

Making Healthcare Safer IV

Deprescribing To Reduce Medication Harms in Older Adults

Rapid Response



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 Evidencebased 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.² 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)³ 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 polypharmacy⁴ and 58 percent to PIMs.⁵ 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. ⁶⁻⁸ 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."9

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. ¹⁰⁻¹² 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. 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, ¹⁸ a separate and distinct patient safety practice that produces a best possible medication history. 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.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 topi cs=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 1. Inclusion and exclusion criteria

Study Parameter	Inclusion Criteria	Exclusion Criteria
Population	Adults aged 65 and older, 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

Study Parameter	Inclusion Criteria	Exclusion Criteria
Outcome	Medication outcome measures (e.g., reduction of polypharmacy or PIMs; total medication count)	Measures of only patient knowledge or levels of engagement No outcome of interest
	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])	
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	Narrative reviews, scoping reviews, pre-post study design, editorials, commentaries, and
	Original studies [published 2019-July 2023]: Randomized controlled trials or observational studies with a comparison group	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. ^{21,22}

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.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.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.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 studies⁴²⁻⁵² 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.

Additional citations identified Citations identified through database searching (PubMed through other sources and Cochrane) n = 7n = 1,464Excluded citations Citations screened (not comparative study, not n = 1,471systematic review, or not on topic) n = 1,179Abstracts screened n = 292Excluded abstracts (not comparative study, not systematic review, or not on topic) n = 209Full-text articles assessed for eligibility n = 83Full-text publications excluded, with reasons n = 42Background Not a topic of interest: n = 7n = 6No intervention of interest: n = 12No outcome of interest: n = 2Toolkits: Setting: n = 14n = 3Study design: n = 7Included studies potentially to abstract n = 30 publications in 32 studies Original research Systematic reviews n = 11n = 21

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)³ 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 polypharmacy⁴ and 58 percent to PIMs.⁵ 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.⁶⁻⁸

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.^{53,54}

- 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. 14,15,24,27,30-32,34-40,46,52 Such deprescribing medication reviews are sometimes guided by explicit criteria (e.g., STOPP). 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. 15,24,30,31,35,37,38,42 Patients, and family as applicable, also are recipients of education about polypharmacy, PIMs, and deprescribing. 14,24,27,34,36-39,42,43,48,52 This most often occurs in written format, but videos are another mode of delivery. 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 medication⁴⁴ (i.e., "interrupt orders) and "nudges"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.^{24,35,37} Some interventions are designed for care transitions and have elements that occur in more than one setting.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 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. 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 2.²⁹ Regarding medication outcome measures, most reviews and original research demonstrated reductions in medication counts, PIMs, or both. 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. 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; 14,15,27,31,39 however, a systematic review by Shrestha (2019) reported that half of the included studies reduced falls. 40 Systematic reviews most often reported no reduction in hospitalization, 14,15,27,30,32,35,46 Similarly, while some reviews found no impact on mortality, ^{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^{15,24} to improvements.^{35,40,50} Many interventions did appear to reduce pharmacy-related costs, ^{14,35} although it was more difficult to draw conclusions about overall healthcare costs. ^{24,40}

Table 2. Characteristics of included systematic reviews

	A 4 la	# Churchina		matic reviews	Deputation	Main Outganas
Type of review	Author, Year	# Studies	Types of Interventions	Setting	Population	Main Outcomes
	Ali, 2022 ²⁴	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
General Reviews	Omuya, 2023 ³⁵	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 costeffective 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

Type of review	Author, Year	# Studies	Types of Interventions	Setting	Population	Main Outcomes
	Rodrigues , 2022 ³⁷	47	Medication review, healthcare professional educational interventions, clinical decision support systems, multifaceted interventions, organizational strategies	Outpatient clinics, emergency department, acute care hospitals, long- term care, community pharmacies	Age ≥65 years	most (31 of 47) interventions reduced PIMs
Reviews Based on	Bloomfield , 2020 ¹⁵ Bloomfield , 2019 ²⁵ Sirois, 2023 ⁴¹	38	Comprehensive medication review, provider education with or without feedback, patient education, patient and provider education computerized decision support	Outpatient clinics	Community- dwelling adults age ≥65 years	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)
Location of Intervent ion	Kua, 2019 ³⁰	41	Drug discontinuation, medication review, healthcare professional education, clinical informatics tool, case conferences	Long-term care	Age ≥60 years, long- term care resident	 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
	Lee, 2022 ³²	16	Comprehensive geriatric assessment, decision support	Pre-operative clinics, acute care hospitals	Age ≥65 years undergoing elective or emergency surgery	3 of 12 studies reduced number of medications 1 of 3 reduced hospital readmissions no difference in mortality, postoperative complications

