

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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The American Heart Association requests that this document be cited as follows: 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. *Circulation*. 2025;152:e000–e000. doi: 10.1161/CIR.0000000000001356

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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

Abstract	eXXX	5.2.1. Initiation of Pharmacological BP Treatment in the Context of Overall CVD Risk	eXXX
What Is New	eXXX	5.2.2. BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension	eXXX
Top Take-Home Messages	eXXX	5.2.3. Initial Medication Selection for Treatment of Primary Hypertension	eXXX
Preamble	eXXX	5.2.4. Choice of Initial Monotherapy Versus Initial Combination Drug Therapy	eXXX
1. Introduction	eXXX	5.2.5. Antihypertensive Medication Adherence Strategies	eXXX
1.1. Methodology and Evidence Review	eXXX	5.2.6. Medication Interactions	eXXX
1.2. Organization of the Writing Committee	eXXX	5.2.7. BP Goal for Patients With Hypertension	eXXX
1.3. Guideline Review and Approval	eXXX	5.2.8. Electrolyte Imbalances	eXXX
1.4. Scope of the Guideline	eXXX	5.2.9. Kidney Dysfunction/Injury	eXXX
1.5. Class of Recommendations and Level of Evidence	eXXX	5.3. Comorbidities	eXXX
1.6. Abbreviations	eXXX	5.3.1. Diabetes	eXXX
2. Definitions and Classification of BP	eXXX	5.3.2. Obesity and Metabolic Syndrome	eXXX
2.1. Definition of High BP	eXXX	5.3.3. Chronic Coronary Disease	eXXX
3. Evaluation and Diagnosis	eXXX	5.3.4. Prevention of HF in Adults With Hypertension	eXXX
3.1. Patient Evaluation	eXXX	5.3.5. Atrial Fibrillation	eXXX
3.1.1. Accurate Measurement of In-Office BP	eXXX	5.3.6. Valvular Heart Disease	eXXX
3.1.2. Patient Evaluation, Including Laboratory Tests and Other Diagnostic Procedures	eXXX	5.3.7. Aortic Disease	eXXX
3.1.3. Out-of-Office BP Monitoring	eXXX	5.3.8. Hypertension Treatment in Patients With CKD	eXXX
3.1.4. ABPM and HBPM	eXXX	5.3.9. Cerebrovascular Disease	eXXX
3.2. Patient Diagnosis	eXXX	5.3.10. Peripheral Artery Disease	eXXX
3.2.1. Causes of Hypertension	eXXX	5.4. Plan of Care for Hypertension	eXXX
3.2.2. White-Coat Hypertension and Masked Hypertension, and White-Coat Effect and Masked Uncontrolled Hypertension	eXXX	5.5. Hypertension and Pregnancy	eXXX
3.2.3. Secondary Forms of Hypertension	eXXX	5.5.1. Gestational Hypertension	eXXX
4. Prevention Strategies	eXXX		
5. BP Management	eXXX		
5.1. Lifestyle and Psychosocial Approaches	eXXX		
5.2. Medical Management	eXXX		

5.5.2.	Preeclampsia and Eclampsia, Including Preeclampsia Superimposed on Chronic Hypertension	eXXX
5.5.3.	Short- and Long-Term Follow-Up of Pregnancy-Associated Hypertension	eXXX
5.6.	Resistant Hypertension and Renal Denervation	eXXX
6.	Complications of Management	eXXX
6.1.	Management of OH	eXXX
6.2.	Hypertensive Emergencies and Severe Hypertension in Nonpregnant and Nonstroke Patients	eXXX
6.2.1.	Medications for Hypertensive Emergencies	eXXX
6.3.	Sexual Dysfunction	eXXX
6.4.	Patients Scheduled for Surgical Procedures	eXXX
7.	Evidence Gaps and Future Directions	eXXX
	Key Words	eXXX
	References	eXXX

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,

- dietitians, 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 $\geq 10\%$ 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, $\geq 7.5\%$ 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 manual⁴ 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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Clinical Practice Guidelines*

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 PREVENT¹ (Predicting Risk of CVD EVENTS) equations regarding populations, outcomes, predictors, and model performance. The PCEs were derived from data on 20338 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 over-predicted 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

Abbreviations	Meaning/Phrase
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	LEVEL (QUALITY) OF EVIDENCE†‡
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	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
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	Level B-R (Randomized) - Moderate-quality evidence‡ from 1 or more RCTs - Meta-analyses of moderate-quality RCTs
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	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
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	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
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 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 consensus 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.

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

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.

(“Out-of-Office BP Monitoring”), and 3.1.4 (“ABPM and HBPM”).



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

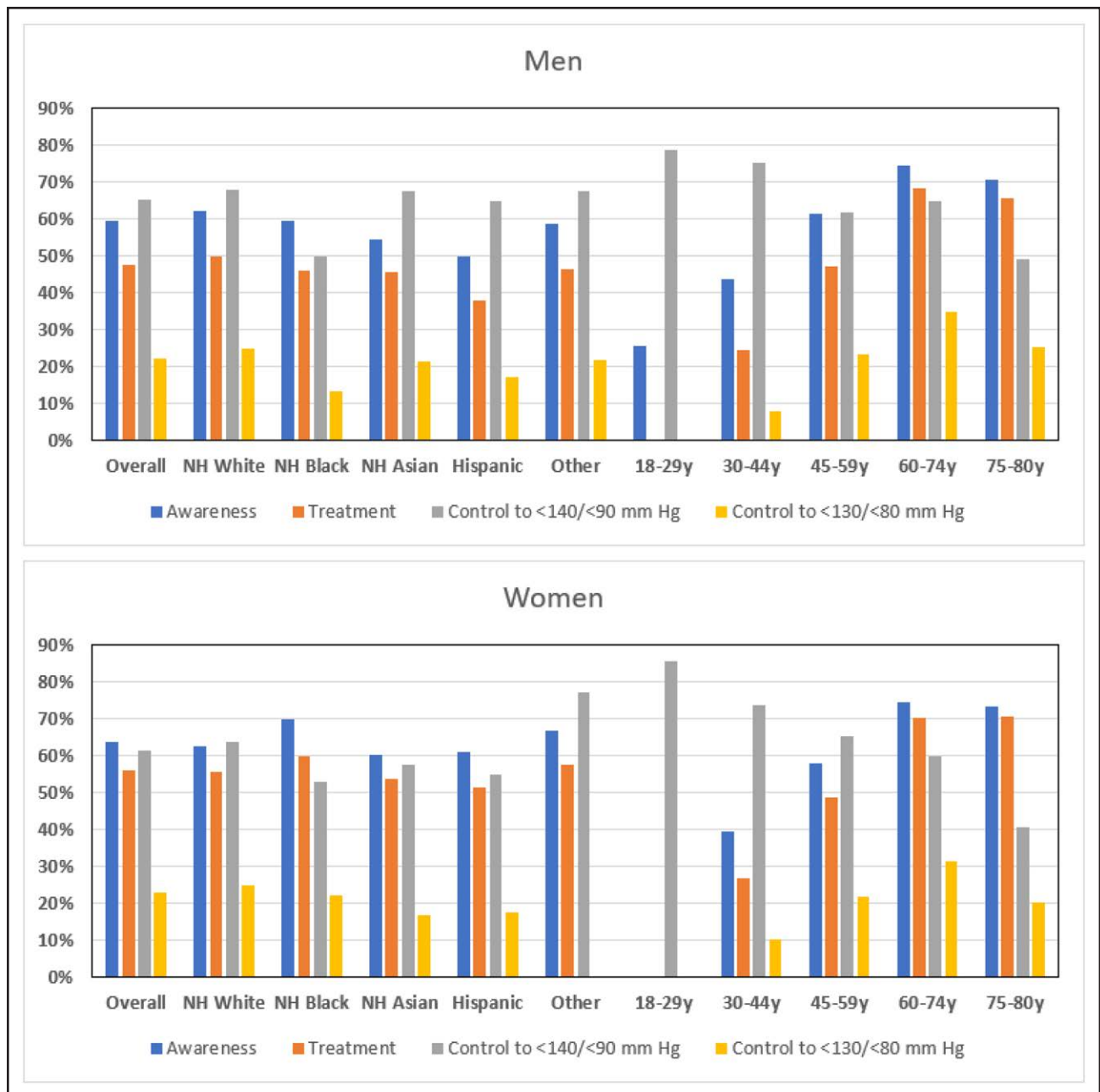


Figure 1. Rates of Awareness, Treatment, and Control of Hypertension Among US Adults Aged 18 to 80 Years, 2017 to 2020*.

*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

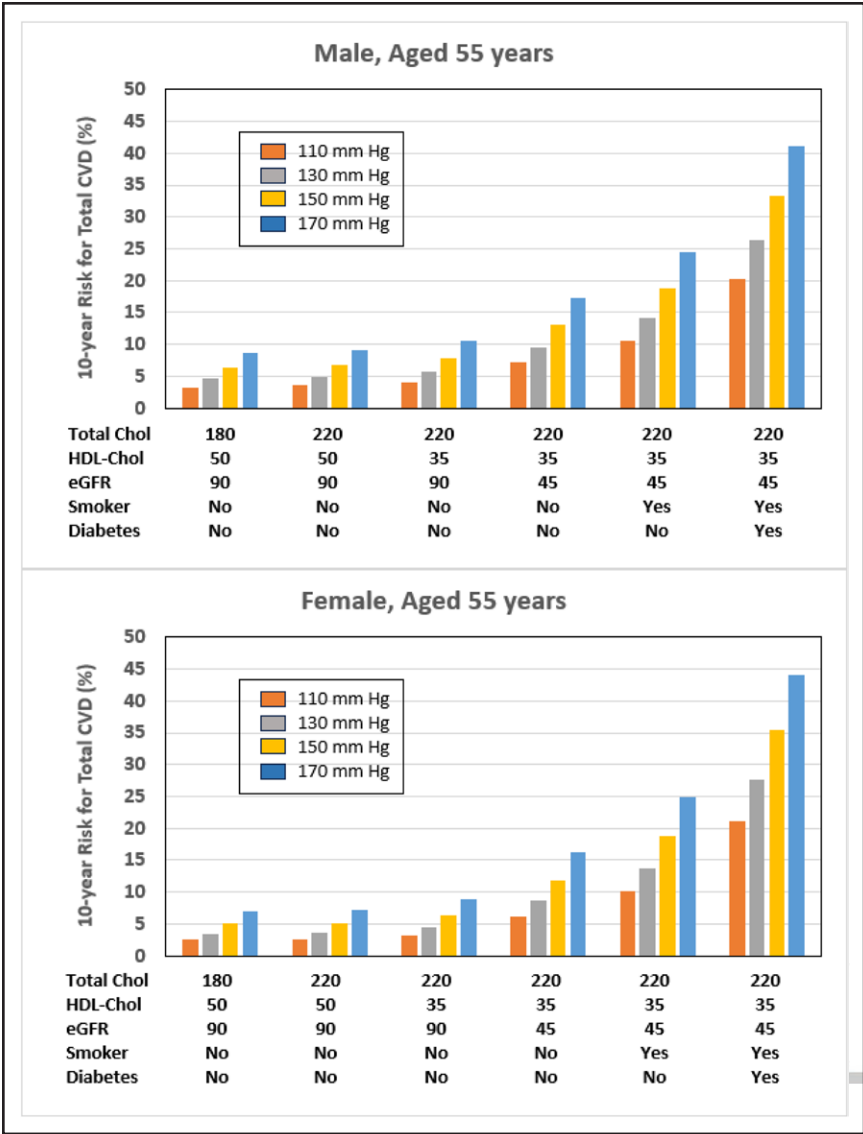


Figure 2. Estimated 10-Year Risks for Total Cardiovascular Disease Using the PREVENT™ CVD Risk Equations, Stratified by Blood Pressure Levels With Selected Combinations of Risk Factors. CVD indicates cardiovascular disease; eGFR, estimated glomerular filtration rate; and HDL, high-density lipoprotein.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

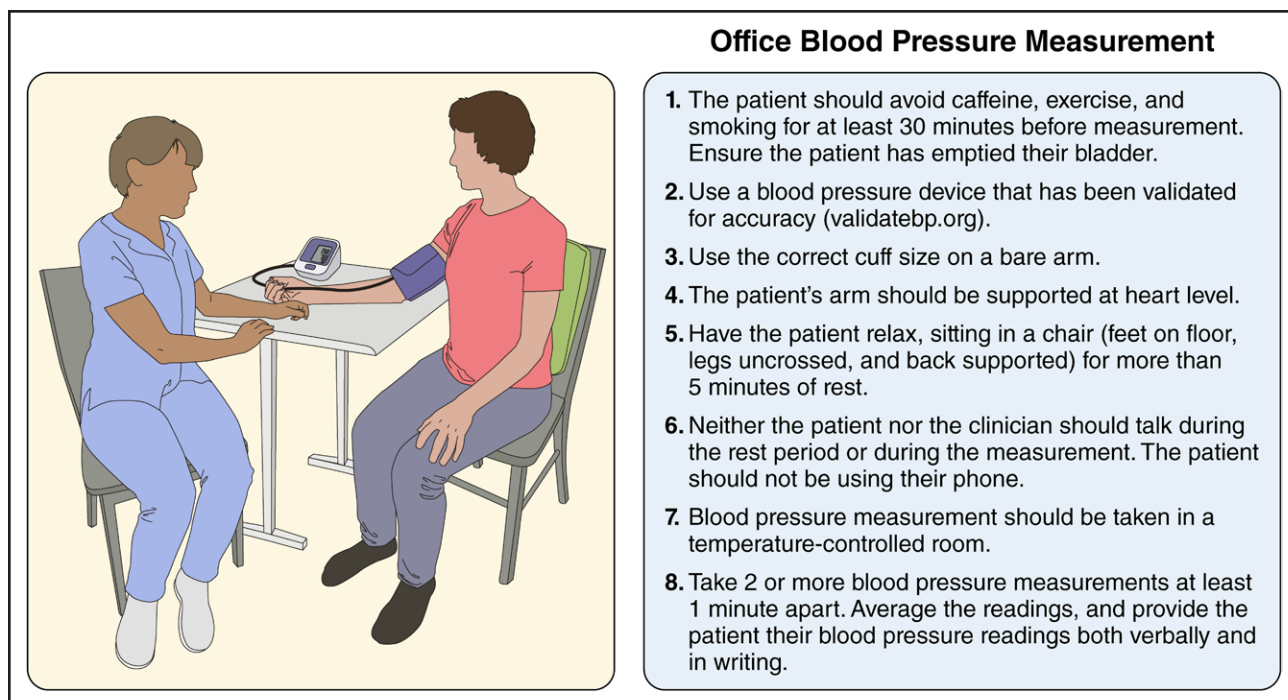


Figure 3. Checklist for Accurate Office Blood Pressure Measurement.

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 measured⁶ 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 test-

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.

ing 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]²), 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”).

