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Review

Deprescribing Cardiovascular Medications in Older Adults Living with Frailty

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ABSTRACT

Certain medications have shown significant effectiveness in reducing the incidence of cardiovascular events and mortality, leading them to be among those that are prescribed most commonly for Canadian seniors. However, polypharmacy, which disproportionately affects older adults, is particularly concerning for frail individuals who are at higher risk for adverse medication-related events. The deprescribing

RÉSUMÉ

Certains médicaments ont montré une efficacité significative dans la réduction de l'incidence des événements cardiovasculaires et de la mortalité, ce qui fait qu'ils figurent parmi les plus couramment prescrits aux aînés canadiens. Cependant, la polypharmacie, qui touche de manière disproportionnée les personnes âgées, est particulièrement préoccupante pour les personnes fragiles qui sont plus exposées

Medications have shown significant effectiveness in reducing cardiovascular (CV) deaths,[1,2] leading to guidelines that prioritize escalation of medical therapies to manage cardiac conditions and address modifiable risk factors.[3-5] However, strict adherence to these guidelines can result in polypharmacy,[6] which disproportionately affects older adults.[7,8] Further, guidelines typically focus on single-illness issues, meaning that complex therapeutic regimens may be required when a patient has multiple comorbidities. Polypharmacy is particularly concerning for frail individuals who face a higher risk of experiencing adverse medication-related events.[9,10] However, the impact of frailty on prescribing extends beyond concerns about adverse events. Although some older adults with frailty may derive benefit from use of medications designed to treat CV conditions, the underrepresentation of this population in clinical trials introduces uncertainty about treatment efficacy.[11] Further, due to their shorter life expectancy, individuals with frailty may not have sufficient time to achieve benefit from treatments that require years to show effect. The balance between risk and benefit must be weighed carefully when deciding whether to continue or stop use of a medication.

The deprescribing process is the discontinuation, either immediate or gradual, of inappropriate medication use, to address polypharmacy and improve outcomes.[12] However, incorporating deprescribing principles into clinical practice presents challenges,[13,14] including the limited amount of data on the benefit of deprescription, and a lack of consensus on how to deprescribe. Although primary-care providers play a key role in the deprescribing process, they may be reluctant to deprescribe CV medications,[14] and therefore, cardiologists' involvement is pivotal. As specialists, cardiologists are key influencers in managing CV conditions. When they are well-informed, they can guide and collaborate more effectively with primary-care and other healthcare providers. This narrative review examines the evidence supporting use of deprescription for common CV conditions and provides practical advice for deprescribing acetylsalicylic acid (ASA), statins, and antihypertensives, to promote safe and effective medication use in the frail older population.

Methods

This narrative review included a targeted search of Google Scholar and PubMed, to identify articles using search terms that included, but were not limited to the following:

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process is the discontinuation, either immediate or gradual, of inappropriate medications, to address polypharmacy and improve outcomes. Nonetheless, the incorporation of deprescribing principles into clinical practice present challenges, including the limited amount of data available on the clinical benefits of deprescription, and a lack of consensus on how to deprescribe.

The current narrative review explores frailty as a basis for deciding to deprescribe medication. The evidence regarding the benefits of use of medications prescribed for common cardiovascular conditions (including acetylsalicylic acid, statins, and antihypertensives) in older adults with frailty is reviewed. The review also examines the issue of who should initiate the deprescribing process, and the associated psychological implications. Although no one-size-fits-all approach to deprescription is available, patient goals should be prioritized. For older adults with frailty, healthcare professionals must consider carefully whether the benefits of use of a cardiovascular medication outweighs the potential harms. Ideally, the deprescribing process should involve shared decision-making among physicians, other health professionals, and patients and/or their substitute decision-makers, with the common goal of improving patient outcomes.

aux événements indésirables liés aux médicaments. Le processus de déprescription consiste en l'arrêt, immédiat ou progressif, des médicaments inappropriés, afin de lutter contre la polypharmacie et d'améliorer les bénéfices. Néanmoins, l'intégration des principes de déprescription dans la pratique clinique présente des défis, notamment en raison du manque de données disponibles sur les avantages cliniques de la déprescription et de l'absence de consensus sur la manière de déprescrire.

