Main Points

• Deprescribing has emerged as a clinical practice to reduce polypharmacy and use of potentially inappropriate medications (PIMs) and serve as a mechanism for quality improvement and increased patient safety. The purpose of this rapid response is to summarize recent literature on the use of deprescribing to improve the safety of medication use among older adults (age ≥ 65 years).

• Our literature search identified 15 systematic reviews and 7 original research studies published since 2019 that evaluated the effectiveness of deprescribing interventions in improving outcomes. All but one of the original research studies was a randomized trial.

• Deprescribing interventions included, but were not limited to, comprehensive medication reviews, patient education, provider education, and clinical decision support systems. Studies were conducted in healthcare settings across the care continuum, including outpatient clinics, emergency departments, acute care hospitals, long-term care facilities, and community pharmacies. Pharmacists were commonly included in interventions.

• Due to heterogeneity, few systematic reviews were able to quantitatively synthesize findings. Combined with findings from the original research studies, deprescribing in general decreased number of medications or potentially inappropriate medications. Clinical outcomes were more variable, with conflicting findings or non-statistically significant results. Few adverse drug withdrawal events resulted from deprescribing interventions.

• There is a large body of literature about barriers and facilitators to implementation of deprescribing interventions. Potentially influential facilitators include agreement by both the patient and the clinician to deprescribe, a standardized process for deprescribing, a strong culture/motivation to reduce medication use, and interprofessional team involvement.
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 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 spring 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. The Evidence-based Practice Center team used a modified Delphi technique to obtain a consensus from the TEP on the PSPs that merited the highest priority for a review. The prioritization took into consideration the team’s assessments of whether a proposed practice meets the definition of a PSP, the likelihood to harm a patient and scope of the condition addressed by the PSP, how widely the PSP is used, whether there are enough studies to merit an updated review on the PSP, and whether guidelines or high-quality systematic reviews on the PSP have been published within the prior 5 years. See the MHS IV Prioritization Report for additional details.

Medication use, whether prescription or nonprescription, 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) or potentially inappropriate medications (PIMs). This is especially common among adults aged 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 percent of older adults are exposed to polypharmacy and 58 percent to PIMs. 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. 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.”

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 implementing deprescribing interventions at the level of the patient, clinician, and healthcare system. Significant efforts have been made to develop and implement deprescribing interventions.
1.1 Overview of the Patient Safety Practice

Deprescribing spans healthcare settings, including outpatient clinics, acute care hospitalizations, long-term care, and community pharmacies. Deprescribing interventions take many forms, including reviews of medications by clinical pharmacists, identifying medications based on established criteria or lists (e.g., Beers, Screening Tool of Older Persons' potentially inappropriate Prescriptions [STOPP]), point-of-prescribing clinical decision support, and “direct-to-patient” educational materials.\textsuperscript{13-17} 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,\textsuperscript{18} a separate and distinct patient safety practice that produces a best possible medication history.\textsuperscript{19} 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 health outcomes.

Making Healthcare Safer III (2019) addressed deprescribing and summarized 14 studies.\textsuperscript{20} The MHS III 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.

For the purposes of this review, we have included evidence published since 2019 on the benefits or harms of deprescribing interventions among adults aged 65 years and over in any healthcare setting.

1.2 Purpose of the Rapid 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 aged 65 years and over within the United States. The response is organized around the review questions listed below.

1.3 Review Questions

1. What are 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 interventions 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 interventions?
2. Methods

For this rapid response, 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 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. We used dual independent review with consensus resolution to screen titles, abstracts, and articles.

We searched for good- or fair-quality systematic reviews published since 2019 and used them as the primary source for content. We did not perform an independent assessment of original studies cited in any such systematic review.

We answered Review Questions 1 and 2 by focusing on the harms and patient safety measures or indicators addressed in the studies identified for Review Question 5. For Review Question 2, we focused on identifying relevant measures 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 answered Review Questions 3 and 4 by citing selected references, including PSPs used and explanations of the rationale presented in the studies found for Review Question 5. For Review Questions 6 and 7, we focused on the barriers, facilitators, and required resources reported in the studies identified in Review Question 5. For Review Question 8, we searched publicly available patient safety toolkits developed by AHRQ and other organizations that could help to support implementation of the PSPs, including 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). We included any toolkits mentioned in the studies found for Review Question 5. We identified toolkits without assessing or endorsing them.

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 1.