Type of review	Author,	# Studies	Types of	Setting	Population	Main Outcomes
Reviews Based	Year Cardona, 2021 ²⁷	7	Interventions 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
on Limited Life Expecta ncy	Shrestha, 2019 ⁴⁰	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
	Ribeiro, 2021 ³⁶	11	Patient education, medication reviews	Outpatient clinics, acute care hospitals, long-term care, community pharmacies	Adults taking benzodiazepi nes	reduced use of benzodiazepines
Reviews Based on Specific Medicati on Class	Salahudee n, 2022 ³⁸	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 anticholinergi c medications	16 of 23 reduced anticholinergic prescribing errors

Type of	Author,	# Studies	Types of	Setting	Population	Main Outcomes
review Reviews Based	Year Buzancic, 2022 ¹⁴	24	Interventions 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"
on Specific Intervent ion Type	Monterio, 2019 ³³	16	Clinical decision support	Outpatient clinics, emergency department, acute care hospitals	Age ≥65 years	reduced PIMs per patient increased PIM discontinuation
	Niznik, 2022 ³⁴	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 benzodiazepi nes and/or opioids	decreased benzodiazepines and/or opioids, with variable effect for different interventions
Reviews	Lee, 2021 ³¹	5	Medication review, patient education, study- recommendatio ns to prescriber	Outpatient clinics, long-term care	Age ≥65 years	no difference in falls or fall-related injuries
Based on Specific Outcome (Falls)	Seppala, 2022 ³⁹	49 for qualitative synthesis; 17 for quantitative analyses	Medication review, patient counseling, clinical decision support, interprofessiona I team review, study- recommendatio ns	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

			Intervention	Comparison	Main Outcomes
County	· opulation	Size	into vontion	Companicon	mani Gatoonioo
Outpatient clinics (Primary care)	Age ≥65 years with dementia or mild cognitive impairment, ≥1 other chronic condition, ≥5 medications	Intervention: 1433 (in 9 clinics) Control: 1579 (in 9 clinics)	Patient and family educational materials; clinician education materials and notifications in the electronic health record	Usual care	no difference in number of medications or PIMs
Care Unit (ICU)	(included subjects had mean age 61.8 years), ICU admission ≥24 hours, delirium, contraindication to haloperidol	99 Control: 101	decision support to interrupt orders for strong anticholinergics, pharmacist review of medication orders; targeted anticholinergics and benzodiazepines		 no difference in anticholinergic burden or benzodiazepin e exposure no difference in delirium duration or severity
Outpatient clinics (Primary care)	Age ≥65 years prescribed anticholinergics: tricyclic antidepressants and urinary antispasmodics	Intervention: 254 n 5 clinics) Control: 298 (in 5 clinics)	Clinical decision support, patient educational videos	Usual care	 no difference in discontinue orders for target anticholinergics no difference in anticholinergic prevalence
Outpatient clinics	Age ≥76 years with ≥10 non- topical prescriptions	Intervention: 1237 Control: 1233	Physician- pharmacist collaboration, including medication reviews and monitoring.	Usual care	 no difference in number of medications no difference in geriatric syndrome conditions no difference in mortality
Outpatient clinics	Age ≥64 years prescribed a z-drug eszopiclone, zolpidem, or zaleplon	Education and prescriber letter (Ed): 50 Education, prescriber letter, and pharmacist counseling session (Ed+): 49	Patient education and letter from prescriber, pharmacist telephone counseling session	Usual care	• 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)
	Outpatient clinics (Primary care) Intensive Care Unit (ICU) Outpatient clinics (Primary care) Outpatient clinics	Setting Population Outpatient clinics (Primary care) Age ≥65 years with dementia or mild cognitive impairment, ≥1 other chronic condition, ≥5 medications Intensive Care Unit (ICU) Age ≥18 years (included subjects had mean age 61.8 years), ICU admission ≥24 hours, delirium, contraindication to haloperidol Outpatient clinics (Primary care) Age ≥65 years prescribed anticholinergics: tricyclic antidepressants and urinary antispasmodics Outpatient clinics Age ≥76 years with ≥10 nontopical prescriptions Outpatient clinics Age ≥76 years with ≥10 nontopical prescriptions	Outpatient clinics (Primary care) Intensive Care Unit (ICU) Outpatient clinics (Primary care) Age ≥18 years (included subjects had mean age 61.8 years), ICU admission ≥24 hours, delirium, contraindication to haloperidol Outpatient clinics (Primary care) Outpatient clinics Age ≥65 years clinics) Intervention: 254 n 5 clinics) Control: 298 (in 5 clinics) Control: 298 (in 5 clinics) Control: 293 Control: 295 Control: 296 Control: 296 Control: 297 Control: 298 C	Setting Population Sample Size Intervention Outpatient clinics (Primary care) Age ≥65 years with dementia or mild cognitive impairment, ≥1 other chronic condition, ≥5 medications Intervention: 1433 (in 9 clinics) Patient and family educational materials; clinician education intervention: porputerized decision support to interrupt orders for strong anticholinergics; pharmacist review of medication orders; targeted anticholinergics and benzodiazepines Outpatient clinics Age ≥65 years and urinary antispasmodics Intervention: prescriber leducation and benzodiazepines Control: 298 (in 5 clinics) Clinical decision support, patient education including medication reviews and monitoring. Outpatient clinics Age ≥64 years prescribed a z-drug eszopiclone, zolpidem, or zaleplon Education and pharmacist counseling session Patient education prescriber, pharmacist telephone counseling session	Setting Population Sample Size Intervention Comparison Outpatient clinics (Primary care) Age ≥65 years with dementia or mild cognitive impairment, ≥1 other chronic condition, ≥5 medications Intervention: 1433 (in 9 clinics) Patient and family educational family educational materials; clinician education materials, clinician education materials and notifications in the electronic health record Intensive Care Unit (ICU) Age ≥18 years (included subjects had mean age 61.8 years), ICU admission ≥24 hours, delirium, contraindication to haloperidol Control: 101 Computerized decision support to interrupt orders for strong anticholinergics, pharmacist review of medication orders; targeted anticholinergics and benzodiazepines Usual care Outpatient clinics (Primary care) Age ≥65 years anticholinergics: tricyclic antichoriergics anticholinergics: tricyclic antichoriergics anticholinergics: tricyclic antichoriergics and urinary antispasmodics Intervention: 254 n 5 clinics) Clinical decision support to interrupt orders; targeted anticholinergics and orders; targeted anticholinergics and videos Usual care Outpatient clinics Age ≥76 years with ≥10 nontopical prescriptions Intervention: 1237 control: 1237 control: 1237 control: 1237 control: 1233 Physician-pharmacist collaboration, including medication reviews and monitoring. Usual care Outpatient clinics Age ≥64 years drug eszopiclone, zolpidem, or zaleplon Education prescriber letter (Ed): pharmacist counselling session