Cette revue narrative explore la notion de fragilité comme base de décision pour la déprescription de médicaments. Les données probantes concernant les avantages de l'utilisation de médicaments prescrits pour des affections cardiovasculaires courantes (notamment l'acide acétylsalicylique, les statines et les antihypertenseurs) chez les personnes âgées fragiles sont passées en revue. L'étude examine également la question de savoir qui devrait initier le processus de déprescription et les implications psychologiques qui en découlent. Bien qu'il n'existe pas d'approche universelle de la déprescription, les objectifs des patients devraient être prioritaires. Pour les personnes âgées fragiles, les professionnels de la santé doivent examiner attentivement si les avantages de l'utilisation d'un médicament à portée cardiovasculaire l'emportent sur les inconvénients potentiels. Idéalement, le processus de déprescription devrait impliquer une prise de décision partagée entre les médecins, les autres professionnels de santé et les patients et/ou leurs mandataires, dans le but commun d'améliorer le pronostic pour le patient.

"deprescribing"; "elderly"; "older adults"; "primary prevention"; "secondary prevention"; "aspirin"; "statin"; and "antihypertensives." The search was limited to articles published in English before June 2024. No restrictions were placed on study type, but relevant systematic reviews and meta-analyses were prioritized. Relevant studies were selected, and their references were searched manually for additional papers. The most-recent guidelines from international societies were also consulted, including the Canadian Cardiovascular Society, Hypertension Canada, the US Preventive Services Task Force, the American Heart Association, the American College of Cardiology, the American College of Physicians, the American Academy of Family Physicians, and the European Society of Cardiology.

Results

Why is deprescribing important?

Polypharmacy is commonly defined as the use of $\geq$ 5 medications.[15] However, this definition alone may not fully capture the complexity and appropriateness of medication regimens. A comprehensive understanding of polypharmacy requires consideration of additional factors, such as indication, medication cost, time to achieve benefit, medication adherence, health status, functional abilities, and the patient's goals of care.

Among older adults, polypharmacy is highly prevalent, with over two-thirds of Canadian adults aged $\geq$ 65 years using $\geq$ 5 medications, and one-quarter taking $\geq$ 10 medications.[16] Polypharmacy is associated with negative effects in older adults,[17] including adverse drug events,[18,19] drug—drug-interactions,[20,21] medication nonadherence,[22] falls,[23,24] functional decline,[25] and increased mortality.[26] Individuals taking 8-10 medications daily have a 7.78 times higher risk of experiencing drug—drug interactions than do those taking 2-4 medications daily.[21] One systematic review found that approximately 10% of hospitalizations for adults aged $\geq$ 65 years can be attributed to adverse drug reactions.[18] Another systematic review of 7 studies showed that patients taking $\geq$ 4 medications daily had an increased risk of falls, with odds ratios (ORs) ranging from 1.14 to 2.6.[23] A meta-analysis of 24 studies, and almost 3 million participants aged $\geq$ 65 years, found a significant increase in the incidence of mortality associated with polypharmacy, with a relative risk of 1.28 in those taking $>$ 5 medications, and 1.44 in those taking $>$ 10 medications.[26]

Among the top 7 drug classes prescribed to Canadian seniors, 5 are used for treating CV disease, including statins, dihydropyridine derivatives, angiotensin-converting enzyme inhibitors, beta-blockers, and angiotensin receptor blockers.[16] Therefore, deprescribing CV medications potentially can mitigate the adverse effects of polypharmacy in older adults and ensure the appropriate use of CV medications based on the care goals of the frail population.

How does frailty factor into the decision to deprescribe?

Although a patient's age is an important factor in assessing the appropriateness of medications, it does not fully capture the variability in health status, functional ability, or cognition.[27] As an alternative to age alone, frailty provides a practical conceptual framework for understanding these complexities.[28] Defined as an age-related syndrome characterized by physiological decline and vulnerability to adverse health outcomes, frailty plays a crucial role in the decision to deprescribe medications. Frailty is defined as diminished physiological reserve and increased vulnerability to adverse

health outcomes.[29] The following 2 constructs predominate: (i) frailty as a syndrome, epitomized by the Fried frailty phenotype[30] (exhaustion, weakness, slowness, physical inactivity, and weight loss); and (ii) frailty as an accumulation of health deficits, measured by tools such as the frailty index,[31] and the Clinical Frailty Scale.[32] Although different tools identify different subpopulations as frail, all predict a person's vulnerability to adverse health outcomes, with advanced levels of frailty correlating with increased vulnerability.[33] The selection of a frailty-assessment tool should be guided by how effectively it can predict the specific health outcomes that align with the patient's goals and priorities.

