

Deprescribing in the Older Patient: A Narrative Review of Challenges and Solutions

Harry Wu¹

Lisa Kouladjian O'Donnell¹

Kenji Fujita¹

Nashwa Masnoon^{1,2}

Sarah N Hilmer¹

¹Departments of Clinical Pharmacology and Aged Care, Faculty of Medicine and Health, The University of Sydney, Kolling Institute, Royal North Shore Hospital, Sydney, NSW, Australia; ²Department of Pharmacy, Royal North Shore Hospital, St Leonards, NSW, Australia

Abstract: Polypharmacy is a major challenge in healthcare for older people, and is associated with increased risks of adverse outcomes, such as delirium, falls, frailty, cognitive impairment and hospitalization. There is significant public and professional interest in the role of deprescribing in reducing medication-related harms in older people. We aim to provide a narrative review of 1) the safety and efficacy of deprescribing interventions, 2) the challenges and solutions of deprescribing research and implementation in clinical practice, and 3) the benefits of using Computerized Clinical Decision Support Systems (CCDSS) and Quality Indicators (QIs) in deprescribing research and practice. Deprescribing is an established management strategy to minimize polypharmacy and potentially inappropriate medications. There is limited clinical evidence for its efficacy on global and geriatric outcomes. Various challenges at patient, healthcare professional and healthcare system levels may impact on the success of deprescribing interventions in research and practice. Management strategies that target all levels of the healthcare system are required to overcome these challenges. Future studies may consider large multicenter prospective designs to establish the effects and sustainability of deprescribing interventions on clinical outcomes.

Keywords: deprescribing, polypharmacy, geriatric, older people, computerized clinical decision support, quality indicator

Introduction

Optimising use of medications is increasingly recognized as an important pillar in the management of older people. Polypharmacy is highly prevalent among older people; it is estimated that more than 15 million Americans aged 65 years and older are prescribed five or more medications.¹ This number is very likely to rise as the population grows older. Population-based studies have demonstrated that polypharmacy is independently associated with increased risks of adverse geriatric outcomes such as delirium, falls, frailty, cognitive impairment and hospitalization.^{2–5} With increasing burdens of geriatric syndromes and age-related diseases,^{6–8} there is significant public interest in reducing medication-related harms in older people.⁹ Reduction of inappropriate polypharmacy is a major public health goal identified by the World Health Organization Third Global Patient Safety Challenge: Medication Without Harm.¹⁰ This has led to a greater awareness of optimising medication use and the need to improve management strategies to prevent medication-related problems in older people.

The term “deprescribing” was first published nearly two decades ago,¹¹ and is defined as the process of supervised withdrawal of inappropriate medications, for which the potential harms outweigh the benefits.¹² The main rationale of

Correspondence: Sarah N Hilmer
Level 13, Kolling Institute of Medical Research, Royal North Shore Hospital, Reserve Road, St Leonards, NSW, 2065, Australia
Tel +612 9926 4481
Email sarah.hilmer@sydney.edu.au

deprescribing is to improve patient outcomes and minimize the adverse events associated with inappropriate medications and polypharmacy, through patient involvement, shared-decision making and goal-directed care.¹³ Given the rapidly expanding field of deprescribing research, this narrative review aims to provide an update on the current evidence on deprescribing to inform and guide clinicians in medication review for older people. Specifically, this review aims to 1) provide a summary of the literature on the safety and efficacy of deprescribing interventions; 2) synthesize challenges and their solutions, for deprescribing interventions in research and practice; and 3) summarize current evidence on two prominent emerging solutions in deprescribing research and practice: Computerized Clinical Decision Support Systems (CCDSS) and Quality Indicators (QIs).

Methods

We performed literature searches in Medline and Embase, focusing on systematic reviews published from January 2016 to March 2021 using the following search terms: “deprescribing”, “polypharmacy”, “inappropriate medications”, “inappropriate prescribing”, “challenges”, “barriers”, “obstacles”, “computerized clinical decision support”, “quality indicator”, “clinical indicator”, “performance measure”, “aged”, “older” and “geriatric”. The search strategy was limited to English language where abstracts were available for review. We excluded studies where patient cohorts were not representative of the older population. In addition, editorials, commentaries, conference abstracts, case reports, un-published studies (grey literature), narrative review articles and non-systematic reviews were excluded. The abstract and title of each publication were reviewed to determine their relevance to the research questions. Systematic reviews were included if they fulfilled the following criteria: a study population that included patients with a median age of 60 years and older, and examined the 1) safety and efficacy of deprescribing interventions on potentially inappropriate medications (PIMs) and patient global health outcomes, such as mortality, hospitalization, quality of life and geriatric syndromes (falls, functional and cognitive impairment), 2) challenges of and solutions for deprescribing research and implementation, 3) use of Computerized Clinical Decision Support Systems (CCDSS) and 4) Quality Indicators (QIs) in deprescribing research. After screening the titles and abstracts of records from literature searches, the full texts of articles deemed potentially eligible were

reviewed. References of included systematic reviews were also screened for their relevance to ensure that no potentially eligible publications were missed. The following data from relevant publications were extracted: first author, year of publication, study population (age, clinical setting: hospital, community or nursing home), deprescribing target (specific medication class or any medication), number and type of studies included in the systematic review (randomized controlled trial, non-randomized controlled trial), impact on medication use, impact on global health outcomes (mortality, hospitalization, quality of life and geriatric syndromes), and adverse drug withdrawal effects. Specific numerical data in the forms of odds ratio (OR), risk ratio (RR) or mean difference (MD) and 95% confidence interval were only reported if the study had performed meta-analyses of the outcomes of interest, and we opted for a narrative summary of our findings.

