The Role of Patient Preferences in Deprescribing

Holly M. Holmes, MD, MS, and Adam Todd, PhD, MPharm

1 Division of Geriatric and Palliative Medicine, University of Texas Health Science Center at Houston McGovern Medical School, 6431 Fannin, MSB 5.116, Houston, Texas 77030.

2 Division of Pharmacy, School of Medicine, Pharmacy and Health, Durham University, UK.

Contact Information:

Holly M. Holmes, UTHealth McGovern Medical School, 6431 Fannin St, MSB 5.116, Houston, Texas 77030, Holly.M.Holmes@uth.tmc.edu

Adam Todd,

Corresponding Author: Holly M. Holmes

Disclosure Statement: The authors have nothing to disclose.

Key Words: Polypharmacy, Inappropriate Medication, Deprescribing

Key Points

- With an increasing population with multimorbidity, polypharmacy and inappropriate medication use, are on the rise, with a greater focus is being placed on deprescribing as an approach to rationalize medication therapy.
- Deprescribing, generally shown to be feasible and safe, is a process of stopping an inappropriate medication under the supervision of a healthcare professional.

- Patient preferences should play a central role in deprescribing approaches, particularly in patients for whom deprescribing is a preference-sensitive decision due to uncertainties about the benefits and harms of medications.

Synopsis: Polypharmacy and the use of inappropriate medications has become an increasing problem globally. Deprescribing, or the systematic process of stopping medications that are harmful or no longer necessary, has gained increasing attention as a means to rationalize medication use. Deprescribing interventions have been shown to be generally feasible and safe; in the few studies in which patient preferences are assessed, such interventions also appear to be acceptable to patients. Qualitative studies of patient attitudes toward deprescribing suggest that patients are interested in reducing medications, and may have high needs for education and communication with their providers around deprescribing. This narrative review focuses on patient preferences for deprescribing and highlights practical recommendations to overcome barriers to deprescribing.

Introduction

The prevalence of polypharmacy continues to rise in the Unites States and elsewhere around the world. With the global aging of the population, we are seeing a shift to a population with comorbidity and subsequent increased medication use. More than half of people over 65 in the United Stated have 3 or more chronic conditions.[1] In the United States the population >65 years in 2010 was 13%; by 2030 the older population is projected to reach 20%, while in other developed countries, older people are expected to reach >30% of the population by 2030.[2]

Increasing medication use is not only on the rise because of higher proportions of older people in the population, but also because more and more older people are exposed to polypharmacy. Based on recent US survey data, >90% of people 65 years and older took at least 1 prescription medication in the prior 30 days, and 39% of older people take 5 or more regular medications on a chronic basis.[3] In the UK, recent registry data shows that 24% of people 80 years and older take 10 or more medications regularly.[4]

While the use of multiple medicines is necessary to treat multiple conditions, taking increasing numbers of medications conveys increasing risks of harm to older patients. Studies of polypharmacy have used different definitions and different methodologies to define the exposure of harmful polypharmacy, and have evaluated different outcomes as measures of harm. There is support to use the definition for polypharmacy as using 5 or more medications; polypharmacy in this regard has been shown to be harmful due to the increased risk of adverse drug events, adverse outcomes, and drug interactions.[5,6] Despite inconsistencies and heterogeneities in study design, polypharmacy has been shown, primarily in observational studies, to be associated with an increased risk of adverse drug events, hospitalizations, and falls.[7] In addition, the use of multiple medications is associated with an increased likelihood of important therapeutic

omissions through non-adherence?, such as beneficial treatments for heart failure or hypertension.[8] It is unknown whether a reduction in polypharmacy results in improved patient outcomes, but there has been increasing interest in the reduction in medication number as a means to mitigate the harmful effects of polypharmacy.[7]

Given the increasing likelihood that healthcare providers will be faced with the complexity of care for adults with multimorbidity and the increasing concerns about the harms of polypharmacy, a greater focus has been placed on deprescribing as an approach to rationalize medication therapy.[9] The purpose of this review is to briefly summarize the definition of deprescribing, review the process of deprescribing, to discuss the role of patient-centered care in guiding deprescribing interventions, and to discuss barriers and possible solutions to deprescribing.

