COMPENDIUM

Blood Pressure Control Among Older Adults With Hypertension: Narrative Review and Introduction of a Framework for Improving Care

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Although antihypertensive medications are effective, inexpensive, and recommended by clinical practice guidelines, a large percentage of older adults with hypertension have uncontrolled blood pressure (BP). Improving BP control in this population may require a better understanding of the specific challenges to BP control at older age. In this narrative review, we propose a framework for considering how key steps in BP management occur in the context of aging characterized by heterogeneity in function, multiple co-occurring health conditions, and complex personal and environmental factors. We review existing literature related to 4 necessary steps in hypertension control. These steps include the BP *measure* which can be affected by the technique, device, and setting in which BP is measured. Ensuring proper technique can be challenging in routine care. The *plan* includes setting BP treatment goals. Lower BP goals may be appropriate for many older adults. However, plans must take into account the generalizability of existing evidence, as well as patient and family's health goals. *Treatment* includes the management strategy, the expected benefits, and potential risks of treatment. Treatment intensification is commonly needed and can contribute to polypharmacy in older adults. Lastly, *monitor* refers to the need for ongoing follow-up to support a patient's ability to sustain BP control over time. Sustained BP control has been shown to be associated with a lower rate of cardiovascular disease and multimorbidity progression. Implementation of current guidelines in populations of older adults may be improved when specific challenges to BP measurement, planning, treating, and monitoring are addressed.

Keywords: blood pressure; blood pressure control; hypertension; older adults

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The prevalence of hypertension and the incidence of hypertension-related cardiovascular disease (CVD) increase with older age, making blood pressure (BP) control among older adults an important population health goal.^{1,2} Although antihypertensive medications are effective, inexpensive, and recommended by clinical practice guidelines, a large percentage of older adults with hypertension have uncontrolled BP.^{3,4} This may be due in part to several factors. For older adults, BP management occurs in the context of aging characterized by heterogeneity in function, multiple co-occurring health conditions, as well as an often complex set of personal and environmental factors.^{5–7} In addition to issues related to aging, there are also specific considerations for measuring and treating hypertension in older age.⁸

In this article, we first review hypertension prevalence, treatment, and control in older adults highlighting current clinical practice guideline definitions and their implications for identifying hypertension in older adults. Next we describe the unique considerations for controlling hypertension at

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older ages and propose a framework for BP management in this population. This framework considers the aging context as well as the specific steps in hypertension management. Based on this framework, we then review the existing literature as it relates to 4 necessary steps in hypertension control: (i) measuring BP, (ii) planning and goal setting, (iii) treating hypertension, and (iv) monitoring BP over time. Lastly, we use this framework to guide a discussion on implementation challenges and opportunities for improving care for older adults with hypertension.

EPIDEMIOLOGY

Guideline definitions and treatment goals

The 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline for the Prevention,

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© Published by Oxford University Press on behalf of American Journal of Hypertension Ltd 2021. This work is written by (a) US Government employee(s) and is in the public domain in the US. SBP 130–139 mm Hg or DBP 80–89 mm Hg and Stage 2 hypertension is defined as SBP \geq 140 mm Hg or DBP \geq 90 mm Hg. These categories replace the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) classification, adding the new category Elevated BP, eliminating the prehypertension category, and lowering the BP levels for defining Stage 1 hypertension.^{4,9} Furthermore, these BP categories are the same for all adults, including the oldest-old.

New to these guidelines are also recommendations for thresholds to initiate BP-lowering medications and BP goals based on CVD risk. Among patients with clinical CVD, guidelines recommend treatment for secondary prevention of CVD events with a BP goal <130 mm Hg/<80 mm Hg. For primary prevention among those without known CVD, guidelines recommend first estimating the 10-year atherosclerotic cardiovascular disease risk. BP-lowering medications are recommended for goal BP levels of <130 mm Hg/<80 mm Hg for patients with an atherosclerotic cardiovascular disease risk of >10%. As 88% of adults over 65 years and 100% of those over 75 years old have an atherosclerotic cardiovascular disease risk of $\geq 10\%$, the recommended BP goal for the vast majority of older adults is <130 mm Hg/<80 mm Hg.⁴ In addition to antihypertensive medication to achieve these goals, the 2017 ACC/AHA guidelines also recommend nonpharmacological interventions including weight loss among those overweight or obese, a heart-healthy diet, sodium restriction, increased physical activity, and reduction in alcohol consumption. These treatment recommendations are the same for adults of all ages.

