Evidence-based Practice Center Rapid Response Protocol

Project Title: *Making Healthcare Safer IV: Deprescribing to Reduce Medication Harms in Older Adults*

1. What is the frequency and severity of harms associated with polypharmacy or potentially inappropriate medications [PIMs])?
2. What patient safety measures or indicators have been used to examine the harm associated with polypharmacy and potentially inappropriate medications?
3. What deprescribing interventions have been used to prevent or mitigate the harm and in what settings have they been used?
4. What is the rationale for deprescribing to prevent or mitigate the harm?
5. What studies have assessed the effectiveness and unintended effects of deprescribing and what new evidence has been published since the search was done for the Making Healthcare Safer (MHS) III report in 2019?
6. What are common barriers and facilitators to implementing deprescribing?
7. What resources (e.g., cost, staff, time) are required for implementation?
8. What toolkits are available to support implementation of deprescribing?

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 patient safety practices (PSPs) that can improve patient safety across the healthcare system—from hospitals to primary care practices, long-term care facilities, and other healthcare settings. In the Spring of 2023, AHRQ launched its fourth iteration of the Making Healthcare Safer Report (MHS IV).

Deprescribing 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]

Medication use, whether prescription or non-prescription, is extremely common for numerous physical and mental health conditions and can have benefits on morbidity and mortality. However, scientific and medical advances have been accompanied with a concurrent increase in the prevalence of polypharmacy (commonly defined as using 5 or more chronic medications)[2] or potentially inappropriate medications (PIMs). This is especially common among adults age 65 years and over, who often have multiple chronic conditions, each of which may be treated with one or more medications. Estimates suggest that 45% of older adults are exposed to polypharmacy[3] and 58% to PIMs.[4] Of concern, both polypharmacy and PIMs are associated with adverse drug events (ADEs), increased healthcare utilization (e.g., emergency department visits, acute care hospitalizations), and greater healthcare costs.[5-7] One approach to minimize these adverse outcomes is to proactively discontinue inappropriate medications. This de-implementation-based approach, known as deprescribing, is defined as a "systematic process of identifying and discontinuing drugs…[where] existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals"[8]

Deprescribing has the potential to improve multiple aspects of patient safety and quality of care, including by reducing drug burden, ADEs, and morbidity. However, there are many barriers to deprescribing at the level of the patient, clinician, and healthcare system.[9-11] Significant efforts have been made to develop and implement deprescribing interventions.

Overview of the PSP

Deprescribing spans various healthcare settings, including outpatient clinics, acute care hospitalizations, and long-term care environments. Deprescribing interventions take many forms, including reviews of medications by clinical pharmacists, identifying medications based on established criteria or lists (e.g., Beers, STOPP), point-of-prescribing clinical decision support, and "direct-to-patient" materials.[12-16] Further, interventions may be isolated or longitudinal, and they may involve one or more individuals involved in decision-making (e.g., prescribers, clinical pharmacists, patients, patients' family/ caregivers). Deprescribing is predicated on a complete and accurate medication list, often elicited through medication reconciliation,[17] a separate and distinct patient safety practice that produces a Best Possible Medication History.[18] As a result of the variety of approaches to deprescribing, questions remain about the most effective interventions, the best strategies to implement them, and their impact on healthcare outcomes. The MHS III[19] report found that reviews by clinical pharmacists and geriatricians could reduce unnecessary medications, and deprescribing reduced medication-related costs for patients and healthcare systems. MHS III also found that patient and family education led to better communication about medication use.

MHS III (2019) addressed deprescribing, and summarized 14 studies. The report concluded that deprescribing reduces medication-related costs for patients and healthcare systems.[19] During the TEP prioritization process, the MHS IV TEP noted that there were no recent high-quality systematic reviews on the subject.[1] For the purposes of this review, we will include evidence published since 2019 on the benefits or harms of any deprescribing intervention among adults age 65 and over in any healthcare setting.

Purpose of the Review

The overall purpose of this rapid response is to summarize the most relevant and recent literature on deprescribing interventions to reduce polypharmacy or PIMs among adults age 65 years and older.

Methodologic Approach

For this rapid response, 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 AHRQ Evidence-based Practice Center (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 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.

We will search for good or fair quality systematic reviews published since 2019 and will rely primarily on the content of any such systematic review that is found. We will not perform an independent assessment of original studies cited in any such systematic review.

We will ask 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. We will focus on the harms and patient safety measures or indicators that are addressed in the studies we find for Review Question 5. For Review Question 2, we will focus 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 (NCQA) patient safety related measures.

We will ask our content experts to answer Review Questions 3 and 4 by citing selected references, including PSPs used and explanations of the rationale presented in the studies we find for Review Question 5.

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 developed by AHRQ or other organizations 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 (see 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	Adults age 65 and over, with polypharmacy or potentially inappropriate medications (PIMs)	Patients younger than 65 years of age
Intervention	Any deprescribing intervention	Studies focused on medication reconciliation only
Comparator	Usual practice	No clear description of comparator
Outcome	**Medication outcome measures** (e.g., reduction of polypharmacy or PIMs; total medication count) **Clinical outcome measures** (e.g., utilization, falls, adverse drug events, adverse drug withdrawal events, mortality) **Implementation measures** (e.g., barriers, facilitators, resources [cost, staff, time])	Measures of only patient knowledge or levels of engagement. No outcome of interest.
Timing	Original studies published from 2019 onwards, the year of the search done for the MHS III report on this topic	Published in 2018 or earlier
Setting	Inpatient, outpatient, and long-term care settings in the United States	
Type of studies	Systematic reviews Original studies [published 2019 - present]: Randomized controlled trials or observational studies with a comparison group	Narrative reviews, scoping reviews, pre-post study design, editorials, commentaries, and abstracts

MHS = Making Healthcare Safer

Literature Searches for Studies of Effectiveness

We will search PubMed and the Cochrane Library for systematic reviews published since 2019 that address the review questions. If no recent high quality systematic review is identified, we will conduct searches of PubMed for original studies since 2019. We plan to use dual

independent review, but if this is not feasible, to efficiently identify articles 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. The team will decide whether it has enough time and resources to ask a second team member to check a 10% sample of citations to verify that important 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.

Description of Included Studies

To efficiently describe eligible studies, the full text of each potentially eligible article will be reviewed by a single team member to confirm eligibility and prepare a summary of the study, including author, year, study design, number of study participants, and main findings relevant to the review questions. Since Review Question 5 calls for identification of studies on the effectiveness of PSPs, we will describe the objectives and basic characteristics of those studies without conducting a detailed analysis of the findings of those studies. If resources permit we will have a second team member check a randomly selected 10% sample of the articles to verify that important studies were not excluded and confirm the accuracy of extracted data.

To describe eligible systematic reviews, a single team member will prepare a summary including the author, year, number of studies by study design, and main findings relevant to each of our review questions. For Review Question 8, we will list the name and source of each relevant toolkit along with a 1-2 sentence description of each toolkit. We will not endorse any specific toolkit.

Risk of Bias (Quality) Assessment

For studies that address Review Question 5 about the effectiveness of PSPs, the primary reviewer 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.[21, 22] When assessing RCTs, we will use the 7 items in Cochrane Collaboration's tool that cover the domains of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[21] 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.[22] 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.[23]

- **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.

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.

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.

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