Review

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Antihypertensive treatment in people of very old age with frailty: time for a paradigm shift?

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The optimal management of hypertension in individuals aged 80 years or older with frailty remains uncertain due to multiple gaps in evidence. Complex health issues, polypharmacy, and limited physiological reserve make responding to antihypertensive treatments unpredictable. Patients in this age group may have limited life expectancy, so their quality of life should be prioritized when making treatment decisions. Further research is needed to identify which patients would benefit from more relaxed blood pressure targets and which antihypertensive medications are preferable or should be avoided. A paradigm shift is required in attitudes towards treatment, placing equal emphasis on deprescribing and prescribing when optimizing care. This review discusses the current evidence on managing hypertension in individuals aged 80 years or older with frailty, but further research is essential to address the gaps in knowledge and improve the care of this population.

Keywords: blood pressure, deprescribing, frailty, hypertension, old age

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; RCTs, randomized controlled trials

INTRODUCTION

Blood pressure (BP)-loweringtreatments are used by over 25% of all adults and 75% of adults older 75 years [1]. Typically started in middle age for primary cardiovascular prevention, they tend to be used life-long. It is estimated that in the UK alone, more than 200 000 people aged 80 or more with frailty receive treatment for hypertension [2–4]. However, the optimal management of hypertension in very old individuals with frailty remains unclear. Decreased physiological reserves and increased vulnerability to stressors in people with frailly increase the risk of falls, hospital admissions, loss of independence and death. Complex health issues and polypharmacy in these individuals make the response to antihypertensive treatments less predictable. Given the limited life expectancy, such people are more likely to prioritize the quality of life over uncertain longevity benefits calling for identifying knowledge gaps and research to improve care for this population [5].

Cardiovascular clinical trials are usually designed to identify populations who benefit from starting a drug [6,7]. It is often unclear when the benefits of the treatment no longer outweigh the risks and the treatment needs to be reduced or stopped. Treatments for chronic conditions are often much longer than clinical trials. Trials exclude people with multi-morbidity and polypharmacy, typical in the frail elderly population. This review article provides an overview of the evidence of optimal antihypertensive pharmacotherapy in people aged 80 years or more living with frailty. Randomized controlled trials (RCT) of antihypertensive treatments and deprescribing in hypertension have been identified from recent systematic reviews detailed below, with a critical appraisal of relevant studies. Observational studies have been selected from PUBMED searches using keywords ('hypertension', 'treatment', 'frailty') and ('hypertension', 'deprescribing').

HYPERTENSION, AGEING AND FRAILTY

Blood pressure (BP) is a key physiological characteristic crucial for tissue perfusion, physical activity and adaptation to various stressors. BP regulation involves multiple body systems, including the heart, muscles, kidneys and neuroendocrine system. Even physiological ageing affects BP control (Fig. 1). Various inter-linking pathophysiological mechanisms are evident.

Arterial wall stiffening decreases arterial recoil during the cardiac cycle, increasing systolic BP, decreasing diastolic BP, and reducing tissue perfusion [8]. An increase in cardiac stroke volume on exertion may be particularly difficult to accommodate by stiff arteries, which may not be reflected by assessments done at rest. Oscillometric BP

