CME

Hypertension guideline update: A new guideline for a new era

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ABSTRACT

In the United States, hypertension affects about one-third of adults and contributes to one out of every seven deaths. Evidence-based treatment is associated with reductions in incidence of stroke, myocardial infarction, and heart failure as well as associated disability and death. This article reviews the ACC/AHA Task Force on Clinical Practice Guidelines' 2017 *Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults*. Key changes include reclassification of BP stages and lowering of hypertension treatment goals.

Keywords: BP, high BP, hypertension, guideline, diagnosis, treatment

Learning objectives

- Compare and contrast the JNC 7 and 2017 guidelines for the diagnosis and management of hypertension.
- List the stages of hypertension and their corresponding treatment recommendations.

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Elevated systolic and diastolic BPs are associated with an increased risk of cardiovascular disease (CVD), including myocardial infarction (MI), heart failure, stroke, and kidney failure, with their associated direct and indirect costs, disability, and premature death.[1,2] The estimated direct and indirect cost of treating hypertension was $51.2 billion in 2012-2013 and total direct cost is estimated to be $200 billion by 2030.[3] Lifestyle modifications and antihypertensive medications reduce elevated BP and the associated morbidity and mortality.[1] Ideal BP targets and treatments optimize the balance between the complications of elevated BP and adverse reactions from excessive BP lowering. Hypertension guidelines are intended to reflect critical evaluation of the available evidence and provide recommendations for the prevention, detection, evaluation, and treatment of hypertension to provide the greatest patient benefit and least amount of harm.

HISTORY OF HYPERTENSION GUIDELINES

Since the first report of the Joint National Committee (JNC) on Detection, Evaluation, and Treatment of High Blood Pressure was published in 1976, six updated reports were commissioned and published by the National Heart, Lung, and Blood Institute (NHLBI), with the last, JNC 7, published in 2003.[4] The JNC 8 panel convened work in 2008 on a strictly evidence-based hypertension

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Key points

- Hypertension affects about one-third of US adults.
- The estimated direct and indirect cost of treating hypertension was $46.4 billion in 2011 and is estimated to be $274 billion by 2030.
- The most recent hypertension guideline reclassifies BP stages and refines hypertension treatment goals.
- Accurate diagnosis and evidence-based treatment can reduce cardiovascular events and associated disability and death in patients with hypertension.

guideline that relied exclusively on evidence from randomized controlled trials and was limited in scope. In 2013, the NHLBI announced it would discontinue developing clinical guidelines, including those in progress.[5] The JNC 8 writing group declined partnership with the American College of Cardiology (ACC) and the American Heart Association (AHA) and published its report in the *Journal of the American Medical Association* in 2014.[6]

To address the lack of a comprehensive hypertension guideline that might incorporate additional forms of evidence beyond that from randomized controlled trials, and because new data were available, the ACC and AHA sponsored development of a new guideline for the prevention, detection, evaluation, and management of high BP in adults.[7] Compared with its JNC predecessors, this guideline used a new methodology and evidence review approach intended to provide clinicians with useful, comprehensive evidence-based recommendations. Evidence was drawn primarily from randomized controlled trials but also included consideration of meta-analyses of randomized controlled trials, systematic reviews, nonrandomized studies, cohort studies, and expert opinion.

For the first time, the ACC/AHA Task Force on Clinical Practice Guidelines excluded members with relevant relationships with industry, to avoid real or perceived bias. The task force included representative experts from diverse backgrounds, perspectives, scopes of practice, and interests: physicians, a pharmacist, a nurse, a physician assistant, epidemiologists, public health experts, and two lay persons; with representatives from the American Academy of PAs, American College of Preventative Medicine, American Geriatric Society, American Pharmacists Association, American Society of Hypertension, Association of Black Cardiologists, National Medical Association, and Preventive Cardiovascular Nurses Association.