Safety and Efficacy Data on Deprescribing

Emerging evidence suggests that deprescribing is safe and feasible as a management strategy in patients at risk of medication-related problems. Deprescribing can reduce the number of potentially inappropriate medications. It rarely causes adverse drug withdrawal events and there is limited evidence of its effects on global and geriatric outcomes. Table 1 summarizes systematic reviews examining the safety and efficacy of deprescribing interventions.

To date, most clinical studies have failed to consistently demonstrate an effect of deprescribing interventions on clinical outcomes such as falls, hospitalization, cognitive and physical function decline.¹⁴ This is partly because most deprescribing studies have relatively small sample sizes and have residual confounding by factors that are not accounted for in the analysis. In addition, it may take many years to reverse some of the geriatric outcomes such as physical and cognitive decline, and the prolonged study duration and intensive multidisciplinary interventions may be cost-prohibitive for most deprescribing trials. In light of these challenges, the data on efficacy of deprescribing interventions is currently limited. The benefits and sustainability of these interventions on long-term quality of life, morbidity and geriatric outcomes remain unclear. Large randomized controlled multicenter trials are needed to define the true efficacy of deprescribing interventions in older population.

Table 1 Summary of Systematic Reviews Examining Safety and Efficacy of Deprescribing Interventions

Citation	Study Population	Deprescribing Target	Number and Type of Studies	Impact on Medication Use*	Impact on Global Health Outcomes (Mortality, Hospitalization, Geriatric Syndromes)*	Adverse Drug Withdrawal Effects*
Cardona et al 2021 ⁷⁴	Palliative care patients aged ≥ 65 years in hospital setting.	Most studies focused on general deprescribing.	5 RCTs, 1 retrospective non-RCT, 1 prospective non-RCT.	Hospital-initiated multi-component, multidisciplinary deprescribing interventions reduced PIMs.	No evidence of reduction in long-term mortality and hospitalization.	3 studies reported no difference between deprescribing intervention and control groups in adverse drug withdrawal effects after 2–3 months.
Bloomfield et al 2020 ⁵²	Community-dwelling older adults aged ≥ 65 years.	Most studies focused on general deprescribing.	12 RCTs and 26 cluster randomized controlled trials.	9/13 studies showed a reduction in PIMs.	Meta-analysis of RCTs showed comprehensive medication review resulted in a 26% relative risk reduction (OR 0.74; 95% CI: 0.58–0.95) or 1.4% absolute reduction in all-cause mortality, but no significant effect on hospitalization (RR 1.07; 95% CI: 0.92–1.26). Most RCTs showed no significant improvement in falls or health-related quality of life.	NR
Kua et al 2019 ⁷⁵	Nursing home residents aged ≥ 60 years.	Most studies focused on general deprescribing.	30 RCTs	Meta-analysis of RCTs showed deprescribing interventions significantly reduced the number of people with PIMs by 59% (OR 0.41; 95% CI: 0.19–0.89).	Meta-analysis of RCTs showed deprescribing was effective in reducing all-cause mortality (OR 0.90; 95% CI: 0.82–0.99) but not falls (OR 0.85; 95% CI: 0.73–1.00) and hospitalization (OR 0.72; 95% CI: 0.31–1.66). Subgroup analysis showed deprescribing interventions involving structured medication review by healthcare professionals were associated with a reduction in all-cause mortality (OR 0.74; 95% CI: 0.65–0.84), and falls (OR 0.76; 95% CI: 0.62–0.93).	NR

(Continued)

Table 1 (Continued).

Citation	Study Population	Deprescribing Target	Number and Type of Studies	Impact on Medication Use*	Impact on Global Health Outcomes (Mortality, Hospitalization, Geriatric Syndromes)*	Adverse Drug Withdrawal Effects*
Ulley et al 2019 ⁴³	Community-dwelling older adults aged ≥ 65 years.	Most studies focused on general deprescribing.	12 RCTs, 1 non-RCT, 9 cross-sectional studies.	4/22 deprescribing intervention studies showed an overall reduction in number of medications.	13/22 deprescribing intervention studies reported improved adherence. However, there is insufficient evidence to conclude that deprescribing interventions routinely improve medication adherence in community-dwelling older adults.	NR
Shrestha et al 2019 ⁴⁶	Older patients aged ≥ 65 years with life-limiting illness and limited life expectancy in hospital and RACF.	Most studies focused on general deprescribing.	3 RCTs and 6 non-RCTs.	Deprescribing interventions reduced PIMs in older patients with life-limiting illness and limited life expectancy.	Impact of deprescribing intervention on mortality, quality of life, falls, physical and cognitive function remain unclear. One non-RCT study reported a significant decrease in mortality at 12 months.	NR
Nakham et al 2019 ⁴⁷	Older adults aged ≥ 65 years in community, hospital, nursing home settings.	Anti-cholinergics	4 RCTs and 4 non-RCTs.	2 of 4 RCTs and all non-RCT studies reported a decrease in anticholinergic burden following deprescribing interventions.	Only 1 RCT reported clinical outcome (cognitive function), and showed no statistically significant difference between deprescribing interventions and control group.	NR
Thillainadesan et al 2018 ⁴⁸	Older adults with a median age of ≥ 65 years in hospital setting.	Most studies focused on general deprescribing.	9 RCTs	Deprescribing interventions in hospital setting were safe and effective at reducing PIM.	Impact on clinical outcomes such as mortality, quality of life, falls and hospitalization was uncertain.	NR
Wilsdon et al 2017 ⁴⁹	Older adults aged ≥ 65 years in community and hospital settings.	7 studies focused on PPI deprescribing, 14 studies focused on general deprescribing.	6 RCTs and 15 non-RCTs	6 of 21 studies demonstrated effective deprescribing interventions, 11 were inconclusive, 4 were ineffective. Types of effective deprescribing interventions included geriatrician-led deprescribing, academic detailing for GPs, population-wide education and promotion strategy.	No clear evidence that PPI deprescribing translates into better clinical outcomes in older people.	NR

