

Implementation considerations of deprescribing interventions: A scoping review

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Over half of older adults experience polypharmacy, including medications that may be inappropriate or unnecessary. Deprescribing, which is the process of discontinuing or reducing inappropriate and/or unnecessary medications, is an effective way to reduce polypharmacy. This review summarizes (1) the process of deprescribing and conceptual models and tools that have been developed to facilitate deprescribing, (2) barriers, enablers, and factors associated with deprescribing, and (3) characteristics of deprescribing interventions in completed trials, as well as (4) implementation considerations for deprescribing in routine practice. In conceptual models of deprescribing, multilevel factors of the patient, clinician, and health-care system are all related to the efficacy of deprescribing. Numerous tools have been developed for clinicians

to facilitate deprescribing, yet most require substantial time and, thus, may be difficult to implement during routine health-care encounters. Multiple deprescribing interventions have been evaluated, which mostly include one or more of the following components: patient education, medication review, identification of deprescribing targets, and patient and/or provider communication about high-risk medications. Yet, there has been limited consideration of implementation factors in prior deprescribing interventions, especially with regard to the personnel and resources in existing health-care systems and the feasibility of incorporating components of deprescribing interventions into the routine care processes of clinicians. Future trials require a more balanced consideration of both effectiveness and implementation when designing deprescribing interventions.

Keywords: clinical trial, deprescriptions, polypharmacy, potentially inappropriate medications, review

Background

Older adults often take multiple medications. Studies show that more than half of older adults take five or more medications concurrently, which

is a geriatric syndrome called polypharmacy [1]. Polypharmacy can increase the risk of medication-related problems such as the use of potentially inappropriate medications (PIMs) [2–7], medication

errors [8–10], medication nonadherence [11], and drug–drug or drug–disease interactions [12]. Additionally, polypharmacy can also contribute to other geriatric syndromes such as falls, depression, and cognitive impairment [13]. Furthermore, inappropriate polypharmacy can increase older adults' risk for hospitalization [14–18] and even mortality [19]. Therefore, polypharmacy should be addressed as part of routine geriatric clinical practice to ensure patient safety and optimize health outcomes.

There are multiple factors that can contribute to polypharmacy among older adults. First, because many older adults have multiple chronic conditions, they often receive care from multiple providers. Discontinuity of care and the lack of shared health information among providers can result in incomplete medication lists and other medication-related errors such as duplications and inconsistent documentation related to indication, dose, or start and stop dates. Additionally, older adults experience frequent care transitions between home, hospital, and post-acute care settings (e.g., short-term skilled nursing facilities and inpatient rehabilitative facilities), and studies have revealed gaps in provider communication and care coordination during these transitions. The complexity of medication regimens combined with many older adults' need for help with medication management further increases the risk of medication errors related to polypharmacy [1, 20].

A recent systematic review shows that numerous intervention studies have been conducted to improve health outcomes among older adults with polypharmacy [21]. These intervention studies have focused on medication review, medication reconciliation, education about medication management, and more recently, deprescribing [21]. For example, medication reconciliation is the process of identifying all medications a patient is taking, with the aim to reduce medication errors [22]. In a study among hospitalized older patients with polypharmacy, medication reconciliation upon hospital discharge led to only a modest reduction in rehospitalization rates. The authors noted that inappropriate polypharmacy remained even after medication reconciliation and prevented further reductions in rehospitalization risk [23].

Deprescribing, which is defined as the clinician-supervised process of discontinuing or reducing medications that are unnecessary and/or no longer beneficial [24, 25], has been shown to be

an effective way to reduce inappropriate polypharmacy. Empirical studies have also demonstrated that deprescribing can effectively reduce medication burden and cost [26], decrease the use of PIMs [26], and increase medication adherence [27]. International campaigns and quality improvement initiatives [28–30] such as “Choosing Wisely” [31] advocate for safe medication use and deprescribing harmful and unnecessary medications in older adults [23–25]. Although deprescribing can also contribute to better clinical outcomes among older adults, existing evidence is mixed among studies reporting the impact of deprescribing on cognitive and physical function [32, 33], falls [33–35], quality of life [33, 36], hospitalizations [33, 36–39], and mortality [33, 36, 37, 40]. One potential reason for these mixed findings is variance in the implementation of deprescribing interventions.

As noted in multiple deprescribing reviews [41–44] and expert opinions [45, 46], more rigorous evaluations of implementation are necessary to (1) separate deprescribing interventions that lacked efficacy from efficacious deprescribing interventions with poor implementation; (2) identify barriers and enablers associated with the implementation of efficacious interventions; (3) determine implementation outcomes such as intervention acceptability and feasibility [47]; and (4) test strategies to enhance both the implementation and sustainability of deprescribing in routine clinical practice.

In this review, we summarize deprescribing frameworks, conceptual models, and tools; barriers, enablers, and factors associated with deprescribing; and the characteristics of deprescribing interventions in completed trials, with a focus on implementation. Our goal is to identify gaps in the existing deprescribing intervention literature to inform recommendations for future deprescribing trials and how these trials can inform changes in routine clinical practice.

Deprescribing frameworks, models, and tools

Medication optimization, which includes prescribing necessary medications and deprescribing unnecessary or high-risk medications, is part of routine clinical practice. Yet, the term “deprescribing” was only introduced in 2015 as a “systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits” [24, 33]. In the seminal paper by Scott et al., the authors describe a five-step process for deprescribing,

which includes (1) ascertaining all medications the patient is taking and the clinical indication for each (i.e., medication review); (2) considering the cumulative risk of drug-induced harm and/or risk for drug–drug interactions in consideration of all medications used by the patient; (3) assessing the benefit and harm or burden of each medication; (4) prioritizing medications with the lowest benefit-to-harm ratio and the lowest likelihood of withdrawal or disease rebound for deprescribing; and (5) implementing a deprescribing plan and monitoring patients closely for improvement in outcomes or onset of adverse effects [24]. Multiple frameworks and models have followed to facilitate and systematize deprescribing in clinical practice in varied health-care settings [48–52], all demonstrating the complexity of the deprescribing process and the relevance of multiple stakeholders in deprescribing decisions. These frameworks and models reflect the importance of considering multilevel factors related to the patient (and/or their caregiver), clinician(s), and health-care systems in the context of deprescribing.

Multiple tools also have been developed to assist clinicians in the identification of potential deprescribing targets [53], including (1) Beers Criteria [54], which is one of the earliest lists of PIMs and the one most commonly used in North America; (2) STOPP/START criteria [55], which is the most commonly used PIMs list in Europe, and its modification (the Rationalization of Home Medication by an Adjusted STOPP in Older Patients [RASP] list [56]); and (3) guidance related to low-value prescribing [57] for the general older adult population. Other lists that target medications with potential for harm among specific subsets of older patients include the STOPPFall criteria designed for those at risk for falls [58], the STOPPFrail criteria [59, 60] for older adults with advanced frailty at the end of life, the Holmes criteria for older persons with advanced dementia [61], and the more general list of Medications Associated with Geriatric Syndromes (MAGS) designed to identify medications that could contribute to or exacerbate common geriatric syndromes [13]. There is substantial overlap among these various lists, and because most of these lists and related criteria are labor-intensive to use, computer-enabled algorithms have been developed to automate screening of PIMs use. However, the use of these algorithms alone has had limited impact on deprescribing practices in routine care [62, 63].

Barriers and enablers of deprescribing

Recognized clinical factors associated with an increased need for deprescribing include multimorbidity, polypharmacy, transitions of care, and the presence of certain chronic conditions that increase the patient's risk for adverse drug events or other medication-related harms, such as Alzheimer's disease and related dementias [64–71].

Studies have revealed multiple factors that can contribute to the efficacy of deprescribing, including factors at the patient, provider, and health-care system levels, each of which may include barriers or enablers to deprescribing. Based on the existing literature, Table 1 summarizes potential barriers and enablers of deprescribing at each of these levels. Patient-level factors that may influence deprescribing include self-efficacy, health literacy and/or decision-making capacity [72–74], attitude toward deprescribing [75, 76], beliefs and perception about benefits, harms, and necessity of specific medications [44], clinical complexity and changes to goals of care [72], and prior experience with deprescribing and/or fear of negative consequences [72, 73, 77–79].

Provider-level factors associated with deprescribing include beliefs and/or attitudes about both prescribing (e.g., preventative medications, symptom management) and deprescribing (e.g., reluctance or fear of stopping medications) [73, 80–84]; clinical expertise, training, and experience with deprescribing [85]; knowledge about the patient, their preferences, and goals of care to inform deprescribing decisions [74, 86]; and clinician time and resources to support collaboration among multiple providers to make deprescribing decisions [72].

Health-care system-level factors associated with deprescribing include clinical guidelines related to both prescribing and deprescribing practices, professional and provider culture about deprescribing [44], incomplete or inaccurate medication use information to inform deprescribing decisions, availability and feasibility of alternative treatments, reimbursement structure, and resources to support deprescribing and shared decision-making among multiple providers.

Deprescribing interventions in previous trials

We conducted a scoping review [87] using the methodological frameworks developed by Arksey

Table 1. Barriers and enablers of deprescribing at the patient, provider and health-care system levels

Level	Potential barriers to deprescribing	Potential enablers of deprescribing
Patient-level factors	• Uncertainty about the benefits and harms of medications; clinical complexity and changes to goals of care • Misperception that all medications are necessary • Past unsuccessful deprescribing experience; poor perceived benefits of deprescribing; and/or fear of negative consequences of deprescribing, such as symptom reoccurrence or withdrawal	• High levels of self-efficacy and/or health literacy • Attitudes toward and/or willingness to consider deprescribing • Patient decision-making capacity, buy-in and advocacy; shared decision-making with health-care providers • Trust in health-care providers
Provider-level factors	• Community and professional attitudes toward more medication use; pressure to prescribe • Beliefs that preventive medications and medications for symptom management are essential to patients; fear a patient's condition may deteriorate after deprescribing • Insufficient evidence and expertise in deprescribing; inertia in stopping medication • Insufficient time for deprescribing consultation; lack of knowledge about the patient's preferences and goals of care • Reluctance to deprescribe medications started by other providers, especially specialists; inadequate communication among multiple providers treating the same patient	• Awareness of deprescribing to reduce risk of harm to patients • Training related to deprescribing for some specialties, such as geriatrics • Involvement of the patient and/or caregiver in deprescribing decisions • Effective communication with patients and/or caregivers that increases willingness to deprescribe • Effective multidisciplinary communication with other providers for the same patient
Health-care system-level factors	• Clinical guidelines for single diseases with prescribing recommendations but without consideration of multimorbidity and polypharmacy • Limited resources to support communication among providers about deprescribing • Incomplete, inaccurate, and/or outdated documentation about medication use • Limited or otherwise infeasible non-pharmacological alternatives for deprescribed medications (e.g., antipsychotics) • Poor information exchange regarding medication information between providers and across different health-care systems (i.e., the data silos); inoperability between different electronic health record platforms that limits communication among providers	• Clear deprescribing guidelines, including benchmarks for deprescribing at the time of initial prescribing • Resources and technologies that facilitate real-time communication among providers (e.g., care liaison personnel and synchronized health information exchange); clear roles and responsibilities of each provider in deprescribing; multidisciplinary network of professionals and resources to support providers and patients with deprescribing • Reimbursement structure that allows for substantial time for providers to consider deprescribing • Integration of deprescribing interventions with existing care processes in medication optimization (e.g., the home medication review program in some countries with universal health insurance coverage)

and O'Malley [88] and Levac et al. [89]. We used the PRISMA for scoping reviews [90] to guide the reporting of this review. Literature was searched to identify English-language publication resources of deprescribing interventions in older adults. We searched six databases (i.e., Medline, EMBASE, CINAHL, The Cochrane Central Register of Controlled Trials, Web of Science, and ProQuest) using keywords (deprescriptions, deprescri*, discontinu*, reduc*, ending, stopping, drug prescriptions, polypharmacy, inappropriate prescribing, prescription*, inappropriate prescriptions, medication*, medicine*, used individually or in combination). The initial database search was conducted on 24 June 2021, with an ongoing search for newly published trials until January 2022. Snowballing was conducted to identify additional publications of deprescribing interventions by reviewing the reference lists of selected articles and published reviews [26, 27, 32, 34, 36, 37, 40, 77, 91–104]. Published protocols of ongoing deprescribing trials identified in this process (database search, snowballing, and ClinicalTrials.gov) were not included in this review because these studies were not yet completed.