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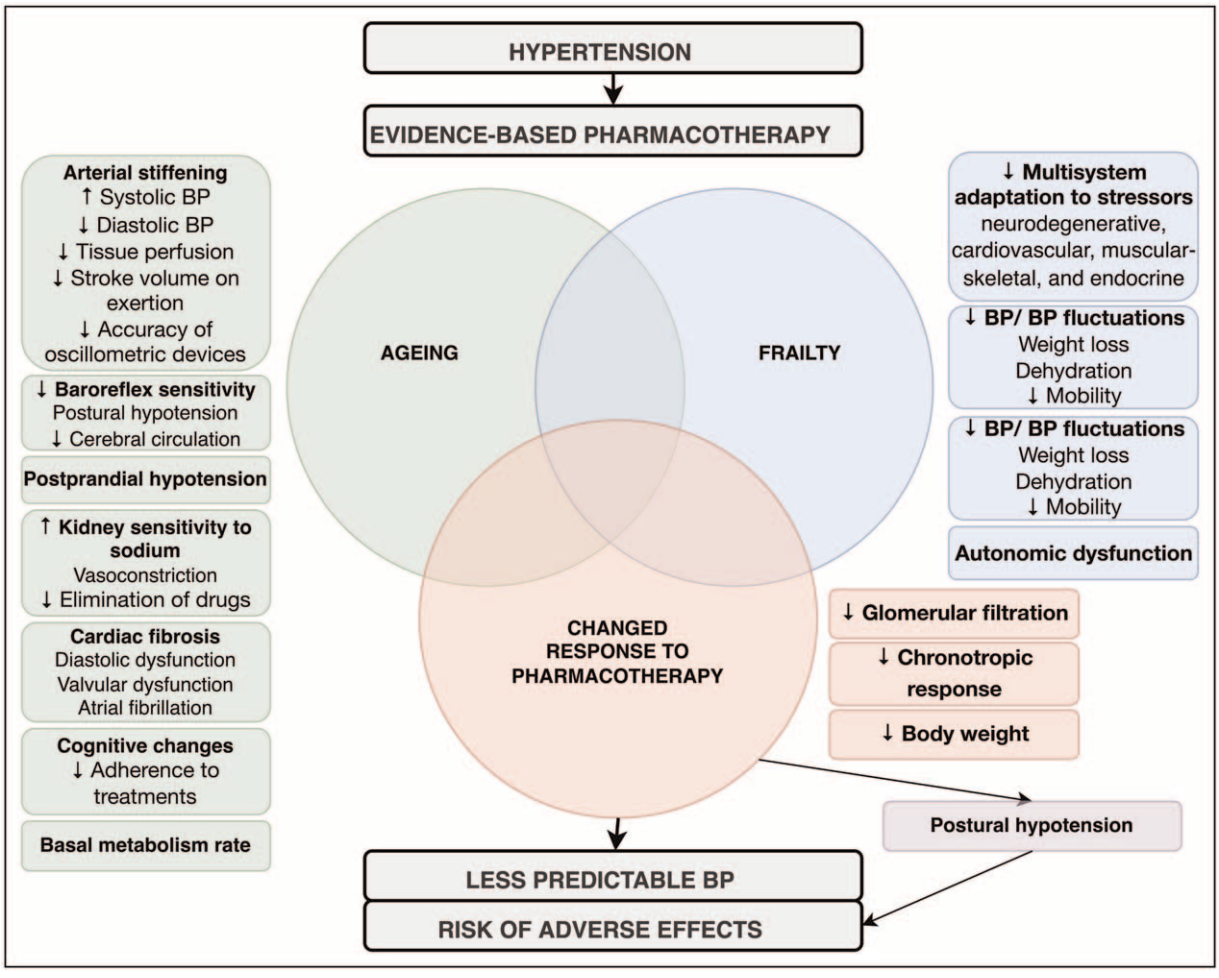

FIGURE 1 Factors affecting blood pressure control in older patients with frailty. Both ageing and frailty status lead to important changes in blood pressure (BP) regulation and response to pharmacotherapy. In some patients, this may result in a less predictable risk/benefit balance from antihypertensive treatment.

devices may overestimate systolic BP and underestimate diastolic BP compared to sphygmomanometers. The error is proportional to arterial stiffening and is hard to establish for individual patients [9].

Reduced baroreflex sensitivity also contributes to postural hypotension observed in 18% of older people, leading to falls [10–12]. Postural hypotension worsens cerebral circulation, already disturbed by cerebral vascular changes and is associated with cerebrovascular events in older hypertensive patients [13].

Postprandial hypotension is common in older people (one in three may be affected), especially in the presence of autonomic dysfunction (e.g. diabetes, chronic kidney disease and Parkinson's disease) [14]. Postprandial hypotension is not part of routine clinical assessment in older people with frailty and is underdiagnosed. Its assessment may improve with the expansion of home BP monitoring. Postprandial hypotension has shared mechanisms with orthostatic hypotension related to autonomic dysfunction, a significant negative prognosticator in older people with potential iatrogenic complications of antihypertensive treatments [15]. Similar to orthostatic hypotensive, postprandial hypotension may remain asymptomatic until cerebral flow autoregulation exhausts its autoregulatory mechanisms.

Increased kidney sensitivity to sodium due to a functional decline in sodium/potassium and calcium adenosine triphosphate pumps leads to vasoconstriction and increased peripheral resistance [16]. Age-related decline in glomerular filtration may reduce the elimination of antihypertensive drugs potentiating their BP-lowering effects [17].