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 pre-specified 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

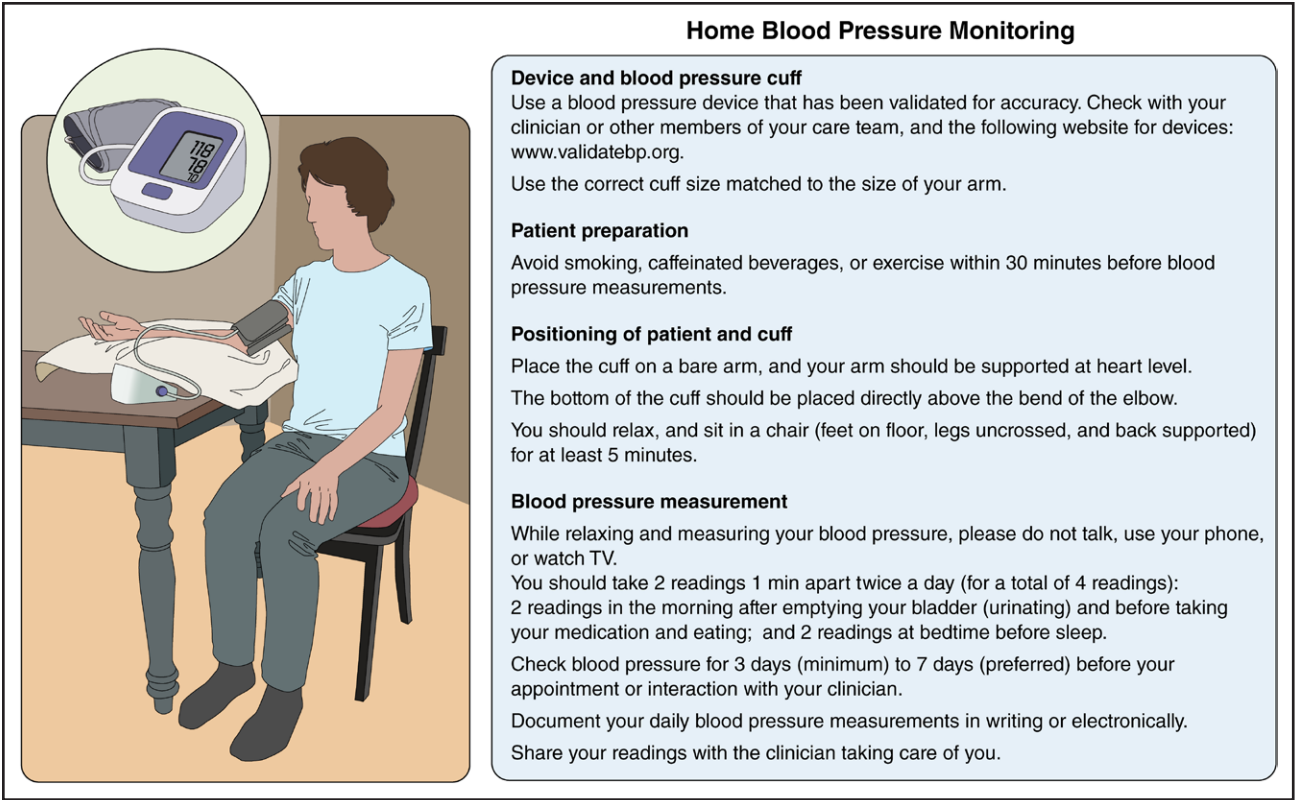


Figure 4. Home Blood Pressure Monitoring.¹⁸
See Table 7 for HBPM targets. BP indicates blood pressure; and HBPM, home blood pressure monitoring. Adapted with permission from Whelton et al.¹⁹ Copyright 2019 American College of Cardiology Foundation and American Heart Association, Inc. Created by Sceyence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

technology with HBPM and the best HBPM counter-
intervention 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 inter-individual 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 study²⁷ 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 $\geq$ 130/80 mm Hg). Individuals with office SBP/DBP $\geq$ 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.

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)			Recommendations for Primary Aldosteronism (Continued)		
COR	LOE	Recommendations	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	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.
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.			

Synopsis

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

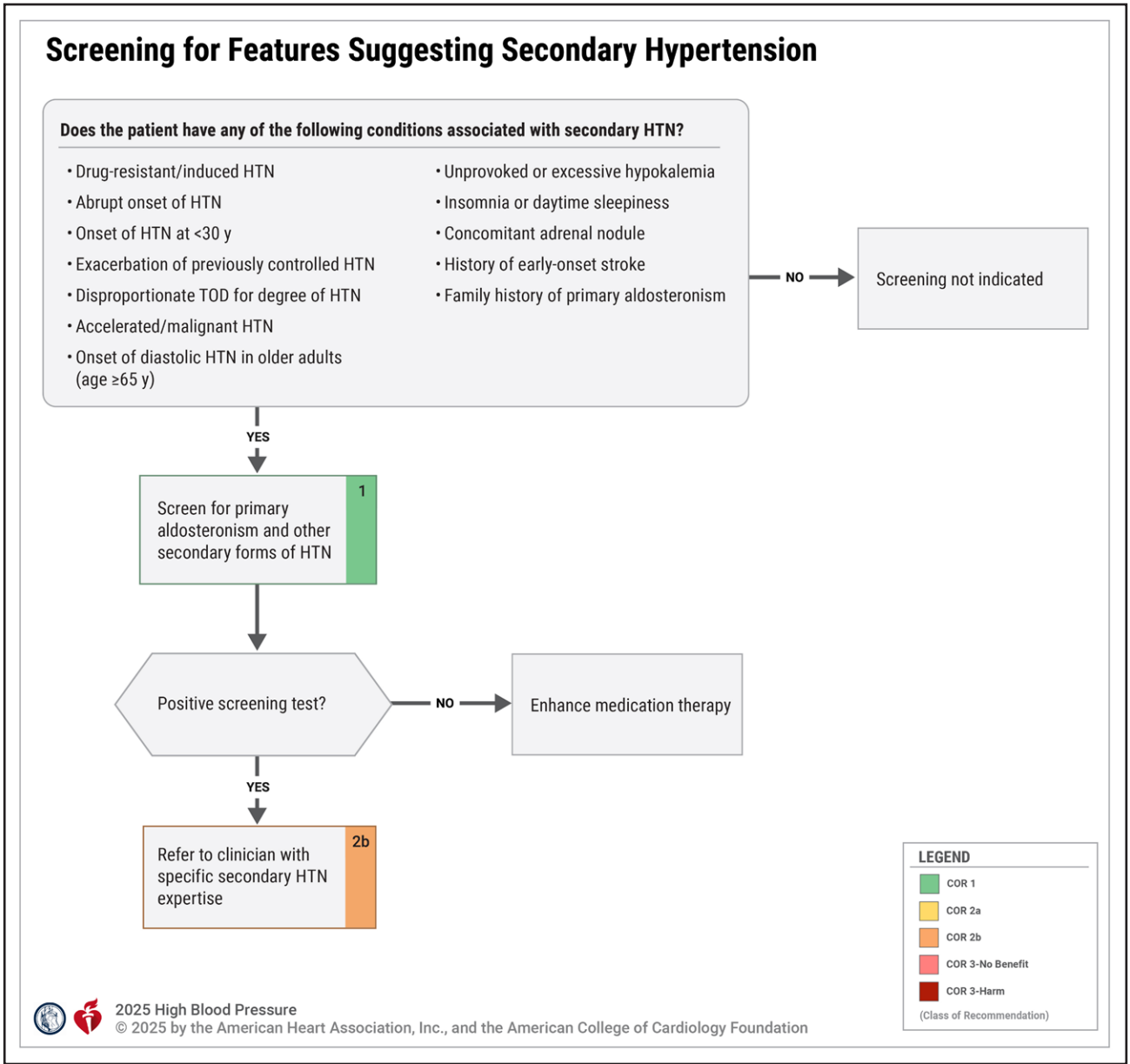


Figure 5. Screening for Features Suggesting Secondary Hypertension. Refer to Table 10 for additional tests for secondary hypertension. HTN indicates hypertension; and TOD, target organ damage (eg, cerebrovascular disease, hypertensive retinopathy, left ventricular hypertrophy, left ventricular dysfunction, 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 aldosterone⁴;

angiotensin-converting enzyme inhibitors (ACEis) and angiotensin receptor blockers (ARBs) may stimulate renin and suppress aldosterone⁴; 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 CCB²¹) 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).¹² 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}

Recommendations for Lifestyle and Psychosocial Approaches (Continued)		
COR	LOE	Recommendations
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 8⁴⁵), 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 con-

trol 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/m² for non-Asian populations and BMI 23.0–27.4 and ≥ 27.5 kg/m² for individuals of Asian heritage⁵⁰), 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).^{79,10,53–55} 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 $\geq 5\%$ of body weight or ≥ 3 kg/m² 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 surgery⁵³ 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 individuals⁶⁶ 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, 20995

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, hand-grip^{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 heterogeneous 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 benzo-thiadiazine 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 $\geq 7.5\%$ 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, $\geq 7.5\%$ 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 $\geq 7.5\%$ 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 $\geq 140/90$ 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 $\geq 130/80$ 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 $\geq 130/80$ 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 $\geq 7.5\%$, 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 5207 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 $\geq 7.5\%$ calculated with PREVENT is also equivalent to the Framingham Risk Score threshold of $\geq 15\%$, 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 $\geq 140/90$ mm Hg and the groups that receive key benefits when average BP is $\geq 130/80$ 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 $\geq 130/80$ mm Hg.^{3,7,8,10–12} The SPRINT trial, which

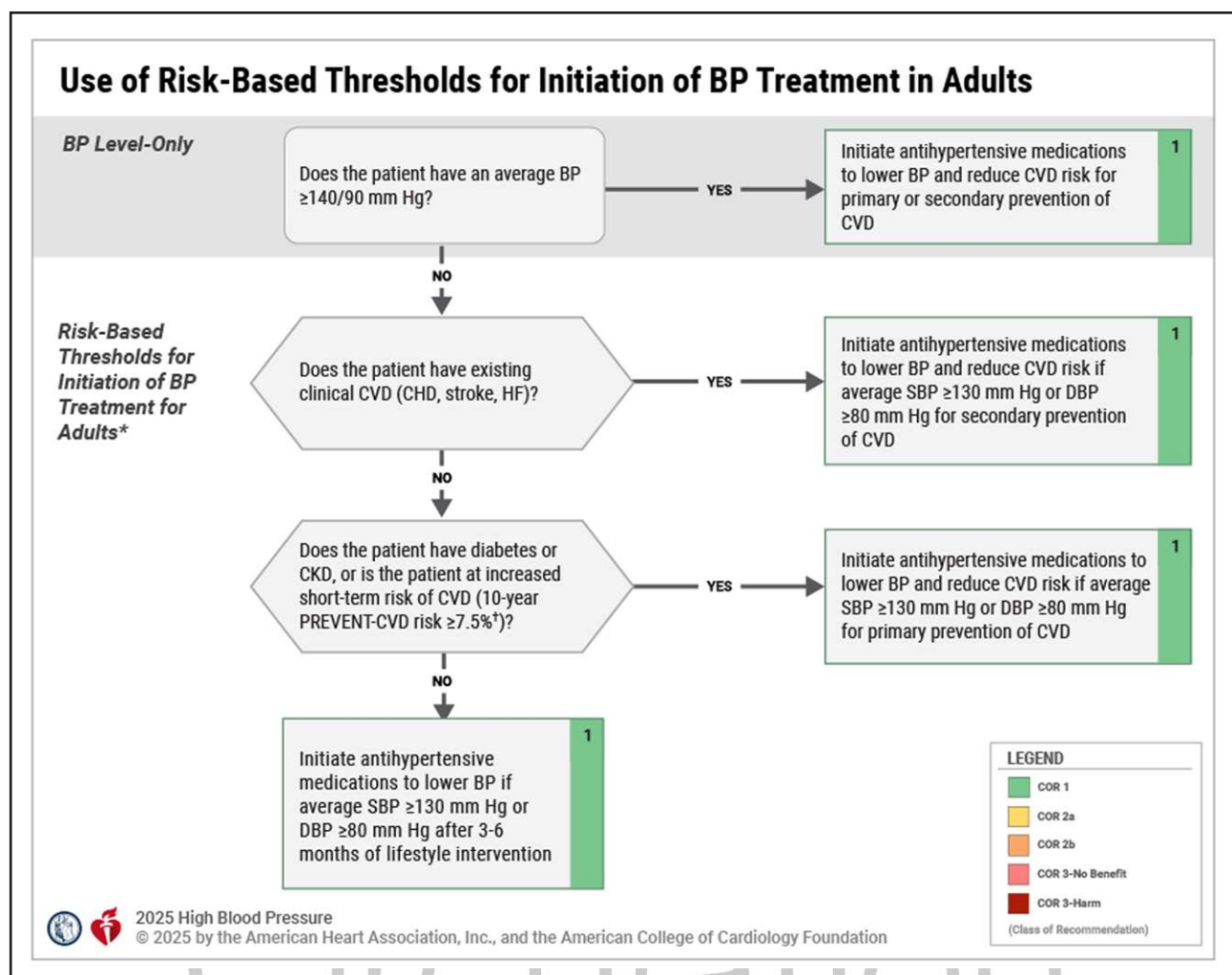


Figure 6. Use of Risk-Based Thresholds for Initiation of BP Treatment in Adults.

*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 $\geq 7.5\%$ 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 $\geq 7.5\%$ with PREVENT. In the SPRINT trial, increased predicted risk of CVD of $\geq 15\%$ based on the Framingham risk score was an inclusion criterion, and 76% of enrolled participants had a Framingham 10-year estimated CVD risk $\geq 15\%$.^{7,8} In the STEP trial, 65% of participants had a Framingham 10-year estimated CVD risk $\geq 15\%$, and this group (but not those at lower predicted risk) benefited from BP lowering. The level of risk estimated by Framingham risk $\geq 15\%$ is roughly equivalent to 10-year estimated CVD risk $\geq 7.5\%$ with PREVENT and 10-year estimated ASCVD risk $\geq 10\%$ with PCEs.^{7,17} Predicted CVD risk $\geq 15\%$ based on Framingham and $\geq 7.5\%$ 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 $\geq 130/80$ 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 ($\geq 140/90$ 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.
	Hydrochlorothiazide	25-50	1	
	Indapamide	1.25-2.5	1	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.
ACEi	Benazepril	10-40	1 or 2	Do not use in combination with ARB or direct renin inhibitor.
	Captopril	12.5-150	2 or 3	
	Enalapril	5-40	1 or 2	There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K+ supplements or K+-sparing drugs.
	Fosinopril	10-40	1	
	Lisinopril	10-40	1	There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis.
	Moexipril	7.5-30	1 or 2	
	Perindopril	4-16	1	Do not use if patient has history of angioedema with ACEi.
	Quinapril	10-80	1 or 2	Avoid use in pregnancy.
	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.
	Candesartan	8-32	1	
	Eprosartan	600-800	1 or 2	There is an increased risk of hyperkalemia in CKD or in those on K+ supplements or K+-sparing drugs.
	Irbesartan	150-300	1	There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis.
	Losartan	50-100	1 or 2	
	Olmesartan	20-40	1	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.
	Telmisartan	20-80	1	
	Valsartan	80-320	1	Avoid use in pregnancy.
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.
	Verapamil IR	120-360	3	
	Verapamil SR	120-360	1 or 2	Do not use in patients with HFrEF.
	Verapamil-delayed onset ER	100-300	1 (in the evening)	There are drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).
Diuretics-loop	Bumetanide	0.5-2	2	These are preferred diuretics in patients with symptomatic HF.
	Furosemide	20-80	2	
	Torsemide	5-10	1	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.

(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.
	Triamterene	50-100	1 or 2	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).
Diuretics—aldosterone antagonists	Eplerenone	50-100	1 or 2	These are preferred agents in primary aldosteronism and resistant hypertension.
	Spironolactone	25-100	1	Spironolactone is associated with greater risk of gynecostasia 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.
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.
	Propranolol IR	80-160	2	Avoid abrupt cessation.
	Propranolol LA	80-160	1	
Beta blockers—intrinsic sympathomimetic activity	Acebutolol	200-800	2	Generally avoid, especially in patients with CHD or HF.
	Penbutolol	10-40	1	Avoid abrupt cessation.
	Pindolol	10-60	2	
Combined alpha and beta blockers	Carvedilol	12.5-50	2	Use of carvedilol is preferred in patients with HFrEF.
	Carvedilol phosphate	20-80	1	Avoid abrupt cessation.
	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.
	Prazosin	2-20	2 or 3	
	Terazosin	1-20	1 or 2	These may be considered a second-line agent in patients with symptomatic benign prostatic hypertrophy.

(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.
	Clonidine patch	0.1-0.3	1 weekly	
	Methyldopa	250-1000	2	Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis.
	Guanfacine	0.5-2	1	Clonidine must be tapered to avoid rebound hypertension.
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	Aprocitan	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 ejection 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
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

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.



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}

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 levels⁷⁻⁹ (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 <120¹⁵ 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 patiomer and sodium zirconium cyclosilicate), noting the importance of taking them (primarily patiomer) 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 (patiomer)	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 12821 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 m², 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/m² 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/m² 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 m² 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

- 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
- 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 nifedipine 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

- 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

- 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}
- 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 PODCAST⁷ 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 diagnosis¹ 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 visits⁶³ 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 collaboration⁴⁰ 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 under-resourced 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

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

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).