<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Adults aged 65 and older, with polypharmacy or potentially inappropriate medications (PIMs)</td>
<td>Patients younger than 65 years of age</td>
</tr>
<tr>
<td>Intervention</td>
<td>Any deprescribing intervention</td>
<td>Studies focused on medication reconciliation only</td>
</tr>
<tr>
<td>Comparator</td>
<td>Usual practice</td>
<td>No clear description of comparator</td>
</tr>
</tbody>
</table>
### Study Parameter | Inclusion Criteria | Exclusion Criteria
--- | --- | ---
**Outcome** | **Medication outcome measures** (e.g., reduction of polypharmacy or PIMs; total medication count)  
**Clinical outcome measures** (e.g., healthcare utilization [e.g., hospitalizations] 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 | None
**Type of studies** | Systematic reviews  
Original studies [published 2019-July 2023]: 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; PIM = potentially inappropriate medication

### 2.2 Literature Searches for Studies of Effectiveness

We searched PubMed and the Cochrane Library for systematic reviews and original research studies published since 2019 to July 2023 that address the review questions (see Appendix A for the full search strategy).

### 2.3 Selection of Studies

The title and abstract of each citation were screened independently by two team members based on predefined eligibility criteria (Table 1), and then conflicts were resolved during team meetings. The full text of each potentially eligible article was reviewed independently by two team members to confirm eligibility and prepare a summary of the study, including author, year, study design, number of study participants, and main findings relevant to each of the review questions. Data extraction was done by one team member and checked by another.

### 2.4 Risk of Bias (Quality) Assessment

For studies that addressed Review Question 5 about the effectiveness of PSPs, we used the Cochrane Collaboration’s tool for assessing the risk of bias of RCTs or the ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions. 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.\textsuperscript{21} For nonrandomized studies, we used 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.\textsuperscript{22} The risk of bias assessments focused on the main outcome of interest in each study.

For a recent eligible systematic review, the primary reviewer used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.\textsuperscript{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.
3. Evidence Base

3.1 Number of Studies

Our search retrieved 1,471 unique titles and abstracts from which we reviewed 83 full-text articles for eligibility. We found 21 systematic reviews\(^{12,14,15,24-41}\) and 11 original research studies\(^{12-52}\) that met the inclusion criteria (Figure 1). Excluded studies are listed in Appendix B along with the background studies. Tables 2 and 3 contain the data tables for Review Question 5. Appendix C contains the critical appraisal tables for Review Question 5.

Figure 1. Results of the search and screening
3.2 Findings for Review Questions

3.2.1 Review Question 1. What Are the Frequency and Severity of Harms Associated With Polypharmacy or Potentially Inappropriate Medications (PIMs)?

Medication use, whether prescription or nonprescription, 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) or potentially inappropriate medications (PIMs). This is especially common among adults aged 65 years and older, who often have multiple chronic conditions, each of which may be treated with one or more medications. Estimates suggest that 45 percent of older adults are exposed to polypharmacy and 58 percent to PIMs. 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.

3.2.2 Review Question 2. What Patient Safety Measures or Indicators Have Been Used To Examine the Harm Associated With Polypharmacy and Potentially Inappropriate Medications?

Three Healthcare Effectiveness Data and Information Set (HEDIS) measures assess polypharmacy and PIMs.

1. Use of High-Risk Medications in the Elderly (HRM), which is the percentage of individuals at least 65 years of age who received at least 2 prescription claims for a high-risk medication during the measurement year. High-risk medications are based on the Beers Criteria.
2. Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (POLY-ACH), which is the percentage of individuals at least 65 years of age older adults with concurrent use of at least 2 unique anticholinergic medications.
3. Polypharmacy Use of Multiple Central Nervous System Active Medications in Older Adults (Poly-CNS), which is the percentage of individuals at least 65 years of age with concurrent use of three or more unique central-nervous system (CNS)-active medications.
3.2.3 Review Question 3. What Deprescribing Interventions Have Been Used To Prevent or Mitigate the Harm and in What Settings Have They Been Used?

A common type of deprescribing intervention is a medication review, sometimes referred to as a comprehensive medication review or comprehensive geriatric assessment. However, interventions labeled as “medication review” or “comprehensive geriatric assessment” can be very broad in scope and goals, and deprescribing is not necessarily a primary goal of all such interventions. So for the purposes of this review, we included interventions of medication review only if it was explicit that the primary goal was deprescribing.\textsuperscript{14,15,24,27,30-32,34-40,46,52} Such deprescribing medication reviews are sometimes guided by explicit criteria (e.g., STOPP).\textsuperscript{55} Medication reviews are often completed by pharmacists, but sometimes are conducted by physicians or nurse practitioners. The involvement of multiple clinicians in deprescribing is also seen in interventions such as case conferences, population health initiatives, and multidisciplinary team-based interventions. However, many interventions are pharmacist-driven, including via consultations, making deprescribing recommendations to other clinicians, and academic detailing.