Author, Year Study Design	Setting	Population	Sample Size	Intervention	Comparison	Main Outcomes
Rashid, 2020 ⁵⁰ Retrospective, propensity score- matched cohort study	Outpatient clinics	Age ≥65 years prescribed ≥270 days-supply of NSAIDs	Intervention: 431 Control: 1724 (1:4 propensity score matched)	Clinical pharmacist-led collaborative drug therapy management protocol	Usual care	reduced pain exacerbation in intervention group no difference in ED visits or hospitalizations for acute kidney injury or gastrointestinal bleeds no difference in NSAID drug costs
Vasilevskis, 2023 ⁵² Randomized clinical trial	Acute care hospital and post-acute care	Age ≥50 years with ≥5 pre-hospital medications	Intervention: 142 Control: 142	Pharmacist- or nurse practitioner-led medication review, deprescribing discussions with patients, deprescribing recommendation s, home visits	Usual care	reduced medications and PIMs at discharge from post-acute care and at 90 days follow-up no difference in ADEs and ADWEs

ADE = adverse drug event; ADWE = adverse drug withdrawal event; CI = confidence interval; ED = emergency department; ICU = intensive care unit; NSAID = non-steroidal anti-inflammatory drug; OR = odds ratio; PIM = potentially inappropriate medication; UC = usual care

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. ²⁶ The other two new reviews both focused on deprescribing in the primary care setting. The first of these, ²⁸ 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 review¹² 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,⁴⁷ aspects of context and implementation in the OPTIMIZE trial,⁵¹ strategies used across different U.S. Department of Veterans Affairs sites as part of a systemwide initiative to reduce benzodiazepine use,⁴⁹ 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.⁴⁵

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.



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Disclaimers

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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.