Frailty is common among older adults in Canada, with approximately 22% of community-dwelling older adults are considered to be frail.[34] The prevalence of frailty increases with age, affecting 15% of those aged 65-74 years, and 48% of those aged $\geq$ 85 years.[34] The prevalence is even higher in people with CV conditions, with a systematic review and meta-analysis finding that 44.5% of patients with heart failure were frail.[35]

Medication efficacy is a significant consideration for older adults with frailty. Individuals with frailty usually are excluded from randomized controlled trials, which limits the generalizability of study findings and introduces uncertainty about treatment benefit. For instance, although tight glycemic control has shown to reduce CV risk in younger cohorts with diabetes, its benefit for older patients is less established. For adults with frailty, tight glycemic control carries an increased risk of adverse events relating to hypoglycemia.[36] Moreover, frailty is associated with a higher risk of medication-related adverse events that potentially outweighs the benefits of treatment. Finally, the pharmacokinetics and pharmacodynamics of medications can change with frailty. A review showed that frail older patients have lower hepatic and renal clearance,[37] leading to altered drug effects and an increased susceptibility to adverse reactions.

In addition to identifying the presence of frailty, an important aspect to consider is the stage or level of frailty, as a greater degree of frailty is correlated with an increased incidence of mortality and increased vulnerability.[38,39] A retrospective cohort study found that higher levels of frailty were associated with 5-year mortality rates of 23.6%, 44.5%, and 69.5%, for mild, moderate, and severe frailty, respectively.[40] A systematic review of heart failure treatment showed that patients with frailty had twice the risk of mortality and hospitalization, compared to that of robust individuals.[10] Conversely, frailty itself is a risk factor for developing CV events,[41] and older adults with frailty still may derive benefit from medications, if such are tolerated. Therefore, identifying the presence of frailty should not lead automatically to deprescription, but rather should prompt a comprehensive assessment of the benefits and risks of medications, in light of patients' goals.

Patient preferences should be a key consideration. The American Geriatrics Society Guiding Principles for the Care of Older Adults with Multimorbidity emphasize that eliciting patient preferences is an important part of shared decision-making.[42] Patients may prioritize different health outcomes at various stages of life, such as increasing longevity, maintaining function, or alleviating symptoms. In caring for individuals with frailty, prescribers also should consider the time required to achieve medication benefit and ensure that this time aligns appropriately with the patient's life expectancy. On a broader scale, guidelines that emphasize frailty as a basis for deprescribing medication should take into account similar factors.[43,44]

Should I stop prescribing ASA if my patient is taking it for primary prevention?

In 1988, the US Food & Drug Administration raised concerns about the findings of the Physicians' Health Study regarding the use of ASA to prevent myocardial infarction.[45] Although the study results showed a reduced risk of acute coronary syndrome, they also indicated an increased risk of hemorrhagic stroke.[45] Similar concerns have been raised in contemporary studies. In 2018, 3 landmark trials—ASPirin in Reducing Events in the Elderly (ASPREE),[46] **A**spirin to **R**educe **R**isk of **I**nitial **V**ascular **E**vents (ARRIVE),[47] and **A** **S**tudy of **C**ardiovascular **E**vents i**N** **D**iabetes (ASCEND)[48]—demonstrated either no benefit or minimal benefit of using ASA for the primary prevention of CV disease (Table 1). Further, a subsequent meta-analysis of 13 trials involving 164,225 participants, with a median follow-up period of 5 years, found that although the use of ASA was associated with a small reduction in the incidence of CV events (hazard ratio [HR], 0.89; absolute risk reduction, 0.41%), this benefit was offset by a significant increase in the incidence of major bleeding (HR, 1.43; absolute risk reduction, 0.47%).[49] However, the 3 trials (ASPREE,[46] ASCEND,[47] and ARRIVE[48]) involved predominantly participants who were not previously taking ASA, making the results more applicable to the initiation of ASA for primary prevention. Little data are available to guide whether ASA use should be discontinued in people who are already taking it. An exploratory meta-analysis of participants in the ASPREE and ARRIVE trials who were taking ASA before enrollment, and were subsequently randomized to stop ASA use, showed a 21% relative excess risk for incident atherosclerotic CV disease (HR, 1.21, 95% confidence interval [CI], 1.05-1.39).[50] Recognizing the limitations of these exploratory data, physicians should be cautious when stopping ASA use that is for primary prevention, particularly in individuals who are at high risk of developing CV disease.

