COURSE #94223 — 5 CONTACT HOURS/CREDITS RELEASE DATE: 10/01/22 EXPIRATION DATE: 09/30/25

# Hypertension: Strategies to Improve Outcomes

## HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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***Faculty***

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***Faculty Disclosure***

Contributing faculty, John J. Whyte, MD, MPH, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

***Audience***

This course is designed for all physicians, physician assistants, nurses, and pharmacy professionals involved in the care of patients with hypertension.

***Accreditations & Approvals***

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*A complete Works Cited list begins on page 21.*

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### *Special Approvals*

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The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

### *Disclosure Statement*

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### *Course Objective*

The purpose of this course is to provide healthcare professionals with the information necessary to develop treatment regimens associated with optimal adherence and provide adequate patient education, counseling, and support to patients with hypertension.

### *Learning Objectives*

*Upon completion of this course, you should be able to:*

1. Apply epidemiologic trends in hypertension to current practice so at-risk patient populations can be more easily identified, assessed, and treated.
2. Utilize knowledge of the pathophysiology of hypertension to create comprehensive treatment strategies that target critical pathways in disease development and progression.
3. Identify the nonpharmacologic interventions for hypertension that are supported by contemporary evidence and are in adherence with guideline recommendations.
4. Discuss the risks and benefits of pharmacologic approaches to hypertension management.
5. Describe strategies to improve patient adherence to hypertension medication by developing treatment regimens associated with optimal adherence and providing adequate patient education, counseling, and support.
6. Analyze necessary modifications in treatment for special populations.

### *Pharmacy Technician Learning Objectives*

*Upon completion of this course, you should be able to:*

1. Outline the epidemiology and pathophysiology of hypertension.
2. Describe pharmacologic and nonpharmacologic options for the management of hypertension.
3. Evaluate adherence to hypertension management recommendations and considerations for special populations.


Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

## INTRODUCTION

Hypertension is a significant cause of morbidity and mortality and a major modifiable risk factor for cardiovascular disease (CVD) as well as stroke, end-stage renal failure, and peripheral vascular disease [1; 2; 3; 4]. The majority (approximately 75%) of adults with CVD comorbidities have hypertension, and poor control of hypertension further exacerbates CVD risk [4; 5]. Hypertension is also associated with shorter overall life expectancy [6]. The goals of hypertensive management are to reduce elevated blood pressure, reduce overall cardiovascular risk, and prevent end-organ damage [3]. These goals can be effectively accomplished through lifestyle interventions, diet, exercise, and appropriate pharmacologic treatment.

While the rates of blood pressure control in hypertensive patients have improved, the management of hypertension remains far from optimal. As of 2018, only 43.7% of all adults with hypertension had adequately controlled blood pressure [1]. One reason for this is poor adherence to antihypertensive medications. About half of patients being treated discontinue their antihypertensive medications within one year [7]. A study of older adults found that 14.1% had low medication adherence and 27.0% had a non-persistent medication possession ratio, reflecting an extended amount of time between prescription fills; 33.7% of the patients studied had uncontrolled blood pressure [8]. Moreover, although certain patient populations (e.g., older adults, non-Hispanic Black Americans, patients with diabetes and/or chronic kidney disease [CKD]) are experiencing higher rates of antihypertensive treatment, they continue to experience high rates of inadequately controlled blood pressure [9]. Importantly, continued efforts are needed to close treatment gaps and establish the benefits of antihypertensive therapy in all patients with hypertension.

## EPIDEMIOLOGY OF HYPERTENSION

Approximately 122 million Americans (47%) have hypertension (defined as systolic blood pressure [SBP] ≥130 mm Hg and/or diastolic blood pressure [DBP] ≥80 mm Hg), while another 28.2% have prehypertension [1]. Prehypertension is defined as blood pressures ranging from 120–139 mm Hg systolic and/or 80–89 mm Hg diastolic in those individuals identified at high risk for developing hypertension and as potentially receiving benefit from early intervention with antihypertensive therapy [1; 10]. However, these data do not reflect how many patients suffer from hypertension but remain undiagnosed. Analysis of electronic medical records reveals that the diagnosis rate of prevalent hypertension is 62.9% while the diagnosis rate of incident hypertension is 19.9%, leaving many patients underdiagnosed [11]. Underdiagnosis is particularly common among survivors of transient ischemic attack (TIA) or minor stroke, due largely to medium-term variability in blood pressure measurements [12].

For individuals with hypertension, roughly 61% are aware of their hypertension, with nearly 43% receiving antihypertensive treatment [1]. However, as noted, only 47% have their hypertension adequately controlled [1]. Of those with uncontrolled hypertension, 39% are not aware of their hypertension [1]. Furthermore, 13.7% of U.S. adults with hypertension meet the criteria for resistant hypertension [1]. Resistant hypertension is defined as blood pressure remaining above goal despite antihypertensive therapy consisting of at least three different classes of antihypertensive agents [13]. Analysis further indicates that approximately 28% of U.S. adults have undiagnosed hypertension [1]. By 2030, it is projected that 41.4% of all U.S. adults will have hypertension, an 8% increase from 2013 [4].

Risk factors for the development of hypertension include, but are not limited to, age, ethnicity, familial history of hypertension and genetic factors, lower levels of physical activity, weight gain, use of tobacco, and dietary factors such as inadequate intake of fruits and vegetables [1]. Importantly, controlling dietary and lifestyle risk factors has the potential to significantly lower or prevent many cases of hypertension [14].

## RACE/ETHNICITY AND SPECIAL POPULATIONS

In the United States, the prevalence of hypertension in Black Americans is among the highest in the world [1]. The overall prevalence of hypertension in Black Americans is nearly 56%, with greater prevalence in Black men (57%) [1]. Black Americans develop hypertension earlier in life, with much higher average blood pressures compared with White Americans [15]. Thus, they face greater morbidity and mortality due to hypertension, with greater rates of fatal and nonfatal stroke, death due to heart disease, and end-stage kidney disease [16]. The highest rates of hypertension within the Black community tend to be among individuals who are middle-aged or older, physically inactive, typically overweight or obese, and have type 2 diabetes [16].

In Hispanic Americans, data indicate that rates of hypertension may be similar or lower than non-Hispanic White Americans [1]. Black Hispanics are at greater risk of hypertension than White Hispanics, as data shows higher income, better-educated Black Hispanics have higher rates of hypertension than lower-income, less-educated White Hispanics [1]. In Mexican Americans, 48.8% of men and 38.1% of women have hypertension [1]. Among Hispanic subpopulations, Puerto Rican Americans experience the highest mortality rate associated with hypertension (154.0 per 100,000) and Cuban Americans report the lowest (82.5 per 100,000) [17].

While efforts to raise awareness about hypertension and the importance of receiving antihypertensive treatment have been successful, substantial ethnic disparities remain in adequately controlling hypertension. Non-Hispanic Black Americans, for example, have the poorest rates of blood pressure control, with 70% higher odds of poorly controlled blood pressure than that of White Americans [1].

Treatment disparities associated with hypertension are not limited to a particular race or ethnicity; the elderly are also affected. While awareness, treatment, and control of hypertension in individuals 65 years of age and older have improved, 78% have blood pressures greater than 140/90 mm Hg [1]. Indeed, among those 80 years of age and older, only 38% of men and 23% of women meet blood pressure targets advocated in clinical guidelines [18]. Hypertension control is extremely poor in women 50 to 79 years of age, with only 36.1% of hypertensive women in this age-group having adequately controlled blood pressure [19]. In postmenopausal women receiving hormonal therapy, hypertension is the most common comorbidity, with a prevalence of 34%, and is associated with significantly higher medical expenditures [20].