What is deprescribing?

While many terms have been used to describe the process of stopping medications, including discontinuation, withdrawal, cessation, stopping, and even debridement, the universal use of the term "deprescribing" has been suggested moving forward to provide consistency.[9,10]

While there are some variations in the definition of deprescribing, common features are the focus on stopping medications based on lack of benefit or increased risk. Definitions include the cessation of a medication no longer necessary,[11] a process of reducing or stopping medications that are harmful or unnecessary,[12] a planned process of stopping medications that are no longer beneficial,[13] and a process of "tapering, stopping, discontinuing, or withdrawing drugs".[10] A recent systematic review and network analysis synthesized the various definitions and proposed the following as a definition of deprescribing:

> *Deprescribing is the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes*.[10]

The focus of this definition is on deprescribing being a process; as has been previously recommended, the medication use process must integrate prescribing and deprescribing.[14] Medications that are candidates for reduction, by this definition, are "inappropriate", which could have different meanings depending on the clinical situation, and would be identified based on being high risk, low benefit, or both.

Deprescribing has been shown to be feasible and generally safe, although the possibility of exacerbating the underlying condition being treated should not be discounted – particularly when the condition involves the cardiovascular or central nervous system.[15,16] Indeed, a recent systematic review of deprescribing interventions found that it was generally feasible, resulted in reduced medication number and minimized inappropriate medication use.

The process of deprescribing

Basic definitions of deprescribing highlight the fact that simply stopping a medication by not renewing the prescription does not capture the process required to deprescribe. Deprescribing requires a systematic identification of all current medications and prioritization of medications to be stopped, a determination of the safest means to stop medications, and a monitoring and follow up plan.[10,18] The five step process, proposed by Scott, et al., is shown in Table 1.

Table 1. The process of deprescribing[19]

Key Step	Detailed Processes
1. Ascertain all drugs the patient is currently taking and the reasons for each one	- Ask patients (and carers) to bring all drugs (prescribed, complementary and alternative medicine, and over the counter) and drug delivery aids to consultation or home visit - Ask patients (in a nonjudgmental way) about any regularly prescribed drugs not being taken and if so why not (eg, too expensive, adverse effects)
2. Consider overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention	- Ascertain and assess risk according to • Drug factors: number of drugs (single most important predictor), use of "high-risk" drugs (see text), past or current toxicity • Patient factors: age >80 y, cognitive impairment, multiple comorbidities, substance abuse, multiple prescribers, past or current nonadherence
3. Assess each drug for its eligibility to be discontinued	- Identify drugs being prescribed • For a diagnosis that is in doubt, ie, not confirmed; highly atypical presentations; • For a confirmed diagnosis but in which evidence of efficacy is nonexistent • That confer no additional benefit after a certain period of continuous use or after a certain age

	- Identify drugs prescribed to counteract adverse effects of other drugs - Reconsider the indications for the initial culprit drug or its substitution by an alternative drug with superior tolerability Identify “drugs to avoid” in older patients - Identify drugs contraindicated in particular patients - Identify drugs causing well-known adverse effects - Ask patient, “Since you started this medicine, has it made such a difference to how you feel that you would prefer to stay on it?” and consider discontinuing the drug if the response is no or probably not - Ask, “Are you still experiencing any troublesome symptoms (cough, headache, dyspepsia, etc)? Do you feel the medicine is still required?” - Consider discontinuing use of the drug if the target condition is self-limiting, mild, intermittent, or amenable to nondrug interventions - Estimate patient’s life expectancy using risk prediction tools or asking “surprise” question - Determine the patient’s expectations and preferences—is present-day quality of life more important than prolonging life or preventing future morbid events? - Identify drugs unlikely to confer benefit (and that may cause harm) over the patient’s remaining