The process of study selection is detailed in Fig. 1. The database search identified 547 records. After removing duplicates ($n = 242$), the remaining records ($n = 305$) were screened for eligibility based on title and abstract review, where 112 were deemed eligible. The full text for these 112 records were reviewed, and 45 were selected. An additional 17 records were identified for review via snowballing—that is, by searching the reference lists of selected articles and those of published reviews. These final 62 records ($45 + 17$) were screened using the following criteria: (1) clinical intervention trials, excluding reviews, descriptive studies, or secondary analysis of existing data; (2) average age of patient sample ≥ 65 -year old; and (3) focus on deprescribing, defined as discontinuation or titration of one or more medications. A total of 37 studies met these criteria. As shown in Fig. 1, we excluded studies that focused on prescribing practices only or other medication-related activities without specific attention to deprescribing. We also excluded studies that treated deprescribing as one component in a multi-component intervention but did not examine the effect of the deprescribing component on outcomes, because we could not determine the unique contribution of deprescribing.

Characteristics of deprescribing studies

Table 2 summarizes the characteristics of the final group of 37 deprescribing studies that met our review criteria.

Study design

We referred to the literature [105] and categorized prior deprescribing intervention studies into four categories: (1) randomized controlled trials (RCT), including parallel-group RCT, cluster RCT, and factorial RCT; (2) quasi-experimental intervention design without randomization; (3) quasi-experimental intervention design without controls; and (4) single-group pre-post studies. Among the reviewed studies, cluster RCT was the most common design ($n = 15$), including one factorial cluster RCT, followed by a single-center RCT ($n = 14$), quasi-experimental studies, including non-randomized controlled clinical trials ($n = 4$), intervention studies without controls ($n = 2$), and single-group pre-post studies ($n = 2$).

Time of study

All reviewed studies were published between 2002 and 2022, with 33 (89%) published in the past 10 years (2012–2022) and 15 (40%) published in the past 5 years (2017–2022).

Country

Most studies were conducted in European countries (e.g., United Kingdom, the Netherlands, Norway), Canada, Australia, and Asia (e.g., Korea). Only three studies were conducted in the United States [106–108].

Setting

Most studies were conducted in either nursing homes ($n = 11$) or hospitals ($n = 11$), with one study in an outpatient ambulatory care setting ($n = 1$). Fewer studies were conducted in the community through primary care ($n = 8$), community pharmacies ($n = 3$), residential care settings such as assisted living facilities ($n = 2$), and the patient's home ($n = 1$) [108]. There were no published studies focused on deprescribing during transitions of care, such as the transition home to the community with or without home health services or to an inpatient post-acute care facility following discharge from an acute care hospital.

Table 2. Study characteristics of reviewed deprescribing trials

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Meredith, 2002	United States	Community	General	Consenting Medicare patients aged 65 and older admitted to participating agency offices	317	RCT	Broad
Fick, 2004	United States	Primary care	General	Primary care physicians in the Medicare + Choice product line of a southeastern managed care organization and their patients 65 years and older	355	Cluster RCT	Broad
Fossey, 2006	United Kingdom	Nursing home	Dementia	Nursing home residents with dementia	350	Cluster RCT	Specific: Neuroleptics
Beer, 2011	Australia	Community	General	Ten volunteers living in the community (recruited by media advertising) and 25 volunteers living in residential aged-care facilities (RCFs)	44	RCT	Specific: Must be taking one of the following: antihypertensive, antianginal, diuretics, NSAIDs, COX-2 inhibitors
Bergh, 2012	Norway	Nursing home	Dementia	128 patients with Alzheimer's disease, dementia or vascular dementia, and neuropsychiatric symptoms (but no depressive disorder), who had been prescribed escitalopram, citalopram, sertraline, or paroxetine for ≥ 3 months	128	RCT	Specific: Escitalopram, citalopram, sertraline, paroxetine

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Dalleur, 2014	Belgium	Hospital	Frailty	Frail patients admitted to a teaching hospital	158	RCT	Specific: Benzodiazepines, antiplatelets, opiates, beta blockers, tricyclic antidepressants, neuroleptics
Tannenbaum, 2014	Canada	Community	General	Adults ≥65-year old receiving long-term benzodiazepine therapy from participating pharmacies	303	Cluster RCT	Specific: Benzodiazepines
Wouters, 2014	The Netherlands	Nursing home	Dementia special care units or if they provided care for residents with disabling conditions	Long-term nursing home residents with a life expectancy >4 weeks who consented to treatment with medication	426	Cluster RCT	Broad
Ballard, 2015	United Kingdom	Nursing home	Dementia	People with dementia in nursing homes	277	Cluster RCT (with factorial design)	Specific: Antipsychotic meds
Clyne, 2015	Ireland	Primary care	General	Practices with at least 80 patients ≥70-year old in greater Dublin	196	Cluster RCT	Broad
McKean, 2016	Australia	Hospital	General	Adults ≥65-year old and receiving ≥8 regularly prescribed medications	50	Intervention studies without concurrent controls	Broad

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Moonen, 2016	The Netherlands	Primary care	Mild cognitive impairment taking antihypertensive without serious CVD	Adults ≥ 75 -year old with mild cognitive deficits (Mini-Mental State Examination score, 21–27) without serious cardiovascular disease who received antihypertensive treatment	385	RCT	Specific: Antihypertensives
Cossette, 2017	Canada	Hospital	Delirium, history of delirium, neurocognitive disorder, Parkinson's, history of falls, hypoglycemia	Adults ≥ 65 -year old, hospitalized, presenting with at least one of the geriatric explicit criteria for PIMs	292	RCT	Broad: Medications selected from the Beers criteria that are most commonly prescribed at the institution (including both specifics and broad PIM: Anticholinergics (delirium/neurocognitive disorder/ Parkinson's/falls) antipsychotics (Parkinson's) antihypertensives (falls) glyburide/chlorpropamide/glimepiride/repaglinide] (hypoglycemia) OR any PIM
Frankenthal, 2017	Israel	Nursing home	General	Residents ≥ 65 -year old, and prescribed with ≥ 1 medication	359	RCT	Broad: PIPs and PPOs according to STOPP/START criteria

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Balsom, 2018	Canada	Nursing home	General	Adults ≥65-year old in a long-term care facility	45	RCT	Broad
Gulla, 2018	Norway	Nursing home	Hypertension	Adults ≥65-year old with antihypertensive treatment	295	Cluster RCT	Specific: Antihypertensives
Martin, 2018	Canada	Community	General	Adults ≥65-year old, prescribed one of four Beers criteria medications (sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs)	489	Cluster RCT	Specific: Focus on four classes of medications in the Beers criteria: sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs
Westbury, 2018	Australia	Community	General	Residential aged care facilities comprised the main participant group; two further groups were consultant pharmacists who delivered staff education, and community pharmacies that provided prescribing data	12,1 [§]	Intervention [‡] studies without concurrent controls	Specific: Antipsychotics and benzodiazepines
Whitty, 2018	Canada	Hospital	End of life care (patients at risk for mortality in 6 months)	Patients: seriously ill or frail elderly patients admitted to the general internal medicine ward who were at elevated risk of 6-month mortality or admission to the intensive care unit admission Health-care team: consenting physician, medical trainee or pharmacist members of general internal medicine clinical teaching units	61	Nonrandomized controlled clinical trial	Broad

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Ee, 2019	Singapore	Hospital	General	Newly admitted patients in 6 subacute and rehabilitative wards of a Singapore rehabilitation hospital	190	RCT	Specific: acid suppressants/proton pump inhibitors (PPIs), laxatives, analgesics (paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), codeine, tramadol), and antiemetics
Gnjidic, 2019	Australia	Hospital	General	Adults ≥ 65 -year old, prescribed a benzodiazepine, and able to consent	42	Nonrandomized controlled clinical trial	Specific: Benzodiazepines
McDonald, 2019	Canada	Hospital	General	Adults ≥ 65 -year old, had an expected prognosis of ≥ 3 months, and were taking ≥ 5 usual home medications	873	Pre-post design	Broad: BEERS list, STOPP/START, and Choose Wisely lists
Parker, 2019	Norway	Hospital	Chronic kidney disease	Adults ≥ 65 -year old, and with Stage 5 chronic kidney disease	180	RCT	Broad: START/STOPP meds
Anderson, 2020	Australia	Primary care	General	20 general practitioners, 2 pharmacists, 145 adults ≥ 65 -year old	153	Nonrandomized controlled clinical trial	Broad
Curtin, 2020	Ireland	Hospital	End of life patients: advanced frailty and polypharmacy (five or more drugs), transferring to long-term nursing home care	Adults ≥ 75 -year old with advanced frailty and polypharmacy (five or more drugs), transferring to long-term nursing home care	130	RCT	Broad: Link to STOPPPFrail Criteria

(Continued)

Table 2. Continued

		Older adult			Sample	N	Trial design	Target medications for	
Study	Country	Setting	population					deprescribing	Specific: Psychotropics
Gedde, 2020	Norway	Nursing home	General		Patients aged ≥ 65 -year old with at least 2 weeks of residency in nursing homes with a life expectancy of > 6 months, without schizophrenia	723	Cluster RCT		
O'Donnell, 2020	Australia	Primary care	General		Patients routinely referred to by general practitioners for home medication review	201	Cluster RCT		Specific: Anticholinergic and sedative medications
Sanyal, 2020	Canada	Community	General		Community-dwelling adults ≥ 65 -year old who were chronic NSAIDS users	489	Cluster RCT		Specific: NSAID
Schapira, 2020	Argentina	Outpatient	General		Patients ≥ 65 -year old with ≥ 1 PCP visit in the last 2 years	879	Pre-post design		Specific: eight common drug classes in their clinical setting—NSAIDs, benzodiazepines, histamine antagonists, opioids, tricyclic antidepressants, muscle relaxants, centrally acting antihypertensives, and cholinergic antagonists
Sheppard, 2020	United Kingdom	Primary care	Mild systolic hypertension		Adults ≥ 80 -year old, had a baseline systolic blood pressure < 150 mm Hg, and were prescribed ≥ 2 antihypertensive treatments for ≥ 12 months; who might potentially benefit from medication reduction due to reasons, including polypharmacy, comorbidity, nonadherence or dislike of medications, or frailty	569	RCT		Specific: Antihypertensives

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
Campbell, 2021	United States	Primary care	General	Patients in 10 primary care clinics within Eskenazi Health in Indianapolis	552	Cluster RCT	Specific: Anticholinergics of two classes—tricyclic antidepressants and urinary antispasmodics Broad
Cateau, 2021	Switzerland	Nursing home	General	Residents in a volunteer nursing home who are ≥65-year old and taking ≥5 medications	62	RCT	Broad
Kua, 2021	Singapore	Nursing home	General	Residents across 4 nursing homes in Singapore who were ≥65-year old and taking ≥5 medications	295	Cluster RCT	Broad
Mahlknecht, 2021	Italy	Primary care	General	Older-aged community-living patients in the Bolzano	579	Cluster RCT	Broad: Beers list/drug-drug interactions algorithm Broad: Assessed
Wauters, 2021	Belgium	Nursing home	General	Nursing home residents ≥65-year old, not residing in short-stay beds or revalidation beds and provided written informed consent; excluded if their GP refused to participate, or if they had a life-expectancy of <3 months	148	Nonrandomized-systematically using controlled clinical trial	Euro PIM, Beers, and STOPP/START criteria using a CDSS toll
Wong, 2021	Singapore	Hospital	General	≥65-year old, newly admitted to rehabilitation or subacute care disciplines and currently taking any of these medicines: Beer's list of PIMs (American Geriatrics Society 2015 version), symptomatic medications (painkillers, laxatives, antiemetics; steroid creams, gastroprotectives) and supplements (chondroitin, glucosamine, multivitamins, and vitamin B complex)	260	RCT	Broad: American Geriatric Society's Beer's List of Potentially Inappropriate Medicine, symptomatic medicine (e.g., analgesics, laxatives), viscosupplements (e.g., glucosamine, chondroitin), and multivitamins and vitamin B complex

(Continued)

Table 2. Continued

Study	Country	Setting	Older adult population	Sample	N	Trial design	Target medications for deprescribing
McDonald, 2022	Canada	Hospital	General	≥65-year old, expected survival of >3 months, and admitted to 1 of 11 acute care hospitals in Canada	5698	Cluster RCT	Broad: BEERS list, STOPP/START, and choose Wisely lists

Abbreviations: PIM, potentially inappropriate medication; RCT, randomized controlled trials.