The task force was assisted by an independent evidence review committee consisting of methodologists, epidemiologists, biostatisticians, and clinicians. The evidence review committee systematically surveyed and assessed evidence to address key clinical questions for review by the task force. Using this approach, the 2017 guideline is the most current, comprehensive, and collaborative guideline for the prevention, detection, evaluation, and management of hypertension.

NEW RECOMMENDATIONS FOR HYPERTENSION

BP classification A log-linear relationship exists between BP and increased CVD risk.[8,9] BP classification is useful for clinical management and population health initiatives. The 2017 guideline classifies BP into four categories: normal, elevated, and stages 1 and 2 hypertension.[7] **Table 1** compares the current classification to the JNC 7 taxonomy. Classification is based on two or more correctly measured BP readings obtained on two or more occasions.

The greatest departures from the JNC 7 are the elimination of prehypertension, the addition of a new definition for elevated BP, and the reclassification of the stages of hypertension. Reclassifying a systolic BP of 130 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg as stage 1 hypertension instead of prehypertension increases awareness of the CVD risk associated with these BP ranges. Earlier recognition of CVD risk can promote intensified lifestyle modification and earlier intensive pharmacologic treatment.

TABLE 1. Comparing BP classifications[4,7]

If the patient's systolic and diastolic BPs fall into different categories, classify the patient's hypertension according to the highest category.

Systolic BP (mm Hg)	Diastolic BP (mm Hg)	2017 guideline	JNC 7
<120	<80	Normal	Normal
120-129	<80	Elevated	Prehypertension
130-139	80-89	Stage 1 hypertension	
140-159	90-99	Stage 2 hypertension	Stage 1 hypertension
≥160	≥100		Stage 2 hypertension

BP treatment The foundation of BP treatment is nonpharmacologic intervention. Weight loss is indicated to reduce BP in adults who are overweight or obese.[7] Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension.[7] In addition, a diet such as the Dietary Approaches to Stop Hypertension eating plan, reduced intake of dietary sodium, enhanced intake of dietary potassium (unless contraindicated), and moderation in alcohol intake are recommended as nonpharmacologic therapies for the treatment of elevated BP and hypertension (**Table 2**).[7]

Nonpharmacologic therapy is the preferred therapy for adults classified with elevated BP.[7] This also should be the first-line therapy in patients with stage 1 hypertension who are not at elevated CVD risk (that is, those without coronary heart disease, heart failure, stroke, or