	lifespan - Ask the patient, “Apart from side effects, are there any other concerns you have with your medicines?” - Identify drugs that are particularly burdensome (eg, difficulty swallowing large tablets, out-of-pocket expense, monitoring requirements)
4. Prioritize drugs for discontinuation	- Deciding the order of discontinuation of drugs may depend on integrating 3 pragmatic criteria: (1) those with the greatest harm and least benefit; (2) those easiest to discontinue, ie, lowest likelihood of withdrawal reactions or disease rebound; (3) those that the patient is most willing to discontinue first (to gain buy-in to deprescribing other drugs) - Suggested approach is to rank drugs from high harm/low benefit to low harm/high benefit and discontinue the former in sequential order
5. Implement and monitor drug discontinuation regimen	- Explain and agree with patient on management plan - Cease 1 drug at a time so that harms (withdrawal reactions or return of disease) and benefits (resolution of adverse drug effects) can be attributed to specific drugs and rectified (if necessary) - Wean patients off drugs more likely to cause adverse withdrawal effects, instruct patient (or

	carer) on what to look for and report in the event of such effects occurring, and what actions they can self-initiate if these were to occur - Communicate plan and contingencies to all health professionals and other relevant parties (carers, family) involved in patient's care - Fully document the reasons for, and outcomes of, deprescribing

From Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, Gnjidic D, Del Mar CB, Roughead EE, Page A, Jansen J, Martin JH. Reducing inappropriate polypharmacy: the process of deprescribing. JAMA Intern Med. 2015;175(5):827-34.

While the process proposed by Scott, et al, suggests multiple possible questions to identify drugs that are candidates for deprescribing (step 3 in the process), there are existing tools that could be employed in this step. For example, to identify drugs that are contraindicated in certain groups, that have well-known adverse effects, or are either unlikely to cause benefit or the benefit is outweighed by harm, explicit lists such as the Beers criteria or the Screening Tool of Older Persons' Prescriptions could be used to determine drugs eligible for deprescribing.[20,21] Scott also proposes an algorithm to determine the order and the mode by which medications could be discontinued.

Patient preferences for deprescribing

The process of deprescribing requires active assessment of patients' attitudes and preferences along the way. For example, patients should be asked whether they think a medication is helpful, if it causing side effects or burden and, ultimately, if they prefer to continue it. Medications that are eligible to be deprescribed and that a patient is willing to stop should be prioritized for deprescribing first, in order to gain patient buy-in and trust during the process.[19]

In adults with multimorbidity, in whom benefits and risks of medication therapy are uncertain, and benefits or risks of stopping medications are also uncertain, deprescribing could be considered a preference-sensitive decision, in which patients' goals and preferences for care should be highly influential in the decision-making process.[1] Identifying medications that are eligible to be deprescribed may be based on an inappropriate benefit-risk ratio, in addition to the complexity and feasibility of the medication regimen, and the alignment with goals and

preferences for care. A proposed framework to identify candidate drugs to stop in such patients is shown in Figure 2.[22]