Reeve et al 2017 ⁸⁰	Older adults aged ≥ 65 years in community, hospital and nursing home settings.	Benzodiazepines or Z-drugs	5 RCTs and 2 non-RCTs	RCTs and non-RCTs showed deprescribing of benzodiazepine and Z-drugs was feasible in older people. However, the benefits and sustainability of these interventions are unclear.	NR	Most RCTs and non-RCTs studies showed no difference in prevalence of withdrawal symptoms or sleep quality.
Page et al 2016 ²²	Older adults aged ≥ 65 years in community, hospital and nursing home settings.	General deprescribing and single medications.	56 RCTs and 60 non-RCTs	Meta-analysis of RCTs showed deprescribing reduced both total number of medications (MD -0.99; 95% CI: -1.83 to -0.14) and PIMs (MD-0.49; 95% CI: -0.70 to -0.28).	Meta-analysis of non-RCTs showed deprescribing polypharmacy (≥ 3 medications) were associated with a significant reduction in mortality (OR 0.32; 95% CI: 0.17–0.60). However, meta-analysis of RCTs showed deprescribing polypharmacy (≥ 3 medications) had no statistically significant mortality benefit (OR 0.82; 95% CI: 0.61–1.11) and no significant change in risk of falls (OR 0.65; 95% CI: 0.40–1.05) or quality of life measures. Deprescribing of single medication class was not associated with a significant difference in mortality and quality of life measures in both RCTs and non-RCTs.	RCTs showed deprescribing interventions were not associated with a significant increase in adverse drug withdrawal events.
Johansson et al 2016 ⁸¹	Older adults aged ≥ 65 years in community, hospital and nursing home settings.	General deprescribing	21 RCTs and 4 non-RCTs	3 RCTs showed deprescribing interventions reduced total number of medications compared to controls.	Meta-analysis of pooled data from RCTs and non-RCTs showed deprescribing strategies had no effect on all-cause mortality (OR 1.02; 95% CI: 0.84–1.23). There was no convincing evidence from RCTs and non-RCTs that deprescribing was effective in improving clinical outcomes (hospitalization and mortality).	NR

Notes: * Specific numerical data in the forms of odds ratio (OR), risk ratio (RR) or mean difference (MD) and 95% confidence interval are only reported if the study has performed meta-analyses of the outcomes of interest.
Abbreviations: GPs, general practitioners; CI, confidence intervals; NR, not reported; OR, odds ratio; PIMs, potentially inappropriate medications; PPI, proton pump inhibitor; RACE, residential aged care facility; RCTs, randomized controlled trials.

Recently, preclinical studies have sought to fill this knowledge gap by determining the impact of polypharmacy and deprescribing on geriatric outcomes.^{15–17} The first polypharmacy mouse model found that administration of therapeutic doses of five drugs (metoprolol, simvastatin, omeprazole, paracetamol and citalopram) for 4 weeks impaired physical function in old but not young male mice.¹⁶ A subsequent study found that 4–6 weeks of polypharmacy with a higher anticholinergic and sedative load (metoprolol, simvastatin, oxycodone, oxybutynin and citalopram) impaired physical function in young and old male and female mice, with greater effects in old age, and greater reduction in grip strength in males.¹⁵ Polypharmacy for 8 weeks (metoprolol, simvastatin, paracetamol, aspirin and citalopram) in young male mice reduced exploration and spatial working memory.¹⁸ A longitudinal study of treatment from middle to old age, found that polypharmacy regimens with increasing Drug Burden Index¹⁹ (a measure of cumulative exposure to drugs with anticholinergic and sedative effects) impaired physical function in old male mice, which was attenuated by deprescribing.¹⁷ This evidence that polypharmacy with high Drug Burden Index causes impaired function in old age, which is reversible with deprescribing, helps to fill the evidence gap on causation and provides a platform for future studies investigating mechanisms, such as complex drug interactions and the effects on aging biology.

Challenges of Deprescribing Studies and Proposed Solutions

Existing studies exploring the outcomes of deprescribing can be broadly categorized as experimental or observational studies.^{20–22} Whilst deprescribing generally appears to be a safe process, there are potential harms, such as return of the condition that was being treated or presence of withdrawal symptoms. Therefore, it is important that deprescribing is closely supervised and informed by the latest evidence.^{20,22,23} Interpreting and applying this evidence, and designing future studies to fill the gaps, requires an understanding of the challenges of existing research and the potential solutions for future studies. These challenges can be divided into challenges relating to patients, relating to healthcare professionals and arising from the current healthcare system structure. Key challenges and potential solutions are outlined below and summarized in Table 2.

