Hypertension

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.

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CLINICAL STATEMENTS AND GUIDELINES

AIM: The "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" retires and replaces the "2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults."

METHODS: A comprehensive literature search was conducted from December 2023 to June 2024 to identify clinical studies, reviews, and other evidence performed on human subjects that were published since February 2015 in English from MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline.

STRUCTURE: The focus of this clinical practice guideline is to create a living, working document updating current knowledge in the field of high blood pressure aimed at all practicing primary care and specialty clinicians who manage patients with hypertension.

Key Words: AHA Scientific Statements ■ antihypertensive agents ■ antihypertensive response ■ blood pressure ■ blood pressure control ■ blood pressure determination ■ blood pressure monitoring ■ cardiovascular disease ■ dosage ■ evaluation ■ hypertension ■ lifestyle ■ major adverse cardiovascular events ■ patient care team ■ quality of life ■ risk factors ■ time factors

TABLE OF CONTENTS

WHAT IS NEW

Table 1 highlights new and/or substantially revised practice-changing recommendations since the last iteration of the guideline and is not a comprehensive list of all updates. Some of these recommendations have corresponding footnotes not captured in this table.

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.
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.
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.
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; and stage 2 hypertension as ≥140 mm Hg systolic or ≥90 mm Hg diastolic.
5. For all adults, lifestyle changes, including maintaining or achieving a healthy weight, following a heart-healthy 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.
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).
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.
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.
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.
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.

Table 1. 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.
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.
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.

(*Continued*)

Table 1. Continued

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.
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.
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.

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker, BP, blood pressure; CKD, chronic kidney disease; COR, Class of Recommendation; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ICH, intracerebral hemorrhage; MRA, mineralocorticoid receptor antagonist; PREVENT = Predicting Risk of CVD EVENTs; RAASi, renin-angiotensin-aldosterone system inhibitor; RDN, renal denervation; and SBP, systolic blood pressure.

PREAMBLE

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts. Guidelines are the official policy of the ACC and AHA. For some guidelines, the ACC and AHA collaborate with other organizations.

Intended Use

Clinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease (CVD). The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances and should not replace clinical judgment.

Clinical Implementation

Management in accordance with guideline recommendations is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions based on individual values, preferences, associated conditions, and comorbidities.

Methodology and Modernization

The ACC/AHA Joint Committee on Clinical Practice Guidelines (Joint Committee) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the National Academy of Medicine (formerly the Institute of Medicine),[1,2] and on the basis of internal reevaluation. Similarly, presentation and delivery of guidelines are reevaluated and modified in response to evolving technologies and other factors to optimally facilitate dissemination of information to health care professionals at the point of care.

Numerous modifications to the guidelines have been implemented to make them shorter and enhance "user friendliness." Guidelines are written and presented in a modular recommendation format in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review.

In recognition of the importance of cost-value considerations, in certain guidelines, when appropriate and feasible, an assessment of value for a drug, device, or intervention may be performed in accordance with the AHA/ACC methodology.[3]

To ensure that guideline recommendations remain current, new data will be reviewed on an ongoing basis by the writing committee and staff. When applicable, recommendations will be updated with new evidence, or new recommendations will be created when supported by published evidence-based data. Going forward, targeted sections/knowledge chunks will be revised dynamically after publication and timely peer review of potentially practice-changing science. The previous designations of "full revision" and "focused update" will be phased out. For additional information and policies on guideline development, readers may consult the AHA/ACC guideline methodology manual[4] and other methodology articles.[5–7]

Selection of Writing Committee Members

The Joint Committee strives to ensure that the guideline writing committee contains requisite content expertise and is representative of the broader cardiovascular community by selection of experts across a spectrum of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and clinical practice settings. Organizations and professional societies with related interests and expertise are invited to participate as collaborators.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found online. Appendix 1 of the guideline lists writing committee members' comprehensive and relevant RWI.

Evidence Review and Evidence Review Committees

In developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data.[4,5] Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only key references are cited.

An independent evidence review committee is commissioned when there are ≥1 questions deemed of

utmost clinical importance that merit formal systematic review to determine which patients are most likely to benefit from a drug, device, or treatment strategy, and to what degree. Criteria for commissioning an evidence review committee and formal systematic review include absence of a current authoritative systematic review, feasibility of defining the benefit and risk in a time frame consistent with the writing of a guideline, relevance to a substantial number of patients, and likelihood that the findings can be translated into actionable recommendations. Evidence review committee members may include methodologists, epidemiologists, clinicians, and biostatisticians. Recommendations developed by the writing committee on the basis of the systematic review are marked "SR".

Guideline-Directed Medical Therapy

The term guideline-directed medical therapy (GDMT) encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and evaluate for contraindications and interactions. Recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

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1. INTRODUCTION

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence-based. An initial extensive evidence review, which included literature derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline published from February 2015, was performed from December 2023 to June 2024. Key search words included but were not limited to the following: ACC/AHA clinical practice guideline; antihypertensive agents; antihypertensive response; blood pressure; blood pressure control; blood pressure determination; blood pressure monitoring; cardiovascular disease; dosage; hypertension; risk factors; and time factors.

Additional relevant studies, which were published through January 2025 during the guideline writing process, were also considered by the writing committee and added to the evidence tables when appropriate. The evidence tables summarize the evidence used by the writing committee to formulate recommendations and are available online. References selected and published in the present document are representative and not all-inclusive.

1.2. Organization of the Writing Committee

The writing committee consisted of general/preventive cardiologists, interventional cardiologists, cardiac imaging experts, nephrologists, internists, a neurologist, a gerontologist, cardiovascular epidemiologists, advanced practice nurses, a clinical pharmacist, a physician associate, and a patient advocate. The writing committee included representatives from the AHA, ACC, Association of Black Cardiologists (ABC), American Academy of Physician Associates (AAPA), American College of Clinical Pharmacy (ACCP), Society of General Internal Medicine (SGIM), Preventive Cardiovascular Nurses Association (PCNA), American Medical Association (AMA), American Association of Nurse Practitioners (AANP), National Medical Association (NMA), American College of Preventive Medicine (ACPM), American Society of Preventive Cardiology (ASPC), and the American Geriatrics Society (AGS). Appendix 1 of the current document lists writing committee members' comprehensive and relevant RWI.

On February 28, 2024, a writing committee member disclosed relationships with Amgen and Novartis, which were deemed to be relevant to the guideline. The member was removed before the guideline writing committee reviewed and approved the manuscript for submission to the Joint Committee, the AHA Science Advisory and Coordinating Committee, the AHA Executive Committee, the ACC Clinical Policy and Approval Committee, the ACC Science and Quality Committee, and the collaborating organizations for consideration of endorsement.

1.3. Guideline Review and Approval

The Joint Committee appointed a peer review committee to review the document. The peer review committee comprised individuals nominated by the ACC, AHA, and the collaborating organizations. Reviewers' RWI information was distributed to the writing committee and is published in this document (Appendix 2). This document was approved for publication by the governing bodies of the ACC and the AHA and was endorsed by the ABC, AAPA, ACCP, SGIM, PCNA, AMA, AANP, NMA, ACPM, ASPC, and AGS.

1.4. Scope of the Guideline

This guideline is intended to be a resource for clinical and public health professionals. Clinicians should be advised that this guideline retires and replaces the previously published "2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults." This guideline does not provide recommendations on blood pressure (BP) prevention and management in patient populations with these conditions: chronic coronary disease (CCD), heart failure (HF), atrial fibrillation (AF), valvular heart disease, aortic disease (AD),

Table 2. Associated Publications

Title	Organization	Publication Year (Reference)
Guidelines		
Lifestyle management to reduce cardiovascular risk	AHA/ACC	2013[2]
Management of overweight and obesity in adults	AHA/ACC/TOS	2014[3]
Primary prevention of cardiovascular disease	ACC/AHA	2019[4]
Management of patients with valvular heart disease	ACC/AHA	2021[5]
Management of heart failure	AHA/ACC/HFSA	2022[6]
Diagnosis and management of aortic disease	AHA/ACC	2022[7]
Management of patients with chronic coronary disease	AHA/ACC/ACCP/ASPC/NLA/PCNA	2023[8]
Management of atrial fibrillation	ACC/AHA/ACCP/HRS	2023[9]
Management of lower extremity peripheral artery disease	ACC/AHA	2024[10]
Perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery	AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM	2024[11]
Other Relevant Documents		
Current science on consumer use of mobile health for cardiovascular disease prevention	AHA	2015[12]
Resistant hypertension: detection, evaluation, and management	AHA	2018[13]
Measurement of blood pressure in humans	AHA	2019[14]
Clinical performance and quality measures for adults with high blood pressure	AHA/ACC	2019[15]
Blood pressure assessment in adults in clinical practice and clinic-based research	ACC	2019[16]
Self-measured blood pressure monitoring at home	AHA/AMA	2020[17]
Revascularization for renovascular disease	AHA	2022[18]
Medication adherence and blood pressure control	AHA	2022[19]
An overview of telehealth in the management of cardiovascular disease	AHA	2022[20]
Hypertension in pregnancy	AHA	2022[21]
Life's essential 8	AHA	2022[22]
Management of heart failure with preserved ejection fraction	ACC	2023[23]
Cardiovascular-kidney-metabolic health	AHA	2023[24]
Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health	AHA	2023[25]
Implementation strategies to improve blood pressure control in the US	AHA	2023[26]
Renal denervation for the treatment of hypertension	AHA	2024[27]

ACC indicates American College of Cardiology; ACCP, American College of Clinical Pharmacy; ACS, American College of Surgeons; AHA, American Heart Association; AMA, American Medical Association; ASNC, American Society of Nuclear Cardiology; ASPC, American Society for Preventive Cardiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; NLA, National Lipid Association; PCNA, Preventive Cardiovascular Nurses Association; SCA, Society of Cardiovascular Anesthesiologists; SCCT, Society of Cardiovascular Computed Tomography; SCMR, Society for Cardiovascular Magnetic Resonance; SVM, Society for Vascular Medicine; and TOS, The Obesity Society.

or peripheral artery disease (PAD); these topics are the focus of other AHA/ACC guidelines as listed in Table 2. The use of risk-based approaches to guide recommendations for initiation of antihypertensive therapy at varying BP thresholds remains the cornerstone of preventive care (Section 5.2.1, "Initiation of Pharmacological BP Treatment in the Context of Overall CVD Risk"). The writing committee discussed and evaluated the optimal approach to estimate risk among adults without clinical cardiovascular disease (CVD) in contemporary clinical practice and compared available data using the pooled cohort equations (PCEs) and the PREVENT[1] (Predicting Risk of CVD EVENTs) equations regarding populations, outcomes, predictors, and model performance. The PCEs were derived from data on 20 338 White adults and 4288 Black adults with baseline examinations dating from the 1960s to the 1990s. In contrast, PREVENT was derived from contemporary data from 3.2 million individuals with baseline examinations from 1992 to 2022 and included a diverse sample of racial and ethnic groups. The PCEs estimate risk for atherosclerotic cardiovascular disease (ASCVD) (eg, myocardial infarction [MI], stroke), whereas PREVENT estimates risk for total

CVD (MI, stroke, and HF), which is especially relevant as trials evaluating antihypertensive therapies and BP thresholds have focused on major adverse cardiovascular events (MACE) as the primary outcome. The PCEs are applicable to adults aged 40 to 79 years who are not on statin therapy. In contrast, PREVENT is applicable to adults aged 30 to 79 years and includes statin therapy as a predictor, making it more broadly applicable to guide preventive decisions regarding antihypertensive therapy. PREVENT incorporates measures of kidney function, as chronic kidney disease (CKD) is an important end-organ manifestation of hypertension and is associated with higher CVD risk. PREVENT includes the integration of place-based social risk (social deprivation index [SDI]), as the burden of hypertension is higher among those who reside in neighborhoods with higher deprivation. As a result of these changes, model performance for PREVENT is superior to PCEs. In a contemporary sample of 3.3 million US adults, PCEs overpredicted risk by 2-fold while PREVENT had excellent calibration, even when examined by race and ethnic group. Taken together, the writing committee recommends the use of PREVENT to estimate 10-year risk for CVD for adults with hypertension without clinical CVD in determining the BP threshold for initiation of therapies (Section 5.2.1, "Initiation of Pharmacological BP Treatment in the Context of Overall CVD Risk") and the BP goal for treatment (Section 5.2.7, "BP Goal for Patients With Hypertension").

In developing this guideline, the writing committee reviewed previously published guidelines and related scientific statements. Table 2 contains a list of AHA/ACC publications deemed pertinent to this writing effort and is intended for use as a resource.

1.5. 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 (Table 3).[28]

1.6. Abbreviations

Abbreviations	Meaning/Phrase
ABPM	ambulatory blood pressure monitoring
ACEi	angiotensin-converting enzyme inhibitor
AD	aortic disease
AF	atrial fibrillation
AKI	acute kidney injury
AOBP	automated office blood pressure
ARB	angiotensin receptor blocker
ASCVD	atherosclerotic cardiovascular disease
BB	beta blocker
BMI	body mass index
BP	blood pressure
CCB	calcium channel blocker
CCD	chronic coronary disease
CKD	chronic kidney disease
CKM	cardiovascular-kidney-metabolic
COR	class of recommendation
CPAP	continuous positive airway pressure
CVD	cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DBP	diastolic blood pressure
eGFR	estimated glomerular filtration rate
EHR	electronic health record
GDMT	guideline-directed medical therapy
GLP-1	glucagon-like peptide-1
HBPM	home blood pressure monitoring
HCTZ	hydrochlorothiazide
HDP	hypertensive disorders of pregnancy
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HbA1c	hemoglobin A1c
HIT	health information technology
HR	hazard ratio
ICH	intracerebral hemorrhage
IV	intravenous
LOE	level of evidence
MACE	major adverse cardiovascular event
MI	myocardial infarction
MRA	mineralocorticoid receptor antagonist
OH	orthostatic hypotension
OSA	obstructive sleep apnea
PAD	peripheral artery disease
PCE	pooled cohort equation
RAS	renin-angiotensin-system
RAASi	renin-angiotensin-aldosterone system inhibitor
RCT	randomized controlled trial
RDN	renal denervation
SBP	systolic blood pressure
SDOH	social determinants of health
SGLT2i	sodium-glucose cotransporter-2 inhibitor
SPC	single-pill combination
T2D	type 2 diabetes
TIA	transient ischemic attack
US	United States

Table 3. Applying the American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated December 2024)

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 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 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 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

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

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consenus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

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2. DEFINITIONS AND CLASSIFICATION OF BP

2.1. Definition of High BP

Recommendation for Definition of High BP References that support the recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
1	**B-NR**	1. In adults, BP should be categorized as normal, elevated, or stage 1 or 2 hypertension to prevent and treat high BP (Table 4).[1,2]

Synopsis

Although a continuous and graded association exists between higher BP and CVD risk (Section 5.2.1, "Initiation of Pharmacological BP Treatment in the Context of Overall CVD Risk"), 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): normal, elevated, and stage 1 or 2 hypertension (Table 4). The rationale for this categorization is based on observational data demonstrating the association between systolic blood pressure (SBP)/diastolic blood pressure (DBP) and CVD risk, as well as outcomes from RCTs of lifestyle modification to lower BP and RCTs of treatment with antihypertensive medication to prevent CVD. An increasing number of individual studies and meta-analyses of observational data have reported a gradient of higher CVD risk from normal BP, to elevated BP, to stage 1 and 2 hypertension.[2,3] BP categories are used for recommendations for prevention and treatment, as are provided in Section 5 ("BP Management"). The relationship of this classification schema with measurements obtained by out-of-office BP monitoring, including ambulatory blood pressure measurement (ABPM) and home blood pressure measurement (HBPM), is discussed in Sections 3.1.1 ("Accurate Measurement of In-Office BP"), 3.1.3 ("Out-of-Office BP Monitoring"), and 3.1.4 ("ABPM and HBPM").

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, "Hypertension and Pregnancy"). Adapted with permission from Whelton et al.[5] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

Table 5. Prevalence of Hypertension* Among US Adults Aged 18 to 80 Years, 2017 to 2020

Demographic group	Prevalence	
	Men	Women
Overall	49.5% (59.0 million)	43.9% (56.3 million)
Age groups, y		
18-29	20.3%	9.0%
30-44	39.6%	23.7%
45-59	57.4%	52.5%
60-74	70.7%	71.4%
75-80	83.7%	84.8%
Racial and ethnic groups (age-adjusted)		
NH White	47.0%	39.0%
NH Black	56.8%	56.7%
NH Asian	49.8%	39.1%
Hispanic	50.4%	36.3%
Other	50.7%	47.9%

*Hypertension defined as diagnosed hypertension, BP ≥130/80 mm Hg, or receiving antihypertensive therapy. Derived from NHANES.[9]

BP indicates blood pressure; and NH, non-Hispanic.

Recommendation-Specific Supportive Text

1. The choice and the naming of BP categories were based on a pragmatic interpretation of BP-related CVD risk and benefit of BP reduction in clinical trials. Meta-analyses of observational studies have demonstrated that elevated BP and hypertension are associated with a higher risk of CVD, end-stage kidney disease, subclinical atherosclerosis, and all-cause death.[1,3,4] The recommended BP classification system is most valuable for untreated adults to make decisions about strategies to prevent or treat high BP. However, it is also useful in assessing the success of interventions to reduce BP.

3. EVALUATION AND DIAGNOSIS

Synopsis

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.[1,2] 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 (Table 5).[3] 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

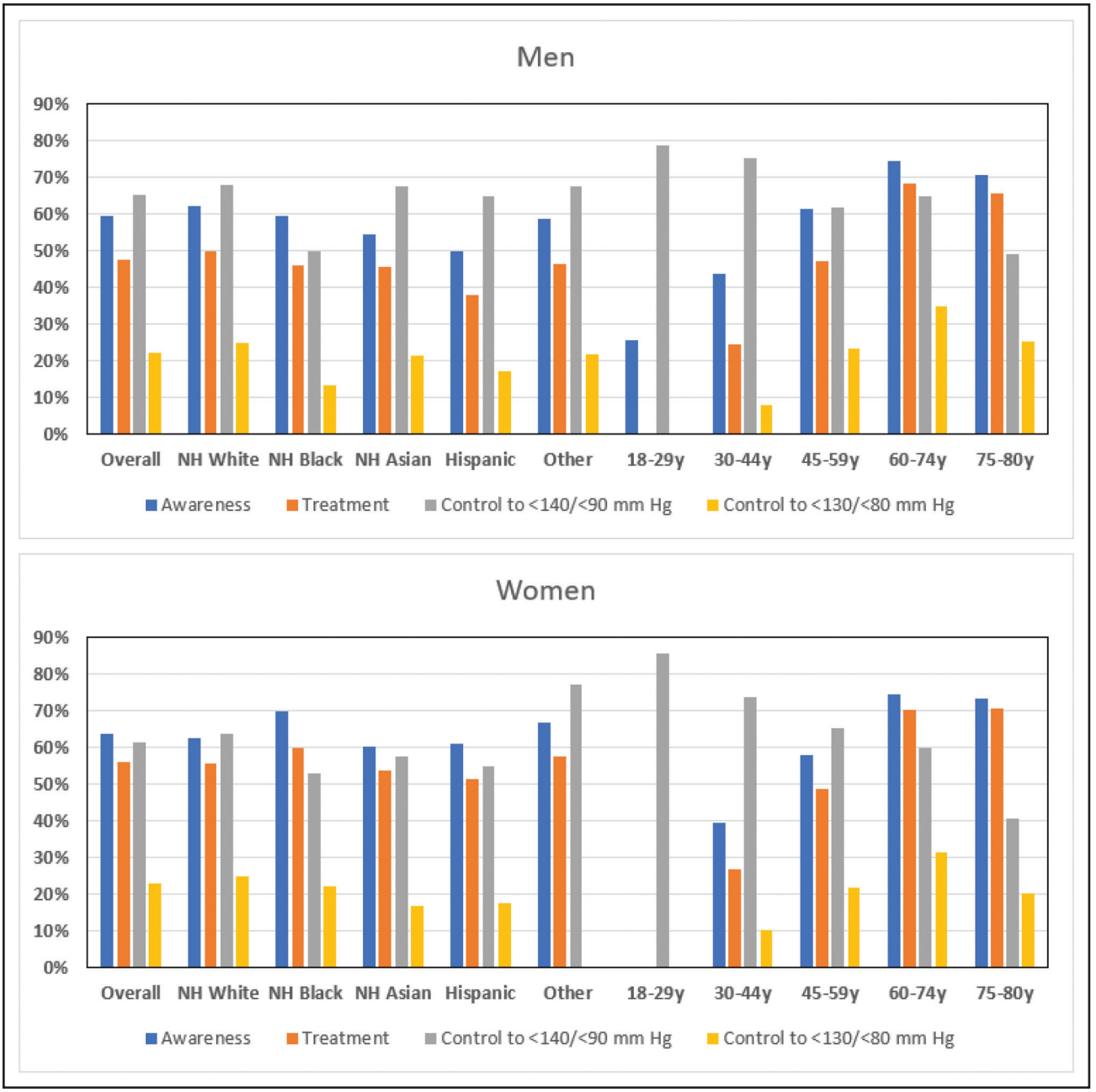


Figure 1. Rates of Awareness, Treatment, and Control of Hypertension Among US Adults Aged 18 to 80 Years, 2017 to 2020*.
*Missing data points indicate uncertain estimates due to small sample sizes for that subgroup. NH indicates non-Hispanic. Derived from NHANES.[9]

decline thereafter.[4] Among middle-aged individuals, the remaining lifetime risks for incident hypertension are as high as 80% to 90%, with earlier onset among men compared with women, and for Black and Hispanic compared with White and Chinese Americans.[5–7] Current rates of awareness, treatment, and control of hypertension remain far below target levels for all groups and demonstrate important age- and race-based disparities (Figure 1).[3]

Hypertension frequently co-occurs with other CVD risk factors.[8] 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 (Figure 2).[10] 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.[11] Among individuals without major risk factors, relative CVD event rates increase, starting at SBP levels as low as 90 mm Hg.[12,13] Higher BP is associated with an elevated

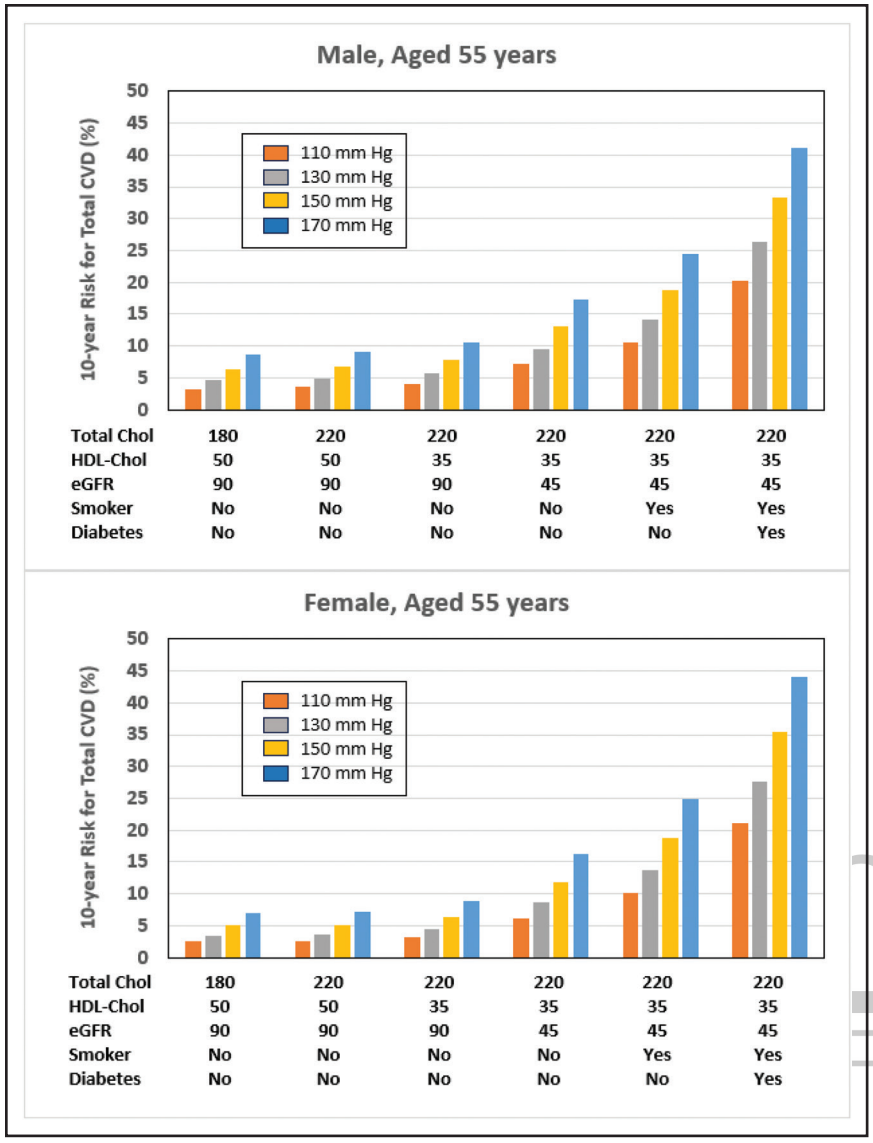


Figure 2. Estimated 10-Year Risks for Total Cardiovascular Disease Using the PREVENT™ CVD Risk Equations, Stratified by Blood Pressure Levels With Selected Combinations of Risk Factors.
CVD indicates cardiovascular disease; eGFR, estimated glomerular filtration rate; and HDL, high-density lipoprotein. Derived from Khan et al[19,20] via PREVENT.

risk for total CVD, coronary heart disease, HF, aortic and peripheral vascular disease, kidney disease, ischemic and hemorrhagic stroke, dementia, and cognitive impairment.[12–16] Relative risks for CVD associated with BP attenuate somewhat, but absolute CVD rates are substantially higher at older compared with younger ages.[11,13] Among middle-aged and older adults, the prevalence and risks associated with higher SBP are greater than those associated with higher DBP.[11,13] 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.[17,18] 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,[17,18] highlighting the importance of primordial prevention of BP elevation.

3.1. 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.

Synopsis

Historically, the measurement of BP in the office setting was performed by using auscultatory BP measurements using a calibrated mercury column, which was later replaced by auscultatory measurements using a nonmercury

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.

Figure 3. Checklist for Accurate Office Blood Pressure Measurement.
BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure. Sourced from Pickering et al.[20] Adapted with permission from Whelton et al.[21] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc. Adapted from Mancia et al[22] by permission of Oxford University Press. Copyright 2013 Oxford University Press. Adapted with permission from Weir et al[23] from Annals of Internal Medicine. Copyright 2014 American College of Physicians. All Rights Reserved. Adapted with permission of American College of Physicians. Created by Sceyence Studios.

device (ie, aneroid). More recently, the use of oscillometric devices has become more common. Oscillometric devices estimate BP by measuring oscillations during cuff inflation or deflation. At the point of maximum cuff oscillations, the BP in the cuff is equivalent to the mean BP in the artery, and SBP and DBP are estimated using proprietary manufacturer algorithms. For this reason, only oscillometric devices that were validated with a rigorous standardized protocol with BP measurement using a reference standard are recommended for use (termed *validated devices*).[4,5] Oscillometric devices can obtain an office BP reading after the device is manually triggered, and typically, the device needs to be triggered repeatedly if multiple measurements are taken. However, some oscillometric devices automatically obtain multiple readings after the device is triggered (ie, automated office blood pressure [AOBP] measurement). In published papers, AOBP is typically measured[6] without a clinician present (ie, unattended AOBP). Regardless of the measurement approach, errors in measurement technique are common if the measurements are taken incorrectly in terms of patient preparation and positioning, environment, and equipment and can result in a misleading estimation of an individual's true in-office BP level.

Recommendation-Specific Supportive Text

1. Accurate measurement of BP is essential to diagnose high BP, ascertain BP-related CVD risk, and assess response to therapy. Many errors in BP measurement, which have been examined in 2 systematic reviews,[2,3] can be avoided by following a standardized protocol that has been a mainstay of clinical trials that include BP measurement.[1] A standardized protocol, provided in Figure 3, includes proper patient preparation, standardized measurement technique and approach, documentation of BP, analysis of the readings, and providing the readings to the patient. The use of a BP device validated against a reference standard with an appropriately sized cuff is paramount for accurate BP measurement (see https://www.validatebp.org for a carefully vetted list of validated devices available in the United States).[5,7–9] Further, because individual BP measurements may vary in an unpredictable or random manner, a single reading is inadequate for clinical decision-making. 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.[10,11] Regardless of the office BP measurement approach, clinicians and staff should have initial and ongoing training,[12] including competency checks ideally every 6 to 12 months to maintain best practices for measuring BP.
2. The use of oscillometric devices has become common in clinical trials, national surveys, and consumer marketplaces[1,13,14] because the use of auscultatory measurements with a calibrated mercury column is

no longer used in clinical practice due to regulatory issues with use of mercury. The use of auscultatory measurements with an aneroid device is a suitable alternative but requires regular device recalibration.[5] Additional potential limitations to the auscultatory method include improper stethoscope placement, inappropriately fast cuff deflation rate, digit preference, and observer hearing deficits.[2,3] As long as a standardized protocol is followed and the oscillometric device has been rigorously validated, the use of an oscillometric device over the auscultatory method is reasonable.[4,5] Oscillometric device validation has been typically done among individuals in sinus rhythm; however, evidence from validation studies of these devices among individuals in AF is limited.[15] Oscillometric devices should be recalibrated on an ongoing basis per the manufacturer's guidance. Mean unattended AOBP is lower than mean office BP obtained with a clinician present and using a standardized protocol.[6] Further, although there is no between-group difference in mean unattended AOBP and mean out-of-office BP,[16,17] there can be large within-person differences between these 2 BP measurements.[6] Among the few available RCTs, there were typically no differences between unattended AOBP versus AOBP measured with a clinician present while using a standardized protocol.[6,18,19]

3.1.2. Patient Evaluation, Including Laboratory Tests and Other Diagnostic Procedures

Recommendation for Laboratory Tests and Other Diagnostic Procedures		
COR	**LOE**	**Recommendation**
1	**C-EO**	1. For adults who are diagnosed with hypertension, laboratory tests (ie, complete blood count, serum electrolytes, serum creatinine, lipid profile, glucose or hemoglobin A1c [HbA1c], thyroid-stimulating hormone, urinalysis, and urine albumin-to-creatinine ratio) and diagnostic procedures (12-lead ECG) should be performed to optimize management.

Synopsis

When a new diagnosis of hypertension is suspected or confirmed, a comprehensive medical history, physical examination, laboratory tests, and other diagnostic procedures should be performed as part of the standard evaluation of a patient. The primary goal of this evaluation is to inform the need for and optimal choice of GDMT for BP lowering. Further, this evaluation is useful for the identification of contributing causes of elevated BP, including secondary causes (Section 3.2.3, "Secondary Forms of Hypertension"), estimation of predicted cardiovascular risk, and evaluation for the presence and extent of target organ damage (eg, impaired kidney function, albuminuria).[1] Basic laboratory testing should be repeated in patients with hypertension at least annually, or sooner if clinical evidence of glucose intolerance, electrolyte imbalances, or uric acid changes is noted. Baseline testing is needed for monitoring of serum electrolytes and serial assessments of kidney function and CVD risk. In addition to the standard diagnostic assessment, optional testing for cardiac biomarkers (eg, high-sensitivity troponin [hs-cTn], B-type natriuretic peptide [BNP]/[NT-proBNP]), echocardiography, and coronary artery calcium may be helpful for CVD risk stratification and for detection of target organ damage in individuals with hypertension. Additional diagnostic evaluation should be considered when secondary causes of hypertension are suspected (Section 3.2.3, "Secondary Forms of Hypertension").

