THE JOURNAL OF FAMILY PRACTICE

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The authors reported no potential conflict of interest relevant to this article.

Hypertension treatment strategies for older adults

This evidence-based review illustrates how to adjust treatment for comorbidities and incorporate frailty and cognitive impairment into the equation.

PRACTICE RECOMMENDATIONS

› *Target a systolic blood pressure (BP) <120 mm Hg in community-dwelling, non-diabetic patients ≥75 years of age if it is achievable without undue burden.* (A)

› *Combine low doses of 2 medications, rather than increase the dose of a single agent, to achieve the desired BP target.* (A)

› *Consider cognitive function, polypharmacy, multimorbidity, and frailty when assessing and treating hypertension in older patients.* (A)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE 1 ▶ An 82-year-old black woman comes in for an annual exam. She has no medical concerns. She volunteers at a hospice, walks daily, and maintains a healthy diet. Her past medical history (PMH) includes osteopenia and osteoarthritis, and her medications include acetaminophen as needed and vitamin D. She has no drug allergies. Her exam reveals a blood pressure (BP) of 148/70 mm Hg, a body mass index of 31, and a heart rate (HR) of 71 beats per minute (bpm). Cardiac and pulmonary exams are normal, and she shows no signs of peripheral edema.

CASE 2 ▶ An 88-year-old white man presents to the office for a 3-month follow-up of his hypertension. His systolic BP at home has ranged from 140 to 170 mm Hg. He denies chest pain, shortness of breath, or lower extremity edema. He lives with his wife and frequently swims for exercise. His PMH is significant for depression and degenerative disc disease. His medications include hydrochlorothiazide 12.5 mg/d, sertraline 50 mg/d, and naproxen 250 mg bid. His BP is 160/80 mm Hg and his HR is 70 bpm with normal cardiovascular (CV) and pulmonary exams.

CASE 3 ▶ An 80-year-old white man with diabetes mellitus (DM), hypertension, and chronic kidney disease (CKD) presents for a 3-month follow-up visit. His home systolic BP has been in the 140s to 150s. He is functional in all of his activities of daily living (ADLs), but is starting to require assistance with medications, finances, and transportation. He takes aspirin 81 mg/d, chlorthalidone 25 mg/d, and atenolol 50 mg/d. Remarkable laboratory test results include a hemoglobin A1c of 8.6%, a serum creatinine of 1.9 mg/dL (normal range: 0.6-1.2 mg/dL), and an albumin-creatinine ratio of 250 mg/g (normal range: <30 mg/g). During the exam, his BP is 143/70 mm Hg, his HR is 70 bpm, he is alert and oriented to person, place, and time, and he has normal CV and pulmonary exams with no signs of peripheral

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A systoloic BP target of <120 mm Hg is appropriate in community-dwelling, non-diabetic adults ≥75 years of age, but if this places an undue burden on the patient, a goal of <140 mm Hg also provides benefit.

edema. He has decreased sensation in his feet, but normal reflexes.

How would you proceed with the care of these 3 patients?

Hypertension is the most common diagnosis made during physician office visits in the United States.[1] Nearly one-third of the population has hypertension, and its prevalence increases with age, such that 67% of men and 79% of women ≥75 years of age have the condition.[2]

Evidence indicates that hypertension is a modifiable risk factor for CV and all-cause mortality (**TABLE W1**,[3-6] available online at jfponline.com). All adults ≥75 years of age are at increased CV risk based on Framingham criteria,[7] making hypertension management paramount. Complicating the situation are findings that indicate nearly half of adults with hypertension have inadequate BP control.[2]

Clinicians require clear direction about optimal BP targets, how best to adjust antihypertensive medications for comorbidities, and how to incorporate frailty and cognitive impairment into management strategies. This article presents recommendations derived from recent evidence and consensus guidelines regarding the management of hypertension in adults ≥75 years of age.