Frailty is also an important consideration in the context of ASA use for primary prevention. A prespecified subgroup analysis in the ASPREE trial found no significant difference in the primary composite endpoint of death, dementia, and persistent physical disability in the population within the frail category (HR, 1.23, 95% CI, 0.87-1.73).[48] Studies also have examined the association between ASA use and the incidence of frailty. A subgroup analysis of 12,101 men aged $\geq$ 60 years who participated in the Physicians' Health Study found that ASA use for $\geq$ 60 days per year was inversely associated with frailty (OR, 0.85, 95% CI, 0.76-0.96).[51] However, another study of a more contemporary cohort, analyzing 19,114 participants in the ASPREE trial (aged $\geq$ 70 years, of both sexes), found that ASA use did not reduce the risk of incident frailty or affect the trajectory of frailty over a median follow-up of 4.7 years (Fried frailty phenotype HR, 1.04, 95% CI, 0.96-1.13; frailty index HR, 1.03, 95% CI, 0.97-1.09).[52]

Table 1. Large randomized controlled trials on the use of acetylsalicylic acid for primary prevention

Trial	Patients' age, y and CVD data	Follow-Up period duration, y	Results
ASPREE (McNeil et al., 2018)[46]	≥ 70; ≥ 65 if in US and Black or Hispanic	Median, 4.7	• No difference in disability-free survival (all-cause mortality, dementia, or persistent physical disability; HR 1.01, 95% CI, 0.92−1.11, $P = 0.79$) • Increased risk of major hemorrhage (HR 1.38, 95% CI, 1.18−1.62, $P < 0.001$)
ARRIVE (Gaziano et al., 2018)[47]	> 55, men; > 65, women; moderate CVD risk (10%−19%)	Median, 5	• No difference in composite endpoint (CV death, MI, UA, stroke, or TIA; HR 0.96, 95% CI, 0.81−1.13, $P = 0.60$) • More (mild) gastrointestinal bleeding (HR 2.11, 95% CI, 1.36−3.28, $P = 0.0007$)
ASCEND (ASCEND Study Collaborative Group et al., 2018)[48]	≥ 40; diagnosis of DM; no known CVD	Mean, 7.4	• 1.1% absolute reduction in serious vascular events (HR 0.88, 95% CI, 0.79−0.97, $P = 0.01$) • 0.9% absolute increase in major bleeding (HR 1.29, 95% CI, 1.09−1.52, $P = 0.003$)

ARRIVE, **A**spirin to **R**educe **R**isk of **I**nitial **V**ascular **E**vents; ASCEND, **A** **S**tudy of **C**ardiovascular **E**vents i**N** **D**iabetes; ASPREE, ASPirin in Reducing Events in the Elderly; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; DM, diabetes mellitus; HR, hazard ratio; MI, myocardial infarction; TIA, transient ischemic attack; UA, unstable angina.

Guidelines from major CV societies have been updated, with most now recommending against the routine use of aspirin for primary prevention in older adults (Table 2). The most-recent 2023 Canadian Cardiovascular Society guidelines for the use of antiplatelet therapy recommend against the routine use of ASA in primary prevention.[53] The 2019 American College of Cardiology/American Heart Association guideline on the primary prevention of CV disease specifies that ASA should not be used for primary prevention in individuals at high risk of bleeding,[54] which includes patients with a history of gastrointestinal bleeding, peptic ulcer disease, age > 70 years, thrombocytopenia, coagulopathy, chronic kidney disease, and the concurrent use of other medications that increase bleeding risk, such as nonsteroidal anti-inflammatory drugs, direct oral anticoagulants, and warfarin.[54] In keeping with the principle of "do no harm," we recommend discontinuing ASA use for primary prevention in patients aged > 70 years and those at high risk of bleeding.

Table 2. Guidelines on the use of acetylsalicylic acid for primary prevention

Guideline	Age, y, or population	Statement
CCS (Bainey et al.,[53] 2024)	N/A	Recommends against the routine use of ASA for primary prevention of ASCVD, regardless of sex, age, or diabetes, in patients without ASCVD
USPSTF(Davidson et al.,[88] 2022)	40−59	In adults who have a >10%, 10-y CVD risk, the decision to initiate ASA should be an individual one; small net benefit
	≥ 60	Recommends against initiating low-dose aspirin use for primary prevention
ACC/AHA (Arnett et al.,[54] 2019)	40−70	Might be considered among select adults who are at higher ASCVD risk but not at increased bleeding risk
	> 70	Should not be administered on a routine basis
ESC (Visseren et al.,[89] 2021)	Low or moderate CV risk	Not recommended

ACC, American College of Cardiology; AHA, American Heart Association; ASA, acetylsalicylic acid; ASCVD, atherosclerotic cardiovascular disease; CCS, Canadian Cardiovascular Society; CV, cardiovascular; CVD, cardiovascular disease; ESC, European Society of Cardiology; N/A, not available; USPSTF, US Preventive Services Task Force.