Cardiac fibrosis (i.e. diastolic dysfunction) and cardiac valve fibrosis impair cardiac haemodynamics and the ability to adequately increase cardiac output during exercise [18]. Impaired cardiac filling may reduce cardiac output due to impaired venous return, ventricle wall stiffness, and impaired chronotropic response.

Other important mechanisms of BP dysregulation include neurogenerative processes affecting the autonomic nervous system, reduced muscle mass and/or strength limiting the effects of muscle pump, decreased blood volume, and reduced vasopressin production. The age-related changes are even more prominent when health reaches the state of frailty, a clinical state characterized by a decrease in homeostatic reserves, vulnerability to endogenous and exogenous stressors, and increased risk of adverse health-related outcomes [19]. Frailty is featured by multisystem changes, including neurodegenerative, cardiovascular, musculoskeletal, and endocrine dysfunction. They disturb maintenance of BP,

especially in response to the stressors and modulate response to antihypertensive agents that were started and titrated up before frailty [20]. BP may also decrease due to weight loss, dehydration, and polypharmacy. In view of these changes and the high prevalence of co-morbidities and polypharmacy, people of very old age with frailty need special consideration regarding optimal BP targets and antihypertensive treatments.

There is no universally accepted clinical or research method to diagnose and quantify frailty, and its definition varies between studies [20]. Frailty Index identifies frailty based on a 'cumulative deficit' model using routine clinical records of the accumulation of a range of deficits (symptoms, signs, or conditions) [21]. The phenotype model uses more direct measures, such as Gate Speed Test or Timed-Up-And-Go test [20]. Different thresholds can be used for both models and must be considered when interpreting study results.

PRESCRIBING OF ANTIHYPERTENSIVE TREATMENTS

There are no randomized controlled trials (RCTs) directly evaluating hypertension pharmacotherapy in octogenarians with frailty. The concept of frailty was more precisely defined in the mid-late 1990s [22], and earlier RCTs did not systematically collect data to allow frailty attribution. A recent Cochrane review identified six RCTs of antihypertensive treatments in older people (Tables 1 and 2) [23]. Only one of those studies, the HYVET, focused on people aged at least 80 years and assessed their frailty status [24]. All six studies excluded non-ambulatory patients and those with dementia and had restrictions on people with cardiovascular and many other co-morbidities (Table 1). A recent secondary analysis of the SHEP trial showed that the benefit of antihypertensive therapy was limited to people with no limitation of physical ability [25].

The HYVET trial [24] ($n = 3845$) is the key study showing benefits of antihypertensive drugs in people aged ≥80 with sustained systolic BP ≥160 mmHg (target BP <150/90 mmHg). The trial mainly recruited in China and Eastern Europe, with 86 patients from Western Europe and none from North America. Compared to placebo, antihypertensive treatment (indapamide, perindopril) reduced the risk of stroke, heart failure, overall and cardiovascular mortality, with fewer adverse effects. The benefits were seen despite the target BP only being achieved in 48% of the intervention groups (vs. 19% in the placebo group).

TABLE 1. Placebo-controlled RCTs of antihypertensive pharmacotherapy in people aged ≥80 years: demography and baseline characteristics