## MORBIDITY AND MORTALITY ASSOCIATED WITH HYPERTENSION

In addition to being a significant risk factor for CVD, hypertension is also a significant risk factor for stroke. For every 20/10 mm Hg increase in blood pressure, the mortality from ischemic heart disease and stroke doubles. Therefore, effectively reducing blood pressure will significantly reduce cardiovascular risk [21]. More specifically, antihypertensive therapy can reduce the incidence of myocardial infarction (20% to 25%), stroke (35% to 40%), and heart failure (> 50%) [22]. Thus, effective antihypertensive treatment is critical in reducing the morbidity and mortality associated with hypertension. Hypertension is frequently comorbid with adverse cardiovascular outcomes and contributes to significant healthcare utilization; 69% of patients with a first myocardial infarction, 77% with a first stroke, and 74% with congestive heart failure have

blood pressure >140/90 mm Hg [3]. Furthermore, essential hypertension contributes to nearly 18 million hospitalizations, nearly 34 million office visits, 914,000 emergency department visits, and 3.7 million outpatient visits annually [1].

In 2019, there were 102,072 deaths attributable to hypertension and 414,477 any-mention deaths attributable to hypertension [1]. The death rate for Black individuals was significantly higher than for White individuals: 233.6 and 157.2 (per 100,000 population) for Black men and women, respectively, compared with 143.1 and 104.3 for White men and women, respectively [1]. As noted, hypertension is associated with significant healthcare expenditures, with estimated annual costs of $51.1 billion [1].

These prevalence and epidemiology data indicate that the prevention and management of hypertension is far from optimal. Addressing missed opportunities for adequate control of hypertension would lead to reduced associated morbidity and mortality [1].

## UNDERSTANDING THE PATHOPHYSIOLOGY OF HYPERTENSION

The underlying pathophysiology of hypertension and coronary heart disease follow two pathways: atherogenesis and increased cardiac afterload [23]. Endothelial injury induced by hypertension impairs the synthesis and release of nitric oxide and promotes inflammatory markers, an inflammatory process that figures prominently in the pathogenesis of both hypertension and atherosclerosis [23; 24]. While hypertension accelerates the development of atherosclerosis, sustained periods of elevated blood pressure have a deleterious effect by destabilizing atherosclerotic lesions (i.e., plaque rupture) in the vasculature and contributing to acute coronary events through thrombogenesis [23]. Similarly, mechanisms responsible for blood pressure maintenance (e.g., the renin-angiotensin-aldosterone system [RAS]) also promote atherosclerosis [23].

Increased cardiac afterload due to sustained periods of uncontrolled hypertension contributes to the development of left ventricular hypertrophy [25; 26]. While left ventricular hypertrophy reduces coronary blood flow, it also serves as an independent predictor of adverse cardiovascular outcomes (e.g., heart failure, cardiac death) [23]. Importantly, even in the absence of coronary heart disease, hypertension can induce myocardial ischemia [23].

Newer hypotheses regarding the pathogenesis of hypertension include sympathetic overactivity, which may result from obesity [27]. For instance, animal studies show that rabbits fed a high-fat diet experienced elevated mean arterial pressure and renal sympathetic nerve activity after one week. When the rabbits resumed a normal diet, mean arterial pressure remained elevated, as did renal sympathetic nerve activity [28]. Additionally, a study of obese hypertensive rats demonstrated that sensory denervation of white adipose tissue decreased renal sympathetic activity and mean arterial pressure, likely through inhibition of the adipose afferent reflex. Lidocaine inhibition of neurons in the paraventricular nucleus produced a similar result, suggesting a central pathway for renal sympathetic overactivity [29]. More research is needed in this area.

It is also proposed that hypertension has an immunologic basis. Studies have revealed that hypertension is associated with renal infiltration of immune cells and that immunosuppression (either pharmacologically or pathologically induced) results in reduced blood pressure. Additionally, T lymphocytes and T-cell derived cytokines (e.g., interleukin 17) may play an important role. One hypothesis is that prehypertension results in oxidation and altered mechanical forces that lead to the formation of neoantigens. The neoantigens are presented to T cells, which leads to T-cell activation and infiltration of critical organs (e.g., the kidneys), resulting in persistent or severe hypertension and end organ damage. Activation of the sympathetic nervous system and noradrenergic stimuli has also been shown to promote T-lymphocyte activation and infiltration and contribute to the pathophysiology of hypertension [30; 31; 32; 33; 34; 35].

In the elderly, alterations in arterial structure and function promote age-associated increases in hypertension. Large blood vessels become less flexible, which initiates a complex cardiovascular cascade that ultimately results in increased myocardial oxygen demand and limited organ perfusion. These effects are further enhanced by coronary stenosis. Progressive renal dysfunction further promotes hypertension through increased sodium, reduced sodium-calcium exchange, and decreased potassium excretion, which may lead to hyperkalemia [36].

While the effects of age and vascular risk factors have been well studied in the elderly, more recent data indicate that subtle effects from hypertension develop insidiously earlier in life, with observed effects in young adults [37]. These data emphasize and support the need for early intervention and optimal control of hypertension.

## SYSTOLIC VERSUS DIASTOLIC HYPERTENSION MANAGEMENT

Historically, clinicians have focused on reducing DBP vis-à-vis SBP in terms of controlling hypertension, and the issue of elevated SBP went largely unaddressed in most patients with hypertension, particularly the elderly. Indeed, survey data show that the majority of physicians (75%) fail to treat elevated SBP (140 –159 mm Hg) in older patients [38]. However, evidence continues to accumulate that indicates SBP is a major risk factor for CVD and thus warrants intervention [39].

Changes occur in blood pressure with increasing age. SBP rises continuously throughout life, whereas DBP rises until about 50 years of age and then plateaus [40]. Thus, diastolic hypertension (with or without elevated SBP) is a prominent cardiovascular risk factor before 50 years of age, and systolic hypertension is after 50 years of age [41]. Importantly, studies show that controlling isolated systolic hypertension reduces total and cardiovascular mortality, stroke, and heart failure [42; 43; 44]. As the population ages, greater emphasis should be placed on treating systolic hypertension, because unattended SBP will lead to increased cardiovascular and renal disease [39].

## WHITE-COAT HYPERTENSION

White-coat hypertension is defined as situational elevated blood pressure observed in the presence of a healthcare professional in a clinical setting in contrast to normal blood pressure measurements (in the same patient) obtained through ambulatory or home blood pressure monitoring [10]. Although its criteria may vary, as many as 20% of patients diagnosed with hypertension may be subject to this effect [45]. Antihypertensive therapy for white-coat hypertension is of limited benefit and typically not indicated [10]. Once diagnosed, the patient can be instructed on the importance of judiciously monitoring his or her blood pressure at home. If home monitoring is used, careful calibration of the blood pressure monitor and thorough patient education are essential [46]. Ambulatory blood pressure monitoring may provide a more accurate depiction of variations in day and nighttime blood pressure and be helpful for further assessment of cardiovascular risk. Evidence supports serial blood pressure monitoring at three months after initial diagnosis, then every six months thereafter [47].

Despite little urgency to treat, white-coat hypertension is not an entirely benign condition, as it has been associated with an elevated stroke risk and cardiovascular risk compared to normotensive controls [48]. Patients also have a 1.5 to 2 times increased risk of developing new-onset diabetes mellitus or sustained hypertension compared to normotensive patients [48]. Firm guidelines for the treatment of white-coat hypertension are lacking, but some experts believe that cardiovascular risk factors and documented end-organ damage should be considerations for beginning treatment [49].