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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

Set #	Search	# of Results
1	elder[tiab] OR elders[tiab] OR elderly[tiab] OR geriatric*[tiab] OR gerontolog*[tiab] OR "old age"[tiab] OR "oldest old"[tiab] OR "senior citizen*"[tiab] OR "very old"[tiab] OR septuagenarian*[tiab] OR octogenarian*[tiab] OR contagenarian*[tiab] OR nonagenarian*[tiab] OR centarian*[tiab] OR centenarian*[tiab] OR supercentenarian*[tiab] OR "older people"[tiab] OR "older person"[tiab] OR "older subject*"[tiab] OR "older patient*"[tiab] OR "older age*"[tiab] OR "older adult*"[tiab] OR "older man"[tiab] OR "older men"[tiab] OR "older male*"[tiab] OR "older woman"[tiab] OR "older women"[tiab] OR "older female*"[tiab] OR "older veterans"[tiab] OR "older population"[tiab] OR "nursing home*"[tiab] OR "Aged"[MAJR] OR "Aged, 80 and over"[MAJR] OR "Health Services for the Aged"[MAJR] OR "Geriatric Assessment"[MAJR] OR "Geriatrics"[MAJR] OR "Geriatric Psychiatry"[MAJR] OR "Homes for the Aged"[MAJR] OR "Nursing Homes"[MAJR]	684,889
2	("deprescrib*"[tiab] OR "de prescribing"[tiab] OR "de prescription*"[tiab] OR "inappropriate prescri*"[tiab] OR "inappropriate medication*"[tiab] OR "potentially inappropriate*"[tiab] OR PIMs[tiab] OR PIMs[tiab] OR "appropriateness medications"[tiab:~2] OR "appropriate prescribing"[tiab] OR (("medication*"[ti] OR "prescribing"[ti] OR prescribing"[ti] OR prescribing"[ti] OR prescribing"[ti] OR ((medication*[ti] OR drugs[ti] OR "drug therap*"[ti] OR overus*[ti])) OR "polypharmacy"[tiab] OR ((medication*[ti] OR drugs[ti] OR "drug therap*"[ti] OR prescription*[ti] OR "prescribing"[ti]) AND (inappropriate*[ti] OR appropriate*[ti]) AND (reduc*[ti] OR discontinu*[ti] OR withdraw*[ti] OR cease[ti] OR ceasing[ti] OR cessation[ti] OR "dose reduction"[ti] OR taper*[ti])) OR ((review*[ti] OR assess*[ti] OR evaluat*[ti] OR screen*[tiab] OR STOPP[tiab] OR START[tiab] OR "STOPP START"[tiab:~1] OR "Beers Criteria"[tiab]) AND (appropriate*[tiab] OR inappropriate*[tiab]) AND ("drug utilization"[ti] OR medication[ti] OR prescrib*[ti] OR prescription*[tiab] OR "drug therap*"[ti])) OR "geriatric pharmacotherap*"[tiab] OR "geriatric pharmacol*"[tiab] OR "Deprescriptions"[MAJR] OR "Inappropriate Prescribing"[MAJR] OR "Drug Utilization Review"[MAJR:NoExp] OR Polypharmacy[MAJR] OR "Potentially Inappropriate Medication List"[MAJR])	27,719
3	(#1 AND #2) AND ((2019/1/1:2023/12/31[pdat]) AND (english[Filter]))	3,889

Set #	Search	# of Results
4	clinicalstudy[Filter] OR clinicaltrial[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR evaluationstudy[Filter] OR governmentpublication[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter] OR researchsupportamericanrecoveryandreinvestmentact[Filter] OR researchsupportnihextramural[Filter] OR researchsupportnihextramural[Filter] OR researchsupportusgovtnonphs[Filter] OR researchsupportusgovtnonphs[Filter] OR researchsupportusgovtnonphs[Filter] OR researchsupportusgovtnonphs[Filter] OR researchsupportusgovtnonphs[Filter] OR researchsupportusgovtnonphs[Filter] OR validationstudy[Filter] OR "randomized control*"[ti] OR "randomised control*"[ti]	6,124,063
5	#3 AND #4	721
6	systematicreview[Filter] OR meta-analysis[Filter] OR review[Filter] OR guideline[Filter] OR practiceguideline[Filter] OR "systematic review"[ti] OR meta-analysis[ti] OR "scoping review"[ti] OR "state of the art"[ti] OR "realist review"[ti] OR "rapid review"[ti] OR "narrative review"[ti] OR "umbrella review"[ti] OR "rapid evidence"[ti] OR "literature review"[ti] OR "evidence synthesis"[ti] OR "evidence summary"[ti] OR guideline*[ti]	3,518,456
7	#3 AND #6	693

References:

<u>Deprescribing Literature Search Strategy - US Deprescribing Research Network</u>

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

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)