Age ≥80, *n* (% of total)	HYVET [24]	SHEP [43,82]	SHEP-P [43,83–85]	EWPHBPE [43,86,87]	Syst-Eur [43,86,88]	STOP [43,89]
	3845 (100%)	650 (14%)	85 (15%)	155 (18%)	441 (9%)	235 (14%)
Treatment	Indapamide, perindopril	Chlorthalidone, atenolol, reserpine	Diuretic, other as needed	HCTZ /triamterene methyldopa	Nitrendipine, enalapril, HCTZ	HCTZ/amiloride, atenolol, pindolol, metoprolol
BP inclusion criteria, mmHg	160–199 <110	160–219 <90	>160 <90	160–239 90–119	160–200 <95	180–230 >90 or 105–120
Target SBP, mmHg	<150	159 if >179 or <21 from baseline	<160 and <20 from baseline	NA	<160 and <20 from baseline	<160
Target DBP, mmHg	<80	NA	NA	NA	NA	<95
Follow up, years	2.1	4.2	2.8	3.1	3.1	2.1
Recruitment countries	Europe (Eastern 2144; Western 86) China 1526; Tunisia 70; Australasia 19	US	US	Western Europe	23 countries, mostly Europe (Western, Eastern, 4.5% from the UK)	Sweden
Key exclusion criteria	Cr ≥150, HF on antihypertensives potassium <3.5 or >5.5 mmol/l, gout	Anticoagulants, recent MI/stroke/TIA, HF, cancer, renal failure, DM, alcohol abuse	Depression, CABG within 2 years, diabetes (insulin)	Diabetes (insulin)	Any severe disease cancer, recent MI, liver dysfunction, cannot stand, HF, Cr ≥180, DM	Recent MI/stroke, uncontrolled angina, severe incapacitating illnesses
Frailty assessment	Yes	No	No	No	No	No
Dementia	Excluded	Excluded	Excluded	Excluded	Excluded	Excluded severe MH illness
Ambulatory patients only	Yes	Yes	Yes	Yes	Yes	Yes
Age, years mean [SD]	83 [5]	83 [3]	83 [3]	85 [4]	84 [4]	82 [1]
Baseline BP, mmHg	173/91	173/73	NA	190/99	177/84	197/101
Female, %	60.5	64	74	90	73	68
Smoker, %	6.5	6	NA	6	11	6
Diabetes, %	6.8	8	NA	14	24	12
Myocardial infarction, %	3.1	4	NA	0	9	4

The table presents characteristics of key placebo-controlled randomized trials (RCTs) of antihypertensive pharmacotherapy in older people and presents characteristics of participants who are aged ≥80. The SHEP programme included 14% of Black Americans [91].
BP, blood pressure; CABG, coronary artery bypass grafting; Cr, creatinine (μmol/l), CV, cardiovascular; CVD, CV disease; DM, diabetes, that requires treatment with insulin, GTN, glycerol trinitrate; HCTZ, hydrochlorothiazide HF, heart failure; MH, mental health, MI, myocardial infarction; NA, not available; PAD, peripheral artery disease; SBP, systolic BP; TIA, transient ischemic attack; US, United States.

TABLE 2. Placebo-controlled RCTs antihypertensive pharmacotherapy in people aged ≥80 years: primary and secondary outcomes

	HYVET [24]	SHEP [43]	SHEP-P [43]	EWPHBPE [43]	Syst-Eur [43]	STOP [43]
Fatal or non-fatal stroke, *n*	51/69[a]	14/42	3/3	11/9 (non-fatal)	27/29	14/9
Any death, *n*	196/235	57/59	10/0	58/60	72/53	11/8
CV death, *n*	99/121	25/29	6/0	NA	32/27	7/3
MI/coronary events, *n*	9/12	19/26	3/0	NA	14/11	0/1
New heart failure, *n*	22/57	12/33	4/0	NA	14/15	3/2

The table presents primary and secondary outcomes in people aged ≥80 who took part in placebo-controlled randomized trials (RCTs) of antihypertensive pharmacotherapy.
[a]Treatment group/placebo; CV, cardiovascular; MI, myocardial infarction; NA, not available.

The SPRINT trial [7] was a large RCT ($n = 2636$, 17.1% Black, 6.6% Hispanic) comparing intensive BP lowering (systolic BP <120 mmHg) with standard BP target (<140 mmHg). Although the study did not report findings for those aged ≥80, the mean age of 79.9 years implied that about 50% belonged to this age category. The SPRINT excluded patients with symptomatic heart failure, type 2 diabetes, clinical dementia, expected survival <3 years, unintentional weight loss, postural hypotension, significant psychiatric and behavioural problems, those struggling with regular appointments or nursing home residents. Overall, the trial provides further support for pharmacological BP lowering in older people but gives little insight about people with frailty.

Post-hoc analyses of the HYVET [6] and SPRINT [7] trials did not find a statistically significant relationship between the benefits of antihypertensive treatment and frailty. However, these trials only recruited relatively fit community-dwelling people, excluding those with significant frailty, cognitive decline, many comorbidities, and orthostatic hypotension [6,7,24]. In the HYVET trial, the Frailty Index (FI) was suggestive of moderate frailty in about 14% and severe frailty in about 6% of patients [6]. Withdrawals from the study were nearly two-fold more frequent in severe frailty vs. least frail group. The study did not provide objective assessment of frailty. Although frailty, defined as frailty index >0.21, was recorded in 31% of the SPRINT patients, it is likely that many patients with more severe frailly were excluded. Those with frailty had 20% higher rates of hypotension, syncope, bradycardia, electrolyte abnormalities, injurious falls, or acute renal failure. Hyponatraemia with sodium <130 mmol/l was 1.5-fold more common in the intensive treatment group. Although hyponatraemia was not specifically reported in people with frailty, this is a common and ominous feature of frailty with poor outcomes.

