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ARTICLE

Deprescribing antihypertensive drugs in frail older adults

SUMMARY

Antihypertensive drugs are commonly used by older adults because of the high prevalence of cardiovascular disease and its risk factors, and the increased absolute benefit of blood pressure reduction with increasing age.

Clinical trials of blood pressure reduction in older adults have generally excluded older adults with multimorbidity, frailty and limited life expectancy. In this population, the benefit–harm ratio of aggressive blood pressure lowering may become unfavourable; a more relaxed blood pressure target may be appropriate; and deprescribing (cessation or dose reduction) of one or more antihypertensive drugs can be considered.

Before deprescribing an antihypertensive drug, it is important to consider other indications for which it may have been prescribed (e.g. heart failure with reduced ejection fraction, diabetic nephropathy, atrial fibrillation).

Evidence from randomised controlled deprescribing trials indicates that it is possible to deprescribe antihypertensives in frail older people. However, some patients may experience an increase in blood pressure that warrants restarting the drug. There are limited data on long-term outcomes (follow-up in deprescribing trials ranged from 4 to 56 weeks).

The risk of adverse outcomes associated with deprescribing, such as withdrawal effects, can be minimised through appropriate planning, patient engagement, dose tapering and monitoring.

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Introduction

Antihypertensive drugs, and often more than one, are commonly used by older adults (65 years and over) because of the high prevalence of cardiovascular disease and its risk factors in this population, and the increased absolute benefit of blood pressure reduction with increasing age.[1] In most older people there are good reasons to continue antihypertensive therapy, but in some cases the benefits of continued prescribing may not outweigh the harms. This is most likely in people who are frail (increased vulnerability to stressors due to decline in reserve and function across multiple physiological systems),[2] or whose goals of care have changed because of limited life expectancy. In this group, blood pressure targets may be relaxed and deprescribing (dose reduction or cessation) of one or more antihypertensive drugs may be considered.[1,3]

Observational studies in residential aged care and hospital wards have reported that deprescribing antihypertensives occurs in 11 to 41% of frail older people with low blood pressure and either a history of falls, advanced dementia or limited life expectancy.[4-6]

The aim of this article is to discuss when deprescribing antihypertensives may be considered in frail older adults, and how the general principles of deprescribing apply to antihypertensives.

Decisions on deprescribing of antihypertensive drugs must consider all the indications for which they are prescribed, including heart failure, diabetic nephropathy and atrial fibrillation. The focus of this article is on frail older adults who are using antihypertensive drugs to lower blood pressure or for primary prevention of cardiovascular disease, as the evidence base for deprescribing is mainly in this group.

Evidence for lowering blood pressure in older adults

Hypertension is a major modifiable risk factor for cardiovascular events and mortality in older people. Australian and international clinical guidelines recommend that blood pressure should be controlled in people at high risk of cardiovascular disease, unless contraindicated or clinically inappropriate,[7,8] owing to the established benefit in preventing cardiovascular events and reducing mortality.[9,10]

There is no chronological age above which antihypertensive drugs are contraindicated. Randomised controlled trials have reported that

lowering elevated blood pressure in older people reduces the risk of cardiovascular events and death, including in people aged over 80 years.[11,12]

However, trials of antihypertensive drugs in older adults have generally been conducted in fitter and healthier populations than many of the people who are prescribed these drugs in practice.[13] For example, people with dementia, with limited life expectancy or living in residential care were excluded from pivotal studies of antihypertensives that recruited older people.[11,12] There is limited evidence about the benefits of ongoing antihypertensive therapy in complex older adults with multimorbidity, polypharmacy and frailty.[3,13-15]

Balancing the benefits and harms of antihypertensive drugs in frail older adults

Antihypertensive drugs can contribute to drug-related harms (e.g. falls, syncope, electrolyte disturbances, acute kidney injury), particularly in older adults with multimorbidity, polypharmacy and frailty.[3,16] Specific adverse effects vary by antihypertensive medication class and have been summarised elsewhere.[17]

Patients may be started on antihypertensive drugs when they are younger (often in their 40s to 60s), but the balance of potential benefits and harms can change over the ensuing decades with changing physiology, comorbidities, concomitant medicines and goals of care, such that the balance of benefits to harms may eventually become unfavourable. Sometimes an antihypertensive drug that was once appropriate may become a candidate for deprescribing.[15,18]

What is deprescribing?

