# Evidence-based Practice Center Rapid Review Protocol

# Project Title: *Making Healthcare Safer IV: Prevention of Transmission of Infection with Multi-Drug Resistant Organisms (MDROs)*

## Review Questions

*(Note: For the scope of this review, these multi-drug resistant organism infections do not include catheter-associated urinary tract infection (CAUTI), central line associated blood stream infection (CLABSI), and ventilator-associated pneumonia (VAP), which are either considered separately or excluded from Making Healthcare Saver IV (MHS IV). Additionally, "health care settings" is defined as acute inpatient settings and long-term care settings, and does not include ambulatory care clinics, free-standing radiology centers, physical therapy offices, etc.)*

1. What is 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 Health Care 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?

# Context and Domain Being Studied

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 of 2023, AHRQ launched its fourth iteration of the MHS Report (MHS IV). Transmission-based Precautions as a 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]

Healthcare-associated infections are those infections which develop in association with a patient's contact with healthcare facilities, treatments, and devices, though this comprises a wide variation in the duration, recency, and nature of contact with healthcare.[2] Hospital-acquired infections are the subset of healthcare-associated infections which develop while a patient is hospitalized and are defined by the CDC National Healthcare Safety Network as those infections in which the first diagnostic test or clinical signs of infection manifest more than 48 hours after hospital admission.[3] The WHO estimates that 7 out of 100 patients hospitalized in high-income countries will develop a hospital-acquired infection, and globally that healthcare-associated infections cause death in 10% of affected patients.[4] In the United States, the HHS HAI National Action Plan estimated in 2013 that hospital-acquired infections are responsible for $28-33 billion annually in preventable healthcare costs.[5] This has prompted efforts to track and reduce the burden of 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).

# Overview of the PSP

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), as well as the broader practices of antimicrobial stewardship and hand hygiene.

The remaining major category of patient safety practices targeting healthcare-associated infection 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.

The risk factors for MDRO infection are complex and include exposure to devices used in invasive medical procedures (central lines, urinary catheters, ventilators, surgical/procedural equipment), the healthcare environment itself (e.g. hospital rooms and beds), contact with other patients and healthcare workers, exposure to antibiotics (with their effects on the patient microbiome as well as evolutionary pressure on pathogens leading to drug-resistance), and patient factors affecting susceptibility to infection including immunocompetence and skin integrity.

Transmission modes of MDROs are therefore also complex. Drug-resistant pathogens enter the healthcare environment from sources including infected patients (who either acquired the MDRO in the community, during prior contact with healthcare systems, or by evolution of a non-resistant pathogen during exposure to antibiotics) as well as via asymptomatic carriage by patients and healthcare workers colonized with MDROs. Infectious agents can transmit directly by contact between source individual and susceptible host (either direct physical contact or through respiratory droplets in close proximity), or indirectly through intermediary vehicles including contaminated surfaces (rooms, beds, equipment, and healthcare worker hands/clothing) as well as airflow (for the subset of respiratory pathogens which can transmit via persistently airborne particles).

This review will focus on patient safety practices for reducing burden and transmission of MDROs within hospital and nursing home environments, including those centering around the patient microbiome (including MDRO surveillance testing and decolonization), 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). We will include literature surrounding vancomycin-resistant Enterococci (VRE), Methicillin-resistant *Staphylococcus* aureus (MRSA), Clostridioides difficile (C.diff), and plan to also include literature covering the multidrug-resistant Enterobacterales (including extended-spectrum beta-lactamase-producing [ESBL] Enterobacterales and carbapenem-resistant Enterobacterales [CRE]) as well as the rare but dangerous invasive yeast *Candida auris*. We will exclude 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 varied infection control practices based on shifting evidence base as well as logistical constraints of limited resources.