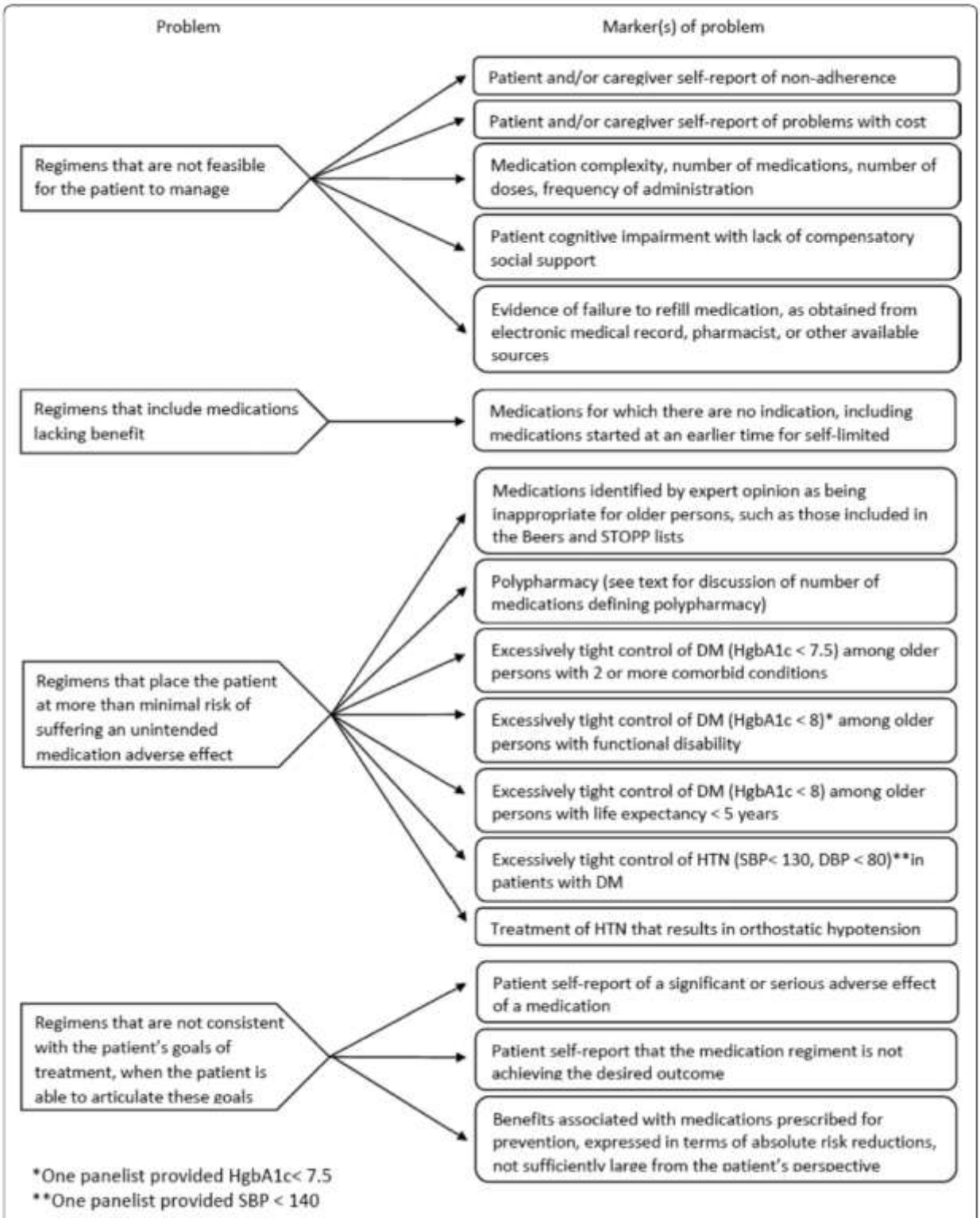

Figure 2. Problems with medications in patients with multimorbidity, reprinted with permission from Fried TR, Niehoff K, Tjia J, Redeker N, Goldstein MK. A Delphi process to address medication appropriateness for older persons with multiple chronic conditions. BMC Geriatr. 2016;16(1):67. Epub 2016/03/17. doi: 10.1186/s12877-016-0240-3.