Prevalence, treatment, and control

The prevalence of hypertension increases with age. Most epidemiologic studies have used BP \geq 140/90 mm Hg to define hypertension. For example, according to an analysis of data from the National Health and Nutrition Examination Survey (NHANES) conducted between 2011 and 2014, the prevalence of hypertension was 10.5%, 29.5%, 52.4%, 63.6%, and 75.1%, among US adults 20-44, 45-54, 55-64, 65-74, and ≥75 years old, respectively.¹ Applying the 2017 ACC/AHA guideline definition of hypertension as BP \geq 130/80 mm Hg classified a higher percentage of US adults as having hypertension (45.6% and 31.9% for 2017 ACC/AHA and JNC7, respectively). However, among those 75 years old and older, the difference in those meeting the definition of hypertension (82.3% vs. 75.1%) or who would receive recommendations for antihypertensive medications (82.3% vs. 78.5%) were small. In the general US population, gender differences in the prevalence of hypertension have also been reported with a higher percentage of men compared with women meeting the definition for hypertension. However, after age 65 years

the prevalence of hypertension is higher among women than men.²

The percentage of older adults with awareness of hypertension and receiving treatment are generally high. Awareness of hypertension, defined as BP $\geq 140/90$ mm Hg has been shown to be 67.3%, 79.3%, 85.4%, and 82.1% among US adults 18-44, 45-64, 65-74, and ≥75 years old, respectively.³ Hypertension awareness has been shown to be more common among those with a usual health care provider, which may explain in part the higher prevalence of awareness at older ages as older adults often require more frequent interactions with the healthcare system. Among those aware they had hypertension, antihypertensive medication use has also been shown to be high among older adults. Among those who reported awareness, the percentage taking antihypertensive medication were 75.8%, 87.7%, 94.1%, and 96.0% at 18-44, 45-64, 65-74, and \geq 75 years old.³

Among older adults with hypertension, the percentage with controlled BP has generally been reported to be less than 50%. A recent analysis reported trends in BP control using NHANES calendar periods across nearly 2 decades.³ Serial cross-sectional surveys took place over 2-year intervals from 1999–2000 through 2017–2018. Overall, an increasing percentage of adults with controlled BP was seen through 2013–2014, followed by a decrease in calendar periods 2015–2016 and 2017–2018. This trend was also seen among those \geq 75 years old (Figure 1). In a pooled analysis from 2015 to 2018, the prevalence ratio for controlled BP among those taking antihypertensive medication was 0.96, 0.84, and 0.63 at ages 45–64, 65–74, and \geq 75 years old, compared with 18–44 years old, respectively.³

Most studies of hypertension have focused on community-dwelling older adults. Therefore, data on the prevalence, treatment, and control of hypertension among special populations of older adults such as the oldest-old or those residing in nursing homes are limited. One analysis of NHANES reported the prevalence among US adults \geq 80 years old to be 76.5%, with similar percentage of those with control among those on hypertension medications to those \geq 75 years old during the same time period.¹⁰ Importantly, a large increase in antihypertensive polypharmacy, defined as 3 or more classes of BP-lowering medications, was found over time. The percentage of US adults ≥ 80 years old with antihypertensive polypharmacy was 7.0%, 19.2%, and 30.9% during calendar NHANES assessments occurring in 1988-1994, 1999-2004, and 2005-2010, respectively.¹⁰ Data on the prevalence of hypertension among older nursing home residents are limited. Because of the high prevalence of multimorbidity in the nursing home population, the prevalence of hypertension in combination with other chronic conditions has been described. For example, 1 report showed that 27% of nursing home patients had co-occurring hypertension and dementia.¹¹ A separate analysis of over 250,000 US nursing home residents with hypertension on antihypertensive medications found that 40% were receiving 2 or more classes of medication.¹² The intensity of treatment did not differ for those with and without moderate-severe

cognitive impairment, raising questions about whether hypertension is overtreated among some nursing home residents who have limited life expectancy.

