Deprescribing for older patients

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The principles that guide optimal prescribing for older patients[1,2] (Box 1) include deprescribing medications that are no longer indicated, appropriate or aligned with evolving goals of care. Deprescribing is a relatively new term that focuses attention on the sometimes overlooked step in medication review of stopping medications to improve outcomes and decrease risks associated with polypharmacy in older people.[3–5] These risks include nonadherence,[6] adverse drug reactions,[7] functional and cognitive decline,[8] and falls.[9,10] In Canada, more than 50% of older people living in long-term care facilities and 27% of those living in the community take more than five medications a day.[11] Although frailty[12] should be a catalyst for deprescribing, the principles and practice of deprescribing apply to all older patients and, if integrated early into care, may play a role in preventing frailty.

In this article, we describe an approach to deprescribing based on principles, practice and available evidence. We reviewed evidence from systematic reviews and randomized controlled trials on the impact of deprescribing (Box 2). Most of the studies failed to measure clinical outcomes relevant to the care of older patients, such as improved functioning. The quality of the evidence was limited by small samples, short study durations and heterogeneous study designs.[13–15] Nonetheless, we found evidence[16] that a substantial proportion of older patients can tolerate careful dosage reduction or withdrawal of certain classes of medications without harmful consequences and with possible improvement in quality of life, especially if the goals of care shift from disease-specific targets to improvements in symptom management and function.

When and for whom is deprescribing appropriate?

Although all older people taking prescribed drugs may benefit from a medication review with a deprescribing lens, those who are frail[12] are the main target of this approach. Frail patients tend to take more medications and have more adverse outcomes related to medications than other older patients. They are also more likely to have limited life expectancy than well older people of similar age.[17] Medication lists tend to lengthen as patients age, and there are few guidelines to inform medication management in the context of polypharmacy, multiple morbidities and age-related changes to pharmacokinetics and pharmacodynamics (Box 1). All prescribers contributing to the medication list need to be alert to "prescribing inertia"[18] (the tendency to automatically renew a medication even when the original indication is no longer present) and should view polypharmacy as an impetus to deprescribe when appropriate.

Any patient interaction can be an opportunity for critical medication review. Certain transitional events in the care of older patients provide identifiable opportunities. For example, medication errors tend to occur during transfers between care settings.[19,20] To reduce this risk, facilities routinely undertake systematic reconciliations of medication lists between sites; this is an opportunity for deprescribing. Similarly, changes in the overall health of a patient that affect life expectancy, such as the diagnosis of a terminal cancer or progression of dementia or clinical frailty,[17] signal the need for medication review to identify drugs that are unlikely to provide meaningful benefit to the individual in their remaining time.[21]

Can deprescribing medications improve clinical outcomes?

It is well recognized that medications can cause harm in older patients, and there is growing rec-

Key Points

- The same principles that guide prescribing for older patients guide deprescribing for this patient group.
- Identify drugs that are no longer indicated, appropriate or align with goals of care.
- Engage the patient, family and other health care providers in the process.
- Develop a tapering/discontinuation plan and monitor adverse outcomes and benefits.

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ognition that careful adherence to disease-specific guidelines in frail patients can result in increased risks of drug interactions and adverse reactions.[22]

Despite this context, the evidence to support deprescribing as a broad strategy to improve clinical outcomes in older patients is weak. According to three recent reviews,[13–15] most of the trials studying deprescribing failed to measure clinical outcomes relevant to the care of older patients, such as improved functioning, and were limited by small samples and short study durations. Although many of the interventions involved pharmacists, the engagement between the pharmacist and prescriber was not adequately described,[14] and few studies incorporated patient perspectives. Heterogeneity in study design, sample selection, choice of outcome measure and intervention made it difficult to synthesize results and draw conclusions.

Nonetheless, when the evidence about deprescribing is organized by the intentions to stop drugs that are no longer indicated, that are no longer appropriate or that no longer align with goals of care, deprescribing appears to be potentially helpful without causing substantial harm, if done well.