Diagnosing hypertension

According to the seventh report of the Joint National Committee (JNC 7), hypertension is defined as a systolic BP ≥140 mm Hg and/or a diastolic BP ≥90 mm Hg.[8] The JNC's more recent report (JNC 8), however, does not define hypertension; instead, it sets forth treatment thresholds (eg, that there is strong evidence to support treating individuals ≥60 years of age when BP ≥150/90 mm Hg).[9]

It starts with an accurate BP measurement. Ensuring the accuracy of a BP measurement requires multiple readings over time. White coat hypertension and masked hypertension can complicate BP measurement. Home measurements better correlate with atherosclerotic cardiovascular disease (ASCVD) risk than do office measurements.[10-12] In fact, the US Preventive Services Task Force recommends obtaining measurements outside of the clinic setting prior to initiating treatment for hypertension.[13]

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TABLE 1

Hypertension evaluations: What to include[10]

Evaluation at initial diagnosis of hypertension
• Urinalysis to look for renal damage, especially albuminuria
• Electrolytes (sodium, potassium) and renal function
• Lipid panel
• Fasting glucose or hemoglobin A1c
• EKG (or obtain prior EKGs) to look for underlying cardiac abnormalities or prior damage
Evaluation for secondary causes of hypertension for resistant hypertension
• Sleep study
• Renal ultrasound with duplex
• Plasma aldosterone/renin ratio
• Thyroid function testing
Evaluation for end-organ damage for symptomatic or poorly controlled patients
• EKG or echocardiogram to evaluate for left ventricular hypertrophy
• Dilated eye exam for retinopathy
• Urine microalbumin for nephropathy

EKG, electrocardiogram.

Common pharmacotherapeutic contributors to uncontrolled BP include NSAIDs, glucocorticoids, high-dose decongestants, and selective norepinephrine reuptake inhibitors.

Educate staff on the proper technique for obtaining BP measurements in the office (ie, taking measurements using an appropriately sized cuff when patients have been seated for at least 5 minutes with feet uncrossed and with their arm supported at heart level). Cold temperatures, coffee consumption, talking, and recent tobacco use can transiently raise BP.

TABLE 1[10] outlines the initial work-up after confirming the diagnosis of hypertension. No other routine tests are recommended for the management of hypertension except those associated with medication monitoring (outlined in **TABLE 2**[10,11,14,15]).

What's the optimal BP target for older patients? No consensus exists on an optimal BP target for older patients. JNC 8 recommends a target BP <150/90 mm Hg in patients ≥60 years of age.[9] The American College of Physicians recommends a systolic BP target <140 mm Hg in patients ≥60 years of age with increased stroke or CV risk.[11] A subgroup analysis of patients ≥75 years of age from the Systolic BP Intervention Trial (SPRINT)[3] was stopped early because of the clear composite CV and mortality benefits associated with targeting a systolic BP <120 mm Hg as compared with <140 mm Hg (**TABLE W1**,[3-6] available online at jfponline.com). Although a criticism of this trial and its results is that the researchers included only adults with high CV risk, all adults ≥75 years of age are considered to have high CV risk by the SPRINT study.[3] Another criticism is that early suspension of the trial may have exaggerated treatment effects.[6]

Lastly, results were seemingly discrepant from previous trials, most notably, the Action to Control CV Risk in Diabetes (ACCORD) trial.[6,16] However, on closer review, the ACCORD trial[16] included only patients with DM, while the SPRINT[3] trial excluded patients with DM, and ACCORD comprised a younger population than the SPRINT subgroup analysis. Also, the ACCORD trial did demonstrate stroke reduction and nonsignificant reduction in CV events, albeit, at the cost of increased adverse events, such as hypotension, bradycardia, and hypokalemia, with tighter BP control.[16]

Population differences presumably explain the discrepancy in results, and a systolic BP target of <120 mm Hg is appropriate in community-dwelling, non-diabetic adults ≥75 years of age. If this target goal cannot be achieved without undue burden (ie, without