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 mmHg and/or DBP ≥90 mmHg 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

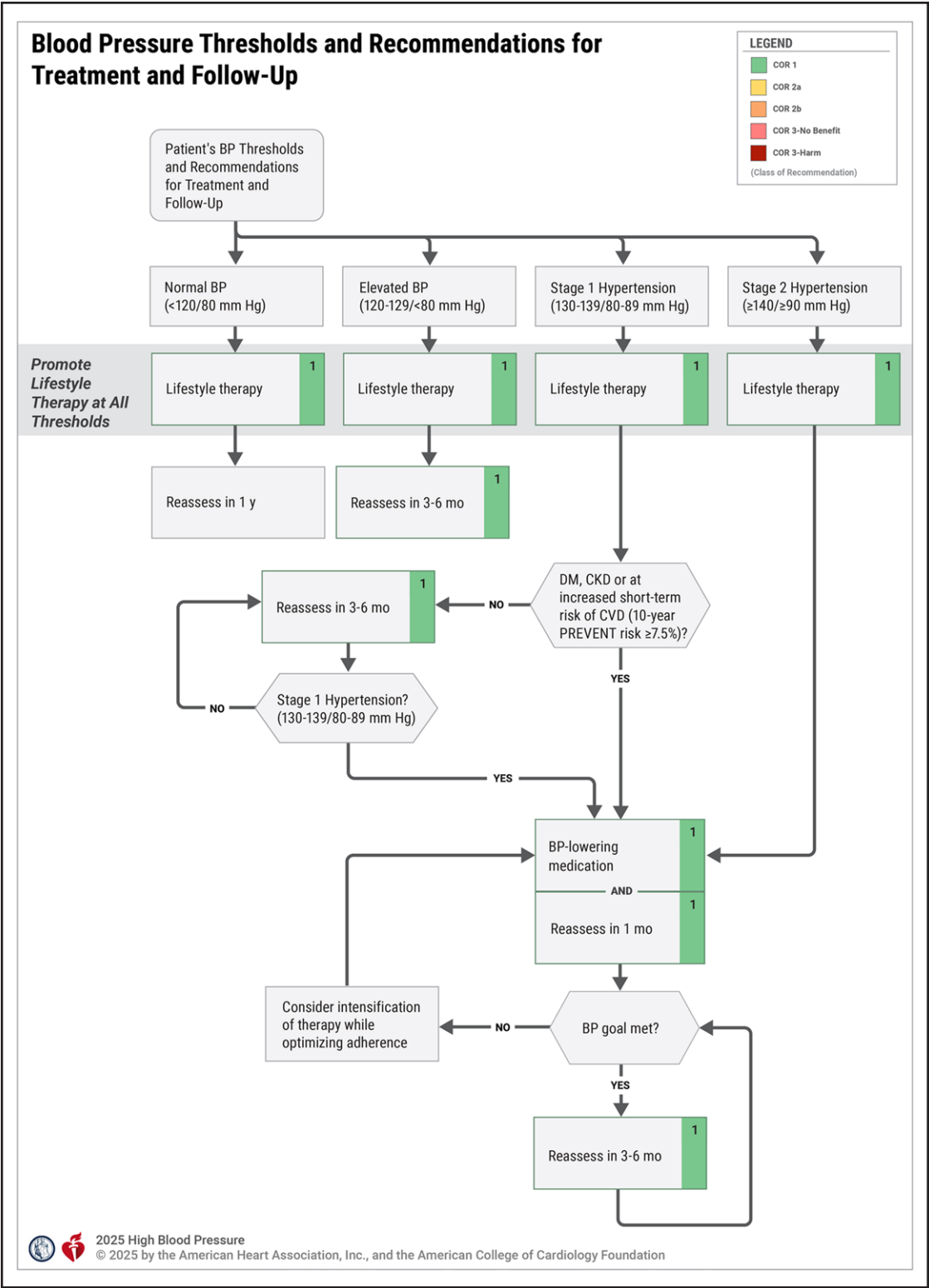


Figure 7. BP Thresholds and Recommendations for Treatment and Follow-Up. BP indicates blood pressure; CVD, cardiovascular disease; DM, diabetes mellitus. Based on the PREVENT calculator.^{52,70} Modified with permission from Whelton et al.⁷¹ Copyright 2018 American College of Cardiology Foundation and 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 preeclampsia² 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.⁴ 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. Atenolol¹¹ 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 Pregnancy²⁰

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

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. LactMed³³ 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,

Table 21. ACOG Diagnostic Criteria for Hypertension in Pregnancy²⁰

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.

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 birth-weight.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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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; <i>or</i> 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; <i>or</i> 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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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	

Reprinted with permission from American College of Obstetricians and Gynecologists.¹⁰ Copyright 2020 American College of Obstetricians and Gynecologists. 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

Recommendations for Resistant Hypertension and Renal Denervation (Continued)		
COR	LOE	Recommendations
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 m².^{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 Aprocritentan, 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. Aprocritentan 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 m².^{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 pre-existing 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).

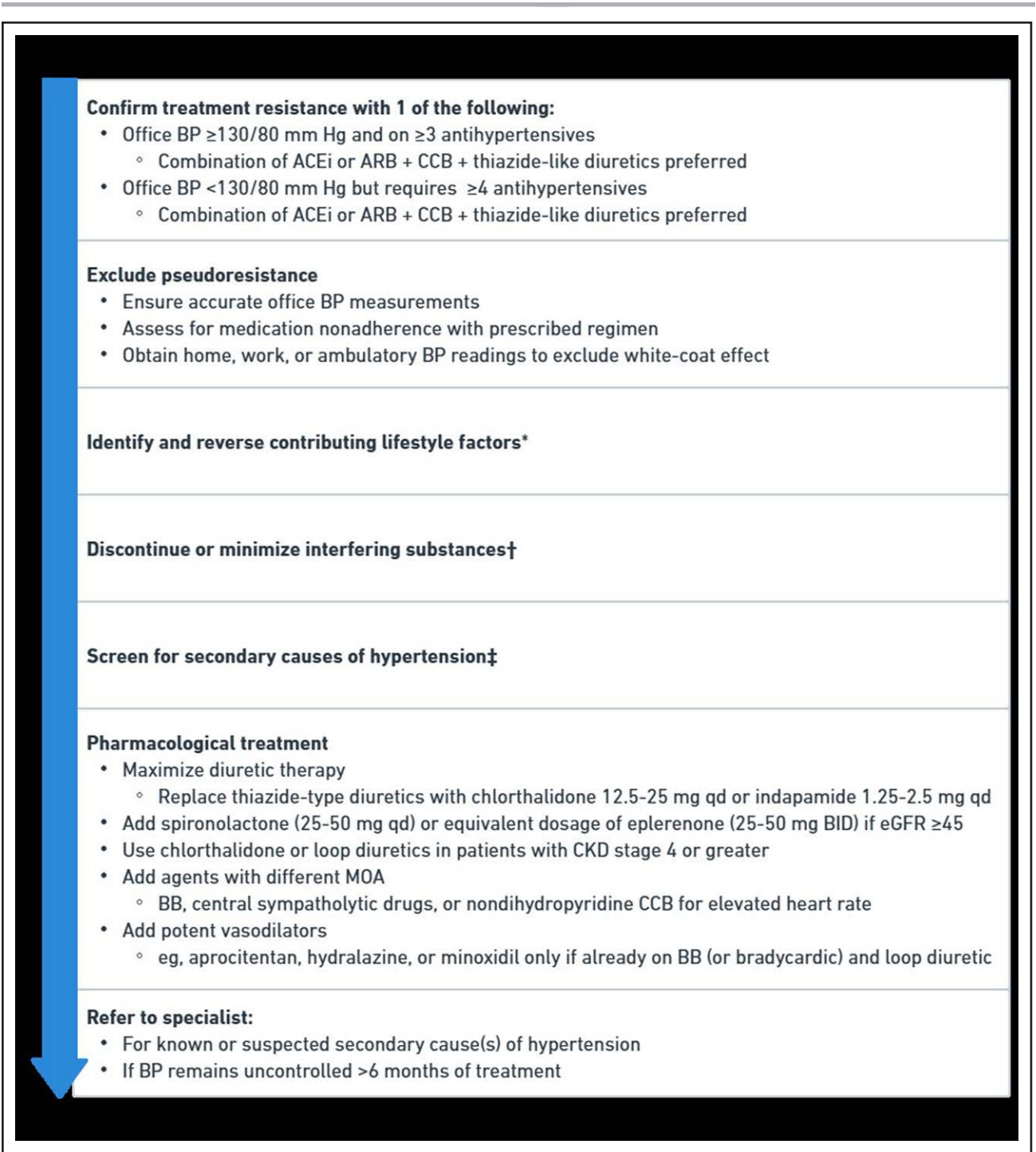


Figure 8. Resistant Hypertension: Diagnosis, Evaluation, and Treatment.
*Please refer to Section 5.2, on lifestyle factors. †Please refer to Table 11 for a complete list of drugs that elevate BP. ‡Please refer to Section 3.2.3, on secondary hypertension, and Subsections 3.2.3.1, 3.2.3.2, and 3.2.3.3. 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.

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 ques-

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.

tions 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

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}

Recommendations for Hypertensive Emergencies and Severe Hypertension in Nonpregnant and Nonstroke Patients* (Continued)		
COR	LOE	Recommendations
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.

- 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.
- 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.

- 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 wish⁷ 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, lipid 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 $\geq 160/90$ mm Hg or SBP elevation $\geq 20\%$ 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

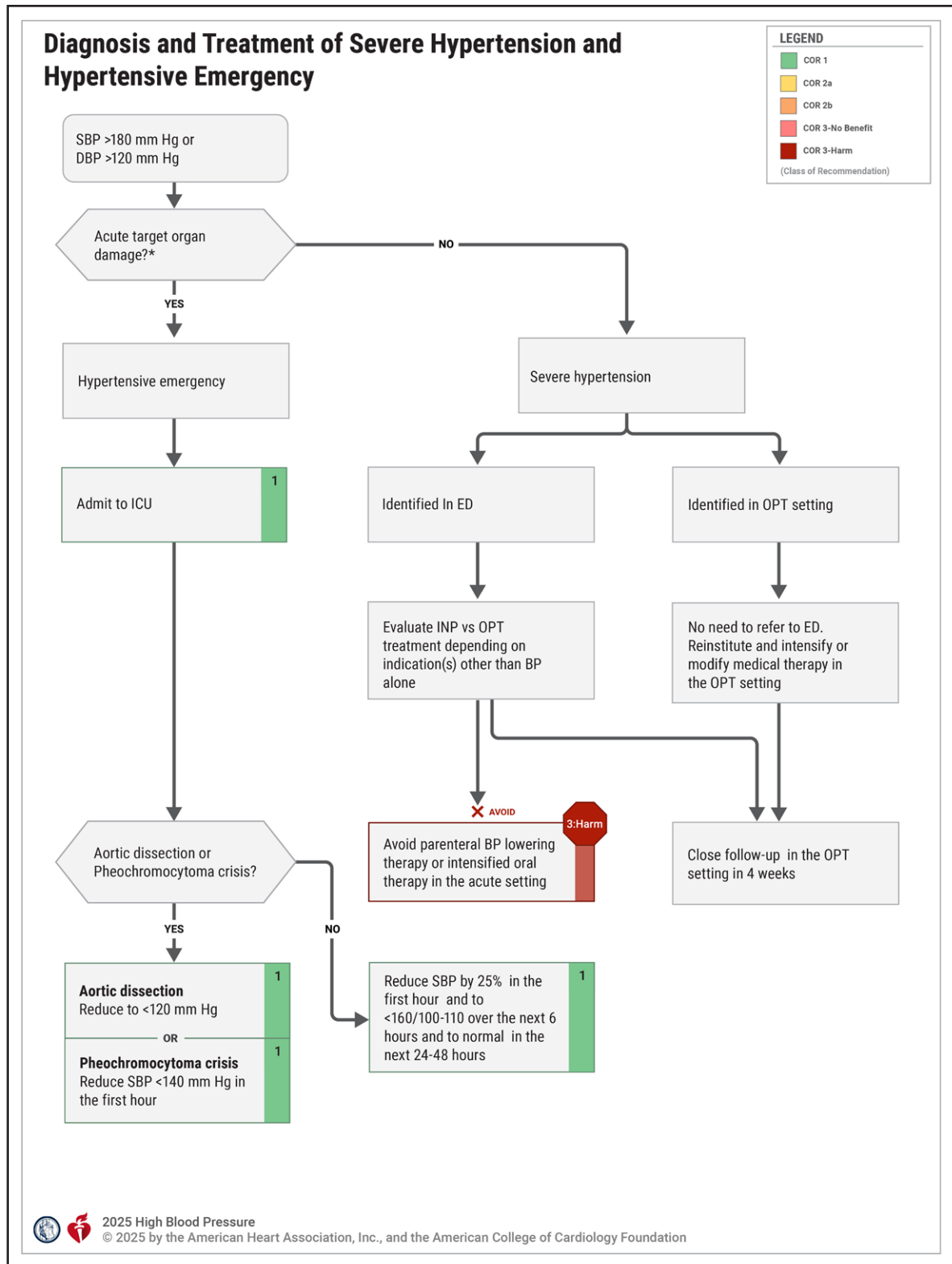


Figure 9. Diagnosis and Treatment of Severe Hypertension and Hypertensive Emergency.

*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

This document was approved by the American College of Cardiology Clinical Policy Approval Committee and the American Heart Association Science Advisory and Coordinating Committee in April 2025, and the American College of Cardiology Science and Quality Committee and the American Heart Association Executive Committee in May 2025.

Supplemental materials are available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000001356>

This article has been copublished in *Hypertension* and *Journal of the American College of Cardiology*.

Copies: This document is available on the websites of the American Heart Association (professional.heart.org) and the American College of Cardiology (www.acc.org). A copy of the document is also available at <https://professional.heart.org/statements> by selecting the "Guidelines & Statements" button. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com.

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REFERENCES

Preamble

1. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Institute of Medicine (US). Clinical Practice Guidelines We Can Trust. *National Academies Press*; 2011.
2. Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine (US). Finding What Works in Healthcare: Standards for Systematic Reviews. *National Academies Press*; 2011.
3. Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. *Circulation*. 2014;129:2329–2345.
4. ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and policies from the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association. 2010. Accessed May 14, 2024. <https://www.acc.org/Guidelines/About-Guidelines-and-Clinical-Documents/Methodology> and https://professional.heart.org/-/media/phd-files/guidelines-and-statements/methodology_manual_and_policies_ucm_319826.pdf.
5. Halperin JL, Levine GN, Al-Khatib SM, et al. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2016;133:1426–1428.
6. Arnett DK, Goodman RA, Halperin JL, et al. AHA/ACC/HHS strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions: from the American Heart Association, American College of Cardiology, and US Department of Health and Human Services. *Circulation*. 2014;130:1662–1667.
7. Levine GN, O'Gara PT, Beckman JA, et al. Recent innovations, modifications, and evolution of ACC/AHA clinical practice guidelines: an update for our constituencies: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139:e879–e886.

Introduction

1. Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149:430–449.
2. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S76–S99.
3. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(suppl 2):s102–s138.
4. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e596–e646.
5. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e72–e227.
6. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e895–e1032.
7. Isselbacher EM, Preventza O, Black JH 3rd, et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;146:e334–e482.
8. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023;148:e9–e119.
9. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149:e1–e156.

10. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS guideline for the management of lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149:e1313–e1410.
11. Thompson A, Fleischmann KE, Smilowitz NR, et al. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM guideline for perioperative cardiovascular management for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;150:e351–e442.
12. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. *Circulation*. 2015;132:1157–1213.
13. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. *Hypertension*. 2018;72:e53–e90.
14. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. *Hypertension*. 2019;73:e35–e66.
15. Casey DE Jr, Thomas RJ, Bhalla V, et al. 2019 AHA/ACC clinical performance and quality measures for adults with high blood pressure: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *Circ Cardiovasc Qual Outcomes*. 2019;12:e000057.
16. Muntner P, Einhorn PT, Cushman WC, et al. Blood pressure assessment in adults in clinical practice and clinic-based research: JACC scientific expert panel. *J Am Coll Cardiol*. 2019;73:317–335.
17. Shimbo D, Artinian NT, Basile JN, et al. Self-measured blood pressure monitoring at home: a joint policy statement from the American Heart Association and American Medical Association. *Circulation*. 2020;142:E42–E63.
18. Bhalla V, Textor SC, Beckman JA, et al. Revascularization for renovascular disease: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e128–e143.
19. Choudhry NK, Kronish IM, Vongpatanasin W, et al. Medication adherence and blood pressure control: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e1–e14.
20. Takahashi EA, Schwamm LH, Adeoye OM, et al. An overview of telehealth in the management of cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2022;146:e558–e568.
21. Garovic VD, Dechend R, Easterling T, et al. Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e21–e41.
22. Lloyd-Jones DM, Allen NB, Anderson CAM, et al. Life's essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a Presidential Advisory from the American Heart Association. *Circulation*. 2022;146:e18–e43.
23. Kittleson MM, Panjath GS, Amancherla K, et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81:1835–1878.
24. Ndumele CE, Rangaswami J, Chow SL, et al. Cardiovascular-kidney-metabolic health: a Presidential Advisory from the American Heart Association. *Circulation*. 2023;148:1606–1635.
25. Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1982–2004.
26. Abdalla M, Bolen SD, Brettler J, et al. Implementation strategies to improve blood pressure control in the United States: a scientific statement from the American Heart Association and American Medical Association. *Hypertension*. 2023;80:e143–e157.
27. Cluett JL, Blazek O, Brown AL, et al. Renal denervation for the treatment of hypertension: a scientific statement from the American Heart Association. *Hypertension*. 2024;81:e135–e148.
28. Methodology manual and policies from the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association. 2010. Accessed June 3, 2020. https://professional.heart.org/-/media/phd-files/guidelines-and-statements/methodology_manual_and_policies_ucm_319826.pdf.

2.1. Definition of High Blood Pressure

1. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903–1913.

2. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014;383:1899–1911.
3. Whelton SP, McEvoy JW, Shaw L, et al. Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. *JAMA Cardiol*. 2020;5:1011–1018.
4. Fuchs SC, Poli-de-Figueiredo CE, Figueiredo Neto JA, et al. Effectiveness of chlorthalidone plus amloride for the prevention of hypertension: the PREVER-Prevention randomized clinical trial. *J Am Heart Assoc*. 2016;5:e004248.
5. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.

3. Evaluation and Diagnosis

1. Global Burden Disease Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1223–1249.
2. Forouzanfar MH, Liu P, Roth GA, et al. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990–2015. *JAMA*. 2017;317:165–182.
3. Martin SS, Aday AW, Almarzooq ZI, et al. 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913.
4. Franklin SS, Gustin Wt, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure. The Framingham Heart Study. *Circulation*. 1997;96:308–315.
5. Chen V, Ning H, Allen N, et al. Lifetime risks for hypertension by contemporary guidelines in African American and White men and women. *JAMA Cardiol*. 2019;4:455–459.
6. Carson AP, Howard G, Burke GL, et al. Ethnic differences in hypertension incidence among middle-aged and older adults: the multi-ethnic study of atherosclerosis. *Hypertension*. 2011;57:1101–1107.
7. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. *JAMA*. 2002;287:1003–1010.
8. Lloyd-Jones DM, Evans JC, Larson MG, et al. Cross-classification of JNC VI blood pressure stages and risk groups in the Framingham Heart Study. *Arch Intern Med*. 1999;159:2206–2212.
9. Jaeger BC, Chen L, Foti K, et al. Hypertension statistics for US adults: an open-source web application for analysis and visualization of National Health and Nutrition Examination Survey data. *Hypertension*. 2023;80:1311–1320.
10. Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1982–2004.
11. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903–1913.
12. Whelton SP, McEvoy JW, Shaw L, et al. Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. *JAMA Cardiol*. 2020;5:1011–1018.
13. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014;383:1899–1911.
14. Weldegioris M, Woodward M. The impact of hypertension on chronic kidney disease and end-stage renal disease is greater in men than women: a systematic review and meta-analysis. *BMC Nephrol*. 2020;21:506.
15. Garofalo C, Borrelli S, Pacilio M, et al. Hypertension and prehypertension and prediction of development of decreased estimated GFR in the general population: a meta-analysis of cohort studies. *Am J Kidney Dis*. 2016;67:89–97.
16. Yaffe K, Vittinghoff E, Pletcher MJ, et al. Early adult to midlife cardiovascular risk factors and cognitive function. *Circulation*. 2014;129:1560–1567.
17. Liu K, Colangelo LA, Daviglius ML, et al. Can antihypertensive treatment restore the risk of cardiovascular disease to ideal levels? The Coronary Artery Risk Development in Young Adults (CARDIA) study and the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Heart Assoc*. 2015;4:e002275.
18. Lieb W, Enserro DM, Sullivan LM, et al. Residual cardiovascular risk in individuals on blood pressure-lowering treatment. *J Am Heart Assoc*. 2015;4:e002155.
19. Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1982–2004.
20. Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149:430–449.

3.1.1. Accurate Measurement of In-Office BP

1. Giorgini P, Weder AB, Jackson EA, et al. A review of blood pressure measurement protocols among hypertension trials: implications for “evidence-based” clinical practice. *J Am Soc Hypertens*. 2014;8:670–676.
2. Kallioinen N, Hill A, Horswill MS, et al. Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings: a systematic review. *J Hypertens*. 2017;35:421–441.
3. Liu J, Li Y, Li J, et al. Sources of automatic office blood pressure measurement error: a systematic review. *Physiol Meas*. 2022;43(9). doi: 10.1088/1361-6579/ac890e.
4. Cohen JB, Padwal RS, Gutkin M, et al. History and justification of a national blood pressure measurement validated device listing. *Hypertension*. 2019;73:258–264.
5. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. *Hypertension*. 2019;73:e35–e66.
6. Roerecke M, Kaczorowski J, Myers MG. Comparing automated office blood pressure readings with other methods of blood pressure measurement for identifying patients with possible hypertension: a systematic review and meta-analysis. *JAMA Intern Med*. 2019;179:351–362.
7. Ishigami J, Charleston J, Miller ER 3rd, et al. Effects of cuff size on the accuracy of blood pressure readings: the Cuff(SZ) randomized crossover trial. *JAMA Intern Med*. 2023;183:1061–1068.
8. Muntner P, Einhorn PT, Cushman WC, et al. Blood pressure assessment in adults in clinical practice and clinic-based research: JACC scientific expert panel. *J Am Coll Cardiol*. 2019;73:317–335.
9. American Medical Association. Blood Pressure Devices (US Blood Pressure Validated Device Listing). Accessed October 17, 2024. <https://www.validatebp.org/>.
10. Powers BJ, Olsen MK, Smith VA, et al. Measuring blood pressure for decision making and quality reporting: where and how many measures? *Ann Intern Med*. 2011;154:781–788, W-289–790.
11. Kronish IM, Edmondson D, Shimbo D, et al. A comparison of the diagnostic accuracy of common office blood pressure measurement protocols. *Am J Hypertens*. 2018;31:827–834.
12. Hayer R, Kirley K, Cohen JB, et al. Using web-based training to improve accuracy of blood pressure measurement among health care professionals: a randomized trial. *J Clin Hypertens (Greenwich)*. 2022;24:255–262.
13. Picone DS, Deshpande RA, Schultz MG, et al. Nonvalidated home blood pressure devices dominate the online marketplace in Australia: major implications for cardiovascular risk management. *Hypertension*. 2020;75:1593–1599.
14. National Health and Nutrition Examination Survey. Blood pressure procedures manual. Centers for Disease Control and Prevention. Updated June 2019. Accessed May, 2024. <https://www.cdc.gov/nchs/data/nhanes/2019-2020/manuals/2019-Blood-Pressure-Procedures-Manual-508.pdf>.
15. Stergiou GS, Kyriakoulis KG, Stamboliu E, et al. Blood pressure measurement in atrial fibrillation: review and meta-analysis of evidence on accuracy and clinical relevance. *J Hypertens*. 2019;37:2430–2441.
16. Fonseca-Reyes S, Fonseca-Cortes K, Coca A, et al. Conventional office blood pressure measurements and unattended automated office blood pressure compared with home self-measurement and 24-h ambulatory blood pressure monitoring. *Blood Press Monit*. 2023;28:59–66.
17. Bauer F, Seibert FS, Rohn B, et al. Attended versus unattended blood pressure measurement in a real life setting. *Hypertension*. 2018;71:243–249.
18. Green BB, Anderson ML, Cook AJ, et al. Automated office blood pressure and the impact of attendance and rest on diagnostic accuracy. *Am J Hypertens*. 2022;35:638–646.
19. Kollias A, Stamboliu E, Kyriakoulis KG, et al. Unattended versus attended automated office blood pressure: systematic review and meta-analysis of studies using the same methodology for both methods. *J Clin Hypertens (Greenwich)*. 2019;21:148–155.

20. Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation*. 2005;111:697–716.
21. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
22. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31:1281–1357.
23. Weir MR. In the clinic: hypertension. *Ann Intern Med*. 2014;161:ITC1–ITC15;quiz ITC16.

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

1. Mahmoodi BK, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet*. 2012;380:1649–1661.
2. Berry JD, Nambi V, Ambrosius WT, et al. Associations of high-sensitivity troponin and natriuretic peptide levels with outcomes after intensive blood pressure lowering: findings from the SPRINT randomized clinical trial. *JAMA Cardiol*. 2021;6:1397–1405.
3. Pandey A, Keshvani N, Ayers C, et al. Association of cardiac injury and malignant left ventricular hypertrophy with risk of heart failure in African Americans: the Jackson Heart Study. *JAMA Cardiol*. 2019;4:51–58.
4. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.

3.1.4. ABPM and HBPM

1. Piper MA, Evans CV, Burda BU, et al. Diagnostic and predictive accuracy of blood pressure screening methods with consideration of rescreening intervals: a systematic review for the US Preventive Services Task Force. *Ann Intern Med*. 2015;162:192–204.
2. Guirguis-Blake JM, Evans CV, Webber EM, et al. Screening for hypertension in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2021;325:1657–1669.
3. Uhlig K, Balk EM, Patel K, et al. Self-Measured Blood Pressure Monitoring: Comparative Effectiveness. *Agency for Healthcare Research and Quality (US)*; 2012.
4. Margolis KL, Asche SE, Bergdall AR, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. *JAMA*. 2013;310:46–56.
5. McManus RJ, Mant J, Haque MS, et al. Effect of self-monitoring and medication self-titration on systolic blood pressure in hypertensive patients at high risk of cardiovascular disease: the TASMIN-SR randomized clinical trial. *JAMA*. 2014;312:799–808.
6. Tucker KL, Sheppard JP, Stevens R, et al. Self-monitoring of blood pressure in hypertension: a systematic review and individual patient data meta-analysis. *PLoS Med*. 2017;14:e1002389.
7. Shimbo D, Abdalla M, Falzon L, et al. Studies comparing ambulatory blood pressure and home blood pressure on cardiovascular disease and mortality outcomes: a systematic review. *J Am Soc Hypertens*. 2016;10:224–234. e217.
8. Panagiotakos D, Antza C, Kotsis V. Ambulatory and home blood pressure monitoring for cardiovascular disease risk evaluation: a systematic review and meta-analysis of prospective cohort studies. *J Hypertens*. 2024;42:1–9.
9. Agarwal R, Bills JE, Hecht TJ, et al. Role of home blood pressure monitoring in overcoming therapeutic inertia and improving hypertension control: a systematic review and meta-analysis. *Hypertension*. 2011;57:29–38.
10. Shimbo D, Abdalla M, Falzon L, et al. Role of ambulatory and home blood pressure monitoring in clinical practice. *Ann Intern Med*. 2015;163:691–700.

11. Schwartz JE, Muntner P, Kronish IM, et al. Reliability of office, home, and ambulatory blood pressure measurements and correlation with left ventricular mass. *J Am Coll Cardiol*. 2020;76:2911–2922.
12. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. *Hypertension*. 2019;73:e35–e66.
13. Ravenell J, Shimbo D, Booth JN 3rd, et al. Thresholds for ambulatory blood pressure among African Americans in the Jackson Heart Study. *Circulation*. 2017;135:2470–2480.
14. Vongpatanasin W, Ayers C, Lodhi H, et al. Diagnostic thresholds for blood pressure measured at home in the context of the 2017 hypertension guideline. *Hypertension*. 2018;72:1312–1319.
15. Muntner P, Carey RM, Jamerson K, et al. Rationale for ambulatory and home blood pressure monitoring thresholds in the 2017 American College of Cardiology/American Heart Association guideline. *Hypertension*. 2019;73:33–38.
16. Shimbo D, Abdalla M, Falzon L, et al. Studies comparing ambulatory blood pressure and home blood pressure on cardiovascular disease and mortality outcomes: a systematic review. *J Am Soc Hypertens*. 2016;10: 224–234. e17.
17. Chappell LC, Tucker KL, Galal U, et al. Effect of self-monitoring of blood pressure on blood pressure control in pregnant individuals with chronic or gestational hypertension: the BUMP 2 randomized clinical trial. *JAMA*. 2022;327:1666–1678.
18. Shimbo D, Artinian NT, Basile JN, et al. Self-measured blood pressure monitoring at home: a joint policy statement from the American Heart Association and American Medical Association. *Circulation*. 2020;142:E42–E63.
19. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.

3.1.4.1. Cuffless BP Devices

1. Islam SMS, Chow CK, Daryabeygikhobensara R, et al. Wearable cuffless blood pressure monitoring devices: a systematic review and meta-analysis. *Eur Heart J Digit Health*. 2022;3:323–337.
2. Han M, Lee YR, Park T, et al. Feasibility and measurement stability of smartwatch-based cuffless blood pressure monitoring: a real-world prospective observational study. *Hypertens Res*. 2023;46:922–931.
3. Stergiou GS, Mukkamala R, Avolio A, et al. Cuffless blood pressure measuring devices: review and statement by the European Society of Hypertension Working Group on blood pressure monitoring and cardiovascular variability. *J Hypertens*. 2022;40:1449–1460.
4. Hu JR, Martin G, Iyengar S, et al. Validating cuffless continuous blood pressure monitoring devices. *Cardiovasc Digit Health J*. 2023;4:9–20.
5. Stergiou GS, Avolio AP, Palatini P, et al. European Society of Hypertension recommendations for the validation of cuffless blood pressure measuring devices: European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability. *J Hypertens*. 2023;41:2074–2087.
6. International Organization for Standardization. Part 3: clinical investigation of continuous automated measurement type (ISO 81060-3:2022). Accessed August 19, 2024. <https://www.iso.org/standard/71161.html>.

3.2.1. Causes of Hypertension

1. Howard G, Cushman M, Moy CS, et al. Association of clinical and social factors with excess hypertension risk in Black compared with White US adults. *JAMA*. 2018;320:1338–1348.
2. Choi Y, Larson N, Steffen LM, et al. Plant-centered diet and risk of incident cardiovascular disease during young to middle adulthood. *J Am Heart Assoc*. 2021;10:e020718.
3. Ndanuko RN, Tapsell LC, Charlton KE, et al. Dietary patterns and blood pressure in adults: a systematic review and meta-analysis of randomized controlled trials. *Adv Nutr*. 2016;7:76–89.
4. Elliott P, Stamler J, Dyer AR, et al. Association between protein intake and blood pressure: the INTERMAP study. *Arch Intern Med*. 2006;166:79–87.
5. Stamler J. The INTERSALT study: background, methods, findings, and implications. *Am J Clin Nutr*. 1997;65:626S–642S.
6. Stamler J, Chan Q, Daviglus ML, et al. Relation of dietary sodium (salt) to blood pressure and its possible modulation by other dietary factors. *Hypertension*. 2018;71:631–637.
7. Lloyd-Jones DM, Liu K, Colangelo LA, et al. Consistently stable or decreased body mass index in young adulthood and longitudinal changes in

metabolic syndrome components: the Coronary Artery Risk Development in Young Adults Study. *Circulation*. 2007;115:1004–1011.