Box 1: Principles to guide prescribing and deprescribing medications in older patients[1,2]

Pharmacokinetics: what the body does to the drug; what factors determine the concentration of the drug at the target receptor or organ

Absorption: little change due to aging alone, but it can be affected by medications and conditions common in older people

Distribution: increased fat:water ratio with aging; protein binding may be affected by malnutrition or medical conditions

Metabolism/excretion: decrease in some liver metabolism with aging may affect different drugs differently; decrease in renal excretion with aging may affect drugs dependent on kidneys for excretion

Pharmacodynamics: what the drug does to the body; what factors affect whether medication will have a greater or lesser affect with same serum concentration

Prescribing tips

- Remember that medications may cause illness
- Know the patient and his or her current medications (and how they are taken)
- Consider nonpharmacologic therapy
- Know the pharmacology of the prescribed drugs
- Keep drug regimens simple
- Establish treatment goals at the time of prescription
- Strive for a diagnosis before prescribing; if a therapeutic trial is done, stop medications if treatment goals are not reached
- Encourage the patient to be a responsible medication user and to participate in his or her medication management
- Consider the patient's current medications and medical conditions before adding or changing new medications
- Start low, go slow (but get there!)
- Monitor closely for adverse effects when starting or stopping medications
- Manage the whole of the patient's treatment regimen

Drugs that are no longer indicated

A systematic review of 31 trials involving older adults, published in 2007, examined the benefits and harms of withdrawing medications felt to be no longer indicated.[16] The studies focused on the complete withdrawal of one of four classes (benzodiazepines, antihypertensives, diuretics for indications other than heart failure and antipsychotics). Although the included studies were limited by small samples and short durations, the results showed that a substantial proportion of participants could tolerate withdrawal of one of these classes and experienced benefits of reduced risk of falling (e.g., psychotropic medication withdrawal, hazard ratio 0.34, 95% confidence interval 0.16–0.74)[23] and improvement in total memory test scores (e.g., benzodiazepine withdrawal, $p < 0.004$).[24]

These results are borne out in current clinical practice. It is almost conventional wisdom that tapering benzodiazepines[25] can improve cognition and reduce the risk of falls. The recent changes in clinical practice guidelines to relax targets for blood pressure (e.g., 150/90 mm Hg)[26,27] and blood glucose (hemoglobin A_{1c} concentration < 7.5%)[28] in older patients is informed by the trade-off between the risk of vascular events with the risk of falling because of orthostatic hypotension[29] or hypoglycemia. Likewise, there is evidence that a systematic approach to reduce the prescribing of antipsychotics for behavioural symptoms of dementia when stable allows many people to be off medications for sustained periods of time or indefinitely.[30]

Drugs that are no longer appropriate

A recent Cochrane review[31] concluded that systematic medication reviews involving a pharmacist working closely with the physician and the patient or caregiver results in a substantial reduction in inappropriate prescribing, either through medication substitution or discontinuation. The results from these studies do not clarify whether improving appropriateness of prescribing improves clinical outcomes; however, this association may be inferred from the evidence about

Box 2: Evidence for this review

We included published systematic reviews that were known to us. We then searched the databases Embase and MEDLINE using the terms "deprescribing" and "drug withdrawal" to identify additional systematic reviews as well as reports of randomized controlled trials of deprescribing published from January 2010 to March 2014. We restricted our review to articles published in English that had a study population aged 65 years or more.

risk of adverse outcomes used to construct tools to identify inappropriate medications in older patients, such as the Beer criteria.[32]

Drugs that no longer align with goals

Frail patients or their substitute decision-makers may shift treatment goals away from prolonging life to controlling symptoms or maximizing function. Eliciting preferences and perspectives on outcomes and goals of therapy is important to guide decisions to reduce or stop medications. In their work on universal health outcomes, Tinetti and colleagues[33] found that the proportion of older patients who identified reducing the risk of falls as their priority equalled the proportion who prioritized stroke prevention with use of antihypertensives. Decreasing the dose or stopping an antihypertensive medication may be an acceptable choice for someone who has had frequent falls or has limited function, a poor prognosis or recent hip fracture, even at the cost of increased stroke risk. More studies are needed to assist with these difficult discussions and decisions about preferences and trade-offs.