BP control and disabling conditions

As many older adults prioritize remaining independent in late life, it is important to recognize the association between BP control and conditions that reduce cognitive and physical function. Uncontrolled BP is a known risk factor for disabling conditions including stroke, heart failure, and coronary heart disease.² Studies have also shown direct associations of hypertension with cognitive and physical function.¹³ For example, BP \geq 120/80 mm Hg during midlife was found to be associated with a greater risk of developing dementia in later life.¹⁴ Therefore, a life-course perspective is helpful for understanding the detrimental effects of uncontrolled BP that may accumulate over many years leading to disability.¹⁵

FRAMEWORK

The combination of an aging US population, a decreasing percentage with controlled hypertension, and recommendations for lower BP goals will likely result in an expanding population of older adults with uncontrolled BP who are at risk for CVD events. Population health efforts to improve BP control often focus on increasing awareness and treatment. However, awareness and treatment have remained high among older adults. An alternative approach may be to recognize specific challenges to BP control among older adults. We proposed a framework for considering how key steps in BP management occur in the context of common issues with aging (Figure 2).

Aging context

A sizable proportion of older adults, including many who are frail, will benefit from intensive BP control, defined as a SBP <120 mm Hg. However, other older adults are unlikely to benefit. The World Health Organization (WHO) has developed a model that is useful for helping to identify those who may be less likely to derive benefit from intense efforts to control BP. The WHO International Classification of Functioning (ICF) model describes 4 aging domains: (i) function, (ii) health conditions (i.e., multimorbidity), (iii) personal factors, and (iv) environmental factors.^{5,16} This model considers the impact of functional limitations on daily activities such as chronic disease self-management tasks. The health conditions domain acknowledges that older adults often experience multiple chronic conditions.^{17,18} Examples of personal factors include individual health goals, personal financial resources, and availability of family caregivers. Examples of environmental factors include living situations such as independent living vs. nursing home residence, and geographic issues such as neighborhood-level poverty. While these considerations may be important regardless of age, the prevalence of functional limitations and complexity of health conditions are known to increase at older age.¹⁹ Consequently, some older adults rely on personal and environmental factors to maintain independence and manage their health conditions.²⁰

The interaction of function, co-occurring health conditions, and personal and environmental factors are relevant to BP control. This is illustrated by considering the multiple self-management tasks necessary for BP control. Limitations with physical and cognitive function may reduce one's capacity to follow physical activity recommendations, adhere to medication scheduling, and refill medications on-time.²¹ While some conditions have overlapping

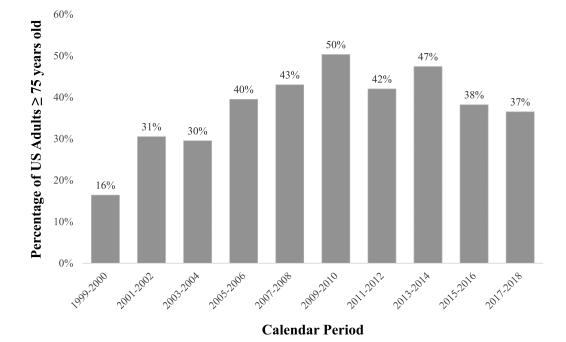


Figure 1. Trends in blood pressure (BP) control among US adults ≥75 years old from the National Health and Nutrition Examination Survey (NHANES).³

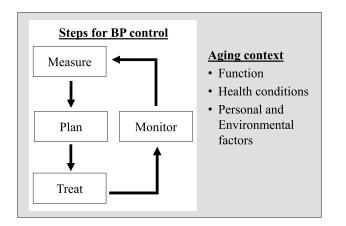


Figure 2. A framework to improve blood pressure (BP) control that considers how key steps in BP management occur in the context of common aging issues.

treatment goals with hypertension, reinforcing the need for treatment (e.g., angiotensin-converting enzyme inhibitor among those with hypertension, chronic kidney disease, and diabetes), the presence of multimorbidity often makes self-management more complex.^{22,23} Older adults may not receive guidance on how to reconcile opposing treatment recommendations.²⁴ This may be especially true when older adults face choices about treating conditions that are symptomatic vs. those that are asymptomatic such as hypertension.²⁵ The presence or absence of a family caregiver or resources to pay caregivers, can influence one's ability to overcome functional and cognitive limitations.

In addition to impacts on ability to self-manage BP, functional limitations and multimorbidity may provide important prognostic information.²⁶ For example, many older adults with poor function and advanced illness are at end-of-life. Those with a life expectancy of less than 2 years are unlikely to live long enough to experience the benefits of intensive BP treatment.^{27,28} Because of the wide range of functional abilities, health conditions, and personal and environmental resources in older age, a one-size-fits-all approach is unlikely to be effective for setting BP goals or controlling BP.