Does the use of statins for primary prevention provide benefits for adults aged ≥ 75 years?

Substantial evidence supports the benefit of using statins for secondary prevention[55] and primary prevention in individuals aged < 75 years.[56] However, the effectiveness of statins in primary prevention for patients aged ≥ 75 years remains a topic of debate.[57] The Canadian Cardiovascular Society recommends that regular CV risk assessment be conducted using the Framingham Risk Score or the Cardiovascular Life Expectancy Model for those aged ≤ 75 years, to guide statin use.[4] However, no formal recommendation has been made regarding statin use in primary prevention for patients aged > 75 years.[4] International guidelines also lack consensus on this issue.[57]

The **Pro**spective **S**tudy of **P**ravastatin in the **E**lderly at **R**isk (PROSPER trial), a randomized controlled trial that specifically enrolled older adults (aged 70-82 years), and compared pravastatin use to placebo use in primary and secondary prevention.[58] In the primary-prevention group, use of statin therapy did not reduce the combined outcome of coronary heart disease mortality and nonfatal myocardial infarction.[58] A meta-analysis of 28 randomized controlled trials assessed the benefit of statin use for primary prevention in a subgroup of older adults.[59] For patients aged > 75 years who were using

Table 3. Guidelines on blood-pressure targets in older adults

Guideline	Age, y	Threshold to initiate treatment, mm Hg	Blood-pressure target, mm Hg
ESC/ESH (Armitage et al.,[69] 2019)	65−79	SBP ≥ 140	SBP 130−139
	≥ 80	SBP ≥ 160	DBP 70−79
Hypertension Canada (Rabi et al.,[3] 2020)	≥ 75	SBP ≥ 130	SBP < 120
ACC/AHA (Yourman et al.,[70] 2020)	≥ 65	SBP/DBP ≥ 130/80	SBP/DBP < 130/80
ACP/AAFP (Joseph et al.,[71] 2023)	≥ 60	SBP ≥ 150	SBP < 150

AAFP, American Academy of Family Physicians; ACC, American College of Cardiology; ACP, American College of Physicians; AHA, American Heart Association; DBP, diastolic blood pressure; ESC, European Society of Cardiology; ESH, European Society of Hypertension; SBP, systolic blood pressure.

statins for primary prevention, no significant reduction occurred in the incidence of major vascular disease.[59] Notably, only 8% of the participants in the included studies were aged > 75 years. A meta-analysis of 8 trials and 65,383 adults aged 50-75 years found that 2.5 years were needed to prevent one CV event in 100 patients treated with a statin, without evidence of any mortality benefit.[60] The current available evidence suggests that initiating statin therapy for primary prevention in patients aged ≥ 75 years has minimal benefit. Two ongoing trials (Pragmatic Evaluation of Events and Benefits of Lipid Lowering in Older Adults [PREVENTABLE][61] and Statin Therapy for Reducing Events in the Elderly [STAREE][62]) will provide additional evidence regarding the value of primary-prevention statin therapy for older adults.

In addition to considering statin-therapy initiation, an important, common scenario to address is that of patients who were started on statin therapy for primary prevention when they were younger, who are now aged ≥ 75 years. Several observational studies showed that statin-use discontinuation was associated with a higher risk of CV events. A cohort study using French national healthcare databases examined patients aged ≥ 75 years, with no history of CV disease, who were taking statins.[63] Among 120,173 subjects who were followed for an average of 2.4 years, statin-use discontinuation was associated with a 33% increased risk of hospital admission for CV events (HR, 1.33, 95% CI, 1.18-1.50).[63] In a retrospective Italian study of 29,047 participants aged ≥ 65 years who were receiving statin therapy, those who discontinued statin use were propensity-matched 1:1 to participants who maintained the therapy.[64] Participants who discontinued statin therapy had a higher risk of hospital admission for heart failure (HR, 1.24, 95% CI, 1.07-1.43), any CV outcome (HR, 1.14, 95% CI, 1.03-1.26), death from any cause (HR, 1.15, 95% CI, 1.02-1.30), and emergency admissions, with no interaction between the primary and secondary prevention cohorts.[64] Another cohort study in Denmark examined people aged ≥ 75 years who were treated with statins for ≥ 5 years.[65] Among 67,418 subjects, the rate of CV events was higher among people who discontinued statin therapy, compared with the rate among those who continued statin therapy for both primary prevention (HR, 1.32, 95% CI, 1.18-1.48) and secondary prevention (HR, 1.28, 95% CI, 1.18-1.39).[65] Although the findings from these studies are congruent, they are confounded by the observational study design, the uncertainty regarding the reasons for statin-use discontinuation, and a lack of information about the adherence to other CV medications.