TABLE 2

How to monitor for common antihypertensive adverse effects[10,11,14,15]

Antihypertensive class	Common adverse effects	Monitoring
Thiazide-type diuretics	Electrolyte disturbances, gastrointestinal discomfort, rashes and other allergic reactions, sexual dysfunction in men, photosensitivity, orthostatic hypotension	Electrolytes (sodium, potassium), creatinine every 3 months
ACE inhibitors	Cough, hyperkalemia	Electrolytes (sodium, potassium), creatinine every 3 months
ARBs	Dizziness, cough, hyperkalemia	
Calcium channel blockers	Dizziness, headache, edema, constipation	Heart rate
Beta-blockers	Bradycardia, fatigue, sexual dysfunction, depression, insomnia	Heart rate
Potassium-sparing diuretics	Hyperkalemia	Electrolytes (sodium, potassium), creatinine every 3 months
Alpha blockers*	Dizziness, lightheadedness, weakness	An option in patients with benign prostatic hyperplasia
Central adrenergics*	Constipation, dizziness, lightheadedness, drowsiness, dry mouth	Heart rate

*Should be avoided in older adults if possible.

ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers.

syncope, hypotension, bradycardia, electrolyte disturbance, renal impairment, or substantial medication burden), a recent meta-analysis found evidence that a systolic BP goal <140 mm Hg also provides benefit.[6]

Initiate treatment, watch for age-related changes

Lifestyle modifications (including appropriate weight loss; reduced caffeine, salt, and alcohol intake; increased physical activity; and smoking cessation) are important in the initial and ongoing management of hypertension.[10,11,17,18] JNC 8 recommends initial treatment with a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin converting enzyme (ACE) inhibitor, or angiotensin receptor blocker (ARB) in the nonblack population, and a CCB or thiazide diuretic in the black population.[9] Specific initial medication choices for comorbid conditions are outlined in **TABLE W2**[3,10,17-22] (available at jfponline.com). JNC 8 recommends against the use of a beta-blocker or alpha blocker for initial treatment of hypertension.[9]

Start a second drug instead of maximizing the dose of the first

If the target BP cannot be achieved within one month of initiating medication, JNC 8 recommends increasing the dose of the initial drug or adding a second drug without preference for one strategy over the other.[9] However, a meta-analysis demonstrates that approximately 80% of the antihypertensive effect of a drug can be achieved with half of the standard dose of the medication; this is true for thiazide-type diuretics, ACE inhibitors/ARBs, beta-blockers, and CCBs.[23]

Furthermore, due to fewer adverse effects and positive synergies, studies show that combining low doses of 2 medications is more beneficial than high-dose monotherapy.[19,23,24] Prescribing combination pills can be helpful to limit pill burden. It is appropriate to combine any of the 4 classes of medications recommended as initial therapy by JNC 8 except for an ACE inhibitor combined with an ARB. If the target BP cannot be achieved with 3 drugs in those classes, other medications such as potassium-sparing diuretics or beta-blockers can be added.[9]

Changes associated with aging

Changes associated with aging include atherosclerosis and stiffening of blood vessels, increased systolic BP, widened pulse pressure, reduced glomerular filtration rate, reduced sodium elimination and volume

expansion, sinoatrial node cellular dropout, and decreased sensitivity of baroreceptors.[10] Because of these alterations, antihypertensive requirements may change, and resistant hypertension may develop. In addition, older patients may be more susceptible to orthostatic hypotension, heart block, electrolyte derangements, and other antihypertensive adverse effects.

When hypertension is difficult to control. Resistant hypertension is defined as hypertension that cannot be controlled with 3 drugs from 3 different antihypertensive classes, one of which is a diuretic. Cognitive impairment, polypharmacy, and multimorbidity may contribute to difficult-to-control hypertension in older adults and should be assessed prior to work-up for other secondary causes of poorly controlled hypertension.