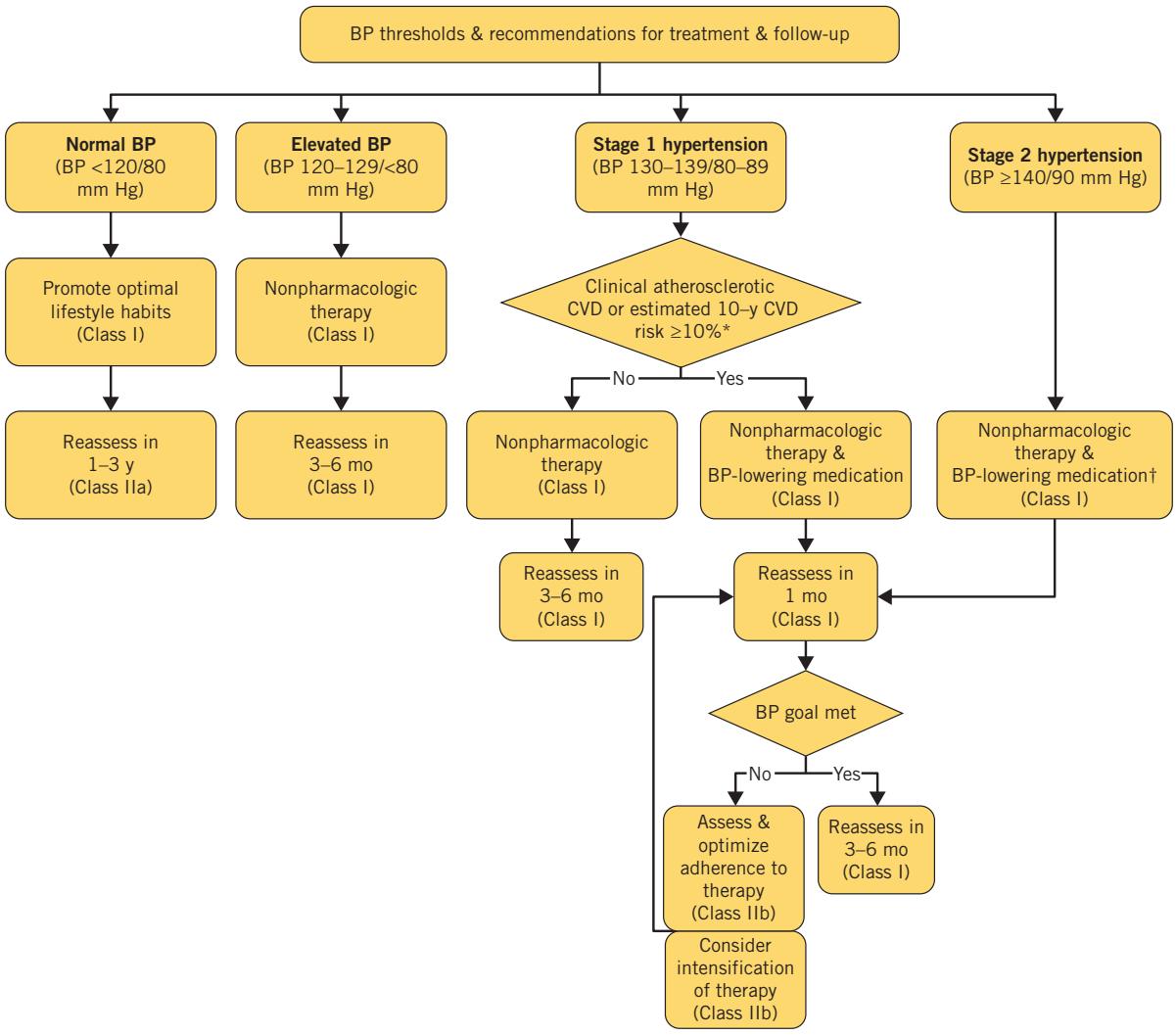

FIGURE 1. BP thresholds and recommendations for treatment and follow-up[7]

* Using the ACC/AHA pooled cohort equations. Patients with diabetes or chronic kidney disease are automatically placed in the high-risk category. For initiation of renin-angiotensin system inhibitor or diuretic therapy, assess blood tests for electrolytes and renal function 2 to 4 weeks after initiating therapy.

† Consider initiating pharmacologic therapy for stage 2 hypertension with two antihypertensive agents of different classes. Patients with stage 2 hypertension and BP ≥ 160/100 mm Hg should be promptly treated, carefully monitored, and subject to upward medication dose adjustment as necessary to control BP. Reassessment includes measuring BP, detecting orthostatic hypotension in selected patients (older adults or those with postural symptoms), identifying white-coat hypertension or white-coat effect, documenting adherence, monitoring response to therapy, reinforcing the importance of adherence, reinforcing the importance of treatment, and assisting with treatment to achieve BP target.

an estimated 10-year risk of CVD of 10% or greater calculated by the ACC/AHA Pooled Cohort Equations).[7,10] Along with lifestyle modification, antihypertensive medication should be initiated in patients with stage 1 hypertension and elevated CVD risk and in patients with stage 2 hypertension.[7] **Figure 1** provides an overview of BP classifications and recommendations for treatment and follow-up.