## RESISTANT HYPERTENSION

As previously stated, resistant hypertension is defined as blood pressure that remains above target goal despite the use of at least three different classes of antihypertensive therapies at optimal doses, with one being a diuretic [13]. Approximately 13% of patients being treated for hypertension meet this criterion [50]. Making the diagnosis, however, requires that all causes of pseudoresistance be ruled out,

namely improper blood pressure measurement, inadequately prescribed medications, poor adherence to an adequate medication regimen, and white-coat hypertension [51]. In resistant hypertension, blood pressure remains uncontrolled due to persistently elevated SBP [13]. Patients with resistant hypertension typically have a high cardiovascular risk factor burden and systemic comorbidities (e.g., obesity, diabetes, CKD) [13]. As the population ages and the incidence of obesity, diabetes, and CKD continues to rise, the number of patients with resistant hypertension will increase as well. Due to the need for multiple antihypertensive therapies, clinical practice guidelines for resistant hypertension indicate that treatment is largely empiric [13].

Despite the resistance to respond to treatment in these patients, there is some evidence that this form of hypertension could be more effectively treated. A 2012 randomized controlled trial demonstrated a significant reduction in SBP and DBP when subjects exercised on a treadmill three times per week for 8 to 12 weeks. By the end of the study, SBP was reduced by 6±12 mm Hg, while DBP was reduced by 3±7 mm Hg [52]. Another way to approach treatment for resistant hypertension is with the addition of spironolactone into the medication regimen. As an add-on to three-drug therapy, spironolactone resulted in significant decreases in SBP as measured by ambulatory monitoring. Significant decreases in DBP were not observed [53].

Newer therapies on the rise for resistant hypertension include denervation of renal arteries and aldosterone synthase inhibition. Sympathetic hyperactivity in the renal arteries is thought to contribute to hypertension via vasoconstriction and renin release; removal of this stimulus by denervation should therefore decrease blood pressure. The procedure can be done as a minimally invasive surgery with the use of a catheter and radiofrequency ablation. Clinical trials show that this procedure can result in reductions in blood pressure of 20/10 mm Hg one month after treatment and 31/14 mm Hg 24 months after treatment. Trials are underway to further explore these findings [54]. The newer drug class of aldosterone synthase inhibitors is also being evaluated. The rationale behind this treatment is to reduce the amount of aldosterone produced in the body, thus modifying one stimulus for blood pressure elevation. Though this approach has been shown to significantly decrease blood pressure in patients with primary hypertension, it is only modestly effective in patients with resistant hypertension [55; 56].

## THE J-CURVE EFFECT IN HYPERTENSION

Although data support that lowering blood pressure improves outcomes in patients with hypertension, this does not apply universally; lower-than-desired DBP can promote adverse cardiovascular outcomes [57]. This inverse relationship between low DBP and adverse cardiovascular outcomes has been known for decades and is referred to as the J-curve effect. The J-curve effect is most pronounced in patients with pre-existing hypertension, coronary heart disease, or left ventricular hypertrophy [57]. Ideally, the DBP should be maintained between 80 and 85 mm Hg in patients with pre-existing cardiac disease [57]. In addition to those with pre-existing CVD, other patient populations who may be impacted by the J-curve effect include the elderly and Black Americans [58]. The effect may be intensified by the natural nocturnal decrease in blood pressure; thus, patients should avoid late-night doses of antihypertensives. Orthostatic hypotension can also intensify the J-curve effect [58].

Causes for the J-curve effect are unknown, though some explanations have been offered. One explanation is that a low DBP is the result of greater comorbidity, not necessarily the other way around. Another explanation holds that lower DBP signifies a sicker heart. Third, lower DBP may be associated with the widened pulse pressure that accompanies aortic disease. A fourth explanation points to reduced coronary perfusion as being responsible for the J-curve [59].

| HYPERTENSION SCREENING RECOMMENDATIONS | | |
|---|---|---|
| **Classification** | **Systolic/Diastolic Blood Pressure (mm Hg)** | **Follow-Up** |
| Normal | <120/80 | Two years |
| Elevated | 120–129/<80 | Three to six months |
| Stage 1 | 130–139/80–89 | Within two months[a] |
| Stage 2 | ≥140/≥90 | Within one month[b] |

[a]Based on physician's clinical judgment of patient's status and cardiovascular risk factors.
[b]If ≥160/≥100 mm Hg, evaluate and treat immediately.

*Source: [63]* *Table 1*

In high-risk elderly with cardiovascular complications, lowering blood pressure should be done slowly and carefully, avoiding lowering of DBP below 60 mm Hg to minimize decreases in coronary perfusion [57; 60]. Because there is limited additional benefit for cardiovascular risk reduction to intensive blood pressure lowering, guidelines are more likely to ease target goals to <140/90 mm Hg, as advocated by the American Diabetes Association and the American Academy of Family Physicians [60; 61; 62; 159].

## SCREENING FOR HYPERTENSION

Accurate measurement and assessment are critical in identifying those patients with or at risk for hypertension. Patients should be actively encouraged to also monitor their blood pressures outside the clinical setting. The 2017 Guideline for High Blood Pressure in Adults screening recommendations for patients without acute end-organ damage are listed in ***Table 1*** [63]. The report of members of the 8th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) was published in 2014, but this new guideline is limited to the pharmacologic management of hypertension; much of the guidance addressing screening, diagnosis, and lifestyle modification has been removed [39]. The U.S. Preventive Services Task Force recommends screening for hypertension in adults 18 years of age and older [64]. A Veterans' Affairs/Department of Defense task force recommends that screening occur periodically (preferably annually) [65].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Department of Veterans Affairs and the Department of Defense recommend screening adults for elevated blood pressure occur periodically, preferably annually.

(https://www.healthquality.va.gov/guidelines/CD/htn/VADoDHypertensionCPG508Corrected792020.pdf. Last accessed September 22, 2022.)

**Strength of Recommendation**: Strong for

## NONPHARMACOLOGIC INTERVENTIONS FOR HYPERTENSION

Lifestyle modifications are critical as first-line therapy for both preventing and managing hypertension [66]. In terms of lifestyle changes to manage blood pressure, the JNC 8 endorses the joint guideline from the American Heart Association (AHA) and the American College of Cardiology (ACC) on lifestyle management to reduce cardiovascular risk [67]. This guideline recommends major lifestyle modifications recommended by JNC 7 known to lower blood pressure, including weight loss, increased physical activity, and adoption of the Dietary Approaches to Stop Hypertension (DASH) eating plan [67]. For patients with hypertension who may be overweight or obese, even modest weight loss can reduce blood pressure [68; 69]. Regular aerobic physical activity can further facilitate weight loss, decrease blood

| LIFESTYLE MODIFICATIONS TO PREVENT AND MANAGE HYPERTENSION | | |
|---|---|---|
| **Lifestyle Modification** | **Recommendation** | **Approximate Systolic Reduction (mm Hg)** |
| Physical activity | ↑aerobic physical activity to at least 30 min/day, most days | 4–9 |
| DASH eating plan | ↑fruits, vegetables, and low-fat dairy products; ↓saturated and total fat | 8–14 |
| Restrict sodium intake | ↓daily dietary sodium intake to 2.4 g sodium | 2–8 |
| Moderate alcoholic intake | Limit daily intake to 1 drink for women and 2 for men | 2–4 |
| Weight loss | Maintain normal body weight (body mass index 18.5–24.9 kg/$m^2$) | 5–20 per 10 kg weight loss |
| Stress reduction | Practice stress reduction measures | 5 |
| Smoking cessation | Any smoking cessation program | 3–4 |