- **Cognitive impairment** is often unrecognized and may impact medication adherence, which can masquerade as treatment failure. Assess for cognitive impairment on an ongoing basis with the aging patient, especially when medication adherence appears poor.
- **Polypharmacy** may also contribute to uncontrolled BP. Common pharmacotherapeutic contributors to uncontrolled BP include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, high-dose decongestants, and selective norepinephrine reuptake inhibitors.[25]
- **Multimorbidity** describes 2 or more chronic medical conditions in one patient. These patients are medically complex. Comorbidities can increase pill burden and make medication adherence difficult for patients. Other poorly controlled disease states can worsen hypertension (eg, renal dysfunction secondary to diabetes). Optimize treatment of comorbid conditions.

Secondary causes. If resistant hypertension persists despite confirming medication adherence and eliminating offending medications, a work-up should ensue for secondary causes of hypertension, as well as end-organ damage. Causes of secondary hypertension include sleep apnea (see this month's HelpDesk available at: jfponline.com), renal dysfunction (renal artery stenosis), aldosterone-mediated hypertension (often with hypokalemia), and thyroid disease. Evaluation for secondary causes of hypertension and end-organ damage is outlined in **TABLE 1**.[10] Patients with well-controlled hypertension do not require repeated assessments for end-organ damage unless new symptoms—such as chest pain or edema—develop.

Consider comorbidities

Clinical trials implicitly or explicitly exclude patients with multiple comorbidities. JNC 8 provided minimal guidance for adjusting BP targets based on comorbidity with only nondiabetic CKD and DM specifically addressed.[9] Guidelines from specialty organizations and recent trials provide some additional guidance in these situations and are outlined in **TABLE W2**,[3,10,17-22] available at jfponline.com.

Heart failure. Hypertension is a major risk factor for heart failure. Long-term treatment of systolic and diastolic hypertension can reduce the incidence of heart failure by approximately half with increased benefit in patients with prior myocardial infarction.[22] Research demonstrates clear mortality benefits of certain antihypertensive drug classes, including diuretics, beta-blockers, ACE inhibitors, ARBs, aldosterone antagonists, combination hydralazine and nitrates, and angiotensin receptor-neprilysin inhibitors.[21,22] The overall treatment goal in heart failure is to optimize drugs with mortality benefit, while lowering BP to a goal <130/80 mm Hg in patients ≥75 years of age.[22]

Increased risk for CV disease. The SPRINT trial[3] defined high risk of CV disease as clinical or subclinical CV disease, CKD, 10-year ASCVD risk of ≥15%, or age ≥75 years. SPRINT supports a systolic BP goal <120 mm Hg, but, as a reminder, SPRINT excluded patients with diabetes. The American College of Cardiology Foundation Task Force and the American Heart Association define high CV risk as a 10-year ASCVD risk ≥10% and recommend a BP goal <130/80 mm Hg.[10]

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Approximately 80% of the antihypertensive effect of a drug can be achieved with half of the standard dose of many medications.

Due to fewer adverse effects and positive synergies, studies show that low doses of 2 drugs is more beneficial than high-dose monotherapy.

Diabetes mellitus. A BP >115/75 mm Hg is associated with increased CV events and mortality in patients with DM.[18] The American Diabetes Association (ADA) and JNC 8 recommend a BP target <140/90 mm Hg.[9,18] ADA suggests a lower target of 130/80 mm Hg in patients with high CV risk if it is achievable without undue burden.[18]

Studies show increased mortality associated with initiating additional treatment once a systolic goal <140 mm Hg has been achieved in patients with DM.[26] The ACCORD trial found increased adverse events with aggressive BP lowering to <120/80 mm Hg.[16]

For patients with DM requiring more than one antihypertensive agent, there are CV mortality benefits associated with administering at least one antihypertensive drug at night, likely related to the beneficial effect of physiologic nocturnal dipping.[27]

Chronic kidney disease. JNC 8 specifically recommends an ACE inhibitor or ARB for initial or add-on treatment in patients with CKD and a BP goal <140/90 mm Hg.[9] The Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group recommends a BP target ≤140/90 mm Hg in patients without albuminuria and ≤130/80 mm Hg in patients with albuminuria to protect against the progression of nephropathy.[17] The SPRINT trial[3] included patients with CKD, and KDIGO has not yet updated its guidelines to reflect SPRINT.