What are some of the guiding principles and steps involved in deprescribing?

In the absence of clear evidence about the best approach to deprescribing, a structured stepwise approach is recommended (Figure 1, Table 1).[3,4] Either a specific clinical concern or a routine medical review may prompt deprescribing. The first step is to ask the patient to bring in all prescribed and over-the-counter medications for a visual "brown bag review" by the physician, nurse or pharmacist. This exercise provides a lot of information about the patient's understanding of and attitudes toward his or her medications and pill-taking habits. The resulting list of current medications should be cross-referenced with the chart and the pharmacy list when possible.

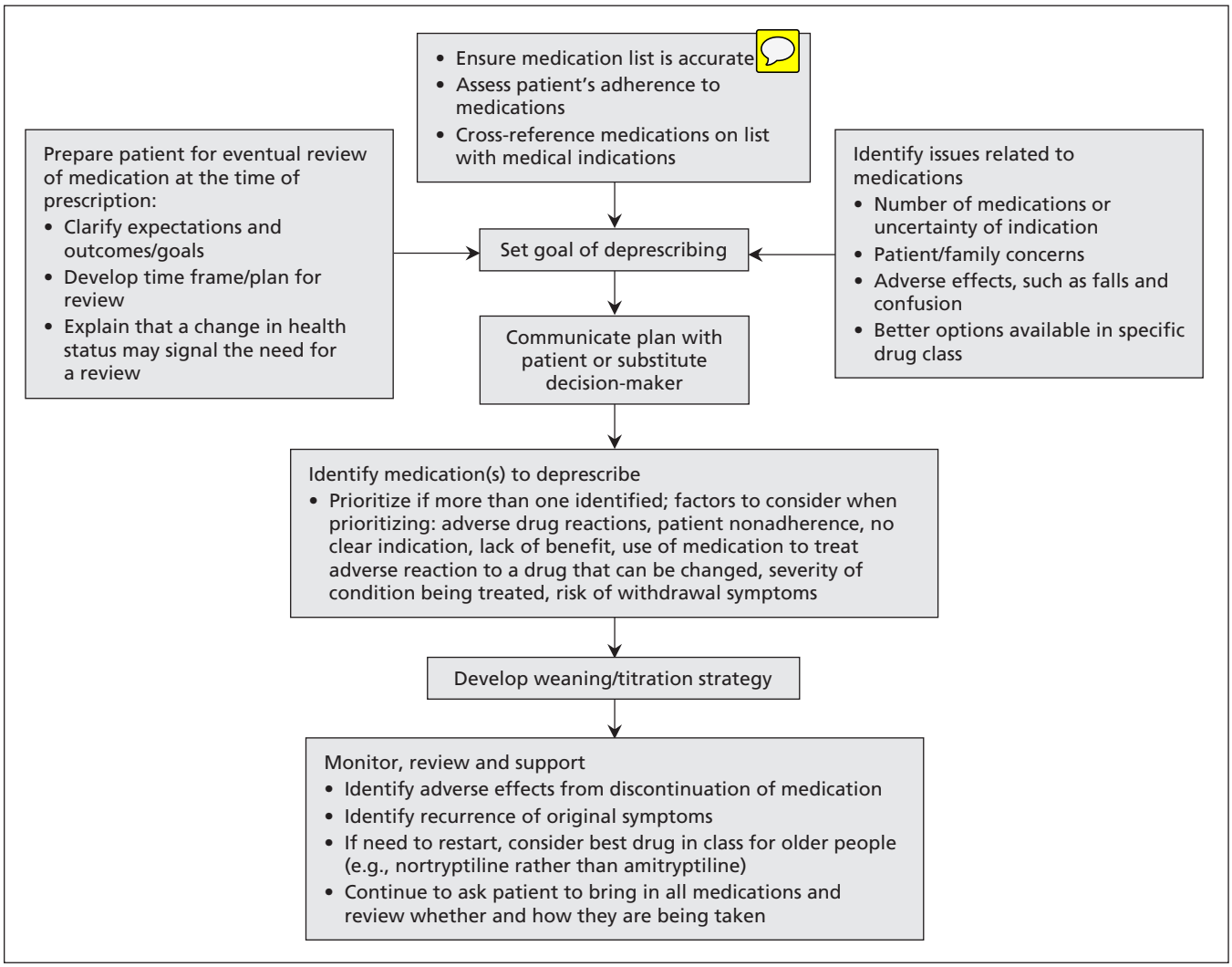

Figure 1: Practical approach to deprescribing.