Set	Search	# of
#		Results
1	deprescrib*:ti,ab,kw OR "de prescribing":ti,ab,kw OR deprescription*:ti,ab,kw OR ("inappropriate" NEAR prescri*):ti,ab,kw OR "inappropriate medication":ti,ab,kw OR ("potentially inappropriate" NEAR medication*):ti,ab,kw OR PIMs:ti,ab,kw OR PIMs:ti,ab,kw OR ("appropriateness" NEAR medication*):ti,ab,kw OR "drug utilization review":ti,ab,kw OR "appropriate prescribing":ti,ab,kw OR polypharmacy:ti,ab,kw OR ("geriatric" NEAR pharmacotherap*):ti,ab,kw OR ("geriatric" NEAR pharmacotherap*):ti,ab,kw OR ("geriatric" NEAR pharmacotherap*):ti,ab,kw OR ("medication*:ti OR prescribing:ti OR prescription*:ti) AND (inappropriate*:ti OR ("over" NEAR prescrib*):ti OR overus*:ti)) OR ((medication*:ti OR drugs:ti OR "drug therapy":ti OR prescription*:ti OR withdraw*:ti OR cease:ti OR ceasing:ti OR cessation:ti OR "dose reduction":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 "STOPP START":ti,ab,kw OR "Beers Criteria":ti,ab,kw) AND (appropriate*:ti,ab,kw OR inappropriate*:ti,ab) AND ("drug utilization":ti OR medication:ti OR prescrib*:ti OR prescription*:ti OR "drug therapy":ti))	2,963
2	#1 Limits: 2019-2023; *Cochrane Reviews: 11 ; Cochrane Protocols: 2 ; Special Collections: 1 ; Clinical Answers: 1	15*

Appendix B. List of Excluded Studies, Background Studies, and Toolkits

Excluded Studies

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

- 1. Impact of deprescribing for people with limited life expectancy. Drug Ther Bull. 2023 May;61(5):69. doi: 10.1136/dtb.2023.000012. PMID: 36882298. *Study Design: Not a SR*
- 2. Alharthi M, Wright D, Scott S, et al. Barriers and enablers to deprescribing for older people in care homes: The theory-based perspectives of pharmacist independent prescribers. Res Social Adm Pharm. 2023 May;19(5):746-52. doi: 10.1016/j.sapharm.2023.01.013. PMID: 36732210. *Setting*
- 3. Aubert CE, Blum MR, Gastens V, et al. Prescribing, deprescribing and potential adverse effects of proton pump inhibitors in older patients with multimorbidity: an observational study. CMAJ Open. 2023 Jan-Feb;11(1):E170-e8. doi: 10.9778/cmajo.20210240. PMID: 36854455. *Setting*
- 4. Baumgartner AD, Clark CM, LaValley SA, et al. Interventions to deprescribe potentially inappropriate medications in the elderly: Lost in translation? J Clin Pharm Ther. 2020 Jun;45(3):453-61. doi: 10.1111/jcpt.13103. PMID: 31873955. *Outcome*
- 5. Bighelli I, Rodolico A, Siafis S, et al. Antipsychotic polypharmacy reduction versus polypharmacy continuation for people with schizophrenia. Cochrane Database of Systematic Reviews. 2022(8). doi: 10.1002/14651858.CD014383.pub2. PMID: CD014383. *Intervention*
- 6. Boersma MN, Huibers CJA, Drenth-van Maanen AC, et al. The effect of providing prescribing recommendations on appropriate prescribing: A cluster-randomized controlled trial in older adults in a preoperative setting. Br J Clin Pharmacol. 2019 Sep;85(9):1974-83. doi: 10.1111/bcp.13987. PMID: 31108564. *Setting*
- 7. Brokaar EJ, van den Bos F, Visser LE, et al. Deprescribing in Older Adults With Cancer and Limited Life Expectancy: An Integrative Review. Am J Hosp Palliat Care. 2022 Jan;39(1):86-100. doi: 10.1177/10499091211003078. PMID: 33739162. *Intervention*
- 8. Christopher CM, Kc B, Blebil A, et al. Clinical and Humanistic Outcomes of Community Pharmacy-Based Healthcare Interventions Regarding Medication Use in Older Adults: A Systematic Review and Meta-Analysis. Healthcare (Basel). 2021 Nov 18;9(11). doi: 10.3390/healthcare9111577. PMID: 34828622. *Intervention: Not about deprescribing interventions*
- 9. Clarkson L, Hart L, Lam AK, et al. Reducing inappropriate polypharmacy for older patients at specialist outpatient clinics: a systematic review. Curr Med Res Opin. 2023 Apr;39(4):545-54. doi: 10.1080/03007995.2023.2185390. PMID: 36847597. *Not on topic: Not specifically deprescribing*