Sample

The majority of studies ($n = 25$) were focused on general older adult populations. Among studies that specified certain medical conditions or diagnoses in eligibility criteria, the most common was dementia and mild cognitive impairment ($n = 5$), followed by advanced frailty and end of life ($n = 3$) [109–111], hypertension ($n = 2$) [112–114], kidney disease ($n = 1$) [115], and miscellaneous other health conditions ($n = 1$) [116].

Sample size

The sample size varied from 42 [117] to 12,157 [118]. Of note, 13 studies did not report power analyses. Among the 24 studies with power analyses, more than half ($n = 13$) [62, 63, 109, 113, 114, 116, 119–125] were underpowered to detect changes in at least one of the outcomes.

Target medications

Among the studies focusing on deprescribing of specific medications, the most common deprescribing targets were psychotropics (e.g., benzodiazepines) ($n = 11$) [63, 106, 110, 117, 118, 126–131], followed by NSAIDs ($n = 5$) [129, 130, 132–134], anticholinergics ($n = 4$) [63, 106, 128, 130], and antihypertensive medications ($n = 3$) [112–114].

Intervention characteristics

Table 3 summarizes the characteristics of the deprescribing interventions in the reviewed studies.

Type of interventions

A total of 35 deprescribing interventions were represented in the 37 included studies (with two interventions published in 4 studies) [62, 112, 124, 128]. Four studies included deprescribing as one intervention component with its effects assessed separately [108, 112, 126, 128]. One study [135] examined deprescribing in both intervention (deprescribing plus behavioral modification) and control groups (deprescribing alone). Several interventions focused on both deprescribing and prescribing [107, 111, 118, 125].

Professional disciplines involved

The most common disciplines involved in the design and delivery of deprescribing interventions were prescribers (e.g., physicians and nurse prac-

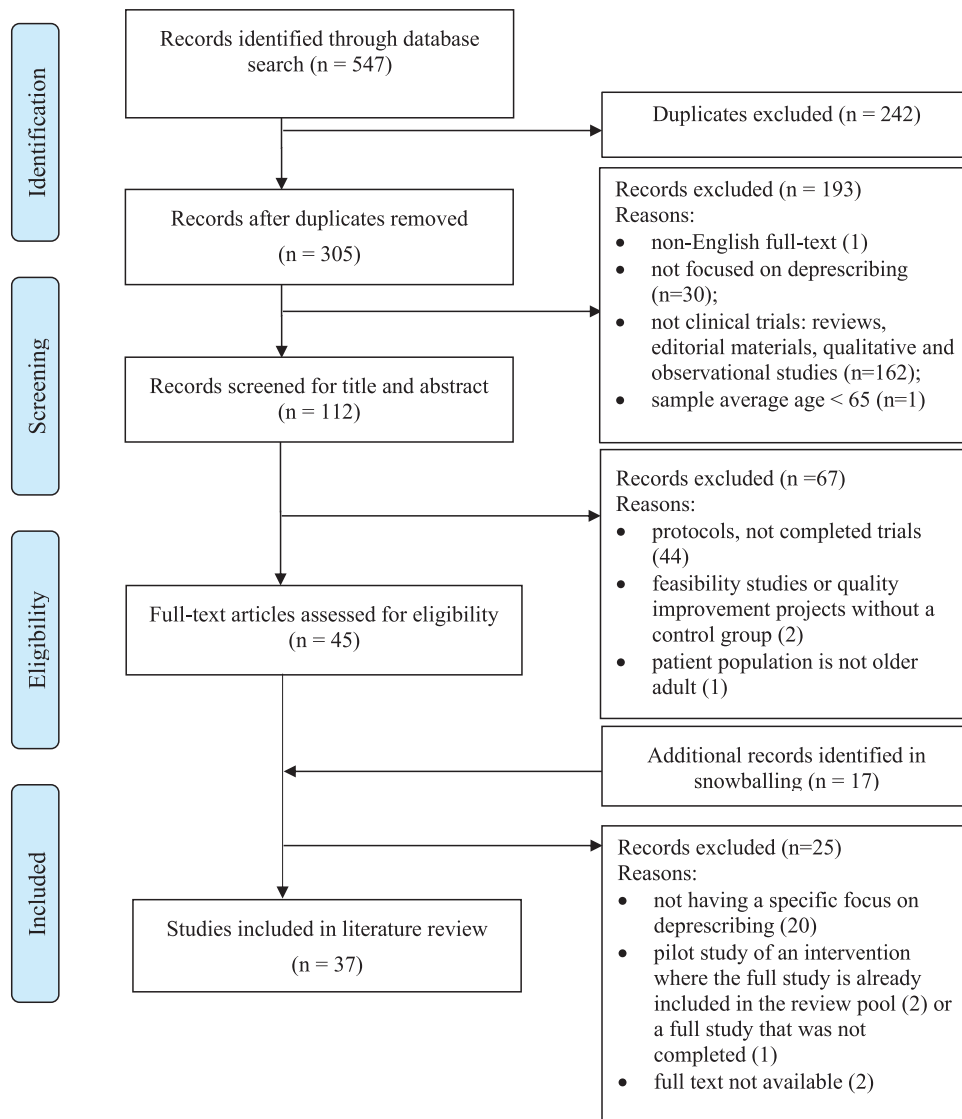


Fig. 1 Literature search flowchart.

tioners) and pharmacists, with fewer studies involving other disciplines such as nursing (mostly registered nurses, except for one study that used advanced practice nurses [118] as interventionists).

Patient engagement in deprescribing decisions

Over half of the interventions ($n = 20$) targeted various types of providers as the recipients of intervention, including physicians ($n = 19$), pharmacists

($n = 12$), registered nurses ($n = 6$), psychologists ($n = 2$), nurse practitioners ($n = 1$), and/or dietitians ($n = 1$). A total of 13 interventions targeted both providers and patients, and 4 interventions targeted patients only. The interventions targeting providers were focused on promoting deprescribing among individual providers [106, 107, 118, 130] or system-level enforcement of deprescribing specific types of medications (e.g., benzodiazepines and antipsychotics) [113, 114, 127, 132] without engaging the patient in the decision-making process.

Among the 17 studies in which patients received the intervention, 7 studies actively engaged patients in the deprescribing decision-making process [111, 112, 120, 125, 133, 136, 137], wherein patients and/or their caregivers participated in deprescribing consultation, and their preferences and/or goals were elicited and considered by the providers when making deprescribing decisions. In addition, three studies informed patients of deprescribing recommendations but did not elicit patients' preferences or care goals [62, 124, 132], one study aimed to empower patients to initiate a conversation about deprescribing with their primary care provider [131], one study aimed to improve patients' attitudes toward deprescribing through the use of an educational booklet [117], and the remaining five studies did not describe to what extent patients were involved in the intervention [106, 126, 127, 129, 134].

Intervention targets

As shown in Fig. 2, there were a number of causal pathways that were the focus of interventions to alter provider and/or patient behaviors related to deprescribing. The intervention targets in these pathways include (1) patients and/or providers' deprescribing beliefs, knowledge or awareness; and (2) enforced deprescribing of specific types of medications. Of the reviewed studies, some were interventions to change patients and/or providers' deprescribing beliefs, knowledge, or awareness ($n = 6$), including providers' deprescribing behavior [106, 107, 118, 130], patients' beliefs about deprescribing [117], and/or patients' initiation of conversations with their providers about deprescribing [131], but without monitoring the impact of deprescribing on patient outcomes. Some were interventions to improve patient outcomes through enforced deprescribing of specific types of medications ($n = 4$) [113, 114, 127, 132], such as antipsychotics. However, the majority of the reviewed studies were interventions to promote patients and providers' deprescribing beliefs or knowledge and awareness of deprescribing. The underlying rationale of these interventions is that deprescribing behaviors lead to discontinuation or reduction of target medications, impacting immediate medication outcomes (e.g., improved adherence) which, in turn, should ultimately change clinical outcomes of the patient (e.g., decreased morbidity) ($n = 27$).

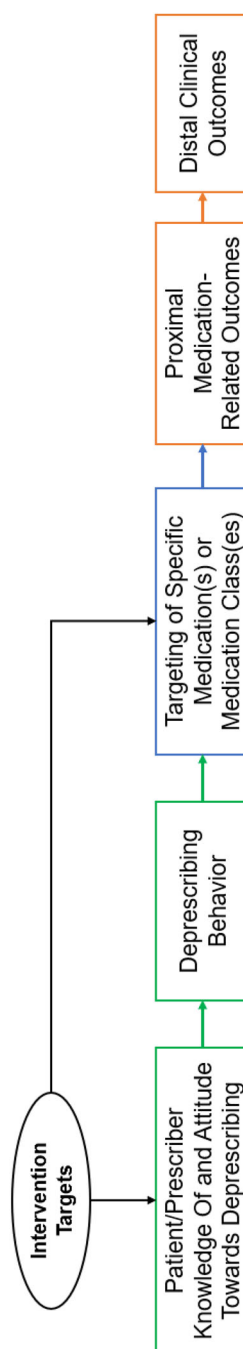


Fig. 2 Intervention pathways to deprescribing.

Intervention components

We did not attempt to categorize the content of deprescribing interventions exhaustively, as it was not the focus of this review and previous reviews have already done so [36, 37]. Rather, we intended to provide a brief overview of the most commonly used components of prior deprescribing interventions.

1. *Education*: The most common intervention component is education, including education for providers, patients, or both. Education for providers was delivered via workshops, seminars, written materials, and academic detailing (i.e., face-to-face contact between prescribers and trained staff, most often the research team). Education for patients was delivered through written materials, videos, and/or communication with providers.
2. *Medication review*: The first step in most deprescribing interventions is to review the medications taken by the patient. Medication reviews, in most of the trials, were limited to prescriptions only (routine and pro re nata). Few studies included over-the-counter medications and dietary supplements in the medication review, [108, 115, 119, 138], and two studies recognized the limitation of not doing so [123, 129]. In most studies, medication reviews were conducted by members of the study team who were physicians ($n = 35$) or pharmacists ($n = 26$), with fewer studies involving nurses or other health-care professionals (e.g., psychologists, therapists, and dietitians) in the process ($n = 13$).
3. *Assessment of target medications for potential deprescribing*: Over half of reviewed studies considered a broad range of medications as potential deprescribing targets ($n = 19$), whereas the remainder focused on specific medications considered harmful based on literature review and clinical practice. Among these 19 studies, most used concrete guidelines and tools (e.g., Beers or STOPP/START criteria) to identify PIMs as deprescribing targets. Few studies reviewed deprescribing targets in the consideration of the patient's specific conditions [112]. Some studies ($n = 6$) used technology to automate screening of PIMs and/or send electronic alerts to clinicians

about potential deprescribing targets [62, 63, 106, 116, 124, 130].