Each medication should be classified according to indication. Medications without a current, credible indication and medications duplicated for the same indication are candidates for deprescribing. In addition, the appropriateness of drug choice and dose within each class of medications may be evaluated at this point and modified if required. A number of tools (Table 2) are available to assist with identifying inappropriate medications[32,34–40] and, occasionally, relevant medications that need to be started.[36]

Often patients will have stopped taking a prescribed medication on their own volition. It is necessary to understand why and to evaluate the justification for continuing with the prescription or not. Medications not being taken regularly are candidates for discontinuation if there are no evident health consequences resulting from the nonadherence.

Current medications should align with current goals of care. With older patients, discussions about goals of care need to be framed in terms of the patient's functional ability, clinical frailty and life expectancy. Predicting life expectancy remains as much the art of medicine as science. According to a recent systematic review of 16 potential prognostic indicators, 10 predicted greater than 50% mortality, but only 3 predicted greater than 80% risk in the highest risk group.[41] Tools focusing on severity of frailty, such as the Clinical Frailty Scale,[12,42] provide general prognostic information that may help to identify patients with limited life expectancy.

As part of the discussion about goals of care, it is important to clarify the patient's preferences for trade-offs between risk reduction (e.g.,"I want to avoid a stroke at all costs") and symptom management (e.g., "I want help with my pain") or between disease-specific targeted goals (e.g., "Please lower

Table 1: Examples of medications to possibly deprescribe at certain steps of medication review[3,4]*

Reason to stop medication or decrease dose	Examples	Comment
Noncompliance without negative health effect	• Antihypertensive • Oral diabetic medication	• Identified through careful visual review of medications brought in by the patient and discussion about his or her understanding of and attitudes toward the medications and pill-taking habits
Taken incorrectly without negative health effect (or without benefit)	• Puffers: some delivery systems are easier to use by older patients	• In some circumstances, use can be corrected by showing patient how to use an aerochamber
Not indicated or relative contraindication	• Statin for primary prevention	• No evidence for benefit in older patients
	• Docusate	• Insufficient evidence for benefit to recommend or not recommend
	• Calcium-channel blocker in patient with systolic heart failure	
No longer indicated	• Bisphosphonate after 5 yr	• No evidence of effectiveness after 5 yr of continuous treatment
	• Clopidogrel: as per guideline after cute coronary syndrome	• Treatment often extends beyond guideline recommendations
	• Benzodiazepine • NSAID • PPI	• Intended for short-term use but susceptible to "prescribing inertia" (tendency to automatically renew a medication even when the original indication is no longer present)
	• Cholinesterase inhibitor (e.g., in patient with very limited prognosis)	• Patient moves to terminal phase of illness
Inappropriate choice for geriatric patient	• Digoxin > 125 μg/d[34]	• Risk of toxicity with age-related decline in renal function
	• Amitriptyline[34]	• Risk of falls and fractures
No longer aligns with goals of care or life expectancy	• Statin in patient with limited life expectancy (< 5 yr) • Bisphosphonate in patient with limited life expectancy (< 2 yr)	
	• Coumadin: decision requires discussion with patient about risk–benefit balance	• No current evidence to guide at what point age-related risk outweighs benefit; frailty and expected life expectancy may be more relevant factors

Note: NSAID = nonsteroidal anti-inflammatory drug, PPI = proton pump inhibitor, START = screening tool to alert doctors to the right treatment.
*START criteria may identify medications that a patient should be taking but is not.

my blood pressure") and universal goals ("Please keep me as independent as possible"). As goals of care evolve from disease-specific to more universal ones, understanding the relative contribution of chronic conditions to universal outcomes such as self-rated health, functioning, symptom burden and mortality can help to elicit priorities and guide clinical decisions.[43]

Once a decision to deprescribe a drug is made, engaging the patient or caregiver in the plan is important. A number of medications require tapering. Health care providers, patients and caregivers need to monitor for withdrawal-related adverse events (Table 3).[44,45] In some instances, it may be necessary to restart the medication.