- 10. Cochrane Special Collections. Achieving sustainable healthcare through deprescribing of unnecessary medications: making sense of the evidence. Cochrane Library. 2022. doi: SC000054. *Study Design*
- 11. Crisafulli S, Luxi N, Coppini R, et al. Anti-hypertensive drugs deprescribing: an updated systematic review of clinical trials. BMC Fam Pract. 2021 Oct 20;22(1):208. doi: 10.1186/s12875-021-01557-y. PMID: 34666689. *Setting*
- 12. Debacq C, Bourgueil J, Aidoud A, et al. Persistence of Effect of Medication Review on Potentially Inappropriate Prescriptions in Older Patients Following Hospital Discharge. Drugs Aging. 2021 Mar;38(3):243-52. doi: 10.1007/s40266-020-00830-6. PMID: 33474671. Setting
- 13. Deng Z, Thompson W, Korenvain C, et al. Benefits and Harms of Deprescribing Antihyperglycemics for Adults With Type 2 Diabetes: A Systematic Review. Can J Diabetes. 2022 Jul;46(5):473-9. doi: 10.1016/j.jcjd.2022.01.009. PMID: 35739041. *Intervention: Not an intervention*
- 14. Elbeddini A, Sawhney M, Tayefehchamani Y, et al. Deprescribing for all: a narrative review identifying inappropriate polypharmacy for all ages in hospital settings. BMJ Open Qual. 2021 Jul;10(3). doi: 10.1136/bmjoq-2021-001509. PMID: 34230053. *Study Design: Not a SR*
- 15. Etherton-Beer C, Page A, Naganathan V, et al. Deprescribing to optimise health outcomes for frail older people: a double-blind placebo-controlled randomised controlled trial-outcomes of the Opti-med study. Age Ageing. 2023 May 1;52(5). doi: 10.1093/ageing/afad081. PMID: 37247404. *Setting*
- 16. Ha M, Furman A, Al Rihani SB, et al. Pharmacist-driven interventions to de-escalate urinary antimuscarinics in the Programs of All-Inclusive Care for the Elderly. J Am Geriatr Soc. 2022 Nov;70(11):3230-8. doi: 10.1111/jgs.17965. PMID: 35900034. *Study Design*
- 17. Hickman E, Seawoodharry M, Gillies C, et al. Deprescribing in cardiometabolic conditions in older patients: a systematic review. Geroscience. 2023 Jul 5. doi: 10.1007/s11357-023-00852-z. PMID: 37402905. *Intervention: Not an intervention*
- 18. Ibrahim K, Cox NJ, Stevenson JM, et al. A systematic review of the evidence for deprescribing interventions among older people living with frailty. BMC Geriatr. 2021 Apr 17;21(1):258. doi: 10.1186/s12877-021-02208-8. PMID: 33865310. *Setting*
- 19. Juraschek SP, Cluett JL, Belanger MJ, et al. Effects of Antihypertensive Deprescribing Strategies on Blood Pressure, Adverse Events, and Orthostatic Symptoms in Older Adults: Results From TONE. Am J Hypertens. 2022 Apr 2;35(4):337-46. doi: 10.1093/ajh/hpab171. PMID: 34718403. *Intervention*
- 20. Kaminaga M, Komagamine J, Tatsumi S. The effects of in-hospital deprescribing on potential prescribing omission in hospitalized elderly patients with polypharmacy. Sci Rep. 2021 Apr 26;11(1):8898. doi: 10.1038/s41598-021-88362-w. PMID: 33903645. *Setting*
- 21. Kose E, Endo H, Hori H, et al. Association of Pharmacist-led Deprescribing Intervention with the Functional Recovery in Convalescent Setting. Pharmazie. 2022 May 1;77(5):165-70. doi: 10.1691/ph.2022.2323. PMID: 35655381. *Setting*