OPTIMAL BLOOD PRESSURE TARGETS AND RISKS OF ANTIHYPERTENSIVE TREATMENTS

BP targets for people aged at least 80 years vary among guidelines. The BP target <150/90 mmHg based on the HYVET trial is currently recommended by NICE [24,26]. However, most guidelines advise stricter BP control of <140/80–90 mmHg influenced by the SPRINT study [7,27,28], but may not suit groups excluded from the trial.

Indeed, observational data show the risks of overtreatment of hypertension in these groups. In a recent UK primary care observational study of 415 980 people older than 75, including 155 821 people with frailty, lower BP values rather than increased BP were related to higher mortality [4]. Systolic BP of 150–159 mmHg compared with the reference range of 130–139 mmHg was associated with reduced mortality, with no increase in strokes or heart failure [4]. There was no excess in mortality associated with diastolic BP ≥90 mmHg in people with moderate-severe frailty aged 75–84 years and in people aged at least 85 years irrespective of frailty status.

The findings are consistent with other observational studies of very old people with frailty receiving antihypertensives, in whom systolic BP <130 mmHg was associated with higher morbidity and mortality [29–34]. Vigorous pharmacological reduction of diastolic BP in older people can reduce coronary perfusion and increase risk of myocardial infarction [35]. In the HYVET trial excessive pharmacological diastolic BP reduction increased risk of incident dementia [36]. Polypharmacy increases the risk of falls, hospital and care home admissions and deaths, especially in the oldest or most frail [37]. Alpha-blockers increase risk of heart failure in older people [38].

In older adults hospitalized for non-cardiac conditions, intensification of antihypertensives at discharge, based on the current guidance, was associated with readmission and serious adverse events, but no reduction in cardiac events within one year [39]. Older people who remain on BP agents despite being hypotensive have increased mortality and hospital admissions [40]. Such occurrences contribute to 6–7% of all acute hospital admissions that are caused by adverse drug reactions at an annual NHS cost in excess of »1 billion [41].

Postural hypotension occurs in more than half of elderly frail nursing home residents [42]. Postural BP changes are highly variable on repeat measurements and can be missed [42]. In an observational study of octogenarians, beta-blocker use was related to postural hypotension [12]. This likely reflects age-related cardiac fibrosis with impaired cardiac chronotropic and inotropic function. In the HYVET, beta-blockers were the only class of antihypertensives independently associated with risk of fractures [hazard ratio (HR) 2.05, 95% confidence interval (CI) 1.03–4.08] [43]. In a 3-year observational study of adults older 70 years, with a previous history of a serious fall injury, a high-intensity antihypertensive treatment was associated with a 2.3-fold increased risk of further injuries [44]. Falls in older people are a common feature of frailly. Because of the high risk of inappropriate postural and reflex hypotension in these patients, the adverse effects of antihypertensive treatments may overweight their benefits. More relaxed BP targets may be more appropriate and shall be agreed upon between the patients and their clinicians [45]. Bradycardia, together with

hypotension, is a pathogenic component of reflex syncope and a likely reason for the risk of beta-blockers in older people. The SynABPM 1 study has shown that ambulatory BP monitoring can identify patients at high risk of reflex hypotension (hypotensive susceptibility), which may help select older patients with daytime hypotensive episodes who may benefit from relaxed BP targets to prevent falls along with considerations for comorbidities, life expectancy, cognitive decline, symptoms impairing quality of life and individual preferences [46]. Unfortunately, the health complexity posed by advanced age, frailty and co-existing comorbidities and polypharmacy makes an informed decision on optimal hypertension management difficult for both clinicians and patients [15]. Ambulatory BP monitoring and dynamic orthostatic tests should be utilized to support the decision, ideally utilizing the multidisciplinary expertise of internists, cardiologists, neurologists, and geriatricians supporting family physicians.

The prevalence of non-adherence is also increased in patients aged over 80 years, likely contributed to by cognitive decline, depression, changing health goals and beliefs, and possibly side effects [47]. As a result, the prescription rates may not reflect the actual use of antihypertensives in this population and the true prevalence of drug intolerance.