Deprescribing is the process of trialling dose reduction or cessation of a medication where the current risk of harm outweighs the potential benefit for the individual, supervised by a clinician, with the goal of improving outcomes.[19] It does not include temporary cessation, such as withholding an antihypertensive drug because of intercurrent illness (e.g. low blood pressure due to sepsis).

Evidence for deprescribing antihypertensive drugs

There is a small but growing body of evidence examining the feasibility and safety of deprescribing antihypertensives in older adults. While the short-term evidence is supportive, there is uncertainty regarding the longer-term benefits and harms.[20]

A Cochrane review of 6 randomised controlled deprescribing trials (total 1073 participants, followed up for 4 to 56 weeks) reported that it may be feasible to stop one or more antihypertensive drugs used for hypertension or primary prevention of cardiovascular disease in adults aged 50 years and older. Up to one-third of participants in the deprescribing group (compared with up to 15% in the continuation group) experienced raised blood pressure or other clinical criteria that required restarting of therapy or removal from the study. Systolic blood pressure was higher in the deprescribing group than the continuation group (mean difference 9.75 mmHg). The impact of deprescribing antihypertensive drugs on cardiovascular events and all-cause mortality was uncertain; odds ratios for these outcomes were increased in the deprescribing group compared with the continuation group, but with wide confidence intervals dipping below 1.0.[21] No studies included in the review reported the frailty of participants.

The Optimising Treatment for Mild Systolic Hypertension in The Elderly (OPTIMISE) study was a randomised controlled deprescribing trial, published after the Cochrane review. It involved 569 patients over 80 years old with clinic systolic blood pressure lower than 150 mmHg who were using 2 or more antihypertensive drugs and, in the investigators' opinion, could potentially benefit from medication reduction due to polypharmacy, comorbidity, nonadherence or frailty. Patients were randomised to cessation of one antihypertensive drug using a deprescribing algorithm, or to standard care. There was no difference between the groups in the proportion of patients who maintained systolic blood pressure below 150 mmHg at 12 weeks follow-up, and no difference in serious adverse events or health-related quality of life. Systolic blood pressure was 3.4 mmHg higher in the deprescribing group than the continuation group, and medication reduction was sustained in 66.3% of patients.[22]

In an Australian observational study of 239 frail older people who had an unplanned hospital admission and were discharged to a nursing home, 44 patients (18.4%) had 52 antihypertensive drugs ceased in hospital. Deprescribing was not limited to drugs that had been prescribed for hypertension or primary prevention of cardiovascular disease (indications were not reported). Patients who had antihypertensive drugs deprescribed had increased 90-day mortality (adjusted odds ratio 2.27, 95% confidence interval 1.00 to 5.12, p=0.05) compared with those without deprescribing. The authors suggested this outcome could be due to residual confounding by indication. For example, older people with low blood pressure are likely to have antihypertensive medications ceased or reduced, and these patients are also known to have higher mortality than older people with normal or high-normal blood pressure. Blood pressure measurements before and after deprescribing were not reported.[6]

When to consider deprescribing antihypertensive drugs

There is limited evidence to guide decisions about when to deprescribe antihypertensive drugs. While current Australian and international guidelines recommend a blood pressure target of less than 140/90 mmHg when managing hypertension,[7] tight blood pressure control may not be appropriate in some older adults because of changes in physiology and sequalae of harms (e.g. outcomes of a fall). Some studies have reported an increased risk of cardiovascular events in older adults with very low systolic (less than 120 mmHg) or diastolic (less than 65 mmHg) blood pressure.[17] The STOPPFrail tool, developed through an expert consensus process, recommends a systolic blood pressure target of 130 to 160 mmHg in older adults who are frail and have limited life expectancy.[23]

The 2023 European Society of Hypertension Guidelines for the management of arterial hypertension recommend 'Reduction of [antihypertensive] treatment can be considered in patients aged 80 years or older with a low systolic blood pressure (less than 120 mmHg) or in the presence of severe orthostatic hypotension or a high frailty level'.[8] They note that antihypertensive deprescribing should be conducted with caution because of a lack of data on the optimal process and likely outcomes.[8]

In lieu of strong evidence on who is suitable for deprescribing antihypertensives, clinicians can be guided by factors that increase risk of harm or signal a decrease in benefit or necessity of the medication, such that potential harms outweigh the benefits.

