthopedic acute care hospital; control affiliated university hospital	128,187 patient-days	Preoperative decolonization protocol (nasal mupirocin and chlorhexidine prior to admission) plus screening MRSA nares cultures to determine perioperative antibiotic choice	Clinical MRSA culture prevalence density reduced from 1.23 to 0.83 per 1000 patient-days (p=0.026) while control hospital saw no difference over timeframe (1.27 vs 1.24 per 1000 patient-days, p=0.787)

Author, Year	Study Design	Setting	Sample Size	Intervention	Outcome
Miller et al, 2023[46]	Cluster randomized controlled trial	28 nursing homes (14 in each arm)	3,109,607 patient-days	Routine bathing vs use of chlorhexidine for all bathing/showering plus nasal povidone-iodine twice daily for 5 day periods (at admission then every other week)	Comparing intervention to baseline period, risk ratio for transfer to hospital due to infection was 1.00 in routine care arm vs 0.83 in decolonization arm (difference in risk ratio 16.6%, 95% CI 11.0-21.8), and risk ratio for transfer to hospital for any reason was 1.08 in routine care arm vs 0.92 in decolonization arm (difference in risk ratio 14.6%, 95% CI 9.7-19.2).
Ray et al., 2017[51]	Randomized controlled trial	15 acute care hospitals (one additional hospital dropped out after randomization)	Not reported	Fluorescent marker room cleaning monitoring and feedback for environmental services staff, vs usual care	No difference in hospital-acquired *C. difficile* infection at intervention hospitals before vs after protocol implementation
Salgado et al., 2013[52]	Randomized controlled trial	3 intensive care units	614 patients	Copper vs standard materials for high-touch surfaces in ICU rooms	Hospital acquired infection and/or acquisition of MRSA or VRE colonization 7.1% vs 12.3% (p=0.02); Hospital acquired infection only 3.4% vs 8.1% (p=0.013)

Abbreviations: CDC = Centers for Disease Control and Prevention; CI= confidence interval; HR = hazard ratio; ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *enterococcus*

Table 4. Characteristics of included systematic reviews

Author, Year Search Dates	Number of Included Studies (Included Study Designs)	Healthcare Setting(s)	Organisms	Outcomes of Interest	Key Findings	Quality of Review
Abad, 2020[17] Nov 30 2019	87 (all observational)	Hospital	Cohorting 60 studies cohorted patient and staff, 27 studies cohorted patients alone Multiple MDRO (C.diff, MRSA, VRE, CRE, Acinetobacter)	Infection or colonization Infection for C diff, infection for MRSA, infection for VRE. CBE and ESBL and more	Effect of cohorting on C diff and MRDO 77 of 87 studies showed a decline in infection or colonization rates after a multifaceted approach that included cohorting. 65 of 87 studies were in the setting of an outbreak and thus evidence is less certain for endemic settings	Good
Afonso, 2013[18] 11/1/2012	15 (9 RCTs)	Hospital Settings included intensive care, hospital, and pre-surgical settings. (5 studies about pediatric populations)	Chlorhexidine wipes Multiple (Acinetobacter, Klebsiella, Psuedomonas, E.coli, *C. difficile*, other MDRO unspecified	Infection or colonization outcomes (HAIs, VAP, CABSI, BSI)	Most included studies favor the use of chlorhexidine wipes to prevent the spread of pathogens, including MDRO	Good

Author, Year Search Dates	Number of Included Studies (Included Study Designs)	Healthcare Setting(s)	Organisms	Outcomes of Interest	Key Findings	Quality of Review
Chang, 2019[22] July 9 2018	8 (4 RCTs)	Hospital + LTC (mostly ICU, includes 2 pediatric studies)	Universal gloving Multiple MDRO (MRSA, VRE, C.diff)	HAI HAI (mostly but not only MRSA, VRE, C diff)	Pooled analysis of 7 studies of universal gloving showed a reduced incident rate ratio of 0.80 (95% confidence interval 0.67, 0.80). Stratified analyses showed no statistically significant association of the intervention in adult ICUs, whereas results were statistically significant in the pediatric ICU setting. Restricting the analysis to only RCTs resulted in a nonsignificant result	Good
Dancer, 2021[25] 3/1/2020	43 (1 RCT)	Hospital + LTC	Decontamination devices (UV, hydrogen peroxide) Multiple (C.diff, MRSA, CRE, MDRGN, VRE)	HAI rates Infection	Automated decontamination devices (hydrogen peroxide or UV light) on HAI rates organisms include C diff, MRSA, CRE, etc. Most studies reported either reductions in HAI rates or resolution of an outbreak, but confounding is likely	Good

Author, Year Search Dates	Number of Included Studies (Included Study Designs)	Healthcare Setting(s)	Organisms	Outcomes of Interest	Key Findings	Quality of Review
Huang, 2016[35] 3/1/2015	15 (1 RCT)	ICU	Chlorhexidine baths Mixed HAIs (CLABSI, CAUTI, VAP) or MDROs (MRSA, VRE)	Infection or colonization CLABSI, CAUTI, VAP	Effectiveness of daily chlorhexidine bathing on numerous organisms – restricted to ICU patients. Pooled analysis of results from 7 observational studies showed a risk ratio of 0.77 (95% confidence interval 0.64, 0.91) for reduction in MRSA acquisition	Good
Kleyman, 2021[37] 8/1/2019	12 in quantitative analysis (no RCTs)	Hospital	Contact precautions MRSA, VRE	Infection or colonization MRSA and VRE Infections	Discontinuation of contact precautions on MRSA and VRE. Pooled analysis of 11 studies showed a risk ratio of 0.84 (95% confidence interval 0.71, 1.01) in HAI from MRSA, faveroing stopping contact precautions. Pooled analysis of 7 studies showed a risk ratio of 0.82 (95% confidence interval 0.72, 0.94) in HAI from VRE, favoring stopping precautions.	Good