Frailty is a clinical syndrome that has been defined as a state of increased vulnerability that is associated with a decline in reserve and function.[28] The largest hypertension studies in older adults address frailty, although often the most frail patients are excluded from these studies (**TABLE W1**,[3-6] available at jfponline.com).

The Hypertension in the Very Elderly Trial (HYVET) categorized patients as frail, pre-frail, or robust and found a consistent benefit of antihypertensive treatment on stroke, CV events, and total mortality—regardless of baseline frailty status.[29] The SPRINT trial included only community-dwelling adults.[3] Other studies suggest that hypertension actually has a protective effect by lowering overall mortality in frail older adults, especially in the frailest and oldest nursing home populations.[30,31]

Although there is a paucity of data to direct the management of hypertension in frail older patients, physicians should prioritize the condition and focus on adverse events from antihypertensives and on slow titration of medications. The JNC 8 BP target of <150/90 mm Hg is a reasonable BP goal in this population, given the lack of evidence for lower or higher targets.[9] Many frail patients have one or more of the comorbidities described earlier, and it is reasonable to strive for the comorbidity-specific target, provided it can be achieved without undue burden.

Cognitive impairment and dementia. The association between hypertension and dementia/cognitive impairment is evolving. Hypertension may impact various forms of dementia, such as Alzheimer's disease (AD) or vascular dementia, differently. There is evidence linking hypertension to AD.[32] The relationship between BP and brain perfusion is complex with the potential existence of an age-adjusted relationship such that mid-life hypertension may increase the risk of dementia while late-life hypertension may not.[33]

A number of studies reveal the evolving nature of our understanding of these 2 conditions:

- A recent systematic review and meta-analysis examining intensive BP treatments in older adults demonstrated that lower BP targets did not increase cognitive decline.[6]
- HYVET's cognitive function assessment did not find a significant reduction in the incidence of dementia with BP reduction over a short follow-up period, but when results were combined in a meta-analysis with other placebo-controlled, double-blind trials of antihypertensive treatments, there was significant reduction in incident dementia in patients randomized to antihypertensive treatment.[34]
- The ACCORD Memory in Diabetes trial (ACCORD-MIND) had the unexpected outcome that intensive lowering of systolic BP to a target <120 mm Hg resulted in a greater decline in total brain volume, compared with the standard BP goal <140 mm Hg. This was measured with magnetic res-

onance imaging in older adults with type 2 DM.[35]
- Results from the SPRINT sub-analysis Memory and Cognition in Decreased Hypertension trial are forthcoming and aim to determine the effects of BP reduction on dementia.[36]

The JNC 8[9] BP target <150/90 mm Hg or a comorbidity-specific target, if achievable without undue burden, is reasonable in patients with dementia. In a systematic review of observational studies in patients with hypertension and dementia, diuretics, CCBs, ACE inhibitors/ARBs, and beta-blockers were commonly used medications with a trend toward prescribing CCBs and ACE inhibitors/ARBs.[37]

As previously highlighted, cognitive impairment may lead to problems with medication adherence and even inadvertent improper medication use, potentially resulting in adverse events from antihypertensives. If cognitive impairment or dementia is suspected, ensure additional measures (such as medication assistance or supervision) are in place before prescribing antihypertensives.

Certain diseases, such as Parkinson's-related dementia and multiple system atrophy, can cause autonomic instability, which can increase the risk of falls and complicate hypertension management. Carefully monitor patients for signs of orthostasis.