*Source: [67; 68; 69; 70; 71; 75; 76; 77; 78; 79; 80; 81]* *Table 2*

pressure, and reduce the overall risk of CVD [70; 71; 72]. Other modes of exercise can provide benefit to patients with hypertension. In addition to aerobic endurance training, dynamic resistance training, combined endurance and resistance training, and isometric resistance training can significantly lower DBP; all of these modes except combined training can lower SBP as well, but this may warrant further study. Additionally, moderate-to-high intensity bouts of aerobic endurance activity, cumulating in less than 210 minutes of exercise per week, demonstrated the largest reduction in blood pressure, suggesting that shorter bouts of more intense exercise are more effective for blood pressure reduction than longer bouts at a lower intensity [73]. The American College of Sports Medicine recommends ≥30 minutes of moderate intensity exercise on most, preferably all, days of the week for patients with hypertension and that this training should be supplemented with resistance exercise as well [74]. Though aerobic activity has been shown to have the greatest blood pressure-lowering effect in hypertensives, the effects of the other modes of training discussed are similar. Clinicians should consider the patient's preference of exercise mode when counseling, as patient choice may improve adherence to an exercise program. Examples of lifestyle modifications and their antihypertensive effects are provided in ***Table 2***.

Nutrition is a key component for the prevention and management of hypertension. Adoption of the DASH eating plan can be very beneficial in reducing blood pressure in hypertensive and normotensive patients and in reducing overall CVD [65; 76; 81]. The DASH eating plan reinforces reductions in saturated fat, cholesterol, and total fat while emphasizing fruits, vegetables, fat-free or low-fat milk, whole-grain products, fish, poultry, and nuts, and reducing lean red meat, sweets, added sugars, and sugar-containing beverages [82]. DASH also focuses on increasing intake of potassium, calcium, and magnesium. Importantly, the DASH diet is highly endorsed by the AHA/ACC as an effective treatment option for patients with elevated blood pressure [67]. Key nutritional provisions of the DASH eating plan are listed in ***Table 3***. When combined with exercise and weight loss in overweight or obese patients with high blood pressure, the DASH diet results in even greater reductions of blood pressure (−11.2/−7.5 mm Hg [DASH alone] vs. −3.4/−3.8 mm Hg [usual diet controls]) and provides physiologic benefits, including improvements in vascular function and reduction in left ventricular mass [83].

| DASH EATING PLAN RECOMMENDATIONS: DAILY NUTRIENT GOALS | | | | | | |
|---|---|---|---|---|---|---|
| Food Group | Daily Servings | | | | Examples | Significance Source |
| | 1,600 cal/day | 2,000 cal/day | 2,600 cal/day | 3,100 cal/day | | |
| Whole grains | 6 | 6 to 8 | 10 to 11 | 12 to 13 | Bread, pasta, cereals, oatmeal, brown rice, popcorn | Energy, fiber |
| Vegetables | 3 to 4 | 4 to 5 | 5 to 6 | 6 | Broccoli, carrots, potatoes, spinach, tomatoes, green beans | Potassium, magnesium, fiber |
| Fruits | 4 | 4 to 5 | 5 to 6 | 6 | Apples, bananas, dates, grapes, oranges, melons, peaches, strawberries | Potassium, magnesium, fiber |
| Fat-free/low-fat dairy | 2 to 3 | 2 to 3 | 3 | 3 to 4 | Reduced-fat cheese/milk/yogurt | Calcium, protein |
| Lean meats, poultry, fish | 3 to 6 | ≤6 | 6 | 6 to 9 | Lean, trim visible fat, remove poultry skin, broil or roast | Magnesium, protein |
| Nuts, seeds, legumes | 3 per week | 4 to 5 per week | 4 to 5 per week | 4 to 5 per week | Almonds, peanuts, kidney beans, lentils, walnuts | Energy, magnesium, protein, fiber |
| Fats and oils | 2 | 2 to 3 | 3 | 4 | Soft margarine, vegetable oil, low-fat mayonnaise | – |
| Sweets/added sugars | 0 | ≤5 per week | ≤2 | ≤2 | Fruit punch, hard candy, jelly, maple syrup, sorbet and ices, sugar | Low in fat |

*Source: [82]* *Table 3*

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Department of Veterans Affairs and the Department of Defense recommend a dietitian-led Dietary Approaches to Stop Hypertension (DASH) Diet for the treatment and/or prevention of hypertension for patients with hypertension and/or interested patients with prehypertension and other cardiovascular risk factors.

(https://www.healthquality.va.gov/guidelines/CD/htn/VADoDHypertensionCPG508Corrected792020.pdf. Last accessed September 22, 2022.)

**Strength of Recommendation**: Strong for

Importantly, dietary sodium restriction, alcohol moderation, stress reduction, and smoking cessation can also lower blood pressure. A higher sodium intake is an independent risk factor for developing hypertension [84]. Using multiple lifestyle modifications concurrently can have a synergistic effect on lowering blood pressure and is actively encouraged to reduce cardiovascular risk. For example, in patients with hypertension, simultaneous use of multiple lifestyle changes, such as weight loss, sodium reduction, increased physical activity, limited alcohol intake, and the DASH diet, not only significantly reduces blood pressure but cardiovascular risk as well [85].

The Academy of Nutrition and Dietetics strongly recommends medical nutrition therapy provided by a registered dietitian nutritionist to reduce blood pressure in adults with hypertension [81]. The Academy recommends that the dietitian nutritionist provide medical nutrition therapy at least once per month for the first year, with follow-up sessions at least two to three times per year thereafter to maintain reductions in blood pressure. Their recommendations are based on research indicating significant reductions in SBP (up to 10 mm Hg) and in DBP (up to 6 mm Hg) at 3 months when therapy was provided every other week for a minimum of three sessions; at 6 to 12 months when therapy was provided at least

monthly or with follow-up after five or more sessions; and up to four years when therapy was provided at least two to three times per year [81].

Data indicate that stress contributes to hypertension and cardiovascular mortality [79; 86]. A meta-analysis examining stress reduction approaches (e.g., biofeedback, relaxation-assisted biofeedback, progressive muscle relaxation, stress management training, transcendental meditation) found that transcendental meditation was effective in significantly lowering blood pressure (−5.0/−2.8 mm Hg) and resulted in improvements in other CVD risk factors [79]. Yoga is an exercise modality that not only reduces high blood pressure in prehypertensive and hypertensive individuals, but can also reduce blood glucose and cholesterol levels, with positive effects on body weight [87; 88]. Data show that acupuncture not only improves the circadian rhythm of blood pressure in patients with hypertension but may be superior to pharmacologic therapy in relieving hypertension [89; 90].

Despite known risks, an estimated 12.5% of U.S. adults (13 of every 100) use tobacco [91]. Tobacco use is associated with higher rates of CVD (e.g., hypertension, atherosclerosis), pulmonary diseases such as chronic obstructive pulmonary disease and emphysema, and cancer [92]. Thus, hypertensive smokers experience greater rates of morbidity and significantly increased risk of cardiovascular and all-cause mortality than nonsmokers with hypertension [92; 93]. Smoking cessation provides immediate benefits, with significant lowering of blood pressure (−3.5/−1.9 mm Hg) and heart rate (−7.3 beats per minute) seen as early as one week after cessation [80].