Making Health Care Safer (2001) chapter 13 primarily focused on the use of barrier precautions in the prevention of healthcare-associated infections with VRE and C.diff. 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. Making Health Care Safer 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.diff, 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 MCHS-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. Making Health Care Safer III had chapters focusing in-depth on individual pathogens including C.diff (chapter 4),[6] other multidrug resistant organisms (chapter 5),[7] and carbapenem-resistant Enterobacter (chapter 6).[8]

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 >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.

# Purpose of the 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.

# Methodologic Approach

For this rapid review, strategic adjustments will be made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. We will follow adjustments and streamlining processes proposed by the Agency for Healthcare Research and Quality (AHRQ) EPC Program. Adjustments include 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 2019 when the search was done for the MHS III report) in English and performed in the United States, and having each study assessed by a single reviewer. Depending on the expected volume of literature, the EPC team may opt to have a randomly selected 10% sample of articles checked by a second reviewer or use the artificial intelligence (AI) feature of DistillerSR (AI Classifier Manager) as a second reviewer at the title and abstract screening stage, as described below in the section on Data Extraction. For Review Questions 6 and 7, we will focus on the barriers, facilitators, and required resources reported in the studies we find for Review Question 5. For Review Question 8, we will identify publicly available patient safety toolkits or guides developed by AHRQ or other organizations such as the Centers for Disease Control or the Infectious Disease Society of America that could help to support implementation of the PSPs. To accomplish that task, we will review AHRQ's Patient Safety Network (PSNet) (https:/psnet.ahrq.gov) and AHRQ's listing of patient safety related toolkits (https://www.ahrq.gov/tools/index.html?search_api_views_fulltext=&field_toolkit_topics=14170&sort_by=title&sort_order=ASC) and we will include any toolkits mentioned in the studies we find for Review Question 5. We will identify toolkits without assessing or endorsing them.

# Eligibility Criteria for Studies of Effectiveness

We will search for original studies and systematic reviews on Review Question 5 according to the inclusion and exclusion criteria presented in Table 1.

**Table 1. Inclusion and Exclusion Criteria**

| Study Parameter | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Population | Adult patients (18+ years) | Pediatric patients (under 18 years) |
| Intervention | • Surveillance testing<br>• Barrier precautions<br>• Cohorting of patients and/or staff<br>• Decolonization of patients<br>• Decontamination of hospital environment<br>  ○ Room cleaning interventions in patient-care wards/ICUs<br>• Dedicated staff | • Hand hygiene-only interventions<br>• Education-only interventions<br>• Respiratory precautions (droplet, airborne, negative pressure airflow)<br>• Decontamination of surgical/procedural environment (operating rooms)<br>• Decontamination of reusable medical equipment (surgical/procedural/endoscopic equipment) |
| Comparator | Usual care or alternative transmission-based precautions | N/A |
| Outcome | • Clinical outcomes<br>  ○ Surveillance testing patients' status for nosocomial pathogens<br>  ○ Clinical healthcare-associated infection<br>• Provider outcomes<br>  ○ Changes in provider behavior such as room entry or physical examination<br>• Cost<br>• Unintended effects<br>  ○ Patient mental health/social isolation/satisfaction<br>  ○ Noninfectious adverse healthcare-associated outcomes (hospital-acquired pressure injuries, inpatient falls) | • Clinical outcomes specifically for:<br>  ○ Central-line associated bloodstream infection (CLABSI)<br>  ○ Catheter-associated urinary tract infection (CAUTI)<br>  ○ Ventilator-associated pneumonia or events (VAP/VAE)<br>  ○ Surgical site infection (SSI)<br>  ○ COVID-19 infection<br>  ○ Tuberculosis infection |
| Timing | • Outcome occurring<br>  ○ During index/current stay in hospital/nursing home<br>  ○ Up to 12 months after discharge from index hospitalization/nursing home stay | Outcome occurring prior to admission to hospital/nursing home study location<br>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<br>• Outside of traditional health care settings<br>• Prison settings<br>• Site not in the United States |

| Study Parameter | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Type of studies | • Systematic reviews<br>• Randomized trials<br>• Non-randomized trials<br>• Case control studies<br>• Controlled before-after studies<br>• Interrupted time series studies and repeated measures studies<br>• De-implementation studies<br>• Studies published since 2011 | • Not published in English<br>• Not original research<br>• Other study designs (e.g., uncontrolled before-after studies or cross-sectional studies) |