8. Wilson PWF, D'Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med*. 2002;162:1867–1872.
9. Zhang Z, Li C, Hong J, et al. Secular trends of population-attributable fractions of obesity for hypertension among US population by sex and race/ethnicity: analysis from NHANES 1999–2018. *Prev Med*. 2024;41:102719.
10. Hou H, Zhao Y, Yu W, et al. Association of obstructive sleep apnea with hypertension: a systematic review and meta-analysis. *J Glob Health*. 2018;8:010405.
11. Wang Y, Mei H, Jiang Y-R, et al. Relationship between duration of sleep and hypertension in adults: a meta-analysis. *J Clin Sleep Med*. 2015;11:1047–1056.
12. Spruill TM, Butler MJ, Thomas SJ, et al. Association between high perceived stress over time and incident hypertension in black adults: findings from the Jackson Heart Study. *J Am Heart Assoc*. 2019;8:e012139.
13. Liu J, Sui X, Lavie CJ, et al. Effects of cardiorespiratory fitness on blood pressure trajectory with aging in a cohort of healthy men. *J Am Coll Cardiol*. 2014;64:1245–1253.
14. Bae S, Hong Y-C. Exposure to bisphenol A from drinking canned beverages increases blood pressure. *Hypertension*. 2015;65:313–319.
15. Liang R, Zhang B, Zhao X, et al. Effect of exposure to PM2.5 on blood pressure: a systematic review and meta-analysis. *J Hypertens*. 2014;32:2130–2140; discussion 2141.
16. Levy D, DeStefano AL, Larson MG, et al. Evidence for a gene influencing blood pressure on chromosome 17. *Hypertension*. 2000;36:477–483.
17. Ehret GB, Munroe PB, Rice KM, et al. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature*. 2011;478:103–109.
18. Keaton JM, Kamali Z, Xie T, et al. Genome-wide analysis in over 1 million individuals of European ancestry yields improved polygenic risk scores for blood pressure traits. *Nat Genet*. 2024;56:778–791.
13. Stergiou GS, Asayama K, Thijs L, et al. Prognosis of white-coat and masked hypertension: International Database of Home blood pressure in relation to Cardiovascular Outcome. *Hypertension*. 2014;63:675–682.
14. Zhang DY, Guo QH, An DW, et al. A comparative meta-analysis of prospective observational studies on masked hypertension and masked uncontrolled hypertension defined by ambulatory and home blood pressure. *J Hypertens*. 2019;37:1775–1785.
15. Thakkar HV, Pope A, Anpalahan M. Masked hypertension: a systematic review. *Heart Lung Circ*. 2020;29:102–111.
16. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. *Hypertension*. 2019;73:e35–e66.
17. Muntner P, Einhorn PT, Cushman WC, et al. Blood pressure assessment in adults in clinical practice and clinic-based research: JACC scientific expert panel. *J Am Coll Cardiol*. 2019;73:317–335.
18. Piper MA, Evans CV, Burda BU, et al. Diagnostic and predictive accuracy of blood pressure screening methods with consideration of rescreening intervals: a systematic review for the US Preventive Services Task Force. *Ann Intern Med*. 2015;162:192–204.
19. Guirguis-Blake JM, Evans CV, Webber EM, et al. Screening for hypertension in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2021;325:1657–1669.
20. Shimbo D, Abdalla M, Falzon L, et al. Studies comparing ambulatory blood pressure and home blood pressure on cardiovascular disease and mortality outcomes: a systematic review. *J Am Soc Hypertens*. 2016;10:224–234.e17.
21. Panagiotakos D, Antza C, Kotsis V. Ambulatory and home blood pressure monitoring for cardiovascular disease risk evaluation: a systematic review and meta-analysis of prospective cohort studies. *J Hypertens*. 2024;42:1–9.
22. Giorgini P, Weder AB, Jackson EA, et al. A review of blood pressure measurement protocols among hypertension trials: implications for “evidence-based” clinical practice. *J Am Soc Hypertens*. 2014;8:670–676.
23. Franklin SS, Thijs L, Asayama K, et al. The cardiovascular risk of white-coat hypertension. *J Am Coll Cardiol*. 2016;68:2033–2043.
24. Shimbo D, Muntner P. Should out-of-office monitoring be performed for detecting white coat hypertension? *Ann Intern Med*. 2019;170:890–892.
25. Shimbo D, Kuruvilla S, Haas D, et al. Preventing misdiagnosis of ambulatory hypertension: algorithm using office and home blood pressures. *J Hypertens*. 2009;27:1775–1783.
26. Verdecchia P, Schillaci G, Borgioni C, et al. White coat hypertension and white coat effect. Similarities and differences. *Am J Hypertens*. 1995;8:790–798.
27. Ugajin T, Hozawa A, Ohkubo T, et al. White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. *Arch Intern Med*. 2005;165:1541–1546.
28. Anstey DE, Booth JN 3rd, Abdalla M, et al. Predicted atherosclerotic cardiovascular disease risk and masked hypertension among Blacks in the Jackson Heart Study. *Circ Cardiovasc Qual Outcomes*. 2017;10(7):e003421.
29. Shimbo D, Newman JD, Schwartz JE. Masked hypertension and prehypertension: diagnostic overlap and interrelationships with left ventricular mass: the Masked Hypertension Study. *Am J Hypertens*. 2012;25:664–671.
30. Sheppard JP, Martin U, Gill P, et al. Prospective external validation of the Predicting Out-of-Office Blood Pressure (PROOF-BP) strategy for triaging ambulatory monitoring in the diagnosis and management of hypertension: observational cohort study. *BMJ*. 2018;361:k2478.
31. Bellows BK, Xu J, Sheppard JP, et al. Predicting out-of-office blood pressure in a diverse US population. *Am J Hypertens*. 2022;35:533–542.
32. Walsh S, Choi E, Fang C, et al. The diagnostic accuracy of using borderline high office blood pressure thresholds to diagnose masked hypertension according to the 2017 American College of Cardiology/American Heart Association blood pressure guideline. *Am J Hypertens*. 2025;38:288–294.
33. Muntner P, Abdalla M, Correa A, et al. Hypertension in Blacks: unanswered questions and future directions for the JHS (Jackson Heart Study). *Hypertension*. 2017;69:761–769.
34. Huang JF, Zhang DY, An DW, et al. Efficacy of antihypertensive treatment for target organ protection in patients with masked hypertension (ANTI-MASK): a multicentre, double-blind, placebo-controlled trial. *EClinicalMedicine*. 2024;74:102736.
35. Hoshida S, Yano Y, Kanegae H, et al. Effect of lowering home blood pressure on subclinical cardiovascular disease in masked uncontrolled hypertension. *J Am Coll Cardiol*. 2018;71:2858–2859.
36. Abdalla M, Goldsmith J, Muntner P, et al. Is isolated nocturnal hypertension a reproducible phenotype? *Am J Hypertens*. 2016;29:33–38.

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

1. Cohen JB, Lotito MJ, Trivedi UK, et al. Cardiovascular events and mortality in white coat hypertension: a systematic review and meta-analysis. *Ann Intern Med*. 2019;170:853–862.
2. Briasoulis A, Androulakis E, Palla M, et al. White-coat hypertension and cardiovascular events: a meta-analysis. *J Hypertens*. 2016;34:593–599.
3. Muntner P, Booth JN, Shimbo D, et al. Is white-coat hypertension associated with increased cardiovascular and mortality risk? *J Hypertens*. 2016;34:1655–1658.
4. Franklin SS, Thijs L, Hansen TW, et al. Significance of white-coat hypertension in older persons with isolated systolic hypertension: a meta-analysis using the International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes population. *Hypertension*. 2012;59:564–571.
5. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta analysis. *Am J Hypertens*. 2011;24:52–58.
6. Siven SS, Niiranen TJ, Kantola IM, et al. White-coat and masked hypertension as risk factors for progression to sustained hypertension: the Finn-Home study. *J Hypertens*. 2016;34:54–60.
7. Mancia G, Bombelli M, Facchetti R, et al. Long-term risk of sustained hypertension in white-coat or masked hypertension. *Hypertension*. 2009;54:226–232.
8. Faria J, Mesquita Bastos J, Bertoquini S, et al. Long-term risk of progression to sustained hypertension in white-coat hypertension with normal night-time blood pressure values. *Int J Hypertens*. 2020;2020:8817544.
9. Pierdomenico SD, Lapenna D, Bucci A, et al. Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. *Am J Hypertens*. 2005;18:1422–1428.
10. Salles GF, Cardoso CR, Muxfeldt ES. Prognostic influence of office and ambulatory blood pressures in resistant hypertension. *Arch Intern Med*. 2008;168:2340–2346.
11. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. *Hypertension*. 2018;72:e53–e90.
12. Cardoso CRL, Salles GF. Prognostic impact of home blood pressures for adverse cardiovascular outcomes and mortality in patients with resistant hypertension: a prospective cohort study. *Hypertension*. 2021;78:1617–1627.

37. Li Y, Staessen JA, Lu L, et al. Is isolated nocturnal hypertension a novel clinical entity? Findings from a Chinese population study. *Hypertension*. 2007;50:333–339.
 38. Gumz ML, Shimbo D, Abdalla M, et al. Toward precision medicine: circadian rhythm of blood pressure and chronotherapy for hypertension – 2021 NHLBI workshop report. *Hypertension*. 2023;80:503–522.
 39. Stergiou G, Brunstrom M, MacDonald T, et al. Bedtime dosing of antihypertensive medications: systematic review and consensus statement: International Society of Hypertension position paper endorsed by World Hypertension League and European Society of Hypertension. *J Hypertens*. 2022;40:1847–1858.
 40. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
- ### 3.2.3. Secondary Forms of Hypertension
1. Rossi GP, Bernini G, Caliumi C, et al. A prospective study of the prevalence of primary aldosteronism in 1125 hypertensive patients. *J Am Coll Cardiol*. 2006;48:2293–2300.
 2. Xu Z, Yang J, Hu J, et al. Primary aldosteronism in patients in China with recently detected hypertension. *J Am Coll Cardiol*. 2020;75:1913–1922.
 3. Brown JM, Siddiqui M, Calhoun DA, et al. The unrecognized prevalence of primary aldosteronism: a cross-sectional study. *Ann Intern Med*. 2020;173:10–20.
 4. Brown JM, Robinson-Cohen C, Luque-Fernandez MA, et al. The spectrum of subclinical primary aldosteronism and incident hypertension: a cohort study. *Ann Intern Med*. 2017;167:630–641.
 5. Jinchai J, Khamsai S, Chattakul P, et al. How common is obstructive sleep apnea in young hypertensive patients? *Intern Emerg Med*. 2020;15:1005–1010.
 6. Pedrosa RP, Drager LF, Gonzaga CC, et al. Obstructive sleep apnea: the most common secondary cause of hypertension associated with resistant hypertension. *Hypertension*. 2011;58:811–817.
 7. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. *JAMA*. 2000;283:1829–1836.
 8. Hundemer GL, Agharazii M, Madore F, et al. Subclinical primary aldosteronism and cardiovascular health: a population-based cohort study. *Circulation*. 2024;149:124–134.
 9. Monticone S, Burrello J, Tizzani D, et al. Prevalence and clinical manifestations of primary aldosteronism encountered in primary care practice. *J Am Coll Cardiol*. 2017;69:1811–1820.
 10. Bhalla V, Textor SC, Beckman JA, et al. Revascularization for renovascular disease: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e128–e143.
 11. Vitarello JA, Fitzgerald CJ, Cluett JL, et al. Prevalence of medications that may raise blood pressure among adults with hypertension in the United States. *JAMA Intern Med*. 2022;182:90–93.
 12. MacIntyre IM, Turtle EJ, Farrah TE, et al. Regular acetaminophen use and blood pressure in people with hypertension: the PATH-BP trial. *Circulation*. 2022;145:416–423.
 13. Patel KA, Bhatt MH, Hirani RV, et al. Assessment of potential drug-drug interactions among outpatients in a tertiary care hospital: focusing on the role of P-glycoprotein and CYP3A4 (retrospective observational study). *Heliyon*. 2022;8:e11278.
 14. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
 15. Pivetta B, Chen L, Nagappa M, et al. Use and performance of the STOP-Bang questionnaire for obstructive sleep apnea screening across geographic regions: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4:e211009.
 16. Bernhardt L, Brady EM, Freeman SC, et al. Diagnostic accuracy of screening questionnaires for obstructive sleep apnoea in adults in different clinical cohorts: a systematic review and meta-analysis. *Sleep Breath*. 2022;26:1053–1078.
 17. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN Task Force on reassessing the inclusion of race in diagnosing kidney disease. *Am J Kidney Dis*. 2022;79:268–288.e261.
 18. Fu EL, Carrero JJ, Sang Y, et al. Association of low glomerular filtration rate with adverse outcomes at older age in a large population with routinely measured cystatin C. *Ann Intern Med*. 2024;177:269–279.
 19. Funder JW, Carey RM, Mantero F, et al. The management of primary aldosteronism: case detection, diagnosis, and treatment: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2016;101:1889–1916.
 20. Young WF Jr, Calhoun DA, Lenders JWM, et al. Screening for endocrine hypertension: an Endocrine Society scientific statement. *Endocrine Rev*. 2017;38:103–122.
 21. Leung AA, Pasieka JL, Hyrcza MD, et al. Epidemiology of pheochromocytoma and paraganglioma: population-based cohort study. *Eur J Endocrinol*. 2021;184:19–28.
 22. Ebbelohj A, Stochholm K, Jacobsen SF, et al. Incidence and clinical presentation of pheochromocytoma and sympathetic paraganglioma: a population-based study. *J Clin Endocrinol Metab*. 2021;106:e2251–e2261.
 23. Isselbacher EM, Preventza O, Black JH 3rd, et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;146:e334–e482.
 24. Fallo F, Di Dalmazi G, Beuschlein F, et al. Diagnosis and management of hypertension in patients with Cushing's syndrome: a position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension. *J Hypertens*. 2022;40:2085–2101.
 25. Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. *Pituitary*. 2021;24:1–13.
 26. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e596–e646.
 27. Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. *Lancet Public Health*. 2017;2:e108–e120.
 28. Teramoto M, Yamagishi K, Muraki I, et al. Coffee and green tea consumption and cardiovascular disease mortality among people with and without hypertension. *J Am Heart Assoc*. 2023;12:e026477.
 29. Penninkilampi R, Eslick EM, Eslick GD. The association between consistent licorice ingestion, hypertension and hypokalaemia: a systematic review and meta-analysis. *J Hum Hypertens*. 2017;31:699–707.
 30. Vongpatanasin W, Kario K, Atlas SA, et al. Central sympatholytic drugs. *J Clin Hypertens (Greenwich)*. 2011;13:658–661.
 31. Luther JM, Dominiczak AF, Jennings GLR, et al. Paroxysmal hypertension associated with presyncope. *Hypertension*. 2019;74:718–725.
 32. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2019;144.
 33. Parks KA, Parks CG, Yost JP, et al. Acute blood pressure changes associated with antipsychotic administration to psychiatric inpatients. *Prim Care Companion CNS Disord*. 2018;20:18m02299.
 34. Li XQ, Tang XR, Li LL. Antipsychotics cardiotoxicity: what's known and what's next. *World J Psychiatry*. 2021;11:736–753.
 35. Cameron NA, Blyler CA, Bello NA. Oral contraceptive pills and hypertension: a review of current evidence and recommendations. *Hypertension*. 2023;80:924–935.
 36. Aggarwal R, Heller G, Hillman DW, et al. PRESTO: a phase III, open-label study of intensification of androgen blockade in patients with high-risk biochemically relapsed castration-sensitive prostate cancer (AFT-19). *J Clin Oncol*. 2024;42:1114–1123.
- ### 3.2.3.1. Primary Aldosteronism
1. Montori VM, Young WF Jr. Use of plasma aldosterone concentration-to-plasma renin activity ratio as a screening test for primary aldosteronism. A systematic review of the literature. *Endocrinol Metab Clin North Am*. 2002;31:619–632, xi.
 2. Maiolino G, Rossitto G, Bisogni V, et al. Quantitative value of aldosterone-renin ratio for detection of aldosterone-producing adenoma: the Aldosterone-Renin Ratio for Primary Aldosteronism (AQUARR) study. *J Am Heart Assoc*. 2017;6:e005574.
 3. Brown JM, Siddiqui M, Calhoun DA, et al. The unrecognized prevalence of primary aldosteronism: a cross-sectional study. *Ann Intern Med*. 2020;173:10–20.
 4. Funder JW, Carey RM, Mantero F, et al. The management of primary aldosteronism: case detection, diagnosis, and treatment: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2016;101:1889–1916.