4. *Communication*: In all trials, deprescribing recommendations were communicated to prescribers, either orally or in writing, for final deprescribing decisions and implementation. Except for a few trials [111, 139], deprescribing recommendations were communicated by study team physicians or pharmacists to the patient's treating providers. It was suggested in one study that direct oral communication about deprescribing recommendations can more effectively lead to implementation [140]. In five studies, patients were informed of the deprescribing recommendations prior to final implementation [62, 121, 122, 124, 132]. Some studies also reported the treating providers' acceptance or implementation of deprescribing recommendations made by the study team [123, 136], noting low [106, 119], or unknown [115] implementation of the deprescribing recommendations by patients' providers [106].

Intervention intensity, duration, and frequency

Only a few studies ($n = 7$) [108, 112, 125, 133, 137, 138, 141] reported the amount of time necessary to deliver the intervention per patient. The reported time needed for completing the intervention largely varied, with the intervention delivered one time only in 24 studies and with regular follow-up in 13 studies. For the 13 studies that included follow-up, the frequency of follow-up ranged from daily (e.g., alerts on workdays) to every 3 months (e.g., medication review and stepwise deprescribing). No study reported the amount of time needed for the patient to receive the intervention.

Though most interventions were delivered by an independent study team, some studies invited the patients' treating providers to participate in deprescribing decisions [111, 139], yet it was not reported how much time providers spent on activities pertinent to the intervention such as reviewing, discussing, and deciding on the study team's deprescribing recommendations. None of the studies provided a rationale for the intensity or duration of the deprescribing intervention, though a few studies noted the low intensity of intervention as one potential reason for null findings [63, 106, 133].

Assessed outcomes

Medication outcomes

All but four studies [113, 123, 126, 127] assessed medication outcomes, such as the use of target medications (e.g., deprescribed, continued, or restarted), total number of medications and PIMs, and/or medication cost.

Clinical outcomes

Relatively fewer studies assessed clinical outcomes, including the following: (1) outcomes related to cognitive, behavioral and/or psychological symptoms ($n = 10$) [63, 113, 120, 126–128, 132, 135, 136, 141], such as apathy, depression, dementia severity, cognitive function, and behavioral and psychological symptoms of dementia; (2) outcomes related to mobility ($n = 13$) [63, 109, 113–115, 120, 121, 125, 127, 128, 136, 140, 141], such as activities of daily living (ADLs) and instrumental ADLs, physical function, physical frailty, and falls; (3) outcomes related to quality of life, symptom control, perception, and belief about medication use ($n = 22$) [62, 108, 109, 111–115, 117, 119–123, 127, 129, 132–135, 137, 141]; (4) outcomes related to health services use (e.g., hospitalization) and mortality ($n = 10$) [62, 109, 112, 116, 121, 123, 126, 136, 137, 140]; and (5) outcomes related to the safety of deprescribing, such as symptom recurrence (e.g., depression [127]), withdrawal symptoms, adverse drug events, or unplanned visits to health-care providers that suggest actual or potential patient harm from deprescribing ($n = 6$) [109, 110, 114, 119, 124, 125].

The choice of control group

Three studies did not use control groups [118, 130, 138]. Among the studies that included a control group ($n = 34$), most ($n = 26$) used unspecified usual care as the control group, and 7 studies used usual care that included either medication review [62, 63, 108, 120, 133], medication reconciliation [124], or medication safety monitoring [125] with potential pharmacist consultation [120] as the control group. For studies focused on increasing deprescribing behaviors among providers, the control group comprised providers who received no additional training on deprescribing [107, 119]. For studies that targeted deprescribing of a specific medication as the intervention, the control group was continued use of the medication [114, 127].

Though not definitive, studies that used medication review and/or reconciliation as the control group [62, 63, 108, 124, 133, 142] tended to have null findings, suggesting that a thorough medication review and reconciliation, both of which are key components of deprescribing, may often exceed routine care standards and overlap with core components of the deprescribing intervention itself. Future deprescribing trials, such as pragmatic embedded clinical trials, should carefully examine the medication management services provided as part of usual care.

The choice of outcomes

Specific details about the reviewed studies are described in Tables 2–4. The limitations in outcomes assessed in deprescribing trials include (1) the absence of patient-centered outcomes in most studies [62], (2) the lack of comparability in outcome measures across studies, and (3) the unknown feasibility of measuring outcomes related to deprescribing using existing datasets (e.g., electronic health records or other available data). Because the outcomes considered important by researchers in deprescribing studies may differ from those perceived as most important to patients [143, 144], it is unknown if deprescribing in routine clinical practice will be accepted by patients without evidence that deprescribing impacts outcomes important to patients, such as quality of life, pain relief or other symptom control, mental health, and cognition, as well as physical function [143]. The lack of overlap in outcomes across varied deprescribing intervention studies [145] makes it difficult for clinicians to compare the effectiveness of deprescribing prior to implementation. Lastly, the fact that most studies used study team members to collect primary data on deprescribing outcomes rather than using existing administrative and electronic health record data suggests that it may be challenging to measure deprescribing outcomes using existing data sources in future pragmatic trials. Ideally, future deprescribing trials should include a standardized set of outcome measures to include patient-centric outcomes and the identification of available data sources for at least some measures [146].

Implementation considerations of deprescribing interventions

To improve the implementation potential of deprescribing interventions, it is important to consider the following: (1) resources in existing health-care

Table 3. *Intervention design of prior deprescribing trials*

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Meredith, 2002	Provider	Pharmacy, nursing (home health care)	1. Structured, pragmatical collaboration between a specially trained clinical pharmacist and the patients' home-care nurses. The intervention procedures were designed to be practical for home care agencies with minimal need for expensive additional staff 2. At each site, an experienced clinical pharmacist was identified and specially trained by the coordinating center to manage the intervention process 3. For each intervention patient, the pharmacist and the patient's nurse jointly reviewed the medication problems identified in light of the available medical history and the study guidelines to determine whether reassessment by the physician was warranted (e.g., to exclude a patient whose physician was known to be addressing the problem) 4. If additional information was needed to assess the problem, it was collected from the patient at the next scheduled visit 5. Structured templates provided by the study then were used to develop a plan to address the identified problem. This was presented to the patient's physician (by the nurse or, for complicated patients, by the pharmacist), who was asked for instructions regarding changes in therapy and patient follow-up		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
			1. The nurse then assisted the patient with the medication changes and monitored their effect. When necessary, consultation was available from the coordinating center clinical pharmacologist	One time: no more than 30 min from the pharmacist per patient	Home health-care agencies' usual care: review of medications and potential medication adverse effects
			2. The clinical pharmacists were provided specially developed educational materials for the nurses that explained the background of each of the problems and suggested ways to resolve them		
			3. We estimated that this procedure required no more than 30 min of pharmacist time per study patient		
Fick, 2004	Provider	Primary care	1. PIMs defined using Beers list criteria	Every 3 months (for 1 year): time not estimated: physician received educational brochure + prescribing letters with fax back forms	Physicians in the control group received no interventions (other than the mass mailing 2001)
			2. PCPs received a mail with an educational letter and brochure on prescribing to the elderly		
			3. PCPs in the intervention received a detailed brochure listing PIMs, suggested alternative medications, and a list of all patients receiving 1 or more PIMs		
			4. Data received in the intervention brochure was for the previous quarter and physicians received four brochures over 1 year		
			5. Physicians received a fax-back form to detail changes made to medications (discontinued, no change, decreased dosage, alternative prescribed, or never prescribed to patient)		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Fossey, 2006	Provider	Psychology, OT, nursing, psychiatry	A. <i>Deprescribing</i>. A psychiatrist and a senior nurse reviewed prescriptions, recommended deprescribing of psychotropics that had been prescribed for >3 months after behavioral problems were resolved; the psychiatrist wrote to care home physicians and telephone if no action was taken within 2 weeks. B. <i>Resolve behavioral problems using patient-centered approach</i> C. Intervention delivered by psychologist, OT, or nurse involved “whole home” issues, such as environmental, care, and attitudinal factors D. Key elements involved skills training, behavioral management, and ongoing support E. Initial skills included philosophy of person centered care, positive care planning, awareness of environmental design, individual interventions, active listening, and involvement of family F. Behavioral management included training in Cohen-Mansfield approach G. Ongoing support included group supervision and development of skills involving individual case supervision	Every 3 months (med review): deprescribing-focused review every 3 months + written to MD with telephone follow-up in 2 weeks to ensure deprescribing + ongoing behavioral resolution intervention	Care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Beer, 2011	Patient	Pharmacy	Information sheets for target drugs were drafted for each drug class and included rationale for withdrawal and general advice. If participants were taking more than 1 target med patients identified which med they would prefer to stop	Every 2 weeks: mean number of visits was 4 ± 1	Control was not specified or described
Bergh, 2012	Patient	Psychiatry	Intervention was merely pharmaceutical: tapering off the antidepressants among NH residents who had dementia, were prescribed antidepressants, and did not have documented depression (investigators were unsure if patients with undocumented depression were included though)	Continuous: 1 week	Continued vs. discontinued antidepressants
Dalleur, 2014	Provider	Nurses, geriatricians, dietitian, occupational therapist, physiotherapist, speech therapist, psychologist	1. ICGT is a multidisciplinary team (nurses, geriatricians, dietitian, occupational therapist, physiotherapist, speech therapist, and psychologist) and evaluate patients who are (need help with ADLs, increase in need related to current illness, memory problems, altered vision, hospitalization within 6 months, daily use of 3+ medications) 2. Patients are screened for geriatric syndromes (falls, polypharmacy, cognitive disorder, malnutrition) 3. Recommendations are communicated to the team and recorded in EMR, ICGT report sent to GP at discharge 4. Using STOPP criteria to screen the medications taken at admission 5. Oral and written recommendations made to ward physician during hospitalization for discontinuation of PIMs	One time: STOPP screening and making recommendations on deprescribing to ward physicians, time not reported	Steps 1–3 in intervention are care as usual, steps 4–5 are the intervention

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Tannenbaum, 2014	Patient	Pharmacy, physician	1. Everything is included in an 8-page booklet: This booklet comprises of a self-assessment about the risks of benzodiazepine use, education about drug interactions, peer champion stories, suggestions for effective therapeutic substitutes for insomnia/anxiety, and stepwise tapering recommendations 2. Tapering recommendations consisted of a visual 21-week protocol with a picture-based diminishing schedule (full pill, half pill, quarter pill), which can be applied regardless of dose or benzodiazepine 3. Patients are asked to discuss deprescribing recommendations with their PCP or pharmacist 4. The material is written in large print at a sixth-grade reading level to be accessible to all and included the name of the specific benzodiazepine the patient was taken based on their pharmacy profile 5. Intervention pamphlet mailed within 1 week of group allocation and the control group received the pamphlet at 6-month follow-up	One time: one booklet for patient	Care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Wouters, 2014	Both	Nursing, pharmacy, elder care physician	1. Pharmacist: Assessing patient perspective and medical information—patient experience/preference about medicine use assessed through questionnaire. Pharmacy interns compiled diagnoses, allergies, and lab results 2. Pharmacist: Medication review—pharmacist reviewed medications to identify potential over-prescribing/under-prescribing using START/STOPP and Beer list 3. Pharmacist: Multidisciplinary meeting/pharmacotherapeutic action—elder care physician and pharmacist reviewed all information and discussed <i>discontinuing, initiating, adjustment of dose, switch to alternatives, taper, and monitoring</i> 4. Physician: Execution and evaluation—actions executed by elder care and communicated to nursing staff, who monitored adverse withdrawal and relapse events. Changes were discussed with nursing home residents and representatives	One time: 45 min	Usual care, including medication safety monitoring and ad hoc medication reviews for individual residents when clinically indicated. These reviews differed in quality and frequency from the standardized 3MRs performed in the intervention group