Some deprescribing interventions provide education to prescribers, staff, or both, occasionally with subsequent audit and feedback.\textsuperscript{15,24,30,31,35,37,38,42} Patients, and family as applicable, also are recipients of education about polypharmacy, PIMs, and deprescribing.\textsuperscript{14,24,27,34,36-39,42,43,48,52} This most often occurs in written format, but videos are another mode of delivery.\textsuperscript{43}

A third broad category of deprescribing interventions are those capitalizing on computerized decision support (CDS). Examples of CDS-based interventions include notifications at the time of prescribing or renewing a medication\textsuperscript{44} (i.e., “interrupt orders) and “nudges”\textsuperscript{43} (e.g., priming, influencing, and setting defaults).

Deprescribing interventions have been designed and implemented in nearly all types of health care settings, including acute care hospitals, emergency departments/urgent care, long-term care (e.g., nursing homes, residency care facilities), palliative care facilities, outpatient clinics, home healthcare, and outpatient pharmacies.\textsuperscript{24,35,37} Some interventions are designed for care transitions and have elements that occur in more than one setting.\textsuperscript{52}

Deprescribing interventions can target specific medications, classes or groups of medications, or the entire medication regimen.

3.2.4 Review Question 4. What Is the Rationale for Deprescribing To Prevent or Mitigate the Harm?

One approach to minimize adverse outcomes associated with polypharmacy and PIMs is to proactively discontinue inappropriate medications. Deprescribing has the potential to improve multiple aspects of patient safety and quality of care, including by reducing drug burden, ADEs, and morbidity. It is also theorized that
deprescribing may improve medication adherence, reduce pharmacy-related and overall healthcare costs, and yield better clinical outcomes (e.g., reduce falls and cognitive impairment).

3.2.5 Review Question 5. What Studies Have Assessed the Effectiveness and Unintended Effects of Deprescribing Interventions and What New Evidence Has Been Published Since the Search Was Done for the Making Healthcare Safer (MHS) III report in 2019?

We identified 15 systematic reviews\textsuperscript{14,15,24,27,30-40} and 7 original research articles that assessed the effectiveness and unintended effects of deprescribing interventions that were published from 2019 to July 2023.\textsuperscript{42-44,46,48,50,52} Full details of findings can be seen in Table 2 and Table 3. We also found the manuscript resulting from MHS III; we did not include that study in Table 2.\textsuperscript{29} Regarding medication outcome measures, most reviews and original research demonstrated reductions in medication counts, PIMs, or both.\textsuperscript{14,15,24,27,30,33,35,37,40,48,52} Related, there were few reported adverse drug withdrawal events or direct harms associated with deprescribing.\textsuperscript{15,35,50,52} Note, similar to noninferiority studies, no statistically significant differences in clinical outcomes can be interpreted as not being associated with harm. Deprescribing less consistently was associated with change in clinical outcomes. Most studies found no reduction in falls;\textsuperscript{14,15,27,31,39} however, a systematic review by Shrestha (2019) reported that half of the included studies reduced falls.\textsuperscript{40} Systematic reviews most often reported no reduction in hospitalization.\textsuperscript{14,15,24,27,30,32,35,46} Similarly, while some reviews found no impact on mortality,\textsuperscript{15,24} Kua (2019) reported reduced mortality with deprescribing (odds ratio 0.90, 95\% confidence interval 0.82 to 0.99), and Shrestha (2019) found one of two included studies reduced mortality. Findings for patient-centered outcomes, such as quality of life, ranged from no impact\textsuperscript{15,24} to improvements.\textsuperscript{35,40,50} Many interventions did appear to reduce pharmacy-related costs,\textsuperscript{14,35} although it was more difficult to draw conclusions about overall healthcare costs.\textsuperscript{24,40}
Table 2. Characteristics of included systematic reviews