What are some of the challenges and barriers to deprescribing?

Establishing a successful deprescribing plan takes time and open discussion between the physician and the patient, which does not always occur. Studies on the topic identify several barri-

Table 2: Examples of tools to assist with medication review and deprescribing[35]

Tool	Description	Level of evidence	Comments
Beers criteria[32]	List of drugs of concern in geriatric care and associated quality of evidence and strength of recommendation	Consensus of expert panel using Delphi technique; strong link between medications on the list and poor patient outcomes confirmed in studies	Many of the drugs are older and out of use; excludes drugs of concern with insufficient evidence
STOPP[34]	Screening tool with 65 indicators; focuses on drug–drug and drug–disease interactions		Items groups by physiologic systems and by drug class; short time to complete
START[36]	Screening tool to identify possible prescribing omissions		Similar to STOPP in structure; it does not relate to deprescribing but may help optimize medications
Anticholinergic risk scale (ARS)[37]	Ranked categorical list of commonly prescribed medications with anticholinergic potential	Statistically significant correlation between higher ARS scores and increased risk of anticholinergic adverse effects	May help identify medications contributing to adverse effects such as confusion, urinary retention
ARMOR[38]	Algorithm that prompts review of drug classes, interactions, functional status, systems review and reassess status	Tested in only 1 nursing facility	Can be used to assess medications, initial assessment, falls or behavioural disturbance, and rehabilitation potential
Geriatric–palliative method[39]	Consensus-based flowchart to reduce polypharmacy	Applied in 6 geriatric nursing departments, (119 patients); significant reduction in mortality, hospital admissions and cost	
Prescribing Optimization Method[40]	6 questions to guide general practitioners to address under-treatment, adherence, inappropriate drugs, adverse drug reactions, interactions and dosing	Improvement in optimal prescribing by 45 physicians when applied to a patient case history	
Choosing Wisely Canada (www.choosingwiselycanada.org/recommendations/canadian-geriatrics-society-2/) and Choosing Wisely (www.choosingwisely.org/doctor-patient-lists/american-geriatrics-society/)	Management recommendations from the American and Canadian Geriatrics Societies	Expert opinion based on variety of evidence levels	Recommendations may advise against use of specific medications in older patients or advise on treatment targets that could facilitate deprescribing (e.g., hemoglobin A_{1c} target and oral agents)

Note: ARMOR = assess, review, minimize, optimize, reassess; START = screening tool to alert doctors to the right treatment; STOPP = screening tool of older persons' potentially inappropriate prescriptions.

ers in attitude and practice to be overcome by both physician and patient.

Schuling and colleagues[46] conducted focus groups with Dutch general practitioners to explore their feelings about and experiences with deprescribing for very old patients with multiple morbidities. They found that the physicians tended to dichotomize medications into symptomatic and preventive types. Physicians expressed more difficulty about withdrawing preventive medications because of the lack of evidence to inform patients about the specifics of risks and benefits with discontinuation and because of the challenge of discussions about life expectancy and quality of life. The general practitioners also expressed concern about stopping medications prescribed by medical specialists. They identified training in shared decision-making to elicit patient preferences and explicit rules for collaborating with medical specialists as potential ways to help them with deprescribing.