Finally, antihypertensive agents may improve frailty, irrespective of their BP-lowering actions. For example, angiotensin-converting enzyme (ACE) inhibitors may directly improve skeletal muscle biochemical function, strength and overall exercise capacity in older people, irrespective of BP [48,49]. ACE inhibitors were commonly used in the HYVET [24] and SPRINT [7] studies, potentially contributing to better outcomes through their effects on muscle.

DEPRESCRIBING OF ANTIHYPERTENSIVE TREATMENTS

Several systematic reviews have synthetized evidence on deprescribing of antihypertensive drugs in the elderly. The 2020 Cochrane review of withdrawal of antihypertensive drugs in older people (i.e. aged $\geq$50) has identified six studies [50]. Another systematic review with different eligibility criteria identified five RCTs (ten different RCTs in total) [51]. However, most of these studies are not relevant to this review (reasons summarized in Online Supplement Table, http://links.lww.com/HJH/C216), leaving only two relevant RCTs discussed below.

The Dutch Discontinuation of Antihypertensive Treatment in Elderly People (DANTE) RCT [52] assessed whether discontinuation of antihypertensive drugs in 385 people aged at least 75 (mean 81.3 years), with mild cognitive impairment without serious cardiovascular disease (CVD), improved cognitive, psychological and general daily functioning. The participants had systolic BP $\leq$160 mmHg ($\leq$140 mmHg if a history of diabetes, peripheral artery disease, myocardial infarction, or coronary reperfusion procedure) and either dementia, heart failure, or a limited life expectancy. The deprescribing intervention aimed for a SBP increase $\leq$20 mmHg. At 16 weeks, the mean BP in the deprescribing arm increased by 5.4/1.3 mmHg (mean 149/82 mmHg). The intervention did not affect the study's outcomes or the occurrence of serious adverse events. However, deprescribing in people with orthostatic hypotension ($n = 162$) [53] increased the proportion of those free from orthostatic hypotension at 4 months from 38% in the control arm to 68% in the deprescribing group.

The UK Optimising Treatment for Mild Systolic Hypertension in the Elderly (OPTIMISE) RCT [54] explored the safety of short-term (12 weeks) deprescribing of antihypertensives vs. standard care in 569 patients aged at least 80 (mean 85 years) with systolic BP <150 mmHg who received two or more antihypertensive drugs. The exclusion criteria included heart failure with left ventricular dysfunction or lack of capacity. The study only included patients when their general practitioner felt that deprescribing would be beneficial because of polypharmacy, co-morbidity, non-adherence, dislike of medicines, or frailty. The population may not be generalizable to the general population as 98% were white, and about 40% had a university education (deprivation status not reported). Based on the Morley FRAIL scale, 49 (8.6%) patients were frail, and the electronic Frailty Index indicated a degree of frailty in 58% of the population (48% mild, 9% moderate, 0.9% severe). The treatment was restarted if BP increased >150/90 mmHg for >1 week, or adverse events occurred. The baseline mean BP was 130/60 mmHg, and adjusted BP was 3.4/2.2 mmHg higher in the medication reduction group at 12 weeks. There was no difference in the main outcome of maintenance of systolic BP <150 mmHg and the secondary outcomes of frailty status, quality of life or adverse events. In the deprescribing group, 86% maintained their target systolic BP, and 66% remained on their deprescribing regime. The findings of this study suggest that reducing antihypertensive drugs in elderly hypertensive patients was safe and was not associated with a significant change in BP control.

When deprescribing, which drug should be stopped first? The effects of deprescribing in the OPTIMISE trial varied depending on the medication withdrawn [55]. Deprescribing of calcium channel blockers was associated with an increase in systolic BP (mean 5 mmHg) and lower rates of systolic BP remaining <150 mmHg compared with usual care. Withdrawal of higher dose treatments increased systolic BP, but did not change BP control status. By contrast, deprescribing beta-blockers or lower dose drugs did not affect BP control. There was no link between deprescribing of specific medication classes and adverse events. The data suggested that deprescribing of higher dose calcium channel blockers should be avoided if BP control were to be maintained. However, information on long-term effects of deprescribing on BP control, clinical outcomes and quality of life is lacking.

The real-life withdrawal of antihypertensive drugs in people aged at least 80 is not well documented. An analysis of US older nursing home residents with limited life expectancy or advanced dementia ($n = 10\,574$, mean systolic BP <120 mmHg) observed reduction in antihypertensives in 41% of treated residents [56]. The deprescribing was more frequent if multiple antihypertensives were used, systolic BP was <100 mmHg, in the presence of recent weight loss, poor appetite, dehydration or pain. The study indicates that that deprescribing is not uncommon in nursing homes.

Many older patients are unaware of the concept of deprescribing but are open to discontinuing medication if suggested by a healthcare professional. Deprescribing shall be part of patient-centred care and include effective communication and shared decisions between HCPshealthcare professionals and patients, involving family members and carers, and shared decision making (SDM). Shared decision making requires trustworthy information about options and considers patient concerns, and personal circumstances (Fig. 2). Engaging patients in medication decisions requires easily understandable educational materials, such as patient decision aids, fact sheets, leaflets, and digital tools/apps. Shared decision making can save resources and improve consultation satisfaction and health outcomes [57,58].

CHALLENGES OF REDUCING OF OVERTREATMENT

Patient surveys have shown that 70–92% of older adults were willing to stop some of their medications if suggested by their doctor, and two-thirds wanted to reduce the number of drugs they were taking [59–61]. Doctors rank antihypertensives first on the list of medications for deprescribing [62]. However, reducing polypharmacy and overtreatment of hypertension has many barriers, including clinical, ethical and medico-legal.

A qualitative study of general practitioners (GPs) in the Netherlands found that deprescribing in older people was challenging [63]. Although GPs were reluctant to start antihypertensive treatment because of frailty and patient preference, they tended to leave previously started treatments unchanged [63]. The most commonly reported barrier for deprescribing in older adults was a gap in GP's knowledge [64–70]. This was particularly influenced by a lack of understanding of the pharmacological properties of the drugs and their interactions with other medications [65,67,71]. The paucity of clinical evidence led to uncertainty about the benefits of long-term medications, especially if used for primary prevention [64,65,67,71]. GPs felt that there was insufficient guidance from current guidelines [63]. Also, GPs lack guidance on how to approach, implement and monitor deprescribing [72].

Deprescribing was facilitated by the GP's experience of patients having a better quality of life after reducing treatment [63]. GPs in England were typically confident about reducing antihypertensive medications in older patients with multimorbidity after a trigger, such as adverse effects or a fall [73]. GPs had to make decisions based on multiple sources of guidance, previous personal experience, nonclinical factors, and often time constraints [73]. Prescribing guidance was focused upon single diseases, and did not take into account older people with frailty and multimorbidity [74]. Consequently, less than half of GPs had a consistent approach to deprescribing [75]. Amongst specialist doctors, there was a clear difference in attitude between specialities. Deprescribing was considered by 73% of geriatricians, but by only 14% of cardiologists [76].

There is a need to balance the potential benefits from primary and secondary cardiovascular prevention with patients' quality of life. Clinical care is fragmented across specialties, with a lack of shared decision-making about prescribing. Concerns about overprescribing of antihypertensives in the elderly, especially in those with frailty, multimorbidity and polypharmacy, are increasingly acknowledged by clinical guidelines [77]. Several tools have been proposed to facilitate the process, such as STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy) [78], Australian Revised Patients' Attitudes Towards Deprescribing (rPATD)

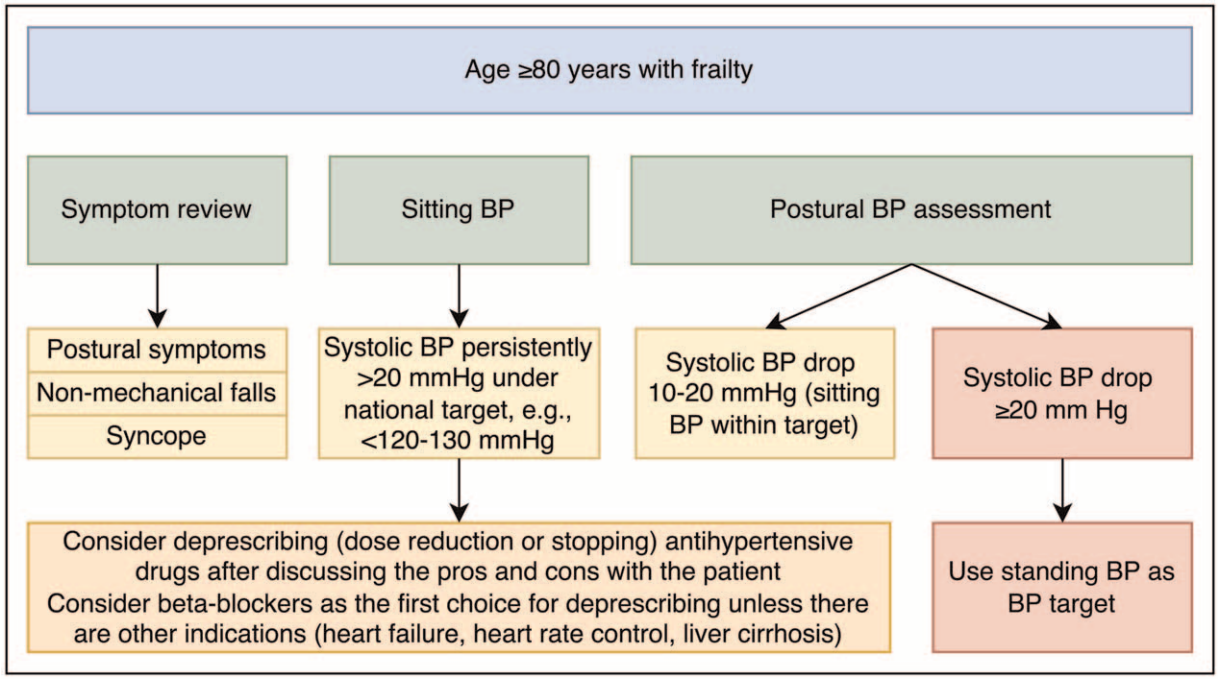

FIGURE 2 Considerations for possible overtreatment of hypertension in older people with frailty. BP, blood pressure.

Questionnaire and Goal-directed Medication review Electronic Decision Support System (G-MEDSS) [61]. However, these tools do not account for the complexities of people with frailty and should be complemented by evidence-based guidance on how to implement deprescribing.

Healthcare professionals need more knowledge and confidence regarding deprescribing, partially due to a lack of awareness about existing deprescribing tools and how to integrate them efficiently into their practice, with further challenges of fear of adverse reactions and time constraints [79]. Psychological and ethical barriers are also important. Educating healthcare professionals about deprescribing and incorporating deprescribing into the undergraduate curriculum may promote deprescribing implementation, but this approach is not widely explored. Embedding digital tools and interventions into existing healthcare systems could be another solution, but it has had variable success in the deprescribing field [80,81].

FUTURE DIRECTIONS

The management of hypertension in older adults with frailty is complex due to various health issues and polypharmacy. This population also has limited physiological reserves to withstand health stressors, making the response to antihypertensive treatments less predictable. Further research is needed to define optimal individualized BP targets and pharmacological means to achieve them. A traditional RCT may not be the best solution to the problem due to the complexity of health vulnerabilities in people progressing from mild to severe frailty, influenced by specific co-morbidities patterns. A better approach would be to predict optimal individual BP targets to improve cardiovascular and safety outcomes. The ongoing Study on Hypertension and Frailty in Older People (HYPER-FRAIL) investigates how BP variability interacts with frailty status in older people. Advancements in data science or broader AI approaches may help future comprehensive algorithms to achieve this using patient health records. Older people with frailty are likely to have different pharmacokinetics compared to healthy people, and pharmacokinetic data for antihypertensives in this population are highly desirable. Moreover, to partially overcome the heterogeneity of this population, pharmacogenetic studies may help identify genetic patterns that influence the treatment choice and dosage, and they may be incorporated into AI models. The field calls for re-evaluating the choice of antihypertensives, which may differ from younger people focusing on tolerability and safety. New, better clinical assessment methods (biochemical or imaging) shall provide a more accurate description of frailty-related vulnerabilities to BP fluctuations and overtreatment. The topic calls for changing attitudes to chronic treatments from life-long to long-term with defined end-of-treatment criteria (deprescribing). An ongoing UK clinical trial evaluates the benefits of deprescribing antihypertensive treatments in older people, including those with frailty, following the experience of the OPTIMISE trial. It is crucial to engage both clinicians and patients in joint decisions, supported by the above data, and qualitative research shall improve the approach for such discussions.

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Conflicts of interest

There are no conflicts of interest.

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