<table>
<thead>
<tr>
<th>Type of review</th>
<th>Author, Year</th>
<th># Studies</th>
<th>Types of Interventions</th>
<th>Setting</th>
<th>Population</th>
<th>Main Outcomes</th>
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</table>
| General Reviews | Ali, 2022<sup>24</sup> | 5 (2 narrative studies, 3 meta-analyses) | Pharmacist-led reviews, physician-led reviews, multidisciplinary team-led interventions; pharmacist consultations, medication reviews, patient education | Primary care, outpatient clinics, urgent care, acute care hospitals, long-term care, pharmacies, home healthcare | Adults with chronic conditions taking ≥5 medications | • reduced PIMs  
• improved medication adherence  
• no impact on ADEs  
• no impact on QoL  
• no impact on mortality  
• 2 of 5 reviews found reduced healthcare utilization  
• 2 of 5 reviews found reduced expenditures |
|                | Omuya, 2023<sup>15</sup> | 14 | Medication reviews, interdisciplinary interventions, staff education, computerized systems. All interventions examined the complete medication profile. | Outpatient clinics, acute care hospitals, long-term care, community pharmacies | Age ≥65 years taking ≥5 medications | • most (12 of 14) studies reduced number of medications  
• 1 study reduced dose of meds  
• 1 study reduced ED visits; no difference in 4 other studies  
• no difference in hospitalizations  
• no difference in falls  
• 4 of 5 studies increased HRQoL  
• 3 of 4 showed lower cost of medications with deprescribing  
• 1 of 4 cost-effective with increase in QALYs and decrease in total cost  
• 3 studies reported that 10-34% of deprescribed medications were restarted  
• 1 study reported 1.81% ADWEs |
<table>
<thead>
<tr>
<th>Type of review</th>
<th>Author, Year</th>
<th># Studies</th>
<th>Types of Interventions</th>
<th>Setting</th>
<th>Population</th>
<th>Main Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviews Based on Location of Intervention</td>
<td>Rodrigues , 2022</td>
<td>47</td>
<td>Medication review, healthcare professional educational interventions, clinical decision support systems, multifaceted interventions, organizational strategies</td>
<td>Outpatient clinics, emergency department, acute care hospitals, long-term care, community pharmacies</td>
<td>Age ≥65 years</td>
<td>• most (31 of 47) interventions reduced PIMs</td>
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<td></td>
<td>Bloomfield , 2020&lt;sup&gt;15&lt;/sup&gt; Bloomfield , 2019&lt;sup&gt;23&lt;/sup&gt; Sirois, 2023&lt;sup&gt;41&lt;/sup&gt;</td>
<td>38</td>
<td>Comprehensive medication review, provider education with or without feedback, patient education, patient and provider education computerized decision support</td>
<td>Outpatient clinics</td>
<td>Community-dwelling adults age ≥65 years</td>
<td>Medication review • reduced PIMs • may reduce mortality • no difference in hospitalizations, HRQoL, falls Education • reduced PIMs • no difference in mortality, hospitalizations, HRQoL Clinical Decision Support • may reduce PIMs • no harms (ADWES, mortality, hospitalizations)</td>
</tr>
<tr>
<td></td>
<td>Kua, 2019&lt;sup&gt;10&lt;/sup&gt;</td>
<td>41</td>
<td>Drug discontinuation, medication review, healthcare professional education, clinical informatics tool, case conferences</td>
<td>Long-term care</td>
<td>Age ≥60 years, long-term care resident</td>
<td>• reduced PIMs (OR 0.41; 95% CI 0.19-0.89) • reduced mortality (OR 0.90; 95% CI 0.82-0.99) • trend to reduced falls (OR 0.85; 95% CI 0.73-1.00) • no difference in hospitalization</td>
</tr>
<tr>
<td></td>
<td>Lee, 2022&lt;sup&gt;32&lt;/sup&gt;</td>
<td>16</td>
<td>Comprehensive geriatric assessment, decision support</td>
<td>Pre-operative clinics, acute care hospitals</td>
<td>Age ≥65 years undergoing elective or emergency surgery</td>
<td>• 3 of 12 studies reduced number of medications • 1 of 3 reduced hospital readmissions • no difference in mortality, post-operative complications</td>
</tr>
<tr>
<td>Type of review</td>
<td>Author, Year</td>
<td># Studies</td>
<td>Types of Interventions</td>
<td>Setting</td>
<td>Population</td>
<td>Main Outcomes</td>
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</table>
| Reviews Based on Limited Life Expectancy | Cardona, 2021 | 7 | Medication review, patient education | Outpatient clinics, acute care hospitals | In last year of life | • decreased number of medications and PIMs  
• no difference in falls  
• no difference in overall readmissions  
• no difference in mortality  |
| | Shrestha, 2019 | 9 | Medication review, interdisciplinary team review; Targeted medications used for prevention of disease (e.g., lipid lowering agents) | Acute care hospital, long-term care | Age ≥65 years with life limiting illness or limited life expectancy (2 years) | • 6 of 9 studies reduced number of medications and PIMs  
• 1 of 2 reduced mortality  
• 1 of 2 increased QoL  
• 1 of 2 reduced falls  
• 1 study reduced medication costs  
• 1 of 2 reduced total costs  |
<p>| Reviews Based on Specific Medication Class | Ribeiro, 2021 | 11 | Patient education, medication reviews | Outpatient clinics, acute care hospitals, long-term care, community pharmacies | Adults taking benzodiazepines | • reduced use of benzodiazepines  |
| | Salahudeen, 2022 | 23 | Medication review, care coordination, pharmacist-led academic detailing, healthcare professional education, population health initiative, clinical decision support | Outpatient clinics, acute care hospitals, long-term care | Age ≥65 years and taking anticholinergic medications | • 16 of 23 reduced anticholinergic prescribing errors  |</p>
<table>
<thead>
<tr>
<th>Type of review</th>
<th>Author, Year</th>
<th># Studies</th>
<th>Types of Interventions</th>
<th>Setting</th>
<th>Population</th>
<th>Main Outcomes</th>
</tr>
</thead>
</table>
| Reviews Based on Specific Intervention Type | Buzancic, 2022<sup>14</sup> | 24 | Community-based pharmacist involved in all; patient education, medication review, pharmacist-led deprescribing intervention, pharmacist-led collaborative intervention | Outpatient clinics | Most studies (n=20) restricted to age ≥65 years | • decreased number of medications  
• “limited or no impact on mortality, QoL, falls, hospitalizations or utilization” |
| | Monterio, 2019<sup>13</sup> | 16 | Clinical decision support | Outpatient clinics, emergency department, acute care hospitals | Age ≥65 years | • reduced PIMs per patient  
• increased PIM discontinuation |
| | Niznik, 2022<sup>14</sup> | 17 | Pharmacist involved in all; patient education, pharmacist medication review, pharmacist-led multidisciplinary team review | Outpatient clinics, acute care hospitals, long-term care | Age ≥65 years and taking benzodiazepines and/or opioids | • decreased benzodiazepines and/or opioids, with variable effect for different interventions |
| Reviews Based on Specific Outcome (Falls) | Lee, 2021<sup>11</sup> | 5 | Medication review, patient education, study-recommendations to prescriber | Outpatient clinics, long-term care | Age ≥65 years | • no difference in falls or fall-related injuries |
| | Seppala, 2022<sup>19</sup> | 49 for qualitative synthesis; 17 for quantitative analyses | Medication review, patient counseling, clinical decision support, interprofessional team review, study-recommendations | Outpatient clinics, acute care hospitals, long-term care | Age ≥65 years | • no difference in falls |