What do patients think about deprescribing? Surprisingly, few qualitative studies have specifically explored patients' attitudes toward deprescribing. A study of the perspectives of long-term care residents and healthcare professionals suggested that to be successful, deprescribing interventions need to take into account the perspectives of multiple stakeholders.[23] For residents in particular, highly ranked concerns included their well being, continuity of care and communication, the ability to continue medications that contributed to their feeling of wellness, the ability to stop medications they believed to be burdensome, having their voices and rights respected, and respecting the opinions of their physicians.[23] A study of frail long-term care residents and healthcare professionals in Australia found a significant disconnect between the perceptions of medication benefits on the part of residents and their family members, whereas physicians recognized that for frail older patients, long-term care was essentially palliative.[24] In addition, residents had poor understanding about the indications and possible adverse effects of their medications, low self-efficacy around medication discontinuation, and high trust in their physician to make medication decisions.[24] Similarly, a study of 85 patients with heart failure and 74 prescribing physicians found a disconnect regarding deprescribing; most of the patients were not dissatisfied about the number of medicines they took regularly, and only 41% could identify at least one drug they would stop, whereas physicians had a high consensus about drugs that could be stopped when presented with clinical heart failure scenarios.[25] In contrast, a study

exploring the medication-related views of patients with life-limiting illness as well as their caregivers found that there was acknowledgement that medications were burdensome, and there was a willingness to rationalize medication use, particularly when they were exposed to polypharmacy.[26] Patients and caregivers also recognized that a transition in care, potentially after the diagnosis of life-limiting illness, was a time when less importance was placed on taking preventive medications, with a willingness to change medications at such transitions.[26]

Trials associated with deprescribing interventions have not consistently explored patient preferences, perceptions or experiences. A recent systematic review included 21 randomized controlled trials (RCTs) on deprescribing specific drugs (rather than an overall approach to reducing medication number), including antipsychotics, diuretics, antidepressants, digoxin, statins, and drugs for benign prostatic hyperplasia. They found that in many of the trials, deprescribing medications led to a relapse or worsening of symptoms or the underlying disease state. The review did, however, not specifically address patient preferences or patient-specific outcomes.[16] In a trial of stopping proton pump inhibitors (PPIs), of 72 patients considered for PPI withdrawal, 8 were considered appropriate to deprescribe, 6 consented, of whom 3 stopped the drug and 3 reduced the dose. Three of the 6 participants returned feedback and reported that they were comfortable with the process and willing to have another medication similarly deprescribed.[11] A cross-sectional study of patients in the last few days of life in a geriatric ward in Belgium found that deprescribing of inappropriate medications at the end of life was more frequent if death was expected, and the authors noted further opportunity to optimize medication use by deprescribing drugs at the end of life. They particularly noted that in cases where prognostication is difficult, early discussions of patient's preferences and wishes for end of life care could help to engender trust with the physician and facilitate the process of deprescribing

life-long medications at the end of life.[27] This is in agreement with a recently published set of recommendations around deprescribing approaches in limited life expectancy that outline the importance of patient-centered, shared decision-making.[ref our paper]

To specifically address patients' willingness to undertake deprescribing, Reeve, et al. developed the Patients' Attitudes Towards Deprescribing questionnaire.[28] The PATD was then employed in an ambulatory setting in a sample of adults, 65% of whom were over 65 years old, and 92% reported willingness to have one or more medications stopped.[29] The PATD was applied in a population of older hospitalized patients in Italy, and found that most of the patients felt that they were taking too many medications, and 89% were willing to have one of their regular medicines deprescribed.[30] The PATD was also applied specifically around stopping statins on older inpatients in Australia, and found that 89% of the participants were willing to stop one or more of their regular medications, and 95% were willing to stop statins.[31]

Patients' willingness to deprescribe may not be enough. Indeed, based on results from qualitative studies highlighting the need for more communication and a focus on patient well being, and based on quantitative studies showing lower uptake of deprescribing interventions and concerns for relapse of underlying symptoms, a successful deprescribing intervention must seek to fully engage both the patient and, where relevant, the caregiver. The EMPOWER trial is an example to describe such an approach: this intervention was developed toward increasing patients' knowledge and self-efficacy around stopping benzodiazepines, and was designed to create a cognitive dissonance around the perception that harmful medications were safe.[32] The intervention consisted of a booklet with an assessment about medication risks, education about harms and drug interactions, and a specific step-wise tapering protocol. Overall, 86% completed a 6-month follow up, at which point 27% of the intervention group had stopped the

benzodiazepine, compared to only 5% of the control group (who received general educational materials). This approach has been expanded to other classes of drugs, with publicly available deprescribing algorithms for practitioners to employ.[33]