Select BP-lowering medications based on evidence and shared decision-making, considering patient preferences, comorbidities, overall health, drug interactions, and drug cost. When a patient has comorbidities (such as heart failure, ischemic heart disease, or chronic kidney disease), choose drugs based on data supporting specific antihypertensive drug classes (**Table 3**).[7] A meta-analysis conducted by the evidence review committee found no evidence of differences in prevention of all-cause mortality for major drug classes: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers, and thiazide diuretics.[9] However, differences did exist in some forms of major morbidity, such as cardiovascular events and heart failure.[11] Therefore, the primary agents that should be employed, in the absence of a specific compelling indication, include ACE inhibitors, ARBs, calcium channel blockers, and thiazide diuretics.[7,11]

Also consider the patient's ethnicity and race in initial antihypertensive drug selection. In black patients without heart failure or nephropathy, including those with diabetes, initial treatment should favor a thiazide diuretic or calcium channel blocker over an ACE inhibitor or ARB, based on the superior results from clinical trials in reducing BP and CV events.[11]

Combination therapy with two or more drugs often is necessary to reach BP goals.[12] For patients with stage 2 hypertension, initiation of drug therapy with two agents, either as separate drugs or in fixed-dose combination, is recommended.[7] Numerous two- and three-drug combinations are available as fixed-dose combinations. Avoid prescribing drugs with similar mechanisms of action or clinical effects (for example, two different nondihydropyridine calcium channel blockers or more than one renin-angiotensin system blocker).

Look for modifiable causes of resistance or secondary causes of hypertension in patients with resistant hypertension and those who need four or more antihypertensive medications to attain goal BP. Ask if the patient is adhering to his or her prescribed medications. Reviewing pharmacy fill rates may be helpful but it can be difficult to accurately verify or disprove adherence. If the patient's BP is resistant to treatment and the patient is thought to be adherent, obtain ambulatory or home BP measurements to exclude a white-coat effect, which is associated with minimal or no increase in CVD risk.[13,14]

TABLE 2. Approximate BP reduction with nonpharmacologic treatment in patients with hypertension[7]

Intervention	Approximate reduction in systolic BP (mm Hg)
Weight loss	5
Healthful diet	11
Dietary sodium reduction	5 to 6
Dietary potassium increase	4 to 5
Physical activity: • Aerobic • Dynamic • Isometric	 • 5 to 8 • 4 • 5
Moderate alcohol intake	4

Assess patients for contributing lifestyle factors, including obesity, physical inactivity, excessive alcohol use, and high sodium intake, and counsel them to make changes. Discontinue substances that may elevate BP, such as nonsteroidal anti-inflammatory drugs, stimulants, oral contraceptives, decongestants, and certain herbal supplements. Evaluate for secondary causes of hypertension and maximize pharmacologic treatment if indicated. Refer patients to a hypertension specialist or an endocrinologist when the treatment of secondary causes of hypertension exceeds the scope of practice of the managing clinician.[7]

BP treatment goals Adequately powered randomized controlled trials and meta-analyses of randomized controlled trials provide the best evidence for optimal BP targets. However, variations in inclusion and exclusion criteria, pharmacologic therapies, and methods of BP measurement may limit extrapolation to the general population. Despite these limitations, the recent Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated that more intensive BP control (systolic BP below 120 mm Hg) compared with standard control (systolic BP below 140 mm Hg) was associated with improved clinical outcomes—including lower risk for heart failure, death from CV events, and death from any cause—particularly among patients at the greatest risk for CV events (number needed to treat [NNT] for primary composite outcome = 61, median follow-up 3.26 years).[15] In patients age 75 years and older in the SPRINT trial who had higher baseline CVD risk, improvement in outcomes was more pronounced (NNT = 27).[16] Meta-analyses, including SPRINT, comparing less-intense versus more-intense BP control demonstrate that more intensive BP reduction (to a systolic BP less than 130 mm Hg, compared with higher targets) significantly reduced the risk of stroke, major CV events,

and CV mortality but not heart failure or all-cause death in patients with elevated CVD risk.[4] Based on these studies, the guideline writing committee concluded that adults with hypertension and at high risk of CVD should be treated to a target BP of less than 130/80 mm Hg.[7,16,17]