Review of antihypertensive drugs needs to be undertaken in the context of the patient's overall medication regimen and current symptoms. There may be other medicines contributing to the patient's adverse effects or risk of harm that could be a higher priority for deprescribing (e.g. psychotropic drugs). Deprescribing requires considering the individual's preferences, values and treatment goals.[24-27]

Table 1 provides a protocol for identifying patients in whom it may be appropriate to deprescribe antihypertensive drugs, and individualising deprescribing, based on the CEASE framework.[28]

How to deprescribe

The risk of adverse outcomes when deprescribing, such as withdrawal effects, can be minimised or prevented through appropriate patient engagement, planning, tapering, monitoring and clinical handover.[17,18,20,29,30] If there are other prescribers involved in the patient's care (e.g. a cardiologist), they should also be engaged in deprescribing decisions.

Engage the patient and carer

Engaging the patient and their carer, if relevant, is essential for the process and the success of deprescribing.[31] Key points for discussion include:

- goals of care and preferences
- current experiences with antihypertensive drugs (e.g. tolerability, burden, possible adverse effects)
- why the drug is suitable for deprescribing (e.g. no longer of benefit, reduction of harms)
- identifying and addressing any fears about deprescribing
- emphasising that deprescribing is a trial, with a plan for monitoring and restarting the drug if necessary
- how to recognise and respond to any withdrawal symptoms
- intrinsic and extrinsic factors that can influence blood pressure (e.g. weather, illness, other medications), which means their antihypertensive regimen may need to be adjusted over time
- advice on modifiable lifestyle cardiovascular disease risk factors where appropriate.

Decide which antihypertensive drug(s) to deprescribe

The CEASE framework (Table 1) can help with deprescribing decisions. After obtaining a complete medication history, consider the indications and evidence for cardiovascular benefits for each of the patient's antihypertensive drugs, including whether there are any other indications (e.g. angiotensin converting enzyme inhibitors for diabetic nephropathy or heart failure) that could warrant continued treatment. Next consider harms that may be related to specific drugs, such as thiazide diuretics exacerbating gout.

Individual patient perceptions, preferences and priorities for the choice and order of drugs for withdrawal are likely to be major determinants of the success of deprescribing. In some cases, where there is an ongoing indication for blood pressure lowering but the patient has an adverse reaction to a specific antihypertensive, switching to a different antihypertensive may be more appropriate than deprescribing.

Deprescribe one drug at a time

One antihypertensive should be reduced or stopped at a time unless there is an urgent need to stop more than one. Adverse drug withdrawal events are less likely, and easier to attribute to a specific drug, if deprescribing occurs one drug at a time. Where possible, patients on a fixed-dose combination

Table 1 Deprescribing protocol for antihypertensive drugs based on the CEASE framework[28]

Steps	Description	Considerations
C: current drugs	Ascertain all drugs the patient is currently taking and their indication(s)	• Indication(s) for the patient's antihypertensive drug(s): – caution required if there is an indication other than hypertension (e.g. heart failure with reduced ejection fraction, diabetic nephropathy), evidence of target organ damage, or a history of secondary or malignant hypertension • Current blood pressure and individualised target: – consider patient's comorbidities, frailty severity, life expectancy, and treatment goals and preferences [NB1] • Other drugs that may affect blood pressure (e.g. sodium-glucose co-transporter 2 inhibitors) or increase the risk of harm (e.g. drugs that increase falls risk)
E: elevated risk	Consider if the patient is at elevated risk of (or experiencing) harm from any of their drugs	• Antihypertensive adverse effects, including: – drug- or class-specific adverse effects (e.g. oedema with calcium channel blockers) – symptoms related to low blood pressure or orthostatic hypotension (e.g. light-headedness, dizziness) [NB2] [NB3] • Prescribing cascades (where a drug is prescribed to manage the adverse effects of another drug). For example: – antihypertensive prescribed following initiation of a nonsteroidal anti-inflammatory drug – drugs prescribed for gout in a person using a thiazide diuretic • Drug–drug interactions
A: assess	Assess the current benefit to harm ratio for each drug	• Strength of indication(s) (likely benefits) for each drug • Presence and severity of existing adverse effects • Risk of future harm associated with continuing treatment: – consider patient factors that may increase risk, such as frailty, impaired cognition, comorbidities, medication nonadherence and other drugs
S: sort and prioritise	Prioritise drugs for deprescribing, according to benefit, harm, ease of stopping and patient preference	• When multiple antihypertensive drugs are being used, prioritise drug(s) with the weakest indication or highest risk of harm
E: eliminate	Implement a discontinuation regimen, and monitor closely for withdrawal syndromes or rebound symptoms that may require restarting treatment	• Usually one drug should be reduced or stopped at a time • The deprescribing regimen (e.g. rate of taper) should take into consideration: – urgency of deprescribing (e.g. whether there are existing adverse effects) – risk of withdrawal syndrome – availability of monitoring (withdrawal may be done more rapidly in a hospital or aged-care setting) – practicality of tapering (e.g. whether the person or their carer can manage a complex tapering regimen) • Monitor for changes in blood pressure and adverse drug withdrawal effects