# Literature Searches for Studies of Effectiveness

Our search strategy will focus on databases expected to have the highest yield of relevant studies, including PubMed and the Cochrane Library, 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 CDC, AHRQ, the National Institutes of Health (NIH), National Quality Forum (NQF), and the American Hospital Association (AHA). We will check ClinicalTrials.gov and PROSPERO for relevant unpublished work.

# Data Extraction

For Review Questions 5-7, we plan to use dual independent review for screening, inclusion and exclusion, and data extraction, unless we find more primary studies than can be managed within the time frame. In that case, to efficiently identify studies that meet the eligibility criteria, we will distribute citations from the literature search to team members, with plans to have the title and abstract of each citation reviewed by a single team member. A second team member will check a 10% sample of citations to verify that relevant studies were not excluded after the review of titles and abstracts. Alternatively, the team may opt to use the DistillerSR AI Classifier Manager as a semi-automated screening tool to conduct the review efficiently at the title and abstract screening stage. In that case, the title and abstract of each citation will be reviewed by a team member, and then the AI Classifier Manager will serve as a second reviewer of each citation. The full text of each remaining potentially eligible article will be reviewed by a single team member to confirm eligibility and extract data. A second team member will check a randomly selected 10% sample of the articles to verify that important studies were not excluded and confirm the accuracy of extracted data.

Data extraction will be organized according to the review questions, and will include author, publication year, data years, study design, population, decision context, intervention, comparator, outcomes (e.g., clinical infection rate, colonization rate, cost, unintended consequences), and implementation barriers and facilitators.

# Risk of Bias (Quality) Assessment

For studies that address Question 5 about the effectiveness of PSPs, we will use the Cochrane Collaboration's tool for assessing the risk of bias of randomized controlled trials (RCTs) or the ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions.[9, 10] When assessing RCTs, we will use the 7 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.[10] When assessing non-randomized studies, we will use specific items in the 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.[9] The risk of bias assessments will focus on the main outcome of interest in each study.

If we identify a recent eligible systematic review, the primary reviewer will use the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[11]

- **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.

The Task Leader will review the risk of bias assessments and any disagreements will be resolved through discussion with the team.

## Strategy for Data Synthesis

Selected data will be compiled into evidence tables and synthesized narratively. For Question 5 about the effectiveness of PSPs, we will record information about the context of each study and whether the effectiveness of the PSP differs across different contexts. If any of the PSPs have more than one study of effectiveness, we will grade the strength of evidence for those PSPs using the methods outlined in the AHRQ Effective Health Care Program (EHC) Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[12] Evidence grading would not add value for PSPs that do not have more than one available study.

## Analysis of Subgroups or Subsets

If possible, for this rapid review, subgroup analyses will be conducted around effectiveness of the PSP across different organisms, and possibly different settings/context, such as the Intensive Care Unit, the general medical/surgical ward, and the nursing home.

## Registration

We will submit the protocol to AHRQ and to the PROSPERO international prospective register of systematic reviews.

## EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators from participation in the review.

## External Peer Review

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers.

We will ask at least one clinical content expert and one methodological expert to review the draft report. Potential peer reviewers must disclose any financial conflicts of interest greater than $5,000 and any

other relevant business or professional conflicts of interest. Invited peer reviewers may not have any financial conflict of interest greater than $5,000.

## Role of the Funder

This project is funded under Contract No. 75Q80120D00003/75Q80122F32009 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The AHRQ Task Order Officer will review contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by AHRQ or the U.S. Department of Health and Human Services.

## Format and Content of Report

The report will follow the most recent template approved by AHRQ at the time of approval of the protocol.

# References


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individual-studies.

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