Deprescribing Research: Issues for Patients/Consumers

Deprescribing studies have explored outcomes such as mortality and hospitalization, based on clinician preferences.^{24,25} Previous research has however shown potential discordance between clinician and patient prioritization of different outcomes of therapy.^{24,26,27} As a result, it is important for future deprescribing studies to assess deprescribing outcomes based on both patient and clinician preferences.^{21,24} Based on existing research, it is also unclear how to best educate patients on the effects of deprescribing, which is essential for shared decision making.²² Future studies should explore the acceptability and effectiveness of different educational programs on deprescribing and how to best tailor these to different patient populations with different levels of health literacy, comorbidities and concurrent medications.²²

Deprescribing Research: Issues for Healthcare Professionals

One of the challenges of existing deprescribing studies for healthcare professionals is the lack of sufficiently powered randomized controlled trials (RCTs) assessing the long-term benefits, safety and sustainability of deprescribing interventions.^{22–24,28} Most studies assess outcomes such as the feasibility and tolerability of deprescribing or reduction in the number of medications, instead of long-term clinical outcomes.^{22–25} Studies do not always explicitly specify the deprescribing schedule used, monitoring or management of patients, making it unclear how to deprescribe those drugs in practice.²² There is a need for information on how to manage adverse drug withdrawal effects, reversal of drug–drug interactions²¹ and provision of alternative non-pharmacological or pharmacological therapy after deprescribing.²⁵ Well powered RCTs with detailed reporting of the intervention and long-term follow-up of clinical outcomes are needed.^{22–25,28}

Studies have explored deprescribing single drug classes, such as benzodiazepines, antipsychotics, antihypertensives and opioids, but patients in practice take a range of other medications.²² Existing studies do not always explicitly specify concurrent medications and chronic conditions present, nor do they consistently account for these potential confounders, making it difficult to apply available evidence to multimorbid patients with polypharmacy seen in clinical practice.^{26,29,30} Additionally, patient populations such as palliative care

Table 2 Summary of Challenges of Existing Deprescribing Research and Potential Solutions for Future Studies

	Challenges	Potential Solutions
Patients	Assessing deprescribing outcomes based on clinician preferences. ^{24,25}	Involving patients in all phases of research including defining relevant outcomes, using patient reported outcome measures, and using individualized goal attainment scale outcomes. ^{21,24}
	Unclear how to best educate patients about deprescribing. ²²	Exploring the acceptability and effectiveness of different educational programs on deprescribing and how to best tailor these to different patient populations such as patients with different levels of health literacy. ²²
Healthcare Professionals	Data on clinical outcomes	
	Lack of sufficiently powered RCTs assessing long-term deprescribing benefits, safety and sustainability. ^{22–24,28} Existing studies assessing outcomes such as the feasibility of deprescribing or reduction in the medicines count instead of clinical outcomes. ^{22–25}	Large RCTs with long-term follow-up assessing prescribing and clinical outcomes and outlining the deprescribing protocols used. ^{22–25,28}
	Detail reported in methods of exiting studies	
	Deprescribing schedule not explicitly reported. ²² Management of patients during deprescribing such as withdrawal symptoms not outlined. ²⁵	Practical guidance regarding appropriate management during deprescribing, including providing safer alternatives such as nonpharmacological therapy. ²⁵
	Generalizability to Clinical Practice	
	Range of drug classes seen in clinical practice not explored for deprescribing. ²² Not specifying comorbidities and concurrent medications and not accounting for these potential confounders. ^{26,29,30} Excluding patient populations such as palliative care. ^{20,30}	Deprescribing different drug classes seen in practice, in different patient populations and explicitly specifying characteristics such as frailty, comorbidities and concurrent medications, adjusting for any potential confounders. ^{20,22,29,30,82}
Health Organizations	Large, robust studies assessing cost-effectiveness of deprescribing interventions, including models of care with time specifically dedicated to deprescribing are limited. ^{25,28} Healthcare organizations undertake deprescribing research as separate groups nationally and internationally. ²⁵	More studies exploring cost-effectiveness of different deprescribing interventions, including models of care with dedicated time for deprescribing. ²⁵ Collaboration between different healthcare organizations to increase capacity to undertake large deprescribing trials.
	Electronic healthcare systems do not always include deprescribing prompts embedded into them. ^{31,32}	Exploring deprescribing interventions embedded into electronic healthcare management systems. ^{31,32}
	Studies exploring specific roles of different healthcare disciplines during the deprescribing process are limited. ²⁸	More research to understand specific roles of different health disciplines which may help develop streamlined, efficient processes around deprescribing. ²⁸

are often excluded from studies, whereas these patients have high uncertainty regarding the benefits of continuing medications.^{20,30} Therefore, there is a need for future research to explore deprescribing different drug classes seen in practice, in different patient populations and explicitly specify characteristics of the study population such as medical conditions and concurrent medications, adjusting for any potential confounders.^{20,22,25,29,30}

Deprescribing Research: Issues for Current Healthcare Systems

Deprescribing interventions can be time-consuming and resource-intensive in addition to the ongoing cost of using different medications.²⁸ Deprescribing harmful medications may however result in potential cost savings such as less visits to the general practitioner and reduced number of hospitalizations.²⁸ Large, robust studies exploring cost-

effectiveness of different deprescribing interventions are limited.²⁸ Therefore, more research is needed exploring the cost-effectiveness of different deprescribing interventions.²⁵ The current healthcare structure does not include time specifically dedicated during medical appointments to explore deprescribing.²⁵ Future studies may explore models of care with time during each appointment specifically dedicated to discuss deprescribing options.²⁵