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Ballard, 2015	Both	NH Staff, therapists, primary care	1. Interventions delivered by therapist who had an intensive 10-day training program and coordinated delivery into nursing homes	One time: 9 months	Care as usual
			2. Training for person centered care—understanding of dementia and person-centered care, assessing each home's care in terms of plan/provision for PCC, developing staff understanding of relationship between experience/well-being, using CBT principles, and implementing PCC planning based on these principles		
			3. Antipsychotic medication review emphasized assessment of underlying causes, use of nonpharmacological interventions, and regular review of antipsychotic medications. This also included trial discontinuation recommendation made to PCP, who will then decide on deprescribing		
			4. Social interaction manual developed in a way to provide positive planned social interactions through individual or group sessions		
			5. Exercise intervention developed to promote exercise through physical activities		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Clyne, 2015	Provider	Pharmacy, GP	- Academic detailing with pharmacist (one 30-min session in which pharmacist visited GPs and discussed PIPs, medicines, and web-based treatment algorithms) - GPs asked to conduct one review per patient using the web-based platform, GP was presented with specific PIPs and treatment algorithm providing the reason for concern, alternatives, background information - Patients received the reasons the PIP may be inappropriate and a list of alternatives	One time: - One 30-min academic detailing - One medication review per patient with feedback for both GP and patient	Care as usual: for public general medical services patients allows GPs to give a prescription on a monthly or 3-month basis. Receipt of simple, patient-level PIP postal feedback in the form of a list summarizing the medication class to which the individual patient's PIM belonged. No academic detailing visit, and no prompts to carry out a medicine review with the individual patients
McKean, 2016	Provider	6 consultant physicians, 6 medical registrars, 11 interns and 3 clinical pharmacists	- Treating clinicians performed medication review on eligible patients identified on post-admission ward rounds using a list of medications - Medications eligible for discontinuation based on: absence of valid indication, likelihood of benefit in remaining lifespan, risk of harm outweighing benefit, no effect on symptoms, or treatment burden in caregivers - Medications were marked as continued, ceased, or titrated down, and final decisions were discussed with the patient and if agreed upon implemented - Treating clinicians attended a seminar on polypharmacy and intervention was performed after reviewing medication indications and effects	Every 2 weeks (reminders) (follow-up of 6 months): medication review (10–15 min per patient) + a seminar	Control was not specified or described

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Moonen, 2016	Provider	Physician	1. Antihypertensive medications were discontinued by physician during a 6-week period after randomization: All physicians were instructed to withdraw antihypertensive treatment until a max increase of 20 mm Hg in SBP was reached 2. After target SBP reached, weekly monitoring until no further changes are made	One time (initial) deprescribing with weekly BP monitoring for 6 weeks: merely pharmaceutical	Care as usual
Cossette, 2017	Provider	Pharmacy, geriatrician	1. Distribution of educational materials to all physicians, medical residents, and pharmacists 2. In-services in the various medical and surgical departments by the geriatricians 3. Comprehensive geriatric assessments 4. CAS-based pharmacist-physician interventions: computer-assisted alert based on EMR and discharge summary, pharmacist reviewed the clinical relevance of alert, and if deemed clinically relevant, developed a geriatric pharmaco-therapeutic plan to discuss with MD to reduce PIM	Daily alert on workdays: study pharmacist analyzed a clinical relevance of CAS alerts and discuss with treating MD if appropriate, mean time 41 ± 16 min	CAS alerts in the control group was only determined by the study pharmacists after the control patient was discharged from the hospital
Frankenthal, 2017	Provider	Pharmacy, physician	Medication review conducted by study pharmacist according to STOPP/START criteria Oral recommendations were given to chief physicians who could choose to implement changes Plans for the control group (medication review) were submitted after 1 year	One time (initial) STOPP/START review + 6-month again): pharmacist med review + oral communication to provider	At the end of 12 months, the study pharmacist conducted a written medication review based on STOPP/START criteria for the control group and submitted it to the chief physician

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Balsom, 2018	Both	Pharmacy (students), with consultation with pharmacist and the team (physician, resident, family member, nursing staff)	Prior to the launch of the study, nursing and support staff of the LTC facility participated in an education session about deprescribing and polypharmacy in older adults provided by pharmacy students. This session presented evidence and facilitated brainstorming amongst the staff about nonpharmacological strategies to manage behaviors and/or withdrawal symptoms when medications were being deprescribed, and foreseeable challenges were discussed 1. Medication review: generating a medical history with associated medications 2. Step-wise, individualized deprescribing (medication causing active harm as highest priority, followed by medications unlikely to be of benefit or to cause adverse withdrawal effects, then by medications with a high potential for adverse withdrawal reaction, and medications for symptom relief where the symptom is already under control) 3. Discussion: The deprescribing plan was discussed with the resident, their family (where appropriate) and nursing care team and documented on the resident's chart. The plan was discussed with the physician when they conducted rounds at the facility 4. Documentation: Deprescribing plan was documented in the resident's chart 5. Implementation: Plans were implemented over 3–6 months with weekly review	Weekly (review to monitor deprescribing process): weeks to months, varied across participant residents	Care as usual: medications were reviewed and reordered by the physician on a quarterly basis and the pharmacist completed an annual medication review to assess for drug interactions, dose adjustments, lab monitoring and any modifications to therapy required, and pharmacist consultation services as required

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Gulla, 2018	Both	Pharmacy, physician, nursing	1. Two-day educational seminar covering research based knowledge on communication, planning, treatment, medicine review. Medication review emphasized blood pressure, pulse, blood tests, neuropsychiatric symptoms, cognitive status, ADLs, pain. Patients wish also considered. Those who received the seminar trained staff in their unit, and distributed assessment tools, including STOPP/START and anticholinergics. Researchers also trained nurses who did not attend the initial seminar 2. Weekly training, 15-min per day, on COSMOS intervention 3. Physicians received a separate booklet on medication review that includes assessment tools used in medication review, STOPP/START criteria, and a list of anticholinergic medications 4. Researchers visited physician/nurses to perform medication reviews to assist with process of deprescribing, trained at least two nurses in the necessary clinical assessments in 4-h sessions 5. Discussions on treatment had a patient-centered focus: before the medication reviews, the staff assessed cognitive function, neuropsychiatric symptoms, pain, ADL, and quality of life in all patients, using tools validated for people with dementia. This information, together with information on diagnoses, drug-drug interactions, blood pressure, pulse, and lab tests were used to assess medication lists	Every day with visit of unknown frequency: Intensive: 2-day seminar + 15 min every day training + tools/list sharing + experienced researcher visit each unit meeting the MD and nurses to perform medication review + researcher further trained >2 nurses for 4 h at an unknown frequency for 4 months	Continued treatment and provided care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Martin, 2018	Both	Pharmacists, physicians	Education intervention 1. Pharmacist-led intervention conducted by distributing educational, drug-specific brochures about inappropriate meds/alternative treatments 2. Brochures for patients was drug specific 3. Optional: Brochures for physicians included an evidence-based pharmaceutical opinion 4. The brochure included rationale, evidence on harms, recommendations, safer alternatives, and personalized data	One time: not specified, not intensive (activity includes sending brochures only)	Care as usual: without any educational materials supplied to pharmacists
Westbury, 2018	Provider	Pharmacy, GP, nurse practitioners	1. Prescribing data: Gathered from electronic medical record used to pack patient medications to generate point prevalence 2. Education session: Consultant pharmacist (trained in evidence-based use of psychotropics) educated staff with a 1-h session at baseline and 3 months with the objective of challenging the belief that antipsychotics and benzodiazepines are effective in older people. Didactic education involving a video and presentation outlining risks and benefits was also used. The second session involved content on nonpharmacological strategies for managing dementia, insomnia, and anxiety	Every 3 months (medication review): 1. 1-h education session by consult pharmacist to change belief 2. Psychotropic medication review 3. Provision of tapering treatment guideline to key prescribers and all staff 4. Optional academic detailing	No control group was used

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Whitty, 2018	Both	Intervention pharmacist/hospital pharmacist/physician	3. Medication review encouraged every 3 months, a three section plan was prepared for each resident, the first two sections were for recommendations by the pharmacist and nurse, the third section was to record the decisions made on medications (the prescriber recorded the decision about whether or not to adjust the medication)		
			4. Treatment guidelines were provided to all staff, and all staff were encouraged to discuss the intervention with the nurse		
			5. Academic detailing sessions were offered to attending GPs and NPs; key prescribers at each facility received intervention information and guidelines, and encouraged to discuss the intervention with the champion nurse. Academic detailing sessions offered to attending GPs and nurse practitioners	One time: the median duration of MERA meetings with the admitting team was 7 min (range 1–12 min) + much time of the study team	Care as usual
Whitty, 2018	Both	Intervention pharmacist/hospital pharmacist/physician	1. The intervention physician and pharmacist review the information and made recommendations to stop, start, or change doses of medications based on guideline-based algorithm		
			2. Study coordinator arranged a meeting between the attending physician, the clinical pharmacist, and the intervention team		
Whitty, 2018	Both	Intervention pharmacist/hospital pharmacist/physician	3. Disagreement by the admitting team led to the recommendations being dropped and not presented to family/patient		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Ee, 2019	Both	Physicians, pharmacists	4. Medication recommendation discussed with patient or decision maker, and changes were only made with the consent of the patient or decision maker		
			5. Summary report provided to patient and caregiver		
Gnjidic, 2019	Patient	Pharmacy, GP	Five-step patient-centered deprescribing process: 1. Review of patient history 2. Assess drug appropriateness 3. Plan for deprescribing 4. Initiating deprescribing Monitoring deprescribing effects 1–3 done by pharmacists (with 1 week of monitoring to decide if the deprescribed med is actually needed), 4–5 done by doctors in the rehab hospital	One time: 1. 19 min of pharmacist and MD's time to cover all five steps of deprescribing (including 11 min for med review, 8 min for discussion with MD) 2. After deprescription medications reviewed by pharmacist at 1, 2, and 6 weeks	Usual practice of medication review, altering and discontinuing medications as necessary, without receiving deprescribing recommendations from pharmacists
			1. Patient-empowering educational booklet using true-false questions about BZDs to correct myths and wrong beliefs (same intervention as that used in the Tananbaum) 2. Booklet provides a successful example patient and a tapering protocol 3. Patients were instructed to read the booklet in their own time and ask their doctor or pharmacist about changes	One time: one booklet (for patients to read in their own time)	Care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	
				One time: not specified	Control group
McDonald, 2019	Both (patient and caregiver received a brochure)	Pharmacy, hospital physicians	1. Computer-generated deprescribing report based on PIMs	One time: not specified	Pre-post design: care as usual (medication reconciliation) before intervention at baseline
			2. Hospital team free to use or not use deprescribing recommendations		
			3. Patient/caregiver provided educational materials		
			4. Patients received a one page brochure on harms of polypharmacy		
			5. For patients who consented to an outpatient postdischarge interview: a copy of deprescribing report and list of medication changes at hospital discharge were faxed to their self-identified most-responsible community physician and pharmacist		
Parker, 2019	Provider	Nephrology	Medication review with one investigator and a nephrologist, using STOPP/START criteria, follow-up recommendations were written in the medical record to inform attending physicians. Attending nephrologist had final say in medication prescription	One time: not specified	The same investigator performed an identical medication review using the STOPP/START criteria, but no notes were entered into the medical record

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Anderson, 2020	Provider	General practitioner, pharmacy	1. A 5-h face-to-face interactive deprescribing training workshop for clinicians, centered on cease deprescribing principles 2. An extended deprescribing consultation between GPs and patients, entailing a CMR, using a standardized software template (Supplement 3) codedigned by GPs during the workshop. The template reminded GPs when to consider deprescribing and served to collect data on changes to medicines, including rationales 3. Optional: Further consultations and referrals to other health professionals occurred at the GP's discretion. To augment deprescribing, intervention GPs could also refer patients for a CMR by participating pharmacists who had full access, with patient consent, to the medical record. The follow-up period from the initial deprescribing consultation was 18 weeks	One time: 1. 5-h workshop, 18-week follow-up 2. One-time deprescribing consultation 3. Optional referral to pharmacist	Care as usual no extra training/workshop or access to pharmacy referrals (GPs did not receive any training and patients continued to receive routine care)