Author, Year Search Dates	Number of Included Studies (Included Study Designs)	Healthcare Setting(s)	Organisms	Outcomes of Interest	Key Findings	Quality of Review
O'Horo. 2012[48] inception – 5/2011	12 (1 RCT)	Mostly ICU (one LTACH study)	Chlorhexidine baths N/A	BSI (mainly CLABSI, some non-CLABSI) Healthcare-associated bloodstream infection incidence, including CLABSI	Inpatient daily chlorhexidine bathing. Pooled analysis of 12 studies showed an odds ratio of 0.44 (95% confidence interval 0.33, 0.59) in reduction in blood stream infections.	Good
Purssell, 2020[50] inception – 2018	26 (no RCTs)	Hospital	Isolation precautions N/A	Non-infectious adverse impacts/mental health/patient experience Psychological (anxiety, depression scores) and non-psychological [noninfectious] outcomes (eg. Attention from HCW, errors, falls, ulcers)	Non-infection-related impact of isolation precautions on patients in isolation. Pooled analysis of 8 studies showed an SMD of 1,45 (95% confidence interval 0.56, 2.34) for more anxiety in patients who were isolated. Pooled analysis of 8 studies showed an SMD of 1.28 (95% confidence interval 0.47, 2.09) for more depression in patients who were isolated.	Good

Author, Year Search Dates	Number of Included Studies (Included Study Designs)	Healthcare Setting(s)	Organisms	Outcomes of Interest	Key Findings	Quality of Review
Schoyer, 2020[53] 2008-2018	12 primary studies (does not report study designs)	Hospital or LTC	Decontamination (bleach, UV, hydrogen peroxide) C.diff	Clostridium difficile infection	Environmental cleaning impact on *C. diff* (including bleach, peroxide, UV). Four of six studies found significant reductions in *C. difficile* infections after the implementation of UV light decontamination after standard bleaching.	Fair
Wong, 2022[56] Database inception – 2020	11 studies included in quantitative analysis (5 RCTs)	LTC	Multiple (vertical eg decolonization; horizontal eg decontaminization, barrier precautions, training/adherence, Multiple MDROs (MRSA, other MDROs)	Infection or colonization Primary MRSA colonization; secondary other MDRO colonization, all MDRO infections	Prevention of MDROs in long-term care setting, with interventions including vertical (decolonization) as well as horizontal strategies (admin, barrier precautions, training, environmental cleaning, performance improvement, source control). 11 studies included in the meta-analysis showed no statistically significant benefit for MRSA outcomes	Good

4.2.5.8. Disparities

Our literature search did not identify any studies about a relationship between transmission-based precautions and disparities.

4.2.5.9. Overall Strength of Evidence

The strength of evidence assessments are in large part based on the included systematic reviews. The newly included original research studies supported the conclusions of the systematic reviews. In one instance, we uprated the systematic review SoE from Low to Medium based on a new large, randomized trial showing benefit for patient decolonization.

Table 5. Overall assessments of the strength (certainty) of evidence

Conclusion From MHS IV	Strength of Evidence
Universal gloving has a small effect in reducing MDRO infections (mostly in the ICU setting)	Low
Contact precautions have mixed evidence for effect in the endemic setting at reducing MDRO infections	Low
Cohorting may be part of an effective strategy to reduce MDRO infections in the setting of an outbreak	Low
Environmental decontamination may reduce MDRO infections	Low
Patient decolonization can reduce MDRO infections in certain populations	Moderate
Bundled infection prevention and control practices in long term care facilities have at most a small effect on rates of MDRO infections in the endemic setting	Low
Infective isolation makes little difference to psychological outcomes, but where it does make a difference this is primarily negative	Low
Non-infectious adverse events may be higher in patients in infective isolation compared to patients who are not isolated	Very Low

4.2.6 Review Question 6. What Are the Most Common Barriers and Facilitators of Implementing the Patient Safety Practices?

Our search identified nine published articles of potential relevance to implementation. Six of these were systematic reviews of aspects of implementation[34,43,47,49,55,57] and three were about specific implementations: a MRSA prevention bundle implemented at seven hospitals more than a decade ago,[27] the effect of participation in a statewide HAI initiative, also more than a decade

ago;[31] and screening bone marrow transplant patients for *C. difficile* at a single tertiary care hospital.[19] We do not discuss these specific implementations in favor of the systematic reviews on the topic.