5. Turcu AF, Yang J, Vaidya A. Primary aldosteronism: a multidimensional syndrome. *Nat Rev Endocrinol*. 2022;18:665–682.
6. Monticone S, D'Ascenzo F, Moretti C, et al. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2018;6:41–50.
7. Monticone S, Sconfienza E, D'Ascenzo F, et al. Renal damage in primary aldosteronism: a systematic review and meta-analysis. *J Hypertens*. 2020;38:3–12.
8. Mulatero P, Stowasser M, Loh KC, et al. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. *J Clin Endocrinol Metab*. 2004;89:1045–1050.
9. Rossi GP, Bernini G, Caliumi C, et al. A prospective study of the prevalence of primary aldosteronism in 1125 hypertensive patients. *J Am Coll Cardiol*. 2006;48:2293–2300.
10. Monticone S, Burrello J, Tizzani D, et al. Prevalence and clinical manifestations of primary aldosteronism encountered in primary care practice. *J Am Coll Cardiol*. 2017;69:1811–1820.
11. Hannemann A, Wallaschofski H. Prevalence of primary aldosteronism in patient's cohorts and in population-based studies—a review of the current literature. *Horm Metab Res*. 2012;44:157–162.
12. Hundemer GL, Curhan GC, Yozamp N, et al. Renal outcomes in medically and surgically treated primary aldosteronism. *Hypertension*. 2018;72:658–666.
13. Hundemer GL, Curhan GC, Yozamp N, et al. Cardiometabolic outcomes and mortality in medically treated primary aldosteronism: a retrospective cohort study. *Lancet Diabetes Endocrinol*. 2018;6:51–59.
14. Cohen JB, Cohen DL, Herman DS, et al. Testing for primary aldosteronism and mineralocorticoid receptor antagonist use among US veterans: a retrospective cohort study. *Ann Intern Med*. 2021;174:289–297.
15. Hundemer GL, Imsirovic H, Vaidya A, et al. Screening rates for primary aldosteronism among individuals with hypertension plus hypokalemia: a population-based retrospective cohort study. *Hypertension*. 2022;79:178–186.
16. Kim V, Shi J, An J, et al. Hyperaldosteronism screening and findings from a large diverse population with resistant hypertension within an integrated health system. *Perm J*. 2024;28:3–13.
17. Kositanurit W, Giacona JM, Xie D, et al. Trends in primary aldosteronism screening among high-risk hypertensive adults. *J Am Heart Assoc*. 2024;13:e036373.
18. Woode ME, Wong K, Reid CM, et al. Cost-effectiveness of screening for primary aldosteronism in hypertensive patients in Australia: a Markov modeling analysis. *J Hypertens*. 2023;41:1615–1625.
19. Sato M, Morimoto R, Seiji K, et al. Cost-effectiveness analysis of the diagnosis and treatment of primary aldosteronism in Japan. *Horm Metab Res*. 2015;47:826–832.
20. Montori VM, Young WF Jr. Use of plasma aldosterone concentration-to-plasma renin activity ratio as a screening test for primary aldosteronism. A systematic review of the literature. *Endocrinol Metab Clin North Am*. 2002;31:619–632.
21. Mulatero P, Rabbia F, Milan A, et al. Drug effects on aldosterone/plasma renin activity ratio in primary aldosteronism. *Hypertension*. 2002;40:897–902.
22. Samnani S, Cenzler I, Kline GA, et al. Time to benefit of surgery vs targeted medical therapy for patients with primary aldosteronism: a meta-analysis. *J Clin Endocrinol Metab*. 2024;109:e1280–e1289.
23. Griffin AC, Kelz R, LiVolsi VA. Aldosterone-secreting adrenal cortical carcinoma. A case report and review of the literature. *Endocr Pathol*. 2014;25:344–349.
6. Bhalla V, Textor SC, Beckman JA, et al. Revascularization for renovascular disease: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e128–e143.
7. Murphy TP, Cooper CJ, Pencina KM, et al. Relationship of albuminuria and renal artery stent outcomes: results from the CORAL randomized clinical trial (Cardiovascular Outcomes with Renal Artery Lesions). *Hypertension*. 2016;68:1145–1152.
8. Misra S, Khosla A, Allred J, et al. Mortality and renal replacement therapy after renal artery stent placement for atherosclerotic renovascular disease. *J Vasc Interv Radiol*. 2016;27:1215–1224.
9. Cooper CJ, Murphy TP, Cutlip DE, et al. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med*. 2014;370:13–22.

3.2.3.3. Obstructive Sleep Apnea

1. Kovacs DK, Gede N, Szabo L, et al. Weight reduction added to CPAP decreases blood pressure and triglyceride level in OSA: systematic review and meta-analysis. *Clin Transl Sci*. 2022;15:1238–1248.
2. Labarca G, Schmidt A, Dreyse J, et al. Efficacy of continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA) and resistant hypertension (RH): systematic review and meta-analysis. *Sleep Med Rev*. 2021;58:101446.
3. Lei Q, Lv Y, Li K, et al. Effects of continuous positive airway pressure on blood pressure in patients with resistant hypertension and obstructive sleep apnea: a systematic review and meta-analysis of six randomized controlled trials. *J Bras Pneumol*. 2017;43:373–379.
4. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13:479–504.
5. Hou H, Zhao Y, Yu W, et al. Association of obstructive sleep apnea with hypertension: a systematic review and meta-analysis. *J Glob Health*. 2018;8:010405.
6. Marshall NS, Wong KK, Cullen SR, et al. Sleep apnea and 20-year follow-up for all-cause mortality, stroke, and cancer incidence and mortality in the Busselton Health Study cohort. *J Clin Sleep Med*. 2014;10:355–362.
7. Kou C, Zhao X, Lin X, et al. Effect of different treatments for obstructive sleep apnea on blood pressure. *J Hypertens*. 2022;40:1071–1084.
8. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2019;15:335–343.
9. McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med*. 2016;375:919–931.
10. Kang KT, Yeh TH, Ko JY, et al. Effect of sleep surgery on blood pressure in adults with obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Med Rev*. 2022;62:101590.
11. Schwartz AR, Jacobowitz O, Eisele DW, et al. Targeted hypoglossal nerve stimulation for patients with obstructive sleep apnea: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2023;149:512–520.
12. Stelmach-Mardas M, Brajer-Luftmann B, Kusnierczak M, et al. Body mass index reduction and selected cardiometabolic risk factors in obstructive sleep apnea: meta-analysis. *J Clin Med*. 2021;10:1485.
13. Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. *N Engl J Med*. 2024;391:1193–1205.
14. Ahmed AM, Nur SM, Xiaochen Y. Association between obstructive sleep apnea and resistant hypertension: systematic review and meta-analysis. *Front Med (Lausanne)*. 2023;10:1200952.
15. Brown J, Yazdi F, Jodari-Karimi M, et al. Obstructive sleep apnea and hypertension: updates to a critical relationship. *Curr Hypertens Rep*. 2022;24:173–184.
16. Navarro-Soriano C, Torres G, Barbe F, et al. The HIPARCO-2 study: long-term effect of continuous positive airway pressure on blood pressure in patients with resistant hypertension: a multicenter prospective study. *J Hypertens*. 2021;39:302–309.

4. Prevention Strategies

1. Lloyd-Jones DM, Allen NB, Anderson CAM, et al. Life's essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a Presidential Advisory from the American Heart Association. *Circulation*. 2022;146:e18–e43.
2. Di Federico S, Filippini T, Whelton PK, et al. Alcohol intake and blood pressure levels: a dose-response meta-analysis of nonexperimental cohort studies. *Hypertension*. 2023;80:1961–1969.

5.1. Lifestyle and Psychosocial Approaches

1. The Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, phase II. *Arch Intern Med*. 1997;157:657–667.
2. Neter JE, Stam BE, Kok FJ, et al. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2003;42:878–884.
3. Whelton PK, Appel L, Charleston J, et al. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: results of the trials of Hypertension Prevention, phase I. *JAMA* 1992;267:1213–1220.
4. Whelton PK, Appel LJ, Espeland MA, et al, TONE Collaborative Research Group. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). *JAMA*. 1998;279:839–846.
5. Whelton PK, Kumanyika SK, Cook NR, et al, Trials of Hypertension Prevention Collaborative Research Group. Efficacy of nonpharmacologic interventions in adults with high-normal blood pressure: results from phase 1 of the Trials of Hypertension Prevention. *Am J Clin Nutr*. 1997;65:652s–660s.
6. Yang S, Zhou Z, Miao H, et al. Effect of weight loss on blood pressure changes in overweight patients: a systematic review and meta-analysis. *J Clin Hypertens (Greenwich)* 2023;25:404–415.
7. Semlitsch T, Krenn C, Jeitler K, et al. Long-term effects of weight-reducing diets in people with hypertension. *Cochrane Database Syst Rev*. 2021;2:CD008274.
8. Zomer E, Gurusamy K, Leach R, et al. Interventions that cause weight loss and the impact on cardiovascular risk factors: a systematic review and meta-analysis. *Obes Rev*. 2016;17:1001–1011.
9. Blumenthal JA, Babyak MA, Hinderliter A, et al. Effects of the DASH diet alone and in combination with exercise and weight loss on blood pressure and cardiovascular biomarkers in men and women with high blood pressure: the ENCORE study. *Arch Intern Med*. 2010;170:126–135.
10. Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA*. 2003;289:2083–2093.
11. Appel LJ, Moore TJ, Obarzanek E, et al, DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med*. 1997;336:1117–1124.
12. Sacks FM, Svetkey LP, Vollmer WM, et al, DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med*. 2001;344:3–10.
13. Filippou CD, Tsioufis CP, Thomopoulos CG, et al. Dietary Approaches to Stop Hypertension (DASH) diet and blood pressure reduction in adults with and without hypertension: a systematic review and meta-analysis of randomized controlled trials. *Adv Nutr*. 2020;11:1150–1160.
14. Fu J, Liu Y, Zhang L, et al. Nonpharmacologic interventions for reducing blood pressure in adults with prehypertension to established hypertension. *J Am Heart Assoc*. 2020;9:e016804.
15. Schwingshackl L, Chaimani A, Schwedhelm C, et al. Comparative effects of different dietary approaches on blood pressure in hypertensive and prehypertensive patients: a systematic review and network meta-analysis. *Crit Rev Food Sci Nutr*. 2019;59:2674–2687.
16. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ*. 2013;346:f1326.
17. Filippini T, Malavolti M, Whelton PK, et al. Blood pressure effects of sodium reduction: dose-response meta-analysis of experimental studies. *Circulation*. 2021;143:1542–1567.
18. Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride. *Cochrane Database Syst Rev* 2020;12:CD004022.
19. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *Lancet*. 2011;378:380–382.
20. Greenwood H, Barnes K, Clark J, et al. Long-term effect of salt substitution for cardiovascular outcomes: a systematic review and meta-analysis. *Ann Intern Med*. 2024;177:643–655.
21. Neal B, Wu Y, Feng X, et al. Effect of salt substitution on cardiovascular events and death. *N Engl J Med*. 2021;385:1067–1077.
22. Aliasgharzadeh S, Tabrizi JS, Nikniaz L, et al. Effect of salt reduction interventions in lowering blood pressure: a comprehensive systematic review and meta-analysis of controlled clinical trials. *PLoS One*. 2022;17:e0277929.
23. Hernandez AV, Emonds EE, Chen BA, et al. Effect of low-sodium salt substitutes on blood pressure, detected hypertension, stroke and mortality. *Heart*. 2019;105:953–960.
24. Jafarnejad S, Mirzaei H, Clark CCT, et al. The hypotensive effect of salt substitutes in stage 2 hypertension: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2020;20:98.
25. Aburto NJ, Hanson S, Gutierrez H, et al. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ*. 2013;346:f1378.
26. Filippini T, Naska A, Kasdagli MI, et al. Potassium intake and blood pressure: a dose-response meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2020;9:e015719.
27. Filippini T, Violi F, D'Amico R, et al. The effect of potassium supplementation on blood pressure in hypertensive subjects: a systematic review and meta-analysis. *Int J Cardiol*. 2017;230:127–135.
28. Dickinson HO, Mason JM, Nicolson DJ, et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. *J Hypertens*. 2006;24:215–233.
29. Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. *Lancet Public Health*. 2017;2:e108–e120.
30. Stewart SH, Latham PK, Miller PM, et al. Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medications and Behavioral Interventions for Alcoholism (COMBINE) study. *Addiction*. 2008;103:1622–1628.
31. Xin X, He J, Frontini MG, et al. Effects of alcohol reduction on blood pressure. *Hypertension*. 2001;38:1112–1117.
32. Carlson DJ, Dieberg G, Hess NC, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. *Mayo Clin Proc*. 2014;89:327–334.
33. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc*. 2013;2:e004473.
34. Rossi AM, Moullec G, Lavoie KL, et al. The evolution of a Canadian hypertension education program recommendation: the impact of resistance training on resting blood pressure in adults as an example. *Can J Cardiol*. 2013;29:622–627.
35. Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med*. 2002;136:493–503.
36. Edwards JJ, Deenmamode AHP, Griffiths M, et al. Exercise training and resting blood pressure: a large-scale pairwise and network meta-analysis of randomised controlled trials. *Br J Sports Med*. 2023;57:1317–1326.
37. Jabbarzadeh Ganjeh B, Zeraattalab-Motlagh S, Jayedi A, et al. Effects of aerobic exercise on blood pressure in patients with hypertension: a systematic review and dose-response meta-analysis of randomized trials. *Hypertens Res*. 2024;47:385–398.
38. Schneider VM, Domingues LB, Umpierre D, et al. Exercise characteristics and blood pressure reduction after combined aerobic and resistance training: a systematic review with meta-analysis and meta-regression. *J Hypertens*. 2023;41:1068–1076.
39. Shariful Islam M, Fardousi A, Sizar MI, et al. Effect of leisure-time physical activity on blood pressure in people with hypertension: a systematic review and meta-analysis. *Sci Rep*. 2023;13:10639.
40. Ooi SL, Giovino M, Pak SC. Transcendental meditation for lowering blood pressure: an overview of systematic reviews and meta-analyses. *Complement Ther Med*. 2017;34:26–34.
41. Hartley L, Dyakova M, Holmes J, et al. Yoga for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2014;2014:CD010072.
42. Wu Y, Johnson BT, Acabchuk RL, et al. Yoga as antihypertensive lifestyle therapy: a systematic review and meta-analysis. *Mayo Clin Proc*. 2019;94:432–446.
43. Chen V, Ning H, Allen N, et al. Lifetime risks for hypertension by contemporary guidelines in African American and White men and women. *JAMA Cardiol*. 2019;4:455–459.
44. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. *JAMA*. 2002;287:1003–1010.
45. Lloyd-Jones DM, Allen NB, Anderson CAM, et al. Life's essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a Presidential Advisory from the American Heart Association. *Circulation*. 2022;146:e18–e43.
46. Lloyd-Jones DM, Liu K, Colangelo LA, et al. Consistently stable or decreased body mass index in young adulthood and longitudinal changes in metabolic syndrome components. *Circulation*. 2007;115:1004–1011.