CASE 1 ▶ Repeat the BP measurement in the office once the patient has been seated for ≥5 minutes, and have the patient monitor her BP at home; schedule a follow-up visit in 2 weeks. If hypertension is confirmed with home measurements, then, in addition to lifestyle modifications, initiate treatment with a CCB or thiazide diuretic to achieve a systolic BP goal <120 mm Hg. Titrate medications slowly while monitoring for adverse effects.

CASE 2 ▶ Consistent with the office measurement, the patient has home BP readings that are above the BP target (<120 mm Hg systolic). He has been taking a single antihypertensive for longer than one month. Discontinue his NSAID prior to adding any new medications. If his BP is still above target without NSAIDs, then add a second agent, such as a low dose of an ACE inhibitor, ARB, or CCB, rather than maximizing the dose of hydrochlorothiazide.

CASE 3 ▶ Given the patient's diabetes, CKD, and albuminuria, a target BP goal <130/80 mm Hg is reasonable. An ACE inhibitor or ARB is a better medication choice than atenolol in this patient with albuminuria. Because of the deterioration in his ADLs, careful assessment of mobility, functionality, comorbidities, frailty, and cognitive function should take place at each office visit and inform adjustments to the patient's BP target. Employ cautious medication titration with monitoring for adverse effects, especially hypotension and syncope. If his functional status declines, adverse effects develop, or the medication regimen becomes burdensome, relax the target BP goal to 150/90 mm Hg. JFP

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A BP target <150/90 mm Hg or a comorbidity-specific target, if achievable without undue burden, is reasonable in patients with dementia.

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TABLE W1

Studies support the benefits of hypertension management in the elderly[3-6]

Trial (n)	Trial overview and BP goals
Systolic Blood Pressure Intervention Trial (SPRINT)[3,6] (2510)	*Design:* RCT comparing systolic BP target <120 mm Hg (intensive treatment) to a target <140 mm Hg (standard treatment)
	Population: Community-dwelling adults ≥75 years in the United States with systolic BP 130-180 mm Hg or higher and increased CV risk (defined as one or more of the following: clinical or subclinical CV disease, chronic kidney disease [estimated glomerular filtration rate, 20-59 mg/min], a 10-year Framingham general CV disease risk ≥15%, or age ≥75 years)
	Exclusion criteria: Type 2 DM, history of stroke, systolic BP <110 mm Hg after one minute of standing, symptomatic heart failure within the past 6 months, or left ventricular ejection fraction <35%
	Conclusion: Intensive treatment resulted in fewer CV composite events and lower mortality than standard treatment. Mortality RR=0.74; 95% CI, 0.60-0.91 Cardiac event RR=0.74; 95% CI, 0.58-0.93
Hypertension in the Very Elderly Trial (HYVET)[4,6] (3845)	*Design:* RCT comparing treatment with indapamide +/- perindopril with placebo for a target BP ≤150/80 mm Hg
	Population: Adults ≥80 years from 11 countries (with many from China and eastern Europe) with sustained elevated systolic BP (160-199 mm Hg) and ~12% with preexisting CV disease
	Exclusion criteria: Heart failure requiring more than digoxin, secondary hypertension, gout, a requirement for nursing care, or the inability to stand or walk
	Conclusion: Active treatment was associated with significantly lower rates of heart failure, death from stroke, and all-cause mortality. Mortality RR=0.82; 95% CI, 0.69-0.99 Cardiac event RR=0.71; 95% CI, 0.57-0.87
Systolic Hypertension in the Elderly Program (SHEP)[5,6] (4736)	*Design:* RCT comparing chlorthalidone-stepped care to placebo for 4.5 years with the goal of reducing systolic BP by at least 20 mm Hg and below 160 mm Hg; both groups were then treated and 22-year follow-up was performed with comparison to age- and gender-matched cohorts
	Population: Adults with an average age of 72 years with isolated systolic hypertension with initial BP 160-219 mm Hg; 57% women and 14% black
	Exclusion criteria: Alcoholic liver disease, renal dysfunction, a competing risk for study endpoint, or presence of medical management problems
	Conclusion: Active treatment was associated with lower rates of fatal and non-fatal stroke. At 22 years, participants had a higher overall life expectancy than actuarial controls, and the active treatment group had longer life expectancy free from CV death than the initial placebo group. Mortality RR=0.88; 95% CI, 0.74-1.05 Cardiac event RR=0.76; 95% CI, 0.62-0.94

BP, blood pressure; CI, confidence interval; CV, cardiovascular; DM, diabetes mellitus; RCT, randomized controlled trial; RR, relative risk.