- 22. Lamarre M, Marcotte M, Laurin D, et al. Discontinuation of bisphosphonates in seniors: a systematic review on health outcomes. Arch Osteoporos. 2021 Sep 15;16(1):133. doi: 10.1007/s11657-021-01000-w. PMID: 34524561. *Intervention*
- 23. Lee JW, Boyd CM, Leff B, et al. Tailoring a home-based, multidisciplinary deprescribing intervention through clinicians and community-dwelling older adults. J Am Geriatr Soc. 2023 May;71(5):1663-6. doi: 10.1111/jgs.18186. PMID: 36515689. *Study Design*
- 24. Mozer C, Madden W, Cursio J, et al. Rates of Inappropriate Dosing in Older Adults at an Urban, Academic Hospital. Am J Med Qual. 2021 Nov-Dec 01;36(6):469-70. doi: 10.1097/01.Jmq.0000751156.52061.64. PMID: 34038914. *Study Design*
- 25. Mucherino S, Casula M, Galimberti F, et al. The Effectiveness of Interventions to Evaluate and Reduce Healthcare Costs of Potentially Inappropriate Prescriptions among the Older Adults: A Systematic Review. Int J Environ Res Public Health. 2022 May 31;19(11). doi: 10.3390/ijerph19116724. PMID: 35682331. *Not on topic*
- 26. Persell SD, Brown T, Doctor JN, et al. Development of High-Risk Geriatric Polypharmacy Electronic Clinical Quality Measures and a Pilot Test of EHR Nudges Based on These Measures. J Gen Intern Med. 2022 Aug;37(11):2777-85. doi: 10.1007/s11606-021-07296-1. PMID: 34993860. *Not on topic*
- 27. Pruskowski JA, Springer S, Thorpe CT, et al. Does Deprescribing Improve Quality of Life? A Systematic Review of the Literature. Drugs Aging. 2019 Dec;36(12):1097-110. doi: 10.1007/s40266-019-00717-1. PMID: 31598908. *Intervention*
- 28. Rantsi M, Pitkälä KH, Kautiainen H, et al. Cost-effectiveness of an educational intervention to reduce potentially inappropriate medication. Age Ageing. 2022 May 1;51(5). doi: 10.1093/ageing/afac112. PMID: 35604803. *Setting*
- 29. Reeve E, Jordan V, Thompson W, et al. Withdrawal of antihypertensive drugs in older people. Cochrane Database Syst Rev. 2020 Jun 10;6(6):Cd012572. doi: 10.1002/14651858.CD012572.pub2. PMID: 32519776. *Intervention*
- 30. Romano S, Figueira D, Teixeira I, et al. Deprescribing Interventions among Community-Dwelling Older Adults: A Systematic Review of Economic Evaluations. Pharmacoeconomics. 2022 Mar;40(3):269-95. doi: 10.1007/s40273-021-01120-8. PMID: 34913143. *Setting*
- 31. Sawan MJ, Moga DC, Ma MJ, et al. The value of deprescribing in older adults with dementia: a narrative review. Expert Rev Clin Pharmacol. 2021 Nov;14(11):1367-82. doi: 10.1080/17512433.2021.1961576. PMID: 34311630. *Study Design: Not a SR*
- 32. Seidu S, Kunutsor SK, Topsever P, et al. Deintensification in older patients with type 2 diabetes: A systematic review of approaches, rates and outcomes. Diabetes Obes Metab. 2019 Jul;21(7):1668-79. doi: 10.1111/dom.13724. PMID: 30938038. *Intervention*
- 33. Seto H, Ishimaru N, Ohnishi J, et al. Multidisciplinary Team Deprescribing Intervention for Polypharmacy in Elderly Orthopedic Inpatients: A Propensity Score-matched Analysis of a Retrospective Cohort Study. Intern Med. 2022 Aug 15;61(16):2417-26. doi: 10.2169/internalmedicine.8929-21. PMID: 35022357. *Setting*

- 34. Shrestha S, Poudel A, Cardona M, et al. Impact of deprescribing dual-purpose medications on patient-related outcomes for older adults near end-of-life: a systematic review and meta-analysis. Ther Adv Drug Saf. 2021;12:20420986211052343. doi: 10.1177/20420986211052343. PMID: 34707802. *Setting*
- 35. Shrestha S, Poudel A, Forough AS, et al. A systematic review on methods for developing and validating deprescribing tools for older adults with limited life expectancy. Int J Pharm Pract. 2023 Mar 13;31(1):3-14. doi: 10.1093/ijpp/riac094. PMID: 36472946. *Intervention: Not about deprescribing interventions*
- 36. Stötzner P, Ferrebus Abate RE, Henssler J, et al. Structured Interventions to Optimize Polypharmacy in Psychiatric Treatment and Nursing Homes: A Systematic Review. J Clin Psychopharmacol. 2022 Mar-Apr 01;42(2):169-87. doi: 10.1097/jcp.0000000000001521. PMID: 35230048. *Not on topic: Not specifically deprescribing*
- 37. Taylor-Rowan M, Alharthi AA, Noel-Storr AH, et al. Anticholinergic deprescribing interventions for reducing risk of cognitive decline or dementia in older adults with and without prior cognitive impairment. Cochrane Database of Systematic Reviews. 2022(12). doi: 10.1002/14651858.CD015405. PMID: CD015405. *Not on topic*
- 38. Thompson W, Lundby C, Graabaek T, et al. Tools for Deprescribing in Frail Older Persons and Those with Limited Life Expectancy: A Systematic Review. J Am Geriatr Soc. 2019 Jan;67(1):172-80. doi: 10.1111/jgs.15616. PMID: 30315745. *Outcome*
- 39. Turk A, Wong G, Mahtani KR, et al. Optimising a person-centred approach to stopping medicines in older people with multimorbidity and polypharmacy using the DExTruS framework: a realist review. BMC Med. 2022 Aug 31;20(1):297. doi: 10.1186/s12916-022-02475-1. PMID: 36042454. *Setting*
- 40. Ulley J, Harrop D, Ali A, et al. Deprescribing interventions and their impact on medication adherence in community-dwelling older adults with polypharmacy: a systematic review. BMC Geriatr. 2019 Jan 18;19(1):15. doi: 10.1186/s12877-019-1031-4. PMID: 30658576. *Not on topic*
- 41. van der Worp H, Jellema P, Hordijk I, et al. Discontinuation of alpha-blocker therapy in men with lower urinary tract symptoms: a systematic review and meta-analysis. BMJ Open. 2019 Nov 7;9(11):e030405. doi: 10.1136/bmjopen-2019-030405. PMID: 31699724. *Intervention*
- 42. Vaughan CP, Burningham Z, Kelleher JL, et al. A cluster-randomized trial of two implementation strategies to deliver audit and feedback in the EQUIPPED medication safety program. Acad Emerg Med. 2023 Apr;30(4):340-8. doi: 10.1111/acem.14697. PMID: 36790188. *Not on topic*