Treating adults without elevated risk of CVD to a goal of less than 130/80 mm Hg also may be reasonable.[7] Although limited data indicate that BP treatment decreases CV morbidity and mortality in lower-risk patients, this group is systemically understudied and clinical trial evidence is lacking. Clinical trials demonstrating reduced morbidity and mortality for lower-risk patients would likely require significant numbers of patients with a prolonged follow-up, which would be unrealistic and cost-prohibitive. However, clinical evidence has shown that both drug and nondrug therapy can interrupt the progressive course of hypertension.[18] In addition, observational studies suggest that more intense BP lowering can slow the progression of hypertension and reduce the lifetime risk of CV events.[7] Based on the most recent and highly powered randomized controlled trials, the 2017 guideline does not recommend different BP goals for patients based on age. Results from SPRINT and the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial demonstrated that treatment goals for adults age 65 years and older need not differ from those for adults under age 65 years.[15,19] Therefore, community-dwelling, ambulatory older adults with hypertension should be treated to a systolic BP of less than 130 mm Hg with careful monitoring for adverse reactions including orthostatic hypotension, falls, and reduced renal function.[6] For older patients with multiple comorbidities and limited life expectancy, advanced cognitive impairment, or frequent falls, a less-aggressive BP target may be reasonable based on clinical judgment and patient preference.[7]

TABLE 3. First-line drugs for patients with hypertension and comorbid diseases[7]

Ischemic heart disease
- First choice for patients with a history of MI: Beta-blockers and ACE inhibitors.
- Beta-blockers are recommended for patients with angina with or without the addition of dihydropyridine calcium channel blockers for further angina control.
- Other drugs, such as dihydropyridine calcium channel blockers, thiazide diuretics, and/or mineralocorticoid receptor antagonists, may be added to achieve target BP.

Heart failure with reduced ejection fraction
- First choice: ACE inhibitors or ARBs, angiotensin receptor-neprilysin inhibitor-ARB combination, mineralocorticoid receptor antagonists, diuretics, and guideline-directed beta-blockers (carvedilol, metoprolol succinate, or bisoprolol).
- Not recommended: Nondihydropyridine calcium channel blockers.
- Do not use ACE inhibitors and ARBs in combination.

Heart failure with preserved ejection fraction
- Prescribe diuretics to control hypertension in patients with symptoms of volume overload.
- Chlorthalidone reduces the risk of heart failure compared with amlodipine, doxazosin, and lisinopril.
- Avoid nondihydropyridine calcium channel blockers, nitrates, and alpha-blockers, which are known to have deleterious consequences in patients with heart failure.

Chronic kidney disease (CKD)
- ACE inhibitors, or ARBS in patients intolerant to ACE inhibitors, may slow kidney disease progression and are reasonable for patients with stage 3 or higher CKD, or stage 1 or 2 CKD with albuminuria greater than 300 mg per day.

Diabetes
- All classes of first-line antihypertensive agents (diuretics, calcium channel blockers, ACE inhibitors, or ARBs) are effective. ACE inhibitors or ARBs may be preferred in patients with albuminuria.

A less-aggressive BP target may be appropriate for older patients with multiple comorbidities.

EVALUATION AND DIAGNOSIS

Before diagnosis and treatment, obtain a thorough history and perform a physical examination. A physical examination can identify features suggestive of secondary hypertension and assess for target-organ damage caused by hypertension.

Historical and physical features suggestive of primary hypertension include a gradual increase in BP over time, lifestyle factors associated with elevated BP (such as decreased physical activity, increased dietary sodium, and excessive alcohol consumption), and overweight or obesity.[7] Evaluate the patient's clinical features for common secondary causes of hypertension (**Table 4**) and address them as appropriate.