ADE = adverse drug event; ADWE = adverse drug withdrawal event; CI = confidence interval; ED = emergency department; HRQoL = health-related quality of life; OR = odds ratio; PIM = potentially inappropriate medication; QALY = quality adjusted life year
Table 3. Characteristics of included original studies

<table>
<thead>
<tr>
<th>Author, Year Study Design</th>
<th>Setting</th>
<th>Population</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Main Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayliss, 2022*2</td>
<td>Outpatient clinics (Primary care)</td>
<td>Age ≥65 years with dementia or mild cognitive impairment, ≥1 other chronic condition, ≥5 medications</td>
<td>Intervention: 1433 (in 9 clinics)</td>
<td>Patient and family educational materials; clinician education materials and notifications in the electronic health record</td>
<td>Usual care</td>
<td>- no difference in number of medications or PIMs</td>
</tr>
<tr>
<td>Campbell, 2019*4</td>
<td>Intensive Care Unit (ICU)</td>
<td>Age ≥18 years (included subjects had mean age 61.8 years), ICU admission ≥24 hours, delirium, contraindication to haloperidol</td>
<td>Intervention: 99</td>
<td>Computerized decision support to interrupt orders for strong anticholinergics, pharmacist review of medication orders; targeted anticholinergics and benzodiazepines</td>
<td>Usual care</td>
<td>- no difference in anticholinergic burden or benzodiazepine exposure</td>
</tr>
<tr>
<td>Campbell, 2021*3</td>
<td>Outpatient clinics (Primary care)</td>
<td>Age ≥65 years prescribed anticholinergics: tricyclic antidepressants and urinary antispasmodics</td>
<td>Intervention: 254 n 5 clinics</td>
<td>Clinical decision support, patient educational videos</td>
<td>Usual care</td>
<td>- no difference in discontinue orders for target anticholinergics</td>
</tr>
<tr>
<td>Herrington, 2023*6</td>
<td>Outpatient clinics</td>
<td>Age ≥76 years prescribed a z-drug eszopiclone, zolpidem, or zaleplon</td>
<td>Intervention: 1237</td>
<td>Physician-pharmacist collaboration, including medication reviews and monitoring.</td>
<td>Usual care</td>
<td>- no difference in number of medications</td>
</tr>
<tr>
<td>Kuntz, 2019*8</td>
<td>Outpatient clinics</td>
<td>Age ≥64 years prescribed a z-drug eszopiclone, zolpidem, or zaleplon</td>
<td>Education and prescriber letter (Ed): 50</td>
<td>Patient education and letter from prescriber, pharmacist telephone counseling session</td>
<td>Usual care</td>
<td>- reduced z-drug use at 6 months (Ed vs. UC: OR 4.02, 95% CI 1.66-9.77; Ed+ vs. UC: OR 4.10, 95% CI 1.65-10.29)</td>
</tr>
</tbody>
</table>
3.2.6 Review Question 6. What Are Common Barriers and Facilitators to Implementing Deprescribing Interventions?