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Curtin, 2020	Provider	Physicians	For participants randomized to the intervention arm, a medication withdrawal plan was devised by the research physician. The recommended medication withdrawal plan was communicated directly to one of the participant's attending physicians and also documented in the patient's medical record. Medications associated with an increased risk of an adverse withdrawal reaction were recommended to be withdrawn slowly according to a standardized trial withdrawal protocol (Supplemental Protocol S1). The attending physician judged whether or not to accept the drug withdrawal plan and implement the recommended changes. Because of the nature of the intervention, the research physician, attending physicians, and participating patients could not be blinded to the intervention or control group assignment after randomization. The intervention was applied at a single time point during the patients' hospital admission at the time of trial enrollment. Attending physicians and nursing staff were encouraged to report any potential adverse consequences of deprescribing (adverse drug withdrawal events or disease relapse) to the research team	One time: not specified, perceived low intensity	Care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Gedde, 2020	Provider	Nursing, physicians, pharmacists	Medication review with a nurse and two research physicians who provided mentoring. Based on validated assessments for behavioral/psych symptoms of dementia, ADLs, pain, cognitive status, QoL. Medication review based on Norwegian Medical Agency guidelines, START/STOPP, and anticholinergic medications. Nurses discussed changes with patients but final decision remained with nursing home physicians	One time: One structured medication review	Care as usual
O'Donnell, 2020	Provider	Clinical pharmacy, medicine (uptake by medicine of deprescribing recommendations is poor)	- The Goal-directed Medication Review Electronic Decision Support System (G-MEDSS) is a computerized clinical decision support system designed to support person-centered medication reviews - The G-MEDSS platform contains three tools and produces reports on these for the general practitioner and patient/carer: - The goals of care management tool that supports documentation of the patient's goals for alignment with their medication management strategies - The Drug Burden Index (DBI) Calculator, a validated tool that provides information on a patient's total exposure to medications with anticholinergic and sedative effects and their risks - The revised patient's attitudes toward deprescribing (rPATD) questionnaire with versions for patients, caregivers, and people living with cognitive impairment	One time: not specified, but seems low	Usual care home medicines reviews (HMRs) alone

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	
				One time: not specified	Control group
Sanyal, 2020	Both	Pharmacists, physicians	Education intervention 1. Pharmacist led intervention conducted by distributing educational, drug-specific brochures about inappropriate meds/alternative treatments (including NSAIDs) 2. Participants received an educational brochure on NSAID risks 3. Optional: Pharmacists could fax an evidence-based pharmaceutical opinion to their physician 4. This intervention is pharmacist led and promotes shared decision making between pharmacists, patients, and physicians		Routine care from community pharmacists and physicians for pain relief and continued filling prescriptions for NSAIDs at community pharmacy. Primary care physicians may have referred patients to specialists depending on disease severity or management of adverse outcomes. Wherever necessary, the specialist communicated with the primary care physician on disease management strategies

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Schapira, 2020	Provider	Physicians	Intervention content	Intervention intensity	Control group
			1. Development of educational materials: Beers criteria used to guide PCPs in working with PIMs	Continuous: education workshops took a total of 2 half-workdays in 2 weeks; other components in the intervention were continuous (materials, email reminders, engagement, etc.) and of low intensity (requiring relatively little workload)	No control was used
			2. Development of simple deprescribing algorithms used for the different drug classes: decision trees developed for eight types of common PIMs (NSAIDs; benzodiazepines; histamine antagonists; opioids; tricyclic antidepressants; muscle relaxants, centrally acting antihypertensives, and cholinergic antagonists)		
			3. Clinician champion: PCP coordinators recruited as champions to promote awareness/participation in the study		
			4. Optional: Educational lectures discussing practical aspects of treatment and clinical cases (a total of 2 half-workday workshops in 2 weeks)		
Sheppard, 2020	Provider	PCP	5. Email alerts: PCPs were asked for their preferred reminder tool and email (in the 48 h prior to patient visit) was used to suggest solutions on PIMs 48 h prior to patient appointments		
			1. PCP performed med review and decided, which antihypertensive to remove from treatment (an algorithm was used for assistance)	4 weeks: one-time medication reduction followed by a 4-week safety BP monitoring period to ensure safety	Usual clinical care, in which they continued to take all antihypertensive medications as prescribed
			2. PCPs asked to follow a safety monitoring algorithm including 4-week follow-up (structured approach, algorithm in figure)		
			3. Treatment reinstated if certain blood pressure cutoffs exceeded		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Campbell, 2021	Both	Medicine, medical assistants	1. Provider-focused component: computerized decision support alert of the presence of a high-risk anticholinergic and offering dose- and indication-specific alternatives (best practice alerts in EPIC) 1. Alerts were triggered each time a patient record was opened on the day of an outpatient visit among patients aged 65 years and older who were current users of one of the target anticholinergics 2. Patient-focused component: a story-based video providing education and modeling an interaction with a health-care provider resulting in a medication change. One of three videos will be played; duration is 3.5–4.5 min; available in Spanish 1. Alerts within the medical record triggered medical assistants to play the video for a patient 3. Both components occur immediately before an outpatient face-to-face interaction 4. Intervention was embedded within EPIC	One day (every time when patient's EMR is opened on the day of outpatient visit): multiple alerts on the day of outpatient visit + one 3.5–4.5 min video played before PCP appointment	Control was not specified or described (assumed to be usual care as it is stated in the tables)

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Cateau, 2021	Provider	Pharmacy, nursing, physician	- Pharmacists attend a 3-day education seminar on the methodology of performing medication review - Pharmacists conducted a deprescribing-focused mediation review - Pharmacist, in collaboration with nurses and physicians, created a treatment modification plan - Agreed upon treatment modification plans were presented to residents and their representatives before implementation - Standardized forms were provided for pharmacists to perform the medication review and to document the treatment modification plan	One time: one time (including a 3-day education session + group meeting medication review + formalization of a deprescribing consensus with treatment modification plan + submitting deprescribing to patients + implementation)	Care as usual: control participants' drug regimen could be adapted freely by the NH staff and physicians

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Kua, 2021	Both	Medicine, nursing, pharmacy	1. Pharmacist: (1) reviewing the necessity of medication using Beers and STOPP criteria to guide the detection and recommendation of PIM use in older adults; (2) checking for drug–drug and drug–food interactions to reduce risks of adverse drug events; (3) discussion with nurses on the feasibility of deprescribing for each resident, with an option to discuss with cognitive-intact residents (or family members of cognitively impaired residents); (4) communication through nurse to physician for reviewing and deprescribing decisions; and finally (5) documentation made available for all agreed action plans with further follow-up as required 2. Nurse: provide input regarding feasibility of deprescribing, communicate between pharmacist and physician 3. Physician: review deprescribing recommendations during the next visit and make final decision on deprescribing implementation	One time: not specified the first 3 months	Active waitlist control for the first 3 months

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Mahlknecht, 2021	Provider	Internal medicine specialist, pharmacology, PCP	1. Pre-review to check for PIMs according to Beers list and for drug-drug interactions 2. The med review and deprescribing recommendations were independently assessed by three experts. Every regimen was assessed by a specialist in internal medicine, a clinical pharmacologist, and an evidence-based practice medication expert and evaluated according to best practices, disease specific guidelines, and the presence of PIMs/DDIs 3. Experts elaborated recommendations for discontinuation based on medication review, if two experts agreed on specific recommendations, an explanation was forwarded to the GP 4. GP was asked to reflect on recommendations with the patient, all responsibility for continuation/discontinuation was with the GP	One time: not specified, but considered moderate: three experts' independent reviews + consensus + GP involvement	Usual care: included potential use of guidelines by GPs and drug changes during routine care but did not include the structured medication review with recommendations by the three experts

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
Wauters, 2021	Provider	Pharmacy, nursing, primary care medicine	1. The nurse uploads the medication regimen to the OptiMEDS platform 2. Using another electronic tool, a list of medication-related symptoms is generated for each individual resident 3. Another automated tool flags PIMs using a database 4. Extracted data are analysed for anticholinergic medications 5. A list of medications for deprescribing is used to flag all medications that can be considered for deprescribing 6. Input is summarized and the pharmacist then proposes alternative treatments 7. A final report is made available for the GP and nurses, and after discussion the nurse implements changes in the medication list	One time: 45 min for nurses, 20 min for pharmacist, 8 min for GP	Care as usual

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	
					Control group
Wong, 2021	Both	Non-ward doctor, pharmacist, ward nurse	1. Five distinct steps of Scott's deprescribing model include ascertaining current meds and indications, risk of harm, current/future benefit, harm, and burden	Weekly: five-step deprescribing at bedside, 7 min per patient	Usual care by the ward doctors, including regular ward rounds, medication changes, and monitoring side effects at their own discretion
			2. Study investigators assessed and decided on deprescribing at patient's bed side		
			3. Patient's ward doctors were informed of changes and the ward team implemented changes		
			4. Patient final preference of deprescribing was considered when deciding on deprescribing		
			5. Training was provided before the intervention was delivered to multidisciplinary treatment team of the patients, who had NO prior training in deprescribing		

(Continued)

Table 3. Continued

Study	Focus	Disciplines	Intervention content	Intervention intensity (frequency: time for each session)	Control group
McDonald, 2022	Both (patient and caregiver received a brochure)	Hospital pharmacy/treatment team	1. CDSS-generated individual deprescribing reports based on evidence-based guidelines for safer prescribing, with tapering instructions when indicated; prioritized deprescribing based on high risk PIMs, intermediate risk PIMs, PIMs with little added value; deprescribing opportunities based on medical conditions, lab values, and home med lists 2. Deprescribing reports provided to treatment team within 3 days of admission and were designed to engage the physician and the hospital pharmacy team 3. Patients or their caregivers received an educational pamphlet on deprescribing, as well as relevant patient oriented deprescribing pamphlets from the Canadian Deprescribing Network for select classes of medications, such as sedative-hypnotics 4. At discharge a report was sent to the community pharmacy and PCP of the patient	One time: not specified	Usual care (medication history), medication reconciliation at hospital admission and discharge. Any deprescribing that took place was based on local and individual practice by the unit physicians and pharmacists

Abbreviations: ADL, activities of daily living; PIM, potentially inappropriate medication; QoL, quality of life.