47. Guo JW, Ning H, Allen NB, et al. Association of cardiovascular health in young adulthood with long-term blood pressure trajectories. *Am J Hypertens*. 2024;37:667–673.
48. Cook NR, Appel LJ, Whelton PK. Lower levels of sodium intake and reduced cardiovascular risk. *Circulation*. 2014;129:981–989.
49. Cook NR, Cutler JA, Obarzanek E, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ*. 2007;334:885–888.
50. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157–163.
51. Garvey WT, Mechanick JL, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016;22 Suppl 3:1–203.
52. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(suppl 2):s102–s138.
53. Schiavon CA, Bersch-Ferreira AC, Santucci EV, et al. Effects of bariatric surgery in obese patients with hypertension the GATEWAY randomized trial (gastric bypass to treat obese patients with steady hypertension). *Circulation*. 2018;137:1132–1142.
54. Siebenhofer A, Winterholer S, Jeitler K, et al. Long-term effects of weight-reducing drugs in people with hypertension. *Cochrane Database Syst Rev*. 2021;1:Cd007654.
55. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384:989–1002.
56. Kherra R, Pandey A, Chandar AK, et al. Effects of weight-loss medications on cardiometabolic risk profiles: a systematic review and network meta-analysis. *Gastroenterology*. 2018;154:1309–1319.e1307.
57. LeBlanc ES, Patnode CD, Webber EM, et al. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2018;320:1172–1191.
58. Iqbal J, Wu HX, Hu N, et al. Effect of glucagon-like peptide-1 receptor agonists on body weight in adults with obesity without diabetes mellitus—a systematic review and meta-analysis of randomized control trials. *Obes Rev*. 2022;23:e13435.
59. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med*. 2022;387:205–216.
60. de Lemos JA, Linetzyk B, le Roux CW, et al. Tirzepatide reduces 24-hour ambulatory blood pressure in adults with body mass index ≥ 27 kg/m²: SURMOUNT-1 ambulatory blood pressure monitoring substudy. *Hypertension*. 2024;81:e41–e43.
61. Jama HA, Snelson M, Schutte AE, et al. Recommendations for the use of dietary fiber to improve blood pressure control. *Hypertension*. 2024;81:1450–1459.
62. Abbasnezhad A, Falahi E, Gonzalez MJ, et al. Effect of different dietary approaches compared with a regular diet on systolic and diastolic blood pressure in patients with type 2 diabetes: A systematic review and meta-analysis. *Diabetes Res Clin Pract*. 2020;163:108108.
63. Siervo M, Lara J, Chowdhury S, et al. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. *Br J Nutr*. 2015;113:1–15.
64. Gay HC, Rao SG, Vaccaro V, et al. Effects of different dietary interventions on blood pressure: systematic review and meta-analysis of randomized controlled trials. *Hypertension*. 2016;67:733–739.
65. Howard G, Cushman M, Moy CS, et al. Association of clinical and social factors with excess hypertension risk in Black compared with White US adults. *JAMA*. 2018;320:1338–1348.
66. Svetkey LP, Simons-Morton D, Vollmer WM, et al. Effects of dietary patterns on blood pressure: subgroup analysis of the Dietary Approaches to Stop Hypertension (DASH) randomized clinical trial. *Arch Intern Med*. 1999;159:285–293.
67. Following the DASH eating plan. National Heart, Lung, and Blood Institute. Accessed July 2, 2024. <https://www.nhlbi.nih.gov/education/dash/following-dash>.
68. What is the DASH diet? Accessed July 2, 2024. <https://dashdiet.org/what-is-the-dash-diet.html>.
69. Your guide to lowering your blood pressure with DASH. National Heart, Lung, and Blood Institute. https://www.nhlbi.nih.gov/files/docs/public/heart/new_dash.pdf.
70. Riegel GR, Ribeiro PAB, Rodrigues MP, et al. Efficacy of nutritional recommendations given by registered dietitians compared to other healthcare providers in reducing arterial blood pressure: systematic review and meta-analysis. *Clin Nutr*. 2018;37:522–531.
71. Bazzano LA, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med*. 2014;161:309–318.
72. He J, Wofford MR, Reynolds K, et al. Effect of dietary protein supplementation on blood pressure: a randomized, controlled trial. *Circulation*. 2011;124:589–595.
73. Nordmann AJ, Suter-Zimmermann K, Bucher HC, et al. Meta-analysis comparing Mediterranean to low-fat diets for modification of cardiovascular risk factors. *Am J Med*. 2011;124:841–851.e842.
74. Yokoyama Y, Nishimura K, Barnard ND, et al. Vegetarian diets and blood pressure: a meta-analysis. *JAMA Intern Med*. 2014;174:577–587.
75. Gholizadeh-Moghaddam M, Shahdadian F, Shirani F, et al. The effect of a low versus high sodium diet on blood pressure in diabetic patients: a systematic review and meta-analysis of clinical trials. *Food Sci Nutr*. 2023;11:1622–1633.
76. Gupta DK, Lewis CE, Varady KA, et al. Effect of dietary sodium on blood pressure: a crossover trial. *JAMA*. 2023;330:2258–2266.
77. Huang L, Trieu K, Yoshimura S, et al. Effect of dose and duration of reduction in dietary sodium on blood pressure levels: systematic review and meta-analysis of randomised trials. *BMJ*. 2020;368:m315.
78. Kalesi S, Williams E, Irwin C, et al. Reducing salt intake: a systematic review and meta-analysis of behavior change interventions in adults. *Nutr Rev*. 2022;80:723–740.
79. Lai JS, Aung YN, Khalid Y, et al. Impact of different dietary sodium reduction strategies on blood pressure: a systematic review. *Hypertens Res*. 2022;45:1701–1712.
80. Ren J, Qin L, Li X, et al. Effect of dietary sodium restriction on blood pressure in type 2 diabetes: a meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis*. 2021;31:1653–1661.
81. Vargas-Meza J, Gonzalez-Rocha A, Campos-Nonato I, et al. Effective and scalable interventions to reduce sodium intake: a systematic review and meta-analysis. *Curr Nutr Rep*. 2023;12:486–494.
82. Xun R, Gao Y, Zhen S, et al. Effects of behavioral interventions for salt reduction on blood pressure and urinary sodium excretion: a systematic review and meta-analysis of randomized controlled trials. *Glob Heart*. 2023;18:65.
83. Yan YY, Chan LML, Wang MP, et al. Technology-supported behavior change interventions for reducing sodium intake in adults: a systematic review and meta-analysis. *NPJ Digit Med*. 2024;7:72.
84. Intersalt Cooperative Research Group. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *BMJ*. 1988;297:319–328.
85. Stamler J. The INTERSALT study: background, methods, findings, and implications. *Am J Clin Nutr*. 1997;65:626S–642S.
86. Bailey MA, Dhaun N. Salt sensitivity: causes, consequences, and recent advances. *Hypertension*. 2024;81:476–489.
87. Barris CT, Faulkner JL, Belin de Chantemele EJ. Salt sensitivity of blood pressure in women. *Hypertension*. 2023;80:268–278.
88. Weinberger MH, Miller JZ, Luft FC, et al. Definitions and characteristics of sodium sensitivity and blood pressure resistance. *Hypertension*. 1986;8:1127–1134.
89. Mattes RD, Donnelly D. Relative contributions of dietary sodium sources. *J Am Coll Nutr*. 1991;10:383–393.
90. Ahmed M, Ng AP, Christoforou A, et al. Top sodium food sources in the American diet-using National Health and Nutrition Examination Survey. *Nutrients*. 2023;15:831.
91. US Department of Agriculture and US Department of Health and Human Services. Dietary Guidelines for Americans, 2020–2025. 9th Edition. December 2020. <https://www.dietaryguidelines.gov/resources/2020-2025-dietary-guidelines-online-materials>.
92. Bibbins-Domingo K, Chertow GM, Coxson PG, et al. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med*. 2010;362:590–599.
93. Tsai YC, Tsao YP, Huang CJ, et al. Effectiveness of salt substitute on cardiovascular outcomes: a systematic review and meta-analysis. *J Clin Hypertens (Greenwich)*. 2022;24:1147–1160.
94. Yin X, Rodgers A, Perkovic A, et al. Effects of salt substitutes on clinical outcomes: a systematic review and meta-analysis. *Heart*. 2022;108:1608–1615.
95. Li Y, Zhang P, Wu J, et al. Twenty-four-hour urinary sodium and potassium excretion and their associations with blood pressure among adults in China. *Hypertension*. 2020;76:1580–1588.

96. Ndanuko RN, Ibrahim R, Hapsari RA, et al. Association between the urinary sodium to potassium ratio and blood pressure in adults: a systematic review and meta-analysis. *Adv Nutr*. 2021;12:1751–1767.
97. Stamler J, Chan Q, Daviglius ML, et al. Relation of dietary sodium (salt) to blood pressure and its possible modulation by other dietary factors. *Hypertension*. 2018;71:631–637.
98. Gan L, Zhao B, Inoue-Choi M, et al. Sex-specific associations between sodium and potassium intake and overall and cause-specific mortality: a large prospective US cohort study, systematic review, and updated meta-analysis of cohort studies. *BMC Med*. 2024;22:132.
99. Zhang Z, Cogswell ME, Gillespie C, et al. Association between usual sodium and potassium intake and blood pressure and hypertension among US adults: NHANES 2005–2010. *PLoS One*. 2013;8:e75289.
100. Vinceti M, Filippini T, Crippa A, et al. Meta-analysis of potassium intake and the risk of stroke. *J Am Heart Assoc*. 2016;5:e004210.
101. Cecchini M, Filippini T, Whelton PK, et al. Alcohol intake and risk of hypertension: a systematic review and dose-response meta-analysis of nonexperimental cohort studies. *Hypertension*. 2024;81:1701–1715.
102. Acin MT, Rueda JR, Saiz LC, et al. Alcohol intake reduction for controlling hypertension. *Cochrane Database Syst Rev*. 2020;9:CD010022.
103. Cushman WC, Cutler JA, Hanna E, et al. Prevention and Treatment of Hypertension Study (PATHS): effects of an alcohol treatment program on blood pressure. *Arch Intern Med*. 1998;158:1197–1207.
104. Anderson BO, Berdzuili N, Ilbawi A, et al. Health and cancer risks associated with low levels of alcohol consumption. *Lancet Public Health*. 2023;8:e6–e7.
105. Saco-Ledo G, Valenzuela PL, Ruiz-Hurtado G, et al. Exercise reduces ambulatory blood pressure in patients with hypertension: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2020;9:e018487.
106. Henkin JS, Pinto RS, Machado CLF, et al. Chronic effect of resistance training on blood pressure in older adults with prehypertension and hypertension: a systematic review and meta-analysis. *Exp Gerontol*. 2023;177:112193.
107. MacDonald HV, Johnson BT, Huedo-Medina TB, et al. Dynamic resistance training as stand-alone antihypertensive lifestyle therapy: a meta-analysis. *J Am Heart Assoc*. 2016;5:e003231.
108. Inder JD, Carlson DJ, Dieberg G, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. *Hypertens Res*. 2016;39:88–94.
109. Edwards J, De Caux A, Donaldson J, et al. Isometric exercise versus high-intensity interval training for the management of blood pressure: a systematic review and meta-analysis. *Br J Sports Med*. 2022;56:506–514.
110. Hansford HJ, Parmenter BJ, McLeod KA, et al. The effectiveness and safety of isometric resistance training for adults with high blood pressure: a systematic review and meta-analysis. *Hypertens Res*. 2021;44:1373–1384.
111. Larsen RN, Kingwell BA, Sethi P, et al. Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis*. 2014;24:976–982.
112. Zeigler ZS, Mullane SL, Crespo NC, et al. Effects of standing and light-intensity activity on ambulatory blood pressure. *Med Sci Sports Exerc*. 2016;48:175–181.
113. Dempsey PC, Sacre JW, Larsen RN, et al. Interrupting prolonged sitting with brief bouts of light walking or simple resistance activities reduces resting blood pressure and plasma noradrenaline in type 2 diabetes. *J Hypertens*. 2016;34:2376–2382.
114. Bhammar DM, Sawyer BJ, Tucker WJ, et al. Breaks in sitting time: effects on continuously monitored glucose and blood pressure. *Med Sci Sports Exerc*. 2017;49:2119–2130.
115. Wheeler MJ, Dunstan DW, Ellis KA, et al. Effect of morning exercise with or without breaks in prolonged sitting on blood pressure in older overweight/obese adults. *Hypertension*. 2019;73:859–867.
116. Egan B. Are there cardiometabolic benefits of low-intensity physical activity in at-risk adults? *J Am Soc Hypertens*. 2018;12:69–70.
117. Cornelissen VA, Arnout J, Holvoet P, et al. Influence of exercise at lower and higher intensity on blood pressure and cardiovascular risk factors at older age. *J Hypertens*. 2009;27:753–762.
118. Costa EC, Hay JL, Kehler DS, et al. Effects of high-intensity interval training versus moderate-intensity continuous training on blood pressure in adults with pre- to established hypertension: a systematic review and meta-analysis of randomized trials. *Sports Med*. 2018;48:2127–2142.
119. Brook RD, Appel LJ, Rubenfire M, et al. Beyond medications and diet: alternative approaches to lowering blood pressure. *Hypertension*. 2013;61:1360–1383.
120. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S76–S99.
121. Filippini T, Malavolti M, Whelton PK, et al. Sodium intake and risk of hypertension: a systematic review and dose-response meta-analysis of observational cohort studies. *Curr Hypertens Rep*. 2022;24:133–144.
122. Rijal A, Adhikari TB, Dhakal S, et al. Effects of adding exercise to usual care on blood pressure in patients with hypertension, type 2 diabetes, or cardiovascular disease: a systematic review with meta-analysis and trial sequential analysis. *J Hypertens*. 2024;42:10–22.
123. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.

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

1. Blood Pressure Lowering Treatment Trialists Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. *Lancet*. 2014;384:591–598.
2. Eddy DM, Adler J, Patterson B, et al. Individualized guidelines: the potential for increasing quality and reducing costs. *Ann Intern Med*. 2011;154:627–634.
3. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016;387:957–967.
4. Karmali KN, Lloyd-Jones DM, van der Leeuw J, et al. Blood pressure-lowering treatment strategies based on cardiovascular risk versus blood pressure: a meta-analysis of individual participant data. *PLoS Med*. 2018;15:e1002538.
5. Karmali KN, Ning H, Goff DC, et al. Identifying individuals at risk for cardiovascular events across the spectrum of blood pressure levels. *J Am Heart Assoc*. 2015;4:e002126.
6. van Dieren S, Kengne AP, Chalmers J, et al. Effects of blood pressure lowering on cardiovascular outcomes in different cardiovascular risk groups among participants with type 2 diabetes. *Diabetes Res Clin Pract*. 2012;98:83–90.
7. Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.
8. Peng X, Jin C, Song Q, et al. Stage 1 hypertension and the 10-year and lifetime risk of cardiovascular disease: a prospective real-world study. *J Am Heart Assoc*. 2023;12:e028762.
9. Bress AP, Bellows BK, King JB, et al. Cost-effectiveness of intensive versus standard blood-pressure control. *N Engl J Med*. 2017;377:745–755.

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

1. He J, Ouyang N, Guo X, et al. Effectiveness of a non-physician community health-care provider-led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): an open-label, blinded-endpoint, cluster-randomised trial. *Lancet*. 2023;401:928–938.
2. Lonn EM, Bosch J, Lopez-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med*. 2016;374:2009–2020.
3. Rahimi K, Bidel Z, Nazarzadeh M, et al. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet*. 2021;397:1625–1636.
4. Guo X, Ouyang N, Sun G, et al. Multifaceted intensive blood pressure control model in older and younger individuals with hypertension: a randomized clinical trial. *JAMA Cardiol*. 2024;9:781–790.
5. Liu J, Li Y, Ge J, et al. Lowering systolic blood pressure to less than 120 mm Hg versus less than 140 mm Hg in patients with high cardiovascular risk with and without diabetes or previous stroke: an open-label, blinded-outcome, randomised trial. *Lancet*. 2024;404:245–255.
6. Peng X, Jin C, Song Q, et al. Stage 1 hypertension and the 10-year and lifetime risk of cardiovascular disease: a prospective real-world study. *J Am Heart Assoc*. 2023;12:e028762.
7. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.