Table 6. 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

Modified with permission from Whelton et al.[4] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.
ECG indicates electrocardiogram.

Recommendation-Specific Supportive Text

1. In adults with a new diagnosis of hypertension, a comprehensive medical history, physical examination, and routine laboratory testing (Table 6) are useful to establish baseline CVD risk and inform management decisions, including the need for additional testing. Pertinent laboratory tests 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.[2,3]

3.1.3. Out-of-Office BP Monitoring

Synopsis

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. Both ABPM and HBPM provide BP estimates that are based on a greater number of BP measurements than are obtained in the office setting, enhancing the accuracy and precision for detecting a patient's true and usual BP levels. 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). 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"; 3) identify the early-morning BP surge pattern; 4) estimate BP variability; and 5) allow for recognition of hypotension. HBPM involves the patient measuring their BP at home using an oscillometric device over days to weeks, which can provide estimates of mean BP over the entire monitoring period and separately during daytime and evening, and determine daytime-to-evening BP variability or BP variability across days.

3.1.4. ABPM and HBPM

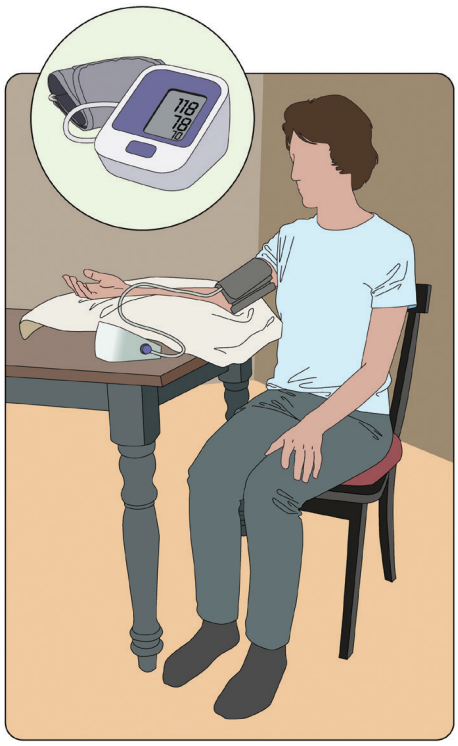
Recommendations for ABPM and HBPM Referenced studies that support the recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	A	1. In adults with suspected hypertension, out-of-office BP measurements by either ABPM or HBPM are recommended to confirm the diagnosis of 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]

Synopsis

High-quality out-of-office BP measurements can be obtained using either ABPM or HBPM. ABPM has been the de facto reference standard for out-of-office BP monitoring as there are more data linking ABPM to CVD events compared with HBPM.[1,2] However, there are scarce data on whether ABPM or HBPM is superior for CVD risk prediction.[7,8] Additional data support the use of HBPM for longitudinal titration of antihypertensive medications. Among adults taking antihypertensive medication, compared with usual care, HBPM use improves office BP control when used in conjunction with other interventions to lower BP.[2,3,6,9] Further, HBPM is often a more practical approach in clinical practice than ABPM and may be more reproducible and accessible, supporting its use for longitudinal management and titration of BP-lowering medication.[10,11] Recommended procedures for the collection of HBPM data are provided in Figure 4. It is important to ensure that the out-of-office BP measurement device has been validated with a rigorous, standardized protocol and the appropriate size cuff is used.[12] A guide to the relationship between HBPM and ABPM readings and corresponding readings obtained in the office is presented in Table 7. These thresholds are provided as a guide but should be interpreted with caution because the data are primarily from European, Australian, and Asian populations, with few data available for establishing appropriate thresholds for US populations.[13,14] Further, the data are derived primarily from observational studies.[15]

Recommendation-Specific Supportive Text

1. Out-of-office BP monitoring with either ABPM or HBPM provides valuable and distinct information compared with office BP for confirming the diagnosis of hypertension. Systematic reviews conducted for the US Preventive Services Task Force reported that ABPM more strongly predicts long-term CVD outcomes than office BP.[1,2] Evidence suggests that HBPM more strongly predicts CVD outcomes than office BP[2,8,16] and may be more reproducible than ABPM.[11] Although ABPM provides distinctive information on nighttime BP, HBPM is often more practical than ABPM in clinical practice.[12] See Section 3.2 ("Patient Diagnosis") for additional details of diagnostic classification. ABPM thresholds corresponding to office BP levels are provided in Table 7.
2. High-quality evidence supports the use of HBPM in combination with cointerventions, such as patient education, telehealth (Section 5.4, "Plan of Care for Hypertension"), and medication titration using prespecified algorithms, for the longitudinal management of BP. Meta-analyses of RCTs have identified modest reductions in office SBP and DBP at 6 months and 1 year with the use of HBPM on its own without cointerventions, as compared with usual care.[2,3,6,9] More clinically meaningful reductions in office SBP and DBP and improved BP control at 6 months and 1 year were noted when HBPM was used in conjunction with cointerventions, compared with usual care. These studies indicate the importance of combining HBPM with cointerventions to make meaningful improvements in office BP control rates. HBPM thresholds corresponding to office BP levels are provided in Table 7. More recent RCTs showed no BP-lowering benefit of HBPM when enhanced only by using a smartphone application (eg, providing reminders to measure BP and with the ability to store and transmit BP) versus HBPM alone in adults with uncontrolled BP.[5] These studies reinforce the importance of combining HBPM with interventions to make meaningful advances in BP control rates. Additional studies are required to determine the optimal approach to implement health



Home Blood Pressure Monitoring

Device and blood pressure cuff

Use a blood pressure device that has been validated for accuracy. Check with your clinician or other members of your care team, and the following website for devices: www.validatebp.org.

Use the correct cuff size matched to the size of your arm.

Patient preparation

Avoid smoking, caffeinated beverages, or exercise within 30 minutes before blood pressure measurements.

Positioning of patient and cuff

Place the cuff on a bare arm, and your arm should be supported at heart level.

The bottom of the cuff should be placed directly above the bend of the elbow.

You should relax, and sit in a chair (feet on floor, legs uncrossed, and back supported) for at least 5 minutes.

Blood pressure measurement

While relaxing and measuring your blood pressure, please do not talk, use your phone, or watch TV.
You should take 2 readings 1 min apart twice a day (for a total of 4 readings):
2 readings in the morning after emptying your bladder (urinating) and before taking your medication and eating; and 2 readings at bedtime before sleep.

Check blood pressure for 3 days (minimum) to 7 days (preferred) before your appointment or interaction with your clinician.

Document your daily blood pressure measurements in writing or electronically.

Share your readings with the clinician taking care of you.

Figure 4. Home Blood Pressure Monitoring.[18]
See Table 7 for HBPM targets. BP indicates blood pressure; and HBPM, home blood pressure monitoring. Adapted with permission from Whelton et al.[19] Copyright 2019 American College of Cardiology Foundation and American Heart Association, Inc. Created by Sceyence Studios.

technology with HBPM and the best HBPM cointervention among pregnant individuals with chronic or gestational hypertension.[17]

3.1.4.1. Cuffless BP Devices

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]

Synopsis

Traditionally, BP measurement includes an upper arm cuff-based device for clinical, home, and 24-hour ABPM measurement. The use of cuffless devices to measure BP in clinical and ambulatory settings offers the potential for continuous, simple, and unobtrusive BP measurements to aid in the evaluation and management of high BP. 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).[4] Many of these approaches require user calibration with periodic cuff BP measurement or by demographic data input. Studies comparing cuffless BP measurement to oscillometric or auscultatory cuff-based methods have revealed mixed results in regard to acceptable agreement.[3,4] Limitations of current models include substantial variation in sensor technologies and validation approaches used for cuffless devices, comparator measures, measurement conditions, and the populations studied.[1,3,4]

Recommendation-Specific Supportive Text

1. The use of BP measurement devices to evaluate and manage BP in adults in clinical practice requires assessment based on internationally accepted validation

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

Modified with permission from Whelton et al.[19] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; HBPM, home blood pressure monitoring; and SBP, systolic blood pressure.

Table 8. 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

protocols. Currently, few protocols exist for validating cuffless BP devices. The Institute of Electrical and Electronics Engineers validation standards recommend using a cutoff of <7 mm Hg for the mean absolute difference between test and reference devices.[4] A systematic review and meta-analysis from 2022 evaluated validation protocols of 15 cuffless devices; 12 of the 16 studies included in the analysis reported mean absolute difference data.[1] Results revealed no statistically significant differences between the wearable cuffless and reference devices, with a pooled mean difference of 3.42 mm Hg SBP (95% CI: −2.17 to 9.01 mm Hg) and 1.16 mm Hg DBP (95% CI: −1.26 to 3.58 mm Hg).[1] Although these data are promising, the use of cuffless devices risks the underestimation or overestimation of BP due to the marked heterogeneity in the devices being tested. These limitations must be overcome before cuffless devices can be recommended for clinical use. In 2022, the International Organization for Standardization published a validation protocol (ISO 81060-3: 2022) for "continuous noninvasive sphygmomanometers" that could be used for cuffless BP devices that continuously measure BP but may not be appropriate for outpatient use.[5,6] In 2023, the European Society of Hypertension Working Group on BP Monitoring and Cardiovascular Variability recommended procedures for validating intermittent cuffless BP devices.[5] Scarce data exist on using these protocols to test cuffless BP devices.

3.2. Patient Diagnosis

3.2.1. Causes of Hypertension

Synopsis

Elevated BP and hypertension reflect a complex interplay of behavioral, environmental, hormonal, and genetic influences across the lifespan (Table 8). Diet quality is significantly associated with elevated BP and its sequelae.[1–3] 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.[4–6] Weight gain,[7] 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.[8,9] Factors such as increasing age, obesity, and insulin resistance influence how BP is affected by sodium, emphasizing the importance of lower sodium intake.[5] Sleep disturbances (Section 3.2.3.3, "Obstructive Sleep Apnea") and psychosocial stressors can exacerbate,[10–12] and increases in BP can be ameliorated by a higher level of physical activity and fitness (Section 5.1, "Lifestyle and Psychosocial Approaches").[13] Emerging data also implicate environmental exposures and chemical toxins (including air pollution and heavy metals) in the increases in BP.[14,15]

BP is a highly heritable trait,[16] and hundreds of independent genetic loci capable of affecting BP have been described to date.[17,18] Each variant has small effects on BP alone, but collectively they may explain larger interindividual differences in BP.[17,18] Nonetheless, all genetic loci described to date explain <10% of BP variance,[18] indicating the importance of other factors and gene-environment interactions.

3.2.2. White-Coat Hypertension and Masked Hypertension, and White-Coat Effect and Masked Uncontrolled Hypertension

Recommendations for White-Coat Hypertension and Masked Hypertension, and White-Coat Effect and Masked Uncontrolled Hypertension
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
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]
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]
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]

Table 9. BP Categories Based on Office and Out-of-Office BP Measurements

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 Whelton et al.[40] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

BP indicates blood pressure.

Synopsis

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 (Table 9).[16,17] ABPM has been the reference standard for out-of-office BP monitoring, as there are more studies that have examined the association between ABPM and CVD outcomes than studies that have examined the association between HBPM and CVD outcomes.[18,19] However, there are scarce data demonstrating that ABPM is superior to HBPM or vice versa for CVD risk prediction.[20,21] ABPM is preferred for excluding white-coat hypertension and masked hypertension among individuals not taking antihypertensive medication. However, 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. In RCTs demonstrating a reduction in CVD events with the lowering of BP with antihypertensive medication, office BP has been used as a target for titration instead of out-of-office BP.[22] There are scarce data on the cardiovascular risks of not treating white-coat hypertension and not intensifying treatment for white-coat effect and the benefits of treating masked hypertension and intensifying treatment for masked uncontrolled hypertension.

Recommendation-Specific Supportive Text

1. 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.[1–5] The risk of CVD associated with white-coat hypertension may only be increased among older adults who have high baseline CVD risk.[1,23] Nonetheless, the risk of CVD is higher in sustained hypertension than in white-coat hypertension among adults with high office BP.[24] Therefore, 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 (Section 5.2, "Medical Management"). The prevalence of white-coat hypertension is low among those with office BP levels in this range.[25,26]
2. 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.[6–8] An additional study[27] demonstrated that compared with individuals with sustained normotension, a higher proportion of individuals with white-coat hypertension had high out-of-office BP during follow-up. Therefore, 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. The frequency of follow-up monitoring is unclear as only a single visit was conducted at follow-up in these studies (ie, approximately 7 to 11 years after the baseline visit).[6–8,27]
3. Studies have consistently demonstrated that compared with controlled hypertension, white-coat effect is not associated with an increased risk of CVD events and mortality.[9,11] 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.[10,12] Out-of-office BP monitoring is a central component of the initial work-up of apparent resistant hypertension (Section 5.6, "Resistant Hypertension and Renal Denervation"). Therefore, it is reasonable to exclude a white-coat effect using out-of-office BP monitoring for individuals with apparent resistant hypertension.
4. 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.[1,4,13] 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 (Section 5.2, "Medical Management").

5. 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.[5,13–15] Studies have examined whether using specific office BP ranges (ie, those approaching the high office BP threshold) or prediction models incorporating demographic and clinical factors for targeting individuals with out-of-office BP monitoring would be a better approach than screening all individuals who do not have high office BP.[28–32] Clinicians may consider using these targeted screening approaches, particularly among those patients with unexplained BP-related target organ damage. However, it remains unclear which diagnostic approach is the best for excluding masked hypertension among individuals without high office BP and what false-positive and -negative rates are acceptable for population screening. Further, these targeted screening approaches should also be examined among populations with a high prevalence of masked hypertension, such as Black populations.[33] Therefore, 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. Recent evidence suggests that compared with placebo, antihypertensive medication may improve target organ damage among adults with masked hypertension.[34] However, the effect on cardiovascular outcomes remains unknown.
6. Systematic reviews and meta-analyses have demonstrated that compared with controlled hypertension, masked uncontrolled hypertension is associated with an increased risk of CVD events and mortality.[13–15] 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.[35] Although the effect of antihypertensive medication intensification on the risk of CVD events among individuals with masked uncontrolled hypertension remains unknown, it may be reasonable to exclude masked uncontrolled hypertension using out-of-office BP monitoring for CVD risk stratification.

3.2.3. Secondary Forms of Hypertension

Recommendations for Secondary Forms of Hypertension
References that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	C-EO	1. In adults with hypertension, screening for specific forms of secondary hypertension is recommended when clinical suspicion is present (Table 10, Figure 5) to increase rates of detection, diagnosis, and specific targeted therapy.
1	B-NR	2. 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.[1,2]
2a	C-EO	3. In adults who have a positive screening test for a form of secondary hypertension, referral to a clinician who has expertise in that form of hypertension is reasonable for diagnostic confirmation and treatment.

American Heart Association.

Synopsis

Secondary causes of hypertension can be identified in approximately 5% to 25% of adult patients with hypertension.[1–3] 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 (Figure 4) with a history and physical examination and laboratory tests, as recommended in Section 3.1.2 ("Patient Evaluation, Including Laboratory Tests and Other Diagnostic Procedures").

Recommendation-Specific Supportive Text

1. Secondary hypertension is 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. Common forms of secondary hypertension include primary aldosteronism and obstructive sleep apnea (OSA).[4–9] 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.[10] Numerous substances, including prescription medications, over-the-counter medications, herbals, and food substances, may affect BP (Table 11).[11,12] Changes in BP

Table 10. Causes of Secondary Hypertension With Indications for Additional Testing and Diagnostic Screening Tests

	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
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
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

(*Continued*)

Table 10. Continued

	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

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ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure; AF, atrial fibrillation; CKD, chronic kidney disease; CT, computed tomography; DOC, 11-deoxycorticosterone; h, hour; IGF-1, insulin-like growth factor-1; IV, intravenous; MAO, monoamine oxidase; mg, milligrams; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; OH, hydroxylase; OSA, obstructive sleep apnea; RCT, randomized clinical trial; VEGF, vascular endothelial growth factor; wk, week; and y, years.

that occur because of drugs and other agents have been associated with the development of hypertension and with worsening BP control in a patient who already has hypertension. 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.[13] When feasible, drugs associated with increased BP should be reduced or discontinued and alternative agents used.

2. Spontaneous hypokalemia is present only in 20% to 50% of patients with primary aldosteronism,[1,2] and therefore, the decision to perform primary aldosteronism screening should not rely on a history of hypokalemia alone. Screening for primary hyperaldosteronism may require sodium loading to induce aldosterone suppression if plasma screening by the aldosterone-to-renin ratio is inconclusive (Section 3.2.3.1, "Primary Aldosteronism").[3]
3. Diagnosis of many secondary causes of hypertension requires a complex set of tests and measurements combined with specialized technical expertise in data interpretation. Similarly, specific treatment often requires additional training and experience. Clinical expertise in secondary forms of hypertension, such as primary aldosteronism, pheochromocytoma, Cushing syndrome, and renovascular hypertension, is practical for prognosis and treatment plans.

3.2.3.1. 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 (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 (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.

Synopsis

Primary aldosteronism is defined as a group of disorders in which aldosterone production is inappropriately high

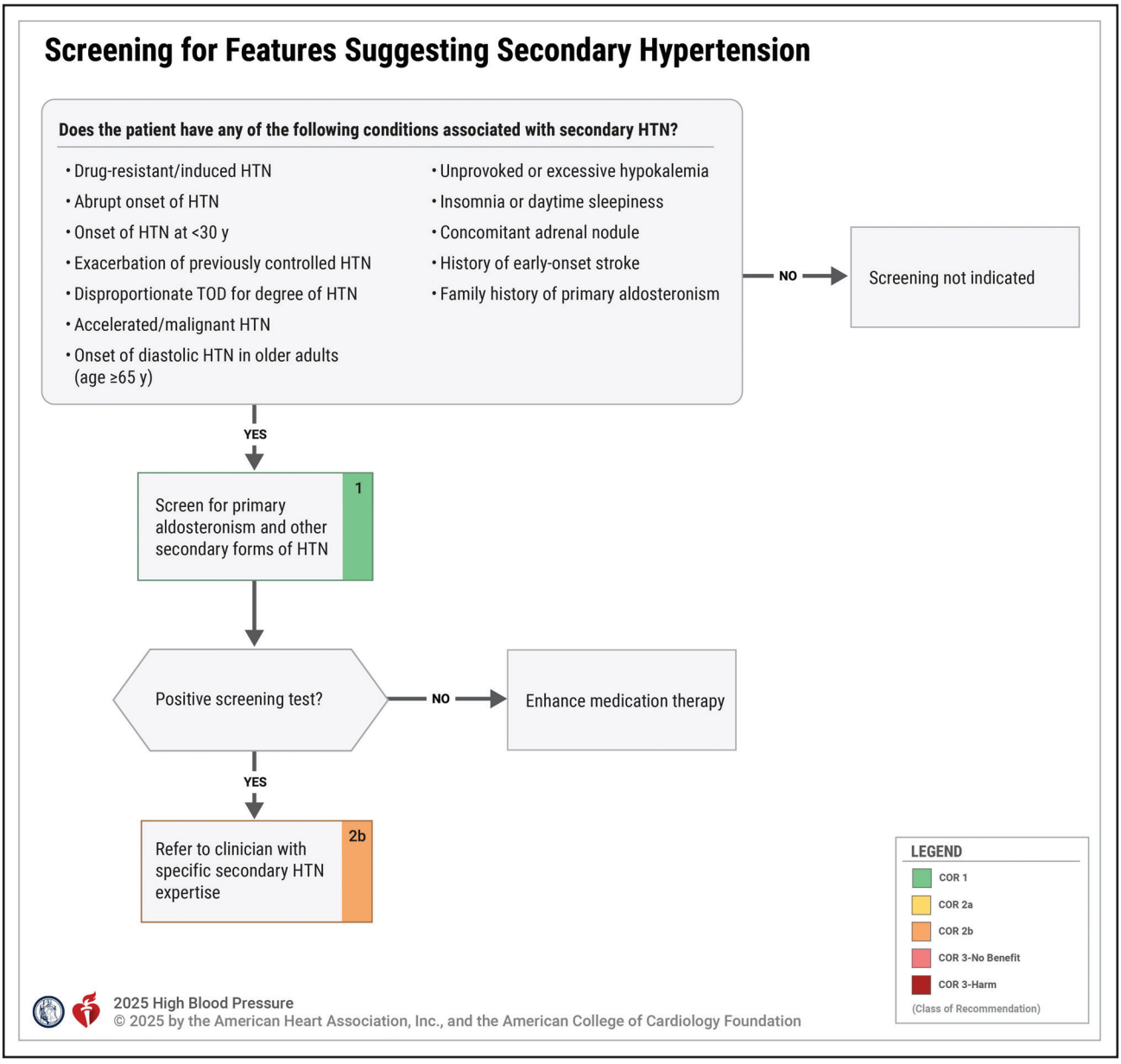

Figure 5. Screening for Features Suggesting Secondary Hypertension.
Refer to Table 10 for additional tests for secondary hypertension. HTN indicates hypertension; and TOD, target organ damage (eg, cerebrovascular disease, hypertensive retinopathy, left ventricular hypertrophy, left ventricular dysfunction, heart failure, coronary artery disease, chronic kidney disease, albuminuria, peripheral artery disease). Modified with permission from Whelton et al.[14] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

Table 11. Selected List of Frequently Used Medications and Other Substances That May Cause Elevated Blood Pressure With Recommendations for Management*

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
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

*List is not all inclusive.

†In specific cases when a specific therapy is needed or the best option for the patient, it is reasonable to continue the medication and initiate or intensify antihypertensive therapy. Modified with permission from Whelton et al.[14] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

ADHD indicates attention-deficit/hyperactivity disorder; BP, blood pressure; CVD, cardiovascular disease; IUD, intrauterine device; MAOI, monoamine-oxidase inhibitors; MDPV, methylenedioxy pyrovalerone; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRI, serotonin norepinephrine-reuptake inhibitor; SSRI, selective serotonin-reuptake inhibitor; and TCA, tricyclic antidepressant.

for sodium and volume status, is relatively autonomous of the major regulators of aldosterone secretion (angiotensin II and potassium), and cannot be completely suppressed with sodium loading.[4,5] The increased production of aldosterone induces intravascular volume expansion, suppressed plasma renin activity, sodium retention, increased potassium excretion, hypertension, and cardiovascular and kidney damage.[4–7] Although the increased potassium excretion, if prolonged and severe, may cause hypokalemia, hypokalemia is absent in the majority of cases in whom normokalemia has a low negative predictive value for the diagnosis of primary aldosteronism.[8,9] In two-thirds of patients with primary aldosteronism, excess aldosterone is caused by bilateral adrenal hyperplasia. In about one-third of patients with primary aldosteronism, excess aldosterone is due to increased unilateral aldosterone production (aldosterone-producing adenoma, less commonly unilateral adrenal hyperplasia, or, rarely, adrenal carcinoma).[4,10] 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.[3,11–13] Nonetheless, rates of screening for primary aldosteronism in appropriate patients are exceptionally low (1% to 2%).[14–17]

Recommendation-Specific Supportive Text

1. Patients with primary aldosteronism are at greater risk for target organ damage than those with primary hypertension due to the toxic tissue effects of aldosterone even when adjusted for degree of hypertension. Meta-analyses of studies that matched patients with primary aldosteronism to those with primary hypertension showed that primary aldosteronism carries a 2.0-fold increased risk of HF, 2.8-fold increased risk of stroke, 1.7-fold increased risk of coronary artery disease, 4.0-fold increased risk of AF, and increased kidney damage compared with primary hypertension.[6,7] Because the deleterious effects of aldosterone overproduction may be blocked with unilateral laparoscopic adrenalectomy or treatment with MRA (eg, spironolactone or eplerenone), patients with hypertension at increased risk of primary aldosteronism are very likely to benefit from screening.[4] These include patients with hypertension and adrenal "incidentaloma," an incidentally discovered adrenal lesion on computed tomography or magnetic resonance imaging performed for other purposes. Additionally, patients with resistant hypertension (regardless of whether hypokalemia is present), hypertension with hypokalemia (either spontaneous or diuretic-induced), and hypertension with OSA have a relatively high prevalence of primary aldosteronism (~20%-35%).[3,4] Patients with hypertension and a history of early-onset hypertension and/or cerebrovascular accident at a young age may have primary aldosteronism due to glucocorticoid-remediable aldosteronism (familial hyperaldosteronism type-1) and therefore also warrant screening.[4] However, the rate of screening for primary aldosteronism in guideline-recommended individuals is <2% in the United States.[14,16,17]
2. Growing evidence supports that primary aldosteronism occurs across the full breadth of hypertension severity, with higher prevalence of primary aldosteronism as the severity of hypertension increases.[3,10] The prevalence of primary aldosteronism is approximately 5% to 10% among individuals with stage 1 hypertension and 11% to 22% among individuals with stage 2 hypertension, which varies depending on the modality of testing and testing thresholds used to diagnose primary aldosteronism.[3,10] The prevalence of primary aldosteronism may be similar among individuals with stage 2 hypertension and those with resistant hypertension.[3] Studies from Australia and Japan suggest that broader screening for primary aldosteronism in individuals with hypertension is cost-effective.[18,19] Nonetheless, the potential burden of additional testing outside of patients with resistant hypertension to confirm the diagnosis of primary aldosteronism and to determine optimal therapy may be taken into consideration prior to screening.
3. The combined interpretation of the plasma aldosterone concentration, renin activity, and aldosterone to renin activity ratio is currently the most accurate and reliable means of screening for primary aldosteronism.[2,3,20] Patients with primary aldosteronism typically have suppressed renin activity (<1 ng/mL/h). Most data support that the plasma aldosterone concentration should be at least 10 ng/dL to interpret the test as positive, but additional evaluation may be indicated if the renin activity is suppressed.[3,4] The most commonly used cutoff value for the aldosterone to renin activity ratio is 30 when plasma aldosterone concentration is reported in nanograms per deciliter (ng/dL) and plasma renin activity in nanograms per milliliter per hour (ng/mL/h), although some data support alternative thresholds (20 or 40).[2–4,20] Patients should have unrestricted salt intake, serum potassium in the normal range (to avoid false-negative testing), and ideally, MRA (eg, spironolactone or eplerenone) withdrawn for at least 4 weeks before testing.[4]
4. Low screening rates may be due to several barriers to screening, such as older guidance to withdraw antihypertensive medications that may affect renin and aldosterone levels, which has since been disputed by growing evidence in support of screening despite treatment with these medications. Specifically, beta blockers (BBs) and central-alpha agonists can suppress both renin and aldosterone[4];

angiotensin-converting enzyme inhibitors (ACEis) and angiotensin receptor blockers (ARBs) may stimulate renin and suppress aldosterone[4]; thiazide-type, loop diuretics, MRA, and potassium-sparing diuretics can stimulate both renin and aldosterone.[4] Throughout this guideline, we use the term thiazide-type diuretic to collectively refer to hydrochlorothiazide (HCTZ), chlorthalidone, and indapamide. Although the literature traditionally differentiates these medications based on their chemical structures, categorizing HCTZ as a thiazide-type diuretic because it possesses a benzothiadiazine ring and categorizing chlorthalidone and indapamide as thiazide-like diuretics because they lack this ring (yet remain closely related sulfonamide derivatives), the interchangeability of thiazide-type and -like agents remains a debated topic. For simplicity and to minimize confusion, in this guideline we have chosen to group them under a single term. In most settings, it is acceptable for clinicians to choose among these agents for treatment. We recognize that 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 (Section 5.6, "Resistant Hypertension"). Initial screening for primary aldosteronism can typically be interpreted in the context of most medications that affect renin and aldosterone. If screening results are negative or borderline in patients in whom there is a high level of suspicion for primary aldosteronism and confirmation of the diagnosis will change management, potentially interfering medications may be temporarily substituted with noninterfering medications (ie, nondihydropyridine calcium channel blockers [CCBs], vasodilators, peripheral alpha-blockers, and potentially dihydropyridine CCB[21]) for at least 2 to 4 weeks prior to repeat testing.