One randomized controlled trial involving 381 patients with an estimated life expectancy of 1 month to 1 year[66] showed that the survival rate was similar for those who stopped vs those who continued statin therapy, with a low incidence of CV events in both groups. The group that discontinued statin use reported a significantly higher level of quality of life, as measured by the McGill Quality of Life Questionnaire (which encompasses physical well-being, physical symptoms, psychological symptoms, well-being, and support).[66] Similarly, a systematic review concluded that statin therapy may not be necessary for secondary prevention in patients with severe frailty, as identified by a Clinical Frailty Scale score of ≥ 7.[67] However, the review also acknowledged that extenuating circumstances might occur in which use of statins is justified, despite the patient's frailty.[67] The 2018 American Heart Association guideline gives a IIB recommendation for using a coronary artery calcium (CAC) score for risk stratification in adults aged 76-80 years.[68] In those with a CAC score of zero, avoiding statin therapy is reasonable.[68]

Taking into account the available evidence, deprescription of statins in individuals with severe frailty or those with limited life expectancy, as well as those with a CAC of zero, should be considered. However, these objective measures need to be considered alongside the patient's goals and preferences. For example, some patients might prioritize taking steps to prevent a CV event because they believe it will help them maintain physical function and independence, whereas others may focus more on minimizing their medication burden. These complex analyses require physician guidance. Therefore, consideration of individualized factors and patient preferences is crucial when making decisions about statin therapy.

What is the optimal blood-pressure target for older, frail adults?

No consensus has been developed, among Canadian,[3] European,[69] and American CV societies,[70,71] in their respective hypertension management guidelines, regarding the definition of older adults, the threshold for initiating antihypertensive treatment in older adults, or the recommended blood-pressure targets for older adults (Table 3). A recent systematic review of 13 hypertension treatment guidelines highlighted the lack of specificity and clarity in the recommendations regarding blood pressure−lowering treatment among the frail population.[72] The Hypertension Canada guideline suggests initiating antihypertensive therapy when systolic blood pressure is > 130 mm Hg, for patients aged ≥ 75 years,[3] a group regarded as being high-risk. The target systolic blood pressure for this population is < 120 mm Hg.[3] These recommendations are based on the findings from the **S**ystolic Blood **Pr**essure **In**tervention **T**rial (SPRINT),[73] a randomized, controlled, open-label trial that involved 9361

patients with a systolic blood pressure of ≥ 130 mm Hg, and an increased CV risk, but without diabetes. Participants were randomized to a systolic blood-pressure target of either < 120 mm Hg or < 140 mm Hg. After 1 year of follow-up, those randomized to the lower blood-pressure target had a 36% relative risk reduction, and a 1.6% absolute risk reduction in the primary composite outcome of myocardial infarction, acute coronary syndrome, stroke, heart failure, and CV death.[73] The reduction in CV events and the lower incidence of all-cause mortality with a lower blood-pressure target persisted at 3 years of follow-up.[74] In a prespecified subgroup analysis, benefit was achieved in all age groups, including those aged > 75 years.[73]

However, concerns have been raised about the generalizability of the SPRINT trial results to all older patients.[75] The exclusion of certain populations, such as adults residing in long-term care facilities, those with orthostatic hypotension, or individuals with a life expectancy of < 3 years limits the applicability of the trial's findings to the older population with frailty.[75] Notably, when the SPRINT inclusion criteria were applied to community-dwelling adults aged ≥ 75 years in a prospective cohort study, the rates of injurious falls and syncope were 5 times higher than those in the standard care group of the trial, which raises concerns about the generalizability of results.[76] In addition, the intensive-therapy group in the SPRINT trial did experience an increased risk of hypotension, syncope, electrolyte abnormalities, and acute kidney injury,[75] which are significant events for older adults with frailty, who may have limited physiological and functional reserve to use to recover from such complications. An interesting point is that mortality data from the SPRINT trial appear to be discordant with results of other trials that assessed blood-pressure targets. A Cochrane review, of 11 studies and 38,688 patients examining blood-pressure targets in adults with hypertension, found that lower blood-pressure targets did not reduce mortality incidence.[77]