Four of the systematic reviews were less informative because: one review was exclusively about HAI which are not within the scope of this review (meaning CLABSI, CAUTI, and VAP);[43] one review included only cross-sectional studies, a study design we excluded, that assessed patient safety climate with adherence to universal precautions;[34] one review explicitly excluded studies of transmission-based precautions;[47] and one review included only studies that were either ineligible pre-post study designs, or about HAIs that were not in scope (CAUTI), or interventions that were not in scope (hand hygiene).[49] The two most informative reviews were about hospital organization, management and structure for preventing HAIs[57] and the effect of hospital culture on HAIs.[55] The former review, which we judged to be of good quality, searched through 2012. Ninety-two articles were included in data extraction, almost all from high-income countries. While the review covered both interventions (such as hand hygiene) and infections (such as VAP and CAUTI) that were not within our scope, there were numerous included studies of within-scope infections and interventions. This review concluded there were a number of implementation characteristics associated with decreased HAI infections, including an infection control program that had nursing staff, a dedicated physician, and data management support; a staff ratio of at least one person for every 250 beds; that high workload and long work hours were associated with increased rates of HAI; that electronic reminders for physicians were effective; that multidisciplinary groups were crucial to focusing programs to targets of interest; audits and checklists improved universal precaution measures and reduced HAI infection rate; multimodal strategies reduced MRSA infections; and that champions and organizational culture were positive factors in implementation. This latter point was reinforced by the findings from the second review, which we judged to be good quality.[55] This review searched through 2018 and identified 20 eligible studies. As in the other review, most studies came from high income countries, and while some studies included in this review would not have met our inclusion criteria there were also many included studies that were about the HAIs and interventions that are the focus of this review. The authors found that almost all studies reported evidence supporting a positive association between organizational culture and lower HAI rates, although strong conclusions were precluded by methodologic limitations of the original studies. The authors additionally identified 8 themes important for positive organizational culture: leadership; fostering a culture of safety; having an innovative culture; seeing the benefits of a non-punitive climate; fitting interventions to a local context; engaging and empowering health professionals; promoting collaboration and communication; and having a global or long-term orientation.

4.2.7 Review Question 7. What Resources (e.g., Cost, Staff, Time) Are Required for Implementation?

Our search did not identify any studies that reported the resource use required for implementation. However, one type of intervention covered in this review is specifically about adding staff, namely infection control and prevention staff. We found one systematic review relevant to the question of dedicated staff.[54] This review, which we judged as good quality, searched through May 2020, and restricted inclusion criteria only to RCTs.[54] Nine eligible studies were identified. Three of the included studies were done in the United States, three more were done in Europe, and the last three were done in Asia. Just over half (5 of 9) of the included studies were conducted in hospitals, an additional three studies were conducted in long term care, and one study was conducted in an outpatient hemodialysis center. About half of studies included an infection control link nurse (ICLN) system in addition to an infection control team. The tasks of the infection control teams in the studies included developing and disseminating guidelines and policies, coordination education, performing surveillance for HAIs, monitoring and auditing practices and standard of care, and building effective links with other staff. Results from five studies yielded a random effects pooled estimate of the incidence risk ratio of healthcare associated infections of 0.65, 95% CI of 0.40, 1.07, I2 = 69%, favoring organizations with an infection control and prevention team. Data from two studies that reported deaths due to healthcare associated infections yielded a random effects pooled estimate of 0.32, 95% CI of 0.04, 2.69, I2=58%, favoring organizations with and infection control and prevention team. Data from two studies about compliance with infection control practices yielded a random effects pooled estimate of 1.17, 95% CI 1.0, 1.38, I2=0%, favoring more compliance in organizations with an infection control and prevention team with an ICLN system. The authors used the GRADE framework to assess the certainty of evidence. They judged the certainty as Very Low that an infection control and prevention team helps reduce the incidence of infection or death from infection. They judged the certainty of evidence as Moderate that infection control and prevention teams with an ICLN system help improve compliance with infection control practices.

4.2.8 Review Question 8. What Toolkits Are Available To Support Implementation of the Patient Safety Practices?

AHRQ published a toolkit in 2022 regarding patient decolonization of non-ICU inpatients with selected indwelling devices,[65] based primarily on data from the 2019 ABATE trial which was discussed in MHS III chapter 5.[66] This was the only toolkit about in-scope safety practices addressing reduction in HAI with MDROs identified for this review which had been published since MHS III in 2019.

5. Discussion

5.1 Summary and Interpretation of Findings

This rapid review of the literature regarding prevention of HAI caused by multidrug-resistant organisms covers a broad and disparate set of patient safety practices. These can broadly be categorized as relating to barrier-type personal protective equipment and its use for contact isolation, patient cohorting, patient decolonization, and disinfection of the hospital environment. There was also literature which discussed the use of several of these practices in combination in long-term care settings.

The literature surrounding barrier-type personal protective equipment included its use both universally for all patients in high-risk settings (i.e., the ICU) as well as on a targeted basis for only those patients known to be infected or colonized with MDROs. A single systematic review of the universal use of gloves in the ICU showed possible reduction in HAI incidence, though did not reach significance when analyzing only RCTs (low strength of evidence). The literature found during our search addressing the routine use of contact isolation (gowns plus gloves) for patients colonized or infected with MDROs was primarily characterized by studies of the effects after discontinuing this practice by policy at the facility level for pathogens other than *C. difficile* (especially MRSA and/or VRE), and this literature showed mixed impact on subsequent rates of MDRO infection. The studies of de-implementation of contact isolation included a systematic review which showed no significant difference in MRSA infection after stopping routine contact isolation (low strength of evidence), though most of the included studies also reported compliance with an alternative intervention after contact isolation was discontinued, such as hand hygiene, bare-below-the-elbows, or chlorhexidine bathing. In contrast, a large prospective cohort study of 123 VA hospitals found significantly higher rates of MRSA HAI in hospitals which stopped using active surveillance testing plus contact isolation for patients colonized or infected with MRSA when compared to hospitals which continued all of these practices. One of the included primary studies showed a decrease of non-infectious adverse events after discontinuing routine contact precautions for MRSA and VRE, though this was from a single acute care hospital. A systematic review of the adverse effects of contact isolation suggested a small detriment to mental health outcomes for isolated patients, but this did not reach significance (low strength of evidence). Aside from the discontinuation studies, a single nonrandomized head-to-head study in two hospitals showed higher costs but no difference in hospitalwide rates of MRSA acquisition or infection when patients already known to be colonized or infected with MRSA were placed in contact isolation (gowns and gloves) vs upgraded standard precautions (gloves only, with conditional use of gowns when anticipating contact with body fluids). Overall, we found that the evidence was mixed for whether contact isolation of patients infected or colonized with MDROs had an impact on rates of infection with those pathogens. This reflects the similarly mixed findings of earlier