5. The diagnosis of primary aldosteronism may require an aldosterone suppression test such as an intravenous (IV) saline suppression test or oral salt-loading test.[4] If the diagnosis of primary aldosteronism is confirmed and the patient agrees that surgery would be desirable, the patient is referred for an adrenal venous sampling procedure to determine whether the increased aldosterone production is unilateral or bilateral in origin. If unilateral excess aldosterone production is documented on adrenal venous sampling, the patient is referred for unilateral laparoscopic adrenalectomy.[4,22] If the patient has bilaterally increased aldosterone secretion on adrenal venous sampling, is not a surgical candidate, or is not interested in pursuing surgery, the patient is treated with an MRA (eg, spironolactone or eplerenone).[4] If primary aldosteronism is confirmed, imaging of the adrenal glands should be considered, even if treatment will be with medication, to exclude a large adrenal mass that may require adrenalectomy if features suggestive of malignancy are present (size >4 cm, imaging characteristics).[23] Treating primary aldosteronism, either with an MRA or unilateral adrenalectomy, if indicated, is associated with resolution of hypokalemia, lower BP, fewer number of antihypertensive medications required, and improved parameters of impaired cardiac and kidney function.[4,12,13] Meta-analysis of observational data suggests that adrenalectomy may be associated with lower risk of MACE and all-cause mortality compared with medical therapy.[22]

3.2.3.2. 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]

Synopsis

Renal artery stenosis refers to a narrowing of the renal artery that can result in a hemodynamically significant restriction of blood flow, usually by >75%. Atherosclerotic disease (90%) is the most common cause of renal artery stenosis, whereas nonatherosclerotic disease, of which fibromuscular dysplasia is the most common, is much less prevalent and tends to occur in younger, otherwise healthier patients with a predilection for women.[5] Atherosclerotic renovascular disease may be present in 14% to 40% of adults with hypertension; however, only a small fraction (0.1%-5%) is considered to be hemodynamically significant to result in renovascular hypertension.[6] With the advent of endovascular procedures to restore blood flow, the risk for postprocedure morbidity and mortality risk dropped substantially from previous surgical reconstruction rates. Several trials designed to compare the efficacy of these procedures with medical therapy suggested no benefit over aggressive medical therapy alone among adults with atherosclerotic renal artery stenosis.[1–3] Nonetheless, there may be benefit in certain subgroups of individuals with atherosclerotic renal artery stenosis who were not represented in the trials, including those with progressively worsening kidney function or sudden onset of pulmonary edema.[3] The absence of severe albuminuria is associated with better outcomes after endovascular renal artery stenosis interventions.[7,8] In contrast, renal artery angioplasty

may cure hypertension in some adults with nonatherosclerotic renal artery stenosis.[4,6]

Recommendation-Specific Supportive Text

1. Atherosclerotic disease in the renal arteries represents systemic disease and indicates higher risk for both kidney failure and cardiovascular morbidity and mortality. No RCT to date has demonstrated a clear clinical advantage of renal artery revascularization (with either angioplasty or stenting) over medical therapy among individuals with hypertension.[1–3] By meta-analysis, renal angioplasty with stenting results in a small reduction in DBP and antihypertensive medication requirement.[2] On the basis of the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trial, the recommended medical approach encompasses optimal management of hypertension with an antihypertensive regimen that includes a renin-angiotensin system (RAS) blocker, in addition to reduction of low-density lipoprotein cholesterol with a high-intensity statin, smoking cessation, HgbA1c reduction in patients with diabetes, and antiplatelet therapy.[9]
2. Revascularization can be favorable for select individuals with uncontrolled hypertension accompanied by progressively worsening kidney function and/or acute HF who were not represented in RCTs.[1–3]
3. Revascularization may be considered for those with nonatherosclerotic renal artery disease (eg, fibromuscular dysplasia, Takayasu arteritis in select cases) and hypertension and may be curative.[6] Fibromuscular dysplasia is most common in women (90%) and may present at a younger age (mean age 53 years) with almost equal frequency in the renal and carotid circulations.[5] Percutaneous transluminal angioplasty alone without stenting can improve BP control and even normalize BP, especially in patients with recent onset of hypertension or resistant hypertension.[4,6]

3.2.3.3. Obstructive Sleep Apnea

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]

Synopsis

OSA is a chronic condition characterized by recurring upper airway obstruction during sleep, resulting in hypoxia and disrupted sleep.[4] Diagnostic criteria and screening methods for OSA can be found in Table 10 and Section 3.2.3 (“Secondary Forms of Hypertension”). Moderate-to-severe OSA is associated with an increased risk of hypertension, CVD events, and mortality.[5,6] Antihypertensive medications can treat hypertension in adults with OSA.[7] Weight loss in conjunction with CPAP therapy can reduce BP levels in adults with OSA who are overweight or obese.[1] Additionally, some studies have shown that CPAP can reduce BP levels in adults with OSA and resistant hypertension.[2,3] Although CPAP is an effective therapy for OSA,[8] data do not support the use of CPAP for the prevention of CVD events or mortality in adults with moderate-to-severe OSA.[9] The role of sleep surgery, including newer device therapy such as hypoglossal nerve stimulation, has been investigated in the treatment of OSA, but the benefit for BP has not been observed in large RCTs to date.[10,11]

Recommendation-Specific Supportive Text

1. Lifestyle interventions are recommended for all individuals with high BP (Section 5.1, “Lifestyle and Psychosocial Approaches”), including adults with OSA and hypertension. Obesity is a risk factor for OSA.[1] A meta-analysis examining the impact of weight loss interventions on BP in adults with OSA demonstrated small effects on SBP (−1.86 mm Hg; 95% CI: −3.57 to −0.15 mm Hg) and DBP (−2.07 mm Hg; 95% CI: −3.79 to −0.35 mm Hg).[1,2] However, weight loss interventions when combined with CPAP therapy have been shown to lower SBP by 8 mm Hg in adults with moderate-to-severe OSA.[1] Recent data from SURMOUNT OSA (Tirzepatide for the Treatment of OSA)[13] demonstrated that tirzepatide versus placebo was associated with a reduction in BP at 48 weeks, a prespecified key secondary endpoint, among adults with moderate-to-severe OSA and obesity. For adults not on CPAP therapy, the estimated treatment difference for SBP was −7.6 mm Hg (95% CI: −10.5 to −4.8 mm Hg) and for DBP was −2.8 mm Hg (95% CI: −5.0 to −0.6 mm Hg), whereas for adults on CPAP therapy the estimated treatment difference for SBP was −3.7 mm Hg (95% CI: −6.8 to −0.7 mm Hg) and for DBP was −1.1 mm Hg (95% CI: −3.2 to 1.0 mm Hg).
2. OSA is a secondary cause of hypertension (Section 3.2.3, “Secondary Forms of Hypertension”) and is associated with nocturnal hypertension and resistant hypertension.[14,15] Several RCTs have demonstrated that short-term treatment with CPAP can reduce high office BP and ambulatory BP by 2 to 5 mm Hg,[3] including among individuals with resistant hypertension.[2] However, these BP outcomes vary based on factors such as patient adherence to CPAP therapy, OSA severity, and presence of daytime sleepiness among study participants. Data

from the HIPARCO-2 (Long-Term Effect of CPAP on BP in Patients With Resistant Hypertension) study demonstrate that participants with OSA and resistant hypertension adherent to CPAP therapy (≥4 hours/night) compared with nonadherent CPAP participants had statistically significant decreases in mean 24-hour ABPM, including nighttime SBP and DBP (−5.5 and −4.9 mm Hg, respectively) over a 59-month follow-up period.[16]

4. PREVENTION STRATEGIES

Synopsis

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 in Section 5.1 ("Lifestyle and Psychosocial Approaches") are useful in primordial prevention of hypertension and should be encouraged.[1] These include weight loss for those with overweight or obesity; a heart-healthy diet such as the DASH (Dietary Approaches to Stop Hypertension) 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 a dose-response manner, including in individuals without hypertension.[2]

5. BP MANAGEMENT

5.1. Lifestyle and Psychosocial Approaches

Recommendations for Lifestyle and Psychosocial Approaches Referenced studies that support the recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
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]
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]
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]
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]

*Dietary sodium reduction may be contraindicated in patients with severe, symptomatic orthostatic hypotension.

†This recommendation refers to potassium-based salt substitutes, which typically contain 25% to 30% potassium chloride, 65% to 75% sodium chloride, and 0% to 10% flavoring agents. Products that refer to themselves as "salt substitutes" that do not contain potassium chloride as a substitute for sodium chloride have unknown effects on BP.

‡Drugs that reduce potassium excretion include: potassium-sparing diuretics (eg, amiloride, triamterene), mineralocorticoid receptor antagonists (eg, spironolactone, eplerenone, finerenone), angiotensin-converting enzyme inhibitors (eg, captopril, enalapril, lisinopril, benazepril, and others), angiotensin receptor blockers (eg, losartan, valsartan, candesartan, telmisartan, and others), and some immunosuppressive agents (eg, cyclosporine, tacrolimus).

§Moderate potassium supplementation is <80 mmol/d (<80 mEq/d).

‖One standard drink (12 to 14 g alcohol) is equivalent to 12 oz of beer (5% alcohol by volume), 5 oz of wine (12% alcohol by volume), or 1.5 oz of distilled spirits (40% alcohol by volume).

Synopsis

BP tends to increase with age from young adulthood, with lifetime risks for incident hypertension exceeding

Table 12. 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
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

*Because inclusion/exclusion criteria and comparator groups vary across interventions, these values should not be compared directly to indicate comparative effectiveness. Modified with permission from Whelton et al.[123] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

BMI indicates body mass index; DASH, Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

80% in US populations.[43,44] Weight gain with age and adverse lifestyles (as defined by Life's Essential 8[45]), rather than aging per se, are potent drivers of BP increases over time.[46,47] Lifestyle modification approaches (Table 12) are critically important strategies to slow the increase in BP and delay or prevent the onset of hypertension. Once patients have been diagnosed with hypertension, specific lifestyle and nonpharmacological strategies can lower BP, slow progression of BP elevation, reduce the amount of medication needed to control BP, and prevent CVD events and mortality.[19–21,48,49] A Bayesian network meta-analysis assessed the comparative effectiveness of 22 lifestyle and stress-reduction strategies for BP lowering.[14] The DASH eating plan ranked as the most effective intervention for BP lowering, followed in order by aerobic exercise, isometric resistance training, low-sodium/high-potassium salt interventions, and comprehensive lifestyle interventions.[14] Meditation and breathing control appeared to be the most effective stress-reduction strategies that

had at least moderate-quality evidence but were judged to be less effective than lifestyle interventions.[14] It is important to note that BP response to any given intervention will vary across subgroups and individuals and is a function of the fidelity and intensity of the intervention, patient adherence, and in some cases, the starting BP level.

Recommendation-Specific Supportive Text

1. In adults who have overweight or obesity (defined as body mass index [BMI] 25.0-29.9 and ≥30 kg/m^2 for non-Asian populations and BMI 23.0-27.4 and ≥27.5 kg/m^2 for individuals of Asian heritage[50]), 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.[51,52] It is somewhat difficult to tease out the effects of weight loss per se on BP lowering from the means by which weight loss is achieved (ie, dietary changes and exercise, which have their own direct effects). Nonetheless, evidence consistently demonstrates BP reduction with weight loss regardless of the mechanism (lifestyle, cognitive behavioral therapy, medication, surgery).[7,9,10,53–55] In general, there is a reduction in BP of approximately 1/1 mm Hg (systolic/diastolic) for each 1 kg (2.2 lbs) of weight loss.[2] Weight reduction ≥5% of body weight or ≥3 kg/m^2 of BMI, compared with lesser amounts, produces greater BP lowering in patients with and without hypertension.[1,2,4–6,8–10,52] Weight loss can amplify the BP-lowering effects of the DASH diet or sodium reduction interventions.[1,4,9] For patients who do not meet weight loss goals with nonpharmacological interventions, pharmacotherapy[54,56] or bariatric surgery[53] can be considered; BP lowering correlates with the amount of weight loss using these approaches, although there is greater potential for adverse effects or harm.[53,57] In the short term, glucagon-like peptide-1 (GLP-1) receptor agonist medications used for other indications (diabetes, obesity) appear to provide concomitant BP lowering.[55,58–60]
2. The DASH eating plan emphasizes fruits, vegetables, low-fat or nonfat dairy, and whole grains, providing high potassium, magnesium, calcium, and fiber intake.[61] It is the most effective eating pattern for lowering BP and has a large and consistent evidence base across BP levels.[10–15,61–64] Conversely, the eating pattern in the Southern United States appears to be the largest mediator of the higher hypertension incidence in Black adults compared with White adults.[65] 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 individuals[66] and individuals with higher baseline BP, younger age (<50 years), or higher sodium intake (>2400 mg/d).[13,63] The DASH eating plan has been effective in both short-term feeding and longer-term behavioral intervention studies,[9–11] and the effect on BP is significantly greater when combined with weight loss or sodium reduction.[9,10,12] Patient information regarding the DASH eating plan is available publicly.[67–69] Counseling by a registered dietician/nutritionist is useful to enhance efficacy.[70] Other eating patterns, including Mediterranean, low-carbohydrate, Paleolithic, high-protein, vegetarian, low-glycemic index, low-sodium, and low-fat dietary approaches, have been shown to lower BP when compared with various control diets, although less effectively than the DASH eating plan.[14,15,64,71–74]
3. Interventions that decrease sodium intake reduce BP elevation across the life course, prevent incident hypertension, and lower BP in adults with hypertension.[17,18,20,22–24,75–87] Sodium substitution interventions prevent CVD events and mortality,[20,21] and dietary interventions that reduce sodium appear to do the same.[19,48,49] There is a linear dose response of BP to sodium intake manipulation, with steeper BP declines at higher than lower baseline BP levels.[17,18,77] On average, low-sodium (≤1500-2300 mg/d) versus high-sodium (≥4500 mg/d) diets safely result in BP reductions of approximately 3/2 mm Hg (systolic/diastolic) in normotensive and 7/3 mm Hg in hypertensive individuals.[4,5,10,16,18] There is greater responsiveness to sodium reduction in older adults and those with salt-sensitive BP.[18,77,86–88] Sodium reduction has additive BP-lowering effects to the DASH eating plan and weight loss.[4,12] Behavioral interventions targeting lower sodium intake, especially if advice is provided by a registered dietitian or low-sodium meals are provided, are most effective in sodium reduction.[22,70,76,78,79,82,83] In the United States, most dietary sodium comes from additions during food processing or during food preparation in restaurants,[89–91] so successful reduction at the population level requires not just a focus on individual behaviors but on societal changes in eating patterns and broad food reformulation strategies and policies.[81] Such population-level strategies could have a profound impact on CVD event reduction.[92]
4. Compared with the use of regular table salt, use of a potassium-enriched salt substitute (in which 100% sodium chloride is partially replaced by potassium chloride and, variably, flavoring agents) causes approximately a 5/1.5 mm Hg (systolic/diastolic) reduction with variability depending on the subgroup and the amount of sodium replacement.[20,22–24,93] In the largest trial to date, 20 995

adults in China, with either a history of stroke or age ≥60 years and uncontrolled BP, were enrolled in a cluster-randomized trial comparing a salt substitute (75% sodium chloride/25% potassium chloride) with regular salt. Use of the salt substitute was associated with SBP reduction by 3.3 mm Hg and significant relative reductions in stroke, MACE, and all-cause mortality of 12% to 14%, with no increase in risk for hyperkalemia.[21] Although most of the data on salt substitutes come from trials performed in East Asia, no significant heterogeneity of effect has been seen by global region.[93,94] Because in the United States the majority of sodium intake comes from consumption of processed foods or meals prepared in restaurants,[89–91] use of a salt substitute may be of greatest benefit in individuals who consume most of their sodium at home, from salt added during food preparation or at the table. Limitations to use of salt substitutes include low availability in the United States of potassium-enriched salt substitutes in the ratios studied to date, potential concerns over taste, and the potential for hyperkalemia in individuals with CKD and those using drugs that reduce potassium excretion (eg, potassium-sparing diuretics).

5. Observational studies have consistently demonstrated that individuals with higher dietary intake of potassium-rich foods (from natural sources such as fruits, juices, vegetables, and legumes) and/or a lower urinary sodium to potassium ratio have lower BP levels and lower stroke and mortality rates.[95–100] Accordingly, a number of studies have examined the effect of potassium supplementation on BP. Moderate potassium supplementation, on average, lowers BP by 6/4 mm Hg, with variation in effects on BP by potassium dose, sodium intake, presence of hypertension, and use of antihypertensive medication.[16,26,27] The BP-lowering effects are greater among participants with hypertension and those with higher urinary sodium excretion (greater intake) at baseline, especially ≥4000 mg/day. There appears to be a U-shaped relationship between potassium supplementation and BP levels, with maximal lowering of BP at approximately 30 mmol/day supplementation and an increase in BP above 80 mmol/day supplementation. The BP increase at higher doses of potassium supplementation (>80 mmol/day) is most evident in those taking antihypertensive therapy.[26]
6. SBP and DBP increase over time with any amount of baseline alcohol intake. Compared with average alcohol intake of 12 g per day (1 standard drink), relative risks for hypertension incidence among individuals drinking 0, 24, 36, and 48 g per day were 0.89 (95% CI: 0.84-0.94), 1.11 (95% CI: 1.07-1.15), 1.22 (95% CI: 1.14-1.30), and 1.33 (95% CI: 1.18-1.49), respectively. Thus, risk for incident hypertension is lowest for those who abstain.[101] Among normotensive individuals who consume alcohol enrolled in controlled trials, reduction of alcohol intake by at least 50% or to abstinence is associated with BP reduction, especially for those drinking ≥4 drinks per day.[29] For patients with hypertension, BP reduction is correlated with the percent reduction in alcohol intake and is greater for those with higher baseline intake.[28–31,102,103] Among individuals with alcohol intake ≥6 drinks per day who reduced intake by 50% on average, mean BP was lowered by 5.5/4.0 mm Hg. Reductions were significant but lower for participants with a baseline intake of 3 to 5 drinks per day. At ≤2 drinks per day, there was no significant reduction in BP observed with reduction of alcohol intake.[29] There are no harms identified with alcohol reduction, but continued alcohol intake is associated with other noncardiovascular harm. Prior observational studies suggesting health benefits with moderate alcohol intake appear to be partially confounded by other positive health factors and socioeconomic position and offset by other health risks.[104] Thus, aiming for abstinence appears to be optimal.[91,104]
7. Increasing leisure-time physical activity reduces BP significantly in adults with hypertension,[39] and it has been an intrinsic component of weight reduction interventions used to reduce BP in patients with and without hypertension.[1,3,4] Structured exercise programs that involve aerobic exercise (eg, endurance activities such as jogging[14,33,35–37,105]), dynamic resistance (eg, weight lifting[14,33,36,106,107]), and static/isometric resistance training (eg, handgrip[14,32–34,36,108–110]) appear particularly effective for BP lowering in adults with or without hypertension. Even lower-intensity physical activity (eg, walking) that interrupts sedentary time can reduce BP.[111–116] All types of structured exercise also appear to be safe, even for older adults with hypertension. Aerobic exercise reduces SBP on average by 4 to 7/3 to 4 mm Hg, with a slightly larger effect in patients with versus without hypertension.[14,33,35] There is a dose response, with an average 2/1 mm Hg reduction for each additional 30 minutes of aerobic exercise per week and the largest BP reduction at 150 minutes per week.[37] Dynamic resistance training alone appears to have a more modest effect on BP reduction (3/2 mm Hg) than aerobic exercise, with larger reductions in people with hypertension versus without.[14,33,36,106,107] Isometric exercise may have the largest effect on BP reduction (mean reductions of approximately 8/4 mm Hg).[14,32–34,36,108–110]

Combination training with aerobic and resistance exercise appears similarly efficacious as either alone.[33,36,38] BP-lowering effects are observed for lower- and higher-intensity exercise and with continuous and interval training.[33,38,106,117,118]

8. A number of stress-reduction strategies have been assessed for their effect on BP lowering.[119] There is consistent moderate- to high-level evidence from short-term clinical trials that transcendental meditation can lower BP in patients without and with hypertension, with mean reductions of approximately 5/2 mm Hg in SBP/DBP.[14,40] Meditation appears to be somewhat less effective than BP-lowering lifestyle interventions, such as the DASH eating plan, structured exercise programs, or low-sodium/higher-potassium intake.[14] The study designs and means of teaching and practicing meditation interventions are heterogeneous across trials, and trials have been of smaller size and short duration, so further data would be beneficial.
9. Among other stress-reducing and mindfulness-based interventions, data are less robust, and evidence is of lower quality because of smaller, short-term trials with heterogenous interventions and results. There is moderate-grade evidence that breathing control interventions lower SBP/DBP by approximately 5/3 mm Hg in people with and without hypertension.[14] There is also low- to moderate-grade evidence that yoga of diverse types lowers BP.[14,41,42]

5.2. Medical Management

Synopsis

Throughout this guideline, we use the term thiazide-type diuretic to collectively refer to HCTZ, chlorthalidone, and indapamide. Although the literature traditionally differentiates these medications based on their chemical structures, categorizing HCTZ as a thiazide-type diuretic because it possesses a benzothiadiazine ring and categorizing chlorthalidone and indapamide as thiazide-like diuretics because they lack this ring (yet remain closely related sulfonamide derivatives), the interchangeability of thiazide-type and -like agents remains a debated topic. For simplicity and to minimize confusion, in this guideline we have chosen to group them under a single term. In most settings, it is acceptable for clinicians to choose among these agents for treatment. We recognize 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 (Section 5.6, "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.

5.2.1. Initiation of Pharmacologic BP Treatment in the Context of Overall CVD Risk

Synopsis

Evidence from meta-analyses of clinical trial data, large observational studies, and simulation models has consistently shown the benefits of antihypertensive therapy initiation can be maximized by prioritizing those at highest cardiovascular risk with the use of absolute risk estimation.[1–7] Although the public health burden is significant at stage 1 hypertension and many will progress to stage 2 hypertension with associated risk,[8] the BP Lowering Treatment Trialists' Collaboration demonstrated that treatment with BP-lowering drugs provides similar relative risk reduction across all levels of predicted total CVD risk and thus greater absolute risk reduction for patients at higher predicted risk.[1] 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.[4] The benefit and efficiency of antihypertensive therapy initiation (ie, number of CVD events prevented for the same cost, or cost savings for the same number of events prevented) is greater using a risk-based strategy rather than a BP level-only strategy in simulation models.[2,9] In support, one of the inclusion criteria for SPRINT (Systolic Blood Pressure Intervention Trial) was having an estimated 10-year predicted CVD risk based on Framingham Heart Study criteria of 15% or greater.[7] Thus, employing quantitative CVD risk estimation in conjunction with BP levels can improve the benefit and efficiency of antihypertensive therapy initiation for individual patients and society.

5.2.2. BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

Recommendations for BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension
Referenced studies that support the recommendations are summarized in the Evidence Table.

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 (Continued)		
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]
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]

*Increased short-term or 10-year risk is defined as a 10-year predicted risk for CVD events of ≥7.5% based on PREVENT (Predicting Risk of cardiovascular disease EVENTs).

Synopsis

For a given BP level, absolute risk for CVD varies according to age, sex, and presence of CVD or CVD risk factors (Figures 1 and 2). Therefore, the decision to initiate antihypertensive treatment should be based on BP level and risk (Section 5.2.1, "Initiation of Pharmacological BP Treatment in the Context of Overall CVD Risk"). Based on BP level alone, all adults with hypertension benefit from antihypertensive therapy at a threshold of ≥140/90 mm Hg.[3,10,11] 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.[3,7,8,10] 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.[7,8,12] 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. As described in Section 1.4 ("Scope of the Guideline"), 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 5 207 517 White adults, 605 036 Black adults, 318 141 Hispanic adults, and 163 741 Asian adults.[13,14] To date, external validation of PREVENT has demonstrated good to excellent discrimination (C-statistic) for CVD in an independent health system not included in development (0.72)[15] and for CVD mortality in a population dataset (0.89).[16] The 10-year risk threshold of ≥7.5% calculated with PREVENT is also equivalent to the Framingham Risk Score threshold of ≥15%, which was an inclusion criterion in SPRINT.[7,17] While the specific risk thresholds or cut points for cardiovascular risk that would result in therapeutic action are based on clinical trial and observational epidemiological data, future research should study the impact of risk-based management of hypertension using these thresholds. Figure 6 summarizes the recommendations to initiate antihypertensive therapy for all adults when average BP level is ≥140/90 mm Hg and the groups that receive key benefits when average BP is ≥130/80 mm Hg.

Recommendation-Specific Supportive Text

1. In adults with hypertension and an average SBP ≥140 mm Hg, observational data, clinical trials, and meta-analyses of individual-level participant data from clinical trials support reduction in CVD event rates with initiation of antihypertensive therapy at an average SBP ≥140 mm Hg for primary and secondary prevention.[1,2,4,5,9] In a large analysis of 344 716 participants from 48 RCTs, similar relative benefit in CVD risk reduction was observed for each 5-mm Hg systolic lowering. The benefit was similar among those with CVD (relative risk: 0.89 [95% CI: 0.86-0.92]) or without CVD (relative risk: 0.91 [95% CI: 0.89-0.94]).[3] In another meta-analysis of 15 266 patients from 13 trials with BPs of 140 to 159/90 to 99 mm Hg and without CVD, antihypertensive treatment resulted in a lower risk of CVD death (relative risk, 0.75 [95% CI: 0.57-0.98]).[10]
2. 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.[1,2,4,5,9] A DBP of ≥90 mm Hg was an entry criterion in several older antihypertensive RCTs (ABCD [Appropriate Blood Pressure Control in Diabetes], ANBP2 [The Second Australian National Blood Pressure Study], UKPDS [UK Prospective Diabetes Study], and EWPHE [European Working Party on High Blood Pressure in the Elderly]) that demonstrated benefit of initiation of antihypertensive therapy in reduction of CVD events.[3]
3. In adults with hypertension and clinical CVD (coronary heart disease, stroke, HF), data from 3 RCTs that evaluated different BP treatment goals provide the evidence base to support initiation of antihypertensive treatment at a lower BP threshold of ≥130/80 mm Hg.[3,7,8,10–12] The SPRINT trial, which

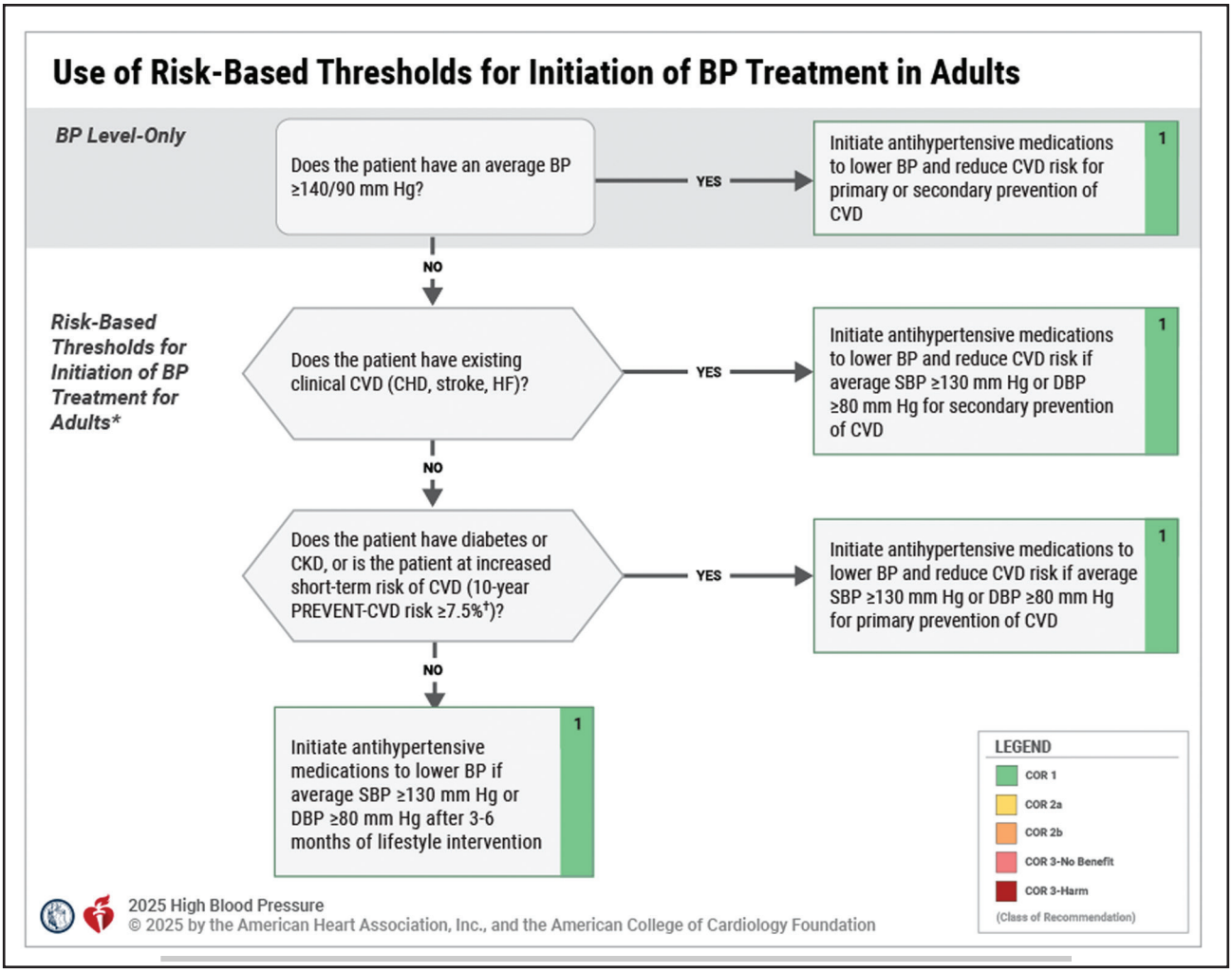

Figure 6. Use of Risk-Based Thresholds for Initiation of BP Treatment in Adults.
*In older adults who may be frail or have a limited life expectancy, a clinician-patient assessment of potential benefits and harms of BP lowering should be pursued to align care with patient goals. †Increased short-term or 10-year risk is defined as a 10-year predicted risk for CVD events of ≥7.5% using PREVENT. BP indicates blood pressure; CHD, coronary heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HF, heart failure; PREVENT, Predicting Risk of cardiovascular EVENTs; and SBP, systolic blood pressure.

enrolled patients aged ≥50 years with high cardiovascular risk and an SBP >130 mm Hg, included 17% of participants with baseline CVD. In the subgroup with CVD, intensive SBP lowering to <120 mm Hg versus standard treatment targeting <140 mm Hg reduced the incidence of the primary outcome to a similar extent of those without CVD. In the STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) trial, which randomized adults aged 60 to 80 years to an SBP target of 110 to 130 mm Hg compared with 130 to 150 mm Hg, 6% of participants had a history of CVD, with similar findings. In the ESPRIT (Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing Risk of Vascular Events) study of 11 255 patients (including 4359 with diabetes and 3022 with a history of stroke), randomization to intensive treatment targeting office SBP <120 mm Hg was associated with better CVD outcomes compared with standard treatment (hazard ratio [HR]: 0.88 [95% CI: 0.78-0.99]) with no heterogeneity of treatment effect by comorbid diabetes or stroke history.[5] In aggregate, these data indicate that the benefit of treatment clearly outweighs the potential harm at a threshold of ≥130 mm Hg for SBP for secondary prevention of CVD.

4. 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 to reduce the risk of cardiovascular events and total mortality. Although elevated diastolic BP ≥80 mm Hg was included as an entry criterion in the ABCD trial that enrolled adults with diabetes and hypertension (with or without CVD), clinical trials have not exclusively enrolled individuals with elevated DBP ≥80 mm Hg. A meta-analysis

of individual-level participant data from the Blood Pressure Lowering Treatment Trialists reported a prerandomization average DBP of 84 mm Hg from 48 RCTs among 157 728 patients with previous CVD who demonstrated benefit with initiation of antihypertensive therapy for BP lowering.[3]

5. 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.[3,7,8,10–12] Three groups of individuals were identified at increased CVD risk without clinical CVD: 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. In the SPRINT trial, increased predicted risk of CVD of ≥15% based on the Framingham risk score was an inclusion criterion, and 76% of enrolled participants had a Framingham 10-year estimated CVD risk ≥15%.[7,8] In the STEP trial, 65% of participants had a Framingham 10-year estimated CVD risk ≥15%, and this group (but not those at lower predicted risk) benefited from BP lowering. 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.[7,17] Predicted CVD risk ≥15% based on Framingham and ≥7.5% based on PREVENT also represent the age- and sex-specific 75th percentile among US adults with untreated SBP 130 to 139 mm Hg, which has been a threshold used in other prevention guidelines.[18] 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.[9]
6. Among individuals without clinical CVD but at increased CVD risk, initiation of antihypertensive therapy at an average DBP threshold of ≥80 mm Hg reduces CVD events.[3,7,8,10–12] While elevated DBP ≥80 mm Hg was included as an entry criterion in the ABCD trial that enrolled adults with diabetes and hypertension (with or without CVD), clinical trials have not exclusively enrolled individuals with elevated DBP ≥80 mm Hg. A meta-analysis of individual-level participant data from the Blood Pressure Lowering Treatment Trialists reported a prerandomization average DBP of 89 mm Hg from 48 RCTs among 186 988 patients without previous CVD who demonstrated benefit with initiation of antihypertensive therapy for BP lowering.[3]
7. 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 mm Hg. Therefore, lifestyle interventions should be encouraged first to lower BP (Section 5.1, "Lifestyle and Psychosocial Approaches"). However, lifestyle interventions may not be successful at lowering SBP, and even when successful initially, it can be difficult to sustain optimal SBP levels. Therefore, 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 (Hypertension Prevention in Pre-Hypertensive Individuals) trial, which demonstrated lower rates of progression to stage 2 hypertension (≥140/90 mm Hg) and end-organ damage (left ventricular mass) following a 3-month lifestyle intervention among participants with elevated BP (120 to 139/80 to 89 mm Hg) who were subsequently randomized to diuretic treatment compared with placebo in adults aged 30 to 70 years.[19] 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 (Section 5.2.7, "BP Goal for Patients With Hypertension") as BP tends to increase over time,[20] and greater cumulative BP exposure is associated with higher risk of clinical CVD.[21,22] Data from observational cohorts of younger adults demonstrate lower risk of subclinical CVD among those with BP <130/80 mm Hg.[23,24] 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.[25,26] 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.[27]
8. In adults without clinical CVD and 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 DBP ≥80 mm Hg. Therefore, lifestyle interventions should be encouraged first to lower BP (Section 5.1, "Lifestyle and Psychosocial Approaches"). However, lifestyle interventions may not be successful at lowering DBP, and even when

successful initially, it can be difficult to sustain optimal DBP levels. Therefore, if average DBP is ≥80 mm Hg after a 3- to 6-month trial, initiation of antihypertensive therapy is advised as an adjunct to lifestyle interventions for adults aged ≥30 years, which was part of the inclusion criterion for the PREVER-Prevention trial.[19] The AHA Life's Essential 8 included DBP <80 mm Hg as optimal based on available epidemiologic data, with higher DBP associated with greater risk of subclinical and clinical CVD.[28] 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.

5.2.3. Initial Medication Selection for Treatment of Primary Hypertension

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]

Synopsis

Many antihypertensive agents are available (Table 13). 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 (Section 5.3, "Comorbidities"). 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.[1–5] 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.[6] A meta-analysis of 50 RCTs with 58 head-to-head comparisons involving 247 006 individuals revealed subtle differences in efficacy between first-line agents.[7] 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 indications.[7]

Recommendation-Specific Supportive Text

1. The primary goal of treatment should be to reduce BP to the target level, considering the underlying CVD risk and compelling indications. High-quality RCTs have demonstrated that 4 drug classes, thiazide-type diuretics, long-acting dihydropyridine CCB, ACEi and ARB, prevent CVD compared with placebo.[1–5] In head-to-head comparisons of first-line therapy, different drug classes show varying capacities to prevent specific CVD events.[6,7] 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. Likewise, the observed CVD prevention with these agents is similar to that expected on the basis of BP lowering.[8] 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.[9] The subgroup of patients with ASCVD had greater benefit with chlorthalidone than HCTZ; however, 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.

5.2.4. Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy
Referenced studies that support the recommendations are summarized in the Evidence Table.

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]

Synopsis

Pharmacological agents are an integral tool in the treatment of hypertension. 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.[2] 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

Table 13. 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	
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	
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)	
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	

(*Continued*)

Table 13. Continued

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–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	
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	
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	

(*Continued*)

Table 13. Continued

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.

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ACEi indicates angiotensin-converting-enzyme inhibitors; ARB, angiotensin receptor blockers, BP, blood pressure; CCB, calcium channel blocker; CNS, central nervous system; CKD, chronic kidney disease; CHD, coronary heart disease; GFR, glomerular filtration rate; HF, heart failure; HFrEF, HF with reduced rejection fraction; and K+, potassium.

and severity of lower leg swelling. Combination therapy is more effective, efficient, and consistent in lowering BP and improves adherence when using an SPC compared with stepped-care therapy.[10] However, a stepped-care approach can be effective for BP lowering if well-executed.[11] 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 (Section 5.2.5, "Antihypertensive Medication Adherence Strategies").[1–3] 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.

Recommendation-Specific Supportive Text

1. 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 (Table 14).[4,5] Moreover, adults with hypertension on SPCs have fewer cardiovascular events and all-cause deaths than those on equivalent multiple-pill combination therapy in observational studies.[6] Evidence favoring this approach comes mostly from studies showing greater BP lowering with SPC agents than with single agents, with higher adherence rates.[1,2,12–14] Several smaller RCTs have demonstrated that low-dose combinations of 3 or 4 drugs together reduces BP more effectively than monotherapy over 3 to 6 months of treatment; however, none of these trials have evaluated CVD prevention.[3] In general, initial combination therapy with 2 drugs is reasonable in adults with stage 2 hypertension and those at high CVD risk. However, BP-lowering medications should be carefully initiated and monitored in older patients because hypotension or orthostatic hypotension (OH) may develop. In most cases, SPCs are a cost-effective alternative to multiple pill combination therapy, and longer follow-up intervals extend the time for intensification of each medication and addition of the next medication in stepped-care treatment.[15,16] Further, as SPCs are not available with every possible dose combination, in some cases the use of separate agents may be more or equally efficient.
2. Although most patients with stage 2 hypertension require at least 2 classes of antihypertensive agents, the stepped-care approach, defined by the initiation of antihypertensive drug therapy with a single agent followed by sequential titration of the dose and addition of other agents if needed, is a

reasonable treatment strategy for initial pharmacotherapy for stage 1 hypertension.[17] This approach remains a reasonable option in older adults and in individuals who have a history of hypotension or multiple drug-associated side effects.

3. 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.[7–9] Additionally, 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). Likewise, 2 drugs from classes that target the same BP control system are less effective and potentially harmful when used together (eg, ACEi and ARB). 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.

5.2.5. Antihypertensive Medication Adherence Strategies

Recommendations for Antihypertensive Medication Adherence Strategies
Referenced studies that support the recommendations are summarized in the Evidence Table.

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]

Synopsis

Studies have documented that up to 50% of patients do not adhere to their antihypertensive medications after 1 year of treatment.[17–19] 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 (Table 15).[20–23] Adherence to medication can be divided into 3 phases: 1) initiation; 2) persistence or implementation, consistent with medication taking; and 3) avoiding permanent discontinuation.[18,19,21]

There are a myriad of factors that contribute to poor adherence, including social determinants of health (SDOH), poor health literacy, stress, anxiety, and depression.[21,23–29] Multiple cointerventions are often needed to improve medication adherence. Once nonadherence is identified, clinicians must work with patients to identify barriers to adherence in a nonjudgmental manner and create a plan that includes patient preferences and shared decision-making to overcome obstacles to adherence.[30] Patients in whom nonadherence is identified should be screened for stress, anxiety, and depression with valid and reliable scales, as studies have found nonadherence rates to be higher in those with these mental health disorders, with referral for appropriate interventions.[23–25,27] Screening for low health literacy should also be conducted, and if identified, patients can be provided with additional education and resources.

Recommendation-Specific Supportive Text

1. Taking medications several times throughout the day requires greater attention to scheduling, transportation, and storage, which can be challenging for some patients. The impact of once-daily dosing of antihypertensive medications versus dosing multiple times daily has been evaluated in several meta-analyses.[1–3] Medication adherence was greatest with once-daily dosing and declined as dosing frequency increased.[1–3] Furthermore, 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.[31]
2. Assessment and modification of drug therapy regimens can improve suboptimal adherence.[1–3,27] Simplifying medication regimens, either by less frequent dosing (ie, once daily versus multiple times daily) or use of combination drug therapy, improves adherence. Findings from a growing body of systematic reviews of nonrandomized controlled trials and observational studies support medication synchronization (ie, coordinating the refill of medications on the same day of each month), especially when dates are appointment-based, as a means to improve adherence.[10–12]
3. RCTs, systematic reviews, and meta-analyses provide evidence that 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.[10–15,22,32–34]

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5.2.6. Medication Interactions

Synopsis

When designing an antihypertensive regimen that minimizes unwanted adverse effects while maximizing beneficial effects for patients taking more than 1 medication (Tables 13 and 14), 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). Important pharmacokinetic interactions relevant to hypertension management involve the CYP3A4 pathway; verapamil and diltiazem are both substrates and inhibitors of CYP3A4 and can alter the metabolism of other medications processed through this pathway. Table 16 summarizes other key clinical pharmacokinetic drug-drug 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. Table 17 lists other key pharmacodynamic drug-drug interactions affecting antihypertensive medications.

5.2.7. BP Goal for Patients With Hypertension

Recommendations for BP Goal for Patients With Hypertension
Referenced studies that support recommendations are summarized in the Evidence Table.

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]

*Increased risk is defined as a 10-year predicted risk for CVD events of ≥7.5% using PREVENT.

Synopsis

In observational studies, BP is associated with CVD risk in a progressive, log-linear fashion from low to high levels[7–9] (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,[2,4,10–15] and clinical trials and meta-analyses support more intensive treatment to prevent CVD.[1,13,16–21] The evidence to support an SBP goal <130 mm Hg is strong.[1] 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.[1,10] Adverse effects of intensive antihypertensive therapy have received less careful scrutiny in clinical trials. Hypotension, syncope, injurious falls, electrolyte abnormalities, and a reduction in eGFR are the most commonly recognized adverse events, but they are infrequent and usually mild.[1] Overall, clinical trials provide strong support for an SBP goal <130 mm Hg and, when feasible, SBP <120 mm Hg. Generalization from clinical trials to clinical practice is challenging, underscoring the need for careful monitoring of patients receiving intensive antihypertensive therapy. Individualization of the BP target may be required in the minority of patients who have difficulty tolerating the antihypertensive treatment, experience side effects, have limited life expectancy, or have other clinical features that warrant a less intensive treatment approach. Clinical judgment and shared decision-making are appropriate in selecting the intensity of antihypertensive therapy in individual patients, and careful monitoring for adverse consequences is warranted. Achievement of target BP should be based on an average of ≥2 readings at ≥2 visits, not on an individual BP measurement. Limited clinical trial results are available to guide the level of antihypertensive intensity in adults with hypertension who are not at high risk for CVD, but on balance, an SBP/DBP target of <130/80 mm Hg seems reasonable. Shared decision-making by clinicians, patients, and their caregivers for BP goals should be utilized when the patient has a limited life expectancy or is institutionalized due to high burden of frailty and comorbidity with limited life expectancy.

Recommendation-Specific Supportive Text

1. In adults at high risk for CVD, 8 trials have compared outcomes in participants randomized to an SBP target <130 mm Hg or to a higher SBP. In a meta-analysis that included 7 of these trials, randomization to an SBP <130 mm Hg resulted in significant reductions in CVD (including reductions in stroke, CHD, HF, and CVD mortality) and all-cause mortality.[1] Hypotension, syncope, injurious falls, electrolyte abnormalities, and acute kidney injury (AKI) were significantly more common in those randomized to

Table 14. Commercially Available Antihypertensive Medication Single-Pill Combinations

Antihypertensive Medication Class Combination	Medication Combination	Generic Available	Doses Available (in Order of Medication Combination Listed)
ACEi or ARB + Thiazide-type diuretic	Benazepril + HCTZ	Yes	10 mg/12.5 mg 20 mg/12.5 mg 20 mg/25 mg
	Captopril + HCTZ	Yes	25 mg/15 mg 25 mg/25 mg 50 mg/15 mg 50 mg/25 mg
	Enalapril + HCTZ	Yes	5 mg/12.5 mg 10 mg/25 mg
	Fosinopril + HCTZ	Yes	10 mg/12.5 mg 20 mg/12.5 mg
	Lisinopril + HCTZ	Yes	10 mg/12.5 mg 20 mg/12.5 mg 20 mg/25 mg
	Moexipril + HCTZ	Yes	7.5 mg/12.5 mg 15 mg/12.5 mg 15 mg/25 mg
	Quinapril + HCTZ	Yes	10 mg/12.5 mg 20 mg/12.5 mg 20 mg/25 mg
	Azilsartan + chlorthalidone	No (est. patent expiration 2030)	40 mg/12.5 mg 40 mg/25 mg
	Candesartan + HCTZ	Yes	16 mg/12.5 mg 32 mg/12.5 mg 32 mg/25 mg
	Irbesartan + HCTZ	Yes	150 mg/12.5 mg 300 mg/12.5 mg 300 mg/25 mg
	Losartan + HCTZ	Yes	50 mg/12.5 mg 100 mg/12.5 mg 100 mg/25 mg
	Olmesartan + HCTZ	Yes	20 mg/12.5 mg 40 mg/12.5 mg 40 mg/25 mg
	Telmisartan + HCTZ	Yes	40 mg/12.5 mg 80 mg/12.5 mg 80 mg/25 mg
	Valsartan + HCTZ	Yes	80 mg/12.5 mg 160 mg/12.5 mg 160 mg/25 mg 320 mg/12.5 mg 320 mg/25 mg
ACEi or ARB + Calcium channel blocker	Benazepril + amlodipine	Yes	10 mg/2.5 mg 10 mg/5 mg 20 mg/5 mg 20 mg/10 mg 40 mg/5 mg 40 mg/10 mg

(*Continued*)

Table 14. Continued

Antihypertensive Medication Class Combination	Medication Combination	Generic Available	Doses Available (in Order of Medication Combination Listed)
	Perindopril + amlodipine	No (est. patent expiration 2029)	3.5 mg/2.5 mg 7 mg/5 mg 14 mg/10 mg
	Trandolapril + verapamil	Yes	1 mg/240 mg 2 mg/180 mg 2 mg/240 mg 4 mg/240 mg
	Olmesartan + amlodipine	Yes	20 mg/5 mg 20 mg/10 mg 40 mg/5 mg 40 mg/10 mg
	Telmisartan + amlodipine	Yes	40 mg/5 mg 40 mg/10 mg 80 mg/5 mg 80 mg/10 mg
	Valsartan + amlodipine	Yes	160 mg/5 mg 160 mg/10 mg 320 mg/5 mg 320 mg/10 mg
ARB + Beta blocker	Valsartan + nebivolol	Yes	80 mg/5 mg
Beta blocker + Thiazide-type diuretics	Atenolol + chlorthalidone	Yes	50 mg/25 mg 100 mg/25 mg
	Bisoprolol + HCTZ	Yes	2.5 mg/6.25 mg 4 mg/6.25 mg 10 mg/6.25 mg
	Metoprolol tartrate + HCTZ	Yes	50 mg/25 mg 100 mg/25 mg 100 mg/50 mg
Potassium-sparing diuretic + thiazide-type diuretics	Amiloride + HCTZ	Yes	5 mg/50 mg
	Triamterene + HCTZ	Yes	37.5 mg/25 mg 75 mg/50 mg
MRA + thiazide-type diuretics	Spironolactone + HCTZ	Yes	25 mg/25 mg
ARB + CCB + thiazide-type diuretics	Olmesartan + amlodipine + HCTZ	Yes	20 mg/5 mg/12.5 mg 40 mg/5 mg/12.5 mg 40 mg/5 mg/25 mg 40 mg/10 mg/12.5 mg 40 mg/10 mg/25 mg
	Valsartan + amlodipine + HCTZ	Yes	160 mg/5 mg/12.5 mg 160 mg/5 mg/25 mg 160 mg/10 mg/12.5 mg 160 mg/10 mg/25 mg 320 mg/10 mg/25 mg

Data are derived from the FDA Orange Book databases.[18]

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; CCB, calcium channel blocker; FDA, Food and Drug Administration; HCTZ, hydrochlorothiazide; and MRA, mineralocorticoid receptor antagonist.

Table 15. Evidence-Based Strategies for Improving Antihypertensive Medication Adherence

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

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an SBP <130 mm Hg but were infrequent, with numbers needed to harm ranging from 508 for hypotension to 3222 for electrolyte abnormalities. The support for SBP <120 mm Hg versus <140 mm Hg was further demonstrated in the BPROAD (Blood Pressure Control Target in Diabetes) trial, with the incidence of MACE being significantly lower in those with type 2 diabetes (T2D).[10]

2. In the PREVER-Prevention trial, conducted in adults who were not at high risk for CVD and had an average SBP between 120 and 139 mm Hg after 3 months of lifestyle counseling, treatment with once-daily low-dose chlorthalidone (12.5 mg) and amiloride (2.5 mg) significantly lowered BP, prevented hypertension, and reduced left ventricular mass as an intermediate endpoint compared with placebo.[5]
3. In adults at high risk for CVD, participants in 2 trials[6,15] were randomized to a DBP <80 mm Hg versus higher DBP antihypertensive treatment goal, concordant with randomization to an SBP goal of <120[15] or <130 mm Hg.[6] In one of these trials, CVD risk and all-cause mortality were significantly reduced in the participants randomized to the lower compared with the higher DBP.[6] The other trial failed to meet its recruitment goal and was substantially underpowered but resulted in a consistent, albeit nonsignificant, reduction for both outcomes in the participants randomized to the lower DBP target.[15] J- and U-shaped associations between DBP and CVD events, including coronary heart disease, have been observed in analyses of nonrandomized clinical trial and disease registry data sets, including a post-hoc analysis of the SPRINT.[22] In randomized comparisons, however, CVD outcomes and all-cause mortality were better in those randomized to an SBP goal of <120 versus <140 for every quintile of baseline DBP, including those with the lowest starting DBP (<68 mm Hg).[22] Although there is no cutoff for level of DBP during antihypertensive treatment, careful monitoring of symptoms and attention to changes in eGFR are important.
4. In the PREVER-Prevention trial, conducted in adults who were not at high risk for CVD and had an average DBP between 80 and 89 mm Hg, treatment with once-daily low-dose chlorthalidone (12.5 mg) and amiloride (2.5 mg) significantly lowered BP, prevented hypertension, and reduced left ventricular mass compared with placebo.[5] Although this is an intermediate endpoint, the results support lowering DBP and are consistent with guidance in an AHA Scientific Statement for those with a high lifetime risk of CVD, including young adults.[23]

5.2.8. Electrolyte Imbalances

Synopsis

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 (Section 3.2.3.1, "Primary 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. 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.[1–3] 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) (Section 5.2.6, "Medication Interactions"). 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.[4,5] If severe or life-threatening electrolyte imbalances occur, the causative medication should be discontinued and the imbalance treated immediately.

Table 16. 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
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
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

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BB indicates beta blocker; BP, blood pressure; CCB, calcium channel blocker; h, hour; and P-gp, P-glycoprotein.

5.2.9. Kidney Dysfunction/Injury

Synopsis

Estimated GFR using serum creatinine should be measured 2 to 4 weeks after initiation or dose titration of antihypertensive medications. Renin-angiotensin-aldosterone 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.[1–3] This expected short-term dip in eGFR is associated with preservation of kidney function in the long-term[4–10] 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. This should prompt evaluation of volume status to rule out hypovolemia and other possible causes of kidney dysfunction. It may be appropriate to initially hold or reduce the diuretic dose and then advance more slowly.

5.3. Comorbidities

Synopsis

Hypertension-related target organ damage describes adverse structural or functional changes in major organ

Table 17. 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
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

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ACEi indicates angiotensin-converting enzyme inhibitors; AKI, acute kidney injury; ARB, angiotensin receptor blockers; BB, beta blocker; BP, blood pressure; CCB, calcium channel blocker; CNS, central nervous system; NSAIDs, nonsteroidal anti-inflammatory drugs; RAASi, renin-angiotensin aldosterone inhibitor; and RAS, renin-angiotensin system.

systems, including the heart, vasculature, kidneys, brain, and retina due to hypertension.[1,2] Common forms of target organ damage include left ventricular hypertrophy, HF, subclinical and clinical atherosclerosis, CKD (ie, reduced eGFR or albuminuria), and cerebrovascular disease (eg, stroke, dementia, retinopathy).[3] Numerous studies demonstrate an association between hypertension and target organ damage,[4–9] and longitudinal data indicate at least 1 form of hypertension-related target organ damage is present in >50% of individuals with hypertension.[1] Recent studies also demonstrate relationships between the severity of hypertension and the number of organs affected by hypertension,[10] as well as the number of affected organs and increased CVD risk.[11] Although there are strong data linking hypertension to target organ damage, recommendations on screening and management of different types of target organ damage beyond hypertension treatment are lacking.[12] The goals of preventing target organ damage and its progression from asymptomatic to symptomatic target organ damage can be achieved by focusing on hypertension control.[13] Future studies are needed to inform how hypertension-related target organ damage should be diagnosed and managed among patients with hypertension.

5.3.1. Diabetes

Recommendations for Diabetes Referenced studies that support the recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	A	1. In adults with T2D and hypertension, antihypertensive drug treatment should be initiated at an SBP of ≥130 mm Hg with a treatment goal of <130 mm Hg, with encouragement to achieve an SBP <120 mm Hg to reduce CVD morbidity and mortality.[1–5]
1	C-LD	2. In adults with T2D and hypertension, antihypertensive drug treatment should be initiated at a DBP of ≥80 mm Hg with a treatment goal of <80 mm Hg to reduce CVD morbidity and mortality.[6]
1	A	3. In adults with T2D and hypertension, all first-line classes of antihypertensive agents (ie, thiazide-type diuretics, long-acting CCB, ACEi, and ARB) are useful and effective for BP lowering.[1,7–9]
1	A	4. 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 diabetes-related kidney disease.[10–12]

Synopsis

More than 80% of adults with T2D also have hypertension. The prevalence rate of hypertension in adults with

T2D is double that of age-matched adults without diabetes.[13] Further, CVD risk in adults with both T2D and hypertension is more than double the risk for either condition alone.[14] Hypertension accelerates CKD, particularly when moderate or severe albuminuria is present.

Recommendation-Specific Supportive Text

1. RCTs have shown that intensive BP goals are associated with improved cardiovascular outcomes in the general population, and recently BPROAD confirmed the benefits of an intensive BP control regimen, specifically in patients with T2D.[5] Of the 12 821 participants, improved cardiovascular outcomes were seen in patients ≥50 years with T2D and elevated SBP if they were assigned to an intensive BP target to lower SBP <120 mm Hg rather than a standard treatment strategy to lower SBP <140 mm Hg. Patients with diabetes were excluded from several major trials, including SPRINT.[15] The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial enrolled patients with T2D at high risk for cardiovascular events but found that targeting an SBP of <120 mm Hg compared with <140 mm Hg did not reduce the rate of a composite outcome of fatal and nonfatal MACE using a multifactorial design.[1,16]
2. There are few studies comparing DBP targets in people with diabetes. Data from the HOT (Hypertension Optimal Treatment) trial, comparing 3 DBP goals in patients with T2D, showed that DBP was reduced in each target group (target DBP ≤90 mm Hg, −20.3 mm Hg; target DBP ≤85 mm Hg, −22.3 mm Hg; target DBP ≤80 mm Hg, −24.3 mm Hg).[6]
3. Any of the recommended antihypertensive drug classes (ACEi, ARB, CCB, and diuretics) are useful in the treatment of hypertension in diabetes.[7–9,12]
4. ACEi and ARB have greater efficacy in reducing urinary albumin excretion among the drug classes. Therefore, an ACEi or ARB is recommended as part of treatment in patients with diabetes and CKD, defined by an eGFR <60 mL/min/1.73 m^2, who also have moderate or severe albuminuria, defined as 30 mg albumin per g creatinine or greater.[10,11] An ACEi or ARB is also appropriate for less severe CKD (stage 1 or 2 when moderate or severe albuminuria is present). No hypoglycemic agents are specifically indicated for BP lowering; however, among the new classes of hypoglycemic agents, sodium-glucose cotransporter inhibitors (SGLT2i) and GLP-1 receptor agonists have been demonstrated to slow decline in kidney function whether or not diabetes is present and may have some beneficial effects on BP.[17] For treatment of hypertension for people with CKD, including those with albuminuria (ie, ACR ≥30 mg/g or 24-hour urine albumin ≥30 mg), trial evidence to support benefits from ACEi or ARB specifically is strongest for those with moderate to severe albuminuria with or without diabetes.[12] For people with CKD and high BP without albuminuria with or without diabetes, ACEi or ARB may be considered for CVD event reduction, although the risk for CKD progression may be lower and there is little evidence to support a unique advantage of these agents for kidney protection.[18]

5.3.2. Obesity and Metabolic Syndrome

Recommendations for Obesity and Metabolic Syndrome Referenced studies that support the recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
2b	B-R	1. In adults with hypertension who also have overweight or obesity with a BMI ≥27 kg/m^2, incretin mimetics (eg, GLP-1 receptor agonists) when used for weight management may be effective as an adjunct to lower BP.[1–4]
2b	B-R	2. In adults with hypertension who have obesity with a BMI ≥35.0 kg/m^2, bariatric surgery (when considered for weight loss) in combination with behavioral interventions and antihypertensive therapies may be effective at lowering BP.[5,6]

Synopsis

Obesity is a major modifiable risk factor for hypertension, with greater degrees of adiposity associated with higher BP levels. Obesity and hypertension often co-occur and with other obesity-related metabolic conditions (eg, dysglycemia, dyslipidemia), and this clustering has traditionally been referred to as the metabolic syndrome, which is associated with increased risk of CVD.[7] Metabolic syndrome, along with hypertension alone, is included in the AHA cardiovascular-kidney-metabolic (CKM) construct.[8,9] CKM syndrome includes both individuals at risk for CVD due to the presence of metabolic risk factors and/or CKD, and individuals with existing CVD that is potentially related to or complicates metabolic risk factors and/or CKD.[8,9] Metabolic syndrome has increased in recent years, with an estimated prevalence of 47% among US adults.[10] Sex-specific risk factors for metabolic syndrome include gestational diabetes and hypertensive disorders of pregnancy (HDP).

As obesity is a major cause of hypertension, strategies that target the underlying pathophysiology of excess or dysfunctional adiposity should be considered in hypertension management, including intensive lifestyle intervention (Section 5.1, "Lifestyle and Psychosocial Approaches"), pharmacotherapies,[1–4,11] and bariatric surgery[12,13] for weight loss. Among lifestyle interventions, the efficacy and safety of time-restricted eating as a strategy to improve metabolic health and lower BP remain unclear.[14] While certain antihypertensive therapies have been suggested to adversely

impact metabolic health (eg, thiazide-type diuretics, BB), outcome data do not demonstrate overt harm. Regardless of the weight loss strategy, weight regain is common and may lead to rebound worsening of BP.[11,12]

Recommendation-Specific Supportive Text

1. In a systematic review and meta-analysis of 6 RCTs of patients with excess weight and without diabetes, use of GLP-1 receptor agonists demonstrated significant reduction in BP, which was a prespecified secondary endpoint in the phase 3 STEP (Once-Weekly Semaglutide in Adults With Overweight or Obesity) trials.[13] In patients with overweight or obesity and without diabetes, the STEP 8 (Research Study to Investigate How Well Semaglutide Works Compared to liraglutide in People Living With Overweight or Obesity) trial demonstrated significant and similar reduction in SBP with semaglutide (−5.7 mm Hg [95% CI: −8.1 to −3.3 mm Hg]) and liraglutide (−2.9 mm Hg [95% CI: −5.3 to −0.5 mm Hg]); significantly greater reduction in DBP was achieved with semaglutide (−5.0 mm Hg [95% CI: −7.0 to −3.1 mm Hg]) compared with liraglutide (−0.5 mm Hg [95% CI: −2.3 to 1.3 mm Hg]).[3] In a prespecified substudy of the SURMOUNT-1 (Study of Tirzepatide in Participants With Obesity or Overweight) trial, 600 participants completed ambulatory BP monitoring with placebo-adjusted SBP change at 36 weeks of −8.0 mm Hg (95% CI: −10.6 to −5.4 mm Hg) for tirzepatide 15 mg, with similar changes in BP for 5- and 10-mg doses and with 70% of the change in BP mediated by change in weight.[5]
2. Bariatric surgery has demonstrated improvement in obesity-related risk factor levels, including BP. In a randomized single-center trial conducted in Brazil, 100 adults aged 18 to 65 years with a BMI 30.0 to 39.9 kg/m^2 were randomized to Roux-en-Y gastric bypass combined with antihypertensive therapy or antihypertensive therapy alone. At 5-year follow-up, there was greater reduction in number of antihypertensive medications, with 81% versus 14% achieving at least a 30% reduction in number of medications in the surgical compared with the medical therapy arm (primary endpoint: relative risk: 5.91 [95% CI: 2.58-13.52]). In addition, SBP was significantly lower in the surgical arm (124 mm Hg [95% CI:119-128 mm Hg]) compared with medical therapy alone (131 mm Hg [95% CI: 126-136 mm Hg]).[6] Similar findings were observed for BP benefit in a prospective observational study of US adults aged 18 to 72 years with a BMI >35.0 kg/m^2 in which 418 patients underwent Roux-en-Y gastric bypass and were compared with 738 patients who did not undergo surgery, demonstrating a significantly lower incidence in hypertension at 12 years follow-up.[15] In LABS-2 (Longitudinal Assessment of Bariatric Surgery-2), a prospective cohort study of adults aged ≥18 years from 10 hospitals in 6 US cities who underwent Roux-en-Y gastric bypass, weight regain was frequent, with median rate of weight regain of 27% of the maximum weight loss at 5 years after reaching nadir weight.[12]

5.3.3. Chronic Coronary Disease

Synopsis

Adults with CCD and hypertension are at increased risk of death compared with adults with CCD who do not have hypertension.[1] Reducing SBP to <130 mm Hg can lower cardiovascular risk and mortality in adults with CCD and hypertension.[2–5] Although there are scarce data on the optimal treatment target for DBP, when SBP is <130 mm Hg, a DBP between 70 and 80 mm Hg is associated with reduced cardiovascular events without an increase in serious adverse events.[5,6] ACEi, ARB, and BB have been shown to reduce CVD events and all-cause death in adults with CCD and hypertension.[7] Conflicting evidence exists regarding the long-term use of BB therapy (>1 year) in adults with CCD (eg, post-MI or post–acute coronary syndrome [ACS]) and hypertension with preserved left ventricular ejection fraction.[5,8] If additional antihypertensive medications are needed to achieve BP control, CCB, thiazide-type diuretics, and/or MRA are recommended.[2,9,10] For additional information on the management of CCD, see Section 4.2.7 ("BP Management") in the "2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease."[5]

5.3.4. Prevention of HF in Adults With Hypertension

Recommendations for the Prevention of HF in Adults With Hypertension
References that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	B-R	1. In adults with hypertension, treating SBP to <130 mm Hg is recommended to lower the risk of developing HF.[1–4]
1	B-NR	2. In adults with hypertension, treating DBP to <80 mm Hg is recommended to lower the risk of developing HF.[1–5]

Synopsis

Antecedent hypertension is present in 71% of patients with HF,[6] and the presence of hypertension in people <40 years of age is highly associated with the development of incident HF.[7] There is a dose-dependent association between BP level and HF risk, and long-term treatment of systolic and diastolic hypertension has been shown to reduce this risk.[6,8,9] Meta-analyses of clinical trials support BP control, rather than a specific medication class, to prevent HF.[10,11]

Recommendation-Specific Supportive Text

1. In adults with systolic hypertension (SBP ≥130 mm Hg) and a high risk of CVD, a strong body of evidence supports treatment with antihypertensive medications

and more-intensive rather than less-intensive intervention (Section 5.2.7, "BP Goal for Patients With Hypertension"). In SPRINT, a more intensive intervention that targeted an SBP <120 mm Hg significantly reduced the incidence of HF, a component of the primary outcome (HR: 0.62; 95% CI: 0.45-0.84).[12] Meta-analyses of clinical trials have identified a similar beneficial effect of more-intensive SBP reduction on the incidence of HF,[2–4] but the body of information from studies confined to trials that randomly assigned participants to different SBP targets is more limited and less compelling.[1] In addition, the available trials were efficacy studies in which BP measurements were more consistent with guideline recommendations than is common in clinical practice, resulting in lower absolute values for SBP. For both of these reasons, the SBP target recommended (<130 mm Hg) is higher than that used in SPRINT.

2. In adults with diastolic hypertension (DBP ≥80 mm Hg) and a high risk of CVD, a strong body of evidence supports treatment with antihypertensive medications (Section 5.2.2, "BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension"). Meta-analyses of clinical trials have identified a similar beneficial effect of DBP reduction on the incidence of HF,[2–4] but the body of information from studies confined to trials that randomly assigned participants to different DBP targets is more limited and less compelling.[1,5]

5.3.4.1. HF With Reduced Ejection Fraction

Synopsis

Hypertension is the most common medical comorbidity in patients with HF, and its prevalence among patients with heart failure with reduced ejection fraction (HFrEF), defined as left ventricular ejection fraction ≤40%, continues to rise.[1] Hypertension is known to be a major risk factor for HFrEF directly through alterations in cardiac structure and function in response to chronic pressure overload and indirectly through its associations with ischemic heart disease.[2] In patients with HFrEF and hypertension, uptitration of HF GDMT to the maximally tolerated dose is recommended for hypertension control (Table 18). Clinical trials assessing the impact of BP reduction on outcomes in patients with HFrEF and hypertension are limited, and the optimal BP goal is unknown; however, a goal SBP <130 mm Hg should at least be attained in patients with hypertension and HFrEF. Diuretics should be added as needed for volume overload. Dihydropyridine CCB may be used to treat hypertension in patients with elevated BP despite the optimization of GDMT. Nondihydropyridine CCB may be harmful in patients with HFrEF due to their negative inotropic effects and are not recommended for hypertension management.[3,4] For information on the management of HFrEF in adults, see the "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure."[5]

5.3.4.2. HF With Preserved Ejection Fraction

Synopsis

Hypertension is a major risk factor for developing heart failure with preserved ejection fraction (HFpEF) and an important target for HF management to reduce hospitalization, CVD events, and mortality.[1] Appropriate use of diuretics is crucial to the success of other antihypertensive medications in the presence of HFpEF and should be used for signs and/or symptoms of volume overload.[1,2] RAASi are indicated for management of HFpEF to attain an SBP of <130 mm Hg, especially with an MRA or ARNi, or ARB when ARNi is not feasible.[1–3] BB are not recommended for hypertension management with HFpEF given negative chronotropic effects and should be restricted to specific comorbid conditions (eg, arrhythmia, ACS).[1,2] SGLT2i are used frequently for HFpEF treatment (with and without diabetes), unless contraindicated, to reduce the risk of hospitalization and cardiovascular mortality.[1,4–6] SGLT2i may lower BP; therefore, adjustment in other antihypertensive medications may be indicated if signs or symptoms of hypotension are present.[2,3,5] For more information on the management of and guidelines for HFpEF in adults, see the "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure," and the "2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction."[1,2]

5.3.5. Atrial Fibrillation

Synopsis

Hypertension has the highest attributable risk for the development of AF.[1,2] It is present in >80% of patients with AF and is the most common comorbid condition, regardless of age.[1,2] Both AF and hypertension increase in frequency with age,[3,4] and because of the close relationship between BP and AF, hypertension remains a key component in several AF and CVD risk prediction scores.[1,5] BP control in individuals with hypertension reduces the risk for incident AF,[3,5] especially in patients with HF.[6] In adults with AF and hypertension, optimal BP control reduces rates of MACE, including stroke.[7] Lifestyle modifications that result in lower BP may decrease the recurrence of AF.[1] Small studies and secondary analyses of RCTs reported lower incident AF with ACEi or ARB,[1] and 2 meta-analyses suggest reduction in recurrent AF with ACEi or ARB,[8] although more definitive evidence is needed. RCTs and observational studies suggest that MRAs reduce AF burden.[1,9] Control of hypertension is a key component of AF management,[8] although optimal treatment targets for the management of hypertension in AF remain unclear. Therefore, it is reasonable to apply general hypertension guidelines to adults with AF,[8] which would include attain-

Table 18. GDMT for Patients With Hypertension and HFrEF

Drug Class	Notes on Use
BB	In patients with HFrEF, even if asymptomatic, use 1 of the 3 BBs proven to reduce mortality and hospitalizations (bisoprolol, carvedilol, metoprolol succinate).
MRA	In patients with symptomatic HFrEF, spironolactone or eplerenone is recommended to reduce morbidity and mortality if eGFR is >30 mL/min/1.73 m^2 and potassium is <5.0 mEq/L.
RAASi with ACEi or ARB or ARNi	In patients with HFrEF and NYHA functional class II to III symptoms, ARNi is recommended to reduce morbidity and mortality. When the use of ARNi is not feasible, ACEi or ARB is recommended to reduce morbidity and mortality.
SGLT2i	SGLT2i are recommended in patients with symptomatic HFrEF to reduce hospitalization and cardiovascular mortality irrespective of the presence of type 2 diabetes.
Additional GDMT to be added as indicated	
Hydralazine and isosorbide dinitrate	For patients self-identified as Black with NYHA functional class III to IV HFrEF who are receiving optimal medical therapy, the combination of hydralazine and isosorbide dinitrate is recommended to improve symptoms and reduce morbidity and mortality. In patients with current or previous symptomatic HFrEF who cannot be given first-line agents, such as ARNi, ACEi, or ARB, because of drug intolerance or renal insufficiency, a combination of hydralazine and isosorbide dinitrate might be considered to reduce morbidity and mortality.

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ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNi, angiotensin receptor-neprilysin inhibitors; BB, beta blocker; eGFR, estimated glomerular filtration rate; GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; RAASi, renin-angiotensin-aldosterone system inhibitors; and SGLT2i, sodium-glucose cotransporter inhibitors.

ing a goal BP of <130/80 mm Hg. For detailed discussion of AF management, see Section 5.2.8 and Table 3 in the "2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation."[1]

5.3.6. Valvular Heart Disease

Synopsis

There are no recommendations based on sufficiently strong evidence for the management of adults with hypertension and valvular heart disease other than for aortic stenosis or chronic aortic regurgitation.[1] Uncontrolled hypertension among individuals with moderate to severe aortic stenosis and/or aortic regurgitation is associated with worsening symptoms, HFrEF, and death.[2–5] Data support the use of antihypertensive medications to control BP in adults with aortic stenosis and/or chronic aortic regurgitation and hypertension. Among adults with severe aortic stenosis who have undergone transcatheter aortic valve implantation, the use of ACEi or ARB to achieve BP control is associated with reduced mortality.[6] However, there are no data from RCTs that examined optimal BP targets for adults with hypertension and chronic aortic regurgitation. Chronic aortic regurgitation is often accompanied by a wide pulse pressure, and medications that lower heart rate may paradoxically increase SBP.[7,8] The use of ACEi and ARB in adults with chronic moderate to severe aortic regurgitation and hypertension is associated with reductions in cardiovascular events and lower all-cause mortality.[9] For additional information on the management of aortic stenosis and chronic aortic regurgitation and mitral regurgitation, including indications for appropriate consultation or referral to a primary or comprehensive Heart Valve Center, see Sections 3, 4.3, and 2.6 in the "2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease."[1]

5.3.7. Aortic Disease

Synopsis

Hypertension is a major risk factor for AD, including thoracic aortic aneurysm,[1] abdominal aortic aneurysm,[2,3] and aortic dissection,[4] resulting in AD-related mortality.[5,6] The risk for abdominal aortic aneurysm rupture increases by 30% for each 10 mm Hg elevation in BP levels.[6–8] Intensive BP management and optimal BP control (<130/80 mm Hg) are important for cardiovascular risk reduction in patients with hypertension and AD, although patients may be asymptomatic.[9] BB are recommended, although limited data exist on the optimal choice of antihypertensive medication and have generally been extrapolated from acute aortic syndrome management, such as for aortic dissection.[9] Future studies should focus on optimal antihypertensive medication therapy for patients with hypertension and AD. For information on the management of hypertension in AD in adults, see Sections 6.4.1, 7.3, and 9.4.1 in the "2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease."[9]

5.3.8. Hypertension Treatment in Patients With CKD

Recommendations for Hypertension Treatment in Patients With CKD
References that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. For adults with hypertension and CKD as identified by eGFR <60 mL/min/1.73 m^2 or albuminuria ≥30 mg albumin/g creatinine, treatment should target an SBP goal of <130 mm Hg to decrease all-cause mortality.[1–3]
1	B-R	2. 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.[4,5]

Synopsis

The prevalence of hypertension is 67% to 92% among people with CKD. CKD is an important risk factor for CVD, and the coexistence of hypertension and CKD further increases the risk of CVD events. Despite this risk, a majority of people with CKD have uncontrolled BP.[6] As demonstrated in SPRINT, intensive BP treatment (mean achieved SBP 121 mm Hg) versus standard treatment (mean achieved SBP 136 mm Hg) reduced the risk of CVD, including among those with CKD.[1] The recommendation in this guideline is for a treatment goal SBP <130 mm Hg and balances the benefits of intensive BP lowering with risks of adverse events.[7] An ACEi or an ARB is recommended for initial treatment of hypertension in CKD due to long-term kidney and CVD benefits in people with moderate or severe albuminuria (≥30 mg/g) and may be considered for those with lower level albuminuria (<30 mg/g) based on expert opinion.[4,5,8–12] These recommendations refer to people with nondialysis-requiring CKD given limited data in patients receiving chronic hemodialysis or peritoneal dialysis. ACEi or ARB is also appropriate for less-severe CKD (stage 1 or 2) when moderate or severe albuminuria is present.

Recommendation-Specific Supportive Text

1. SPRINT data demonstrated adults with CKD and hypertension can be effectively and safely treated to SBP <130 mm Hg.[1] Additionally, meta-analyses have shown benefit of treating SBP <130 mm Hg versus higher SBP targets. An analysis of CKD patients from 4 trials found that an SBP target of <130 mm Hg (versus <140 mm Hg) decreased all-cause mortality.[2] A meta-analysis of the CKD subsets from 18 trials reported that more-intensive SBP (mean SBP 132 mm Hg) versus less-intensive SBP (mean SBP 140 mm Hg) control resulted in 14% reduction in all-cause mortality.[3] While <120 mm Hg is more effective at preventing CVD events,[3] meta-analyses of trial data support an SBP <130 mm Hg to balance the benefits of intensive BP-lowering with the risks of adverse events.[7]
2. There is robust evidence to support ACEi or ARB as first-line antihypertensive therapy in CKD for CVD benefits.[4,5,8–12] The evidence to support kidney benefit is strongest when albuminuria is moderate or severe (>30 mg/g), with consideration for using ACEi or ARB with mild albuminuria based on expert opinion. ACEi or ARB reduce intraglomerular pressure, which may cause a transient decrease, or dip, in eGFR up to 30%. This short-term decline in eGFR is not associated with decreased long-term outcomes and should not prompt discontinuation of the ACEi or ARB.[13–15] Electrolytes should be rechecked 2 to 4 weeks after initiating or intensifying ACEi or ARB dosage, monitoring for hyperkalemia or a decline in eGFR of >30%, which may require reducing or holding the agent temporarily or additional evaluation. ACEi or ARB can be continued in people with eGFR <30 mL/min/1.73 m^2 as an RCT found that discontinuation was not associated with a significant difference in long-term decrease in eGFR.[16] The combined use of an ACEi and an ARB should be avoided because of increased harm, as discussed further in Section 5.2.8 ("Electrolyte Imbalances").[12,17,18]

5.3.8.1. Hypertension After Kidney Transplantation

Synopsis

Hypertension is common after kidney transplantation because of pre-existing kidney disease, effects of immunosuppressive medications, and presence of allograft pathology.[1–3] One study reported high prevalence of masked hypertension in kidney transplant recipients,[4] who frequently have multiple risk factors that increase the risk of CVD events. Hypertension may accelerate kidney function decline and increase the risk for CVD and mortality.[2,5] Immunosuppression may contribute to the risk of hypertension in organ transplant recipients (including kidney and other organs). Calcineurin inhibitor-based immunosuppression regimens are associated with a high (70% to 90%) prevalence of hypertension.[3] There are no robust trials in post-transplant patients comparing different BP targets or drug choices. A systematic review did not find that any BP-lowering medication class reduced the risk of graft loss, withdrawal because of adverse events, death, cardiovascular outcomes, or kidney outcomes compared with placebo/other drug classes.[6] One trial of 188 kidney transplant recipients randomized patients to spironolactone versus placebo for 3 years and found no difference in kidney function or proteinuria.[7] Overall, there is insufficient evidence to support specific recommendations on BP targets or recommended agents for kidney transplant recipients.

5.3.9. Cerebrovascular Disease

Synopsis

Stroke is a major cause of death, disability, and dementia.[1] Due to its heterogeneous causes and hemodynamic consequences, the management of BP in adults with stroke is complex and challenging. To accommodate the variety of important issues pertaining to BP management in the stroke patient, treatment recommendations require recognition of stroke acuity, stroke type, and therapeutic objectives. Future studies should focus on identifying more precise BP targets, accounting for stroke etiology, personalized cerebrovascular hemodynamics, and appropriate antihypertensive agents.

5.3.9.1. Acute Intracerebral Hemorrhage

Recommendations for Acute Intracerebral Hemorrhage		
COR	**LOE**	**Recommendations**
2a	A	1. For adult patients with acute spontaneous intracerebral hemorrhage (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.[1–3]
2a	B-NR	2. 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.[3,4]
3: Harm	B-NR	3. For adult patients with acute spontaneous ICH who present with SBP >220 mm Hg, SBP should not be lowered below 130 mm Hg to reduce adverse events.[5–7]

Synopsis

Spontaneous, nontraumatic ICH is a significant global cause of morbidity and mortality.[8] Elevated BP is highly prevalent in the setting of acute ICH and is linked to greater hematoma expansion, neurological worsening, and death and dependency after ICH.[1–3,9]

Recommendation-Specific Supportive Text

1. INTERACT-2 (The Second Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial) showed improvement in secondary outcomes of overall function and quality of life with lowering SBP to <140 mm Hg and maintaining for 7 days for noncomatose spontaneous ICH patients who presented with an SBP of 150 to 220 mm Hg within 6 hours of onset of ICH.[2] INTERACT 3 (Third Intensive Care Bundle With Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial) concluded that an early intensive SBP lowering of <140 mm Hg (bundled with strict blood glucose control, antipyrexia treatment, and rapid reversal of warfarin treatment within 1 hour) and maintenance for 7 days was associated with overall improved long-term functional outcome compared with usual care.[3] Both trials protocolized stopping antihypertensive medications if SBP lowered <130 mm Hg. A meta-analysis of INTERACT-2 and ATACH-2 (Antihypertensive Treatment of Acute Cerebral Hemorrhage II) trial showed an improved 90-day global disability with incrementally lower achieved SBP up to 130 mm Hg.[3] In a post-hoc analysis of the INTERACT-2 trial, SBP <130 mm Hg was harmful.[6]
2. A post hoc analysis of INTERACT-2 found that increased standard deviation of SBP during the first 24 hours had a linear association with death and severe disability at 90 days.[4] A meta-analysis of INTERACT-2 and ATACH-2 also showed a continuous association between achieved SBP and lesser variability during the first 24 hours after ICH and the distribution of modified Rankin scale scores at 90 days, suggesting that avoiding large fluctuations in BP is beneficial.[3] There is a lack of evidence to guide the choice of BP-lowering agents during the hyperacute phase after ICH, including bolus versus drip management. IV nicardipine was the drug used in ATACH-2, whereas a range of IV and oral BP-lowering agents were used in INTERACT-2 and INTERACT 3. Any antihypertensive drug with rapid onset and short duration of action to facilitate easy titration and sustained BP control to minimize SBP variability seems appropriate, although venous vasodilators may be harmful because of unopposed venodilation and its effect on hemostasis and intracranial pressure.[10] In a meta-analysis of 50 studies, use of a titratable agent and CCB and alpha- and beta-adrenoceptor blockers were associated with favorable outcomes compared with other fixed agent use and RAS blockers, nitrates, and magnesium.[3]
3. A post-hoc analysis of the ATACH-2 trial showed that among 228 participants with ICH of mild-to-moderate severity who had SBP >220 mm Hg at presentation, intensive lowering of their SBP where the achieved values were <130 mm Hg was harmful.[7] However, given the consistent nature of the data linking high BP with poor clinical outcomes and data favoring modest SBP lowering in patients with moderately high initial SBP levels,[1–3] cautious, modest lowering of SBP (in the range of 160-180 mm Hg) in ICH patients with markedly high SBP levels (>220 mm Hg) might be reasonable.

5.3.9.2. Acute Ischemic Stroke

Recommendations for Acute Ischemic Stroke References that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	C-LD	1. In patients with acute ischemic stroke, hypotension and hypovolemia should be corrected to maintain systemic perfusion levels necessary to support organ function.[1–3]
1	B-NR	2. Patients who have elevated BP and are otherwise eligible for treatment with IV thrombolytics should have their BP lowered to SBP <185 mm Hg and DBP <110 mm Hg before IV thrombolytic therapy is initiated and should be maintained below 180/105 mm Hg for at least the first 24 hours after initiating thrombolytic therapy to avoid complications.[4,5]
2a	B-NR	3. In patients who undergo endovascular treatment, it is reasonable to maintain the BP at ≤180/105 mm Hg during and for 24 hours after the procedure to improve long-term functional outcomes and prevent death.[6,7]
2b	C-LD	4. In patients with BP of ≥220/120 mm Hg who did not receive IV thrombolytic or endovascular treatment and have no comorbid conditions requiring acute antihypertensive treatment, it might be reasonable to lower BP by 15% during the first 24 hours after onset of stroke to improve outcomes.[2,3]

Recommendations for Acute Ischemic Stroke (Continued)		
COR	LOE	Recommendations
3: No Benefit	A	5. In patients with BP <220/120 mm Hg who do not receive IV thrombolysis or endovascular treatment and do not have a comorbid condition requiring urgent antihypertensive treatment, initiating or reinitiating treatment of hypertension within the first 48 to 72 hours after an acute ischemic stroke is not effective to prevent death or disability.[8–11]
3: Harm	A	6. 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.[12–14]

Synopsis

High BP occurs in up to 80% of acute stroke patients.[15] Counteracting concerns about hypertension during acute ischemic stroke include enhancing cerebral perfusion while minimizing brain edema and hemorrhagic transformation of the ischemic tissue.[2,16] Some studies have shown a U-shaped relationship between the admission BP and favorable clinical outcomes.[3] Cerebral autoregulation in the ischemic penumbra of the stroke is grossly abnormal, and adequate systemic perfusion pressure is needed for blood flow and oxygen delivery. Rapid reduction of BP, even to levels within the hypertensive range, can be detrimental. Treatment of hypertension in acute ischemic stroke is dependent on the following conditions: 1) treatment with IV thrombolysis, 2) treatment with endovascular thrombectomy with successful reperfusion, 3) patients with SBP >220 mm Hg or DBP >120 mm Hg, and 4) comorbid conditions requiring treatment. For all other acute ischemic stroke patients, the advantage of lowering BP early to reduce death and dependency is uncertain.[8,9,17,18] It should be noted that early treatment of hypertension is indicated when required by comorbid conditions (eg, concomitant acute coronary event, acute HF, aortic dissection, postfibrinolysis symptomatic ICH, or preeclampsia/eclampsia).

Recommendation-Specific Supportive Text

1. The BP level that should be maintained in patients with acute ischemic stroke to ensure the best outcome is unknown. Observational studies conflict with an association between worse outcomes and lower BP.[1–3,19] No studies have addressed the treatment of low BP in patients with stroke. In a systematic analysis of 12 studies comparing the use of IV colloids and crystalloids, the odds of death or dependence were similar. Clinically important benefits or harms could not be excluded. There are no data to guide volume and duration of parenteral fluid delivery.[20] No studies have compared different isotonic fluids.
2. The RCTs of IV alteplase required the SBP to be <185 mm Hg and DBP <110 mm Hg before treatment and SBP <180 mm Hg and DBP <105 mm Hg for the first 24 hours after treatment.[4,5] Observational studies and meta-analyses suggest that the risk of hemorrhage after administration of alteplase is greater in patients with higher BPs and in patients with more BP variability.[21,22] The exact BP at which the risk of hemorrhage after IV alteplase increases is unknown. It is thus reasonable to target the BPs used in the RCTs of IV alteplase. ENCHANTED (Enhanced Control of Hypertension and Thrombolysis Stroke Study) showed that antihypertensive treatment to target SBP 130 to 140 mm Hg within 6 hours of stroke onset in patients treated with IV thrombolytic did not show improvement in outcome.[9]
3. Data from large observational studies and meta-analyses suggest that higher BP after endovascular thrombectomy, particularly for those who undergo successful reperfusion, is associated with worse functional outcomes.[6,7,23] The majority of the RCTs of endovascular thrombectomy for acute ischemic stroke protocolized an SBP target of <180 mm Hg after treatment. No RCT has studied a post-endovascular thrombectomy SBP target higher than 180 mm Hg.
4. Patients with severe hypertension (most commonly SBP/DBP >220/>120 mm Hg) were excluded from clinical trials evaluating BP lowering after acute ischemic stroke.[8–11] Rapid BP reduction has traditionally been advised for these cases, but the benefit of such treatment in the absence of comorbid conditions that may be acutely exacerbated by severe hypertension has not been formally studied, and the benefit of initiating or reinitiating treatment of hypertension within the first 48 to 72 hours is uncertain. Ideal management in these situations should be individualized, with an initial BP reduction of 15% a reasonable goal. Excessive drop in BP could result in complications, such as stroke progression, by compromising cerebral perfusion in penumbral tissue and AKI from renal hypoperfusion. There are no data to show that one strategy to lower BP is better than another after acute ischemic stroke.
5. Multiple RCTs and meta-analyses of these trials have consistently shown that initiating or reinitiating antihypertensive therapy within the first 48 to 72 hours after an acute ischemic stroke is safe, but this strategy is not associated with improved mortality or functional outcomes.[8,10,11,17,18] However, none of these trials included patients with extreme hypertension or coexistent indications for rapid BP reduction.
6. RCTs and meta-analysis of RCTs evaluating BP lowering after successful endovascular thrombectomy to date have shown either harm or no benefit.[12–14,24]

In BP TARGET (Blood Pressure Target in Acute Stroke to Reduce Hemorrhage After Endovascular Therapy), the rate of any and symptomatic ICH was similar between post endovascular thrombectomy SBP goals of 110 to 129 mm Hg and 130 to 185 mm Hg. The ENCHANTED-2 MT (Enhanced Control of Hypertension and Thrombectomy Stroke Study) comparing post-endovascular thrombectomy SBP goals of <120 mm Hg and 140 to 180 mm Hg was stopped early due to an increased rate of worse global disability in the <120-mm Hg group (OR: 1.53 [95% CI: 1.18-1.97]).[12] OPTIMAL BP (Enhanced Control of Hypertension and Thrombectomy Stroke Study), which compared post-endovascular thrombectomy SBP goals of <140 mm Hg versus 140 to 180 mm Hg, was also stopped early due to lower rates of improved outcomes at 90 days (modified Rankin scale score 0 to 2 of 39.4% in the <140-mm Hg group versus 54.4% in the 140- to 180-mm Hg group).[13] The BEST-II trial (Blood Pressure After Endovascular Stroke Therapy-II) showed that an SBP target of <140 mm Hg was potentially harmful based on the utility-weighted modified Rankin score, with a low probability of a future, larger trial showing benefit of post-endovascular thrombectomy BP lowering in a prespecified analysis.[14]

5.3.9.3. Secondary Stroke Prevention

Recommendations for Secondary Stroke Prevention
References that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In patients with hypertension who have experienced an ischemic stroke, transient ischemic attack (TIA), or ICH, treatment with a thiazide-type diuretic, ACEi, or ARB is recommended for lowering BP and reducing recurrent stroke and ICH risk.[1–3]
1	B-R	2. In patients with hypertension who have experienced an ischemic stroke, TIA, or ICH, an office SBP/DBP goal of <130/80 mm Hg is recommended to reduce the risk of recurrent stroke, ICH, and other vascular events.[1,3–5]
2a	B-R	3. In patients with no history of hypertension who have experienced an ischemic stroke, TIA, or ICH and have an average office SBP/DBP of ≥130/80 mm Hg, antihypertensive medication treatment can be beneficial to reduce the risk of recurrent stroke, ICH, and other vascular events.[5–7]

Synopsis

Each year in the United States, >750 000 adult patients experience a stroke, of which about 23% are recurrent strokes.[8] More than 75% of ischemic stroke or ICH survivors have hypertension.[9] Hypertension is the most important risk factor for stroke and ICH recurrence.[10,11] Yet, hypertension remains poorly controlled in the outpatient setting among these patients, particularly among Black and Hispanic patients.[12–14] For patients with prior stroke or TIA, there is concern that lower BP thresholds may increase the risk of stroke. New data from RCTs and large meta-analyses provide compelling evidence that neurologically stable patients with cerebrovascular disease benefit from an SBP/DBP goal of <130/80 mm Hg and that BP targets for stroke, ICH, and major vascular event prevention should be aligned with targets for prevention of other cardiovascular conditions. There is insufficient evidence to recommend a lower limit of BP within the normal range for patients with prior stroke or ICH. Like all patients with hypertension, antihypertensive drug regimens for those with cerebrovascular diseases should consider patient comorbidities, pharmacological agent class, and patient preference. The optimal timing for BP reduction after stroke is unclear; therefore, the recommendations in this section pertain to outpatient management of neurologically stable patients.

Recommendation-Specific Supportive Text

1. Thiazide-type diuretics, ACEis, and ARBs have demonstrated benefit in RCTs or systematic reviews of RCTs.[1,2,4,15,16] Although CCBs are recommended for the treatment of hypertension, there are limited data on their efficacy for secondary stroke prevention. However, the use of CCBs is acceptable for patients with stroke who require additional medication options.[1,17]
2. Data from 4 RCTs and recent meta-analyses support the benefit of treating patients with prior stroke or TIA to achieve a BP goal of <130/80 mm Hg. The RESPECT (Recurrent Stroke Prevention Clinical Outcome),[5] PAST-BP (Prevention After Stroke-Blood Pressure),[18] and PODCAST (Prevention of Decline in Cognition after Stroke Trial)[7] RCTs compared intensive control of BP (SBP targets <120 to <130 mm Hg) with standard BP control (SBP targets <140 to <150 mm Hg) in patients with prior cerebrovascular disease. These trials reported nonsignificant tendencies toward lower recurrent stroke rates in the intensive treatment groups. However, a meta-analysis of these trials showed a significant reduction in recurrent stroke risk with an intensive versus standard target (relative risk: 0.78 [95% CI: 0.64-0.96]). An independent Cochrane analysis of SPS3 (Secondary Prevention of Small Subcortical Strokes), PAST-BP, and PODCAST reported a trend toward benefit of intensive BP targets (pooled relative risk for recurrent stroke, 0.80 [95% CI: 0.63-1.00]).[1] In addition, the largest meta-analysis to date including >40 000 patients from 14 RCTs (including ischemic stroke, TIA, and

ICH) showed a significantly lower rate of recurrent stroke in patients with an achieved SBP of <130 mg Hg.[3] It should be noted that in subgroups of 2 large meta-analyses, the greatest benefit of tighter BP control was noted in patients with ICH as an index event.[3,5]

3. The recommended threshold BP of >130/80 mm Hg for starting antihypertensive medications is informed by the baseline BPs of patients with cerebrovascular disease studied in trials of BP treatment. Among the 4 RCTs comparing intensive and standard BP targets in patients with prior cerebrovascular disease, the RESPECT,[5] PAST-BP,[6] and PODCAST[7] trials included patients with baseline SBPs as low as 125 mm Hg. In PAST-BP,[6] approximately 50% of patients had baseline SBP <140 mm Hg. Similarly, in the PROFESS (Prevention Regimen for Effectively Avoiding Second Strokes) trial of >20 000 patients with ischemic stroke, approximately 33% of patients had baseline SBP <135 mm Hg.[19] The large number of subjects with prior stroke and SBP <140 mm Hg included in these trials supports the safety and efficacy of the use of antihypertensive medications in patients with SBP ≥130 mm Hg.

5.3.9.4. Mild Cognitive Impairment and Dementia

Recommendation for Prevention of Mild Cognitive Impairment and Dementia
Referenced studies that support the recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
1	A	1. In adults with hypertension, a goal of <130 mm Hg SBP is recommended to prevent mild cognitive impairment and dementia.[1–5]

Synopsis

Dementia affects the memory and other cognitive functions, behavioral functioning, and social abilities, impairing daily life and resulting in most nursing home placements. Prior studies estimate that more than 9 million Americans could have dementia by 2030 and nearly 12 million by 2040.[6] The prevalence of mild cognitive impairment, a transitional state between normal cognitive aging and dementia, is also expected to markedly increase.[7] Interventions that produce a 5-year delay in onset of dementia would likely decrease the number of cases of incident dementia and accompanying institutionalizations by about 50% after several decades.[8] Hypertension has been identified as a prevalent modifiable risk factor for cognitive decline and dementia.[9–12] Cerebrovascular disease, a complication of hypertension, is commonly present in Alzheimer disease and related forms of dementia, where it frequently co-occurs with beta-amyloid and tau neuropathology.[12,13] Hypertension is the primary risk factor for small-vessel ischemic disease and cortical white matter abnormalities[14–16] in the brain, which are highly predictive of cognitive decline and dementia.[17] Most observational studies and clinical trials have suggested that better control of SBP reduces Alzheimer disease and related dementias, with the strongest association for BP lowering in middle age.[18,19] These data support intensive BP treatment as an important strategy for the prevention of cognitive impairment and suggest some degree of persistent benefit on the development of cognitive impairment from even a few years of intensive treatment.

Recommendation-Specific Supportive Text

1. Meta-analyses of RCTs, excluding the 2 most recent large trials, have strongly supported a beneficial effect of BP reduction on dementia risk.[2,20,21] Of the 7 large trials finding a lower risk for dementia, the trials showing a reduction in dementia achieved relative SBP reductions of 7 to 21 mm Hg. The largest meta-analysis and 2 large recent BP-lowering trials each demonstrated a 12% to 19% reduction in dementia incidence; however, the reduction in SPRINT was not significant.[19,20,22] Early cognitive decline was reduced in participants without adjudicated incident dementia in the 2 largest RCTs (SPRINT and CRHCP [China Rural Hypertension Control Project]), each with a treatment goal of 120 mm Hg SBP.[20,22] New results from the SPRINT-MIND legacy follow-up show that unlike mortality, significant benefit in reducing the risk of incident mild cognitive impairment alone with or without dementia continued for at least 7 years.[4] A nonstatistically significant reduction in dementia risk remained, with each of these findings a result of only 3.5 years of intensive BP treatment. Other work has shown that the 12-mm Hg SBP reduction achieved in SPRINT rapidly dissipated after the trial was stopped.[23] Importantly, no RCT of BP lowering has demonstrated an adverse impact on dementia incidence or cognitive function, nor have the 2 large RCTs of BP lowering demonstrated harm, such as increase in overall adverse events, falls, fall-related fractures, or kidney failure, even at an SBP treatment goal of 120 mm Hg.[24]

5.3.10. Peripheral Artery Disease

Synopsis

Hypertension is present in 35% to 55% of patients at the time of their PAD diagnosis[1] and is the most common risk factor for PAD. Hypertension is associated with a longitudinal decline in ankle brachial index in adults >65 years of age.[2] Treatment of hypertension to a goal BP of <130/80 mm Hg in adults with PAD is optimal to reduce the risk of MACE, including stroke, MI, HF, and cardiovascular death. Historically, some concern has been

expressed that lower BP targets may compromise blood flow to an extremity with impaired perfusion caused by PAD and worsen symptoms.[3] However, to date, multiple studies have shown no deterioration in symptoms of claudication and functional status caused by antihypertensive treatments in adults with PAD.[4–6] Although no single antihypertensive medication appears to be more effective at treating hypertension in adults with PAD, cardiovascular benefits are shown with the use of ACEi or ARB, and these agents should be first line for adults with PAD and hypertension.[7,8] For additional information on the management of hypertension in adults with PAD, see Section 5.3 in the "2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/AVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease."[9]

5.4. Plan of Care for Hypertension

Recommendations for Plan of Care for Hypertension
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
Team-Based Care		
1	A	1. For adults with uncontrolled hypertension, a team-based care approach is recommended to achieve and maintain BP control.[1–4]
1	C-LD	2. For adults with uncontrolled hypertension, an evidence-based care plan utilizing HBPM, and team-based care that is responsive to addressing adverse SDOH, is recommended to achieve and maintain BP control.[5,6]
Framework in Clinical Practice to Improve Hypertension Control		
1	B-NR	3. For adults with uncontrolled hypertension, an integrated treatment model that includes accurate BP measurement, prompt treatment, patient engagement, and ongoing review of HBPM is recommended to improve BP control.[7–10]
Follow-Up After Initial BP Evaluation and Initiation of Antihypertensive Therapy		
1	B-R	4. Adults with uncontrolled hypertension placed on new or intensified medical therapy should have follow-up evaluations for medication adherence and response to treatment at monthly intervals until control is achieved.[11–13]
Health Information Technology		
1	B-R	5. For adults with uncontrolled hypertension, health information technology (HIT) by synchronous (eg, phone, video call) or asynchronous (eg, text, e-mail) communication is beneficial in improving BP control, access to care, and adherence to standards of care and should be incorporated in the management of hypertension, including the titration of BP medications.[14–17]
1	B-NR	6. In adults with undiagnosed or uncontrolled hypertension, use of the electronic health record (EHR) and patient registries is beneficial for screening and identification of hypertension to focus on those who need additional care.[15]
2a	B-R	7. In adults with uncontrolled hypertension, telehealth interventions can be useful to reduce BP[18–26] and improve office BP control.[19,21,23–26]

Synopsis

Team-based care is a health systems level organizational intervention that incorporates a trained multidisciplinary team and is frequently implemented as part of a multifaceted approach to improve hypertension outcomes using strategies outlined in Table 19.[1–3,27–36] Multidisciplinary teams can be effective in assessing and addressing individual social determinants of health, such as access to medications and other structural barriers to optimize patient-centered cardiovascular care for all patients with hypertension and reduce the disparities in hypertension control.[36] Delineation of individual team member roles based on knowledge, skill set, availability, and patient needs allows the primary care clinician more time to manage complex and critical issues.[27,31,37] Team-based care often requires organizational change and reallocation of resources.[27,38] Although cost-effective,[39] current payment models do not support reimbursement for hypertension care that is provided by health care team members other than physicians. A comprehensive care plan for hypertension should incorporate current best practices, including standardized treatment protocols, team-based care, and HBPM with clinical support, while considering the local environment, associated risk factors, and SDOH.[5,6,40] This personalized approach should integrate strategies to enhance medication adherence (SPC therapy),[5,41] utilize technology for self-management, and implement case management through a multidisciplinary team to effectively address the complexities of hypertension management.[1–3,5,6,27–35,37,38,40–45] Integration of HIT, including computerized clinical decision support systems like EHR and patient registries, facilitates large-scale queries to support population health by effective identification and management of patients with hypertension.

Telehealth interventions (Section 3.1.3, "Out-of-Office BP Monitoring") allow the exchange of medical information between patients and their health care team for chronic disease management at a distance by synchronous (eg, phone, video call) or asynchronous (eg, text, email) communication using Wi-Fi, Bluetooth, cellular, and/or mobile communication technologies ("mHealth"; mobile apps).[20,42,46,47] Effective telehealth interventions include proactive outreach by health care professionals to integrate remote BP data exchange with lifestyle education and medication management.[20,24,42,46–48] The frequency of follow-up depends on the stage of hypertension, target organ damage, medication use, and BP control.[49–52] Uncontrolled hypertension is the average BP above the patient's goal BP. Please refer to Table 4 and Section 3 ("Evaluation and Diagnosis") for nuances on accurate BP measurement.

Recommendation-Specific Supportive Text

1. The hypertension care team may include primary care clinicians, specialists, nurses, pharmacists, dieticians,

community health workers, or social workers (Table 19). RCTs and meta-analyses of RCTs of team-based hypertension care involving nurse or pharmacist intervention demonstrated reductions in SBP and DBP and/or greater achievement of BP goals when compared with usual care.[1–4,31,34,53–56] Systematic reviews of team-based care, including a review of studies that included nurses, pharmacists, and community health workers, showed reductions in SBP and DBP and improvements in BP control, appointment keeping, and hypertension medication adherence compared with usual care.[1,31,35,53,57] Team-based care interventions that include medication titration by a nonphysician health care clinician or titration by a physician had the greatest reduction in SBP (−7.1 and −6.2 mm Hg) compared with other implementation strategies.[56]

2. Studies demonstrate that implementing an evidence-based care plan for hypertension can lead to sustained reduction of BP and attainment of BP targets.[43,45] The care plan should take into account the local environment,[6] patient preferences, SDOH, and readiness for behavioral change,[58,59] with resources matched to the needs of each patient to promote health equity. Several RCTs have evaluated the effectiveness of team-based care on changes in BP and hypertension control for up to 12 months with case management provided by nurses or pharmacists.[43,44] These studies demonstrate that case management utilizing strategies such as individualized training and education,[44,60–62] home BP monitoring,[43] telenursing, and home visits[63] can improve hypertension control. Given that hypertension is a chronic disease requiring ongoing long-term care to prevent or delay complications,[43,61] consideration should be given to implementing longitudinal case management strategies to assist in health promotion, support medication adherence, foster and support behavioral change, and address comorbidities that impact BP control.[44,63] As HBPM is incorporated into the care plan, it is important to facilitate active collaboration[40] and relay of BP data back to the care team so that appropriate and timely advice can be provided to the patient.
3. A clinical framework including accurate BP measurement, timely initiation of pharmacotherapy, regular interval follow-up and therapeutic intensification for uncontrolled BP, active engagement and support of adults with hypertension, and ongoing data monitoring and reporting enables rapid and sustained improvement in hypertension control.[64] Using this approach, improvement in hypertension control has been observed in historically underresourced groups,[7–10] including those receiving care in resource-limited care settings.[8–10]
4. The addition of new medications or intensified dosing of current medications requires follow-up to monitor BP response and the potential for adverse effects. High-quality RCTs have successfully and safely developed strategies for follow-up, monitoring, and reassessment for management of BP from which recommendations can be made (Figure 7). Components of the follow-up evaluation should include assessment in the office, and when possible, outside of the office (eg, telehealth), for BP control, including evaluation for OH, adverse drug effects, adherence to medication and lifestyle therapy, need for additional therapeutic intensification of medication dosing, and indicated laboratory testing (eg, electrolytes, renal function, target organ damage).

Table 19. Responsibilities and Roles of the Hypertension Team

Hypertension Team Responsibilities	
Communication, shared decision-making, and care coordination among various clinical team members, the patient, and patient caregivers	
Effective use of evidence-based diagnosis and management guidelines	
Regular, structured follow-up mechanisms and reminder systems to monitor patient progress	
Medication adherence support and patient education about hypertension medication	
Medication initiation, addition, and titration using evidence-based treatment algorithms	
Use of evidence-based tools and resources designed to maximize self-management (including health behavior change, lifestyle modification, etc)	
Individual Hypertension Team Members	**Roles (examples)**
Primary care physician/cardiologist, physician assistant or associate/nurse practitioner/advanced practice nurse	Routine and complex hypertension care, managing primary care issues
Cardiologist/physician assistant or associate/nurse practitioner/advanced practice nurse	Routine and complex hypertension care, especially for patients with cardiac disease or high risk for major cardiovascular events
Nephrologist, endocrinologist, hypertension specialist	Management of complex hypertension care, especially due to secondary causes, and/or resistant hypertension
Nurse (including in-office, home care, internal and external population health personnel)	Accurate assessment of BP, medication reconciliation, patient education, self-management, lifestyle modification, and adherence
Clinical Pharmacist	Comprehensive medication management, identification of medication-related interactions, and educating patients on their medication regimen
Dietician	Ongoing patient-centered counseling to assess dietary habits and preferences and set and monitor goals for healthy lifestyle
Social Worker	Assess for psychosocial, cultural, and financial barriers and find solutions to overcome these barriers
Community health worker	Assess and address social determinants of health and identify and promote acceptable community-based resources to overcome these barriers

5. The implementation of HIT improves hypertension control and adherence to guidelines using clinical decision support pathways.[15,17] Hypertension control to lower home BP targets (<135/85 mm Hg) has shown to be greater after intervention via self-monitoring and telemonitoring (HBPM or ABPM, Section 3.1.3, "Out-of-Office BP Monitoring") compared with standard office-based care.[14–16] Self-monitoring is recommended for the ongoing management of hypertension in all patients willing to use it, and clinicians should consider readings obtained from self-monitoring in titrating medications and ruling out white-coat hypertension and masked hypertension.[48] In an RCT, SBP was lower in both self-monitoring and telemonitoring intervention groups compared with usual care with no difference between the self-monitoring and telemonitoring groups. Enhanced self-monitoring of BP paired with an advanced application was not shown to be superior to standard self-monitoring in BP control.[16] Further, additional medications were prescribed to individuals using self-monitoring or telemonitoring in the titration of antihypertensive medications.[14]
6. Health systems are developing and using patient registries and EHRs for large-scale queries to support population health management strategies by identifying undiagnosed or uncontrolled hypertension as ongoing quality improvement initiatives.[17] Multifaceted approaches studied to date include: 1) application of hypertension screening algorithms to EHR databases to identify at-risk patients; 2) contacting at-risk patients to schedule BP measurements; 3) monthly feedback to clinicians about at-risk patients who have yet to complete a BP measurement; and 4) electronic prompts for BP measurements whenever at-risk patients visit the clinic. The role of the EHR is paramount in supporting interventions in primary care and to maximize hypertension management in under-represented racial and ethnic groups. Some clinical interventions implementing clinical decision support systems and best practice alert applications in primary care clinics show promising results.[15]
7. RCTs and meta-analyses of RCTs of telehealth interventions demonstrate greater office SBP and DBP reductions[18–26,65] and a larger proportion of patients achieving hypertension control compared with individuals receiving usual clinic-based care without telehealth interventions, but results are mixed on improving medication adherence.[19–21,23–26,42,46,47] Telehealth interventions, including out-of-office BP monitoring using HBPM (Section 3.1.4, "ABPM and HBPM") with remote BP data transfer between the patient and health care staff, lifestyle education, and/or medication management, demonstrated greater BP lowering compared with usual clinic care alone.[19,22,48,66] Trial results are inconsistent for interventions solely using mobile apps, but a growing number of studies demonstrate significant BP reduction based on strengthening patients' self-management skills.[46,67,68] Limited telehealth RCTs have focused on under-represented racial and ethnic populations, with some demonstrating reduced BP among Black and Hispanic populations.[25,46] Hypertension telehealth interventions demonstrated significant BP reduction in patients with comorbid conditions (eg, diabetes, stroke); however, there are insufficient data on reduction of MACE.[46] Even as there is increasing use of hypertension telehealth interventions, significant barriers remain for equitable access to telehealth services, including patient internet access, digital literacy, equipment/infrastructure costs, clinical staffing/workflow, and integration with EHRs.[46,47] Additional studies are needed, particularly among high-risk underrepresented racial and ethnic populations.[46,47,69]

5.5. Hypertension and Pregnancy

Recommendations for Individuals With Hypertension and Pregnancy* Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. For individuals with hypertension who are planning a pregnancy or who become pregnant, labetalol and extended-release nifedipine are preferred agents to treat hypertension and minimize fetal risk.[1]
1	B-R	2. Individuals with hypertension who are planning a pregnancy or who become pregnant should be counseled about the benefits of low-dose (81 mg/day) aspirin to reduce the risk of preeclampsia and its sequelae.[2]
1	B-R	3. Pregnant individuals with SBP ≥160 mm Hg or DBP ≥110 mm Hg confirmed on repeat measurement within 15 minutes should receive antihypertensive medication (Table 23) to lower BP to <160/<110 mm Hg within 30 to 60 minutes to prevent adverse events.[3–7]
1	B-R	4. Pregnant individuals with chronic† hypertension (defined as prepregnancy hypertension or SBP 140 to 159 mm Hg and/or DBP 90 to 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.[1,8,9]
3: Harm	C-LD	5. 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.[10–14]

*ACOG diagnostic criteria and classification of hypertensive disorders of pregnancy are found in Tables 22 and 23.

†Chronic hypertension in pregnancy is defined as a preexisting diagnosis of hypertension or SBP ≥140 mm Hg and/or DBP ≥90 mm Hg on 2 occasions at least 4 hours apart before 20 weeks' gestation.

Synopsis

HDP are strongly associated with maternal and fetal/neonatal complications and are a leading cause of

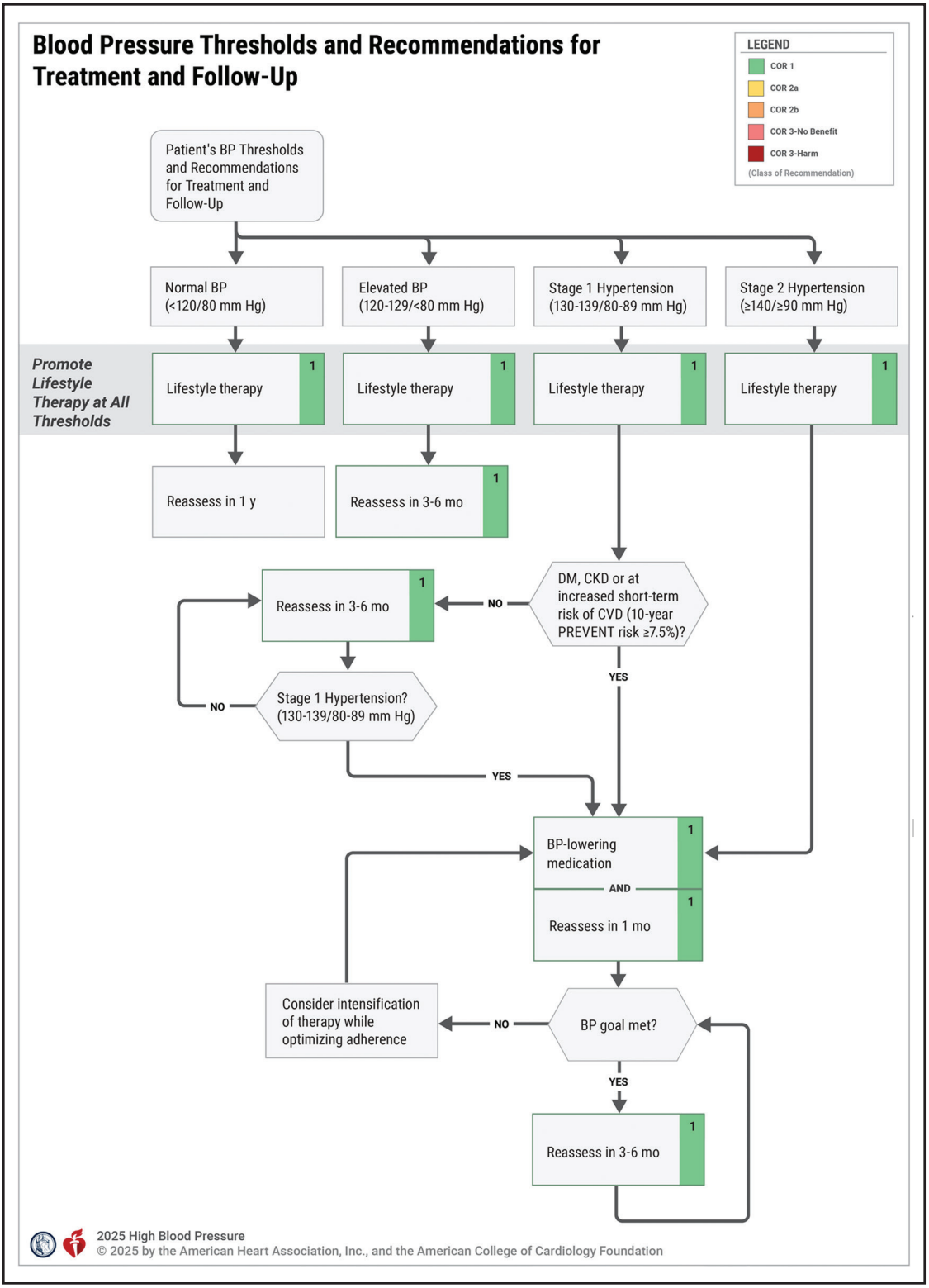

Figure 7. BP Thresholds and Recommendations for Treatment and Follow-Up.
BP indicates blood pressure; CVD, cardiovascular disease; DM, diabetes mellitus. Based on the PREVENT calculator.[52,70] Modified with permission from Whelton et al.[71] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

pregnancy-associated mortality. HDP are increasingly common in the United States, affecting 15.9% of deliveries, with the highest prevalence experienced by Black and American Indian and Alaska Native women,[15,16] women aged ≥35 years,[17,18] and women with obesity.[19]

The management of BP in pregnancy-capable individuals requires special considerations. The overarching goals of antihypertensive treatment during pregnancy are aimed at preventing severe hypertension and preeclampsia and optimizing maternal and fetal/neonatal clinical outcomes. Compared with the diagnostic criteria for hypertension in adults presented in this document, the American College of Obstetricians and Gynecologists (ACOG) defines hypertension in pregnancy as an SBP ≥140 mm Hg or DBP ≥90 mm Hg on 2 occasions at least 4 hours apart, and severe-range hypertension as sustained SBP ≥160 mm Hg or DBP ≥110 mm Hg with verification in 15 minutes to avoid treatment delays (Table 20).[6,20,21] Pregnant individuals with elevated BP are further classified as having 1 of the HDP based upon gestational age at diagnosis and the presence of target organ involvement (Table 21). Vascular and hemodynamic alterations in pregnancy result in a decline of BP by 10% in early pregnancy, reaching a nadir in the second trimester and slowly rising back to baseline by the end of the third trimester.[22] It is because of these alterations that the classification of HDP depends on gestational age, and the use of BP monitors that have been specifically validated for accuracy (www.validatebp.org) in pregnancy is advised.[23,24]

Recommendation-Specific Supportive Text

1. When antihypertensive therapy is indicated in individuals planning a pregnancy or who become pregnant, labetalol and extended-release nifedipine are the preferred first-line agents.[6,20] Among them, no specific agent is preferred because there is a lack of data supporting the use of 1 over the other, although nifedipine is dosed once daily, which may improve adherence.[3–5,25] In a meta-analysis, BB and CCB appear more effective than methyldopa for the prevention of severe hypertension.[1] Table 22 lists antihypertensive agents that can be used alone or in combination for chronic maintenance therapy in pregnant individuals. There are limited data available on the safety of amlodipine in pregnancy,[26–28] but it does not appear to be associated with a heightened risk of major congenital malformations.
2. Chronic hypertension, defined as high BP that predates pregnancy or is diagnosed before 20 weeks' gestation, is associated with a high risk of developing preeclampsia, a multiorgan system inflammatory syndrome that is thought to result from abnormalities in placental development, leading to placental ischemia and oxidative stress.[6] In a meta-analysis, daily low-dose aspirin taken during pregnancy after 12 weeks' gestation has been shown to significantly reduce the risk for preeclampsia in individuals at moderate or high risk compared with placebo (pooled relative risk: 0.85 [95% CI: 0.75-0.95]).[2] Aspirin use was also associated with significantly reduced risk for preterm birth, small-for-gestational age/intrauterine growth restriction, and perinatal mortality in pregnant persons at increased risk for preeclampsia[2] without increased risk of postpartum hemorrhage. Only individuals with no prior adverse events or allergy to aspirin should be advised to take low-dose aspirin for preeclampsia prevention.
3. Severe hypertension in pregnancy is defined as SBP ≥160 mm Hg or DBP ≥110 mm Hg. When left untreated, it can result in maternal stroke, renal insufficiency or kidney failure, MI, HF, placental abruption, preterm birth, fetal growth restriction, and maternal death from intracerebral hemorrhage and/or stillbirth or perinatal death. Table 23 describes the preferred agents, doses, and routes of administration for the expeditious treatment of severe-range hypertension in pregnant individuals. Immediate-release oral nifedipine has been shown in a meta-analysis to be associated with faster time to achieve target BP specifically in pregnancy, although it is not generally recommended for the acute treatment of other types of hypertension.[3]
4. A Cochrane review and meta-analysis of 58 trials evaluating the treatment of nonsevere-range hypertension in pregnancy (SBP <160 mm Hg and DBP <110 mm Hg) concluded that the use of antihypertensive medications reduced the risk of severe-range hypertension (risk ratio: 0.49; 95% CI: 0.40-0.60) but did not significantly reduce the risk of preeclampsia.[1] However, the CHAP (Chronic Hypertension and Pregnancy) trial, which randomized 2408 women with chronic hypertension to receive antihypertensive medications to reach target BP <140/90 mm Hg compared with no treatment unless SBP ≥160 mm Hg or DBP ≥105 mm Hg, demonstrated an 18% absolute risk reduction in the primary composite endpoint of preeclampsia with severe features, preterm birth, placental abruption, or fetal/neonatal death without evidence of increased risk of fetal growth restriction.[8]
5. BP management during pregnancy is complicated by the fact that many commonly used antihypertensive agents are contraindicated because of potential harm to the fetus. Therapeutic classes are not universally recommended or avoided because potential toxicity differs among agents within classes. Atenolol[11] has been associated with growth restriction and lower fetal weight and should be avoided in pregnancy.[12] This is likely not a class effect, as other beta-1-selective agents like metoprolol have not demonstrated similar associations with growth restriction, and labetalol is a preferred agent with the most reassuring fetal safety data. ACEi, ARB, and direct renin inhibitors are

Table 20. Classification of Hypertensive Disorders of Pregnancy[20]

Condition	Definition
Chronic hypertension	Diagnosis prior to pregnancy or at <20 wks' gestation
Gestational hypertension	De novo hypertension at ≥20 wks' gestation in the absence of proteinuria or other signs of preeclampsia
Preeclampsia	Gestational hypertension with proteinuria or other maternal end-organ dysfunction including neurologic findings, pulmonary edema, hematologic findings, acute kidney injury, hepatic dysfunction (Section 5.5.2 "Preeclampsia and Eclampsia, Including Preeclampsia Superimposed on Chronic Hypertension")
Preeclampsia superimposed on chronic hypertension	Preeclampsia in a woman with a history of hypertension before pregnancy or before 20 weeks' gestation

Table 21. ACOG Diagnostic Criteria for Hypertension in Pregnancy[20]

Condition	Definition
Hypertension in pregnancy	SBP ≥140 mm Hg and/or DBP ≥90 mm Hg
Severe-range hypertension	SBP ≥160 mm Hg and/or DBP ≥110 mm Hg

ACOG indicates American College of Obstetricians and Gynecologists; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

fetotoxic in the second and third trimesters of pregnancy due to their effects on the developing renal system, leading to oligohydramnios and AKI.[10,13,14] Adverse effects in the first trimester may be secondary to hypertension or medications. Based on the mechanism of action and data from animal studies, fetal exposure to spironolactone may cause feminization of a male fetus or growth restriction and is generally not recommended,[29–32] even for individuals with primary aldosteronism. The feminizing effects appear to be dose-dependent. There are few human data on nitroprusside safety in pregnancy, but data from animal studies show that nitroprusside crosses the placenta and may lead to fetal cyanide toxicity. Following delivery, many antihypertensive medications can be safely used again. LactMed[33] is a searchable database of medication safety for lactating individuals.[34,35]

5.5.1. Gestational Hypertension

Synopsis

Gestational hypertension is the de novo development of hypertension after 20 weeks' gestation in the absence of new proteinuria or target organ damage (Table 20).[1] Gestational hypertension is associated with an increased risk of maternal and fetal/neonatal adverse events, and up to 30% of women with gestational hypertension ultimately develop preeclampsia.[2] Following delivery, individuals with gestational hypertension have an increased risk of future hypertension and CVD. Most RCTs examining BP targets for pregnant individuals with gestational hypertension have been small and of poor to moderate quality. The highest-quality randomized trial that included women with nonproteinuric hypertension examined tight versus less-tight DBP targets (85 mm Hg and 100 mm Hg, respectively) and demonstrated a reduction in severe maternal hypertension with tight DBP control.[3,4] There were no other significant differences in maternal, fetal, or neonatal complications or pregnancy loss between treatment groups. In post-hoc analyses, the development of severe hypertension was also associated with an increased risk of pregnancy loss, neonatal intensive care unit admission, preterm delivery, and low birthweight.[4] Current treatment recommendations by ACOG in the 2020 Practice Bulletin advocate that individuals with gestational hypertension who present with severe-range blood pressures, which is defined as persistent SBP ≥160 mm Hg or DBP ≥110 mm Hg, be managed with the same approach as those with preeclampsia and severe-range blood pressures, highlighting the overlap in risks associated with both of these HDP (Table 23).

5.5.2. Preeclampsia and Eclampsia, Including Preeclampsia Superimposed on Chronic Hypertension

Synopsis

Preeclampsia, a multiorgan system inflammatory syndrome, is an HDP characterized by hypertension, as well as proteinuria or target organ dysfunction (Table 24).[1] Preeclampsia also develops in 20% to 50% of individuals with chronic hypertension and is termed *superimposed preeclampsia* in that scenario, which often presents as an increase in baseline hypertension or proteinuria. In an individual with preeclampsia, the development of severe features or hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome are associated with increased rates of maternal and fetal/neonatal morbidity and mortality. Eclampsia, the occurrence of convulsive seizures, is one of the most severe forms of preeclampsia. Both preeclampsia and eclampsia can occur before, during, or after delivery, and magnesium sulfate in addition to antihypertensive medications are the mainstay of treatment. Low-dose aspirin is the only routinely recommended intervention that has been demonstrated to reduce the risk of preeclampsia and its sequelae when taken from 12 weeks of gestation in pregnant people at moderate and greater risk.[2–4] Pravastatin has been investigated in small studies as a potential therapy for the treatment of preeclampsia, but larger prospective studies are needed to confirm safety and efficacy.[5] The measurement of the antiangiogenic markers soluble fms-like tyrosine kinase -1 (sFlt-1), placental growth factor (PlGF), and their ratio is emerging as a diagnostic test with high

Table 22. Common Oral Antihypertensive Agents in Pregnancy

Drug	Dosage	Comments
Labetalol	200-2400 mg/d orally in 2 to 3 divided doses. Commonly initiated at 100-200 mg twice daily.	Potential bronchoconstrictive effects. Avoid in women with asthma, preexisting myocardial disease, decompensated cardiac function, and heart block and bradycardia.
Nifedipine	30-120 mg/d orally of an extended-release preparation. Commonly initiated at 30-60 mg once daily (extended release).	Do not use sublingual form. Immediate-release formulation should generally be reserved for control of severe, acutely elevated blood pressures in hospitalized patients. Should be avoided in tachycardia.
Methyldopa	500-3000 mg/d orally in 2 to 4 divided doses. Commonly initiated at 250 mg 2 or 3 times daily.	Safety data up to 7 y of age in offspring. May not be as effective as other medications, especially in control of severe hypertension. Use limited by side effect profile (sedation, depression, dizziness).
Hydrochlorothiazide	12.5-50 mg daily	Second- or third-line agent.

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IM indicates intramuscular; and IV, intravenous.

negative predictive value to rule out preeclampsia.[6–9] To date, the heterogeneity in prospective studies limits definitive conclusions about their clinical utility for diagnosing preeclampsia.

5.5.3. Short- and Long-Term Follow-Up of Pregnancy-Associated Hypertension

Synopsis

BP measurement and medication titration in the early postpartum period should be individualized and patient centered. ACOG recommends a BP check for individuals with an HDP within 3 to 10 days of discharge,[1] and HBPM has been shown to improve BP ascertainment. When combined in a team-based approach, including medication self-management and telehealth, HBPM for postpartum individuals with a history of HDP has been associated with lower BP and improved measures of cardiac structure and function at 6 and 9 months' postpartum compared with usual care.[2,3] These remote strategies may also help compensate for racial disparities in office-centric follow-up strategies, although there is insufficient evidence to definitively confirm reduction of maternal morbidity or mortality or racial disparity outcomes.[4] Individuals with a history of gestational hypertension and preeclampsia are at increased risk for the development of CKM risk factors, including chronic hypertension and overt cardiovascular and cerebrovascular morbidity and mortality that often occurs prematurely.[5–7] Much of this increased risk is mediated through the development of chronic hypertension; thus, early detection, diagnosis, and management of hypertension in this high-risk group is essential. Postpartum individuals with a history of pregnancy-associated hypertension in whom BP elevations resolve and antihypertensive medications are discontinued are encouraged to have their BP measured at least annually.[8] HDP are also recognized as sex-specific risk enhancers that should be taken into consideration when stratifying individuals and discussing the initiation of a statin for primary prevention of CVD.[9,10] A discussion of effective contraception in pregnancy-capable individuals with chronic hypertension being treated with potentially teratogenic medications is essential.[11–13] Barring no medical contraindications, individuals with a history of HDP should be educated about the benefits of low-dose aspirin and prescribed low-dose aspirin to be taken starting at 12 weeks of gestation during subsequent pregnancies to reduce the risk of preeclampsia.

Table 23. Antihypertensive Agents Used for Urgent Blood Pressure Control in Pregnancy

Drug	Dose	Comments	Onset of Action
Labetalol	10-20 mg IV, then 20-80 mg every 10-30 min to a maximum cumulative dosage of 300 mg; *or* constant infusion 1-3 mg/min IV	Tachycardia is less common with fewer adverse effects. Avoid in women with asthma, preexisting myocardial disease, decompensated cardiac function, and heart block and bradycardia.	1-2 min
Hydralazine	5 mg IV or IM, then 5-10 mg IV every 20-40 min to a maximum cumulative dosage of 20 mg; *or* constant infusion of 0.5-10 mg/h	Higher or frequent dosage associated with maternal hypotension, headaches, and abnormal fetal heart rate tracings; may be more common than other agents.	10-20 min
Nifedipine (immediate release)	10-20 mg orally, repeat in 20 min if needed; then 10-20 mg every 2-6 h; maximum daily dose is 180 mg	May observe reflex tachycardia and headaches.	5-10 min

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IM indicates intramuscular; and IV, intravenous.

Table 24. Diagnostic Criteria for Preeclampsia

Blood pressure	SBP ≥140 mm Hg or DBP ≥90 mm Hg on 2 occasions at least 4 h apart after 20 wks of gestation in a woman with previously normal BP *or* SBP ≥160 mm Hg or DBP ≥110 mm Hg (severe hypertension can be confirmed within a short interval [min] to facilitate timely antihypertensive therapy).
AND	
Proteinuria	≥300 mg per 24-h urine collection (or this amount extrapolated from a timed collection) *or* Protein/creatinine ratio ≥0.3 *or* Dipstick reading of 2+ (used only if other quantitative methods are not available)
OR in the Absence of Proteinuria, New Onset Hypertension With the New Onset of Any of the Following:	
Thrombocytopenia: Platelet count <100 × 10^9/L	
Renal insufficiency: Serum creatinine concentrations >1.1 mg/dL or a doubling of serum creatinine concentration in the absence of other renal disease	
Impaired liver function: Elevated blood concentration of liver transaminases to twice normal concentration	
Pulmonary edema	
New-onset headache unresponsive to medication and not accounted for by the alternative diagnoses or visual symptoms	

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BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

5.6. Resistant Hypertension and Renal Denervation

Recommendations for Resistant Hypertension and Renal Denervation
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
Resistant Hypertension		
1	B-NR	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.[1–5]
1	B-R	2. In adults with uncontrolled resistant hypertension despite optimal treatment with first-line antihypertensive therapy (ie, a combination of ACEi or ARB plus CCB and thiazide-like diuretic [chlorthalidone or indapamide] and with an eGFR of ≥45 mL/min/1.73 m^2), addition of a MRA is recommended to control BP.[6,7]
2a	B-NR	3. In adults with uncontrolled resistant hypertension who cannot tolerate or have contraindications to MRA, the addition of one of the following agents or classes—amiloride, BBs, alpha-blockers, central sympatholytic drugs, dual endothelin receptor antagonists, or direct vasodilators—is reasonable to control BP.[8–11]
Renal Denervation		
2b	B-R	4. In carefully selected patients with systolic and diastolic hypertension (office SBP 140-180 mm Hg and DBP ≥90 mm Hg) and eGFR ≥40 mL/min/1.73 m^2 who have resistant hypertension despite optimal treatment, or intolerable side effects to additional antihypertensive drug therapy, renal denervation (RDN) may be reasonable as an adjunct treatment to BP medications and lifestyle modification to reduce BP.[12–14]
1	B-NR	5. All patients with hypertension who are being considered for RDN should be evaluated by a multidisciplinary team with expertise in resistant hypertension and RDN.[12–14]
1	C-EO	6. 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.

Synopsis

Resistant hypertension is defined as BP above goal despite treatment with 3 antihypertensive medications with complementary mechanisms of action, including a diuretic at maximally tolerated doses or BP at goal but requiring ≥4 medications (Figure 8).[15] Based on the current BP goal of <130/80 mm Hg, the prevalence of resistant hypertension is approximately 8.5% to 20% among hypertensive US adults.[16–18] Multiple cohort studies have identified common risk factors for resistant hypertension, including older age, obesity, CKD, and diabetes.[15,19] Resistant hypertension is more common in Black populations, which may be related to adverse social factors, including living in a professional shortage area or disadvantaged neighborhood and clinical inertia.[20] Patients with resistant hypertension are known to have at least a 50% higher risk of MI, stroke, end-stage kidney disease, and cardiovascular death than adults with hypertension without resistance to treatment.[21–23] Evaluation of resistant hypertension requires exclusion of pseudoresistance, including inaccurate BP measurement (Section 3.1.3, "Out-of-Office BP Monitoring"), use of interfering medications (Section 5.2.6, "Medication Interactions"), white-coat hypertension via out-of-office BP monitoring (Sections 3.1.3, "Out-of-Office BP Monitoring," and 3.2.2, "White-Coat Hypertension and Masked Hypertension, and White-Coat Effect and Masked Uncontrolled Hypertension"), and medication nonadherence (Section 5.2.5, "Antihypertensive Medication Adherence Strategies"). Routine measurement of out-of-office BP is an important component of resistant hypertension management as both home BP and 24-hour ABPM are shown to be superior to office BP in predicting cardiovascular events.[24,25] Screening for secondary hypertension (Section 3.2.3, "Secondary Forms of Hypertension") should be performed because, depending on the specific cause, these conditions require a distinct management strategy.

RDN is an additional option to consider in managing resistant hypertension. In the absence of antihypertensive medications, RDN induced a reduction in 24-hour or daytime ambulatory SBP by 4 to 6 mm Hg during a follow-up duration of 2 to 3 months.[26–28] In the pres-

ence of a 2- to 5-agent antihypertensive drug regimen or resistant hypertension, the efficacy of newer-generation devices appears variable. While some trials showed a small but significant reduction in 24-hour ambulatory SBP by 3 to 5 mm Hg over the sham arm,[13,14] others failed to reach their primary endpoint.[29–31] Although broader indications are approved for the RDN devices by the FDA, given the relatively short duration of follow-up in clinical trials with modest BP-lowering effects and the absence of CVD outcome trials, RDN should not be considered as a curative therapy for hypertension or full replacement for antihypertensive drugs.

Recommendation-Specific Supportive Text

1. Approximately 20% of adults with hypertension reported regular use of over-the-counter or nonprescription medications that may directly raise BP or interfere with antihypertensive drug efficacy, such as NSAIDs or nasal decongestants (Table 17).[2] These medications are associated with uncontrolled BP and should be reviewed during evaluation of patients with resistant hypertension.[2] Some prescription drugs are known to elevate BP and should be replaced with alternative agents that avoid hypertensive side effects, if possible; however, in some settings, such as the treatment of malignant diseases, the contributing medication should be continued if hypertension can be controlled. Secondary hypertension is more common among adults with resistant hypertension, particularly primary aldosteronism, OSA, renal parenchymal disease, and renovascular disease.[1] Screening for secondary hypertension is discussed in Section 3.2.3 ("Secondary Forms of Hypertension").
2. Antihypertensive drug therapy should start with a combination of an ACEi or ARB, a CCB, and a diuretic.[15] Replacing thiazide-type diuretics (eg, HCTZ or bendroflumethiazide) with thiazide-like diuretics (eg, chlorthalidone and indapamide) may offer additional BP reduction[32,33] and cardiovascular protection among patients with previous MI or stroke. [34] RCTs have shown that addition of spironolactone (25-50 mg/day) as the fourth drug reduced home and 24-hour SBP by 6.6 to 8.7 mm Hg when compared with placebo in patients with resistant hypertension and eGFR ≥45 mL/min/1.73 m^2.[6,7] The reduction in BP was greater than with addition of doxazosin or bisoprolol.[6] The magnitude of reduction in 24-hour systolic and diastolic BP was greater with spironolactone than clonidine in a separate clinical trial.[8] Nevertheless, 4% to 40% of adults with resistant hypertension cannot tolerate spironolactone due to hyperkalemia or antiandrogenic side effects.[35–38] Eplerenone, a more selective steroidal MRA that avoids the antiandrogenic side effects but may cause hyperkalemia, is a potential alternative to spironolactone, but RCTs have not demonstrated reduction of home BP or 24-hour BP at doses between 25 and 100 mg daily when compared with placebo, and effective treatment may require higher dosages.[39–41] Use of nonsteroidal MRA for treating resistant hypertension in patients with moderate to advanced CKD has not been tested in a clinical trial but may be considered in selected patients with close monitoring of serum potassium.
3. When spironolactone or eplerenone are not tolerated due to side effects or cost, amiloride (10-20 mg) has been shown to be as effective as spironolactone in adults with resistant hypertension.[42] Other alternative fourth- and fifth-line drug therapies include BBs, alpha blockers, central sympatholytic drugs, and direct vasodilators.[6,8,9,11,43] However, direct vasodilators such as hydralazine and minoxidil should be used in combination with a BB and a loop diuretic given their effects on sympathetic tone, sodium reabsorption, and fluid retention.[44] Aprocitentan, a dual endothelin A and B receptor antagonist, was shown to reduce 24-hour ambulatory SBP by 4 to 6 mm Hg compared with placebo in adults with resistant hypertension when added to a CCB, RAS inhibitor, and HCTZ. Aprocitentan has not been directly compared with spironolactone in the treatment of resistant hypertension, and the side effects of leg edema and fluid retention (9%-18%) may be prohibitive in some patients.[45]
4. Almost all RDN trials included only patients with elevation in both systolic and diastolic BP and eGFR of at least 40 mL/min/1.73 m^2.[13,14,26–28,46] The benefit of RDN for isolated systolic hypertension or advanced CKD remains uncertain. In addition, only patients with suitable renal anatomy with artery diameters between 3 and 8 mm were included in the trials, while presence of preexisting renal artery abnormalities, such as fibromuscular dysplasia, renal artery stenosis, renal stent, and renal artery aneurysm were excluded. Among patients with resistant hypertension, the magnitude of SBP reduction achieved by RDN was shown to be inferior to or similar to the addition of spironolactone as the fourth agent in 2 RCTs[38,47]; however, between 10% and 40% of patients in the trials[36,38] could not tolerate spironolactone. Given the modest BP-lowering effects of RDN over the sham arm or addition of spironolactone, RDN should be reserved for adults with hypertension who develop intolerable side effects to optimal antihypertensive regimens. Patient selection should be made in the same manner as used in clinical trials to maximize clinical outcomes while minimizing potential complications (Table 25).

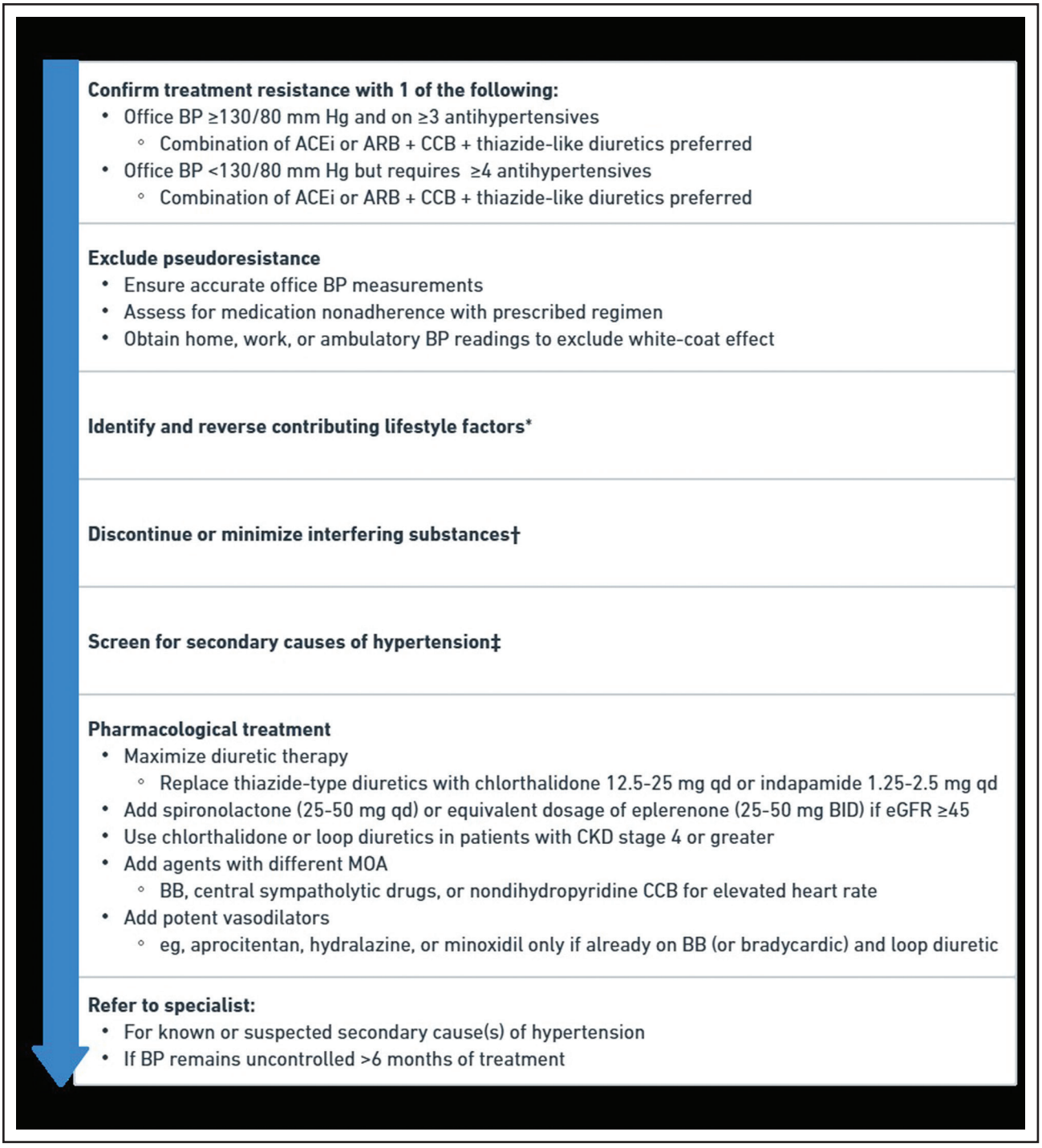

Figure 8. Resistant Hypertension: Diagnosis, Evaluation, and Treatment.
*Please refer to Section 5.2, on lifestyle factors. †Please refer to Table 11 for a complete list of drugs that elevate BP. ‡Please refer to Section 3.2.3, on secondary hypertension, and Subsections 3.2.3.1, 3.2.3.2, and 3.2.3.3. ARB indicates angiotensin receptor blocker; BB, beta blocker; BP, blood pressure; BID, 2 times daily; CCB, calcium channel blocker; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; mo, month; MOA, mechanisms of action; NSAIDs, nonsteroidal anti-inflammatory drugs; OSA, obstructive sleep apnea; qd, daily; and SBP, systolic blood pressure. Modified with permission from Whelton et al.[54] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc. Adapted with permission from Calhoun et al.[55] Copyright 2008 American Heart Association, Inc.

5. Potential candidates for RDN are recommended for evaluation by a hypertension specialist with expertise in screening for secondary hypertension or conditions in which RDN is inappropriate and an interventionalist with sufficient training in performing the specific procedure and managing procedural complications to evaluate for potential eligibility and procedural contraindications.

Secondary hypertension that may be directly treated, white-coat hypertension, and the presence of supine hypertension with OH were exclusion criteria in most RDN trials; therefore, evaluation should include measurement of 24-hour ambulatory BP and orthostatic vital signs in addition to screening for secondary hypertension. The presence of renal artery disease (stenosis, dissection, renal stenting) is considered a contraindication to the procedure. After RDN, it is estimated that the risk of renal artery stenosis requiring intervention is approximately 0.2% per year, with the highest risk within the first 6 months.[48] Thus, surveillance for renal artery stenosis or dissection using noninvasive imaging studies (eg, duplex Doppler, computed tomography angiogram, or magnetic resonance angiography) is suggested after RDN.

6. Shared medical decision-making with patients regarding the procedural risks and potential cardiovascular benefits from lowering BP is essential to ensure the outcome meets the patient's expectations. Predictors of BP response to RDN have not been consistently demonstrated among clinical trials.[49] Only 60% to 70% of patients undergoing RDN experienced a meaningful reduction in ambulatory SBP of at least 5 mm Hg in clinical trials.[12,50] RDN is currently performed strictly via the femoral artery approach, with the immediate risk associated with an RDN procedure not significantly greater than the risk associated with femoral access alone.[51–53] Due to the risk for renal artery stenosis after the procedure, patients will require ongoing surveillance imaging.

Table 25. Patient Selection for Renal Denervation

Resistant hypertension OR uncontrolled hypertension*
• Patients with stage 2 hypertension (with both office SBP ≥140 mm Hg and office DBP ≥90 mm Hg) in whom BP is not at goal despite taking ≥4 antihypertensive medications at optimal dosages (ACEi/ARB +CCB +thiazide-type diuretics, and MRA)[38,47] • Patients with stage 2 hypertension (with both office SBP ≥140 mm Hg and office DBP ≥90 mm Hg) who are unable to take antihypertensive medications at the optimal dosages or additional medications[11,12,14]
Contraindications[13,14,26–28,46]
• Neurogenic orthostatic hypotension • Pregnancy • Fibromuscular dysplasia • Stented renal artery • Renal artery aneurysm • Significant renal artery stenosis • Known kidney or secreting adrenal tumors

*After evaluation by a multidisciplinary team to screen for secondary hypertension and contraindications and following a shared decision-making process.[49]

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DBP, diastolic blood pressure; MRA, mineralocorticoid receptor antagonist; and SBP, systolic blood pressure.

6. COMPLICATIONS OF MANAGEMENT

6.1. Management of OH

Recommendations for Management of OH
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In adults with hypertension, improved BP control is recommended to reduce the risk for OH.[1–4]
2a	A	2. In adults receiving intensive BP-lowering therapy with asymptomatic OH, treatment with a goal of SBP <130 mm Hg is reasonable due to increased CVD and mortality benefit.[3,5]
2a	B-R	3. In adults with hypertension initiating treatment or adding medication with a goal of SBP <130 mm Hg, assessment for symptomatic OH is reasonable to detect other chronic conditions.[1–4,6,7]

Synopsis

Emerging evidence for the benefits of intensive versus standard BP treatment among the general population of middle- and older-aged adults has raised questions about the approach to patients with OH. OH affects an estimated 7% to 10% of community-dwelling adults with hypertension, especially older adults, and is predictive of adverse health outcomes, including CVD events.[7–11] Institutionalized older adults (age >65 years) have a much higher prevalence of OH and are not included in the scope of these recommendations, nor are persons with neurologic etiologies of OH, such as Parkinson disease and other autonomic neuropathies. OH is also associated with antihypertensive medication and specific classes of medication use.[6,7,12–15] These association studies led to recommendations for screening to identify OH prior to initiation or intensification of antihypertensive treatment and for monitoring of hypotension-related safety during treatment. Concerns about worsening OH have also contributed to advice against more intensive BP treatment, particularly among older adults, and for deprescribing antihypertensive medications.[16,17] Contrary to this perspective that intensive BP therapy increases risk of hypotension-associated adverse events, evidence from RCTs demonstrates no association between OH and intensive BP treatment using first-line antihypertensive medication classes.[1–3] However, because antihypertensive agents may sometimes unmask OH in patients with an underlying autonomic or other impairment, thoughtful assessment is warranted. Taken together, these results support the assessment for OH symptoms as helpful in the management of adults with hypertension.

Recommendation-Specific Supportive Text

1. Individual analyses of large randomized BP-lowering trials, plus a meta-analysis of several well-conducted

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hypertension trials (31 043 participants with 275 098 assessments for OH), have together shown that more intensive BP treatment and active antihypertension treatment lower the risk for OH.[1–3] In SPRINT, there was an increase in self-reported syncope for intensively treated participants; however, the intensively treated group experienced no increase in falls or injurious falls but rather a nonstatistically significant decrease in injurious falls. This finding was the same for the intensively treated arm in the CRHCP (goal for both trials <120 mm Hg).[4,18]

2. The impact of OH on the CVD and mortality benefit from intensive BP control in the SPRINT trial found no difference in the risk reduction for CVD or all-cause mortality, regardless of OH status, and no evidence for harm among those with standing hypotension (SBP <110 mm Hg).[3] A similar post-hoc analysis of the NAILED (Nurse-Based Age-Independent Intervention to Limit Evolution of Disease) study population (n=814, 35% experiencing OH at least once) showed that intensification of BP control was not associated with an increased risk of cardiovascular events or death in this stroke/TIA population.[5] Systematic titration of antihypertensive treatment did not increase the prevalence of OH compared with usual care. Thus, there is emerging evidence that OH does not reduce the gains of intensive antihypertensive treatment.
3. Assessment for OH prior to initiation of treatment is equitable as this was part of the eligibility process for the most valid trials of BP lowering.[1–4,18] An assessment for OH in symptomatic patients, particularly after initiation of treatment or adding a new class of antihypertensive medication, is acceptable to detect unmasked autonomic system dysfunction or other acute or chronic conditions.[6,7]

6.2. Hypertensive Emergencies and Severe Hypertension in Nonpregnant and Nonstroke Patients

Recommendations for Hypertensive Emergencies and Severe Hypertension in Nonpregnant and Nonstroke Patients* References that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	B-NR	1. In adults with a hypertensive emergency (BP >180 and/or >120 mm Hg and evidence of acute target organ damage), admission to an intensive care unit is recommended for continuous monitoring of BP and target organ damage and for consideration of parenteral administration of appropriate therapy (Tables 26 and 27, Figure 9).[1–3]
1	C-LD	2. For adults with a hypertensive emergency related to a compelling condition (eg, acute aortic syndrome or acute aortic dissection), SBP should be reduced to <140 mm Hg for most conditions and to <120 mm Hg in aortic dissection during the first hour, while monitoring for other target organ dysfunction.[4–7]
1	C-LD	3. For adults with a hypertensive emergency but without a compelling condition, SBP should be reduced with oral or parenteral therapy by no more than 25% within the first hour; then, if stable, to <160/100 mm Hg within the next 2 to 6 hours; and then cautiously to 130 to 140 mm Hg during the next 24 to 48 hours to limit target organ injury.[2,8,9]
3: Harm	B-NR	4. 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 IV or oral antihypertensive medications are not recommended to acutely reduce BP.[8,10,11]

*Hypertensive emergencies in patients with acute ICH and acute ischemic stroke are discussed in Section 5.3.9 ("Cerebrovascular Disease") and in pregnant adults in Section 11.5 ("Hypertension and Pregnancy").

Synopsis

Hypertensive emergencies are defined as severe elevations in BP (>180/120 mm Hg) associated with evidence of acute target organ damage. Patients with hypertensive emergencies experience a high in-hospital mortality rate of 10% with a 1-year cardiovascular morbidity and mortality rate of 20% to 30%.[12,13] Common forms of acute hypertension-related target organ damage include acute HF/pulmonary edema, neurologic disorders (encephalopathy, ICH, acute ischemic stroke), and AKI, with aortic dissection the least common presentation.[12] Hypertensive emergencies demand immediate reduction of BP to prevent or limit further target organ damage. However, the rapid correction of BP in patients with longstanding hypertension to normal range may result in vital organ hypoperfusion due to loss of autoregulation.[6,7] In contrast, patients with severe hypertension without evidence of acute target organ damage (previously called hypertensive urgency) should not have aggressive BP lowering in the short-term or be given parenteral antihypertensive drug therapy. Reinstitution or intensification of oral antihypertensive medications, preferably in the outpatient setting, is recommended for these patients.

Recommendation-Specific Supportive Text

1. There is no RCT evidence that antihypertensive drugs reduce morbidity or mortality in patients with hypertensive emergencies.[3] There is also no high-quality RCT evidence to inform clinicians as to which first-line

antihypertensive drug class provides more benefit than harm in hypertensive emergencies. This lack of high-quality RCT evidence is related to the small size of trials, lack of double-blinding design, lack of long-term follow-up, and failure to report outcomes. The therapeutic goal is to minimize target organ damage safely by rapid recognition of the problem and early initiation of appropriate antihypertensive treatment. To achieve rapid BP control and avoid large swings in BP, continuous infusion of short-acting titratable antihypertensive agents is often preferable in the intensive care setting. Antihypertensive agents available for the treatment of hypertensive emergencies are shown in Tables 26 and 27. Clinical trials suggested that IV nicardipine is more effective than labetalol in reaching short-term BP target, while clevidipine was shown to induce faster reduction in BP than nicardipine.[1,2] However, selection of an antihypertensive agent should be based on the drug's pharmacology, underlying mechanisms of hypertension, degree of progression of target organ damage, the desirable rate of BP decline, and the presence of comorbidities.

2. Other than for stroke/ICH (Section 5.3.9, "Cerebrovascular Disease"), there is no RCT evidence comparing different strategies to reduce BP acutely. Observational studies have indicated exponential dose-response relationship between SBP and an increasing risk of aortic dissection and death, with an HR of more than 2-fold for SBP >120 mm Hg.[4] However, BP measurement was not performed during hospitalization or IV drug treatment. Nevertheless, the current guideline endorses SBP target to <130 mm Hg in most patients with AD and <120 mm Hg in selected high-risk patients in the chronic setting.[14] Pheochromocytoma hypertensive crisis is also considered a medical emergency that requires prompt lowering of BP. However, the relationship between BP and mortality risk has not been characterized during adrenergic crisis. Despite potential cardiovascular complications of pheochromocytoma crisis, including a takotsubo-like cardiomyopathy,[5] pheochromocytoma should not be considered a compelling indication to reduce SBP immediately to less than <120 or 140 mm Hg in the first hour. In addition, clinical trials in patients without aortic dissection or pheochromocytoma showed increased risk of adverse kidney events associated with early intensive lowering of SBP to 110 to 139 mm Hg, particularly among patients with extremely high initial SBP of >220 mm Hg.[6,7] Thus, an attempt should be made to reduce SBP to <120 mm Hg in aortic dissection during the first hour and <140 mm Hg for most other conditions while monitoring for the presence and extent of other target organ function.
3. There is no RCT evidence for the treatment of other forms of hypertensive emergency without compelling indication. Small clinical trials in patients with acute HF and severe hypertension showed improvement in dyspnea when SBP was reduced by 15% (ie, 20 to 40 mm Hg) within 30 minutes without increased adverse events.[2,9] Thus, strategies to reduce BP should be more conservative to achieve 25% reduction in the first hour, followed by gradual further reduction within 24 to 48 hours.
4. Antihypertensive drug treatment should be used with extreme caution in hospitalized patients with asymptomatic severe hypertension because spontaneous falls in BP without any antihypertensive agents occur commonly, at a rate of 40% to 50%.[10] Observational studies have shown that initiation or intermittent use of additional IV or oral antihypertensive medications in patients hospitalized for noncardiac conditions are associated with increased risk of in-hospital mortality, AKI, and prolonged hospital stay.[8,11] Asymptomatic patients with severe hypertension can be treated with careful and frequent monitoring using standing medications and avoiding as-needed medications.

6.2.1. Medications for Hypertensive Emergencies

Treatment of hypertensive emergencies requires rapid recognition of the condition and knowledge of the unique treatment approaches appropriate for the causal condition or emergency consequences. A full discussion of these factors are in Sections 6.2 ("Hypertensive Emergencies and Severe Hypertension in Nonpregnant and Nonstroke Patients") and 5.3.9 ("Cerebrovascular Disease"). Tables 26 and 27 provide preferred agents for specific conditions.

6.3. Sexual Dysfunction

Synopsis

Sexual dysfunction frequently occurs in individuals with hypertension and has been more commonly reported by women than men.[1–6] Sexual dysfunction is defined as a person's inability to participate in sexual relationships as they would wish[7] and can be assessed in men and women using sex-specific validated tools that query emotional and physical symptoms in several domains, including thoughts and desires, arousal, frequency of sexual activity, pleasure and orgasm, and problems affecting sexual function.[8,9] The association between hypertension and sexual dysfunction may be due to shared mechanistic pathways of impaired vascular function and atherosclerosis, in addition to common risk factors of increasing age, hormonal shifts, diabetes, and depression.[10] Antihypertensive medications may also contribute as treated patients with hypertension are more likely to report sexual dysfunction than untreated ones.[11] Discussing sexual function with patients is essential as concerns about antihypertensive medications' negative impact on sexual function can lead to decreased adherence.[12] Diuretics and BBs, except nebivolol, are most commonly associated with erectile dysfunction in men,[10] and BBs are associated with a worsening of sexual function in women.[13,14] ARBs have the most favorable profile in men and women.[6,10] Phospho-

Table 26. Intravenous Antihypertensive Drugs for Treatment of Hypertensive Emergencies

Class	Drug(s)	Usual Dose Range	Comments
CCB–dihydropyridines	Nicardipine	Initial 5 mg/h, increasing every 5 min by 2.5 mg/h to maximum 15 mg/h	Contraindicated in advanced aortic stenosis; no dose adjustment needed for persons aged ≥65 y. No negative inotropic or chronotropic effects.
	Clevidipine	Initial 1-2 mg/h, doubling every 90 s until BP approaches target, then increasing by less than double every 5-10 min; maximum dose 21 mg/h; maximum duration 72 h	Contraindicated in patients with soybean, soy product, egg, and egg product allergy and in patients with defective lipid metabolism (eg, pathological hyperlipidemia, lipoid nephrosis [minimal change disease] or acute pancreatitis). No negative inotropic or chronotropic effects. Decreased risk of reflex tachycardia.
Vasodilators–nitric-oxide dependent	Sodium nitroprusside	Initial 0.3-0.5 mcg/kg/min; increase in increments of 0.5 mcg/kg/min every 5 min to achieve BP target; maximum dose 10 mcg/kg/min; duration of treatment as short as possible	Due to potency, intra-arterial BP monitoring is recommended to prevent "overshoot." Lower dose required for older adults. Tachyphylaxis is common with extended use. No negative inotropic or chronotropic effects. Due to increased mortality risk, should be avoided in acute cerebrovascular disease unless other agents are not available. Use cautiously in pregnancy or older adults. Cyanide toxicity (increased risk in liver dysfunction and chronic kidney disease) and thiocyanate toxicity (increased risk in kidney dysfunction, sCr >3) may occur for infusion rates ≥3 mcg/kg/min and/or duration ≥3 d. Cyanide toxicity and thiocyanate toxicity may present similarly with metabolic acidosis, altered mental status, and cardiac arrhythmia. For either toxicity state, nitroprusside should be discontinued and sodium thiosulfate or cyanocobalamin should be administered.
	Nitroglycerin	Initial 5 mcg/min; increase in increments of 5 mcg/min every 3-5 min to a maximum rate of 200 mcg/min	Use only in patients with acute coronary syndrome and/or acute pulmonary edema. Do not use in volume-depleted patients. Tachyphylaxis is common with extended use.
Vasodilators–direct	Hydralazine	Initial 10 mg via slow IV infusion (maximum initial dose 20 mg); repeat every 4-6 h as needed. Adjust rate up to total cumulative dose of 200 mg/24 h	BP begins to decrease within 10-30 min, and the fall lasts 2-4 h. Hydralazine is an undesirable first-line agent for acute treatment in most patients due to unpredictability of response and prolonged duration of action.
Adrenergic blockers–beta-1 receptor selective antagonist	Esmolol	Loading dose 500-1000 mcg/kg/min over 1 min followed by a 50-mcg/kg/min infusion. For additional dosing, the bolus dose is repeated, and the infusion increased in 50-mcg/kg/min increments as needed to a maximum of 300 mcg/kg/min	Contraindicated in patients with concurrent beta-blocker therapy, bradycardia, or decompensated HF. Monitor for bradycardia. Higher doses may block beta-2 receptors and impact lung function in reactive airway and obstructive pulmonary disease.
Adrenergic blockers–combined alpha-1 and nonselective beta receptor antagonist	Labetalol	Initial 0.3- to 1.0-mg/kg dose (maximum 20 mg) slow IV injection every 2 min or 0.4-1.0-mg/kg/h IV infusion up to 3 mg/kg/h. Adjust rate up to total cumulative dose of 300 mg/24 h	Contraindicated in reactive airway or obstructive pulmonary disease. Especially useful in hyperadrenergic syndromes. May worsen HF and should not be given in patients with second- or third-degree heart block or bradycardia.
Adrenergic blockers–nonselective alpha receptor antagonist	Phentolamine	IV bolus dose 5 mg. Additional bolus doses every 10 min as needed to lower BP to target. Adjust rate up to total cumulative dose of 50 mg/24 h	Used in hypertensive emergencies induced by catecholamine excess (pheochromocytoma, interactions between monoamine oxidase inhibitors and other drugs or food, cocaine toxicity, amphetamine overdose, or clonidine withdrawal).
Dopamine-1-receptor selective agonist	Fenoldopam	Initial 0.1-0.3 mcg/kg/min; may be increased in increments of 0.05-0.1 mcg/kg/min every 15 min until target BP is reached. Maximum infusion rate 1.6 mcg/kg/min	Contraindicated in patients at risk of increased intraocular pressure (glaucoma) or intracranial pressure and those with sulfite allergy.
ACE inhibitor	Enalaprilat	Initial 1.25 mg over a 5-min period. Doses can be increased up to 5 mg every 6 h as needed to achieve BP target. Adjust rate up to total cumulative dose of 50 mg/24 h	Contraindicated in pregnancy and should not be used in acute MI or bilateral renal artery stenosis. Mainly useful in hypertensive emergencies associated with high plasma renin activity. Poorly defined dose adjustments for kidney failure and may worsen kidney injury in those with CKD. Relatively slow onset of action (15 min) and unpredictability of BP response.

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BP indicates blood pressure; CCB, calcium channel blocker; CKD, chronic kidney disease; HF, heart failure; IV, intravenous; and MI, myocardial infarction.

diesterase-5 inhibitors are a safe and effective therapy for erectile dysfunction and can be administered with antihypertensive medications. Caution should be exercised when sildenafil, tadalafil, vardenafil, and avanafil are coadministered with CYP3A4 inhibitors (such as diltiazem, verapamil; Section 5.2.6, "Medication Interactions") or ingested with grapefruit juice or alcohol, which may increase the risk of hypotension. These drugs should not be taken with nitrates due to the risk of severe hypotension.

6.4. Patients Scheduled for Surgical Procedures

Recommendations for Patients Scheduled for Surgical Procedures Referenced studies that support the recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	B-NR	1. In patients with hypertension scheduled for major surgery who have been on BBs chronically, BBs should be continued throughout the perioperative period to assist with BP control.[1–5]
2a	C-EO	2. In patients with hypertension scheduled for elective major surgery, it is reasonable to continue most medications for hypertension throughout the perioperative period.
2b	B-R	3. In patients with hypertension scheduled for major surgery, discontinuation of ACEi or ARB preoperatively may be considered to prevent hypotension during surgery.[6–10]
Recommendations for Patients Scheduled for Surgical Procedures (Continued)		
COR	**LOE**	**Recommendations**
2b	C-LD	4. In patients scheduled for elective major surgery with SBP ≥180 mm Hg or DBP ≥110 mm Hg, deferring surgery may be considered especially in high-risk patients to minimize perioperative complications.[11–13]
3: Harm	B-NR	5. In patients with hypertension scheduled for surgery, abrupt preoperative discontinuation of BB or clonidine may result in rebound hypertension and is potentially harmful.[14]
3: Harm	B-R	6. For patients with hypertension scheduled for surgery, BB should not be started on the day of surgery in BB-naïve patients because of increased risk of postoperative mortality.[4,15,16]

Synopsis

Hypertension in the perioperative period increases the risk of cardiovascular and cerebrovascular events and bleeding.[17,18] As many as 25% of patients who undergo major noncardiac surgery and 80% of patients who have cardiac surgery experience perioperative hypertension.[18–20] In general, the level of risk is related to the severity of the hypertension. Uncontrolled hypertension is associated with increased perioperative and postoperative complications. Certain medications (eg, BB, clonidine) may be associated with rebound hypertension if discontinued abruptly. In addition to RCT results, several general strategies and

Table 27. Intravenous Antihypertensive Drugs for Treatment of Hypertensive Emergencies in Patients With Selected Comorbidities

Comorbidity	Preferred Drug(s)*	Comments
Acute aortic dissection	Esmolol, labetalol	Requires rapid lowering of SBP to ≤120 mm Hg. Beta blockade should precede vasodilator (eg, nicardipine or nitroprusside) administration, if needed for BP control or to prevent reflex tachycardia or inotropic effect; SBP ≤120 mm Hg should be achieved within 20 min.
Acute pulmonary edema	Clevidipine, nitroglycerin, nitroprusside	Beta blockers contraindicated.
Acute coronary syndromes	Esmolol†, labetalol, nicardipine, nitroglycerin†	Nitrates given in the presence of PDE-5 inhibitors may induce profound hypotension. Contraindications to beta blockers include moderate-to-severe LV failure with pulmonary edema, bradycardia (<60 beats/min), hypotension (SBP <100 mm Hg), poor peripheral perfusion, second- or third-degree heart block, and reactive airways disease.
Acute kidney injury	Clevidipine, fenoldopam, nicardipine	N/A
Eclampsia or preeclampsia	Hydralazine, labetalol, nicardipine, nifedipine	Requires rapid BP lowering. ACE inhibitors, ARB, renin inhibitors, and nitroprusside contraindicated.
Perioperative hypertension (BP ≥160/90 mm Hg or SBP elevation ≥20% of the preoperative value that persists for >15 min)	Clevidipine, esmolol, nicardipine, nitroglycerin	Intraoperative hypertension is most frequently seen during anesthesia induction and airway manipulation.
Acute sympathetic discharge or catecholamine excess states (eg, pheochromocytoma, postcarotid endarterectomy status)	Clevidipine, nicardipine, phentolamine	Requires rapid lowering of BP.
Acute ICH	Clevidipine, nicardipine, esmolol, labetalol, hydralazine	Section 5.3.9.1
Acute ischemic stroke	Clevidipine, nicardipine, esmolol, labetalol, hydralazine	Section 5.3.9.2

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*Agents are listed in alphabetical order, not in order of preference.
†Agent of choice for acute coronary syndromes.
ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; ICH, intracerebral hemorrhage; LV, left ventricular; PDE-5, phosphodiesterase type-5; and SBP, systolic blood pressure.

principles based on experience and observation are recommended for this section. In the management of patients with perioperative hypertension, it is important to assess other potential contributing factors, such as volume status, pain control, oxygenation, and bladder distention, when the use of pharmacological therapy to control BP is under consideration. For additional recommendations on perioperative hypertension management for noncardiac surgery, including the use of BB, ACEi, and ARB, please refer to the "2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery."[21]

Recommendation-Specific Supportive Text

1. If well tolerated, BBs should be continued in patients who are currently receiving them for GDMT indications (eg, recent MI, hypertension, arrhythmias). Multiple observational studies support the benefits of continuing BBs in patients who are undergoing surgery and who are taking these agents for GDMT.[1,3,4] Clinical judgment is useful in titrating BB during the perioperative period, focusing on continuing the medication through the hospital stay and at discharge unless clear contraindications arise.
2. In the absence of conclusive RCTs, the expert opinion of this writing committee is that control of BP to levels recommended by this guideline (BP <130/80 mm Hg) or other target levels specified for a particular individual is reasonable before undertaking major elective procedures in either the inpatient or outpatient setting. If the patient is unable to take oral medications, it is reasonable to use IV medications as necessary to control BP. Special consideration of parenteral therapy usually occurs for patients taking clonidine or BB because of the risk associated with stopping these medications acutely. Withdrawal syndromes, accompanied by sympathetic discharge and acute hypertension, can occur on cessation of these agents.[16] Caution is advised when continuing antihypertensive therapy in patients with low perioperative BPs, older adults (age ≥65 years),[22] and patients in whom the risk for perioperative hypotension is high.
3. Data on the potential risk and benefit of ACEi in the perioperative setting have been mostly limited to observational analyses and are controversial. Evidence from a large cohort study demonstrates that patients who stopped their ACEi or ARB 24 hours before noncardiac surgery were less likely to suffer the primary composite outcome (all-cause death, stroke, or myocardial injury) and intraoperative hypotension than were those continuing these medications until surgery.[10] However, the results from POISE-3 (Perioperative Ischemic Evaluation-3), which randomized 7490 patients undergoing noncardiac surgery with at least 1 high-risk factor, did not find a significant difference between patients randomized to a strategy that involved perioperative discontinuation of ACEi/ARB therapy and those with maintenance of such therapy during the operative and immediate perioperative periods.[9] Omitting RAASi before surgery has been shown to reduce intraoperative hypotension, whereas RCTs have failed to prove their continuation or implementation improves clinical outcomes.[6,7,23]
4. There is conflicting evidence for patients with DBP >110 mm Hg regarding recommending delay of surgery to provide for gradual reduction in DBP before proceeding with surgery.[24] In a systematic review and meta-analysis, preoperative hypertension was associated with a 35% increase in cardiovascular complications.[12] An increase in cardiovascular and cerebrovascular complications and renal failure has been reported in patients with DBP >110 mm Hg immediately before surgery.[25] In contrast, patients with DBP <110 mm Hg do not appear to be at significantly increased risk.[26] The relationship of systolic hypertension to surgical risk is less certain. During induction of anesthesia for surgery, a sympathetic reaction can result in a 20 to 30 mm Hg increase in BP among patients with normal BP.[25] Lability in BP appears more likely in patients with poorly controlled hypertension, whereas studies have observed that patients with controlled hypertension respond similarly to those who are normotensive.[26] An elevated BP on the day of surgery may represent a situational ("white-coat hypertension") response if there was evidence of controlled hypertension or normotension prior to surgery.[27] Therefore, referring to patients' baseline ambulatory BP is recommended to guide BP management. Without evidence for increased risk for perioperative complications in patients whose preoperative SBP/DBP is <180/110 mm Hg, there is little evidence to defer surgery, and the patient can be evaluated and BP can be controlled postoperatively or after discharge.[12]
5. Although few studies describe risks of withdrawing BB in the perioperative period, longstanding evidence from other settings suggests that abrupt withdrawal of long-term BB is harmful and should be avoided.[1,2,28] There are fewer data to describe whether short-term (1 to 2 days) perioperative use of BB, followed by rapid discontinuation, is harmful.[21,29] Importantly, abrupt discontinuation of clonidine can result in rebound hypertension associated with norepinephrine surge.[30]
6. This guideline recommends against starting a BB on the day of surgery in BB-naïve patients, particularly at high initial doses, in long-acting form, and if there are no plans for dose titration or monitoring for adverse events.[4,15,16] Evidence has been summarized in at least

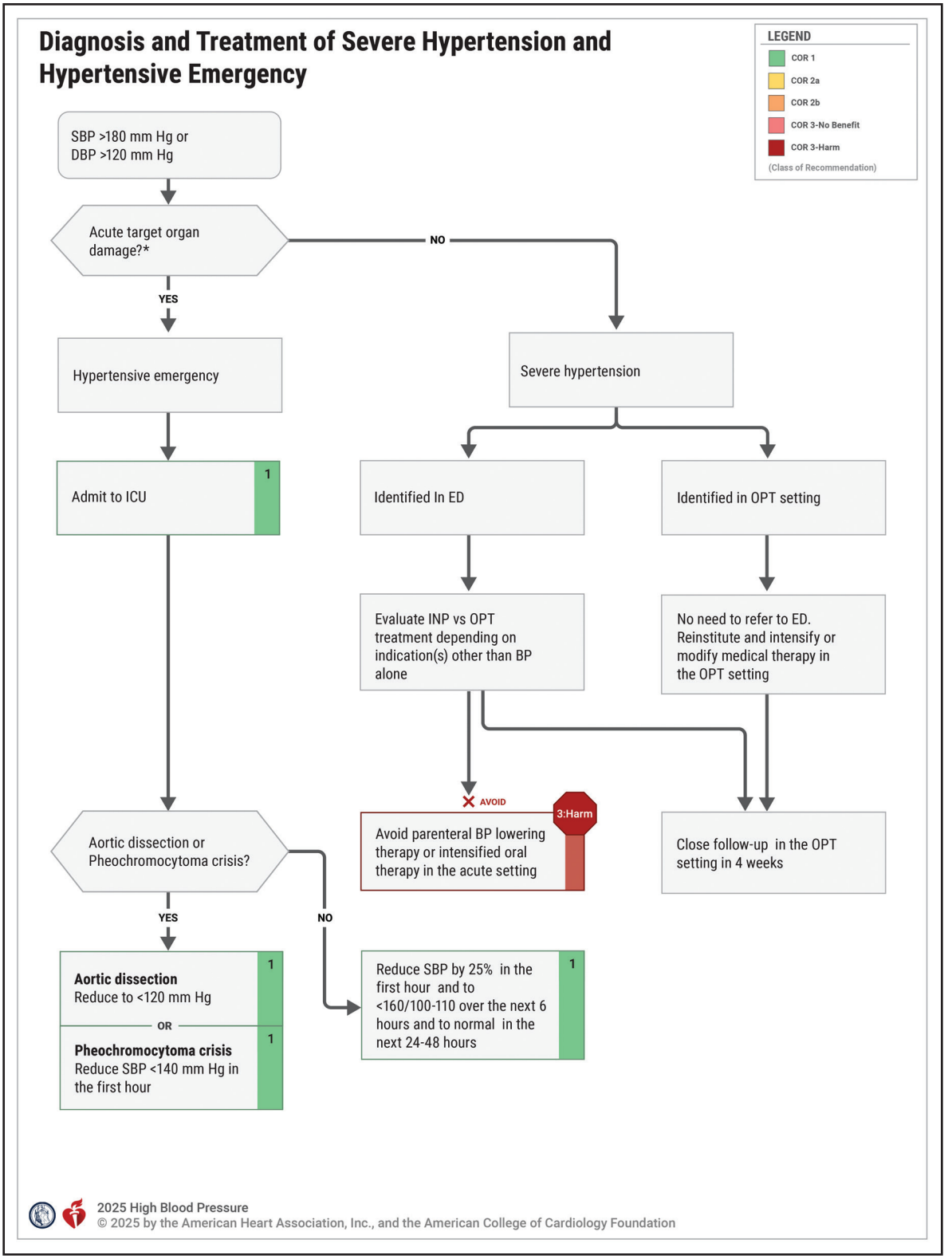

Figure 9. Diagnosis and Treatment of Severe Hypertension and Hypertensive Emergency.
*Defined as acute heart failure/pulmonary edema, neurologic disorders (posterior reversible encephalopathy syndrome, encephalopathy, retinal hemorrhage, papilledema, intracranial hemorrhage, acute ischemic stroke), acute decompensated heart failure, acute coronary syndrome, acute kidney injury, acute aortic syndrome (penetrating aortic ulcer, aortic dissection). DBP indicates diastolic blood pressure; ED, emergency department; ICU, intensive care unit; INP, inpatient; OPT, outpatient; and SBP, systolic blood pressure. For reinstitution, modification or intensification of medical therapy, refer to Sections 5.2.2. through 5.2.4. Modified with permission from Whelton et al.[15] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

3 well-performed meta-analyses.[15,21,31] The first 2 of these meta-analyses called into question the strength of evidence for benefit of BB, while raising concerns about harms related to hypotension and stroke.[21,31] A more recent review confirmed earlier meta-analytic results while assessing that the certainty of evidence was low given biases and heterogeneity among the studies reviewed; each of these meta-analyses results were driven in part by the large POISE (Perioperative Ischemic Evaluation)[29] sample size.

7. EVIDENCE GAPS AND FUTURE DIRECTIONS

Since the 2017 high BP guideline was published, there have been numerous advancements in high BP management. However, key questions on the awareness of high BP and optimal management of high BP remain, and these knowledge gaps suggest areas for future research as described in this section.

Among adults with hypertension in the United States, most are not controlled to <130/80 mm Hg. More than 50% are unaware that they have hypertension. Population management strategies are just beginning to utilize the EHR and consider community-engaged strategies to identify those with undiagnosed or uncontrolled hypertension to focus resources. There is a need for research regarding effective screening methods and for more effective implementation strategies within and outside the health care system to control BP and reduce CVD risk.

Observational data demonstrate increased risk of CVD among younger adults with stage 1 hypertension, and elevated BP can be associated with evidence of target organ damage. There is a need to clarify those areas where current clinical trial evidence is sufficient on which to base our treatment decisions for younger adults, and where the needs for additional research are greatest. There is a lack of evidence to support BP targets for diastolic hypertension, which is more common in younger adults who have low short-term CVD risk but have a longer time horizon to consider for prevention. Research related to this issue should include detection of CVD endpoints organized outside academic centers, such as by pragmatic trial designs, to allow financial feasibility, use of surrogate endpoints such as left ventricular hypertrophy, which are not widely measured clinically, and evaluations for target organ damage performed at baseline and during longitudinal follow-up.

Accurate BP measurement remains a major challenge. Trials are needed that compare measurements taken by attended AOBP and unattended AOBP methods. Continued studies are needed in the realm of alternative methods for measurements, including accurate wearable and cuffless devices to provide near-continuous monitoring, HBPM, ABPM, and other novel approaches to measuring or estimating BP load. Additional studies comparing home and ambulatory BP measurements in estimating CVD risk are greatly needed to reduce treatment disparities due to lack of availability of ABPM to all populations. There is a need for studies utilizing HBPM combined with interventions to effectively achieve and maintain BP control utilizing health technology and to minimize nonadherence.

Further studies are needed at the intersection of BP, race/ethnicity, and SDOH, which includes those who are underinsured or uninsured to allow more precise predictions of needs and better focused prevention and management. To ensure optimal application of guidelines and evidence-based approaches that are effective and equitable for all groups, the BP treatment thresholds and treatment targets for different subpopulations need to be further clarified. With these efforts, there will be a need for additional data monitoring to evaluate new approaches and their effects on BP control and CVD outcomes across differences in sex/gender, race/ethnicity, socioeconomic status, education level, and access to medical care.

Further studies are needed to help us understand the role of genetic and epigenetic factors in BP. Using risk estimates that consider the influence of environmental and behavioral factors on genetic risk may add clarity to the areas of greatest need and potential benefit. Overall, further studies of environmental and lifestyle issues are needed, including nutrition, physical activity, and especially obesity and the role of emerging interventions for weight management in persons living with obesity and hypertension. We need additional studies of patients with white-coat hypertension to determine whether this condition carries additional long-term risk.

Using risk estimates that incorporate genetic risk, but that also consider the influence of environmental and behavioral factors on this risk, may add clarity to areas of greatest need and potential benefit.

In the realm of treatment approaches, there is prior evidence to support the contribution of sleep apnea to hypertension and resistant hypertension, but evidence of BP lowering from sleep apnea treatment is limited. This is an area ripe for research, particularly as sleep apnea treatment includes serial monitoring, which could incorporate BP tracking.

Early studies using stress management techniques have shown promise but need to be tested across a greater breadth of patients with adverse SDOH. We need additional trials comparing combinations of medications, dosed as separate agents and using SPCs to improve adherence and therefore effectiveness while monitoring for patient tolerance.

While pregnancy is an area where different concepts apply and decisions must account for optimal management of both the pregnant individual and the fetus, pregnancy planning and management have important implications for women with or at risk for high BP. Among women with preexisting hypertension or at risk for hypertension, safety and effectiveness of antihypertensive therapies should be considered, along with counseling on appropriate contraction options and recommendations for prophylactic aspirin therapy among those at greatest risk for acute onset or worsening of prior hypertension.

Other considerations relate to the management of patients with severe hypertension accompanied by symptoms and signs of acute CVD events and to management of hypertension during the perioperative period. Trials are challenging in these areas, and pragmatic study designs may be helpful.

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ARTICLE INFORMATION

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2.1. Definition of High Blood Pressure

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Appendix 1. Writing Committee Relationships With Industry and Other Entities–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

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Daniel W. Jones	University of Mississippi Medical Center–Professor of Medicine and Dean Emeritus	None	None	None	None	None	None
Keith C. Ferdinand	Tulane University School of Medicine–Professor of Medicine, Gerald S. Berenson Chair in Preventative Cardiology	RELEVANT • Amgen* • Janssen • Medtronic* • Novartis • Sanofi	None	None	RELEVANT • Boehringer Ingelheim	NOT RELEVANT • Alnylam Pharmaceuticals	None
Sandra J. Taler	Mayo Clinic–Professor of Medicine	None	None	None	None	NOT RELEVANT • *American Journal of Hypertension*	None
Marwah Abdalla	Columbia University Irving Medical Center–Associate Professor of Medicine	None	None	None	NOT RELEVANT • NIH*	None	None
M. Martine Altieri	My Cardiologist–Physician Assistant	NOT RELEVANT • CAPP • Gather Ed	None	None	None	NOT RELEVANT • AAPA RELEVANT • Medtronic	None
Nisha Bansal	University of Washington–Professor, Division of Nephrology	NOT RELEVANT • UpToDate	None	None	None	NOT RELEVANT • AHA† • ASN • NIH*	None
Natalie A. Bello	Cedars Sinai Medical Center–Associate Professor of Cardiology; Atria Physician Practice, P.A.–Director of Women's Cardiovascular Health & Cardiology (effective January 2025)	None	None	None	NOT RELEVANT • Cardiovascular Research Foundation (DSMB) • Global Clinical Trial Partners (CEC)† • NIH (DSMB)† • NIH (PI)*	None	None
Adam P. Bress	University of Utah School of Medicine–Associate Professor of Population Health Sciences; US Department of Veterans Affairs–Data Scientist	None	None	None	NOT RELEVANT • NIH* RELEVANT • Amarin Pharma* • Amgen*	None	None
Jocelyn Carter	Massachusetts General Hospital, Division of General Internal Medicine–Assistant Professor, Harvard Medical School	None	None	None	None	None	None
Jordana B. Cohen	University of Pennsylvania Perelman School of Medicine–Associate Professor of Medicine and Epidemiology	None	None	NOT RELEVANT • UpToDate	NOT RELEVANT • NIH*	NOT RELEVANT • *American Heart Journal* • *Journal of Human Hypertension*	None

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Karen J. Collins	Collins Collaboration, LLC–Founder and President	None	None	None	None	NOT RELEVANT • Steel Jupiter, Inc.†	None
Yvonne Commodore-Mensah	John Hopkins University School of Nursing–Associate Professor	None	None	None	None	None	None
Leslie L. Davis	University of North Carolina, Chapel Hill–Associate Professor, PhD Division, School of Nursing	None	None	None	NOT RELEVANT • AANP* • UNC-Chapel Hill-REHEARSe (PI)*	NOT RELEVANT • AANP • ACC • KANPNM • NCDR Chest Pain-MI Registry† • NPACE • *Nursing Clinics of North America* • PCNA • Skin, Bones, Hearts & Private Parts* • *The Journal for Nurse Practitioners**	None
Brent Egan	American Medical Association–Vice President, Cardiovascular Health	NOT RELEVANT • Mineralys Therapeutics, Inc.†	None	NOT RELEVANT • UpToDate*	NOT RELEVANT • Yeshiva University (DSMB)	None	None
Heather M. Johnson	Baptist Health South Florida–Preventive Cardiologist, Director of Preventive Cardiology for Women's Services	NOT RELEVANT • Esperion* RELEVANT • Amgen • Medtronic • Novartis	NOT RELEVANT • Esperion*	None	None	NOT RELEVANT • ASPC† • North American Thrombosis Forum	None
Sadiya S. Khan	Northwestern University Feinberg School of Medicine–Associate Professor of Medicine, Medical Social Sciences, and Preventative Medicine	None	None	None	NOT RELEVANT • NIH*	NOT RELEVANT • AHA* • *JAMA Cardiology*†	None
Donald M. Lloyd-Jones	Boston University–Director, Framingham Center for Population and Prevention Science, and Section Chief, Preventive Medicine and Epidemiology; (prior) Northwestern University–Professor of Preventive Medicine, Medicine, and Pediatrics, and Chair, Department of Preventive Medicine	None	None	None	NOT RELEVANT • NIH*	NOT RELEVANT • AHA (National Board of Directors)†	None

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Bernadette Mazurek Melnyk	Ohio State University–Professor and Dean Emeritus; CEO and Founder COPE2Thrive, LLC; (prior) Ohio State University–Vice President of Health Promotion and Chief Wellness Officer	None	None	NOT RELEVANT • Cope for Hope* • COPE2Thrive, LLC* • Springer Publishing* • *Worldviews on Evidence-Based Nursing* (Editor)*	None	NOT RELEVANT • AACN* • AANP • AFSP* • Binghamton University* • CANP* • Case Western Reserve School of Nursing • College of Nursing Pennsylvania State University* • Delaware Health Force* • Eck Institute for Global Health, University of Notre Dame* • Florida Nursing University* • Florida Organization for Nursing Leadership* • Florida Southwestern State College* • Galen College of Nursing* • Greater St. Louis Regional Consortium* • Loyola University Marcella Niehoff School of Nursing • Medstar Health Center for Well-being • NINR* • Northern Arizona University • NSNA* • NWINRC* • Pennsylvania State University* • Sacred Heart University* • Sigma Theta Tau International, Greater St. Louis Regional Consortium* • The Morel Company* • The Nurse Practitioner Association NYS Region 2* • University of Virginia School of Nursing* • The University of Texas MD Anderson Cancer Center* • Wolters Kluwer*	None
Eva A. Mistry	University of Cincinnati–Associate Professor, Department of Neurology and Rehabilitation Medicine	NOT RELEVANT • AbbVie • RapidAI	None	None	NOT RELEVANT • NIH* • NINDS* • PCORI* • Silver Creek Pharmaceuticals* • SVIN*	NOT RELEVANT • CSL Behring • *Stroke** • *Stroke: Vascular and Interventional Neurology* • Translational Sciences†	None

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Modele O. Ogunniyi	Emory University School of Medicine–Professor of Medicine	RELEVANT • Novartis	None	None	NOT RELEVANT • Cardurion Pharmaceuticals (PI)* • Emory University (DSMB)† • Johns Hopkins Bloomberg School of Public Health (DSMB)† • Mayo Clinic College of Medicine & Science (DSMB) • Wake Forest Baptist Health School of Medicine (DSMB)† RELEVANT • AstraZeneca (PI)* • Boehringer Ingelheim (PI)* • Novartis	RELEVANT • Pfizer*	None
Stacey L. Schott	Johns Hopkins University School of Medicine–Assistant Professor of Medicine	NOT RELEVANT • ACPM*	None	NOT RELEVANT • BioNTech • Novo Nordisk RELEVANT • Eli Lilly • Merck • Pfizer	None	NOT RELEVANT • AHA† • Maryland Department of Health and Mental Hygiene†	None
Daichi Shimbo	Columbia University–Professor of Medicine, Director, Cardiovascular Physiology Research	None	None	None	NOT RELEVANT • AHA* • NIH*	None	None
Sidney C. Smith Jr	UNC School of Medicine–Professor of Medicine	None	None	None	None	None	None
Amy W. Talbot‡	American Heart Association/American College of Cardiology–Science & Health Advisor, Guidelines	None	None	None	None	None	None
Sabrina Singleton-Times§	American Heart Association/American College of Cardiology–Science & Health Advisor, Guidelines	None	None	None	None	None	None

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Wanpen Vongpatanasin	University of Texas Southwestern Medical Center–Director of Hypertension, Professor of Internal Medicine	RELEVANT • AstraZeneca† • Medtronic	None	NOT RELEVANT • University of Texas System Board of Regents (patent)	None	None	None
Karol E. Watson	UCLA - David Geffen School of Medicine–Professor of Medicine/Cardiology	RELEVANT • Amgen* • Boehringer Ingelheim* • Eli Lilly • Novartis • Novo Nordisk	None	None	None	RELEVANT • Merck Sharp & Dohme	None
Paul K. Whelton	Tulane University–Chair, Global Public Health, Department of Epidemiology	None	None	None	None	NOT RELEVANT • *Hypertension* • NIH* • World Hypertension League (President)†	None
Jeff D. Williamson	Wake Forest University–Professor of Internal Medicine and Epidemiology	NOT RELEVANT • Alzheimer's Association*	None	None	None	NOT RELEVANT • Alzheimer's Association* • Biogen, Inc.† • NIH*	None
Daniel Duprez‖	University of Minnesota, Academic Health Center–Professor of Medicine	None	None	None	None	NOT RELEVANT • Arrowhead Pharmaceuticals • NIH RELEVANT • Amgen* • Novartis*	None

This table represents all relationships of committee members with industry and other entities that were reported by authors, including those not deemed to be relevant to this document, at the time this document was under development. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to https://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.

†No financial benefit.

‡Amy Talbot is an AHA/ACC joint staff member and acts as the Science & Health Advisor for the AHA/ACC Guideline for High Blood Pressure. No relevant relationships to report. Nonvoting author on measures and not included/counted in the RWI balance for this committee.

§Sabrina Singleton-Times was a former AHA/ACC joint staff member and Science & Health Advisor for the AHA/ACC Guideline for High Blood Pressure. No relevant relationships to report. Nonvoting author on measures and not included/counted in the RWI balance for this committee.

‖Dr. Duprez disclosed relationships with relevant companies during document development. Given the current policy that at least 51% of the writing committee must be free of relevant RWI, the decision was made to remove Dr. Duprez from the writing committee.

AACN indicates American Association of Colleges of Nursing; AANP, American Association of Nurse Practitioners; AAPA, American Academy of Physician Assistants; ABC, Association of Black Cardiologists; ACC, American College of Cardiology; ACPM, American College of Preventative Medicine; AFSP, American Foundation for Suicide Prevention; AHA, American Heart Association; ASN, American Society of Nephrology; ASPC, American Society of Preventive Cardiology; CANP, California Association for Nurse Practitioners; CAPP, Cardiology Advanced Practice Providers; CEC, clinical endpoint committee; DSMB, data safety monitoring board; KANPNM, Kentucky Association of Nurse Practitioners & Nurse-Midwives; NCDR, National Cardiovascular Data Registry; NIH, National Institutes of Health; NINDS, National Institute of Neurological Disorders and Stroke; NINR, National Institute for Nursing Research; NMA, National Medical Association; NPACE, Nurse Practitioners Associates for Continuing Education; NSNA, National Student Nurses Association; NWINRC, Northwest Indiana Nursing Research Consortium; NYS, New York State; PCNA, Preventive Cardiovascular Nurses Association; PCORI, Patient-Centered Outcomes Research Institute; PI, principal investigator; SVIN, Society of Vascular and Interventional Neurology; and UNC, University of North Carolina.

Appendix 2. Reviewer Relationships With Industry and Other Entities–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

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Donna Arnett	University of South Carolina–Executive Vice President and Provost	None	None	None	None	None	None
Eugene Yang	University of Washington–Professor of Medicine, Division of Cardiology	• Genentech USA • Idorsia • Measure Labs • Mineralys • Qure.ai • Sky Labs	None	• Measure Labs	• Microsoft Research*	None	None
David Aguilar	University of Texas Southwestern Medical Center-Professor of Medicine; General Cardiology Section Chief; (prior) LSU Health New Orleans School of Medicine–Professor of Medicine	None	None	None	None	None	None
Vivek Bhalla	Stanford University School of Medicine–Associate Professor of Medicine, Nephrology	• AMA† • AstraZeneca • Bayer* • Idorsia* • Janssen Biotech • Johnson & Johnson • Medtronic • Nephrogen* • Pyrames • Reata	None	• HrtEx • Nephrogen*	• NIH*	• AHA* • NIH*	None
Sarah J. Billups	University of Colorado Denver–Associate Professor, Department of Clinical Pharmacy	None	None	None	None	None	None
Margaret Bowers	Duke University School of Nursing–Clinical Professor	None	None	None	None	• American Association of Nurse Practitioners • Skin, Bones, Hearts & Private Parts*	None
Beverly B. Green	Kaiser Permanente Bernard J Tyson School of Medicine–Professor; Kaiser Foundation Research Institute–Senior Investigator and Family Physician	None	None	None	None	• ACS • NCI • NHLBI • NYU Langone Medical Center (DSMB) • PCORI	None

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Appendix 2. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Steven M. Greenberg	Massachusetts General Hospital–Neurologist	• Alnylam Pharmaceuticals*	None	• UpToDate	• Bayer (DSMB) • Bristol Myers Squibb (DSMB) • Washington University School of Medicine in St. Louis (DSMB)	• NIH*	None
Eileen Handberg	University of Florida College of Medicine–Research Professor of Medicine, Director of the Clinical Trials Program, Director of the College of Medicine Clinical Research Hub, Program Co-Director One-Florida+ Clinical Research Consortium	• Novo Nordisk* • PCNA	None	None	None	• Abbott Laboratories* • Abiomed* • Alexion Pharmaceuticals* • Alpha Phi Foundation* • Amgen* • BioCardia* • Biogen* • Biotronik* • Cedars-Sinai Medical Center* • EvaHeart* • Medtronic* • MyoKardia* • Priovant Therapeutics* • Private donor* • Roche Diagnostics* • SIREN* • US Department of Defense*	None
Christopher Jackson	University of South Florida–Associate Professor, Department of Medicine	• Southern Medical Association† • US Medical Licensing Examination	None	None	None	None	None
Wallace Robert Johnson Jr	University of Maryland School of Medicine–Assistant Professor of Medicine	None	None	None	• Novartis* • Novo Nordisk*	None	None
Min Ji Kwak	University of Texas Medical School at Houston–Assistant Professor	• Diabetes and Endocrine Plus Clinic* • Institute for Healthcare Improvement* • Novo Nordisk	None	• Eli Lilly*	Medical AI*	None	None
Renee Langstaff	Alvernia University–Assistant Professor, Department of Medical Science Chair; Physician Associate Program Director	• Simon's Heart†	None	None	None	None	None

(*Continued*)

Appendix 2. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Carlos Jose Rodriguez	Yeshiva University Albert Einstein College of Medicine–Professor of Medicine		• Merck	None	• Amgen*	• NHLBI*	None
Mark Santillan	University of Iowa–Professor, Department of Obstetrics and Gynecology	• Companche Biopharma*	None	• Patents†	None	None	None
Michael D. Shapiro	Wake Forest Baptist Health School of Medicine–Fred M. Parrish Professor of Cardiology and Molecular Medicine, Director of Center for Preventive Cardiology	• Agepha Pharma • Amgen • Ionis* • Merck • New Amsterdam Pharma • Novartis* • Novo Nordisk • Regeneron* • Tourmaline	None	None	None	None	None
Prentiss Taylor	Advocate Health Care–Internal Medicine Clinic physician	• Oakstone Publishing*	None	• Doctor On Demand	None	None	None
Jennifer Thibodeau	UT Southwestern Medical Center–Professor, Medical Director of Heart Failure; Medical Director of ECMO	None	None	None	None	• ACC Foundation† • *Circulation* • *Journal of Cardiac Failure*† • UpToDate	None
Greg Wozniak	American Medical Association–Vice President, Health Outcome Analytics	None	None	None	None	None	None
Jackson T. Wright, Jr	University Hospitals Cleveland Medical Center–Professor of Medicine and Director of Clinical Hypertension Program; Case Western Reserve University–Emeritus Professor of Medicine	• Medtronic*	None	None	• AHRQ* • Ohio Department of Medicaid* • Tulane University (DSMB)	None	None
Wendy C. Ziai	Johns Hopkins University–Assistant Professor of Neurology, Neurosurgery, Anesthesia, and Critical Care Medicine		None	None	None	*Neurocritical Care**	None

This table represents all reviewers' relationships with industry and other entities that were reported at the time of peer review, including those not deemed to be relevant to this document, at the time this document was under review. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to https://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.

†No financial benefit.

ACC indicates American College of Cardiology; ACS, American Cancer Society; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; DSMB, data and safety monitoring board; ECMO, extracorporeal membrane oxygenation; NCI, National Cancer Institute; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; PCNA, Preventive Cardiovascular Nurses Association; PCORI, Patient Centered Outcomes Research; SIREN, Strategies to Innovate Emergency Care Clinical Trials Network; and UT, University of Texas.