Barriers and pitfalls to deprescribing

Despite the perceived acceptability of deprescribing and the momentum toward reducing medication use, there are significant barriers to stopping medications. The biggest barrier to deprescribing is an emotional and psychological one: our belief as a society and healthcare system that every patient-doctor interaction needs to end in the addition of a medication, and that additional medication will either prolong life or promote health.[34] Much has been written about prescribers' discomfort in stopping medications, and emerging discussion of these barriers incorporates a consideration of patient and system barriers to the process.[35] While there is a disconnect between patients and prescribers regarding the belief about the benefit of medications, the widespread dislike of overmedication is a major enabler of deprescribing as an acceptable intervention.[35] Recent evidence regarding the willingness of patients to stop medications and their reliance on physicians to communicate the need to stop drugs puts the onus back on prescribers to take on responsibility to make deprescribing more commonplace.[18] The barriers to deprescribing are summarized in the **Box**.

Box. Potential Barriers to Deprescribing[18,23,35-37]

Prescriber	Lack of guidelines, lack of decision support
	Lack of time
	Fixed beliefs about benefits and harms of medications
	Lack of awareness; incomplete medical or medication history

	Clinical inertia
	Lack of knowledge or skills
	Beliefs about external constraints
	Need for multiple points of contact/communication to deprescribe
	Reluctant to change specialists' medications
Patient	Lack of decision making capacity
	Difficulty in comprehension or communication around deprescribing
	Need for caregiver engagement
	Misalignment with goals of care
System	Lack of reimbursement
	Fragmentation during transitions of care
	Lack of facilitators for communication
	Absence of integrated electronic medical records system across different sites
	Discoordinated care

Prescribers' opinions vary widely, particularly about preventive medications, highlighting the need for consensus guidelines around deprescribing.[12] The optimal time at which to deprescribe, the ideal patient situations in which deprescribing should occur, and the ideal settings are unclear and may very widely based on the individual clinical situation. For example, while transitions of care may represent an ideal time to reconcile and critically rethink all medication therapy, deprescribing in the hospital could be a problem for sustaining change. Deprescribing requires active participation of the patient, including communication and agreement to the change, and an acutely ill patient may not be able to participate in

deprescribing.[38] Similarly, the ideal patient situations that should prompt deprescribing are uncertain. As an example, patients with dementia may have frequently changing goals of care, making deprescribing necessary as care shifts at the end of life; however, the inability to engage the patient in deprescribing and the need to engage caregivers with frequent communication may present obstacles.[36]

Ultimately, addressing these specific barriers could help to facilitate deprescribing and make stopping medications as facile as prescribing them in the first place. This could be accomplished by a number of changes, not the least of which includes:

1) Systematically screen patients for their willingness to have medications deprescribed. Much in the same way that providers systematically screen for depression or for falls, tools such as the PATD could be employed to elicit a patient's attitudes, which could help inform providers about preferences and could facilitate patient-centered decision-making about medicines.[28]
2) Provide health information systems that facilitate communication between multiple specialists and with the patient and caregiver, to reduce the concerns about stopping medicines that other prescribers have started.
3) Leverage data systems to identify medications that are eligible for deprescribing or patients that are ideal candidates for deprescribing interventions.[39] This could be accomplished through the use of existing tools to identify inappropriate medications and tools to identify patients with high-risk conditions.
4) Promote reimbursement for deprescribing activities by members of a multidisciplinary team, and specifically facilitate the input of pharmacists in making recommendations to deprescribe.