Background/Introductory Information

1. O'Mahony D. STOPP/START criteria for potentially inappropriate medications/potential prescribing omissions in older people: origin and progress. Expert Rev Clin Pharmacol. 2020 Jan;13(1):15-22. doi: 10.1080/17512433.2020.1697676. PMID: 31790317. *Background*

- 2. Reeve E, To J, Hendrix I, et al. Patient barriers to and enablers of deprescribing: a systematic review. Drugs Aging. 2013 Oct;30(10):793-807. doi: 10.1007/s40266-013-0106-8. PMID: 23912674. *Background*
- 3. Reeve J, Maden M, Hill R, et al. Deprescribing medicines in older people living with multimorbidity and polypharmacy: the TAILOR evidence synthesis. Health Technol Assess. 2022 Jul;26(32):1-148. doi: 10.3310/aafo2475. PMID: 35894932. *Background*
- 4. Saeed D, Carter G, Parsons C. Interventions to improve medicines optimisation in frail older patients in secondary and acute care settings: a systematic review of randomised controlled trials and non-randomised studies. Int J Clin Pharm. 2022 Feb;44(1):15-26. doi: 10.1007/s11096-021-01354-8. PMID: 34800255. *Background*
- 5. Santos NSD, Marengo LL, Moraes FDS, et al. Interventions to reduce the prescription of inappropriate medicines in older patients. Rev Saude Publica. 2019 Jan 31;53:7. doi: 10.11606/s1518-8787.2019053000781. PMID: 30726488. *Background*
- 6. Steinman MA, Boyd CM, Spar MJ, et al. Deprescribing and deimplementation: Time for transformative change. J Am Geriatr Soc. 2021 Dec;69(12):3693-5. doi: 10.1111/jgs.17441. PMID: 34499742. *Background*

Toolkits

- 1. Eastern AHSN. Opioid deprescribing toolkit. n.d. https://easternahsn.org/about-us/our-projects/opioid-deprescribing-toolkit/. Accessed on September 22, 2023.
- 2. GeriatricsCareOnline.org. AGS Deprescribing Toolkit. n.d. https://geriatricscareonline.org/toc/ags-deprescribing-toolkit/TK013. Accessed on September 22, 2023.
- 3. National Hospice and Palliative Care Organization. Hospice Medication Deprescribing Toolkit. November 2020. https://www.nhpco.org/wp-content/uploads/NHPCO Deprescribing Toolkit.pdf.

Appendix C. Critical Appraisal Tables

Table C-1. 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
Rashid, 2020 ⁵⁰	Unclear	Low	Low	Unclear	Low	Unclear	Low

Table C-2. Cochrane Risk of Bias for RCTs

Author, Year	Random	Allocation Concealment	Blinding Participants	Blinding Outcome Assessment	Selective Reporting	Attrition
Bayliss, 2022 ⁴²	Low Risk	Low Risk	Low Risk	Uncertain Risk	Low Risk	Low Risk
Campbell, 2019 ⁴⁴	Low Risk	Uncertain Risk	High Risk	Low Risk	Low Risk	Low Risk
Campbell, 2021 ⁴³	Low Risk	Uncertain Risk	High Risk	High Risk	Low Risk	High Risk
Herrinton, 2023 ⁴⁶	Low Risk	Low Risk	High Risk	High Risk	Low Risk	Low Risk
Kuntz, 2019 ⁴⁸	Low Risk	Uncertain Risk	High Risk	High Risk	Low Risk	Low Risk
Vasilevskis, 2023 ⁵²	Low Risk	Uncertain Risk	High Risk	High Risk	Low Risk	Uncertain Risk

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