The shift towards using electronic healthcare systems globally, presents the opportunity for future studies to explore deprescribing interventions embedded into electronic systems.^{31,32} Whilst medication management involves different healthcare disciplines such as medical practitioners, pharmacists and nurses, more research is necessary to understand specific roles of different disciplines which may help develop streamlined, efficient, multidisciplinary processes around deprescribing.²⁸

Different healthcare organizations undertake deprescribing research as separate groups nationally and internationally, resulting in unnecessary research duplication and lack of sharing of findings.²⁵ Future studies should consider collaboration between different healthcare organizations. Deprescribing networks, which have emerged internationally since the first was established in Australia in 2014, should ideally increase capacity to undertake large trials and help address the different challenges of existing studies.^{25,33}

Implementation Challenges: Patients, Healthcare Professionals and Healthcare Systems

In addition to the knowledge gaps in deprescribing research, implementation of deprescribing in clinical practice faces many challenges at patient, healthcare professional and healthcare system levels (Figure 1). At the

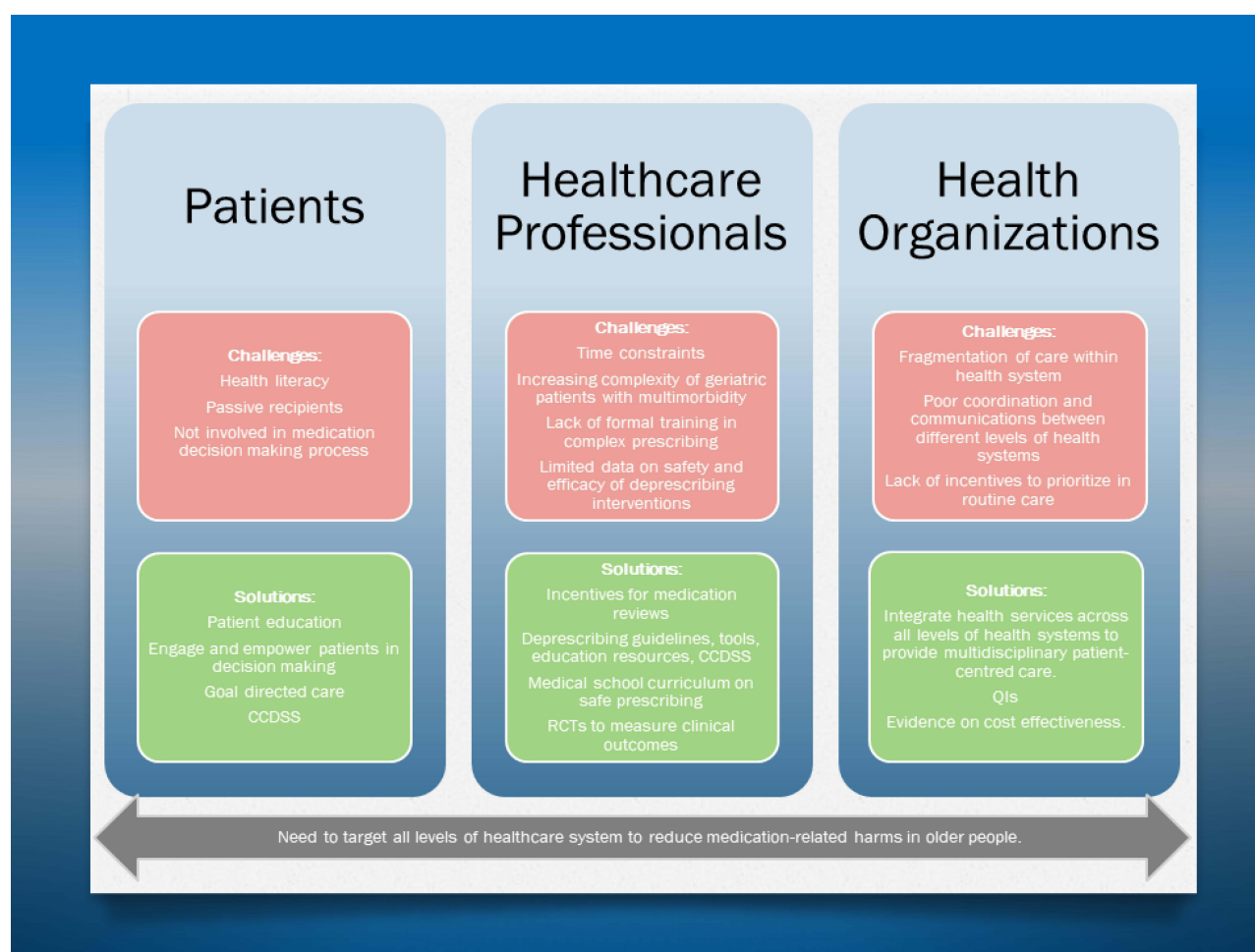


Figure 1 Deprescribing challenges and their solutions across different levels of healthcare system, informed by multiple sources.^{36,38}