To confirm the diagnosis of hypertension, obtain accurate patient BP measurements using the average of two to three measurements obtained on two to three occasions and measured while the patient is relaxed and has been sitting in a chair for at least 5 minutes.[7] Use a validated

TABLE 4. Features that suggest a secondary cause of hypertension[7]

Features	Possible cause of hypertension
Snoring, daytime sleepiness, fitful sleep, breathing pauses during sleep	Obstructive sleep apnea
Muscle cramps, weakness, hypokalemia	Primary aldosteronism
Weight loss, heat intolerance, palpitations, diarrhea, insomnia	Hyperthyroidism
Weight gain, cold intolerance, dry skin, constipation	Hypothyroidism
Labile BP, headache, sweating, palpitations	Pheochromocytoma
Use of nonsteroidal anti-inflammatory drugs; stimulants; oral contraceptives; certain herbal supplements; tobacco; alcohol; cocaine, amphetamines, or other illicit drugs	Drug- or alcohol-induced

device and appropriate size cuff, and support the patient's arm during measurement.[4] Initially, obtain and record BP from both arms. Use the arm with the higher reading for subsequent measurements.[7] Although office measurements are recommended for initial diagnosis and management, out-of-office measurement using home BP monitoring or ambulatory BP monitoring is useful to confirm the diagnosis, screen for white-coat effect and masked hypertension, and to monitor patient response to treatment.

Several basic and optional tests are recommended in patients newly diagnosed with hypertension to establish a baseline for medication use, screen for secondary causes, and identify other CVD risk factors. Basic testing should include a fasting blood glucose level, complete blood cell count, metabolic profile, lipid profile, thyroid-stimulating hormone, urinalysis, and ECG.[7] Optional studies include a urinary albumin to creatinine ratio, serum uric acid, and an echocardiogram.[7] Additional screening tests for secondary causes of hypertension are included in the guideline.

TREATMENT FOLLOW-UP

Appropriate follow-up is necessary to assess patient adherence and response to treatment. Patients with elevated BP or stage 1 hypertension who have initiated lifestyle modifications should have a repeat BP evaluation in 3 to 6 months.[7] Patients started on antihypertensive therapy should have a repeat BP evaluation in 1 month.[7] The follow-up evaluation should include BP measurement, assessment of adherence to medication and lifestyle modifications, review of medication adverse reactions, assessment of target organ damage, determination of the need for laboratory testing (including electrolyte and renal function status), and need for adjustment of medication regimen.[7] Consider intensifying therapy if the BP goal is not met.[7]

The inconsistencies between office and out-of-office BP measurements increasingly are being recognized. These inconsistencies, together with more aggressive targets for hypertension control, have led to increased focus on out-of-office BP readings, especially home BP monitoring. Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for medication titration.[7]

TREATMENT STRATEGIES

Promote medication adherence and lifestyle modification

Educate patients about hypertension and its consequences: adhering to prescribed medications and/or a healthful lifestyle helps patients achieve optimal BP control and reduce CVD morbidity and mortality. Patient factors affecting poor adherence include low health literacy, health beliefs, lack of involvement in the treatment decision-making process, complexity or inconvenience of medication regimen, and resource constraints.[7]

> Once-daily medications may improve patient adherence.

Clinicians can improve patient health literacy by using the teach-back method, using visual education, and empowering patients to ask questions.[7] Encourage patients to use adherence support tools such as reminders and pillboxes.[7] Prescribing medications dosed once daily rather than multiple times daily and using combination antihypertensive drugs rather than multiple individual drugs are recommended to improve adherence.[7] Consider the costs and potential adverse reactions when choosing antihypertensive therapy for patients.

Screen all adults for tobacco, alcohol, and substance abuse, and provide behavioral interventions if needed.[7] Cognitive behavioral interventions and support groups may help patients lose weight and increase their physical

activity.[4] Address barriers to healthful behavior, such as lack of access to affordable, healthful foods; unsafe environments; transportation and language barriers; and lack of knowledge of healthful foods and activities. Dietitians, social workers, nurses, and community healthcare providers may be helpful in addressing barriers to lifestyle modification.