versions of prior versions of Making Healthcare Safer. MHS I found evidence supporting contact precautions for reducing rates of MDRO infection, but the underlying literature studied isolation precautions in combination with other patient safety practices.[67] MHS II found mixed evidence for contact precautions, with some studies showing a reduction in infection rates while other studies did not show a difference; the report noted that "the studies with negative results had stronger study designs".[68] MHS III reviewed literature related to contact isolation specifically for infection with *C. difficile* (chapter 4) and carbapenem-resistant *Enterobacterales* (chapter 6), and for both pathogens they found that there was evidence showing that multicomponent infection control bundles reduced infections; all literature reviewed for CRE included contact isolation in combination with other practices, while only half of the studied bundle protocols in the *C. difficile* literature included contact isolation.[69]

The literature related to cohorting of patients infected or colonized with MDROs comprised a single systematic review which suggested some (but inconsistent) reduction of rates of infection when cohorting was used to address local MDRO outbreaks in combination with other infection prevention/control PSPs (low strength of evidence). The benefits of cohorting were unclear in endemic settings (very low strength of evidence). This practice was addressed in the literature reviewed in all three prior versions of MHS, but always studied in combination with other practices so no specific conclusions about patient cohorting itself were made in prior editions of MHS.[68,69]

Patient decolonization practices varied in study context and in whether they were applied universally or only to those patients known to be colonized or infected with MDROs, but overall we found that these practices had some of the more convincing potential benefit for reducing HAI among the PSPs we reviewed (albeit still with limited evidence). A systematic review showed reduction of both MRSA acquisition and VRE acquisition with daily chlorhexidine bathing for all ICU patients (moderate strength of evidence). A multicenter RCT showed reduction of MRSA infections and rehospitalization with a post-discharge decolonization regimen targeting patients already infected or colonized with MRSA, though this fairly intensive regimen entailed 6 months of repeated courses of nasal mupirocin, chlorhexidine mouthwash, and chlorhexidine bathing. Another multicenter RCT in nursing homes found lower rates of hospitalization for infection or for any cause with use of universal decolonization with chlorhexidine bathing and nasal iodophor, compared to routine bathing. A smaller controlled before-after study showed reduced MRSA infections in one orthopedic hospital after universal preoperative decolonization with nasal mupirocin and chlorhexidine bathing in combination with targeted perioperative antibiotic adjustments. Overall, the evidence we reviewed builds on the findings of MHS III chapter 5.1, which found that chlorhexidine bathing could reduce colonization and infection with MDROs, especially in ICU populations and in terms of infections related to invasive medical devices. Like MHS III, the majority of the evidence we reviewed addressed infection or colonization with gram-positive MDROs such as MRSA and VRE. We also did not find new evidence regarding decolonization

practices during acute care hospitalization for non-ICU patients, which in MHS III was supported only in those non-ICU patients with invasive medical devices based on subgroup analysis from the ABATE trial.[69]

Regarding practices related to decontamination of patient rooms, the literature published since this topic was addressed in MHS III showed little evidence for specific room-cleaning interventions. A systematic review of automated room cleaning technology with ultraviolet light or hydrogen peroxide vapor found no significant benefit over traditional cleaning methods (low strength of evidence). This contrasts the findings of MHS III chapter 4.3, which found evidence of significant reductions in facility-level *C. difficile* infection rates when hydrogen peroxide or UV decontamination were added to standard cleaning;[6] MHS III chapter 5.4 found that these no-touch disinfection technologies were promising for reducing MDRO infections but had limited evidence so merited further study.[7] In terms of other room decontamination practices, our search also identified an RCT which showed no change in rates of *C. difficile* infection after implementing a fluorescent-marker-based feedback system for cleaning staff. Another RCT showed fewer HAIs and/or MDRO acquisition with use of copper for high-touch surfaces in ICU rooms, but the study was small so this primarily serves as proof of concept for further study of the use of intrinsically antimicrobial materials in healthcare environments to augment room cleaning practices. Our review did not identify new literature to address the choice of manual cleaning agent, which MHS III found the most established for chlorine-based solutions for *C. difficile* as well as other MDROs, with some evidence for quaternary ammonium compounds for certain MDROs other than *C. difficile.*[69]

We found some literature regarding infection prevention and control practices specifically in long-term care settings, though aside from the RCT studying chlorhexidine/povidone decolonization discussed above in context of the other decolonization studies, the underlying literature largely addressed multiple PSPs bundled in various combinations rather than separately assessing individual practices. A systematic review showed no statistically significant reduction in MRSA infection rates with infection prevention and control practices (low strength of evidence), except small nonsignificant in narrow subgroup analyses of so-called vertical interventions including patient decolonization practices. An RCT suggested some improvement in infection rates with a multi-component infection control bundle in nursing homes, but this was not significant by difference-in-difference analysis and did not alter rates of antibiotic use or hospitalization.