8. Zhang W, Zhang S, Deng Y, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med*. 2021;385:1268–1279.
9. Rahimi K, Bidel Z, Nazarzadeh M, et al. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis. *Lancet*. 2021;398:1053–1064.
10. Sundstrom J, Arima H, Jackson R, et al. Effects of blood pressure reduction in mild hypertension: a systematic review and meta-analysis. *Ann Intern Med*. 2015;162:184–191.
11. Blood Pressure Lowering Treatment Trialists Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. *Lancet*. 2014;384:591–598.
12. Karmali KN, Lloyd-Jones DM, van der Leeuw J, et al. Blood pressure-lowering treatment strategies based on cardiovascular risk versus blood pressure: a meta-analysis of individual participant data. *PLoS Med*. 2018;15:e1002538.
13. Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1982–2004.
14. Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149:430–449.
15. Zinzuwadia AN, Mineeva O, Li C, et al. Tailoring risk prediction models to local populations. *JAMA Cardiol*. 2024;9:1018–1028.
16. Scheuermann B, Brown A, Colburn T, et al. External validation of the American Heart Association PREVENT cardiovascular disease risk equations. *JAMA Network Open*. 2024;7:e2438311-e2438311.
17. D'Agostino Sr RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*. 2008;117:743–753.
18. Muntner P, Carey RM, Gidding S, et al. Potential US population impact of the 2017 ACC/AHA high blood pressure guideline. *Circulation*. 2018;137:109–118.
19. Fuchs SC, Poli-de-Figueiredo CE, Figueiredo Neto JA, et al. Effectiveness of chlorthalidone plus amlodipine for the prevention of hypertension: the PREVER-Prevention randomized clinical trial. *J Am Heart Assoc*. 2016;5:e004248.
20. Bao W, Threefoot SA, Srinivasan SR, et al. Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogalusa Heart Study. *Am J Hypertens*. 1995;8:657–665.
21. Chen V, Ning H, Allen N, et al. Lifetime risks for hypertension by contemporary guidelines in African American and White men and women. *JAMA Cardiol*. 2019;4:455–459.
22. Reges O, Ning H, Wilkins JT, et al. Association of cumulative systolic blood pressure with long-term risk of cardiovascular disease and healthy longevity: findings from the lifetime risk pooling project cohorts. *Hypertension*. 2021;77:347–356.
23. Allen NB, Siddique J, Wilkins JT, et al. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. *JAMA*. 2014;311:490–497.
24. Gidding SS, Liu K, Colangelo LA, et al. Longitudinal determinants of left ventricular mass and geometry: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Circ Cardiovasc Imaging*. 2013;6:769–775.
25. McEvoy JW, Martin SS, Dardari ZA, et al. Coronary artery calcium to guide a personalized risk-based approach to initiation and intensification of antihypertensive therapy. *Circulation*. 2017;135:153–165.
26. Pandey A, Patel KV, Vongpatanasin W, et al. Incorporation of biomarkers into risk assessment for allocation of antihypertensive medication according to the 2017 ACC/AHA high blood pressure guideline: a pooled cohort analysis. *Circulation*. 2019;140:2076–2088.
27. Haug EB, Horn J, Markovitz AR, et al. Association of conventional cardiovascular risk factors with cardiovascular disease after hypertensive disorders of pregnancy: analysis of the Nord-Troendelag Health study. *JAMA Cardiol*. 2019;4:628–635.
28. Lloyd-Jones DM, Allen NB, Anderson CA, et al. Life's essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association. *Circulation*. 2022;146:e18–e43.
29. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 4. Effects of various classes of antihypertensive drugs-overview and meta-analyses. *J Hypertens*. 2015;33:195–211.
30. Wei J, Galaviz KI, Kowalski AJ, et al. Comparison of cardiovascular events among users of different classes of antihypertension medications: a systematic review and network meta-analysis. *JAMA Netw Open*. 2020;3:e1921618.
31. Fretheim A, Odgaard-Jensen J, Brors O, et al. Comparative effectiveness of antihypertensive medication for primary prevention of cardiovascular disease: systematic review and multiple treatments meta-analysis. *BMC Med*. 2012;10:33.
32. Czernichow S, Zanchetti A, Turnbull F, et al. The effects of blood pressure reduction and of different blood pressure-lowering regimens on major cardiovascular events according to baseline blood pressure: meta-analysis of randomized trials. *J Hypertens*. 2011;29:4–16.
33. Law MR, Morris JK, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009;338:b1665.
34. The Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*. 2002;288:2981–2997.
35. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure-lowering on outcome incidence in hypertension: 5. head-to-head comparisons of various classes of antihypertensive drugs - overview and meta-analyses. *J Hypertens*. 2015;33:1321–1341.
36. Law MR, Morris JK, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009;338.
37. Ishani A, Cushman WC, Leatherman SM, et al. Chlorthalidone vs. hydrochlorothiazide for hypertension-cardiovascular events. *N Engl J Med*. 2022;387:2401–2410.
38. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
39. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42:1206–1252.

5.2.4. Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

1. Parati G, Kjeldsen S, Coca A, et al. Adherence to single-pill versus free-equivalent combination therapy in hypertension: a systematic review and meta-analysis. *Hypertension*. 2021;77:692–705.
2. Wald DS, Law M, Morris JK, et al. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11 000 participants from 42 trials. *Am J Med*. 2009;122:290–300.
3. Wang N, Rueter P, Atkins E, et al. Efficacy and safety of low-dose triple and quadruple combination pills vs monotherapy, usual care, or placebo for the initial management of hypertension: a systematic review and meta-analysis. *JAMA Cardiol*. 2023;8:606–611.
4. Schmieder RE, Wassmann S, Predel HG, et al. Improved persistence to medication, decreased cardiovascular events and reduced all-cause mortality in hypertensive patients with use of single-pill combinations: results from the START-Study. *Hypertension*. 2023;80:1127–1135.
5. Verma AA, Khuu W, Tadrus M, et al. Fixed-dose combination antihypertensive medications, adherence, and clinical outcomes: a population-based retrospective cohort study. *PLoS Med*. 2018;15:e1002584.
6. Webster R, Salam A, de Silva HA, et al. Fixed low-dose triple combination antihypertensive medication vs usual care for blood pressure control in patients with mild to moderate hypertension in Sri Lanka: a randomized clinical trial. *JAMA*. 2018;320:566–579.
7. Fried LF, Emanuele N, Zhang JH, et al. Combined angiotensin inhibition for the treatment of diabetic nephropathy. *N Engl J Med*. 2013;369:1892–1903.
8. Parving HH, Brenner BM, McMurray JJ, et al. Cardiorenal end points in a trial of aliskiren for type 2 diabetes. *N Engl J Med*. 2012;367:2204–2213.
9. Investigators O, Yusuf S, Teo KK, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med*. 2008;358:1547–1559.

5.2.3. Initial Medication Selection for Treatment of Primary Hypertension

1. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 4. Effects of various classes of antihypertensive

10. Abdalla M, Bolen SD, Brettler J, et al. Implementation strategies to improve blood pressure control in the United States: a scientific statement from the American Heart Association and American Medical Association. *Hypertension*. 2023;80:e143–e157.
 11. He J, Ouyang N, Guo X, et al. Effectiveness of a non-physician community health-care provider-led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): an open-label, blinded-endpoint, cluster-randomised trial. *Lancet*. 2023;401:928–938.
 12. Law M, Wald N, Morris J, et al. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ*. 2003;326:1427.
 13. Bangalore S, Kamalakkannan G, Parkar S, et al. Fixed-dose combinations improve medication compliance: a meta-analysis. *Am J Med*. 2007;120:713–719.
 14. Du LP, Cheng ZW, Zhang YX, et al. The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for hypertension: a meta-analysis. *J Clin Hypertens (Greenwich)*. 2018;20:902–907.
 15. Bellows BK, Ruiz-Negron N, Bibbins-Domingo K, et al. Clinic-based strategies to reach United States Million Hearts 2022 blood pressure control goals. *Circ Cardiovasc Qual Outcomes*. 2019;12:e005624.
 16. Ratanawongsa N, Zikmund-Fisher BJ, Couper MP, et al. Race, ethnicity, and shared decision making for hyperlipidemia and hypertension treatment: the DECISIONS survey. *Med Decis Making*. 2010;30:65S–76S.
 17. Joint National Committee on Prevention Treatment of High Blood Pressure National High Blood Pressure Education Program. Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Public Health Service, National Institutes of Health, National Heart and Lung; 1997.
 18. US Food and Drug Administration. Approved drug products with therapeutic equivalence evaluations [Orange book. Accessed September 30, 2024. <https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book>.
- ### 5.2.5. Antihypertensive Medication Adherence Strategies
1. Weeda ER, Coleman CI, McHorney CA, et al. Impact of once- or twice-daily dosing frequency on adherence to chronic cardiovascular disease medications: a meta-regression analysis. *Int J Cardiol*. 2016;216:104–109.
 2. Iskedjian M, Einarson TR, MacKeigan LD, et al. Relationship between daily dose frequency and adherence to antihypertensive pharmacotherapy: evidence from a meta-analysis. *Clin Ther*. 2002;24:302–316.
 3. Schroeder K, Fahey T, Ebrahim S. How can we improve adherence to blood pressure-lowering medication in ambulatory care? Systematic review of randomized controlled trials. *Arch Intern Med*. 2004;164:722–732.
 4. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents: a meta-analysis. *Hypertension*. 2010;55:399–407.
 5. Du LP, Cheng ZW, Zhang YX, et al. The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for hypertension: a meta-analysis. *J Clin Hypertens (Greenwich)*. 2018;20:902–907.
 6. Webster R, Salam A, de Silva HA, et al. Fixed low-dose triple combination antihypertensive medication vs usual care for blood pressure control in patients with mild to moderate hypertension in Sri Lanka: a randomized clinical trial. *JAMA*. 2018;320:566–579.
 7. Lauffenburger JC, Tesfaye H, Solomon DH, et al. Investigating the ability to adhere to cardiometabolic medications with different properties: a retrospective cohort study of >500 000 patients in the USA. *BMJ Open*. 2023;13:e075840.
 8. Nsiah I, Imeri H, Jones AC, et al. The impact of medication synchronization programs on medication adherence: a meta-analysis. *J Am Pharm Assoc (2003)*. 2021;61:e202–e211.
 9. Nguyen E, Sobieraj DM. The impact of appointment-based medication synchronization on medication taking behaviour and health outcomes: a systematic review. *J Clin Pharm Ther*. 2017;42:404–413.
 10. Al-Arkee S, Mason J, Lane DA, et al. Mobile apps to improve medication adherence in cardiovascular disease: systematic review and meta-analysis. *J Med Internet Res*. 2021;23:e24190.
 11. Choudhry NK, Krumme AA, Ercole PM, et al. Effect of reminder devices on medication adherence: the REMIND randomized clinical trial. *JAMA Intern Med*. 2017;177:624–631.
 12. Conversano C, Orru G, Pozza A, et al. Is mindfulness-based stress reduction effective for people with hypertension? A systematic review and meta-analysis of 30 years of evidence. *Int J Environ Res Public Health*. 2021;18:2882.
 13. Morawski K, Ghazinouri R, Krumme A, et al. Association of a smartphone application with medication adherence and blood pressure control: the MediSAFE-BP randomized clinical trial. *JAMA Intern Med*. 2018;178:802–809.
 14. Van Truong P, Wulan Apriyasyari R, Lin MY, et al. Effects of self-management programs on blood pressure, self-efficacy, medication adherence and body mass index in older adults with hypertension: meta-analysis of randomized controlled trials. *Int J Nurs Pract*. 2021;27:e12920.
 15. Reeves L, Robinson K, McClelland T, et al. Pharmacist interventions in the management of blood pressure control and adherence to antihypertensive medications: a systematic review of randomized controlled trials. *J Pharm Pract*. 2021;34:480–492.
 16. Xu H, Long H. The effect of smartphone app-based interventions for patients with hypertension: systematic review and meta-analysis. *JMIR Mhealth Uhealth*. 2020;8:e21759.
 17. Abegaz TM, Shehab A, Gebreyohannes EA, et al. Nonadherence to antihypertensive drugs: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2017;96:e5641.
 18. Lee EKP, Poon P, Yip BHK, et al. Global burden, regional differences, trends, and health consequences of medication nonadherence for hypertension during 2010 to 2020: a meta-analysis involving 27 million patients. *J Am Heart Assoc*. 2022;11:e026582.
 19. Brinker S, Pandey A, Ayers C, et al. Therapeutic drug monitoring facilitates blood pressure control in resistant hypertension. *J Am Coll Cardiol*. 2014;63:834–835.
 20. Pandey A, Raza F, Velasco A, et al. Comparison of Morisky Medication Adherence Scale with therapeutic drug monitoring in apparent treatment-resistant hypertension. *J Am Soc Hypertens*. 2015;9:420–426.e422.
 21. Choudhry NK, Kronish IM, Vongpatanasin W, et al. Medication adherence and blood pressure control: a scientific statement from the American Heart Association. *Hypertension*. 2022;79:e1–e14.
 22. Peeters LEJ, Kappers MHW, Hesselink DA, et al. Antihypertensive drug concentration measurement combined with personalized feedback in resistant hypertension: a randomized controlled trial. *J Hypertens*. 2024;42:169–178.
 23. Calderon-Larranaga A, Diaz E, Poblador-Plou B, et al. Non-adherence to antihypertensive medication: the role of mental and physical comorbidity. *Int J Cardiol*. 2016;207:310–316.
 24. Alvarez C, Hines AL, Carson KA, et al. Association of perceived stress and discrimination on medication adherence among diverse patients with uncontrolled hypertension. *Ethn Dis*. 2021;31:97–108.
 25. Bautista LE, Vera-Cala LM, Colombo C, et al. Symptoms of depression and anxiety and adherence to antihypertensive medication. *Am J Hypertens*. 2012;25:505–511.
 26. Taff C, Hallberg I, Bengtsson U, et al. Links between blood pressure and medication intake, well-being, stress, physical activity and symptoms reported via a mobile phone-based self-management support system: a cohort study in primary care. *BMJ Open*. 2018;8:e020849.
 27. Stamoulis T, Dragioti E, Gouva M, et al. Unveiling the Nexus: depressive symptoms and medication adherence in hypertensive patients' self-care: a systematic review. *Mater Sociomed*. 2024;36:65–72.
 28. Farhadi F, Aliyari R, Ebrahimi H, et al. Prevalence of uncontrolled hypertension and its associated factors in 50-74 years old Iranian adults: a population-based study. *BMC Cardiovasc Disord*. 2023;23:318.
 29. Qi M, Santos H, Pinheiro P, et al. Demographic and socioeconomic determinants of access to care: a subgroup disparity analysis using new equity-focused measurements. *PLoS One*. 2023;18:e0290692.
 30. Schesing KB, Chia R, Elwood B, et al. Assessment of patient and provider attitudes towards therapeutic drug monitoring to improve medication adherence in low-income patients with hypertension: a qualitative study. *BMJ Open*. 2020;10:e039940.
 31. Mackenzie IS, Rogers A, Poulter NR, et al. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial. *Lancet*. 2022;400:1417–1425.
 32. Geiger C, Cramer H, Dobos G, et al. A systematic review and meta-analysis of mindfulness-based stress reduction for arterial hypertension. *J Hum Hypertens*. 2023;37:161–169.
 33. Lee EKP, Yeung NCY, Xu Z, et al. Effect and acceptability of mindfulness-based stress reduction program on patients with elevated blood pressure or hypertension: a meta-analysis of randomized controlled trials. *Hypertension*. 2020;76:1992–2001.
 34. Zaugg V, Korb-Savoldelli V, Durieux P, et al. Providing physicians with feedback on medication adherence for people with chronic diseases taking long-term medication. *Cochrane Database Syst Rev*. 2018;1:CD012042.

5.2.6. Medication Interactions

- Fravel MA, Ernst M. Drug interactions with antihypertensives. *Curr Hypertens Rep.* 2021;23:14.

5.2.7. BP Goal for Patients With Hypertension

- Whelton PK, O'Connell S, Mills KT, et al. Optimal antihypertensive systolic blood pressure: a systematic review and meta-analysis. *Hypertension.* 2024;81:2329–2339.
- Zhang W, Zhang S, Deng Y, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med.* 2021;385:1268–1279.
- Bi Y, Li M, Liu Y, et al. Intensive blood-pressure control in patients with type 2 diabetes (BPROAD). *N Engl J Med.* 2025;392:1155–1167.
- Liu J, Li Y, Ge J, et al. Lowering systolic blood pressure to less than 120 mm Hg versus less than 140 mm Hg in patients with high cardiovascular risk with and without diabetes or previous stroke: an open-label, blinded-outcome, randomised trial. *Lancet.* 2024;404:245–255.
- Fuchs SC, Poli-de-Figueiredo CE, Figueiredo Neto JA, et al. Effectiveness of chlorthalidone plus amloride for the prevention of hypertension: the PREVER-Prevention randomized clinical trial. *J Am Heart Assoc.* 2016;5:e004248.
- He J, Ouyang N, Guo X, et al. Effectiveness of a non-physician community health-care provider-led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): an open-label, blinded-endpoint, cluster-randomised trial. *Lancet.* 2023;401:928–938.
- Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet.* 2002;360:1903–1913.
- Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet.* 2014;383:1899–1911.
- Whelton SP, McEvoy JW, Shaw L, et al. Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. *JAMA Cardiol.* 2020;5:1011–1018.
- Bi Y, Li M, Liu Y, et al. Intensive blood-pressure control in patients with type 2 diabetes. *N Engl J Med.* 2024;.
- ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med.* 2010;362:1575–1585.
- The SPS3 Study Group. Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial. *Lancet.* 2013;382:507–515.
- Reboussin DM, Allen NB, