Cardio-Pharmacotherapy Course

Review of 2025 ACC/AHA Hypertension Guideline; Part 1

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Circulation

CLINICAL PRACTICE GUIDELINES

2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Developed in Collaboration With and Endorsed by American Academy of Physician Associates; American Association of Nurse Practitioners; American College of Clinical Pharmacy; American College of Preventive Medicine; American Geriatrics Society; American Medical Association; American Society of Preventive Cardiology; Association of Black Cardiologists; National Medical Association; Preventive Cardiovascular Nurses Association; and the Society of General Internal Medicine.

Disclosure

- I have no actual or potential conflict of interest in relation to this presentation

Collaboration

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WHAT IS NEW?

New or Revised	Section Title	2017 Recommendation	2025 Recommendation
New terminology	N/A	Hypertensive urgency	Severe hypertension
New recommendation	3.2.3. Secondary Forms of Hypertension	N/A	COR 1: In adults with resistant hypertension, screening for primary aldosteronism is recommended regardless of whether hypokalemia is present to increase rates of detection, diagnosis, and specific targeted therapy.
New recommendation	3.2.3.1. Primary Aldosteronism	N/A	COR 1: In adults with an indication for screening for primary aldosteronism, it is recommended to continue most antihypertensive medications (other than MRA) prior to initial screening to minimize barriers to or delays in screening.
New recommendation	5.1. Lifestyle and Psychosocial Approaches	N/A	COR 2a: In adults with or without hypertension, potassium-based salt substitutes can be useful to prevent or treat elevated BP and hypertension, particularly for patients in whom salt intake is related mostly to food preparation or flavoring at home, except in the presence of CKD or use of drugs that reduce potassium excretion where additional monitoring is probably indicated.

WHAT IS NEW?

Revised recommendation	5.2.2. BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension	COR 1: Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average of SBP ≥130 mm Hg or an average DBP ≥80 mm Hg and for primary prevention in adults with an estimated 10-year ASCVD risk of ≥10% and an average SBP ≥130 mm Hg or an average DBP ≥80 mm Hg	COR 1: In adults with hypertension without clinical CVD but with diabetes or CKD or at increased 10-year CVD risk (ie, ≥7.5% based on PREVENT), initiation of medications to lower BP is recommended when average SBP is ≥130 mm Hg and average DBP is ≥80 mm Hg to reduce the risk of CVD events and total mortality.
Revised recommendation	5.2.2. BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension	COR 1: Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP ≥140 mm Hg or a DBP ≥90 mm Hg	COR 1: In adults with hypertension without clinical CVD and with estimated 10-year CVD risk <7.5% based on PREVENT, initiation of medications to lower BP is recommended if average SBP remains ≥130 mm Hg or average DBP remains ≥80 mm Hg after a 3- to 6-month trial of lifestyle intervention to prevent target organ damage and mitigate further increases in BP.

WHAT IS NEW?

Revised recommendation	5.3.1. Diabetes	COR 2b: In adults with diabetes and hypertension, ACEi or ARB may be considered in the presence of albuminuria.	COR 1: In adults with diabetes and hypertension, ACEi or ARB are recommended in the presence of CKD as identified by eGFR <60 mL/min/1.73 m^2 or albuminuria ≥30 mg/g and should be considered when mild albuminuria (<30 mg/g) is present to delay progression of diabetic kidney disease.
Revised recommendation	5.3.8. Hypertension Treatment in Patients With Chronic Kidney Disease	COR 2a: In adults with hypertension and CKD (stage 3 or higher or stage 1 and 2 with albuminuria ≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void), treatment with an ACEi is reasonable to slow kidney disease progression. AND COR 2b: In adults with hypertension and CKD (stage 3 or higher or stage 1 and 2 with albuminuria ≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void), treatment with an ARB may be reasonable if an ACEi is not tolerated.	COR 1: For adults with hypertension and CKD as identified by eGFR <60 mL/min/1.73 m^2 with albuminuria of ≥30 mg/g, RAASi (either with ACEi or ARB but not both) is recommended to decrease CVD and delay progression of kidney disease.
New recommendation	5.3.9.1. Acute Intracerebral Hemorrhage	N/A	COR 2a: For adult patients with acute spontaneous ICH who present with SBP between 150 and 220 mm Hg, it can be beneficial to immediately lower SBP to 130 to <140 mm Hg for at least 7 days after ICH to improve functional outcomes, but stop antihypertensive medications if SBP <130 mm Hg.

WHAT IS NEW?

New or Revised	Section Title	2017 Recommendation	2025 Recommendation
Revised recommendation	5.3.9.1. Acute Intracerebral Hemorrhage	COR 2a: In adults with ICH who present with SBP >220 mm Hg, it is reasonable to use continuous intravenous drug infusion and close BP monitoring to lower SBP.	COR 2a: In adults with acute spontaneous ICH requiring acute BP lowering, careful titration to ensure smooth, nonlabile, and sustained control of BP, avoiding peaks and large variability in SBP, can be beneficial for improving functional outcomes.
Revised recommendation	5.3.9.2. Acute Ischemic Stroke	COR 3 Harm: Immediate lowering of SBP to <140 mm Hg in adults with spontaneous ICH who present within 6 hours of the acute event and have an SBP between 150 and 220 mm Hg is not of benefit to reduce death or severe disability and can potentially be harmful.	COR 3 Harm: In patients undergoing successful brain reperfusion with endovascular treatment for a large vessel occlusion, lowering SBP <140 mm Hg within the first 24 to 72 hours after reperfusion can worsen long-term functional outcome.
Revised recommendation	5.3.9.4. Mild Cognitive Impairment and Dementia	COR 2a: In adults with hypertension, BP lowering is reasonable to prevent cognitive decline and dementia.	COR 1: In adults with hypertension, a goal of <130 mm Hg SBP is recommended to prevent mild cognitive impairment and dementia.
New recommendation	5.5. Hypertension and Pregnancy	N/A	COR 1: Pregnant individuals with SBP ≥160 mm Hg or DBP ≥110 mm Hg confirmed on repeat measurement within 15 minutes should receive antihypertensive medication to lower BP to <160/<110 mm Hg within 30 to 60 minutes to prevent adverse events.

WHAT IS NEW?

New recommendation	5.5. Hypertension and Pregnancy	N/A	COR 1: Pregnant individuals with chronic hypertension (defined as prepregnancy hypertension or SBP 140-159 mm Hg and/or DBP 90-109 mm Hg prior to 20 weeks gestation) should receive antihypertensive therapy to achieve BP <140/90 mm Hg to prevent maternal and perinatal morbidity and mortality.
New recommendation	5.5. Hypertension and Pregnancy	N/A	COR 1: Individuals with hypertension who are planning a pregnancy or who become pregnant should be counseled about the benefits of low-dose aspirin to reduce the risk of preeclampsia and its sequelae.
Revised recommendation	5.5. Hypertension and Pregnancy	COR 3 harm: Women with hypertension who become pregnant should not be treated with ACEi or direct renin inhibitors.	COR 3 Harm: Individuals with hypertension who are planning a pregnancy or who become pregnant should not be treated with atenolol, ACEi, ARB, direct renin inhibitors, nitroprusside, or MRA to avoid fetal harm.

WHAT IS NEW?

New recommendation	5.6. Resistant Hypertension and Renal Denervation	N/A	COR 1: In adults with resistant hypertension, a more detailed evaluation for secondary causes, to include careful review of all medications and removal of those with interfering effects on BP, is beneficial for lowering BP and simplifying treatment.
New recommendation	5.6. Resistant Hypertension and Renal Denervation	N/A	COR 1: All patients with hypertension who are being considered for RDN should be evaluated by a multidisciplinary team with expertise in resistant hypertension and RDN.
New recommendation	5.6. Resistant Hypertension and Renal Denervation	N/A	COR 1: For patients with hypertension for whom RDN is contemplated, the benefits of lowering BP and potential procedural risks compared with continuing medical therapy should be discussed as part of a shared decision-making process to ensure patients choose the therapy that meets their expectations.
New recommendation	6.2. Hypertensive Emergencies and Severe Hypertension for Nonpregnant and Nonstroke Patients	N/A	COR 3 Harm: For adults with severe hypertension (>180/120 mm Hg) who are hospitalized for noncardiac conditions without evidence of acute target organ damage, intermittent use of additional intravenous or oral antihypertensive medications are not recommended to acutely reduce BP.

TOP TAKE-HOME MESSAGES

- 1.
  - High blood pressure is the most prevalent and modifiable risk factor for the development of cardiovascular diseases, including coronary artery disease, heart failure, atrial fibrillation, stroke, dementia, chronic kidney disease, and all-cause mortality.
  - The overarching blood pressure treatment goal is <130/80 mm Hg for all adults, with additional considerations for those who require institutional care, have a limited predicted lifespan, or are pregnant

TOP TAKE-HOME MESSAGES

- 2.
  - Clinicians should collaborate with community leaders, health systems, and practices to implement screening of all adults in their communities and implement guideline-based recommendations regarding prevention and management of high blood pressure to improve rates of blood pressure control

TOP TAKE-HOME MESSAGES

- 3.
  - Multidisciplinary team-based care is effective in assessing and addressing patient access to medications and other structural barriers to support individual patient needs and thereby reduce barriers to achieving hypertension control. Team members may include physicians, pharmacists, nurse practitioners, nurses, physician assistants/associates, dieticians, community health workers, and other
  - health care professionals.

TOP TAKE-HOME MESSAGES

- 4.
  - Blood pressure is classified by the following framework:
    - normal blood pressure is defined as <120 mm Hg systolic *and* <80 mm Hg diastolic;
    - elevated blood pressure as 120 to 129 mm Hg systolic *and* <80 mm Hg diastolic;
    - stage 1 hypertension as 130 to 139 mm Hg systolic *or* 80 to 89 mm Hg diastolic;
    - stage 2 hypertension as ≥140 mm Hg systolic or ≥90 mm Hg diastolic.

TOP TAKE-HOME MESSAGES

- 5.
  - For all adults, lifestyle changes, including maintaining or achieving a healthy weight, following a hearthealthy eating pattern (such as DASH [Dietary Approaches to Stop Hypertension]), reducing sodium intake, increasing dietary potassium intake, adopting a moderate physical activity program, managing stress, and reducing or eliminating alcohol intake are strongly recommended to prevent or treat elevated blood pressure and hypertension

TOP TAKE-HOME MESSAGES

- 6.
  - Initiation of medication therapy to lower blood pressure in addition to lifestyle interventions is recommended for all adults with average blood pressure ≥140/90 mm Hg and/or for selected adults with average blood pressure ≥130/80 mm Hg who have clinical cardiovascular disease, previous stroke, diabetes, chronic kidney disease, or increased 10-year predicted cardiovascular risk of ≥7.5% defined by PREVENT™ (Predicting Risk of CVD EVENTs)

TOP TAKE-HOME MESSAGES

- 7.
  - In adults with average blood pressure ≥130/80 mm Hg and at lower 10-year cardiovascular disease risk defined by PREVENT of <7.5%, initiation of medication therapy to lower blood pressure is recommended if average blood pressure remains ≥130/80 mm Hg after an initial 3- to 6-month trial of lifestyle modification

TOP TAKE-HOME MESSAGES

- 8.
  - For all adults with stage 2 hypertension, the initiation of antihypertensive drug therapy with 2 first line agents of different classes in a single-pill, fixed-dose combination is preferred over 2 separate pills to improve adherence and reduce time to achieve blood pressure control

TOP TAKE-HOME MESSAGES

- 9.
  - Home blood pressure monitoring combined with frequent interactions with multidisciplinary team members using standardized measurement and treatment protocols and home measurement protocols is an important integrated tool to improve rates of blood pressure control.
  - Reliance on cuffless devices, including smartwatches, for accurate blood pressure measurements should be avoided until these devices demonstrate greater precision and reliability.

TOP TAKE-HOME MESSAGES

- 10.
  - Severe hypertension in nonpregnant individuals, defined as blood pressure >180/120 mm Hg, without evidence of acute target organ damage, should be evaluated and treated in the outpatient setting with initiation, reinstitution, or intensification of oral antihypertensive medications in a timely manner

Class of Recommendations and Level of Evidence

- The Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk.
- The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources

Class of Recommendations and Level of Evidence

CLASS (STRENGTH) OF RECOMMENDATION

Class 1 (STRONG) **Benefit >>> Risk**

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

Class of Recommendations and Level of Evidence

Class 2a (MODERATE) **Benefit >> Risk**

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/ indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

Class of Recommendations and Level of Evidence

Class 2b (WEAK) **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

Class of Recommendations and Level of Evidence

Class 3: No Benefit (MODERATE) **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

Class 3: HARM (STRONG) **Risk > Benefit**

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

Class of Recommendations and Level of Evidence

LEVEL (QUALITY) OF EVIDENCE‡
Level A • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
Level B-R (Randomized) • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
Level B-NR (Nonrandomized) • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
Level C-LD (Limited Data) • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Level C-EO (Expert Opinion) • Consensus of expert opinion based on clinical experience

Classification and Definitions

- Although a continuous and graded association exists between higher BP and CVD, it is useful to categorize BP levels for clinical and public health decision-making.
- In the present document, BP is categorized into 4 levels based on average BP measured in a health care setting (office BP)

Table 4. Categories of Blood Pressure in Adults*

	SBP		DBP
BP Category			
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120 to 129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130 to 139 mm Hg	or	80 to 89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in Section 3 ("Evaluation and Diagnosis"); DBP, diastolic blood pressure; and SBP, systolic blood pressure.

*Adults with SBP and DBP in 2 categories should be designated to the higher BP category. This table excludes individuals who are pregnant (see Section 11.5,

Definition (2024 ESC guideline)

- The 2024 Guidelines continue to define hypertension as office systolic BP of ≥140 mmHg or diastolic BP of ≥90 mmHg. However, a new BP category called 'Elevated BP' is introduced. Elevated BP is defined as an office systolic BP of 120–139 mmHg or diastolic BP of 70–89 mmHg.
- A major, evidence-based change in the 2024 Guidelines is the recommendation to pursue a target systolic BP of 120–129 mmHg among adults receiving BP-lowering medications.

Table 5 Comparison of office, home, and ambulatory blood pressure measurement thresholds for elevated blood pressure and hypertension

	Office BP (mmHg)[a]	Home BP (mmHg)	Daytime ABPM (mmHg)	24 h ABPM (mmHg)	Night-time ABPM (mmHg)
Reference					
Non-elevated BP	<120/70	<120/70	<120/70	<115/65	<110/60
Elevated BP	120/70–<140/90	120/70–<135/85	120/70–<135/85	115/65–<130/80	110/60–<120/70
Hypertension	≥140/90	≥135/85	≥135/85	≥130/80	≥120/70

ABPM, ambulatory blood pressure monitoring; BP, blood pressure.

[a]The BP thresholds provided assume that a standardized approach to office BP measurement is performed (*Figure 3*). However, evidence indicates that office BP measurement in routine clinical settings is often not done using a standardized approach and, in this case, the routine office BP value may be 5–10 mmHg higher than it would have been if measured using the recommended standardized approach.[65,66]

Evaluation and Diagnosis

- Hypertension is the most prevalent modifiable CVD risk factor and is the leading cause of death and disability worldwide, with an increasing burden over the last several decades.
- From 2017 to 2020, the prevalence of hypertension (defined as BP ≥130/80 mm Hg or receiving antihypertensive therapy) among adults in the United States was 46.7%, with the prevalence varying by age, sex, and race/ethnicity
- With aging, population SBP levels tend to rise steadily to the end of life, whereas DBP levels rise until the fifth decade of life, plateau for a decade, and decline thereafter.
- 80% to 90%, with earlier onset among men compared with women,
- Hypertension frequently co-occurs with other CVD risj factors.

Evaluation and Diagnosis

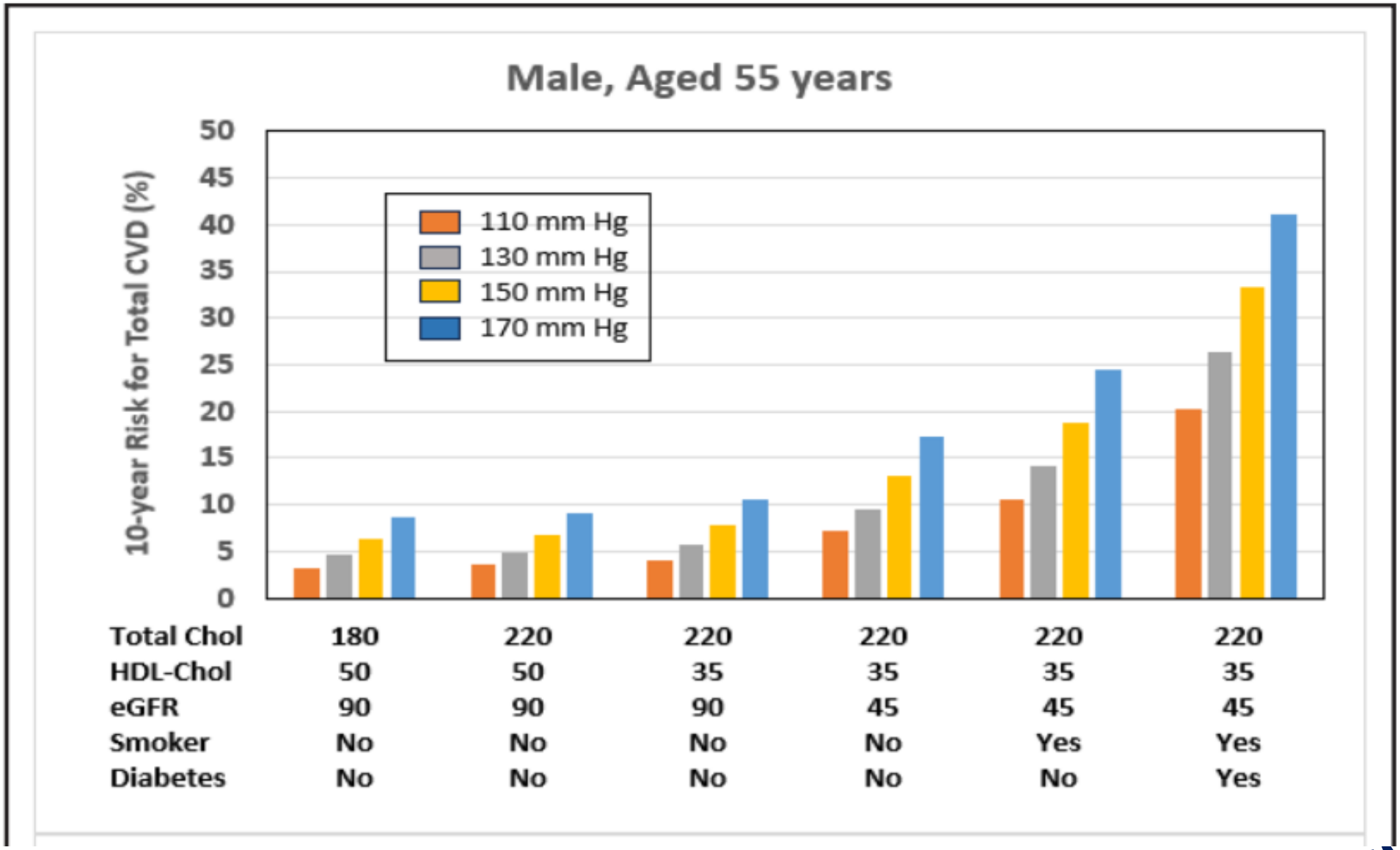
- From 2017 to 2020, 16.6% of adults with hypertension in the United States were current smokers, 72.6% were overweight or obese, 12.3% had diabetes, and 13.4% had diagnosed CKD,9\ leading to additive and synergistic risks for CVD
- BP is associated with fatal and nonfatal cardiovascular events in a graded, log-linear fashion, with an approximate doubling of risk for each 20-mm Hg higher SBP and 10-mm Hg higher DBP level
- Among individuals without major risk factors, relative CVD event rates increase, starting at SBP levels as low as 90 mm Hg.
- Among middle-aged and older adults, the prevalence and risks associated with higher SBP are greater than those associated with higher DBP.

Evaluation and Diagnosis

- Once BP is above normal (SBP ≥120 mm Hg or DBP ≥80 mm Hg), there may be irreversible vascular damage and residual risk, even if antihypertensive treatment is started.
- Individuals with a diagnosis of hypertension who have treated SBP/DBP levels <120/80 mm Hg have twice the risk for CVD of adults without hypertension who have untreated SBP/DBP levels <120/80 mm Hg
  - highlighting the importance of primordial prevention of BP elevation

Risk prediction

Estimated 10-Year Risks for Total Cardiovascular Disease Using the PREVENT™ CVD Risk Equations, Stratified by Blood Pressure Levels With Selected Combinations of Risk Factors.



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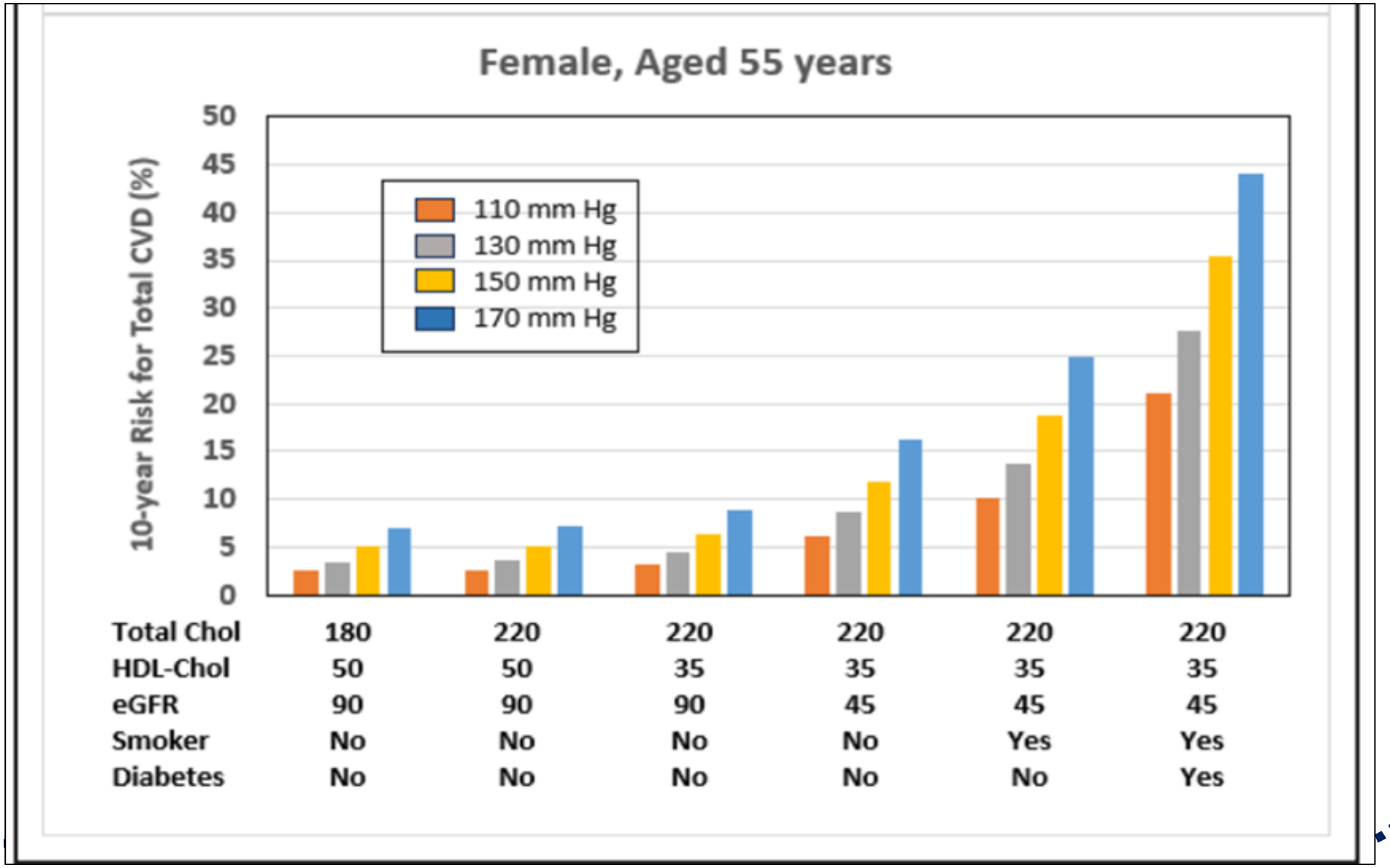


Patient Evaluation

- Accurate measurement of BP is essential to diagnose high BP, ascertain BP-related CVD risk, and assess response to therapy
- A standardized protocol, includes proper patient preparation, standardized measurement technique and approach, documentation of BP, analysis of the readings, and providing the readings to the patient.
- Office BP should be based on the average of available readings, and an average of ≥2 BP measurements obtained on ≥2 separate occasions may minimize error and provide a more accurate estimation of office BP

Patient Evaluation

3.1.1. Accurate Measurement of In-Office BP

Recommendations for Accurate Measurement of In-Office BP		
COR	**LOE**	**Recommendations**
1	**C-LD**	1. When diagnosing and managing high BP in adults, standardized methods are recommended for the accurate measurement and documentation of in-office BP (Figure 3).[1–3]
2a	**C-EO**	2. When measuring in-office BP in adults, it is reasonable to use the oscillometric method with an automated device over the auscultatory method.

Office Blood Pressure Measurement

1. The patient should avoid caffeine, exercise, and smoking for at least 30 minutes before measurement. Ensure the patient has emptied their bladder.
2. Use a blood pressure device that has been validated for accuracy (validatebp.org).
3. Use the correct cuff size on a bare arm.
4. The patient's arm should be supported at heart level.
5. Have the patient relax, sitting in a chair (feet on floor, legs uncrossed, and back supported) for more than 5 minutes of rest.
6. Neither the patient nor the clinician should talk during the rest period or during the measurement. The patient should not be using their phone.
7. Blood pressure measurement should be taken in a temperature-controlled room.
8. Take 2 or more blood pressure measurements at least 1 minute apart. Average the readings, and provide the patient their blood pressure readings both verbally and in writing.

Laboratory Tests and Other Diagnostic Procedures

- In adults with a new diagnosis of hypertension, a comprehensive medical history, physical examination, and routine laboratory testing are useful to establish baseline CVD risk and inform management decisions, including the need for additional testing
  - should be repeated at least annually to monitor for potential adverse effects of therapies (eg, serum electrolytes), to assess for development or progression of kidney disease (eg, urine albumin-to-creatinine ratio,1 creatinine-based or cystatin-C based estimated glomerular filtration rate [eGFR]), and to monitor for changes in predicted CVD risk (eg, lipid profile)
  - Electrocardiography can provide important information on subclinical CVD (eg, left ventricular hypertrophy), and cardiac biomarkers, echocardiography, and coronary artery calcium scoring allow more refined risk estimation for CVD and assessment of the prevalence and extent of subclinical CVD.

Routine Laboratory Testing for New Diagnosis of Hypertension

Diagnostic Tests
Complete blood count
Serum sodium, potassium, calcium
Serum creatinine with estimation of glomerular filtration rate (based on the 2021 CKD-EPI Creatinine Equation)
Lipid profile
Fasting blood glucose or Hemoglobin A1c
Thyroid-stimulating hormone
Urinalysis
Urine albumin-to-creatinine ratio; urine protein-to-creatinine ratio
ECG

Out-of-Office BP Monitoring

- Hypertension screening and management, including the use of BP targets, have primarily relied on BP measured in the office setting
- Out-of-office measurement of BP using ABPM or HBPM, which is also known as self-measurement of BP at home, can provide valuable information beyond office BP for the confirmation and management of hypertension
  - Evidence suggests that HBPM more strongly predicts CVD outcomes than office BP and may be more reproducible than ABPM
  - ABPM typically involves wearing a fully automated device, usually over a period of 24 hours, with out-of-office BP readings obtained at relatively frequent intervals during the daytime (ie, 15-30 minutes) and less frequent intervals at nighttime (ie, 30-60 minutes).

Out-of-Office BP Monitoring

- ABPM can
  - 1) provide estimates of mean BP over the entire monitoring period, and separately during daytime and nighttime;
  - 2) determine the daytime-to-nighttime BP ratio to identify the extent of nocturnal “dipping”; (non dipper: <10% Decrease in Mean BP During Sleep; associated with higher cardiovascular risk)
  - 3) identify the early-morning BP surge pattern;
  - 4) estimate BP variability; and
  - 5) allow for recognition of hypotension

3.1.4. ABPM and HBPM

Recommendations for ABPM and HBPM
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In adults with suspected hypertension, out-of-office BP measurements by either ABPM or HBPM are recommended to confirm the diagnosis of hypertension.[1,2]
1	A	2. In adults who are taking antihypertensive medication, HBPM is recommended for monitoring the titration of BP-lowering medication, along with cointerventions such as patient education, telehealth counseling, and clinical interventions.[2–6]

Table 7. Values of Systolic/Diastolic Blood Pressure for Ambulatory and Home Blood Pressure Monitoring Corresponding to Office Systolic/Diastolic Blood Pressure Levels

Office, mm Hg	HBPM, mm Hg	Daytime ABPM, mm Hg	Nighttime ABPM, mm Hg	24-Hour ABPM, mm Hg
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

Cuffless BP Devices

- Cuffless technology options, often embedded in wearable, nonwearable, or smartphone devices, estimate BP through various approaches (eg, pulse wave velocity, pulse transit time, pulse wave analysis, volume clamping, and applanation tonometry).
- Many of these approaches require user calibration with periodic cuff BP measurement or by demographic data input

Recommendation for Cuffless BP Devices		
COR	**LOE**	**Recommendation**
3: No Benefit	**C-LD**	1. In adults, the use of cuffless BP devices is not recommended for the diagnosis or management of high BP.[1–3]

Causes of Hypertension

- Elevated BP and hypertension reflect a complex interplay of behavioral, environmental, hormonal, and genetic influences across the lifespan
- Diet quality is significantly associated with elevated BP and its sequelae.
- Among dietary factors influencing BP, **higher** sodium intake, **lower** potassium intake (measured by urinary excretion), and alcohol overuse predominate; **low** intake of fiber, calcium, magnesium, and plant protein also influence BP
- Weight gain, overweight or obesity, and related metabolic issues (ie, insulin resistance) contribute to the increase in BP and hypertension across the lifespan, particularly in recent decades
- Factors such as increasing age, obesity, and insulin resistance influence how BP is affected by sodium, emphasizing the importance of lower sodium intake

Causes of Hypertension

- Sleep disturbances and psychosocial stressors can exacerbate, and increases in BP can be ameliorated by a higher level of physical activity and fitness.
- Emerging data also implicate environmental exposures and chemical toxins (including air pollution and heavy metals) in the increases in BP
- BP is a highly heritable trait, and hundreds of independent genetic loci capable of affecting BP have been described to date.
  - Nonetheless, all genetic loci described to date explain <10% of BP variance, indicating the importance of other factors and gene environment interactions

Environmental, Behavioral, and Genetic Causes of Hypertension

Dietary Intake Factors	Nondietary Factors
Higher sodium intake	Genetic variants
Lower potassium intake	Overweight/obesity
Lower calcium/magnesium intake	Lower physical activity/fitness
Lower diet quality (lower intake of fruits/vegetables, plant proteins, fiber)	Sleep disturbances (related to duration, quality, regularity, and/or disordered breathing)
Alcohol intake	Psychosocial stressors
	Air pollution

White-Coat Hypertension and Masked Hypertension

- The availability of out-of-office BP monitoring provides differentiation of hypertension into several clinically relevant categories based on the concordance or discordance of office BP and out-of-office BP, including *white-coat hypertension* and *masked hypertension* for individuals not taking antihypertensive medication and *white-coat effect* and *masked uncontrolled hypertension* for those taking antihypertensive medication
- Systematic reviews and meta-analyses of observational studies have demonstrated that compared with sustained normotension, white-coat hypertension is associated with no risk to a moderately increased risk of CVD.
- The risk of CVD associated with white-coat hypertension may only be increased among older adults who have high baseline CVD risk

White-Coat Hypertension and Masked Hypertension

- ABPM is preferred for excluding white-coat hypertension and masked hypertension among individuals not taking antihypertensive medication.
- HBPM is preferred for excluding a white-coat effect and masked uncontrolled hypertension among individuals taking antihypertensive medication as ABPM is more difficult to conduct repeatedly in clinical practice

BP Category	High BP in the Office Setting?	High BP Outside of the Office Setting?*
Among individuals not taking antihypertensive medication		
Sustained normotension	No	No
Sustained hypertension	Yes	Yes
Masked hypertension	No	Yes
White-coat hypertension	Yes	No
Among individuals taking antihypertensive medication		
Controlled hypertension	No	No
Uncontrolled hypertension	Yes	Yes
Masked uncontrolled hypertension	No	Yes
White-coat effect	Yes	No

*Please refer to Table 7 for office BP and out-of-office BP thresholds used to define high BP. High out-of-office BP is defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg when using awake BP and SBP ≥125 mm Hg or DBP ≥75 mm Hg when using 24-hour BP. These BP thresholds correspond to an office SBP ≥130 mm Hg or DBP ≥80 mm Hg. Out-of-office BP is primarily based on mean awake BP or mean 24-hour BP. It remains unclear whether asleep BP should be used to determine high out-of-office BP as the prevalence and reproducibility of isolated nocturnal hypertension (high asleep BP without high awake BP) are both low.[36,37] Further, there is no high-quality randomized controlled trial evidence to indicate that lowering asleep BP reduces CVD risk.[38,39] Modified with permission from

White-Coat Hypertension and Masked Hypertension

- Nonetheless, the risk of CVD is higher in sustained hypertension than in white-coat hypertension among adults with high office BP.
- It is reasonable to exclude white-coat hypertension using out-of-office BP monitoring for adults with high office BP (ie, SBP/DBP ≥130/80 mm Hg)
- One caveat is that adults with office SBP/DBP ≥160/100 mm Hg should be promptly treated and antihypertensive medication dose titrated as necessary to control BP
  - The prevalence of white-coat hypertension is low among those with office BP levels in this range.
- Studies have demonstrated that compared with individuals with sustained normotension, a higher proportion of individuals with white-coat hypertension or masked hypertension have sustained hypertension during follow-up

White-Coat Hypertension and Masked Hypertension

- it is reasonable to conduct out-of-office BP monitoring to exclude sustained hypertension among those initially identified with white-coat hypertension or masked hypertension
- Studies have consistently demonstrated that compared with controlled hypertension, white-coat effect is not associated with an increased risk of CVD events and mortality
- Evidence also suggests that higher out-of-office BP is associated with an increased risk of CVD events, independent of office BP, among individuals with apparent resistant hypertension
  - Out-of-office BP monitoring is a central component of the initial work-up of apparent resistant hypertension
  - it is reasonable to exclude a white-coat effect using out-of-office BP monitoring for individuals with apparent resistant hypertension

White-Coat Hypertension and Masked Hypertension

- Systematic reviews and meta-analyses have demonstrated that compared with controlled hypertension, white-coat effect is not associated with an increased risk of CVD events.
- These studies primarily did not focus on individuals with apparent resistant hypertension, indicating that it is reasonable to conduct out-of-office BP monitoring for the larger group of individuals who are taking antihypertensive medication and who have high office BP (ie, office SBP/DBP ≥130/80 mm Hg).
- Individuals with office SBP/DBP ≥160/100 mm Hg should have antihypertensive medication intensification as necessary to control BP

White-Coat Hypertension and Masked Hypertension

- Systematic reviews and meta-analyses of observational studies have demonstrated that compared with sustained normotension, masked hypertension is associated with an increased risk of CVD events with a risk range similar to that of sustained hypertension
- In the absence of knowing the best approach for targeted screening, the use of out-of-office BP monitoring may be reasonable to exclude masked hypertension among adults with office SBP/DBP <130/80 mm Hg
- There are some data to suggest that antihypertensive medication targeting out-of-office BP among individuals with masked uncontrolled hypertension reduces hypertension-related target organ damage measures, including urinary albumin-to-creatinine ratio, pulse wave velocity, and left ventricular mass index.

White-Coat Hypertension and Masked Hypertension

2a	**B-NR**	1. In adults with untreated office SBP ≥130 mm Hg or DBP ≥80 mm Hg, and without office SBP ≥160 mm Hg or DBP ≥100 mm Hg, it is reasonable to exclude white-coat hypertension using out-of-office BP monitoring before a diagnosis of hypertension is made.[1–5]
2a	**B-NR**	2. In adults with white-coat hypertension or masked hypertension, out-of-office BP monitoring is reasonable to exclude transition to a diagnosis of sustained hypertension.[6–8]

White-Coat Hypertension and Masked Hypertension

2a	**C-LD**	3. In adults with apparent treatment-resistant hypertension on office BP, it is reasonable to exclude white-coat effect, a form of pseudoresistance, using out-of-office BP monitoring.[9–12]
2a	**B-NR**	4. In adults who are taking antihypertensive medication and have elevated office BP (office SBP ≥130 mm Hg or DBP ≥80 mm Hg) but do not have resistant hypertension or office SBP ≥160 mm Hg or DBP ≥100 mm Hg, it is reasonable to exclude white-coat effect using out-of-office BP monitoring.[1,4,13]

White-Coat Hypertension and Masked Hypertension

2b	B-NR	5. In adults with untreated office SBP <130 mm Hg and DBP <80 mm Hg, it may be reasonable to exclude masked hypertension using out-of-office BP monitoring.[5,13–15]
2b	B-NR	6. In adults who are taking antihypertensive medication and have office SBP <130 mm Hg and DBP <80 mm Hg, it may be reasonable to exclude masked uncontrolled hypertension using out-of-office BP monitoring.[13–15]

Secondary causes of HTN

- Secondary causes of hypertension can be identified in approximately 5% to 25% of adult patients with hypertension.
- If a cause can be correctly diagnosed and treated, patients with secondary hypertension may experience a marked improvement in BP control with a reduction in CVD risk.
- Patients with a new diagnosis of hypertension and concomitant conditions should be screened with a history and physical examination and laboratory tests
- More common with stage 2 hypertension, treatment-resistant hypertension, sudden onset of hypertension, increased BP in patients with hypertension previously controlled on drug therapy, early-onset hypertension (age <30 years), diastolic hypertension in older adults, and target organ damage disproportionate to the duration or severity of the hypertension.

Secondary causes of HTN

- Common forms of secondary hypertension include primary aldosteronism and obstructive sleep apnea (OSA).
- Atherosclerotic renovascular disease may be present in 14% to 40% of adults with hypertension; however, only a small fraction (0.1% to 5%) is considered to be hemodynamically significant to result in renovascular hypertension.
- Numerous substances, including prescription medications, over the-counter medications, herbals, and food substances, may affect BP
  - A careful history should be taken with close attention paid to prescription medications and over-the-counter substances, illicit drugs, and herbal products
  - A change in BP may also result from drug-drug or drug-food interactions.
  - When feasible, drugs associated with increased BP should be reduced or discontinued and alternative agents used

Secondary causes of HTN

- Spontaneous hypokalemia is present only in 20% to 50% of patients with primary aldosteronism, and therefore, the decision to perform primary aldosteronism screening should not rely on a history of hypokalemia alone.
- Primary aldosteronism is a common cause of secondary hypertension (occurring in 5% to 10% of patients with hypertension and 20% of patients with resistant hypertension), and targeted treatment is associated with improved kidney and cardiovascular outcomes

Secondary causes of HTN

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Common causes					
OSA[5–7]	25%-50%	Snoring, choking, gasping during sleep; daytime sleepiness; resistant hypertension	Obesity, large neck size (eg, >17 inches [men]; >16 inches [women], Mallampati class 3-4; loss of normal nocturnal BP fall	STOP-Bang Questionnaire[15]; Berlin Questionnaire[16]; overnight oximetry	Referral for polysomnography or home sleep apnea testing if no suspicion of nonrespiratory sleep disorders (eg, narcolepsy)
CKD[17,18]	14%	Diabetes, obstruction, hematuria; urinary frequency and nocturia; urinary incontinence, analgesic abuse; family history of polycystic kidney disease; elevated serum creatinine; abnormal urinalysis	Abdominal mass or large palpable kidneys (polycystic kidney disease); skin pallor	Electrolytes, including sodium, potassium, chloride, and bicarbonate, serum creatinine, urinalysis, urine microalbumin, serum cystatin C, renal ultrasound	Tests to evaluate cause of CKD
Primary aldosteronism[1–3,9,19]	5%-25%	Resistant hypertension; hypertension with hypokalemia (spontaneous or diuretic induced); hypertension and muscle cramps or weakness; hypertension and incidentally discovered adrenal mass; hypertension and obstructive sleep apnea; hypertension and family history of early-onset hypertension or stroke	Arrhythmias (with hypokalemia); especially AF	Electrolytes, including sodium and potassium, plasma aldosterone/renin activity ratio (correction of hypokalemia and withdrawal of MRA for 4-6 wks)	Oral sodium loading test (with 24-h urine aldosterone) or IV saline infusion test with plasma aldosterone at 4 h of infusion or captopril suppression test (in patients not on ACEi or ARB treatment), adrenal CT scan, adrenal vein sampling

Secondary causes of HTN

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Common causes					
Drug or alcohol induced[11]	2%-20%	Sodium-containing antacids; antidepressants; nicotine (smoking); alcohol; NSAIDs; oral contraceptives; cyclosporine or tacrolimus; sympathomimetics (decongestants, anorectics); cocaine, amphetamines and other illicit drugs; neuropsychiatric agents; erythropoiesis-stimulating agents; cancer treatment (VEGF inhibitors, Bruton tyrosine kinase inhibitors and others), clonidine withdrawal; herbal agents (Ma Huang, ephedra)	Fine tremor, tachycardia, sweating (cocaine, ephedrine, MAO inhibitors); acute abdominal pain (cocaine)	Urinary drug screen (illicit drugs)	Response to withdrawal of suspected agent
Renovascular hypertension[10]	0.1%-5%	Resistant hypertension; hypertension of abrupt onset or worsening or increasingly difficult to control; flash pulmonary edema (atherosclerotic); early-onset hypertension, especially in women (fibromuscular hyperplasia)	Abdominal systolic-diastolic bruit; bruits over other arteries (carotid, femoral)	Electrolytes, including sodium, potassium, chloride, and bicarbonate, renal duplex Doppler ultrasound; magnetic resonance arteriography; abdominal CT arteriography	Bilateral selective renal intra-arterial angiography

Secondary causes of HTN

Uncommon causes					
Hypothyroidism[20]	<1%	Dry skin; cold intolerance; constipation; hoarseness; weight gain	Delayed ankle reflex; periorbital edema; coarse skin; cold skin; slow movement; goiter	Thyroid-stimulating hormone; free thyroxine	None
Hyperthyroidism[20]	<1%	Warm, moist skin; heat intolerance; nervousness; tremulousness; palpitations, insomnia; weight loss; diarrhea; proximal muscle weakness	Lid lag; fine tremor of the outstretched hands; warm, moist skin, goiter, thyroid nodule	Thyroid-stimulating hormone; free thyroxine	Radioactive iodine uptake and scan
Pheochromocytoma/paraganglioma[21,22]	<0.6%	Resistant hypertension; paroxysmal hypertension or crisis superimposed on sustained hypertension; "spells," BP lability, headache, sweating, palpitations, piloerection; positive family history of pheochromocytoma/paraganglioma; adrenal incidentaloma	Skin stigmata of neurofibromatosis (café-au-lait spots; neurofibromas); orthostatic hypotension	24-h urinary fractionated metanephrines or plasma metanephrines under standard conditions (supine position with indwelling IV cannula)	CT or MRI scan of abdomen/pelvis, Ga-DOTATATE PET/CT scan

Secondary causes of HTN

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Aortic coarctation (undiagnosed or repaired)[23]	0.1%	Young adult with hypertension (age <30 y)	BP higher in upper extremities than in lower extremities; absent femoral pulses; continuous murmur over patient's back, chest, or abdominal bruit; left thoracotomy scar (postoperative)	Echocardiogram	Thoracic and abdominal CT angiogram or magnetic resonance arteriography
Cushing syndrome[24]	<0.1%	Rapid weight gain, especially with central distribution; proximal muscle weakness; depression; hyperglycemia	Central obesity, "moon" face, dorsal and supraclavicular fat pads, wide (1 cm) violaceous striae, hirsutism	Overnight 1-mg dexamethasone suppression test	24-h urinary free cortisol excretion (preferably multiple); midnight salivary cortisol
Primary hyperparathyroidism[20]	Rare	Hypercalcemia	Usually none	Serum calcium	Serum parathyroid hormone
Congenital adrenal hyperplasia[20]	Rare	Hypertension and hypokalemia; virilization (11-beta-hydroxylase deficiency [11-beta-OH]); incomplete masculinization in men and primary amenorrhea in women (17-alpha-hydroxylase deficiency [17-alpha-OH])	Signs of virilization (11-beta-OH) or incomplete masculinization (17-alpha-OH)	Hypertension and hypokalemia with low or normal aldosterone and renin	11-beta-OH: elevated DOC, 11-deoxycortisol, and androgens; 17-alpha-OH; decreased androgens and estrogen but elevated DOC and corticosterone
Mineralocorticoid excess syndromes other than primary aldosteronism[20]	Rare	Early-onset hypertension; resistant hypertension; hypokalemia or hyperkalemia	Arrhythmias (with hypokalemia)	Low aldosterone and renin	Urinary cortisol metabolites; genetic testing
Acromegaly[25]	Rare	Acral features, enlarging shoe, glove, or hat size; headache, visual disturbances; diabetes	Acral features; large hands and feet; frontal bossing	Serum growth hormone ≥1 ng/mL during oral glucose load	Elevated age- and sex-matched IGF-1 level; MRI scan of the pituitary

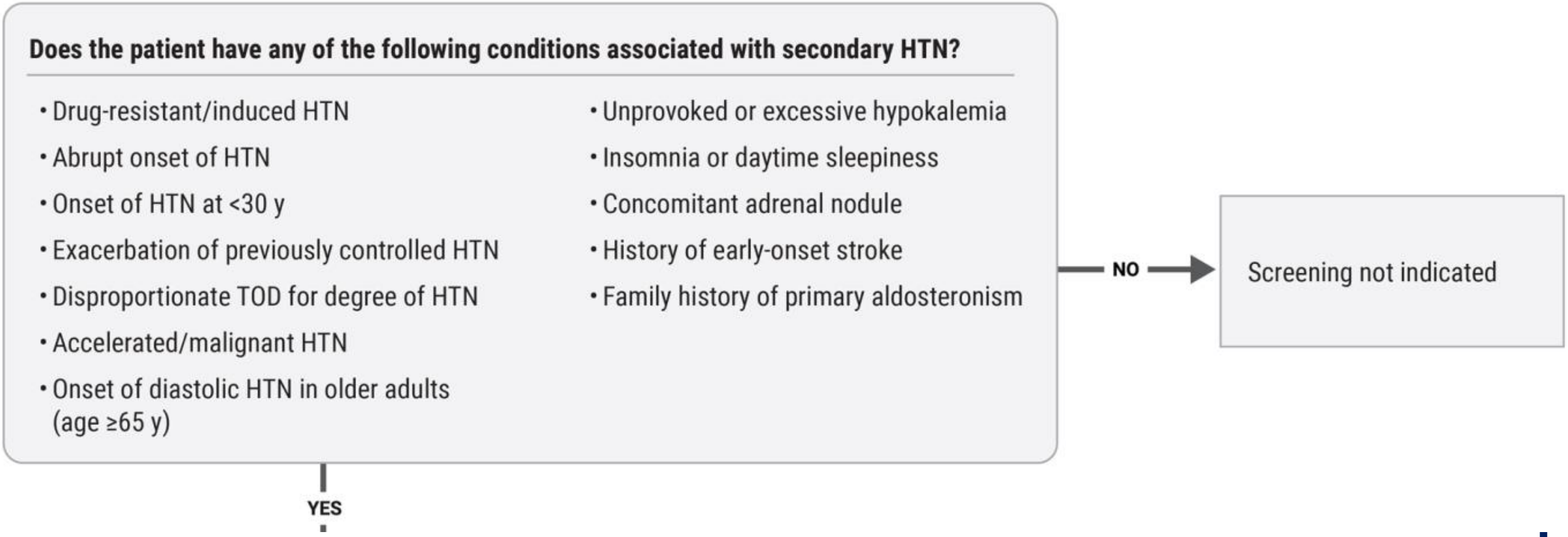
Medication induced HTN

Agent	Possible Management Strategy
Nonprescription drugs/substance	
Alcohol	Options include abstinence or limit alcohol to ≤1 drink daily for women and ≤2 drinks daily for men[26,27]
Caffeine[28]	Limit caffeine intake to <300 mg/d Avoid more than 1 cup daily in patients with severe uncontrolled hypertension
Decongestants (eg, phenylephrine, pseudoephedrine)	Use for shortest duration possible and avoid in severe or uncontrolled hypertension Consider alternative therapies (eg, nasal saline, intranasal corticosteroids, antihistamines) as appropriate
Herbal supplements (eg, Ma Huang, ephedra, St. John's wort [with MAO inhibitors, yohimbine])	Avoid use
Black licorice[29]	Avoid use
NSAIDs; acetaminophen	Avoid systemic NSAIDs when possible Limit acetaminophen to less than 4 g/d[12] Consider alternative analgesics (eg, topical NSAIDs), depending on indication and risk
Recreational drugs (eg, "bath salts" [MDPV], cocaine, methamphetamine, etc)	Discontinue or avoid use

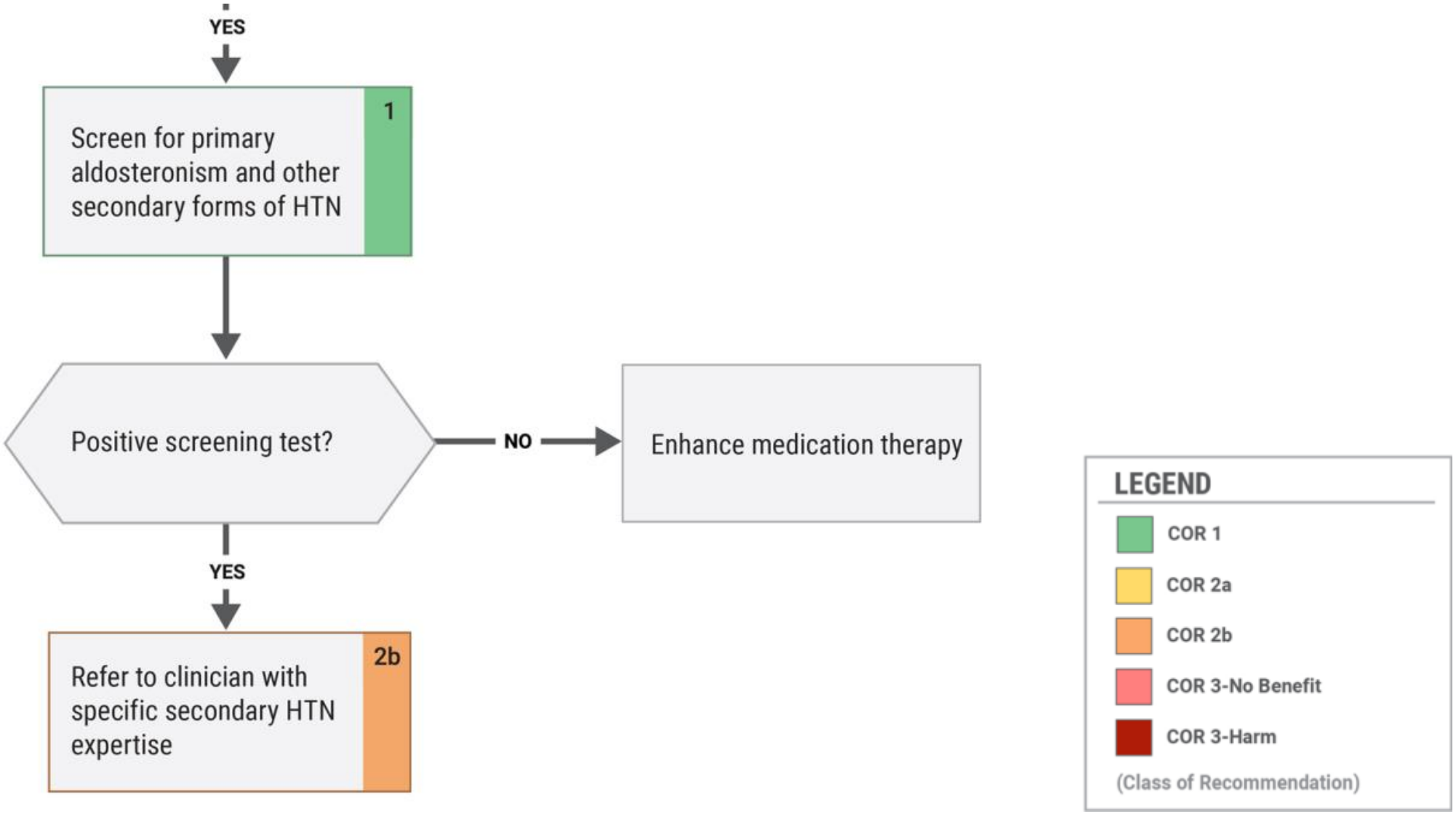
Medication induced HTN

Prescription drugs	
Sudden withdrawal of central-acting sympatholytic drugs such as clonidine and tizanidine	Recommend avoiding oral clonidine for treatment of hypertension whenever possible and tapering upon discontinuation[30]; use cyclobenzaprine or other muscle relaxants instead of tizanidine[31]
Amphetamines† (eg, amphetamine, methylphenidate dexmethylphenidate, dexamfetamine, lisdexamfetamine, dextroamphetamine)	Discontinue or decrease dose Consider behavioral therapies or nonstimulants (such as guanfacine) for ADHD[32]
Antidepressants† (eg, MAOIs, SNRIs, TCAs)	Consider alternative agents (eg, SSRIs) depending on indication Avoid tyramine-containing foods with MAOIs
Atypical antipsychotics† (eg, risperidone, olanzapine)[33,34]	Discontinue or limit use when possible Consider behavior therapy where appropriate Recommend lifestyle modification (Section 5.1 "Lifestyle and Psychosocial Approaches") Consider alternative agents associated with lower risk of weight gain, diabetes, and dyslipidemia
Immunosuppressants† (eg, cyclosporine)	Consider converting to tacrolimus, which may be associated with fewer effects on BP
Oral contraceptives†	Use low-dose (eg, 20-30 mcg ethinyl estradiol) agents or a progestin-only form of contraception, or consider alternative forms of birth control where appropriate (eg, barrier, abstinence, nonhormonal IUD) Avoid use in women with uncontrolled hypertension[35]
Systemic corticosteroids† (eg, dexamethasone, fludrocortisone, methylprednisolone, prednisone, prednisolone)	Avoid or limit use when possible Consider alternative modes of administration (eg, inhaled, topical) when feasible
Angiogenesis inhibitor† (eg, bevacizumab) and tyrosine kinase inhibitors (eg, sunitinib, sorafenib)	Avoid or limit use when possible
Androgen deprivation therapy† such as CYP 17 inhibitors (eg, abiraterone, orteronel) or androgen receptor antagonist (eg, enzalutamide)[36]	Avoid or limit use when possible Consider alternative chemotherapy

Screening for Features Suggesting Secondary Hypertension



Screening for Features Suggesting Secondary Hypertension



Recommendations for Primary Aldosteronism

Recommendations for Primary Aldosteronism		
COR	**LOE**	**Recommendations**
1	**C-EO**	1. In adults with hypertension, screening for primary aldosteronism is recommended in the presence of any of the following conditions to increase rates of detection, diagnosis, and specific targeted therapy: resistant hypertension (regardless of whether hypokalemia is present), hypokalemia (spontaneous or diuretic induced), OSA, incidentally discovered adrenal mass, family history of early-onset hypertension, or stroke at a young age (<40 years).
2b	**C-EO**	2. In adults with stage 2 hypertension, screening for primary aldosteronism may be considered to increase rates of detection, diagnosis, and specific targeted therapy.

Recommendations for Primary Aldosteronism

Recommendations for Primary Aldosteronism (Continued)		
COR	**LOE**	**Recommendations**
1	**C-LD**	3. In adults with an indication for screening for primary aldosteronism, use of plasma aldosterone, renin activity, and the plasma aldosterone to renin activity ratio is recommended for initial screening to assess if there is biochemical evidence of primary aldosteronism.[1–3]
1	**C-EO**	4. In adults with an indication for screening for primary aldosteronism, it is recommended to continue most antihypertensive medications (other than mineralocorticoid receptor antagonists [MRAs]) prior to initial screening to minimize barriers to or delays in screening.

Recommendations for Primary Aldosteronism

Recommendations for Primary Aldosteronism (Continued)		
COR	**LOE**	**Recommendations**
1	**C-EO**	5. In adults with hypertension and a positive screening test for primary aldosteronism or continued suspicion for primary aldosteronism based on suppressed plasma renin or disproportionate target organ damage, referral to a hypertension specialist or endocrinologist is recommended for further evaluation and treatment.

Recommendations for Renal Artery Stenosis

Recommendations for Renal Artery Stenosis
References that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In adults with hypertension and atherosclerotic renal artery stenosis, medical therapy is recommended to reduce kidney and CVD morbidity and mortality.[1–3]
2a	C-EO	2. In adults with hypertension and atherosclerotic renal artery stenosis for whom medical management has failed (eg, resistant hypertension, worsening kidney function, and/or acute HF), it is reasonable to refer patients for revascularization by percutaneous renal artery angioplasty and/or stent placement.
2b	C-LD	3. In adults with hypertension and nonatherosclerotic renal artery stenosis, including fibromuscular dysplasia, it may be reasonable to refer patients for revascularization by percutaneous renal artery angioplasty.[4]

Recommendations for OSA

Recommendations for OSA
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
2a	**B-R**	1. In adults with hypertension and OSA who are overweight or obese, weight loss interventions when combined with continuous positive airway pressure (CPAP) treatment can be effective in reducing SBP.[1]
2a	**B-R**	2. In adults with resistant hypertension and moderate-to-severe OSA, CPAP treatment can be useful in reducing BP.[2,3]

Prevention Strategies For HTN

- The etiology of primary (previously termed essential) hypertension is a complex interplay of genetics, lifestyle choices, and chronic stress
- Even in those with a genetic predisposition to hypertension, healthy lifestyle behaviors can prevent hypertension
- All of the therapies recommended for the treatment of hypertension are useful in primordial prevention of hypertension and should be encouraged.
  - weight loss for those with overweight or obesity; a heart-healthy diet such as the DASH eating plan; no more than 2300 mg of sodium per day (with the ideal limit of no more than 1500 mg per day for most adults); dietary potassium 3500 to 5000 mg per day; aerobic and resistance exercise (≥150 minutes of moderate physical activity per week and resistance exercise ≥2 days per week); and stress management practices.
  - Intake of any alcohol is associated with higher SBP in dose-response manner, including in individuals without HTN

BP Management
Lifestyle and Psychosocial Approaches

- Lifestyle modification approaches are critically important strategies to slow the increase in BP and delay or prevent the onset of hypertension.
- The DASH eating plan ranked as the most effective intervention for lowering, followed in order by aerobic exercise, isometric resistance training, low-sodium/high-potassium salt interventions, and comprehensive lifestyle interventions.
- In adults who have overweight or obesity, weight loss is a core strategy to improve current health and reduce risk for multiple diseases, and for management of chronic conditions, including elevated BP and hypertension
- In general, there is a reduction in BP of approximately 1/1 mm Hg (systolic/diastolic) for each 1 kg of weight loss.

Lifestyle and Psychosocial Approaches

- Weight reduction ≥5% of body weight or ≥3 kg/m2 of BMI, compared with lesser amounts, produces greater BP lowering in patients with and without hypertension
- Reduction in BP with the DASH eating plan varies across trials, from 1 to 13 mm Hg for SBP and from 1 to 10 mm Hg for DBP.
  - BP reduction with the DASH eating plan is generally greater among Black individuals66 and individuals with higher baseline BP, younger age (<50 years), or higher sodium intake (>2400 mg/d).
- Interventions that decrease sodium intake reduce BP elevation across the life course, prevent incident hypertension, and lower BP in adults with hypertension.
- There appears to be a U-shaped relationship between potassium supplementation and BP, with maximal lowering of BP at approximately 30 mmol/day supplementation and an increase in BP above 80 mmol/day supplementation.

Lifestyle and Stress Reduction Interventions to Lower Blood Pressure

Intervention	Target/Biomarker	Evidence-Based Goals	Approximate Mean Change in SBP (mm Hg)*		References
			With Hypertension	Without Hypertension	
Weight loss	Body weight or BMI	Aim for sustained ≥5% reduction in body weight or ≥3 kg/m^2 reduction in BMI; expect about 1 mm Hg reduction for every 1-kg reduction in body weight	−6 to −8	−3 to −5	2,6,14,52
Heart-healthy diet	DASH eating pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat	−5 to −8	−3 to −7	13–15,64,120
Reduced intake of sodium	Dietary sodium intake; 24-h urinary sodium	Optimal goal is <2300 mg/d, but aim for an ideal limit of <1500 mg/d	−6 to −8	−1 to −4	16–18,79,120,121
Use of salt substitute	Replace cooking/table salt (100% sodium chloride) with salt substitute (25%-30% potassium chloride, 65%-75% sodium chloride, and 0%-10% flavoring agents); 24-h urinary sodium and potassium	Reduce dietary sodium intake as above	−5 to −7	−5	20–22,93
Enhanced intake of potassium	Dietary potassium intake; 24-h urinary potassium	Aim for 3500-5000 mg/d, ideally by consumption of a diet rich in potassium; or alternative use of moderate-dose pharmacological potassium supplementation (<80 mmol)	−6	−3 to −6	25–27

Lifestyle and Stress Reduction Interventions to Lower Blood Pressure

Intervention	Target/Biomarker	Evidence-Based Goals	Approximate Mean Change in SBP (mm Hg)*		References
			With Hypertension	Without Hypertension	
Reduced alcohol intake	Alcohol consumption	Optimal goal is abstinence for all adults for best health outcomes; in patients who consume alcohol, aim for >50% reduction in daily intake to no more than 2 drinks/d in men or 1 drink/d in women	−4 to −6	−3	29
Exercise	Aerobic exercise	90-150 min/wk 65%-75% heart rate reserve	−4 to −8	−2 to −7	14,33,36,120,122
	Dynamic resistance	90-150 min/wk 50%-80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set	−2 to −7	−2 to −5	33,36,106,107
	Isometric resistance	4 × 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk	−5 to −10	−4 to −6	14,32,33,36,109,110
Meditation	Transcendental meditation	Training by a professional, followed by 2 × 20 min sessions/d while seated comfortably with eyes closed	−5 to −7	−5	14,119
Breathing control	Slowing respiration	Device-guided session to decrease respiration to <10 breaths/min for 15 min/d	−5	−5	14

Recommendations for Lifestyle and Psychosocial Approaches

Weight		
1	A	1. In adults who have overweight or obesity, weight loss is recommended with a goal of at least 5% of body weight reduction to prevent or treat elevated BP and hypertension.[1–9]
Diet and Nutrients		
1	A	2. In adults with or without hypertension, a heart-healthy eating pattern, such as the DASH eating plan, is recommended to prevent or treat elevated BP and hypertension.[9–15]
1	A	3. In adults with or without hypertension, reduction of dietary sodium intake* is recommended to <2300 mg/d, moving toward an ideal limit of <1500 mg/d to prevent or treat elevated BP and hypertension.[4,12,16–19]

Recommendations for Lifestyle and Psychosocial Approaches

2a	A	4. In adults with or without hypertension, potassium-based salt substitutes† can be useful to prevent or treat elevated BP and hypertension, particularly for patients in whom salt intake is related mostly to food preparation or flavoring at home, except in the presence of CKD or use of drugs that reduce potassium excretion where monitoring of serum potassium levels is indicated.‡[20–24]
1	A	5. In adults with elevated BP or hypertension, moderate potassium supplementation,§ ideally from dietary sources, is recommended to prevent or treat elevated BP and hypertension, except in the presence of CKD or use of drugs that reduce potassium excretion where monitoring of serum potassium levels is indicated.‡ [25–27]

Recommendations for Lifestyle and Psychosocial Approaches

Alcohol		
1	A	6. Adults with or without hypertension who currently consume alcohol should be advised to pursue a recommended goal of abstinence, or at least to reduce alcohol intake to ≤1 drink/d for women and ≤2 drinks/d for men to prevent or treat elevated BP and hypertension.‖ [28–31]
Physical Activity		
1	A	7. In adults with or without hypertension, increasing physical activity, through a structured exercise program that includes aerobic exercise and/or resistance training, is recommended to prevent or treat elevated BP and hypertension.[1,3,4,14,32–39]

Recommendations for Lifestyle and Psychosocial Approaches

Stress Reduction		
2b	**B-R**	8. In adults with or without hypertension, stress reduction through transcendental meditation may be reasonable to prevent or treat elevated BP and hypertension, as an adjunct to lifestyle or medication interventions.[7,8,14,40]
2b	**B-R**	9. In adults with or without hypertension, other forms of stress management, such as breathing control techniques or yoga, may be reasonable to prevent or treat elevated BP and hypertension, as an adjunct to lifestyle or medication interventions.[14,41,42]

Medical Management

- Throughout this guideline, they use the term thiazide-type diuretic to collectively refer to HCTZ,
- chlorthalidone, and indapamide; For simplicity and to minimize confusion.
  - In most settings, it is acceptable for clinicians to choose among these agents for treatment
  - There are differences in potency and half-life between these agents that may be relevant in some situations, particularly in the management of resistant hypertension
    - In that setting, thiazide like diuretics are preferred due to their greater efficacy; therefore, treatment recommendations in this setting continue to advocate thiazide-like diuretics.
- Across a wide range of BP thresholds and predicted CVD risk, a risk-based strategy for targeting antihypertensive therapy in primary prevention patients is more effective than a BP-alone based strategy in terms of events avoided and numbers-needed-to-treat to prevent 1 CVD event

Medical Management

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Medical Management

- For a given BP level, absolute risk for CVD varies according to age, sex, and presence of CVD or CVD risk factors.
  - Therefore, the decision to initiate antihypertensive treatment should be based on BP level and risk.
- Based on BP level alone, all adults with hypertension benefit from antihypertensive therapy at a threshold of ≥140/90 mmHg.
- Adults with hypertension and clinical CVD (coronary heart disease, stroke, or HF) are at increased risk for CVD events and benefit from antihypertensive therapy at a lower BP threshold of ≥130/80 mm Hg to prevent recurrent events.

Medical Management

- Among adults without clinical CVD, identification of patients at increased risk for CVD selects those who derive greatest benefit from antihypertensive therapy at a threshold of ≥130/80 mm Hg.
- Adults with hypertension are defined at increased risk if they have diabetes, CKD, or an estimated 10-year CVD risk of ≥7.5%, according to PREVENT
  - The PREVENT equations are validated for US adults aged 30 to 79 years and represent the most accurate, contemporary, and generalizable risk prediction tool available, including data from 5207517 White adults, 605036 Black adults, 318141 Hispanic adults, and 163741 Asian adults.
  - The level of risk estimated by Framingham risk ≥15% is roughly equivalent to 10-year estimated CVD risk ≥7.5% with PREVENT and 10-year estimated ASCVD risk ≥10% with PCEs

Medical Management

- In adults with hypertension and an average DBP of ≥90 mm Hg, observational data, clinical trials, and meta-analyses of individual-level participant data from clinical trials support reduction in CVD with initiation of antihypertensive therapy for primary and secondary prevention.
- In adults with hypertension and clinical CVD (coronary heart disease, stroke, HF), initiation of medications to lower BP is recommended when average DBP is ≥80 mm Hg
- Among individuals without clinical CVD but at increased CVD risk, initiation of antihypertensive therapy at an SBP threshold of ≥130 mm Hg reduces CVD events:
  - 1) individuals with diabetes;
  - 2) individuals with CKD;
  - 3) individuals aged 30 to 79 years without CVD, diabetes, or CKD who have a 10-year estimated CVD risk of ≥7.5% with PREVENT

Medical Management

- Initiation of antihypertensive treatment for adults aged ≥80 years (for whom estimated risk models are limited) is recommended at ≥130/80 mm Hg when clinical judgment suggests benefits will outweigh harms and when aligned with the patient's goals of care.
  - In the SPRINT trial, 12.5% of participants were aged ≥80 years, and there was no difference in benefit by age.
  - Observational data also suggest a similar relative risk reduction of BP lowering across age categories, including those aged ≥85 years
- In adults without clinical CVD who are at lower 10-year predicted CVD risk based on PREVENT (<7.5%), there are limited data about the net benefit of initiation of antihypertensive therapy at a lower threshold with an average SBP ≥130 mmHg.
  - If average SBP is ≥130 mm Hg after a 3- to 6-month trial, initiation of antihypertensive therapy is advised as an adjunct to lifestyle interventions. This is supported by the PREVER-Prevention trial

Medical Management

- For those adults age <30 years for whom models estimate risk is limited, initiation of antihypertensive therapy could be considered at an average SBP ≥130 mm Hg after a trial of lifestyle modification, but data are limited.
  - In addition, BP should continue to be monitored as BP tends to increase over time, and greater cumulative BP exposure is associated with higher risk of clinical CVD
  - Other modalities for risk assessment, such as imaging (eg, echocardiography) or biomarkers (eg, BNP, hs-cTn) or applying the long-term 30-year risk estimation with PREVENT, may be useful to guide clinician-patient discussions
  - Having a history of hypertensive disorders of pregnancy may also identify individuals who have higher long-term predicted risk and may benefit from earlier initiation of antihypertensive therapy
- While initiation of antihypertensive therapy for adults <30 years for whom estimated risk models are limited, initiation of therapy could be considered after attempts at lifestyle intervention have not achieved optimal BP levels, but data are limited in this age range.

Medical Management

- Initiation of antihypertensive treatment for adults aged ≥80 years (for whom estimated risk models are limited) is recommended at ≥130/80 mm Hg when clinical judgment suggests benefits will outweigh harms and when aligned with the patient's goals of care.
  - In the SPRINT trial, 12.5% of participants were aged ≥80 years, and there was no difference in benefit by age.
  - Observational data also suggest a similar relative risk reduction of BP lowering across age categories, including those aged ≥85 years
- In adults without clinical CVD who are at lower 10-year predicted CVD risk based on PREVENT (<7.5%), there are limited data about the net benefit of initiation of antihypertensive therapy at a lower threshold with an average SBP ≥130 mmHg.
  - If average SBP is ≥130 mm Hg after a 3- to 6-month trial, initiation of antihypertensive therapy is advised as an adjunct to lifestyle interventions. This is supported by the PREVER-Prevention trial

Recommendations for BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

COR	LOE	Recommendations
1	A	1. In all adults with hypertension, initiation of medications to lower BP is recommended when average SBP is ≥140 mm Hg to reduce the risk of cardiovascular events and total mortality.[1–6]
1	A	2. In all adults with hypertension, initiation of medications to lower BP is recommended when average DBP is ≥90 mm Hg to reduce the risk of cardiovascular events and total mortality.[1–6]
1	A	3. In adults with hypertension and clinical CVD, initiation of medications to lower BP is recommended when average SBP is ≥130 mm Hg to reduce the risk of cardiovascular events and total mortality.[5–8]
1	C-LD	4. In adults with hypertension and clinical CVD, initiation of medications to lower BP is recommended when average DBP is ≥80 mm Hg to reduce the risk of cardiovascular events and total mortality.[5–8]

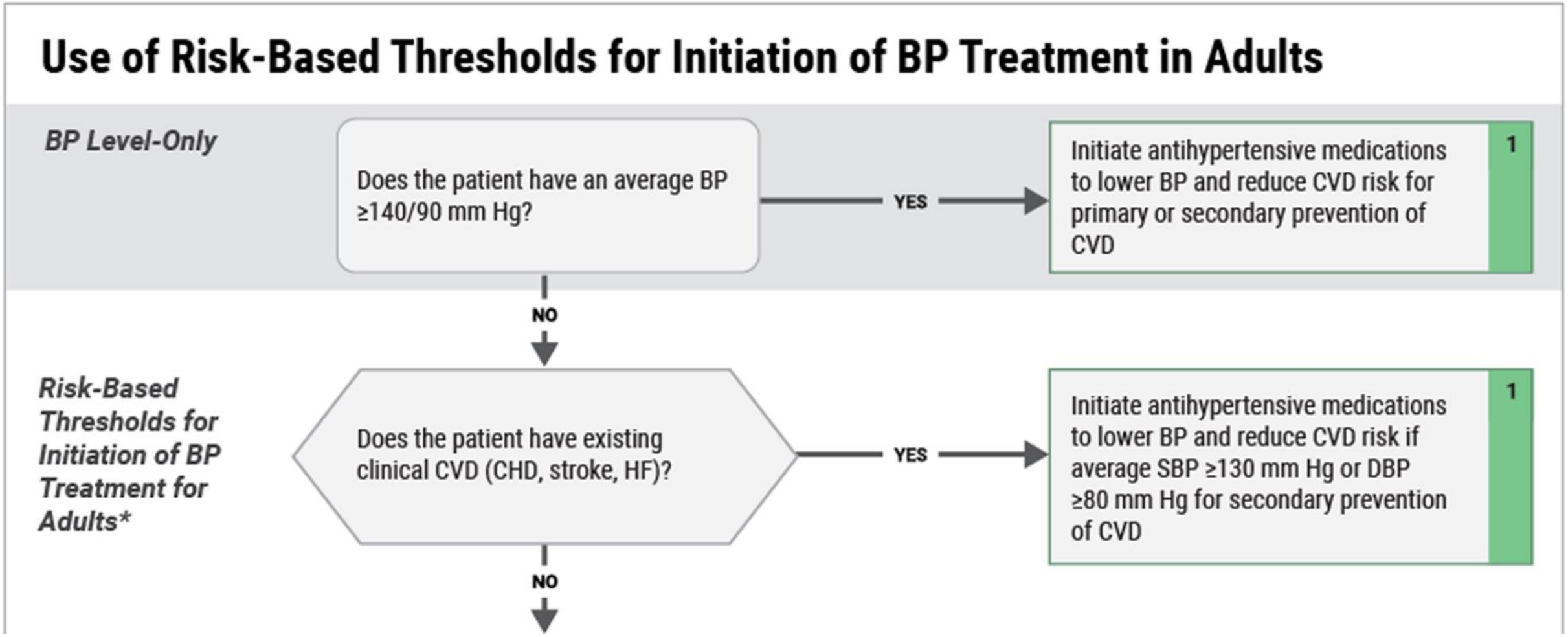
Recommendations for BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

COR	LOE	Recommendations
1	A	5. In adults with hypertension without clinical CVD but with diabetes or CKD or at increased short-term CVD risk (ie, estimated 10-year CVD risk ≥7.5% based on PREVENT*), initiation of medications to lower BP is recommended when average SBP is ≥130 mm Hg to reduce the risk of CVD events and total mortality.[5–10]
1	C-LD	6. In adults with hypertension without clinical CVD but with diabetes or CKD or at increased 10-year CVD risk (ie, ≥7.5% based on PREVENT*), initiation of medications to lower BP is recommended when average DBP is ≥80 mm Hg to reduce the risk of CVD events and total mortality.[5–10]

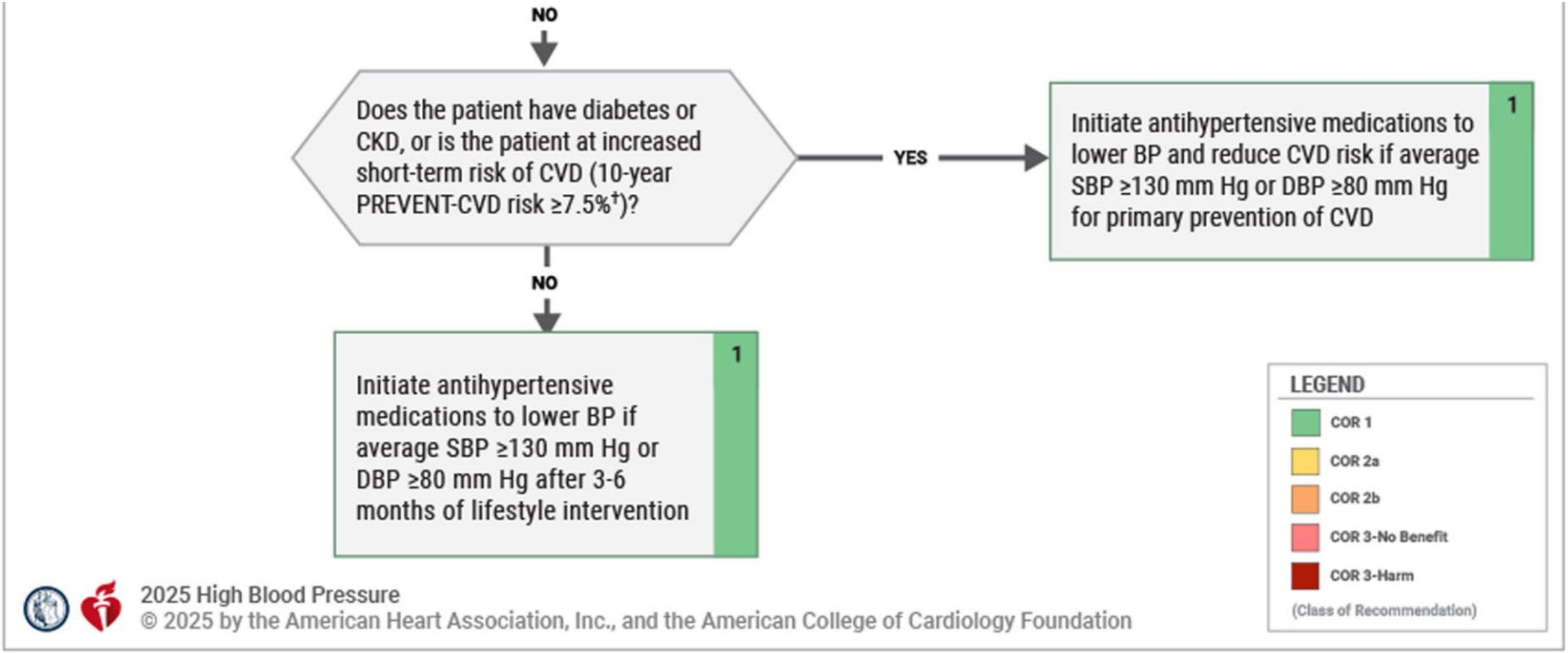
Recommendations for BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

1	B-R	7. In adults with hypertension without clinical CVD and with estimated 10-year CVD risk <7.5% based on PREVENT,* initiation of medications to lower BP is recommended if average SBP remains ≥130 mm Hg after a 3- to 6-month trial of lifestyle intervention to prevent target organ damage and mitigate further rise in BP.[7,9,10]
1	B-R	8. In adults with hypertension without clinical CVD and with estimated 10-year CVD risk <7.5% based on PREVENT,* initiation of medications to lower BP is recommended if average DBP ≥80 mm Hg after a 3- to 6-month trial of lifestyle intervention to prevent target organ damage and mitigate further rise in BP.[7,9,10]

Use of Risk-Based Thresholds for Initiation of BP Treatment in Adults



Use of Risk-Based Thresholds for Initiation of BP Treatment in Adults



Initial Medication Selection for Treatment

- When initiating pharmacological therapy, primary consideration should be given to comorbidities (eg, coronary artery disease, HF, stroke, diabetes, CKD) for which specific BP-lowering medication classes are indicated
- Strong RCT evidence supports 4 classes of first-line agents compared with placebo (thiazide-type diuretics, long-acting dihydropyridine CCB, and ACEi and ARB) due to their favorable profiles for BP lowering, CVD prevention, and tolerability
  - In a carefully designed head-to-head comparison of initial antihypertensive drug therapies, a long-acting thiazide type diuretic was more effective than a CCB or ACEi for prevention of HF and slightly better than ACEi for prevention of stroke.
  - All other antihypertensive agents are considered secondary.
  - BBs were less effective than first-line antihypertensive classes in preventing strokes and had a less favorable side effect profile; therefore, they should be reserved for adults with compelling indication

Medical Management

- The primary goal of treatment should be to reduce BP to the target level, considering the underlying CVD risk and compelling indications
- While there are subtle differences among thiazide-type diuretics, long-acting dihydropyridine CCB, and ACEi and ARB, the general pattern indicates a similar effect in preventing CVD
- In a large pragmatic RCT comparing HCTZ 25 mg to chlorthalidone 12.5 mg, switching from HCTZ to chlorthalidone did not lower the rates of MACE.
  - The subgroup of patients with ASCVD had greater benefit with chlorthalidone than HCTZ
  - The design of the study made it difficult to exclude the possibility that choice of a longer-acting diuretic such as chlorthalidone is preferable to use of a shorter-acting agent such as HCTZ.

Recommendation for Initial Medication Selection

Recommendation for Initial Medication Selection for Treatment of Primary Hypertension
Referenced studies that support the recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
1	A	1. For adults initiating antihypertensive drug therapy, thiazide-type diuretics, long-acting dihydropyridine CCB, and ACEi or ARB are recommended as first-line therapy to prevent CVD.[1,2]

Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

- As BP is regulated by several complementary biological systems, most patients require ≥2 antihypertensive medications to achieve BP control.
- Historically, a stepped-care approach was recommended, starting with monotherapy then titrating the dose or adding a second agent as needed
- No RCTs have compared initial stepped care with initial combination therapy.
- Combining antihypertensive medications with complementary mechanisms enhances BP-lowering effects and may reduce side effects.
  - For example, combining an RAS blocker with a thiazide-type diuretic reduces the likelihood of hypokalemia or hyperkalemia, and combining an ACEi or ARB with a dihydropyridine CCB reduces the incidence and severity of lower leg swelling

Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

- Combination therapy is more effective, efficient, and consistent in lowering BP and improves adherence when using an SPC compared with stepped-care therapy
- a stepped-care approach can be effective for BP lowering if well executed.
  - Exceptions include stage 1 hypertension, where some patients can achieve and maintain BP control with a single agent, especially those with initial BP close to target.
- Initial combination therapy is recommended for stage 2 hypertension and some high-risk patients with stage 1 hypertension (eg, non-Hispanic Black adults, ASCVD risk >7.5%) using 2 agents from different classes, preferably in an SPC to improve adherence and BP control
- Few RCTs have compared different combinations head-to-head.
  - Available RCT evidence supports using an RAS blocker with either a thiazide-type diuretic or a dihydropyridine CCB as initial therapy

Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

- Because most patients with hypertension require multiple agents for control of their BP, for those who are candidates for initial combination therapy (nonfrail adults with SBP ≥20 mm Hg and DBP ≥10 mm Hg from target), starting treatment with SPCs rather than equivalent free-pill combinations improves adherence
- Evidence favoring this approach comes mostly from studies showing greater BP lowering with SPC agents than with single agents, with higher adherence rates
- BP-lowering medications should be carefully initiated and monitored in older patients because hypotension or orthostatic hypotension (OH) may develop.
- As SPCs are not available with every possible dose combination, in some cases the use of separate agents may be more or equally efficient.

Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

- the stepped-care approach remains a reasonable option in older adults and in individuals who have a history of hypotension or multiple drug-associated side effects.
- High-quality RCT reports demonstrate that simultaneous administration of RAS blockers (ie, an ACEi combined with an ARB or an ACEi or ARB combined with the direct renin inhibitor, aliskiren) increases the risk of CVD, kidney disease, and hyperkalemia.
- drug combinations with agents that have similar mechanisms of action or clinical effects should be avoided.
  - For example, 2 drugs from the same class should not be administered together (eg, 2 different BB, ACEi, or dihydropyridine CCB)
  - 2 drugs from classes that target the same BP control system are less effective and potentially harmful when used together (eg, ACEi and ARB).

Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

- Exceptions include concomitant use of thiazide-type and potassium sparing diuretics, and thiazide-type and loop diuretics.
- Dihydropyridine and nondihydropyridine CCB can be combined for additional BP-lowering in selected patients

Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

COR	LOE	Recommendations
1	B-R	1. In adults with stage 2 hypertension (SBP ≥ 140 mm Hg and DBP ≥90 mm Hg), initiation of antihypertensive drug therapy with 2 first-line agents of different classes, ideally in a single-pill combination (SPC), is recommended to improve BP control and adherence.[1–6]
2a	C-EO	2. In adults with stage 1 hypertension (SBP 130-139 mm Hg and DBP 80-89 mm Hg), initiation of antihypertensive drug therapy with a single first-line antihypertensive drug is reasonable, with dosage titration and sequential addition of other agents as needed to achieve BP control.
3: Harm	A	3. In adults with hypertension, simultaneous use of an ACEi, ARB, and/or renin inhibitor in combination is not recommended due to the potential for harm.[7–9]

FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Agents recommended for initial therapy				
Thiazide-type diuretics	Chlorthalidone	12.5-25	1	Chlorthalidone has a longer half-life and is more potent than hydrochlorothiazide on a mg-to-mg basis. Monitor for hyponatremia and hypokalemia, increased glucose, uric acid, and calcium levels. Monitor patients with history of acute gout unless patient is on uric acid-lowering therapy.
	Hydrochlorothiazide	25-50	1	
	Indapamide	1.25-2.5	1	

FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Agents recommended for initial therapy				
ACEi	Benazepril	10-40	1 or 2	Do not use in combination with ARB or direct renin inhibitor. There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K+ supplements or K+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ACEi. Avoid use in pregnancy.
	Captopril	12.5-150	2 or 3	
	Enalapril	5-40	1 or 2	
	Fosinopril	10-40	1	
	Lisinopril	10-40	1	
	Moexipril	7.5-30	1 or 2	
	Perindopril	4-16	1	
	Quinapril	10-80	1 or 2	
	Ramipril	2.5-20	1 or 2	
	Trandolapril	1-4	1	
ARBs	Azilsartan	40-80	1	Do not use in combination with ACEi or direct renin inhibitor. There is an increased risk of hyperkalemia in CKD or in those on K+ supplements or K+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive an ARB beginning 6 weeks after ACE inhibitor is discontinued. Avoid use in pregnancy.
	Candesartan	8-32	1	
	Eprosartan	600-800	1 or 2	
	Irbesartan	150-300	1	
	Losartan	50-100	1 or 2	
	Olmesartan	20-40	1	
	Telmisartan	20-80	1	
	Valsartan	80-320	1	

FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Agents recommended for initial therapy				
CCB–dihydropyridines	Amlodipine	2.5-10	1	Associated with dose-related lower extremity edema, which is more common in women than men.
	Felodipine	2.5-10	1	
	Isradipine	5-10	2	
	Nicardipine SR	60-120	2	
	Nifedipine LA	30-90	1	
	Nisoldipine	17-34	1	
Alternative agents				
CCB–nondihydropyridines	Diltiazem ER	120-360	1	Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. Do not use in patients with HFrEF. There are drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).
	Verapamil IR	120-360	3	
	Verapamil SR	120-360	1 or 2	
	Verapamil-delayed onset ER	100-300	1 (in the evening)	

FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Diuretics–potassium-sparing	Amiloride	5-10	1 or 2	As monotherapy, these agents are minimally effective antihypertensive agents. Combination therapy of a potassium-sparing diuretic with a thiazide-type diuretic can be considered in patients with hypokalemia on thiazide-type diuretic monotherapy. Avoid use in patients with significant CKD (eg, GFR <45 mL/min).
	Triamterene	50-100	1 or 2	
Diuretics–loop	Bumetanide	0.5-2	2	These are preferred diuretics in patients with symptomatic HF. They are preferred over thiazide-type diuretics in patients with moderate-to-severe CKD (eg, GFR <30 mL/min). The longer-acting choice of torsemide is preferred for treatment of hypertension. A loop diuretic is an option for patients who develop thiazide-type diuretic associated hyponatremia.
	Furosemide	20-80	2	
	Torsemide	5-10	1	

FDA-Approved Drugs for Treatment of Hypertension

Diuretics–aldosterone antagonists	Eplerenone	50-100	1 or 2	These are preferred agents in primary aldosteronism and resistant hypertension. Spironolactone is associated with greater risk of gynecomastia and impotence compared with eplerenone. Demonstrated efficacy as fourth-agent add-on therapy for resistant hypertension. Avoid use with K+ supplements, other K+-sparing diuretics, or significant renal dysfunction (eg, GFR <45 mL/min). Eplerenone often requires twice-daily dosing for adequate BP lowering. Avoid use in pregnancy.
	Spironolactone	25-100	1	

FDA-Approved Drugs for Treatment of Hypertension

Beta blockers–cardioselective	Atenolol	25-100	2	Beta blockers are not recommended as first-line agents unless the patient has CHD or HF. These are preferred in patients with bronchospastic airway disease requiring a beta blocker. Bisoprolol and metoprolol succinate are preferred in patients with HFrEF. Avoid abrupt cessation.
	Betaxolol	5-20	1	
	Bisoprolol	2.5-10	1	
	Metoprolol tartrate	100-200	2	
	Metoprolol succinate	50-200	1	
Beta blockers–cardioselective and vasodilatory	Nebivolol	5-40	1	Nebivolol induces nitric oxide-induced vasodilation. Avoid abrupt cessation.
Beta blockers–noncardioselective	Nadolol	40-120	1	Avoid use in patients with reactive airways disease. Avoid abrupt cessation.
	Propranolol IR	80-160	2	
	Propranolol LA	80-160	1	
Beta blockers–intrinsic sympathomimetic activity	Acebutolol	200-800	2	Generally avoid, especially in patients with CHD or HF. Avoid abrupt cessation.
	Penbutolol	10-40	1	
	Pindolol	10-60	2	
Combined alpha and beta blockers	Carvedilol	12.5-50	2	Use of carvedilol is preferred in patients with HFrEF. Avoid abrupt cessation.
	Carvedilol phosphate	20-80	1	
	Labetalol	200-1200	2	

FDA-Approved Drugs for Treatment of Hypertension

Direct renin inhibitor	Aliskiren	150-300	1	Do not use in combination with ACEi or ARB. Aliskiren is very long acting. There is an increased risk of hyperkalemia in CKD or in those on K+ supplements or K+-sparing drugs. Aliskiren may cause acute renal failure in patients with severe bilateral renal artery stenosis. Avoid use in pregnancy.
Alpha-1 blockers	Doxazosin	1-16	1	These are associated with orthostatic hypotension, especially in older adults with a greater BP drop with first dose effect. These may be considered a second-line agent in patients with symptomatic benign prostatic hypertrophy.
	Prazosin	2-20	2 or 3	
	Terazosin	1-20	1 or 2	

FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Central alpha-2-agonist and other centrally acting drugs	Clonidine oral	0.1-0.8	2	These are generally reserved as last-line choices because of significant CNS adverse effects, especially in older adults. Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis. Clonidine must be tapered to avoid rebound hypertension.
	Clonidine patch	0.1-0.3	1 weekly	
	Methyldopa	250-1000	2	
	Guanfacine	0.5-2	1	
Direct vasodilators	Hydralazine	100-200	2 or 3	These are associated with sodium and water retention and reflex tachycardia and should be used with a diuretic and beta blocker. Hydralazine is associated with a drug-induced lupus-like syndrome at higher doses. Minoxidil is associated with hirsutism and requires a loop diuretic. Minoxidil can induce pericardial effusion.
	Minoxidil	5-40	1-2	
Dual endothelin receptor antagonist	Aprocitentan	12.5	1	Associated with mild-to-moderate fluid retention usually occurring within the first 4-6 wks of therapy. Indicated as add-on therapy for patients whose BP is not adequately controlled on other antihypertensive medications. Avoid use in pregnancy.

Antihypertensive Medication Adherence Strategies

- Studies have documented that up to 50% of patients do not adhere to their antihypertensive medications after 1 year of treatment.
- Adherence to medications can be assessed in multiple ways, including self-report, medication adherence questionnaires, review of prescription refills, pill counting, electronic pill boxes, and chemical adherence testing of antihypertensive drug levels
- Adherence to medication can be divided into 3 phases: 1) initiation; 2) persistence or implementation, consistent with medication taking; and 3) avoiding permanent discontinuation.
- Medication adherence was greatest with once-daily dosing and declined as dosing frequency increased.

Antihypertensive Medication Adherence Strategies

- a large RCT showed a significantly higher adherence rate among hypertensive adults with morning dosing (6:00 am to 10:00 am) versus evening dosing of once-daily medications.
- Simplifying medication regimens, either by less frequent dosing (ie, once daily versus multiple times daily) or use of combination drug therapy, improves adherence.
- The following interventions can improve adherence: medication reminder aids (eg, text, telephone, smartphone apps); patient education and self-management programs; mindfulness-based stress reduction or counseling for high stress, anxiety, or depression; simplification of antihypertensive regimen; electronic/home blood pressure monitoring, feedback to clinicians about antihypertensive adherence via displaying prescription refills or undetected drug levels; and education/coaching by health care professionals.

Recommendations for Antihypertensive Medication Adherence Strategies

COR	LOE	Recommendations
1	B-R	1. In adults with hypertension, antihypertensive medication dosing once daily rather than multiple times daily is beneficial to improve medication adherence.[1–3]
1	B-R	2. In adults with hypertension, the use of a SPC to reduce pill burden rather than taking separate pills is effective to improve medication adherence.[4–9]
2a	B-R	3. In adults with hypertension, use of medication reminder aids and educational or self-management interventions can be useful to improve medication adherence.[10–16]

Evidence-Based Strategies for Improving Antihypertensive Medication Adherence
Dose consolidation
Single pill combination rather than separate pills
Education/coaching by pharmacists and other health professionals
Electronic/home blood pressure monitoring and feedback
Integration of patient preferences and values/shared decision-making into management plan
Medication synchronization and reminder aids
Mindfulness-based stress reduction or counseling for high stress, anxiety, and/or depression
Self-management interventions

Medication Interactions

- When designing an antihypertensive regimen that minimizes unwanted adverse effects while maximizing beneficial effects for patients taking more than 1 medication, knowledge of pharmacology and drug-drug interactions is essential.
- Drug-drug interactions are categorized as either pharmacokinetic (when 1 medication affects the absorption, metabolism, distribution, or elimination of another) or pharmacodynamic (when 1 medication affects the end-pharmacological response to another medication without impacting the drug's disposition within the body)
- verapamil and diltiazem are both substrates and inhibitors of CYP3A4 and can alter the metabolism of other medications processed through this pathway

Medication Interactions

- Examples of beneficial pharmacodynamic interactions include the combination of an RAS inhibitor with a thiazide-type diuretic to minimize diuretic-induced hypokalemia, or a dihydropyridine CCB with an RAS inhibitor to reduce the incidence or severity of lower extremity edema
- Conversely, combining drugs with overlapping mechanisms, like ACEi and ARB or direct renin inhibitors, leads to an increased risk of hyperkalemia, an adverse pharmacodynamic interaction.

Pharmacokinetic Drug–Drug Interactions With Antihypertensive Medications

Blood Pressure Drug	Potential Interacting Drug	Clinical Effect
Absorption		
Thiazide-type diuretics	Cholestyramine	Decreased absorption leading to reduced BP lowering
Amlodipine, furosemide, metoprolol, carvedilol, bisoprolol, nebivolol, telmisartan	Potassium binder (patiromer)	Decreased absorption of antihypertensives leading to reduced BP-lowering effects. To mitigate this, administer the antihypertensives at least 3 h before or after taking the potassium binder
Furosemide	Potassium binder (sodium zirconium cyclosilicate)	Increased absorption of furosemide due to increased gastric pH leading to increased clinical effects (eg, diuresis or risk of hypokalemia); effect diminished with separation of administration by 2 h
Methyldopa	Iron salts	Decreased absorption of methyldopa leading to reduced BP lowering

Pharmacokinetic Drug–Drug Interactions With Antihypertensive Medications

Blood Pressure Drug	Potential Interacting Drug	Clinical Effect
Metabolism		
Bisoprolol, carvedilol, metoprolol	CYP2D6 inhibitors (eg, amiodarone, cimetidine, diphenhydramine, fluoxetine, paroxetine, terbinafine)	Increased BB concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inhibitors (eg, clarithromycin, erythromycin itraconazole, ketoconazole)	Increased nondihydropyridine concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, St. John's Wort, rifampin)	Decreased nondihydropyridine CCB concentration leading to reduced clinical effects (eg, minimization of blood pressure and pulse lowering)
CYP3A4 inhibition via amlodipine, verapamil, or diltiazem or other CYP3A4 inhibitors	Tacrolimus, cyclosporine	Increased calcineurin inhibitor concentration leading to increased risk for side effects (eg, renal impairment)
	Dabigatran, rivaroxaban	Increased concentration leading to increased risk for bleeding
	Atorvastatin, simvastatin	Increased statin concentration leading to increased risk for side effects (eg, myopathy)
	Colchicine	Increased colchicine concentration leading to increased risk for adverse effects (eg, neuromuscular toxicity)
	Eplerenone	Increased risk of hypotension and hyperkalemia Using a lower dose of eplerenone when combined with diltiazem could be considered a productive interaction, as the inhibition of eplerenone's metabolism might allow for lower doses to be effective, reducing the risk of adverse effects while maintaining efficacy

Pharmacokinetic Drug–Drug Interactions With Antihypertensive Medications

Blood Pressure Drug	Potential Interacting Drug	Clinical Effect
Elimination		
Lithium	Thiazide-type diuretics, RAS blockers	Reduced lithium clearance leading to increased lithium toxicity risk
P-glycoprotein (P-gp)		
Verapamil via P-gp inhibition	Dabigatran	Reduced P-gp efflux of dabigatran leading to increased dabigatran levels, which results in a higher risk of bleeding
Verapamil and carvedilol via P-gp inhibition	Digoxin	Reduced P-gp efflux of digoxin leading to increased digoxin levels, resulting in a higher risk of digoxin toxicity

Pharmacodynamic Drug–Drug Interactions With Antihypertensive Medications

Drug Combinations		Clinical Effect
Cautionary interactions		
Any antihypertensive medication	NSAIDs	Reduced BP lowering via sodium retention
	Sympathomimetic (eg, pseudoephedrine, dextroamphetamine)	Reduced BP lowering
	Venlafaxine	Reduced BP lowering
Nondihydropyridine CCB	Beta blockers	Bradycardia or atrioventricular block
ACEi	ARBs	AKI, hyperkalemia
	Potassium-sparing diuretics (Spironolactone, eplerenone, triamterene, amiloride)	Hyperkalemia
	Sulfamethoxazole/trimethoprim	Hyperkalemia
	Potassium supplements	Hyperkalemia
	NSAIDs (eg, ibuprofen, naproxen)	AKI
Clonidine, methyldopa, guanfacine	CNS depressants (eg, zolpidem, alprazolam)	Sedation
Clonidine	Noncardioselective BB (eg, nadolol or propranolol)	Unopposed alpha agonism upon BB withdrawal leading to hypertensive crisis

Pharmacodynamic Drug–Drug Interactions With Antihypertensive Medications

Drug Combinations		Clinical Effect
Advantageous interactions		
Dihydropyridine CCB	RAS inhibitor	Reduced risk of dihydropyridine CCB-induced lower leg swelling
RAS inhibitors	Diuretics	Balanced effects on serum potassium levels with diminished possibility for hypokalemia (with diuretic) or hyperkalemia (with RAASi)
RAS inhibitors	Potassium binder	Lowers risk of hyperkalemia from the RAS inhibitor
Diuretic	Potassium supplement	Lowers risk of hypokalemia from the diuretic

Electrolyte Imbalances

- Assessment of electrolytes is important in evaluating causes of hypertension and in monitoring adverse effects with treatment.
- A basic metabolic panel should be checked at the time of diagnosis of hypertension to evaluate for secondary hypertension, including primary or secondary aldosteronism and other endocrine causes.
- A basic metabolic panel should be checked 2 to 4 weeks after initiation or dose titration of specific antihypertensive medication classes, including diuretics, ACEi, ARB, and MRA.
- Common lab disturbances relate to changes in potassium, sodium, or creatinine.
- In addition to secondary causes of hypertension, hypokalemia may be caused by kaliuresis from thiazide-type and loop diuretics

Electrolyte Imbalances

- Hyperkalemia may be caused by ACEi, ARB, MRA, and potassium-sparing diuretics especially when used in combination or in the setting of CKD
- ACEi and ARB should not be used concurrently due to several trials demonstrating an increased risk for AKI or renal dysfunction
- Hyponatremia may be caused by diuretics, in particular thiazide-type diuretics.
- Strategies to mitigate electrolyte disturbances related to antihypertensive medications include dietary changes, electrolyte supplementation, and combination use of medications with complementary effects on electrolytes (eg, ACEi plus thiazide-type or loop diuretic, which may normalize potassium levels)

Electrolyte Imbalances

- Treatment of hyperkalemia, other than emergency treatment for life-threatening hyperkalemia, can also be managed with initiation of potassium-lowering binders (including patiromer and sodium zirconium cyclosilicate), noting the importance of taking them (primarily patiromer) mid-day apart from other medications to avoid interfering with absorption.
- If severe or life-threatening electrolyte imbalances occur, the causative medication should be discontinued and the imbalance treated immediately

Kidney Dysfunction/Injury

- Estimated GFR using serum creatinine should be measured 2 to 4 weeks after initiation or dose titration of antihypertensive medications
- Renin-angiotensinaldosterone system inhibitor (RAASi) (including ACEi, ARB, and MRA) may lead to an expected reduction, or dip, in eGFR of up to 30% via vasodilation of efferent arterioles
  - This expected short-term dip in eGFR is associated with preservation of kidney function in the long-term and should not lead to discontinuation of the RAASi unless the decline in eGFR is persistently >30%.
  - A referral to a nephrologist is appropriate for evaluation for other causes of AKI, CKD, progression, and possible renal artery stenosis
  - The presence of new kidney dysfunction/injury may also be observed with the addition or dose increase of diuretics; rule out hypovolemia
  - initially hold or reduce the diuretic dose and then advance more slowly

BP Goal for Patients With Hypertension

- In observational studies, BP is associated with CVD risk in a progressive, log-linear fashion from low to high levels (eg, SBP 100-180 mm Hg), suggesting the likelihood of CVD benefits with more intensive treatment
- In adults at high risk for CVD, RCTs, including those that randomized adults to different BP treatment targets, and clinical trials and meta-analyses support more intensive treatment to prevent CVD
- The evidence to support an SBP goal <130 mm Hg is strong.
- There is also evidence for an SBP goal <120 mm Hg versus <140 mm Hg, but this is based on a smaller, albeit growing, number of trials
  - Achievement of target BP should be based on an average of ≥2 readings at ≥2 visits, not on an individual BP measurement

Recommendations for BP Goal

COR	LOE	Recommendations
1	A	1. In adults with confirmed hypertension who are at increased risk* for CVD, an SBP goal of at least <130 mm Hg, with encouragement to achieve SBP <120 mm Hg, is recommended to reduce the risk of cardiovascular events and total mortality.[1–4]
2b	B-NR	2. In adults with confirmed hypertension who are not at increased risk* for CVD, an SBP goal of <130 mm Hg, with encouragement to achieve SBP <120 mm Hg, may be reasonable to reduce risk of further elevation of BP.[5]
1	B-R	3. In adults with confirmed hypertension who are at increased risk* for CVD, a DBP target of <80 mm Hg is recommended to reduce the risk of cardiovascular events and total mortality.[6]
2b	B-NR	4. In adults with confirmed hypertension who are not at increased risk* for CVD, a DBP target of <80 mm Hg may be reasonable to reduce the risk of cardiovascular events.[5]

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Intensive Blood-Pressure Control in Patients with Type 2 Diabetes

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Among patients with type 2 diabetes, the incidence of major cardiovascular events was significantly lower with intensive treatment targeting a systolic blood pressure of less than 120 mm Hg than with standard treatment targeting a systolic blood pressure of less than 140 mm Hg. (Funded by the National Key Research and Development Program of the Ministry of Science and Technology of China and others; BPROAD ClinicalTrials.gov number, NCT03808311.)