In terms of implementing infection prevention and control practices, we found some evidence in two systematic reviews supporting a reduction of hospital-acquired infections with certain staffing and logistical features of infection prevention/control programs, as well as with features of underlying organizational culture. A separate systematic review of the practice of having a dedicated infection prevention and control team suggested that such a team likely improves the rates of compliance with infection control practices (moderate strength of evidence) with possible but nonsignificant reductions in the incidence of HAI (very low strength of evidence).

5.2 Limitations

This rapid review had limitations related to the review process. It is possible that there were additional relevant studies that we did not identify using our search strategy and querying specific databases (i.e., PubMed and Cochrane Library). Our rapid review was limited to studies performed in the United States, so there may be additional relevant studies which were performed outside the United States.

There were several limitations related to the sources of evidence that were located through the search. This rapid review relied heavily on evidence from systematic reviews, some of which included observational studies. As a result, some reviews were assessed as providing low or very low strength of evidence. Most of the reviews did not include statements around the strength of the evidence, which had to be assessed by the authors of this rapid review.

A strength of this review was the inclusion of a broad scope of literature across various healthcare settings (i.e., ICU, general medical ward, nursing homes).

5.3 Implications for Clinical Practice and Future Research

More prospective controlled studies are needed to evaluate individual infection prevention and control practices; as prior evidence discussed in earlier reviews of this topic in MHS supports multicomponent bundles of these practices, this may require standardization of infection control practices across study arms aside from the individual practice being studied, which may be challenging to implement across multiple sites. Such prospective controlled studies need not be randomized: statistical process control methods can be used to assess the de-implementation of components of the bundle of interventions one-at-a-time, to assess the effect on infection rates.

Given that there is often a lag between acquisition of an MDRO (i.e., colonization) and subsequent development of infection with that pathogen, longer followup times may help better illustrate the effects of practices seeking to reduce transmission of MDROs. Furthermore, future analyses can evaluate whether interventions such as decolonization can decrease MDRO infections at the population level, such as unit level analyses of prevention of MDRO acquisition by patients in neighboring areas. And then lastly there may be novel approaches not-yet-developed that can be tested.

The literature appears to be limited for the most dangerous, extremely-drug resistant organisms such as carbapenem-resistant bacteria and *Candida auris*. This is likely in part due to their relative rarity compared to more common drug-resistant pathogens such as MRSA and *C. difficile*, but it may also reflect the less robust systems for tracking and reporting these pathogens compared to the mandated, ubiquitous reporting standards dictated by CMS for MRSA bacteremia and *C. difficile* infection.

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Authors

Sean T. McCarthy, M.D.
Aneesa Motala, B.A.
Emily Lawson, M.S.
Paul G. Shekelle, M.D., Ph.D.

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Peer Reviewers

This list of Peer Reviewers follows:

Matthew Goetz, M.D.
Chief, Infectious Diseases, VA Greater Los Angeles Healthcare System
Professor, University of California, Los Angeles
Los Angeles, CA

Marin Schweizer, Ph.D.
Professor
Division of Infectious Disease
School of Medicine and Public Health
University of Wisconsin-Madison
Madison, WI

Arjun Srinivasan, M.D.
Deputy Director for Program Improvement
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention
Atlanta, GA

Disclaimers

This report is based on research conducted by the Southern California Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 75Q80120D00003). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

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

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

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe. AHRQ recognizes that people are struggling with urgent questions on how to make healthcare safer. AHRQ is using this rapid format for the fourth edition of its Making Healthcare Safer series of reports, produced by the EPC Program and the General Patient Safety Program. To shorten timelines, reviewers make strategic choices about which processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

AHRQ expects that these rapid evidence products will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to AHRQ. If you have comments related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to MHS@ahrq.hhs.gov.

Robert Otto Valdez, Ph.D., M.H.S.A.
Director
Agency for Healthcare Research and Quality

Therese Miller, D.P.H.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Christine Chang, M.D., M.P.H.
Acting Director
Evidence-based Practice Center Division
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

David W. Niebuhr, M.D., M.P.H., M.Sc.
Evidence-based Practice Center Division Liaison
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Craig A. Umscheid, M.D., M.S.
Director
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Margie Shofer, B.S.N., M.B.A.
Director, General Patient Safety Program
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Jennifer Eskandari
Task Order Officer
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Farzana Samad, Pharm.D., FISMP, CPPS
Health Scientist Administrator
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Appendixes

Appendix A. Methods

Search Strategies for Published Literature

Databases:

- PubMed
- Cochrane Library

Limits:

- 2011 – May 2023
- English

Results:

- # of results post-dup for review: **701**

Table A-1. PubMed search strategy

Set #	Search	# of Results
1	"cross infection*"[ti] OR "cross transmission*"[ti] OR "health care associated infection*"[ti] OR "healthcare associated infection*"[ti] OR "nosocomial infection*"[ti] OR "healthcare acquired infection*" OR "health care acquired infection*"[ti] OR "hospital acquired infection*"[ti] OR "hospital associated infection*"[ti] OR "hospital onset infection*"[ti] OR "vancomycin resistan*"[ti] OR "methicillin resistan*"[ti] OR "MRSA"[ti] OR "VRE"[ti] OR "antibiotic resistant bacter*"[tiab] OR "Cross Infection"[Mesh] OR "Gram-Positive Bacterial Infections"[MAJR] OR "Methicillin-Resistant Staphylococcus aureus"[MAJR] OR "Vancomycin-Resistant Enterococci" OR "Vancomycin Resistance"[Mesh] OR "Disease Transmission, Infectious"[MAJR] OR "healthcare infection"[ti:~3]	514,538
2	"contact precaution*"[ti] OR "isolation precaution*" OR "patient isolat*"[ti] OR "infection control*"[ti] OR "infection prevent*"[ti] OR "universal precaution*"[ti] OR "transmission precaution*"[ti] OR "transmission prevent*"[ti] OR "transmission reduction*"[ti] OR "preventative measure*"[ti] OR "Infection Control"[MAJR] OR "Patient Isolation"[MAJR] OR "Universal Precautions"[MAJR] OR "infection prevention"[ti:~2] OR "infection prevention control"[ti:~3]	48,891
3	inpatient*[tiab] OR hospital*[tiab] OR "healthcare facilit*"[tiab] OR Inpatients[Mesh] OR Hospitalization[Mesh] OR Hospitals[MAJR] OR "Health Facilities"[Mesh:NoExp]	1,810,459
4	Austria* OR Australia* OR Belgium OR Canada* OR Denmark OR Finland OR France OR French OR German* OR Ireland OR Irish OR Italy OR Italian OR Netherlands OR Norway OR Portugal OR Spain OR Spanish OR Sweden OR "New Zealand" OR "United Kingdom" OR "United States" OR "UK" OR "USA" OR England OR Scotland OR Wales	
5	#1 AND #2 AND #3 AND #4	6,042
6	#5 AND (2011/01/01:2023/12/31[Date - Publication] AND "english"[Language]) AND ("systematic review"[ti] OR "randomized controlled"[ti] OR evidence[ti] OR "meta analysis"[ti] OR comparativestudy[Filter] OR evaluationstudy[Filter] OR guideline[Filter] OR meta-analysis[Filter] OR multicenterstudy[Filter] OR practiceguideline[Filter] OR preprint[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter] OR validationstudy[Filter])	**698**

Table A-2. Cochrane Library search strategy

Set #	Search	# of Results
1	("cross" NEXT infection*):ti,ab,kw OR ("cross" NEXT transmission*):ti,ab,kw OR ("health care associated" NEXT infection*):ti,ab,kw OR ("healthcare associated" NEXT infection*):ti,ab,kw OR ("nosocomial" NEXT infection*):ti,ab,kw OR ("healthcare acquired" NEXT infection*):ti,ab,kw OR ("health care acquired" NEXT infection*):ti,ab,kw OR ("hospital acquired" NEXT infection*):ti,ab,kw OR ("hospital associated" NEXT infection*):ti,ab,kw OR ("hospital onset" NEXT infection*):ti,ab,kw OR (healthcare NEAR infection*):ti,ab,kw OR ("vancomycin" NEXT resistan*):ti,ab,kw OR ("methicillin" NEXT resistan*):ti,ab,kw OR MRSA:ti OR VRE:ti,ab,kw OR ("antibiotic resistant" NEXT bacter*):ti,ab,kw OR ("gram-positive bacteria" NEAR infection*):ti,ab,kw OR "methicillin-resistant staphylococcus aureus":ti,ab,kw OR ("infectious disease" NEAR transmission*):ti,ab,kw	5,487
2	("contact" NEXT precaution*):ti,ab,kw OR ("isolation" NEXT precaution*) OR ("patient" NEXT isolat*):ti,ab,kw OR ("infection" NEXT control*):ti,ab,kw OR ("infection" NEXT prevent*):ti,ab,kw OR ("universal" NEXT precaution*):ti,ab,kw OR ("transmission" NEXT precaution*):ti,ab,kw OR ("transmission" NEXT prevent*):ti,ab,kw OR ("transmission" NEXT reduction*):ti,ab,kw OR ("preventative" NEXT measure*):ti,ab,kw OR ("prevention" NEAR measure*):ti,ab,kw OR (safety NEAR precaution*):ti,ab,kw OR (safety NEAR measure*):ti,ab,kw	15,142
3	inpatient*:ti,ab,kw OR hospital*:ti,ab,kw OR ("healthcare" NEXT facilit*):ti,ab,kw OR ("health care" NEXT facility*):ti,ab,kw OR ("health" NEXT facilit*):ti,ab,kw OR hospitaliz*:ti,ab,kw	241,220
4	Austria*:ti,ab,kw OR Australia*:ti,ab,kw OR Belgium:ti,ab,kw OR Canada:ti,ab,kw OR Canadian*:ti,ab,kw OR Denmark:ti,ab,kw OR Finland:ti,ab,kw OR France:ti,ab,kw OR French:ti,ab,kw OR German*:ti,ab,kw OR Ireland:ti,ab,kw OR Irish:ti,ab,kw OR Italy:ti,ab,kw OR Italian:ti,ab,kw OR Netherlands:ti,ab,kw OR Norway:ti,ab,kw OR Portugal:ti,ab,kw OR Spain:ti,ab,kw OR Spanish:ti,ab,kw OR Sweden:ti,ab,kw OR "New Zealand":ti,ab,kw OR "United Kingdom":ti,ab,kw OR "United States":ti,ab,kw OR "UK":ti,ab,kw OR "USA":ti,ab,kw OR England:ti,ab,kw OR Scotland:ti,ab,kw OR Wales:ti,ab,kw	196,416
5	#1 AND #2 AND #3 AND #4	189
6	#5 Limits: 2011 – 2023	**4**

Appendix B. List of Excluded Studies Upon Full-Text Review

Excluded Studies

The reason for exclusion is noted at the end of the citation.

1. Abubakar S, Boehnke JR, Burnett E, et al. Examining instruments used to measure knowledge of catheter-associated urinary tract infection prevention in health care workers: A systematic review. Am J Infect Control. 2021 Feb;49(2):255-64. doi: 10.1016/j.ajic.2020.07.025. PMID: 32707131. *Intervention*

2. Adams C, Peterson SR, Hall AJ, et al. Associations of infection control measures and norovirus outbreak outcomes in healthcare settings: a systematic review and meta-analysis. Expert Rev Anti Infect Ther. 2022 Feb;20(2):279-90. doi: 10.1080/14787210.2021.1949985. PMID: 34225537. *Intervention*

3. Almeida D, Cristovam E, Caldeira D, et al. Are there effective interventions to prevent hospital-acquired Legionnaires' disease or to reduce environmental reservoirs of Legionella in hospitals? A systematic review. Am J Infect Control. 2016 Nov 1;44(11):e183-e8. doi: 10.1016/j.ajic.2016.06.018. PMID: 27524259. *Intervention*

4. Amirov CM, Binns MA, Jacob LE, et al. Impact of chlorhexidine bathing on methicillin-resistant Staphylococcus aureus incidence in an endemic chronic care setting: A randomized controlled trial. Am J Infect Control. 2017 Mar 1;45(3):298-300. doi: 10.1016/j.ajic.2016.10.007. PMID: 27839752. *Setting*

5. Andalib E, Faghani M, Zia Ziabari SM, et al. The Effectiveness of the Anteroom (Vestibule) Area on Hospital Infection Control and Health Staff Safety: A Systematic Review. Front Public Health. 2022;10:828845. doi: 10.3389/fpubh.2022.828845. PMID: 35558527. *Intervention*

6. Anderson DJ, Chen LF, Weber DJ, et al. Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and Clostridium difficile (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study. Lancet. 2017 Feb 25;389(10071):805-14. doi: 10.1016/s0140-6736(16)31588-4. PMID: 28104287. *Assessed in MHS II or III*

7. Backman C, Taylor G, Sales A, et al. An integrative review of infection prevention and control programs for multidrug-resistant organisms in acute care hospitals: a socio-ecological perspective. Am J Infect Control. 2011 Jun;39(5):368-78. doi: 10.1016/j.ajic.2010.07.017. PMID: 21429622. *Assessed in MHS II or III*

8. Birgand G, Moore LSP, Bourigault C, et al. Measures to eradicate multidrug-resistant organism outbreaks: how much do they cost? Clin Microbiol Infect. 2016 Feb;22(2):162.e1-.e9. doi: 10.1016/j.cmi.2015.10.001. PMID: 26482264. *Study design, systematic review of costs*

9. Bishop J, Parry MF, Hall T. Decreasing Clostridium difficile infections in surgery: impact of a practice bundle incorporating a resident rounding protocol. Conn Med. 2013 Feb;77(2):69-75. PMID: 23513633. *Study design, pre-post study*

10. Calfee DP, Salgado CD, Milstone AM, et al. Strategies to prevent methicillin-resistant Staphylococcus aureus transmission and infection in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014 Jul;35(7):772-96. doi: 10.1086/676534. PMID: 24915205. *Timing*

11. Daeschlein G, von Podewils S, Bloom T, et al. Active surveillance for methicillin-resistant Staphylococcus aureus including polymerase chain reaction-based screening prevents transmission in a dermatology ward. Infect Control Hosp Epidemiol. 2012 Sep;33(9):957-9. doi: 10.1086/667372. PMID: 22869274. *Timing*

12. de França SR, Sant'Ana EA, Nunes Mafra ACC, et al. The Impact of Isolation Precautions on Hand Hygiene Frequency by Healthcare Workers. Infect Control Hosp Epidemiol. 2018 Feb;39(2):245-7. doi: 10.1017/ice.2017.275. PMID: 29345607. *Population*

13. Dubberke ER, Rohde JM, Saint S, et al. Quantitative Results of a National Intervention to Prevent Clostridioides difficile Infection: A Pre-Post Observational Study. Ann Intern Med. 2019 Oct 1;171(7_Suppl):S52-s8. doi: 10.7326/m18-3545. PMID: 31569233. *Study Design*

14. Falagas ME, Thomaidis PC, Kotsantis IK, et al. Airborne hydrogen peroxide for disinfection of the hospital environment and infection control: a systematic review. J Hosp Infect. 2011 Jul;78(3):171-7. doi: 10.1016/j.jhin.2010.12.006. PMID: 21392848. *Outcome*