Table 4. Outcomes assessed in prior deprescribing trials

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Meredith, 2002	N	1. Therapeutic duplication: <i>stopping</i> at least one of the potentially duplicative medications 2. Use of cardiovascular med: masked review of the medication regimen to determine whether changes had been made that addressed the problem related to cardiovascular med use 3. Psychotropic med use: <i>dose reduction</i> of 25% or greater or change to a preferred drug 4. NSAID use: a <i>dose reduction</i> of 25% or greater or stopping the NSAID		1.5–3 months: 6–12 weeks
Fick, 2004	Physician response, documented action regarding PIMs, and type of PIMs responded to	Documented action regarding PIMs and type of PIMs responded to		12 months
Fossey, 2006	N	Proportion of residents in each home who were prescribed neuroleptics	Mean levels of agitated and disruptive behavior (Cohen-Mansfield agitation inventory) in each nursing home	12 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Beer, 2011	N	1. Medication withdrawal achieved among intervention participants 2. Medication adherence	Quality of life, medication adherence, sleep quality, and cognitive function	
Bergh, 2012	N	N	Scores on the Cornell scale for depression in dementia and the neuropsychiatric inventory; scores on the unified Parkinson's disease rating scale, quality of life-Alzheimer's disease scale, Lawton and Brody's physical self-maintenance scale, severe impairment battery score, and clinical dementia rating scale	6.25 months: 25 weeks
Dalleur, 2014	Clinical significance/relevance of the STOPP-related recommendations (6-point scale rated by 3 experts: minor, moderate, major, extreme, life-saving, deleterious; increased risk of adverse event; N/A)	1. Proportion of PIMs discontinued between hospital admission and discharge 2. Proportion of PIMs that were still discontinued 1 year after discharge	Characteristics associated with discontinuation of PIMs at discharge	12 months
Tannenbaum, 2014	N	Complete cessation of benzodiazepine use in the 6 months following randomization Cessation was defined as an absence of any benzodiazepine prescription renewal at the time of the 6-month follow-up that was sustained for 3 consecutive months or more, in the absence of substitution to another benzodiazepine		6 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Wouters, 2014	Visits to outpatient clinics, visits by elder care physicians, and consultations by other health-care professionals	- Proportion of residents who successfully discontinued use of at least 1 inappropriate medication - Number of residents for whom at least 1 under-prescribed medication was initiated, at least 1 dose was adjusted, and at least 1 potentially hazardous drug was replaced by a safer alternative - Cumulative exposure to anticholinergic and sedative drugs (drug burden index)	Number of falls, visits to outpatient clinics, visits by elder care physicians, and consultations by other health-care professionals	4 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Ballard, 2015	N	N	Antipsychotic and other psychotropic drugs were classified according to the British National Formulary Depression evaluated by using the Cornell Scale for Depression in Dementia Agitation evaluated by informant interview using the 29-item Cohen-Mansfield Agitation Inventory neuropsychiatric symptoms measured through the 10 domains of the Neuropsychiatric Inventory, nursing home version (which also includes a domain for depression), mortality, and dementia severity as measured by the Clinical Dementia Rating and Functional Assessment Staging instrument	9 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Clyne, 2015	N	1. Proportion of patients with PIP 2. Mean number of PIP drugs per group 3. Absolute number of PIP drugs per group of the top 5 reported nationally: proton pump inhibitor at full therapeutic dosage for more than 8 weeks, long-term use (>3 months) of nonsteroidal anti-inflammatories (NSAIDs), long-term use (>1 month) of long-acting benzodiazepines, therapeutic duplication, and tricyclic antidepressants with an opiate or calcium channel blocker	Secondary outcomes included individual measures of the composite drug-specific outcome, including the absolute number of PIP drugs per group of the top 5 reported nationally 7: proton pump inhibitor at full therapeutic dosage for more than 8 weeks, long-term use (>3 months) of nonsteroidal anti-inflammatories (NSAIDs), long-term use (>1 month) of long-acting benzodiazepines, therapeutic duplication, and tricyclic antidepressants with an opiate or calcium channel blocker. Patient-reported outcomes included responses on the Patients' Beliefs about Medicines Questionnaire¹⁹ and the Well-Being Questionnaire²⁰ collected via self-completed questionnaires	6 months
McKean, 2016	N	Change in medications per patient	/	6 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Moonen, 2016	N	N	Change in overall cognition compound score between baseline and follow-up. Changes in the different cognitive domains and separate cognitive tests were secondary outcome measures. Further secondary outcome measures were changes in psychological and general daily functioning. The Apathy Scale was used to measure symptoms of apathy (range, 0–42 points, with higher scores indicating more symptoms of apathy), 23 and the Geriatric Depression Scale-15 was used to measure symptoms of depression (range, 0–15 points, with higher scores indicating more symptoms of depression) [24]. General daily functioning was assessed with the Groningen Activity Restriction Scale (range, 18–72 points, with higher scores indicating lower functioning) [25], and quality of life was assessed with the Cantril Ladder (range, 1–10 points, with higher scores indicating better quality of life) [26]	4 months; 16 weeks

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Cossette, 2017	N	1. Number of discontinued drugs or drugs with a dosage decrease	Length of stay, in-hospital death, and emergency room visits and readmissions within 30 days of hospital discharge	1 month; 30 days
Frankenthal, 2017	N	1. Quality of prescribing: number of residents with at least one PIP or PPO according to the STOPP/START criteria 2. Medication cost	Falls and hospitalizations All-cause mortality 24 months after randomization Time to death	24 months
Balsom, 2018	N	Number of prescribed and OTC medications	Survival, quality of life, cognitive performance, pain, social engagement, ADLs	6 months
Gulla, 2018	N	1. Number of antihypertensive drugs	Systolic blood pressure and pulse	9 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Martin, 2018	Process outcomes: assessment of the delivery of the educational brochures to the patients by their pharmacists; the prevalence, timing, and type of pharmaceutical opinions sent by the pharmacists to the patients' primary care physicians; the effect of the educational material on participants' beliefs about the use of their inappropriate medications and their intent to discuss cessation with their physician or pharmacist; the effect of the pharmaceutical opinion on the prescribing physician's behavior; participant-physician encounters to discuss inappropriate prescriptions; and participant improvement in self-efficacy to discontinue medication	Y: Complete cessation of prescription fills for any of the 4 medication classes 6 months after randomization	/	6 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Westbury, 2018	N	1. Prevalence of regular antipsychotic and benzodiazepine prescribing at baseline, and at 3 and 6 months 2. Chlorpromazine and diazepam-equivalent doses/day/resident 3. Proportions of residents for whom drug was ceased or the dose reduced 4. Prevalence of antidepressant and PRN (as required) psychotropic prescribing (to detect any substitution practice)	/	6 months
Whitty, 2018	Enrolment rate and the acceptability of the MERA intervention to patients/SDMs	1. Number of medications prescribed 2. Number of recommended discontinuations 3. Number of accepted discontinuations	Medication use 3 months after discharge using the Ontario Drug Benefit (ODB) program database (which would have information for many medications taken by participants over age 65 year)	3 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Ee, 2019	1. Feasibility: time required to complete the deprescribing process (19 min in total: pharmacists spend 11 min on medication review, and another 8 min to discuss with MD about deprescribing plan)	1. Cost of 1 month of medications 2. Total number of medications	Possible adverse consequences of deprescribing, which comprise constipation indicated by no bowel movement (BNO $\geq 2/7$), other two days (BNO $\geq 2/7$), other symptom recurrence, adverse drug withdrawal events (ADWEs) and the need for deprescribed medications to be restarted, or initiation of new symptomatic control medications after deprescribing, were monitored. The feasibility of implementation was also determined through the time required to complete the deprescribing process and the limitations and challenges encountered, as documented by the pharmacists	1.5 months; 6 weeks
Gnjidic, 2019	N	Use of benzo at 1 month follow-up after hospital discharge	Beliefs on BZD use	1 month

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
McDonald, 2019	Adverse events within 30 days after hospital discharge	- Proportion of patients who had at least 1 PIM deprescribed by hospital discharge - Adverse drug events within 30 days after hospital discharge - Estimated NNT = 12 (it takes doing the intervention on 12 patients for the intervention to make an impact on 1 patient)	/	1 month; 30 days
Parker, 2019	N	- Number of patients with potentially inappropriate prescriptions (identified using the STOPP criteria) - Total number of medications per patient - Medication adherence	/	6 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Anderson, 2020	- Instances of actual or potential patient harm from deprescribing - Self-reported unplanned hospitalizations	- Number of regular medicines deprescribed (ceased/reduced) per patient - Proportion of patients having at least one medication deprescribed	Secondary outcomes comprised: (1) the number of agreed regular medicines per patient over the study period that were ceased and dose reduced; (2) the number of medicines deprescribed, ceased, dose reduced, started, and dose increased; and (3) the medicine classes deprescribed. The Patient Attitude Towards Deprescribing (PATD) Questionnaire²² was applied to intervention patients to investigate: (1) changes in PATD scores between baseline and follow-up and (2) whether baseline responses predicted the primary outcome. The proportion of intervention patients who underwent a deprescribing appointment was measured, while the mean number of GP visits per patient and proportion of patients receiving a CMR by a pharmacist during the study period were measured in both patient groups.	4.5 months: 18 weeks

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
			Potential adverse effects of deprescribing were assessed by: (1) changes in health-related quality of life (HRQoL), as measured by the EQ-5D-5L Questionnaire—Telephone Version, 23 which included questions on five health domains and a “visual” analogue scale (EQ-VAS) for global health; (2) unplanned hospitalizations, as measured by patient self-report (as cross-referencing with GP and hospital records proved infeasible); (3) instances of actual or potential patient harm from deprescribing, as reported directly to the research team by either patient or GP	

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Curtin, 2020	1. Potential adverse consequences of deprescribing (adverse drug withdrawal events or disease relapse) 2. Unscheduled medication reviews	1. Number of regular medications 2. 28-day medication cost 3. Prescriptions of neuroleptic antipsychotic medications	Unscheduled hospital presentations, falls, quality of life, monthly medication costs, and mortality	3 months
Gedde, 2020	N	1. Numbers of prescribed psychotropic drugs	Mean changes in (1) BPSD estimated by the Neuropsychiatric Inventory–Nursing Home Version (NPI–NH) and the Cornell Scale for Depression in Dementia (CSDD), and (2) ADL evaluated by Physical Self Maintenance Scale (PSMS)	4 months
O'Donnell, 2020	N	Y: Proportion of patients with any reduction in DBI at 3 months follow-up, change in continuous DBI score at 3 months, change in change in DBI category (binary) that would result from HMR (unsure how)	Physical function, falls, cognitive function, institutionalization, mortality	3 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Sanyal, 2020	N	Y: Health-care services use and total cost include cost of medication use and management of symptoms related to NSAIDS deprescribing were derived from the literature; probability was derived from the study	Costs and Quality-Adjusted Life Years	12 months (cost effectiveness analysis only)
Schapira, 2020	Process measures: 28% participating PCPs received both educational workshops, 41% received 1 of the 2 educational workshops	Prevalence of PIM use of eight drug classes	/	12 months
Sheppard, 2020	1. Relative risk of systolic blood pressure control 2. Adverse effects to medications 3. Serious adverse events 4. Change in systolic and diastolic blood pressure over 12 weeks	Proportion of participants in the intervention group who maintained medication reduction	Relative risk of systolic blood pressure control (<150 mm Hg; defined by UK National Institute for Health and Care Excellence as the target blood pressure for those older than 80 years) between groups at 12-week follow-up. Frailty, quality of life, adverse effects, serious adverse events, and change in systolic and diastolic blood pressure over 12 weeks	3 months: 12 weeks

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Campbell, 2021	Process measures: % of alerts enacted upon by providers and staff	- Proportion of the population - Using target anticholinergics - Anticholinergic orders	- Prescribing behavior: number of discontinue orders - Population prevalence of anticholinergic users (extracted from Medication orders in electronic medical record system)	12 months
Cateau, 2021	N	- Number of PIMs used at baseline and 4 months (assessed using STOPP criteria) - The number of chronic (not in reserve or short-term treatment) drugs - The number of inappropriate defined daily doses (DDD) per day - The number of chronic DDD per day - The number of common complaints frequently related to drug use	Health-related quality of life (QoL), measured with EuroQol-5 Dimension-5 Levels (EQ-5D-5L), all assessed at baseline and 4 months after intervention. Safety outcomes were the mortality rate, the number of participants hospitalized, the number of days spent in hospital, the number of participants having experienced at least one fall, the number of falls, and the number of days spent with physical restraints	4 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Kua, 2021	Process measure: deprescribing acceptance rate	Y: Pill burden (number of pills per day and number of medications); medication cost-saving from deprescribing for the study population; type and percentage of drug-related problems (DRPs)	The co-primary outcomes of interest was a reduction in both fall rates (number of fallers) and fall risks, assessed using the fall risk assessment tool (FRAT). Number of fallers was defined as the number of residents with reported falls within the past 3 months Pill burden (number of pills per day and number of medications), number of deprescribing interventions, as well as cost-related measures such as medication cost-saving from deprescribing for the study population Post hoc mortality rate, hospitalization rate, the acceptance rate of the deprescribing intervention, as well as the type and percentage of drug-related problems (DRPs) and categorized them into percentages of unnecessary medication use according to therapeutic classes, using the Beers criteria	12 months