NB1: There is limited evidence to guide the selection of an optimal blood pressure target for frail older adults. The target range needs to be individualised based on the person's goals of care, and assessment of potential benefits and harms. As a guide, the STOPPFrail consensus tool for identifying potentially inappropriate medicines in frail older adults with limited life expectancy recommends a systolic blood pressure target of 130 to 160 mmHg.[23] Systolic blood pressure below 120 mmHg, and diastolic blood pressure below 60 mmHg, should be avoided in frail older adults.[3,8,17]

NB2: Orthostatic hypotension is defined as more than a 20 mmHg fall in systolic blood pressure or more than a 10 mmHg fall in diastolic blood pressure on standing.

NB3: Not all antihypertensive drugs are associated with orthostatic hypotension.[1]

antihypertensive should be converted to individual drugs to facilitate deprescribing one drug at a time.

There may be circumstances when deprescribing more than one antihypertensive drug concurrently is appropriate; for example, if the patient is experiencing significant adverse effects related to the overall regimen (e.g. severe hypotension). This should usually occur in a supervised setting with close monitoring (e.g. in hospital).

Taper the dose

In most cases, antihypertensive doses should be tapered before stopping the drug.[17,18,20,29,30] Abrupt cessation of beta blockers can lead to a rebound phenomenon of angina, anxiety, severe hypertension, tachycardia and can cause a myocardial infarction. Clonidine can also cause a withdrawal syndrome if it is not tapered. While the other classes of antihypertensive drugs have not been clearly

associated with withdrawal effects, abrupt cessation can lead to rapid return of hypertension, or in the case of diuretics, fluid accumulation.[17,20,29,30]

Tapering also enables identification of the lowest effective dose if the drug cannot be completely stopped. Additionally, tapering may encourage patient acceptance of, and comfort with, deprescribing.[31]

Although there is limited evidence to guide the process of deprescribing antihypertensive drugs, a general approach is to taper the dose by 25 to 50% every 4 weeks. A faster rate of taper or immediate cessation may be required if the patient is experiencing adverse reactions to antihypertensive treatment, and there is a low risk of drug withdrawal effects or a high level of supervision with close monitoring is available.

Written instructions and adherence aids are often required to support complex deprescribing regimens. Currently there are no widely available patient resources for deprescribing antihypertensives, but resources for other drug classes could be adapted.[21,32]

Monitor outcomes and provide clinical handover

Monitor blood pressure and watch for symptoms of withdrawal or rebound at every tapering step. Continue to closely monitor blood pressure for at least 4 weeks after cessation, followed by ongoing routine monitoring. The frequency and method of ongoing monitoring should be individualised based on the patient's treatment goals.[8,10]

Document the deprescribing plan and outcomes in the patient's medical record and clinical handover summary where relevant. This should include the reason for deprescribing, the targeted drug(s), the tapering schedule, the monitoring plan, and the threshold for reinstating therapy.

Conclusion

Antihypertensive drugs have established benefits in cardiovascular disease risk reduction in older adults. Use of multiple antihypertensives is common and, while this can be appropriate and beneficial in many cases, their continuation should be regularly reviewed. Deprescribing one or more antihypertensive drugs may be considered when the potential benefits are outweighed by the risk of harms, or no longer align with the patient's goals of care. <

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Sarah Hilmer is a member of the Australian Deprescribing Network Executive Committee, and chairs the New South Wales Therapeutic Advisory Group and Sydney Health Partners Geriatric Medicine Clinical Academic Group.

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