Abbreviations: CCDSS, Computerized Clinical Decision Support Systems; QIs, Quality Indicators

patient level, people may have limited health literacy and false beliefs that medications are always superior to non-pharmacological approaches in treating diseases. Patients and/or their carers may be resistant to stop medications that they have been taking for a long time due to unrealistic expectations in the efficacy of the medications.³⁴ Other patient level challenges to deprescribing include lack of knowledge of the potential side effects of the medications and socioeconomic factors, where access to regular health services may be limited.^{34,35} At the healthcare professional level, the increasing complexity of older patients as a result of multimorbidity and polypharmacy can pose challenges for medical practitioners to distinguish between medication side effects and new complaints. Often, inadequate time is spent on reviewing patient's medication list.³⁶ On the other hand, clinical inertia or reluctance to talk to patients about therapy appropriateness,³⁷ reluctance to interfere with management initiated by other healthcare professionals, and lack of formal training in prescribing for older people have been identified as a potential barriers to deprescribing. At the healthcare system level, there can be issues with fragmentation of care,³⁸ difficulty accessing patient's health

information and poor coordination and communication between specialists and general practitioners when medications are initiated, changed or ceased.³⁹

Implementation Solutions: Patient, Healthcare Professional and Healthcare System

Given the growing burden of medication-related problems in older people, and the complexity of deprescribing process, the success of deprescribing interventions depends on simultaneous strategies and policies across all levels (Figure 1, Table 3), involving patients and the public, healthcare professionals, health organizations, regulatory and policymakers. Patient education and improvement in health literacy are potential strategies to help patient develop realistic expectations about their health treatment. Physicians and other healthcare professionals can provide suitable evidence-based advice about benefits and harms of each medication the patient is taking. These strategies are likely to be more effective if delivered using a patient-centered approach.⁴⁰ It is important that treating physicians understand patient's preferences and goals of care, and how they can contribute to improving clinical outcomes through goal-directed medication reviews.

Table 3 Summary of Challenges and Solutions of Implementing Deprescribing in the Healthcare System, Data from Multiple Sources^{36,38}

	Challenges	Solutions
Patients	Poor health literacy, reluctant to discontinue medications due to false belief. Patients are often passive recipients of medications, not involved in the decision making process on the use of medications.	Provide educational materials and tools (eg patient-held medication record, medication passport) to enhance patient awareness about inappropriate polypharmacy and understand the benefits and harms of each medication. Engage and empower patients to play an active role in their health care, so they can safely manage their own medications.
Healthcare Professionals	Increasing number of complex geriatric patients with multimorbidity. Lack of formal training in prescribing for older patients with complex polypharmacy. Time constraints to counsel patients on medication-related harms.	Provide health professionals with tools, guidelines and educational resources on how to manage polypharmacy in older people. Develop educational curricula on safe medication management and deprescribing for both undergraduate and postgraduate health professionals. Provide additional incentives to health professionals that conduct a medication regimen review as part of routine health check-up.
Health Organizations	Healthcare systems and practices of medication are often complex and dysfunctional. Fragmentation of care within healthcare system. Poor coordination and communication between different health professionals (eg specialists and general practitioners) when new medications are initiated.	Integrate health services across all levels of healthcare systems to provide multidisciplinary patient-centered care. Establish a national deprescribing working group of leading experts, regulators and policymakers to develop strategies, guidelines and action plans on polypharmacy and deprescribing in older people.

Continued involvement of patients throughout the deprescribing process has been shown to be instrumental in improving the success of deprescribing interventions.⁴¹ There are opportunities to include deprescribing in the evidence-based recommendations in the **4Ms** Framework for an Aged-Friendly Health System that aims to align what **matters** to the older patients and their family caregivers with their **medications**, **mentation** and **mobility**.⁴² Potential advantage in adherence maybe another incentive for implementation.⁴³ At healthcare professional level, deprescribing requires a close interdisciplinary collaboration between the general practitioners, physicians, pharmacists, nurses and allied health professionals. This multidisciplinary care approach is likely to provide the most optimal management of patient's medication regimen based on consensus from all healthcare professionals involved.³⁶ In addition, hospital-based initiatives aimed to improve awareness and skills of clinicians and pharmacists through provision of deprescribing protocols, and use of explicit criteria to guide medication review have proven to be effective in achieving deprescribing.^{44,45} Introducing prescribing education in medical schools and continuing medical education programs for health professionals can improve the skills and confidence of healthcare professionals managing medication-related problems in older people.^{36,46,47} At the healthcare system level, specialist medical colleges and other professional and consumer groups have important roles in advocacy and can influence policies related to health literacy and coordination between primary, secondary and tertiary health care providers. Therefore, a concerted effort from all levels of healthcare systems will be needed to make a significant impact on reducing inappropriate medication use.

Implementation Solutions: Computerized Clinical Decision Support Systems

Computerized Clinical Decision Support Systems (CCDSS) are defined as multiple integrated systems that can apply algorithms to individual patient data to generate suggested actions intended to improve or support clinical decision-making for healthcare practitioners.⁴⁸ CCDSS are considered to be one of the many solutions to optimising prescribing of medications and medication safety in older adults.⁴⁹ The types of CCDSS can vary, from simple electronic medical record alerts directed towards healthcare practitioners at the point of prescribing or medication review, to integrated complex features such as recommending a medication for deprescribing or substituting

for a therapeutic equivalent. The success of CCDSS interventions in deprescribing relies on the design, user interface and integration into practice. A systematic review of the features of effective CCDSS interventions identified that successful interventions included systems that required practitioners to provide reasons when overriding advice, and systems that were designed to provide advice to the patient and practitioner simultaneously, allowing for a person-centered focus of care.⁵⁰ However, many interventional studies poorly describe the CCDSS design and implementation features, which may hinder future development of successful CCDSS interventions focused on deprescribing inappropriate medications.