Steps in BP management

In addition to issues related to older age influencing BP control, there are specific components involved in achieving and sustaining BP control (Table 1). This framework acknowledges that the BP *measure* can be affected by the technique, device, and setting in which BP is measured. The *plan* refers to setting a goal BP in the context of the patient and family's overall health goals. *Treatment* refers to the management strategy including the use of BP-lowering medications, the expected benefits of treatment, and risk for adverse events. Lastly, *monitor* refers to need for ongoing follow-up to support a patient's ability to sustain BP control over time. Below we highlight some of the relevant literature for each of these 4 steps.

Measure

Differences in BP measurement based on the technique and setting are common at all ages, but especially true in this population. The AHA Scientific Statement on Measurement of BP in Humans describes 6 overall steps and 20 specific instructions for the proper technique to obtain seated BP in the office.²⁹ Large-scale studies have demonstrated that implementing the proper technique is feasible, however approaches used in clinical trials have not been widely adopted in practice. Clinic-level challenges include ensuring a 3- to 5-minute relaxation period, not talking to the patient during the measurement, as well as determining the proper cuff size. At the patient-level, challenges include removing clothing among those with functional limitations or arthritis, bladder emptying among those with prostate or bladder dysfunction, and following instructions for those with cognitive limitations. These challenges may explain the recent report showing higher SBP in the electronic health record compared with BP obtained under a standardized research protocol.³⁰ Despite these challenges, there are several examples of how outpatient clinics can overcome clinic- and patient-level barriers to care (e.g., blood draws, laboratory calibration, crash cart maintenance) when standardized policies are put into place. This might also involve an expanded use of home blood pressure monitoring following AHA Scientific Statement recommendations for proper technique.²⁹ While this approach may overcome the cliniclevel deficiencies, some patient-level challenges remain. Concerns about device validation have also been reported.³¹

Research has shown differences based on the setting in which BP is measured, an important example being the higher prevalence of white coat hypertension with aging.^{8,32} One way to identify white coat hypertension is by using ambulatory blood pressure monitoring (ABPM). In ABPM, a BP monitor is worn for 24 hours and obtains automatic readings in the out-of-office setting.⁸ ABPM has been shown to have similarly feasible in older and younger adults.³³ Using ABPM, white coat hypertension is defined as having elevated clinic BP without elevated daytime BP on ABPM. The term "treated white coat hypertension" has been used to describe elevated clinic BP without elevated daytime BP on ABPM among those on antihypertensive medications.⁸ Prior studies have shown that among older adults, clinic BP is higher in relationship to daytime BP resulting in a higher prevalence of treated white coat hypertension at older age. For example, an analysis of data from the Jackson Heart Study, compared the difference in clinic and daytime SBP among Black US adults with hypertension <60 vs. \geq 60 years old.³⁴ The difference between clinic SBP and daytime SBP was on average higher among those ≥ 60 years old compared with <60 years old (12 mm Hg higher vs. 8 mm Hg higher). The prevalence of white coat hypertension may be greater among special populations of adults. The prevalence of treated white coat hypertension among participants who were all 80 years and older in the HYVET study was 50%.35 Among nursing home residents, 1 study found that 70% of all nursing home residents with high BP were found to have white coat hypertension when ABPM was conducted.³⁶ Taken together, these findings suggest that clinic BP obtained as part of routine

	Description	Relevance to older adults	
Measure	Technique, device, setting	 Proper technique limited by physical and cognitive impairment or geriatric conditions 	
		 Competing demands for clinical assessments among older adults with multimorbidity (i.e., proper technique a low priority) 	
		Higher prevalence of treated white coat hypertension at older age	
Plan	Setting goals	Concerns about generalizability of clinical trial evidence for some older adults	
		 Wide range in health goals and willingness to accept tradeoffs between benefits and harms at older age 	
Treat	Management strategy, benefits vs.	Treatment intensification likely to result in polypharmacy	
	harms	Physical and cognitive impairment may limit self-management	
		Dependence on caregivers for self-management support	
		 Falls are a common cause and death and disability in older adults. Fear of precipitating a fall may affect treatment decisions 	
Monitor	Follow-up over time	 Heterogeneity in life expectancy and time for which BP monitoring may be necessary 	
		 Intervening health events and declining function occur at older age and may affect BP control or treatment goals 	

Table 1.	Description of steps in	hypertension con	trol and relevant	considerations for older adults

Abbreviation: BP, blood pressure.

care may not always reflect the out-of-clinic BP and should be considered when addressing BP control in older adults.