Mallery et al. published a consensus guideline for blood-pressure targets for older adults with frailty in the Canadian context.[43] According to the guideline, for patients with severe frailty (ie, those with a Clinical Frailty Scale score of ≥ 7,[32] indicating dependency in completing basic activities of daily living), treatment should be considered when systolic blood pressure is ≥ 160 mm Hg, with a target, seated systolic blood pressure of 140-160 mm Hg.[43] Clinicians should taper or discontinue use of antihypertensives if seated systolic blood pressure is < 140 mm Hg or if orthostasis is present.[43] Similarly, the American Heart Association recommended a systolic blood-pressure goal of 150 mm Hg for older adults who have lost autonomy in conducting activities of daily living or who have a limited life expectancy.[44] Use of antihypertensive therapy should be re-evaluated when systolic blood pressure is < 130 mm Hg, or if orthostatic hypotension is present.[44] Although the 2 guidelines have slight differences in blood-pressure targets, both provide guidance on when to stop antihypertensive therapy in patients with frailty.

When deprescribing antihypertensives, the class of medication needs to be considered. For example, in patients with hypertension and orthostatic hypotension, priority should be given to discontinuing antihypertensives that have a higher risk of precipitating orthostasis, such as alpha-blockers, alpha-agonists, and beta-blockers.[78] Before deciding whether to discontinue use of a medication, another important point to consider is whether the antihypertensive agent has another indication, such as rate control for patients with atrial fibrillation, or treatment of heart failure in patients with reduced ejection fraction.[43]

A multicentre, cluster-randomized, controlled trial conducted in Norwegian nursing homes investigated the impact of systematic medication reviews on antihypertensive prescriptions.[79] The study included 765 patients aged ≥ 65 years who were taking at least one antihypertensive medication. Most subjects had dementia of various stages (94% in the intervention arm; 89% in the control arm). CV comorbidities were prevalent, with atrial fibrillation, heart failure, and stroke being the most common. At baseline, each patient used an average of 9.2 ± 3.5 medications, and 1.6 ± 0.7 antihypertensives. Clusters were randomized to either the intervention arm, in which physicians received mentoring on how to perform systematic medication review, or the control arm, in which usual care was provided. The intervention group showed a higher incidence of deprescription of antihypertensive medications, compared to that in the control group (32% vs 10%). Important to note is that such deprescription did not impact patients' pulse or blood pressure, but it did lead to a decrease in the number of hospitalizations.

Taken together, these findings indicate that when establishing blood-pressure targets, consideration of the patient's overall health and functional status is important. In addition, they show that factors such as frailty, orthostatic hypotension, life expectancy, and medical comorbidities should be considered, as they may indicate a need for less-intensive treatment, a higher blood-pressure target, or avoidance of a specific antihypertensive agent that may increase the severity of orthostasis.

Who should initiate the deprescribing process?

The party responsible for deprescribing CV medications depends on multiple factors and may vary for each patient. Based on a systematic review of 22 studies, the establishment of a positive, trusting relationship between older patients and their attending clinicians is crucial for successful deprescription of CV medications.[80,81] Providing gradual deprescription, ongoing support, and follow-up care also were identified as essential contributors to positive outcomes.[82] Although primary-care providers play a key role in the deprescribing process, they may be hesitant to deprescribe CV medications, due to concerns about interfering with another physician's treatment plan.[14] Additionally, patients may be reluctant to discontinue use of medications when they were initiated by specialists, especially if they have been told that the medication is necessary for them lifelong.[82] Therefore, cardiologists play a crucial role in leading the deprescribing process.

These issues highlight the importance of a collaborative, multidisciplinary approach to deprescribing CV medications, with effective communication among healthcare providers.[83] The circle of care may include the patient's family physician, cardiologist, and pharmacist. As specialists, cardiologists are key influencers in managing CV conditions. Well-informed cardiologists can guide and collaborate more effectively with primary-care providers and other healthcare