There is a large literature about barriers and facilitators of deprescribing interventions, both original research and systematic reviews. Studies of barriers and facilitators are fundamentally different than studies of effectiveness, and thus the evidence in these reviews includes data from surveys, case studies, focus groups, and other study designs that would not be relevant to a review question about effectiveness. Our literature search identified three new good quality systematic reviews\(^{12,26,28}\) and three original research studies assessing barriers and facilitators for specific deprescribing interventions.\(^{47,49,51}\) One systematic review cited as evidence for Review Question 5 also contained data on barriers and facilitators.\(^{35}\)

Recent studies tend to cite and build on the foundational 2013 systematic review by Reeve and colleagues.\(^{10}\) That review included 21 articles and posited 4 main domains of barriers and facilitators: appropriateness of cessation (the degree to which the patient and/or the clinician agreed with cessation); a process for cessation; negative and positive influences on cessation; and fear of cessation versus dislike of the medication. The category with the greatest number of articles reporting a barrier or enabler was appropriateness. One new systematic review built on the existing review by Reeve, for a specific clinical context (cardiovascular...
medications) and found that for patients, informal caregivers, and healthcare providers the lack of evidence, fear of negative consequences, and social influences were the largest barriers to deprescribing. The other two new reviews both focused on deprescribing in the primary care setting. The first of these, which searched through 2019, included 40 studies (24 of which were qualitative studies, and 7 of the 40 were from the United States) and categorized barriers and enablers using the socio-ecological model, which includes patient, interpersonal, organizational, and cultural domains. This review found “a complex of barriers and facilitators to safe deprescribing interventions.” Cultural and organization barriers included a culture of diagnosing and prescribing, evidence-based guidance focused on single diseases, a lack of evidence-based guidance and a lack of shared communication, tools and resources. Interpersonal and individual level barriers included fragmented care, professional etiquette, and uncertainties. The second primary care-focused review searched through 2020, included 56 articles (of which 21 were qualitative studies and 8 articles were from the United States), and categorized barriers and enablers using constructs from normalization process theory – coherence, cognitive participation, collective action, and reflexive monitoring. This review found that most barriers and enablers were in the collective action construct, which included specifics such as a suboptimal deprescribing environment or a strong culture of prescribing, lack of confidence in deprescribing, or conversely confidence in deprescribing, availability of deprescribing resources, supportive guidance for patients, and the presence of a predefined deprescribing process. Specific barriers in the Coherence construct included deprescribing being seen as an abandonment of care, a money-saving exercise, threatening to current stable conditions with a fear of alienating patients, deviation from standard therapy, and the perceived negative consequences of deprescribing. The systematic review cited in Review Question 5 reported findings consistent with the above, with common barriers being clinician time constraints, lack of agreement with the recommendation to stop the medication, and “incomplete professional team involvement” as the most common barriers; common facilitators were reassurance that the medication can be restarted at a later date if needed and interprofessional consensus on which medications can be deprescribed.35 These newer systematic reviews continue to support the conclusions of the 2013 review by Reeve.

Four new original research studies assessed barriers and enablers for specific deprescribing initiatives, using the Reeve categorization scheme to assess deprescribing in the Shed-MEDS trial, aspects of context and implementation in the OPTIMIZE trial, strategies used across different U.S. Department of Veterans Affairs sites as part of a systemwide initiative to reduce benzodiazepine use, using Loentjevas’ model of process evaluation and the Consolidated Framework for Implementation Research to assess barriers and facilitators to implementation of an intervention to reduce psychotropic use in nursing home residents with dementia.
3.2.7 Review Question 7. What Resources (e.g., Cost, Staff, Time) Are Required for Implementation?

Our literature review did not identify any data on costs of implementing the interventions identified for Review Question 5.