Plan

In the proposed framework, the plan refers to setting goals for BP control levels. As described above, the guideline recommended goal BP for the vast majority of older adults is <130 mm Hg/<80 mm Hg. This recommendation is supported by clinical trial evidence including findings from the Systolic Blood Pressure Intervention Trial (SPRINT) which tested intensive vs. standard control.²⁷ While the results of SPRINT have been extensively reported,³⁷ it is worth reviewing 3 findings that are relevant to older adults. First, among the prespecified subgroup of participants \geq 75 years old, treating to an SBP goal of <120 mm Hg (intensive control) vs. <140 mm Hg (standard control) resulted in lower rates of fatal and nonfatal CVD events and death.²⁸ This was true in exploratory subgroups in which participants were categorized as fit, less fit, or frail or had a low gait speed and among those ≥ 80 years old.³⁸ Second, findings from SPRINT maybe generalizable to a large number of ambulatory older adults, including those with frailty. In SPRINT, 31% of participants \geq 75 years old were frail, a similar prevalence seen in community-dwelling older adults.³⁹ Third, findings from the SPRINT MIND study found a lower incidence of mild cognitive impairment and the combination of mild cognitive impairment or probable dementia with intensive SBP control.⁴⁰ There was no difference seen in the primary outcome of probable dementia, perhaps due to the intervention being terminated early and inadequate follow-up time. However, because maintaining cognitive function is such an important goal in aging, findings of lower risk of mild cognitive impairment are clinically relevant for older adults.

While SPRINT is a landmark study and representative of a large percentage of older adults with hypertension, it is not possible for a randomized trial to be generalizable to all older adults. Therefore, it is important to consider the study exclusions most relevant to older adults when planning BP goals. For example, SPRINT excluded adults residing in nursing homes and those with standing hypotension of <110 mm Hg, type 2 diabetes, prior history of stroke, estimated glomerular filtration rate <20 ml/min/1.73 m², dementia, unintentional weight loss, or symptomatic heart failure.²⁷ As these conditions are common at older age and may be associated with risk for adverse events, it is not known if intensive SBP control would confer the same benefits for some subgroups of older adults. In addition to the exclusion criteria, it has been well documented that barriers exist to inclusion of older adults in research.⁴¹ For example, older adults with functional limitations and limited social support face additional barriers to participation even when not explicitly excluded, reinforcing the need to consider the aging context when making plans for BP treatment goals.⁴¹

Treat

After making plans for BP goals, the next step is to choose a managementstrategy. This includes both nonpharmacological interventions, such as low sodium diets and weight loss, as well as the use of BP-lowering medications. Several nonpharmacological interventions have additional benefits such as improvement of function and should be considered regardless of the need for antihypertensive medication. The clinician and patient should have an understanding of the expected benefits and potential for risk for adverse events when considering antihypertensive medication initiation or intensification. In general, guideline recommendations for specific antihypertensive medications do not differ by age.⁴ As the majority of older adults with hypertension are

on treatment, treatment decisions less often focus on which antihypertensive medication to initiate, but more on when to intensify treatment by adding medications from other classes. For example, among adults \geq 75 years old in SPRINT, 85% of participants in the intensive treatment group and 57% in the standard treatment group required 2 or more antihypertensive medication classes to achieve the targeted BP goals (mean number 2.6 vs. 1.8).²⁸ The most commonly used antihypertensive medications for both randomization groups were angiotensin-converting enzyme inhibitors/ ARBs followed by diuretics and calcium channel blockers. Therefore, in this population it is important to anticipate and manage polypharmacy, specifically antihypertensive polypharmacy, when treating hypertension.

Another aspect of treatment to consider is the risk for adverse events. Falls are leading cause of injury and death among older adults.⁴² Although concerns about fall risk likely lead to less intensive hypertension treatment, evidence on the association between hypertension treatment and falls is mixed. Clinical trials, including SPRINT, have not shown intensive BP treatment to be associated with a higher risk of injurious falls.^{27,43} However, rates of falls have been shown to be lower in trial populations than in observational studies.^{44,45} Among Medicare beneficiaries \geq 70 years old with hypertension, antihypertensive medications use was shown to be associated with a higher risk of serious fall injuries.⁴⁴ In a separate study of over 90,000 Medicare beneficiaries, antihypertensive medication initiation or intensification was associated with risk for serious fall injuries within 14 days, but not longer-term risk.⁴⁶ In an analysis of data from the REasons for Geographic and Racial Differences in Stroke (REGARDS) study participants on antihypertensive medication, indicators of frailty, but not BP levels or number of antihypertensive medications, was shown to be associated with risk for serious fall injuries.⁴⁷ These findings suggest that the risk for falls should not preclude hypertension treatment for most older adults, but careful titration, short-term monitoring, and addressing multiple fall risk factors should be part of comprehensive hypertension treatment.