5) Strengthen the evidence based around deprescribing by including patient goal-driven interventions and patient-reported outcomes in deprescribing studies.

Conclusions

Deprescribing is more complex than simply stopping medications: it is a multiple stage process that should be patient-centred and a part of the wider remit of shared care decision-making. Despite the acknowledgment that patient preferences – alongside those of healthcare professionals and caregivers – are crucial for any successful deprescribing intervention there is, at present, a dearth of literature in this area. Future studies – particularly randomized controlled trials – should be encouraged to include a qualitative aspect to enable the better understanding of perceptions and experiences for patients who have undergone deprescribing interventions. It will be crucial for future deprescribing interventions to be able to adapt to new evidence as it emerges and still allow for the application of clinical judgment and the consideration of ethical issues.

References

1. American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. *J. Am. Geriatr. Soc.* 2012;60(10):E1-E25.
2. Ortman JM, Velkoff VA, Hogan H. An aging nation: the older population in the United States. US Census Bureau; 2014:25-1140.
3. Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. Trends in Prescription Drug Use Among Adults in the United States From 1999-2012. *JAMA.* 2015;314(17):1818-1831.
4. Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995-2010. *BMC Med.* 2015;13:74.
5. Turner JP, Jamsen KM, Shakib S, Singhal N, Prowse R, Bell JS. Polypharmacy cut-points in older people with cancer: how many medications are too many? *Support. Care Cancer.* 2015.
6. Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J. Clin. Epidemiol.* 2012;65(9):989-995.
7. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J. Am. Geriatr. Soc.* 2014;62(12):2261-2272.

8. Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Sen S, Kaboli PJ. Polypharmacy and prescribing quality in older people. *J. Am. Geriatr. Soc.* 2006;54(10):1516-1523.

9. Alldred DP. Deprescribing: a brave new word? *Int. J. Pharm. Pract.* 2014;22(1):2-3.

10. Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging de fi nition of 'deprescribing' with network analysis: implications for future research and clinical practice. *Br. J. Clin. Pharmacol.* 2015;80(6):1254-1268.

11. Reeve E, Andrews JM, Wiese MD, Hendrix I, Roberts MS, Shakib S. Feasibility of a patient-centered deprescribing process to reduce inappropriate use of proton pump inhibitors. *Ann. Pharmacother.* 2015;49(1):29-38.

12. Ailabouni NJ, Nishtala PS, Mangin D, Tordoff JM. General practitioners' insight into deprescribing for the multimorbid older individual: a qualitative study. *Int. J. Clin. Pract.* 2016;70(3):261-276.

13. Potter K, Flicker L, Page A, Etherton-Beer C. Deprescribing in Frail Older People: A Randomised Controlled Trial. *PLoS One.* 2016;11(3):e0149984.

14. Bain KT, Holmes HM, Beers MH, Maio V, Handler SM, Pauker SG. Discontinuing medications: a novel approach for revising the prescribing stage of the medication-use process. *J. Am. Geriatr. Soc.* 2008;56(10):1946-1952.

15. Iyer S, Naganathan V, McLachlan AJ, Le Couteur DG. Medication withdrawal trials in people aged 65 years and older: a systematic review. *Drugs Aging.* 2008;25(12):1021-1031.

16. Nguyen T, Gurwitz JH. Deprescribing in older adults: a systematic review. American Geriatrics Society Annual Meeting, Long Beach, California, 2016.

17. Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The feasibility and the effect of deprescribing in older adults on mortality and health: A systematic review. *Br. J. Clin. Pharmacol.* 2016.

18. Scott IA, Le Couteur DG. Physicians need to take the lead in deprescribing. *Intern. Med. J.* 2015;45(3):352-356.

19. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med.* 2015;175(5):827-834.

20. By the American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J. Am. Geriatr. Soc.* 2015;63(11):2227-2246.

21. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing.* 2015;44(2):213-218.