Many systematic reviews have been conducted to specifically assess whether CCDSS are a successful solution to deprescribing medications in older adults (Table 4). Monteiro et al aimed to evaluate the evidence of CCDSS to address polypharmacy and prevent its occurrence.⁵¹ In this review, almost all studies reported that the CCDSS interventions reduced the number of PIMs that were deprescribed or improved medication appropriateness, however, statistical significance was not always achieved.

In a systematic review that aimed to evaluate the effectiveness, comparative effectiveness, and harms of deprescribing interventions among community-dwelling older adults, four trials were identified that evaluated the effect of CCDSS.⁵² These trials were conducted in the USA and Canada, and only two out of the four trials reported a significant reduction of potentially inappropriate medications in the intervention group compared with the control group.

A systematic review conducted in 2018 examined the evidence for efficacy of CCDSS designed to reduce potentially inappropriate prescribing in hospitalized older adults.⁵³ This review found that seven out of the eight studies included demonstrated a statistically significant reduction in the proportion of patients prescribed an inappropriate medication; however, interpretation of the results was discussed given the limitations of generalizability of the studies and single-center studies.

Iankowitz et al examined the effect of CCDSS on the frequency of prescribing potentially inappropriate medications at discharge and related unplanned hospitalizations.⁵⁴ The authors concluded that although CCDSS had the potential for decreasing the number of potentially inappropriate medications in older adults, conclusions about unplanned hospitalizations could not be made, given the lack of evidence.

Overall, although many systematic reviews have demonstrated that CCDSS interventions can affect deprescribing inappropriate medications in older adults, there are no reviews that provide evidence on CCDSS interventions on clinical outcomes, such as falls, frailty, quality of life or mortality.

Implementation Solutions: Quality Indicators

Another example of a key implementation tool is the use of Quality Indicators (QIs). QIs are a recognized mechanism for improving quality use of medicines if they have

been robustly developed and their measurement properties scientifically tested.⁵⁵ QIs are measurable elements of practice performance for which there is evidence or consensus that it can be used to assess the quality, and hence change in the quality, of care provided.⁵⁶ QIs are usually described with a denominator and a numerator. The denominator is the total number of cases in the intended population, and the numerator is the number of cases in the denominator that fulfil a predetermined criterion, and the calculated QI score indicates the quality of care. QIs can be used for monitoring process performance, assessing quality improvement activities, providing feedback to

Table 4 Summary of Systematic Reviews to Evaluate Computerized Clinical Decision Support Systems (CCDSS) in Deprescribing in Older Adults

Citation	Study Population	Deprescribing Target	Number and Type of Studies	Impact on Medication Use*	Impact on Global Health Outcomes (Mortality, Hospitalization, Geriatric Syndromes)*	Adverse Drug Withdrawal Effects*
Bloomfield et al 2020 ⁵²	Community-dwelling older adults aged ≥ 65 years.	Most studies focused on general deprescribing.	4 RCTs	2 studies reported reduction in PIMs in the intervention group, and 2 reported no effect.	NR	NR
Monteiro et al 2019 ⁵¹	Older adults aged ≥ 65 years in community and hospital settings.	General deprescribing and single medications.	10 RCTs and 6 non-RCTs	CCDSS may reduce PIMs.	NR	NR
Dalton et al 2018 ⁵³	Older adults aged ≥ 65 years in hospital setting.	General deprescribing and single medications.	2 RCTs and 6 non-RCTs	Intervention patients were less likely to be prescribed a PIM (OR 0.6; 95% CI: 0.38–0.93)	Most studies did not assess global health outcomes such as falls, hospitalization or mortality. One non-RCT study showed CCDSS resulted in a statistically significant reduction in inpatient falls.	NR
Iankowitz et al 2012 ⁵⁴	Older adults aged ≥ 65 years in community and hospital settings.	General deprescribing and single medications.	4 RCTs and 1 non-RCTs	CCDSS had the potential for decreasing the number of PIMs, conclusions about unplanned hospitalizations could not be made. The computer systems were significantly effective in decreasing frequency of ordering PIMs.	NR	NR

Notes: * Specific numerical data in the forms of odds ratio (OR), risk ratio (RR) or mean difference (MD) and 95% confidence interval are only reported if the study has performed meta-analyses of the outcomes of interest.

Abbreviations: RCT, randomized controlled trial; c-RCT, cluster randomized controlled trial; CCDSS, computerized clinical decision support systems; NR, not reported; PIMs, potentially inappropriate medications; OR, odds ratio; CI, confidence intervals.

healthcare providers, assisting patients in choosing their providers, or detecting unsafe situations. Therefore, the purpose of QIs could vary depending on the stakeholders (eg patients, practitioners, payers, healthcare inspectorate, researchers, or governments).