15. Farbman L, Avni T, Rubinovitch B, et al. Cost-benefit of infection control interventions targeting methicillin-resistant Staphylococcus aureus in hospitals: systematic review. Clin Microbiol Infect. 2013 Dec;19(12):E582-93. doi: 10.1111/1469-0691.12280. PMID: 23991635. *Outcome*

16. French CE, Coope C, Conway L, et al. Control of carbapenemase-producing Enterobacteriaceae outbreaks in acute settings: an evidence review. J Hosp Infect. 2017 Jan;95(1):3-45. doi: 10.1016/j.jhin.2016.10.006. PMID: 27890334. *Assessed in MHS II or III*

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Toolkits

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Appendix C. Evidence Tables–Risk of Bias of Included Studies

Table C-1. Cochrane risk of bias for randomized-controlled trials

Author, Year	Random	Allocation Concealment	Blinding Participants	Blinding Outcome Assessment	Selective Reporting	Attrition
Huang et al., 2019[36]	Low risk	Unclear risk	High risk	Low risk	Low risk	Unclear risk
McConeghy et al., 2017[44]	Unclear risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Miller et al, 2023[46]	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk
Ray et al., 2017[51]	Unclear risk	Low risk	High risk	Low risk	High risk	Unclear risk
Salgado et al., 2013[52]	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk

Table C-2. ROBINS-I risk of bias assessment for nonrandomized studies

Author, Year	Confounding	Selection Bias	Bias in Measurement Classification of Interventions	Bias Due to Deviations From Intended Interventions	Bias Due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Result
Bessesen et al., 2013[20]	High	High	Low	Unclear	Unclear	Low	Low
Evans et al, 2023[28]	Unclear	Low	Low	High	Low	Low	Low
Martin, 2018[41]	Unclear	Low	Low	Unclear	Unclear	Low	Low
Mehta et al., 2013[45]	High	High	Low	Unclear	Unclear	Low	Low

Table C-3. SOE table for systematic reviews of selected transmission-based precaution interventions effectiveness

Author, Year	Type of Evidence	Number of Included Studies	Heterogeneity (either quantitative estimate or narrative from the authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Abad, 2020[17]	Narrative	All observational	Heterogeneity	"…studies were too heterogenous…"	"cohorting may be reasonable....in outbreaks" "whether effective in endemics is unknown"	Low for outbreaks, Very Low for endemics
Afonso, 2013[18]	Narrative	15 studies, 9 RCTs	Heterogeneity	"…studies were included regardless of the research methodology utilized…a more severe approach would have increased statistical integrity and homogeneity…"	"use of chlorhexidine wipes prevent the spread of pathogens, including multidrug resistant strains"	Low
Chang, 2019[22]	Meta-analytic	4 RCTs 4 higher quality observational studies	Heterogeneity I2 = 60%.	"..only 8 publications met inclusion criteria,and they were heterogeneous." "The included studies were of moderate quality" "Only 3 studies reported hand	"Universal gloving may be associated with a small protective effect…" (result was nonsignificant when only RCTs were assessed)	Low

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Author, Year	Type of Evidence	Number of Included Studies	Heterogeneity (either quantitative estimate or narrative from the authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
				hygiene and gloving compliance…"		
Dancer, 2021[25]	Narrative	43 studies 3 reports from 1 RCT	Heterogeneity	None mentioned	"clear benefits in vitro…insufficient objective assessment of patient outcome…"	Low
Huang, 2016[35]	Meta-analytic	15 studies included (1 RCT)	Minimal I2 = 12%	"only 3 eligible RCTs were included…" "..overall quality of the included studies was low." "studies did not adequately evaluate the long-term effects…"	"suggests intervention reduces HAI"	Low
Kleyman, 2021[37]	Meta-analytic	12 studies included (all observational)	Minimal I2 = 0% no effect of stopping	"we note the inherent biases attributed to the nonrandomized nature of studies…"	No significant differences after stopping contact precautions	Low
O'Horo. 2012[48]	Meta-analytic	12 studies 1 RCT	Heterogeneity	"Only a single randomized controlled trial met our inclusion	"Among ICU patients, daily chlorhexidine bathing reduces the risk of health-case	Low

Author, Year	Type of Evidence	Number of Included Studies	Heterogeneity (either quantitative estimate or narrative from the authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
			I2 = 53% and 64% in two pooled analyses	criteria…" "…variability in the choice of study outcome…"" variability in implementation of the interventions…" "…evidence of publication bias…"	associated blood stream infections"	
Purssell, 2020[50]	Meta-analytic	26 studies All observational	Heterogeneity	"Because this evidence is comprised of cohort and case-control studies, a claim for a casual relationship cannot be made…"	Data "suggest that isolation.….has a number of negative" effects on patients	Very Low
Schoyer, 2020[53]	Narrative	12 studies Does not report study designs	Heterogeneity	"…[included studies] were undermined by several weaknesses such as not including a control group…"	"environmental cleaning and decontamination were associated with significant decreases in facility level *C. difficile* infection rates	Low
Wong, 2022[56]	Meta-analytic	11 studies included in the quantitative analysis 5 RCTs	Varies	"very few data on adherence reported…" "…multiplicity of	Results "did not show any beneficial effect of IPC interventions	Low

Author, Year	Type of Evidence	Number of Included Studies	Heterogeneity (either quantitative estimate or narrative from the authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
			I2 between 0% and 77% depending on analysis	outcome measures could limit the potential to synthesize results…" "…low quality of the study affects the internal validity of our review…"	on MRSA reductions."	