22. Fried TR, Niehoff K, Tjia J, Redeker N, Goldstein MK. A Delphi process to address medication appropriateness for older persons with multiple chronic conditions. *BMC Geriatr.* 2016;16(1):67.

23. Turner JP, Edwards S, Stanners M, Shakib S, Bell JS. What factors are important for deprescribing in Australian long-term care facilities? Perspectives of residents and health professionals. *BMJ Open.* 2016;6(3):e009781.

24. Palagyi A, Keay L, Harper J, Potter J, Lindley RI. Barricades and brickwalls--a qualitative study exploring perceptions of medication use and deprescribing in long-term care. *BMC Geriatr.* 2016;16:15.

25. Hopper I, de Silva C, Skiba M, Tonkin A, Krum H. Attitudes of Patients and Prescribing Clinicians to Polypharmacy and Medication Withdrawal in Heart Failure. *J. Card. Fail.* 2016.

26. Todd A, Holmes H, Pearson S, et al. 'I don't think I'd be frightened if the statins went': a phenomenological qualitative study exploring medicines use in palliative care patients, carers and healthcare professionals. *BMC Palliat. Care.* 2016;15:13.

27. Van Den Noortgate NJ, Verhofstede R, Cohen J, Piers RD, Deliens L, Smets T. Prescription and Deprescription of Medication During the Last 48 Hours of Life: Multicenter Study in 23 Acute Geriatric Wards in Flanders, Belgium. *J. Pain Symptom Manage.* 2016.

28. Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. Development and validation of the patients' attitudes towards deprescribing (PATD) questionnaire. *Int. J. Clin. Pharm.* 2013;35(1):51-56.

29. Reeve E, Wiese MD, Hendrix I, Roberts MS, Shakib S. People's attitudes, beliefs, and experiences regarding polypharmacy and willingness to Deprescribe. *J. Am. Geriatr. Soc.* 2013;61(9):1508-1514.

30. Galazzi A, Lusignani M, Chiarelli MT, et al. Attitudes towards polypharmacy and medication withdrawal among older inpatients in Italy. *Int. J. Clin. Pharm.* 2016;38(2):454-461.

31. Qi K, Reeve E, Hilmer SN, Pearson SA, Matthews S, Gnjidic D. Older peoples' attitudes regarding polypharmacy, statin use and willingness to have statins deprescribed in Australia. *Int. J. Clin. Pharm.* 2015;37(5):949-957.

32. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. *JAMA Intern Med.* 2014;174(6):890-898.

33. Deprescribing Algorithms, available at deprescribing.org, Accessed May 21, 2016.

34. Garfinkel D, Ilhan B, Bahat G. Routine deprescribing of chronic medications to combat polypharmacy. *Ther Adv Drug Saf.* 2015;6(6):212-233.

35. Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging.* 2013;30(10):793-807.

36. Reeve E, Bell JS, Hilmer SN. Barriers to Optimising Prescribing and Deprescribing in Older Adults with Dementia: A Narrative Review. *Curr. Clin. Pharmacol.* 2015;10(3):168-177.

37. Ailabouni NJ, Nishtala PS, Mangin D, Tordoff JM. Challenges and Enablers of Deprescribing: A General Practitioner Perspective. *PLoS One.* 2016;11(4):e0151066.

38. Ramanathan J. Sustainability of deprescribing post discharge. *Intern. Med. J.* 2015;45(8):885.

39. Niehoff KM, Rajeevan N, Charpentier PA, Miller PL, Goldstein MK, Fried TR. Development of the Tool to Reduce Inappropriate Medications (TRIM): A Clinical Decision Support System to Improve Medication Prescribing for Older Adults. *Pharmacotherapy.* 2016.

40. Todd A, Holmes HM. Recommendations to support deprescribing medications late in life. *Int. J. Clin. Pharm.* 2015;37(5):678-681.