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
Mahlknecht, 2021	N	N	Composite binary outcome of all-cause mortality or unplanned hospitalizations. Additionally, all-cause mortality and non-elective hospitalizations were analysed as single secondary outcomes	24 months
Wauters, 2021	1. Feasibility: challenges and time spent 2. Acceptability: user experience	Percentage of residents with a decrease of at least one PIM (potentially inappropriate medication, an anticholinergic or a candidate for deprescribing)	/	1 month
Wong, 2021	Feasibility of implementing intervention: rounding time per patient (7 min); inconvenience of assembling the team for rounding and spending time to address patients' concerns about deprescribing	1. Percentage reduction of total daily dose (TDD) of medications from baseline upon inpatient discharge 2. Percentage reduction of TDD at 3 other timepoints	Secondary outcomes include other efficacy outcomes (namely percentage reduction of TDD at three other timepoints mentioned below, TNM and total daily cost of medicine [TDC] at all four timepoints), safety outcomes (i.e., recurring or worsening symptoms; medicine reinitiation or substitution, hospitalization and death)	1 month: 28 days

(Continued)

Table 4. Continued

Study	Process outcomes	Medication outcomes	Clinical outcomes	Follow-up period
McDonald, 2022	N	1. Proportion of patients experiencing an adverse drug events (ADE) within the first 30 days after hospital discharge 2. Proportion of patients with 1 or more PIMs deprescribed at hospital discharge	Proportion of patients with 1 or more PIMs deprescribed at hospital discharge compared with usual care, and 30-day postdischarge adverse effects, falls, emergency department visits and/or hospitalizations, deaths, quality of life (using the EQ-5D-5L questionnaire with a Canadian value set33), and sleep disturbance (using the PROMIS SD 4a)	1 month; 30 days

Abbreviations: ADL, activities of daily living; PIM, potentially inappropriate medication; PRN, pro re nata.

systems, (2) target patient populations, and (3) intervention design, including content, intensity, and duration.

Resources in existing health-care systems

The setting and geographic region where trials were conducted are important considerations when translating evidence into practice (i.e., implementation), due to the variation in providers and other resources across clinical settings and regions. The countries that initially spearheaded deprescribing efforts (e.g., the United Kingdom, Canada, and Australia) tend to have more community-based pharmacists available and existing reimbursement structures for community pharmacists to assist with medication review and deprescribing [147]. For example, one trial (reported in two studies) [129, 134] featured a deprescribing intervention led by community pharmacists, who are heavily utilized within community-based care in public health-care systems such as in Canada and Australia. A similar role for community pharmacists was employed in deprescribing interventions in Singapore [136]. However, in other countries such as the United States where community pharmacy services are more limited and payment is often not sponsored by federal health-care insurance widely available to older adults (i.e., Medicare), the potential of deprescribing interventions to utilize community-based pharmacy services is uncertain.

In addition, we noted that deprescribing interventions in long-term-care settings are the most common, and these interventions also tend to be more effective relative to interventions in other clinical settings. However, the long-term (nursing home) care setting is unique in many ways that may limit the generalizability of these interventions to other care settings, particularly the community. For example, the long-term care setting allows for a longer follow-up period after medication changes, continuous supervision and symptom monitoring by licensed personnel, direct access to and control over all medications [110], and regulatory oversight with standardized quality measures related to the use of psychotropics, antianxiety, and hypnotic medications [148] as well as other standardized measures related to mobility and functional decline, falls, and hospitalizations. All these factors may contribute to the effectiveness of deprescribing interventions in long-term care settings that may be difficult to replicate in other care settings.

Target patient populations

Also related to the variability in geographic region is the heterogeneity in target patient populations who received the deprescribing intervention. In countries with intensive home-care support to allow older adults to remain at home for longer periods of time, such as the United Kingdom, Switzerland [149], and Sweden [150], and to some degree, the United States (i.e., with the rise of assisted living facilities [151, 152]), nursing home residents tend to be more frail, older, and have more functional impairments. There is also a need to consider a wider range of patient populations regarding their underlying medical conditions and medications targeted for deprescribing. Specifically, many of the reviewed deprescribing trials were focused on patients with dementia who were prescribed antipsychotics. However, the prevalent focus on antipsychotic deprescribing among persons with dementia may limit the generalizability of these findings to deprescribing other commonly used medications with potential for harm (e.g., benzodiazepines) among older adults who may or may not have dementia. Moreover, deprescribing interventions should be targeted to patient populations most likely to benefit. Multiple studies have noted that deprescribing interventions are likely more effective if they are targeted toward patients with high levels of frailty, comorbidity, and hyperpolypharmacy (taking ≥ 10 medications concurrently) [132, 142]. Patient education trials may be more or less effective based on patients' attitudes toward deprescribing, health literacy, and/or the involvement of a caregiver in medication management. Future studies should include more broadly and clearly defined criteria for the target patient populations to allow deprescribing interventions to be evaluated among more patients likely to benefit.

Design of intervention

The key components of most deprescribing interventions included education, medication review and reconciliation, assessment of deprescribing targets, and communication with patients, caregivers, and/or health-care providers. These care processes are often part of routine clinical practice, to at least some degree, though often not by the same provider in a single visit.

Implementation outcomes

Eight studies measured the feasibility and acceptability of deprescribing, such as the physician or

patient acceptance of deprescribing recommendations, time spent on deprescribing tasks, challenges to deprescribing implementation, as well as the process of deprescribing [106, 111, 129, 130, 133, 136, 137, 141], to assess intervention fidelity. The follow-up period for outcome measurements ranged from 1 month [117] to 24 months, including ≤ 3 months ($n = 12$), 3–12 months ($n = 15$), and ≥ 12 months ($n = 9$).

In multiple deprescribing trials, researchers noted the importance of monitoring patients after deprescribing to ensure safety and adherence to the revised medication regimen. A monitoring phase also allows for the identification of symptom recurrence or worsening, such as increasing depressive symptoms among patients with dementia [127] and increasing blood pressure in those with hypertension [114]. We noted that few trials [125] incorporated a monitoring phase in the study design. In addition, follow-up interventions may improve the effectiveness and sustainability of deprescribing [36], yet most interventions were delivered one-time only, with no subsequent efforts to assess either patient adherence or safety outcomes. Authors of deprescribing intervention studies that focused primarily on technological innovations with limited human efforts and null findings suggested that more intensive human efforts are needed to monitor deprescribing implementation [63, 106].

Alignment with existing care processes of clinicians

Deprescribing implementation must consider how this process can be incorporated into clinical care workflows and what types of providers within the care team are best suited to accomplish each of the tasks delineated in the deprescribing process [94]. In deprescribing trials, a notable challenge is the degree to which providers actually implemented the deprescribing recommendations provided by the research team [108, 110]. This finding is consistent with prior reviews wherein few trials reported implementation rates of deprescribing recommendations [94]. We also noted limited, or uncertain, implementation potential of deprescribing interventions in routine clinical practice or in the community, particularly among studies that aimed to improve deprescribing outcomes for patients by intervening on deprescribing behaviors of providers.

In addition, researchers from one of the earliest deprescribing trials [107] noted that, because medication use is a complex issue that involves multiple parties, including the patient, the prescriber(s), and other health-care professionals (e.g., pharmacists and nurses), deprescribing interventions should target multiple disciplines rather than focus on a single discipline. Yet, in prior deprescribing trials, we noted the lack of involvement of multidisciplinary health-care workers, such as licensed registered nurses and advanced practice nurses who could potentially play an essential role in home-based medication review and patient education. Therefore, we suggest that researchers consider the feasibility of future deprescribing interventions, such as the existing workforce, relevant disciplines, and available training to facilitate implementation of the intervention in routine care practice.

Potential strategies to improve the implementation potential of deprescribing interventions include (1) systems or practices to support a Best Possible Medication History (BPMH) using multiple data sources beyond the electronic health record, such as a patient/caregiver self-report that includes explicit questions about over-the-counter medication use and pharmacy refill history [153]; (2) specific criteria for the identification of PIMs (e.g., the Beers or STOPP criteria) into comprehensive geriatric assessment [110] to improve deprescribing assessment; and (3) written deprescribing recommendations to primary care providers in a familiar, succinct format [63] such as the Situation–Background–Assessment–Recommendation (SBAR) communication tool [154], with direct oral communication when needed [140] to support provider implementation.

For example, community-embedded pharmacists and nurses (depending on availability in the existing health-care system) could complete the initial medication review and patient education, as well as obtain feedback from the patient (and/or caregiver) about their preferences and goals, ideally within the patient's home. Then, primary care providers—with the support of pharmacists if available—could reconcile the medication list, identify deprescribing targets, and discuss deprescribing recommendations with the patient during a routine outpatient visit. If deprescribing aligns with the patient's preferences and goals, the home-visiting nurses (available in multiple countries such as the United States, Canada, Australia, Japan, and Singapore)

could then facilitate the implementation of deprescribing by helping the patient adhere to the new medication regimen, monitoring symptoms and side effects, and ensuring that deprescribed medications are appropriately disposed of or stored separately to avoid medication use errors.

Implications for clinical practice and future research on deprescribing

This scoping review of deprescribing interventions provides insights into the implementation of deprescribing in clinical practice. First, interoperability of electronic health records is needed to improve communication between providers to support deprescribing, such as by providing an accurate, comprehensive list of medications, and prioritized deprescribing recommendations accessible to all members of the health-care team as well as the patient. The deprescribing recommendations should aim to align the treatment regimen with the patient's elicited goals of care, preferably including oral or electronic communication with prescribers, and patients and/or caregivers whenever possible to enhance patient involvement in the deprescribing decision process.

Second, deprescribing for older adults with multimorbidity and complex medication regimens can be time-consuming. In fact, time constraints of clinicians are a major barrier to implementing both medication reconciliation and deprescribing in clinical practice [155]. Therefore, we recommend that future deprescribing trials consider using existing data from electronic health records for risk profiling and automatic screening to target high-risk patients and identify potential deprescribing targets. Additionally, it would be beneficial to incorporate dedicated personnel who can bill for medication management in out-patient clinics or team-based clinical practices to support deprescribing.

Third, there is a need for more deprescribing intervention studies in the United States (although there are currently multiple active [49] and recently completed trials [142]), more studies in varied care settings (e.g., home health care and hospice care) as well as during care transitions (hospital to skilled nursing facility to home or hospital to home with/out home health care). Fourth, more work is needed to enhance interdisciplinary collaboration so as to broaden the impact of deprescribing to more disciplines in health care. For example, various "deprescribing networks" have been devel-

oped in the United States and other countries such as Canada and Australia [156–161], promoting a more concerted effort to share findings, identify common measures, and available databases, and explore implementation strategies of deprescribing research on the international level.

Limitations

This review has several limitations. First, we did not grade the quality of reviewed studies. Because our focus was on assessing the characteristics and implementation potential of deprescribing interventions in trials, all relevant studies were included regardless of methodological quality. Second, we did not include unpublished or active trials, but note that some currently active trials have incorporated more patient-centeredness in the design and might have also included considerations of future implementation of the tested interventions in existing health-care systems [49, 112].

Perspectives

As the world population is living longer and often experiencing multimorbidity, polypharmacy and related issues will continue to grow both in prevalence and impact. These changes in demographic and health profiles require our health-care systems to provide more holistic "age-friendly" care that considers not only medications but also other domains important to the well-being of older adults. Specific to the field of deprescribing, we have seen exponential growth in the development of tools, conceptual models and frameworks and the examination of factors associated with deprescribing. Deprescribing interventions examined in prior studies have not included adequate consideration of the necessary workforce, training, and resources within existing health-care systems, limiting the potential to translate evidence into improvements in comprehensive geriatric clinical care. Deprescribing interventions and practices that incorporate patient-centeredness in the delivery, design and outcome assessments are needed to advance the field. Efforts are also needed to improve the implementation of deprescribing interventions by providers in routine clinical practice across clinical settings.

Conflicts of interest

The authors declare no conflicts of interest.

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