Another nonpharmacologic approach to reducing blood pressure is flaxseed supplementation. Adding flaxseed to the diet of patients with peripheral arterial disease significantly reduced SBP by 10 mm Hg and DBP by 7 mm Hg after six months [94]. Clinical investigators hypothesized that such a drop in blood pressure would equate to a 30% and 50% reduction in the incidence of myocardial infarctions and strokes, respectively [94].

Coenzyme Q-10 is another dietary supplement with potential blood pressure control capabilities. When it is added to conventional medications, patients may experience significant reductions in SBP and DBP after eight weeks. Further reductions remain significant after one year [95]. However, experts agree that more well-conducted trials are needed [96].

Fish oil is a popular supplement used by patients suffering from CVD. Meta-analyses reveal that fish oil supplementation can result in statistically significant reductions in SBP and DBP of 2.56 mm Hg and 1.47 mm Hg, respectively. This effect was only observed in patients with hypertension, as normotensive patients experienced only nonsignificant reductions of blood pressure [97].

In 2013, the American Heart Association issued a scientific statement on alternative approaches to lowering blood pressure [98]. It concludes that it is reasonable for clinicians to consider and recommend alternative approaches (such as exercise, yoga, medication, breathing exercises, and acupuncture) as long as they are used under appropriate circumstances and physician supervision. It is important for clinicians to remember that many of these alternative therapies have benefits beyond lowering of blood pressure.

## PHARMACOLOGIC INTERVENTIONS FOR HYPERTENSION

The major change in the JNC 8 was an adjustment in the blood pressure levels at which pharmacotherapy should be initiated. In the general population of adults younger than 60 years of age, the Committee recommends pharmacologic treatment to lower BP be initiated at SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg [39; 46]. The threshold levels are slightly higher for adults 60 years of age or older (i.e., ≥ 150/90 mm Hg) [46].

| SELECTED ANTIHYPERTENSIVE TREATMENT OPTIONS | |
|---|---|
| **Drug Class** | **Agents** |
| Thiazide diuretics | Bendroflumethiazide, hydrochlorothiazide, chlorthalidone, indapamide |
| Loop diuretics | Bumetanide, furosemide, torsemide |
| Potassium-sparing diuretics[a] | Amiloride, triamterene |
| Aldosterone receptor antagonists[a] | Eplerenone, spironolactone |
| $\alpha_1$-adrenergic antagonists[b] | Doxazosin, prazosin, terazosin |
| β-blockers[a] | Acebutolol, atenolol, bisoprolol, metoprolol, nadolol, nebivolol, propranolol |
| α- and β-blockers[a] | Carvedilol, labetalol |
| ACE inhibitors | Benazepril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril |
| Angiotensin II receptor blockers | Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan |
| Calcium channel blockers | Amlodipine, clevidipine, diltiazem, felodipine, isradipine, nifedipine, nitrendipine, verapamil |
| Direct renin inhibitors | Aliskiren |
| Central $\alpha_2$ agonists[a] | Clonidine, methyldopa, reserpine, guanfacine |
| Direct vasodilators[a] | Hydralazine, minoxidil |
| [a]The JNC 8 does not recommend for the initial treatment of hypertension.<br>[b]The JNC 8 does not recommend for the treatment of hypertension. | |
| *Source: [39; 102; 103; 104; 105]* | *Table 4* |

As discussed, the goals of hypertensive management are to reduce blood pressure, reduce overall cardiovascular risk, and prevent end-organ damage without adversely affecting quality of life, and effectively treating hypertension significantly reduces the incidence of fatal stroke, myocardial infarction, and heart failure and prolongs life expectancy [22; 39; 99; 100]. While lifestyle modifications and nonpharmacologic treatment options are beneficial in reducing blood pressure, approximately 70% of patients with hypertension will require at least two antihypertensive agents to reduce blood pressure to within acceptable ranges [3; 39; 46; 99] To reduce cardiovascular risk in patients with hypertension, antihypertensive agents should ideally provide effective and sustained blood pressure reduction throughout the 24-hour dosing period while attenuating early morning surges in blood pressure and reducing blood pressure variability [101]. After antihypertensive therapy is initiated, patients should be monitored and treatment adjustments made monthly until the desired blood pressure goal is reached [39]. The JNC 7 recommended that serum potassium and creatinine should be monitored every 6 to 12 months for patients receiving antihypertensive therapy; however, monitoring these levels is not addressed by the JNC 8 [3; 39; 46]

Pharmacologic treatment options for hypertension include, but are not limited to, thiazide diuretics, aldosterone receptor antagonists, α-adrenergic antagonists, β-blockers, angiotensin converting enzyme (ACE)-inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and direct renin inhibitors (***Table 4***). The management of hypertension can be challenging given the number of possible combinations of antihypertensive agents that may be needed to effectively reduce blood pressure to target goals.

An extensive review of all antihypertensive agents is beyond the scope of this course. However, an overview of the most commonly used and recommended approaches will be provided.

## DIURETICS

For uncomplicated hypertension in the general non-Black population, the JNC 8 recommends the use of a thiazide-type diuretic, CCB, ACE inhibitor, or ARB as initial antihypertensive therapy due to their propensity to prevent cardiovascular complications associated with hypertension [39]. In the Black population, the preferred first-line agents are thiazide diuretics or CCBs. The panel noted that heart failure outcomes were improved with initial treatment with a thiazide diuretic compared to a CCB or ACE inhibitor; all other outcomes measures were similar among the four drug classes [39]. Thiazide-type diuretics are generally well-tolerated and effective at low doses; higher doses may be associated with hypokalemia and adverse effects such as increased uric acid and sexual dysfunction, with little added benefit [3]. At particularly high doses, thiazide-induced hypokalemia may contribute to ventricular ectopy [106]. Other medication classes (e.g., statins) may be considered if the patient does not respond to initial treatment or combination therapy with these agents [39].

## COMBINATION THERAPY IN MANAGING HYPERTENSION

Blood pressure elevation is typically the result of multiple physiologic factors, so it is very difficult to treat and manage through singular mechanisms of action [3; 99]. As stated, the majority of patients with hypertension will require two or more antihypertensive agents to achieve target blood pressure goals, making combination therapy necessary [3; 39; 99]. Using combinations of antihypertensive agents that have complementary mechanisms of action allows for synergistic lowering of blood pressure, and such a strategy is far more effective in reducing blood pressure than increasing doses of any single antihypertensive agent [107; 108]. Not only is combination therapy effective in reducing blood pressure, but it also offers the opportunity to use lower doses of each component, which may potentially lead to decreased side effects and improved adherence [107]. It is important to note that ACE inhibitors and ARBs should not be prescribed together for combination therapy [39].

Combination antihypertensive therapy also reduces blood pressure variability, which is associated with an increased risk of myocardial infarction and stroke [109]. For example, data show that reducing SBP variability with combination therapy consisting of a diuretic, a CCB, and an ACE inhibitor improves outcomes [109]. Importantly, combination antihypertensive therapy should be approached cautiously in older patients and individuals who are at risk for orthostatic hypotension [3]. However, despite demonstrated benefits, combination therapy for hypertension remains considerably underutilized [110].


In the treatment of hypertension, the Department of Veterans Affairs and the Department of Defense found there is insufficient evidence to recommend for or against initiating combination therapy over initiating monotherapy with the sequential addition of another medication.

(https://www.healthquality.va.gov/guidelines/CD/htn/VADoDHypertensionCPG508Corrected792020.pdf. Last accessed September 22, 2022.)