Monitor

Population level reports on BP control provide a snapshot in time. However, in practice, clinicians diagnose and treat individuals with hypertension over many visits and patients live with hypertension over many years. Older adults often experience intermittent health events, many unrelated to hypertension, that may affect their ability to achieve BP control. Therefore, monitoring BP control over time with the goal of sustaining BP control is an important step in hypertension management. Recent studies have shown that sustained BP control is associated with better health outcomes.⁴⁸ For example, an analysis of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) linked to Medicare health insurance claims examined the association between sustained SBP control and the progression of multimorbidity, defined by the co-occurrence of up to 14 separate chronic conditions.⁴⁹ SBP control was categorized as <140 mm Hg at <50%, 50% to <75%, 75% to <100%, and 100% of visits over a 48-month assessment period.

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	Clinical trials	Routine care	Implementation opportunities
Measure	 Standardized technique Calibrated equipment Certified research staff Multiple measures Routine orthostatic BP 	 Multiple techniques Available equipment Busy clinical staff Single measure Additional measures when clinically indicated/ symptoms 	Develop practical approaches to BP measurement that can be achieved in busy clinic settings or accurately obtained outside of the clinic.
Plan	 Eligibility screening prior to enrollment BP goals determined by protocol or randomization group 	 All comers Provider variability in knowledge and comfort with guideline recommended goals Variability in patient and family goals 	Use risk stratification tools to identify patients for whom guideline recommended BP is appropriate. Incorporate shared decision-making tools to help align patient goals with BP treatment goals.
Treat	 Determined by standardized protocols or by randomization group Frequent assessment for study specific adverse events including minor events 	 Provider, patient, and clinic variability in drug choice and timing of initiation/intensification Adverse events are multifactorial in etiology Adverse events may not be identified unless they result in acute or emergent care 	Develop treatment protocols that address polypharmacy, drug–drug, and drug–condition interactions that are common among older adults with multimorbidity. Following existing guidelines for addressing multifactorial geriatric conditions such as falls.
Monitor	 Standard device and setting Routine interval Set study endpoint 	 Multiple devices and settings As needed or when acute events occur No endpoint 	Report meaningful metrics for sustained BP control that support patient- provider communication and quality improvement. Follow flexible monitoring schedules that respond to changes in BP control, acute health events, or health goals.
Abbreviation: BF	Abbreviation: BP, blood pressure.		

 Table 2.
 Identifying implementation opportunities that address differences in clinical trials and routine care

Participants with sustained SBP control at a higher percentage of visits had a slower rate of multimorbidity progression and developed multimorbidity when they were 5–10 years older than their counterparts without sustained SBP control. As older adults often consider their overall health when assessing the risks and benefits of treatment, not just the disease-specific outcomes, evidence on reducing multimorbidity could be used to guide patientcentered discussions about monitoring and improving BP control over time.

Implementation needs

Understanding the unique challenges and opportunities for BP control in older adults may facilitate better implementation of hypertension guidelines in this population. In **Table 2**, we describe some differences between clinical trials and routine care related to measuring, planning, treating, and monitoring BP control among older adults. Recognizing these differences can be used to identify implementation opportunities. For example, in clinical trials, strict inclusion criteria are applied to populations to identify eligible participants before any plan for BP treatment is initiated. In clinical practice, identifying patients who might benefit is not done in a coordinated way. Therefore, implementation strategies that include risk stratification tools to identify patients for whom guideline recommended BP is appropriate are needed.

Despite effective and inexpensive treatments, clinical trial evidence on the benefits of treatment, and guideline recommendations, a large percentage of older adults do not have adequately controlled BP. A framework that recognizes both the broader aging context and the specific challenges and opportunities in BP management may be helpful for improving BP control. Implementation of current guidelines in populations of older adults may be improved when barriers to BP measurement, planning, treating, and monitoring are addressed.

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DISCLOSURE

The authors declared no conflict of interest.

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