professionals. A recent review outlined a framework for deprescribing CV medications that includes medication reconciliation, risk assessment, medication use discontinuation, and implementation of a monitoring protocol.[84] When a cardiologist identifies a CV medication for which use should be tapered or discontinued, they can implement this change and communicate with the patient, the patient's primary-care physician, and the community pharmacist, regarding the rationale for the change and the need for subsequent monitoring. Cardiologists should provide patients and their pharmacists with prescriptions for tapering doses or stopping medications. If tapering use of a medication is recommended, pharmacists can ensure that the correct doses of medications are dispensed. If use of a medication is to be discontinued, a prescription for such prompts the pharmacist to cancel out any remaining refills, and to update the patient's electronic medication records. Collaboration between primary-care providers and specialists enhances comprehensive care. For example, if falls due to hypotension are a concern, the cardiologist may recommend deprescription of antihypertensives. The patient's primary-care physician can address the patient's fracture risk and consult a geriatrician for fall-prevention strategies. Overall, although cardiologists play an important role in initiating the deprescribing process, the involvement of a range of healthcare providers ensures that all aspects of the patient's care are considered.

What are the psychological implications of the deprescription of medications?

A survey of 453 physicians—40.6% geriatricians, 40.2% general internists, and 19.2% cardiologists—identified patient reluctance regarding deprescription as a major barrier to its implementation.[14] Patients may not understand the intent behind deprescription. Instead of recognizing it as a personalized intervention to reduce their medication burden and improve their quality of life, they may perceive deprescription as being age-based discrimination.[80] Patients' limited knowledge about medications also can hinder their confidence and willingness in engaging in discussions about deprescription.[81,85] However, fostering open and respectful communication about the rationale behind deprescription, and its potential benefits, can empower patients and caregivers to participate in shared decision-making. An interesting finding is that patients' reluctance regarding deprescription may reflect the perceptions of physicians rather than patient attitudes. A meta-analysis and systematic review of 40 studies involving 10,816 participants found that 84% of patients and 80% of caregivers were willing to discontinue at least one medication if their physician suggested that doing so was feasible.[86,87]

Patients may be hesitant to accept the deprescription of CV medications, owing to apprehension about potential negative consequences.[82] They may adhere to the adage "If it ain't broke, don't fix it," which can lead to clinical inertia. However, the pharmacokinetics and pharmacodynamics of medication use undergo significant changes with age,[36,37] resulting in a shifting risk–benefit ratio over time. Although an adverse drug reaction can provide strong motivation for deprescribing the medication,[81] clinicians should take a proactive approach by discontinuing use of medications that have a high risk of adverse reactions, before these are manifested. In addition, recognizing that patients may lack awareness of existing adverse effects, due to acclimation, is important. To address patient concerns, depicting deprescription as a process, rather than an isolated event, may be helpful.[80,82] Reassuring patients and caregivers that potential side effects are being monitored, with a contingency plan to reintroduce the medication or resume the original dose if needed, can provide them with a sense of control.[82] Such empowerment ensures that patients and their families feel comfortable when considering the possibility of embarking on the deprescribing process.

Conclusion

CV medications can benefit older adults significantly, but they also increase polypharmacy and carry the potential for inducing harm. Polypharmacy is a common issue among older adults in Canada, and it is associated with negative health outcomes. The decision to start the deprescribing process involves conducting a critical appraisal of the available literature and an individualized risk–benefit analysis. However, many trials lack the representation of older adults with frailty, which limits the generalizability of the trial findings to this population. As a result, limited evidence supports deprescribing decision-making, especially for older adults with frailty.

Based on the existing evidence, ASA use should be discontinued for primary prevention in patients aged > 70 years, or those with a high risk of bleeding. Uncertainty remains about the benefit of continuing statin therapy in older adults. However, discontinuation of statin therapy can be considered in older patients with severe frailty and/or with a limited life expectancy, taking individualized factors and patient preferences into account. Ongoing trials, such as PREVENTABLE[62] and STAREE,[63] are expected to provide more-definitive evidence on the benefits and risks of statin-therapy use in older adults, which will help in efforts to further refine recommendations.

Finally, providers should consider tapering or discontinuing antihypertensive treatments in older adults with significant frailty, whose systolic blood pressure is < 140 mm Hg, and/or those with orthostatic hypotension. No one-size-fits-all approach to implementing the deprescribing process is available, but decision-making surrounding this process always should prioritize patient goals. For older adults who are healthy and robust, aggressive management of risk factors may be reasonable. However, for older adults with advanced frailty, healthcare professionals must carefully consider whether the benefits of medication use outweigh the potential harms. Ideally, the deprescribing process should involve shared decision-making among physicians, other health professionals, and patients and/or their substitute decision-makers, with the common goal of improving patient outcomes.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a narrative review of published literature; therefore the IRB did not require consent.

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