3.2.8 Review Question 8. What Toolkits Are Available To Support Implementation of Deprescribing Interventions?

We identified several toolkits. Herrinton (2023) described multiple tools to support intervention implementation, with elements including an operational playbook, protocols, and workflow guidance.46 Several toolkits are also available on the internet:

- The American Geriatrics Society has a compendium of resources, including educational materials, tools to identify PIMs, and guidance for communication strategies.56
- The National Hospice and Palliative Care Organization similarly published deprescribing guidance, algorithms, and checklists, and other resources.57
- The Eastern Academic Health Science Network disseminated a toolkit on its website to support opioid deprescribing.58
4. Discussion

4.1 Interpretation of Findings

In MHS III, the topic of deprescribing was reviewed for the first time. That review focused on both deprescribing interventions and the STOPP criteria, presenting 14 studies specifically on deprescribing. Key findings included effective reduction of PIMs from geriatrician and clinical pharmacist medication reviews, patient and family education can improve communication about medication use, and deprescribing reduces medication-related costs.59

In this report, focused only on deprescribing, 15 new systematic reviews and 7 new original studies were identified. The findings of the included studies generally support those from MHS III; that is, deprescribing can reduce polypharmacy and PIMs (i.e., medication outcomes directly influenced by the intervention), lowering drug burden and potential for harm. Because of the close relation, deprescribing also lowered medication costs. While MHS III reported fewer clinical outcomes, this update found few robust findings for clinical and utilization outcomes, such as falls, hospitalizations, and mortality, which precludes a clear conclusion of the impact of deprescribing on these more distal outcomes. While the rationale for deprescribing is to improve health outcomes (via reduction of adverse events due to medications), this update provides evidence to support the safety of deprescribing, with few reported adverse drug withdrawal events and often no difference in mortality.

The multifactorial nature of many of the interventions also makes it difficult to determine which component was the driver of successful interventions; future work to delineate the most effective aspects of deprescribing interventions—as well as the strategies needed to successfully implement them—is still needed.

4.2 Limitations

This rapid response has several limitations. First, rapid responses use streamlined processes to complete the effort in a short timeline. We limited the studies discussed in Review question 5 to published works since 2019, the year of the MHS III review on this topic. We also restricted original research studies to those performed within the clinical practices and healthcare systems of the United States, and we required systematic reviews to include at least one study that was conducted within the United States. Second, many of the systematic reviews included heterogeneous studies, resulting in narrative syntheses rather than quantitative assessments of the effectiveness of deprescribing. Third, the complexity of many interventions, with multiple components and multiple clinical roles involved, makes it difficult to determine the magnitude of effect of individual aspects of the intervention. Finally, many studies—both those included in the systematic reviews and original research—
had followup assessments that may have occurred too soon or had sample sizes too small to detect differences in meaningful clinical outcomes (e.g., falls, mortality).

### 4.3 Implications and Conclusions

Deprescribing as an explicit, specific intervention is a relatively newer practice with the objective of reducing harms associated with polypharmacy and inappropriate medication use. Numerous systematic reviews continue to support the effectiveness of this practice to reduce proximal outcomes related to medications: medication count and number of potentially inappropriate medications. The evidence also indicates that deprescribing reduced medication-related costs, a conclusion also reached in MHS III. Importantly, deprescribing was associated with few adverse drug withdrawal events.

There remain numerous gaps and limitations in the evidence. Many deprescribing interventions, even if they reduce polypharmacy and PIMs, have not yet consistently been associated with improved clinical outcomes. There is also uncertainty about the impact of deprescribing on mortality and overall healthcare expenditures. Studies are needed that assess outcomes at a longer follow-up interval (i.e., beyond 1 year) to better determine the ability of deprescribing to effect change on clinically meaningful outcomes.

Deprescribing has potential to improve the safety and quality of medication use, with benefits to patients in multiple domains (clinical outcomes, quality of life, financially); however, further research is needed to support the benefit of deprescribing on those and other important domains. Until then, because there are still proximal benefits and minimal identified harms from deprescribing, it remains a practice with potential to improve the safety of medication use among older adults.
5. References


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Disclaimers

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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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Agency for Healthcare Research and Quality. February 2024. 
https://doi.org/10.23970/AHRQEPCEPC_MHS4DEPRESCRIBING. Posted final reports are located on the Effective Health Care Program search page.
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.