More than 2400 content validated medication-related QIs exist covering most diseases and conditions.⁵⁷ These QIs for measuring adherence to medication guideline could be applied to minimize potentially inappropriate medications (eg % of persons age 65+ years prescribed antidepressants using an anticholinergic antidepressant drug).⁵⁸ In addition, QIs for polypharmacy management were developed and implemented in some countries. For example, Swedish Indicators for Quality of Drug Therapy in Older Persons includes three polypharmacy management indicators (eg % of persons age 75+ years prescribed ten or more drugs).⁵⁹ NHS Scotland published one polypharmacy indicator and six high risk prescribing indicators for the older person (eg % of persons age 75+ years prescribed an antipsychotic drug).⁶⁰ In Australia, a set of QIs for reducing inappropriate polypharmacy (ie, polypharmacy QUM indicators) was developed by a team led by the authors (Table 5).⁶¹ The polypharmacy QUM indicators are designed to evaluate processes involved in identification of medication-related harm in older hospitalized patients and the management of inappropriate polypharmacy. Specifically, of the seven polypharmacy QUM indicators, three QIs are related to the identification of older patients at high risk of medication-related harm, one QI to the implementation of hospital-based medication review, and three QIs to optimising discharge communications and continuation of medication care at transitions of care. As causes of inappropriate polypharmacy could vary, a combination approach using the seven QIs is important.

To stimulate continuous quality improvement activities, QI scores are tied to financial incentives,⁶² public reporting,⁶³ quality management accreditation,⁶⁴ or continued professional development.⁶⁵ Note that the use of QIs also has the potential for unintended negative consequences. These consequences are likely to become prominent when QIs are linked with financial incentives.⁶⁶ In such a case, data manipulation could occur to reach predetermined threshold values. In addition, healthcare institutions may turn away specific types of patients who may decrease QI scores. Furthermore, under pay-for-performance models, institutions may focus only on the quality of care linked with financial incentives and pay less attention to the quality of care

Table 5 New South Wales Therapeutic Advisory Group (NSW TAG) Polypharmacy Quality Use of Medicines (QUM) Indicators⁸³

Identification of Older Patients at High Risk of Medication-Related Harm
1. Percentage of older patients that are appropriately assessed for risk of harm from inappropriate polypharmacy 2. Percentage of older patients that are appropriately assessed for risk of medication-related falls 3. Percentage of older patients that are appropriately assessed for risk of medication-related impairment of cognitive and/or physical function
Intervention: a hospital-based medication review (HBMR)
4. Percentage of older patients at high risk of medication-related harms that receive a hospital-based medication review and, if applicable, a deprescribing plan
Optimising discharge communications and continuation of medication care at transitions of care
5. Percentage of older patients at high risk of medication-related harms with a recommendation for a post-discharge medication review, when hospital-based medication review is not performed 6. Percentage of older patients whose discharge summaries contain a current, accurate and comprehensive list of medicines, including explanations for any medication therapy changes and, if applicable, details of a deprescribing plan 7. Percentage of older patients who receive a current, accurate and comprehensive medication list, including explanations for any medication changes and, if applicable, details of a deprescribing plan, at the time of hospital discharge

Notes: Reproduced with permission from New South Wales Therapeutic Advisory Group (NSW TAG) Polypharmacy Quality Use of Medicines (QUM) Indicators. Available from: <https://www.nswtag.org.au/qum-indicators/> Accessed May 6, 2021. © NSW Therapeutic Advisory Group Inc 2020.⁸³

not being measured. It is not surprising that some healthcare providers do not welcome the use of QIs for fear of being judged or blamed for their poor performance.⁶⁷ Hence, the users of QIs should be aware of which aspects of care are not being measured, and of these unintended negative consequences.

When using QIs, standardized data collection systems are expected to be established so that QIs can be measured automatically using routine clinical practice data sets. These systems will also be of importance for reducing the burden of data collection, assuring data accuracy, linking to other routine data, and enabling real-time decision support. Given the dynamic nature of healthcare, ongoing quality improvement activities, using methodology such as the Plan-Do-Study-Act cycles, are expected to facilitate deprescribing inappropriate polypharmacy.

There are several limitations in our review merit comments. First, this is not a systematic review of systematic reviews, as we have not followed the protocol of a systematic review.^{68,69} Second, we acknowledge the limitations of traditional narrative reviews, such as the risk of bias (publication bias and selection bias), variation in study quality and potential overlapping reviews in the included systematic reviews have not been rigorously accounted for.^{70–73}

Conclusions

Inappropriate medication use contributes to significant morbidity and mortality in older people. Deprescribing is an established management strategy to minimize polypharmacy and potentially inappropriate medications. Knowledge of the efficacy of deprescribing polypharmacy on clinical outcomes in older patients is limited. This has recently been supplemented by preclinical data, demonstrating that deprescribing in old age attenuates frailty and functional impairment caused by chronic polypharmacy. The benefits and sustainability of deprescribing interventions on long-term quality of life, morbidity and geriatric outcomes in older people remain unclear. Various patient level, healthcare professional level and healthcare system level challenges influence the success of deprescribing studies and implementation. Researchers, healthcare professionals and policymakers have a great responsibility to promote quality use of medication in older people by overcoming these challenges. Deprescribing networks emerging internationally can further facilitate novel research and successful implementation of deprescribing in clinical practice. Future large multicenter prospective studies of deprescribing are needed to establish the efficacy of deprescribing interventions in older populations, and to clarify which subgroups would benefit most from this approach. This will help deprescribing find its place in routine prescribing, under the umbrella of personalized medicine.

Disclosure

Prof Sarah N Hilmer and Dr Lisa Kouladjian O'Donnell are both members of the executive committee of the Australian Deprescribing Network (voluntary roles). The authors report no other conflict of interest in this work.

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