Team-based care Effective BP reductions can be improved through team-based care.[7] Team members may include physicians, physician assistants, nurses, pharmacists, and other healthcare professionals who can provide patient support and increase access to care. Team members, within the scope of their knowledge and training, can diagnose and manage hypertension, titrate and change medications, provide patient education, facilitate lifestyle changes, coordinate care, and implement process changes to improve care and outcomes.

CONCLUSION

Detection, accurate diagnosis, and evidence-based treatment of hypertension are important to reduce CV events. Once diagnosed with hypertension, patients should be treated to achieve a target BP of less than 130/80 mm Hg. Nonpharmacologic therapy with appropriate lifestyle modification is recommended for all patients with elevated BP or hypertension. In addition, antihypertensive medication is recommended for patients with stage 1 hypertension who are at high risk for CVD and patients with stage 2 hypertension, and should be considered in others who have not achieved goal BP despite nonpharmacologic therapy.

Choose antihypertensive medications based on the patient's comorbid conditions, contraindications, potential drug interactions and adverse reactions, ethnicity and race, and patient preference. Follow up appropriately to assess for possible adverse medication reactions and to ensure that patients reach their BP targets. Evaluate each patient's adherence to nonpharmacologic and pharmacologic therapies and use team-based approaches to improve BP control and reduce hypertension-associated morbidity and mortality. **JAAPA**

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REFERENCES

1. Yoon PW, Gillespie CD, George MG, et al. Control of hypertension among adults—National Health and Nutrition Examination Survey, United States, 2005-2008. *MMWR Suppl*. 2012;61(2):19-25.
2. Kung HC, Xu J. Hypertension-related mortality in the United States, 2000-2013. *NCHS Data Brief*. 2015;(193):1-8.
3. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *Circulation*. 2017;135(10):e146-e603.
4. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560-2572.
5. Gibbons GH, Shurin SB, Mensah GA, Lauer MS. Refocusing the agenda on cardiovascular guidelines: an announcement from the National Heart, Lung, and Blood Institute. *Circulation*. 2013;128(15):1713-1715.
6. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520.
7. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *J Am Coll Cardiol*. [e-pub Nov. 7, 2017].
8. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360(9349):1903-1913.
9. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014;383(9932):1899-1911.
10. American College of Cardiology. ASCVD risk estimator plus. http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate. Accessed March 14, 2018.
11. Reboussin DM, Allen NB, Griswold ME, et al. Systematic review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *J Am Coll Cardiol*. [e-pub Nov. 7, 2017].
12. Gradman AH, Basile JN, Carter BL, et al. Combination therapy in hypertension. *J Clin Hypertens (Greenwich)*. 2011;13(3):146-154.
13. Tientcheu D, Ayers C, Das SR, et al. Target organ complications and cardiovascular events associated with masked hypertension and white-coat hypertension: analysis from the Dallas Heart Study. *J Am Coll Cardiol*. 2015;66(20):2159-2169.
14. Briasoulis A, Androulakis E, Palla M, et al. White-coat hypertension and cardiovascular events: a meta-analysis. *J Hypertens*. 2016;34(4):593-599.
15. Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103-2116.
16. Williamson JD, Supiano MA, Applegate WB, et al. Intensive versus standard blood pressure control and cardiovascular disease outcomes in adults aged ≥ 75 years: a randomized clinical trial. *JAMA*. 2016;315(24):2673-2682.
17. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels—updated overview and meta-analyses of randomized trials. *J Hypertens*. 2016;34(4):613-622.
18. Julius S, Nesbitt SD, Egan BM, et al. Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med*. 2006;354(16):1685-1697.
19. Cushman WC, Evans GW, Byington RP, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362(17):1575-1585.