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Appendixes

Appendix A. Methods

Search Strategies for Published Literature

Databases:
- PubMed (NIH/NLM)
- Cochrane Library

Limits:
- 2019 – July 2023
- In English

Results:
- Total # imported to EndNote Library: 2,013
- Total # for review post-deduplication of EN Library: 1,463

Table A-1. PubMed search strategy

<table>
<thead>
<tr>
<th>Set #</th>
<th>Search</th>
<th># of Results</th>
</tr>
</thead>
<tbody>
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<td>3</td>
<td>(#1 AND #2) AND ((2019/1/1:2023/12/31[pdat]) AND (english[Filter]))</td>
<td>3,889</td>
</tr>
</tbody>
</table>
Deprescribing Literature Search Strategy - US Deprescribing Research Network

Development and validation of search filters to identify articles on deprescribing in Medline and Embase | BMC Medical Research Methodology | Full Text (biomedcentral.com)

A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice - PubMed (nih.gov)

Table A-2. Cochrane Database of Systematic Reviews (CDSR)

<table>
<thead>
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<th>Set #</th>
<th>Search</th>
<th># of Results</th>
</tr>
</thead>
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<td>1</td>
<td>deprescrib*:ti,ab,kw OR &quot;de prescribing&quot;:ti,ab,kw OR deprescription*:ti,ab,kw OR (&quot;inappropriate&quot; NEAR prescri*):ti,ab,kw OR (&quot;potentially inappropriate&quot; NEAR medication*):ti,ab,kw OR PIMs:ti,ab,kw OR PIM:ti,ab,kw OR &quot;appropriateness&quot; NEAR medication*:ti,ab,kw OR &quot;appropriate prescribing&quot;:ti,ab,kw OR polypharmacy:ti,ab,kw OR (&quot;geriatric&quot; NEAR pharmacotherap*):ti,ab,kw OR ((medication*:ti OR prescription*:ti) AND (inappropriate*:ti OR (&quot;over&quot; NEAR prescri*):ti OR overus*:ti)) OR ((medication*:ti OR drugs*:ti OR &quot;drug therapy&quot;:ti OR prescription*:ti OR prescribing*:ti) AND (inappropriate*:ti OR appropriate*:ti) AND (reduce*:ti OR discontinu*:ti OR &quot;dose reduction&quot;:ti OR taper*:ti) OR ((review*:ti OR assess*:ti OR evaluat*:ti OR screen*:ti) OR STOPP:ti,ab,kw OR START:ti,ab,kw OR &quot;Beers Criteria&quot;:ti,ab,kw) AND (appropriate*:ti,ab,kw OR inappropriate*:ti,ab) AND (&quot;drug utilization&quot;:ti OR medication*:ti OR prescription*:ti OR &quot;drug therapy&quot;:ti))</td>
<td>2,963</td>
</tr>
<tr>
<td>2</td>
<td>Limits: 2019-2023; *Cochrane Reviews: 11; Cochrane Protocols: 2; Special Collections: 1; Clinical Answers: 1</td>
<td>15*</td>
</tr>
</tbody>
</table>
Appendix B. List of Excluded Studies, Background Studies, and Toolkits

Excluded Studies
The reason for exclusion are noted at the end of the citation.


**Background/Introductory Information**


Toolkits


## Appendix C. Critical Appraisal Tables

### Table C-1. ROBINS-I risk of bias assessment for nonrandomized studies

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Confounding</th>
<th>Selection Bias</th>
<th>Bias in Measurement Classification of Interventions</th>
<th>Bias Due to Deviations From Intended Interventions</th>
<th>Bias Due to Missing Data</th>
<th>Bias in Measurement of Outcomes</th>
<th>Bias in Selection of the Reported Result</th>
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<td>Rashid, 2020</td>
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<td>Low</td>
<td>Unclear</td>
<td>Low</td>
<td>Unclear</td>
<td>Low</td>
</tr>
</tbody>
</table>

### Table C-2. Cochrane Risk of Bias for RCTs

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Random Allocation</th>
<th>Allocation Concealment</th>
<th>Blinding Participants</th>
<th>Blinding Outcome Assessment</th>
<th>Selective Reporting</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayliss, 2022</td>
<td>Low Risk</td>
<td>Low Risk</td>
<td>Low Risk</td>
<td>Uncertain Risk</td>
<td>Low Risk</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Campbell, 2019</td>
<td>Low Risk</td>
<td>Uncertain Risk</td>
<td>High Risk</td>
<td>Low Risk</td>
<td>Low Risk</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Campbell, 2021</td>
<td>Low Risk</td>
<td>Uncertain Risk</td>
<td>High Risk</td>
<td>High Risk</td>
<td>Low Risk</td>
<td>High Risk</td>
</tr>
<tr>
<td>Herrinton, 2023</td>
<td>Low Risk</td>
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<tr>
<td>Kuntz, 2019</td>
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<tr>
<td>Vasilevskis, 2023</td>
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<td>High Risk</td>
<td>Low Risk</td>
<td>Uncertain Risk</td>
</tr>
</tbody>
</table>

Note: For attrition, 80% followup used to assign low risk; 70%–80% = uncertain risk, <70% = high risk