**Strength of Recommendation**: Neither for nor against

### Renin-Angiotensin System Inhibition: Preferred Combinations

The American Society of Hypertension has reviewed treatment combinations and classified them as preferred, acceptable, and less effective based on efficacy, tolerability, and adherence (***Table 5***) [104].

Blockade of the RAS system has become the cornerstone of antihypertensive management because ACE inhibitors and ARBs have additional benefits for comorbidities (e.g., CKD) [3]. Indeed, ACE inhibitors or ARBs are recommended as foundation therapy for patients with comorbid diabetes [111]. As a result, ACE inhibitors or ARBs are frequently used in combination with a thiazide diuretic (e.g., hydrochlorothiazide, chlorthalidone) to synergistically provide effective reductions in blood pressure [99]. An ACE inhibitor or ARB may attenuate thiazide-induced hypokalemia but can alternatively cause hyperkalemia in susceptible patients [99; 109]. Although hydrochlorothiazide is used most

**AMERICAN SOCIETY OF HYPERTENSION RECOMMENDATIONS FOR DRUG SELECTION IN HYPERTENSIVE PATIENTS WITH OR WITHOUT OTHER MAJOR CONDITIONS**

| Patient Type | First Drug | Add Second Drug If Needed to Achieve a BP <140/90 mm Hg | If Third Drug is Needed to Achieve a BP <140/90 mm Hg |
|---|---|---|---|
| **When hypertension is the only or main condition** | | | |
| Black patients (African ancestry): All ages | CCB[a] or thiazide diuretic | ARB[b] or ACE inhibitor (If unavailable, can add alternative first drug choice) | Combination of CCB + ACE inhibitor or ARB + thiazide diuretic |
| White and other non-Black patients: Younger than 60 years of age | ARB[b] or ACE inhibitor | CCB[a] or thiazide diuretic | Combination of CCB + ACE inhibitor or ARB + thiazide diuretic |
| White and other non-Black patients: 60 years of age and older | CCB[a] or thiazide diuretic (although ACE inhibitors or ARBs are also usually effective) | ARB[b] or ACE inhibitor (or CCB or thiazide if ACE inhibitor or ARB used first) | Combination of CCB + ACE inhibitor or ARB + thiazide diuretic |
| **When hypertension is associated with other conditions** | | | |
| Hypertension *and* diabetes | ARB or ACE inhibitor Note: In Black patients, it is acceptable to start with a CCB or thiazide. | CCB or thiazide diuretic Note: In Black patients, if starting with a CCB or thiazide, add an ARB or ACE inhibitor. | The alternative second drug (thiazide or CCB) |
| Hypertension *and* chronic kidney disease | ARB or ACE inhibitor Note: In Black patients, good evidence for renal protective effects of ACE inhibitors | CCB or thiazide diuretic[c] | The alternative second drug (thiazide or CCB) |
| Hypertension *and* clinical coronary artery disease[d] | β-blocker plus ARB or ACE inhibitor | CCB or thiazide diuretic | The alternative second step drug (thiazide or CCB) |
| Hypertension *and* stroke history[e] | ACE inhibitor or ARB | Thiazide diuretic or CCB | The alternative second drug (CCB or thiazide) |
| Hypertension *and* heart failure | Patients with symptomatic heart failure should usually receive an ARB or ACE inhibitor + β-blocker + diuretic + spironolactone regardless of BP. A dihydropyridine CCB can be added if needed for BP control. | | |

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, BP = blood pressure, CCB = calcium channel blocker, eGFR = estimated glomerular filtration rate.
[a]CCBs are generally preferred, but thiazides may cost less.
[b]ARBs can be considered because ACE inhibitors can cause cough and angioedema, although ACE inhibitors may cost less.
[c]If eGFR <40 mL/min, a loop diuretic (e.g., furosemide or torsemide) may be needed.
[d]If history of myocardial infarction, a β-blocker and ARB/or ACE inhibitor are indicated regardless of blood pressure.
[e]If using a diuretic, there is good evidence for indapamide (if available).

*Source: Reprinted with permission from Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community a statement by the American Society of Hypertension and the International Society of Hypertension. J Hypertens. 2014;32(1):3-15.* *Table 5*

often as the diuretic in fixed-dose combination antihypertensive products, a fixed-dose combination of azilsartan and chlorthalidone was approved by the U.S. Food and Drug Administration in 2011 [103; 105]. Expert consensus and clinical trial data indicate that chlorthalidone may be more effective in reducing blood pressure and cardiovascular risk than hydrochlorothiazide [109; 112; 113]. However, the findings of more recent research do not support the recommendations to prefer chlorthalidone over hydrochlorothiazide [114]. In one large study, chlorthalidone use was not associated with significant cardiovascular benefits compared with hydrochlorothiazide, while its use was associated with greater risk of renal and electrolyte abnormalities [114]. Additionally, one network meta-analysis suggests that hydrochlorothiazide may be the safer choice, based on serum potassium levels [115].

The addition of an ACE inhibitor or ARB to a CCB not only provides effective reduction in blood pressure, but in the case of dihydropyridine-type CCBs (e.g., nifedipine) also improves their tolerability by attenuating the reflex tachycardia and peripheral edema that may be associated with their use [99; 109; 116; 117]. Although providing comparable reduction in blood pressure in high-risk diabetic patients with ischemic heart disease, the combination of ACE inhibitor plus CCB provides greater reductions in cardiovascular risk factors (e.g., myocardial infarction, stroke) than ACE inhibitor plus diuretic [118].

While effective antihypertensive agents when used as monotherapy, data show that dual inhibition with both an ACE inhibitor and ARB may not only ineffectively reduce blood pressure but may cause significant adverse effects as well. In patients with vascular disease or high-risk diabetes, the combination of telmisartan and ramipril was associated with significantly increased risk of syncope, hypotension, and renal dysfunction [119]. Similarly, when combined with an ACE inhibitor or ARB, the renin inhibitor aliskiren led to an increase in nonfatal stroke, renal dysfunction, hyperkalemia, and hypotension, which led to a premature study termination [120].

### Acceptable Combinations for Managing Hypertension

Data show that the combination of the CCB amlodipine plus hydrochlorothiazide is well-tolerated and has similar mortality reduction to valsartan [109; 121]. The combination of a dihydropyridine CCB plus a β-blocker (e.g., felodipine and metoprolol) may effectively reduce blood pressure, although β-blockers should be used cautiously with the CCBs diltiazem and verapamil due to their synergistic effects on heart rate and atrioventricular conduction potentially leading to bradycardia or heart block [99; 109]. Although β-blockers reduce cardiovascular end points, meta-analyses indicate less effectiveness in treating hypertension than diuretics, ACE inhibitors, ARBs, and CCBs [122; 123; 124]. However, there is some evidence that β-blockers may be a reasonable first-line choice in younger-to-middle-aged (younger than 60 years of age) individuals [125; 126]. β-blockers in combination with thiazide diuretics effectively lower blood pressure, but they may be associated with an increased risk of glucose intolerance, fatigue, and sexual dysfunction [99].

### Special Populations

In addition to the American Society of Hypertension clinical practice guidelines on hypertension, clinical practice guidelines are also available on the management of hypertension in the elderly (65 years of age or older), in patients with diabetes, and in patients with CKD [36; 111; 127; 128].