TABLE W2

BP target goals and drug choices by comorbidity[3,10,17-22]

Comorbidity (Society)	Target goal (mm Hg)	Drug choices
Heart failure (AHA/ACC/ASH)	<130/80	*ACE inhibitors* are equivalent to *ARBs* (candesartan or valsartan) *Beta-blockers* (carvedilol, metoprolol succinate, bisoprolol, nebivolol) *Thiazides*: For BP control or with volume overload *Aldosterone receptor antagonists (spironolactone or eplerenone)*: For patients with NYHA II-IV and EF <40% (may be substituted for thiazides or used in combination); monitor potassium frequently in patients taking ACE inhibitors/ARBs; do not use if Cr ≥2.5 mg/dL in men or ≥2.0 mg/dL in women or if serum potassium ≥5 mEq/L *Hydralazine + isosorbide dinitrate*: For African Americans with NYHA III-IV with reduced EF *Loop diuretics*: For severe heart failure or severe renal impairment with volume overload *HCN channel blocker (ivabradine)*: For patients with NYHA II-IV and EF ≤35% with resting HR ≥70 bpm on maximum dose of beta-blockers or who can't tolerate beta-blockers; do not use in patients with hepatic impairment *Angiotensin receptor-neprilysin inhibitor (sacubitril/valsartan)*: For patients with NYHA II-III in place of an ACE inhibitor or ARB in select patients with adequate BP tolerating a reasonable dose of an ACE inhibitor or ARB Avoid *non-dihydropyridine calcium channel blockers (verapamil and diltiazem)*, *clonidine*, *moxonidine*, and *hydralazine without a nitrate* in patients with reduced EF Use *adrenergic blockers (doxazosin)* only if control cannot be achieved with other drugs at maximum doses tolerated
Increased CV risk (ACCF/AHA)	≤130/80 <120 systolic (SPRINT)	Thiazide-like diuretic ACE inhibitor or ARB Beta-blocker ARB + CCB is superior to a high-dose ARB alone or ARB + hydrochlorothiazide
Diabetes mellitus (ADA)	<140/90 <130/80 may be appropriate in patients with higher CV risk if achievable without undue treatment burden	With micro- or macro-albuminuria:* An ACE inhibitor or ARB (at the maximum dose tolerated) Thiazide-like diuretic Dihydropyridine-CCBs
CKD (with or without DM; KDIGO)	≤140/90 ≤130/80 with albuminuria* Consider SPRINT: <120 systolic	With micro- or macro-albuminuria:* An ACE inhibitor or ARB No strong evidence to support preferential use of other agents

*Micro-albuminuria is defined as an albumin/creatinine ratio 30 to 300 mg/g; macro-albuminuria is defined as an albumin/creatinine ratio >300 mg/g.

ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACE, angiotensin-converting enzyme; ADA, American Diabetes Association; AHA, American Heart Association; ARB, angiotensin receptor blocker; ASH, American Society of Hypertension; BP, blood pressure; BPM, beats per minute; CCB, calcium channel blocker; CKD, chronic kidney disease; Cr, creatinine; CV, cardiovascular; DM, diabetes mellitus; EF, ejection fraction; HCN, hyperpolarization-activated cyclic nucleotide-gated; HR, heart rate; KDIGO, Kidney Disease: Improving Global Outcomes; NYHA, New York Heart Association; SPRINT, Systolic blood PRessure INtervenion Trial.