Reeve and colleagues[47] published a systematic review of 21 studies related to medication cessation and patients' beliefs. Three themes emerged: beliefs about the appropriateness of the medication being deprescribed, concerns about

Table 3: Medications commonly associated with withdrawal-related adverse events[44,45]

Medication	Effect of discontinuation*	Withdrawal-related manifestations
Increased risk of discontinuation syndrome		
Antianginal agent	Recurrence	Angina
Anticonvulsant	Withdrawal, recurrence	Anxiety, depression, seizures
Benzodiazepine	Withdrawal, rebound, recurrence: common strategy is to taper by 10% of the dose every 1–2 wk until the dose is at 20% of the original dose, then taper by 5% every 2–4 wk	Seizures, agitation, anxiety, delirium, insomnia
Beta-blocker	Rebound, recurrence	Angina, hypertension, acute coronary syndrome, tachycardia
Corticosteroid	Withdrawal, rebound, recurrence if used long term	Anorexia, hypotension, nausea, suppression of the hypothalamic–pituitary–adrenal axis
Decreased risk of discontinuation syndrome		
ACE inhibitor	Recurrence	Heart failure, hypertension
Antipsychotic	Withdrawal, recurrence: • When used for behavioural and psychiatric symptoms of dementia, taper dose with goal to stop drug every 3 mo or more if clinically appropriate (taper by 25% every 1–2 wk) • Some behaviours decline as disease worsens	Dyskinesias, insomnia, nausea, restlessness
Anticholinergic	Withdrawal	Anxiety, nausea, vomiting, headaches, dizziness
Digoxin	Recurrence: patients can usually be followed for signs and symptoms of heart failure and medication restarted as needed	Heart failure, tachycardia
Diuretic	Recurrence	Heart failure, hypertension, edema
Narcotic analgesia	Withdrawal: if medication used long term, tapering will decrease risk of physical withdrawal	Abdominal cramping, anxiety, chills, diaphoresis, diarrhea, insomnia

Note: ACE = angiotensin-converting enzyme.
*Recurrence = recurrence of original symptoms, withdrawal = symptoms associated with withdrawal, rebound = recurrent symptoms that are worse than the original symptoms.

the process for cessation, and attitudes of family and physicians about the deprescribing process. Not surprisingly, patients' beliefs that the prescribed medication was doing something or was "better than doing nothing" presented barriers to stopping the medication, whereas beliefs that the medication was no longer appropriate enabled cessation. Patients reported that ensuring the process for deprescribing was monitored, supported and suitably paced assisted discontinuation, as did good relationships with the physicians and support of family over the process.

Recognition of terminal illness is an important reason to review goals of care and medications. However, even when faced with a terminal illness, some patients will be concerned about stopping medications they have been taking for years, especially when a physician in the past has stressed its importance. One example may be stopping a medication for the primary prevention of cardiovascular disease, even though there is little evidence to support its use in individuals aged over 80 years and even less evidence in those aged over 90. A randomized controlled trial is currently under way to determine whether there is a difference in survival time and quality of life between patients with advanced life-limiting illness whose statins are discontinued and those whose statins are continued (ClinicalTrials.gov trial no. NCT01415934).

Medications commonly used in palliative and end-of-life care can have adverse effects such as confusion, drowsiness, constipation and fatigue. To optimize the use of these medications, it may be prudent to minimize the use of other medications that could potentially worsen these effects. For example, ferrous gluconate may no longer provide achievable benefit for anemia but may exacerbate constipation caused by opiates.

Paradoxically, stopping a medication with a previously unrecognized adverse effect can sometimes improve overall function and change the short-term outlook at end of life. Although not well described in the literature, many physicians caring for patients with end-stage heart failure have had the experience of patients rallying with short-term improvement when high doses of cardiac medications are stopped or decreased because of apparently imminent death.

These practical lessons reinforce the importance of understanding the current indication for each medication prescribed to an older patient and a readiness to review and deprescribe as appropriate.

Unanswered questions

Which approach to deprescribing is most effective in improving clinical outcomes? Most approaches seem to involve a pharmacist and prescriber. Available study interventions are too heterogenous or poorly described to permit comparisons between approaches.

How effective are medication reviews in improving patient-centred results such as quality of life? Most existing trials fail to measure outcomes such as improved functioning and are of too short a duration or too small a size to show significant clinical improvements with deprescribing.

Does primary prevention of cardiovascular disease at end of life improve quality of life? Studies looking at the role of statins in end-of-life care are underway.

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