#### *Elderly Patients*

Guidelines for the elderly recommend identifying reversible and/or treatable causes of hypertension, evaluating for end-organ damage, assessing for other CVD risk factors/comorbid conditions, and identifying barriers to treatment adherence [129]. In addition to history, physical exam, and lab testing, there is particular emphasis on accurate assessments of blood pressure, kidney function, and CVD [36]. Recommended lab tests include urinalysis, blood chemistries, lipids, fasting blood glucose, and electrocardiogram. Care should be

taken to address pseudohypertension due to noncompressible arteries and white-coat hypertension [129]. Recommended target blood pressure goals in the elderly are <150/90 mm Hg for uncomplicated hypertension and <140/90 mm Hg for those with coronary artery disease or CKD if they are able to tolerate antihypertensive therapy [39]. However, treatment need not be adjusted for older patients who have achieved a lower blood pressure without adverse effects on health or quality of life [39]. After lifestyle modifications, thiazide diuretics should be the initial pharmacotherapy. However, in elderly patients with coronary artery disease and stable angina or prior myocardial infarction, β-blockers should be the initial pharmacotherapy. Clinicians should pay particular attention to polypharmacy in these patients, and quality of life should be always considered when making therapeutic decisions [1; 129]. Management of hypertension in the elderly is made more difficult by limited clinical trial data upon which to base clinical decision-making.

### *Patients with Diabetes*

The American Diabetes Association (ADA) has issued guidelines for the management of hypertension in diabetic patients [62]. Blood pressure should be measured at every routine visit and, if elevated, measured again on a separate day. The ADA and the JNC 8 agree that the goal for people with diabetes and hypertension is SBP <140 mm Hg, though the ADA states a goal of 130 mm Hg is appropriate in individuals at higher cardiovascular risk (i.e., existing CVD or 10-year CVD risk greater than 15%) [62]. Both the JNC 8 and the ADA recommend DBP should be treated to <90 mm Hg; the ADA has set a lower threshold of <80 mm Hg in individuals at higher cardiovascular risk [39; 62]. Patients who have blood pressure >120/80 mm Hg should initially be advised to undertake lifestyle changes without further pharmacotherapy. Patients who have blood pressure >140/80 mm Hg, however, should promptly begin pharmacotherapy in addition to lifestyle modifications [62]. Pharmacotherapy for this patient population centers on either an ACE inhibitor or an ARB but not both, and multi-drug therapy is generally required to achieve target blood pressure. These medications should be managed by monitoring of serum creatinine/estimated glomerular filtration rate and serum potassium levels [62].

### *Patients with CKD*

The National Kidney Foundation published guidelines on the management of hypertension in CKD in 2004 and revised them in 2021 [127; 128]. Because hypertension is a risk factor for faster progression of kidney disease, antihypertensive therapy not only helps to control blood pressure but also slows this progression. Lifestyle modifications should be initiated, and sodium intake should be limited to <2 grams per day. In patients with CKD with or without hypertension, antihypertensive treatment with ACE inhibitors or ARBs is recommended to lower blood pressure (<130/80 mm Hg), reduce CVD, and slow the rate of kidney decline, with adjustments based on proteinuria [128]. Most patients should also receive diuretics. Long-acting agents should be used when possible, and patients who have SBP >20 mm Hg above goal should begin initial therapy with two agents. A multidisciplinary approach is highly recommended to optimize outcomes in patients with CKD [127].

Since the publication of the National Kidney Foundation guidelines in 2004, the JNC 8 published its own recommendations for blood pressure management in patients with CKD. The JNC 8 recommends initiating pharmacologic treatment at ≥140/90 mm Hg for adults with CKD [39].

## ADHERENCE ISSUES

Successful management of hypertension can only be accomplished through appropriate selection of antihypertensive therapy to effectively lower blood pressure and maintenance of adherence to such therapy by both the patient and clinician. Indeed, successful antihypertensive treatment must be carried out continuously for many years [130]. However, patient nonadherence to antihypertensive therapy is a major barrier to effective control of blood pressure [131; 132]. Research indicates that as many as 70% of hypertensive patients do not take their antihyper-

tensive medications as prescribed [100]. Long-term data indicate that less than 60% of patients are still on their antihypertensive treatment 2 years after starting and only 39% of patients with hypertension remain adherent after 10 years of therapy [133]. Thus, the ultimate challenge is to individualize antihypertensive therapy to achieve optimal levels of blood pressure control while ensuring patient adherence to and continuation of prescribed therapy [134]. The increasing prevalence of uncontrolled or suboptimally controlled blood pressure in the face of significant advances in antihypertensive management has been characterized as the "hypertension paradox" [135].

Factors that contribute to suboptimal patient adherence to antihypertensive therapy are multifactorial, complex, and involve both the patient and his or her healthcare providers. Data from the World Health Organization have categorized factors associated with long-term adherence as social and economic, disease-related, therapy-related, patient-related, and healthcare system/healthcare team-related [136]. Clearly, a number of issues can potentially adversely influence patient adherence. Interestingly, simply forgetting is the most common reason patients give for not taking antihypertensive medication [137]. Other barriers that contribute to nonadherence include cost of care and medication, lack of insurance, transportation issues, and comorbidities [134].

Increasingly complex antihypertensive treatment regimens and unfavorable tolerability profiles are associated with poorer adherence [132; 138; 139]. Simply switching from twice-daily to once-daily antihypertensive agents can improve adherence up to 20% [140]. Moreover, use of single-pill, fixed-dose combination therapy can improve adherence by 26% [141]. Commercially available fixed-dose product formulations may incorporate two or three separate antihypertensive agents.

Clinicians often overestimate levels of adherence to antihypertensive therapy [131]. Furthermore, therapeutic or clinical inertia by clinicians contributes to suboptimal control of blood pressure [142; 143; 144]. Data indicate that in patients with cardiovascular risk factors or established CVD, physicians are frequently less likely to intensify antihypertensive treatment when blood pressure goals have not been met [143]. The quality of the patient-clinician relationship for communicating and building trust can favorably impact adherence; the risk for patient nonadherence increases by 19% in patients whose clinician communicates poorly [134; 145]. Communication skills training programs targeting healthcare professionals' behaviors are promising strategies to reduce disparities and build trust in ethnic minority patients with hypertension [146]. Encouragement and continual reinforcement of patients' active participation in their own care improves adherence to antihypertensive therapy as well as improves self-monitoring of their blood pressure [134].

In a study of older Mexican American patients, those who reported using Spanish more often than English in mass media were more likely to have undiagnosed hypertension [147]. Language barriers can be a serious consideration when engaging in patient education and elucidating possible causes of non-adherence to the established treatment regimen. When a patient does not speak the same language as the clinician, a professional interpreter should be consulted to ensure accurate communication. Use of professional interpreters has been associated with improvements in communication (errors and comprehension), utilization, clinical outcomes, and satisfaction with care [148].

Studies show that suboptimal control of blood pressure is not limited to the primary care setting. For example, one study found that 30.3% of patients with hypertension being seen in a cardiology clinic had suboptimal control of blood pressure (≥140/90 mm Hg) [149]. Moreover, clinic physicians failed to document a treatment plan to address hypertension in 38% of patients with elevated blood pressure [149]. Thus, there are many cases where blood pressure is not only suboptimally controlled but elevated blood pressure is not acted upon when observed. Such data demonstrate a potential opportunity for improvement in hypertension management.

| RECOMMENDATIONS FOR IMPROVING ADHERENCE IN HYPERTENSION | |
|---|---|
| **Strategy** | **Recommendations** |
| Focus on clinical outcomes | Follow clinical practice guidelines.<br>Simplify the antihypertensive regimen.<br>Reassess uncontrolled blood pressures.<br>Remind patients to take medications as directed.<br>Encourage self-monitoring of blood pressure.<br>Use technologic tools to monitor progress toward goals. |
| Empower patients and encourage self-care | Assess patient barriers to adherence.<br>Probe patient knowledge and confidence.<br>Encourage problem solving and behavioral changes.<br>Help patients to ensure prescriptions are refilled. |
| Implement a team approach | Use a collaborative team approach.<br>Apply policies to improve blood pressure control.<br>Support self-management and problem prevention. |
| *Source: [134]* | *Table 6* |

Suboptimal adherence to antihypertensive therapy adversely affects clinical outcomes in patients with hypertension and increases the risk of cardiovascular morbidity and mortality. Acknowledging the need to improve outcomes, the American Society of Hypertension has proposed several strategies to improve patient adherence and persistence to antihypertensive therapy that will result in more effective control of blood pressure (***Table 6***).

## TREATMENT CONSIDERATIONS IN SPECIAL POPULATIONS

### MINORITIES

As noted, the prevalence and control of hypertension differ across racial subgroups. In Black individuals, hypertension is more common, more severe, develops at an earlier age, and is associated with greater sequelae (e.g., higher rates of stroke, heart disease, end-stage renal disease, and mortality) than in non-Hispanic White individuals [1; 150]. Blacks have a greater prevalence of other cardiovascular risk factors, especially obesity [151]. In fact, hypertension is the single most common contributor to the mortality gap between Black and White Americans [3]. For every 10-mm Hg increase in SBP, the risk of stroke in Black Americans is triple that of White Americans (24% vs. 8%, respectively) [152]. Non-Hispanic Black and Mexican Americans have poorer blood pressure control rates than non-Hispanic White Americans [1]. Differences in outcomes may be attributable to differences in socioeconomic conditions, access to healthcare services, attitudes regarding health care, and cultural beliefs [3].

Before initiation of antihypertensive therapy, weight and sodium reduction are particularly effective in minorities [153]. For example, the low-sodium DASH eating plan is associated with significant blood pressure reductions in Black patients [154]. However, monotherapy with ACE inhibitors, ARBs, or β-blockers is less effective in lowering blood pressure in Black patients than White patients [3; 104]. Moreover, Black and Asian patients have a three- to fourfold higher risk of angioedema and have more cough attributed to ACE inhibitors than White patients [3; 155]. The use of combination antihypertensive drug therapy, including a thiazide diuretic, will lower blood pressure and reduce the cardiovascular and renal burden in minorities [39; 104; 153]. Chlorthalidone is particularly beneficial in low-renin patients as well as the elderly and patients with diabetes [155]. Importantly, identifying and addressing treatment barriers is critical to improving outcomes in minority populations [150].

### ELDERLY PATIENTS

Hypertension affects most elderly people, and these individuals are more likely to have organ damage or clinically relevant CVD. On average, elderly patients are taking more than six prescription drugs, so polypharmacy, nonadherence, and potential drug-drug interactions are all important concerns that should be monitored and addressed [36]. Caution is advised when initiating antihypertensive agents in the elderly, and treatment must be individualized. For example, hypertensive elderly patients have a 43% increased risk of hip fracture during the first 45 days after starting antihypertensive treatment [156]. Conducting a risk factor assessment for falls in older adults initiating antihypertensive therapy may improve the recognition of those at risk for serious fall injuries. Independent risk factors include older age; female sex; White race; history of stroke, syncope, osteoporosis, depression or dementia; use of more than 10 medications; and a serious fall injury in the 12 months prior to initiation of antihypertensive therapy [157].

In the elderly, thiazide diuretics are recommended for initiating therapy and are generally well tolerated [36]. Thiazide diuretics reduce cardiovascular events in the elderly but may also exacerbate hyperuricemia, glucose abnormalities, and dyslipidemia, which are frequently seen in the elderly [36]. A 2015 scientific statement from the AHA/ACC/ASH urges caution when using thiazide diuretics in the elderly to avoid decreases in DBP due to reduced coronary perfusion [158]. β-blockers are best suited for patients with migraine and/or cardiovascular comorbidities such as heart failure and coronary artery disease [36]. All β-blockers may result in a decreased response in the elderly as compared with younger adults. Dose reduction, initial lower dose, or dose titrated to the response should be considered [105]. In the elderly, α-adrenergic antagonists are not recommended as first-line therapy due to a possible increase in cardiovascular events [36; 39; 158]. Similar to β-blockers, CCBs are considered safe and effective in elderly patients with cardiovascular comorbidities (e.g., angina, supraventricular arrhythmias) [36; 105]. However, dosing should start at the lower end of dosing range and be titrated to response [36]. Elderly patients have shown a decreased clearance of amlodipine [105]. Immediate-release nifedipine should be avoided due to the potential for postural hypotension, which may precipitate dizziness and falls [36]. Generic versions of verapamil that are bioequivalent in young adults may not be bioequivalent in the elderly [105]. The CCBs verapamil and diltiazem may precipitate heart block in those with underlying defects in cardiac conduction [36]. ACE inhibitors and ARBs are well tolerated, are renal protective, and reduce cardiovascular morbidity and mortality [36]. As with younger patients, combination therapy in the elderly offers an opportunity for enhanced effectiveness, more convenience, and potentially more favorable tolerability in a simplified antihypertensive regimen.

## CONCLUSION

Hypertension is a major risk factor for CVD and is associated with significant morbidity and mortality. Despite a multitude of treatment options, management of hypertension remains suboptimal. Patient adherence with antihypertensive therapy has historically been less than ideal, and the fact that the majority of patients with hypertension will require two or more antihypertensive agents further complicates its management. While the increased use of multiple antihypertensive agents has led to improvement in blood pressure control, disparities in the treatment of hypertension still exist. As new clinical practice guidelines for hypertension will be issued in the near future, clinicians should take the opportunity to incorporate the latest evidence-based medicine into clinical practice and improve outcomes in patients with hypertension.

## FACULTY BIOGRAPHY

**John J. Whyte, MD, MPH**, is currently the Chief Medical Officer at WebMD. In this role, he leads efforts to develop and expand strategic partnerships that create meaningful change around important and timely public health issues. Previously, Dr. Whyte was the Director of Professional Affairs and Stakeholder Engagement at the FDA's Center for Drug Evaluation and Research and the Chief Medical Expert and Vice President, Health and Medical Education at Discovery Channel, part of the media conglomerate Discovery Communications.

Prior to this, Dr. Whyte was in the Immediate Office of the Director at the Agency for Healthcare Research Quality. He served as Medical Advisor/Director of the Council on Private Sector Initiatives to Improve the Safety, Security, and Quality of Healthcare. Prior to this assignment, Dr. Whyte was the Acting Director, Division of Medical Items and Devices in the Coverage and Analysis Group in the Centers for Medicare & Medicaid Services (CMS). CMS is the federal agency responsible for administering the Medicare and Medicaid programs. In his role at CMS, Dr.Whyte made recommendations as to whether or not the Medicare program should pay for certain procedures, equipment, or services. His division was responsible for durable medical equipment, orthotics/prosthetics, drugs/biologics/therapeutics, medical items, laboratory tests, and non-implantable devices. As Division Director as well as Medical Officer/Senior Advisor, Dr. Whyte was responsible for more national coverage decisions than any other CMS staff.

Dr. Whyte is a board-certified internist. He completed an internal medicine residency at Duke University Medical Center as well as earned a Master's of Public Health (MPH) in Health Policy and Management at Harvard University School of Public Health. Prior to arriving in Washington, Dr. Whyte was a health services research fellow at Stanford and attending physician in the Department of Medicine. He has written extensively in the medical and lay press on health policy issues.

**Implicit Bias in Health Care**

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

## Works Cited


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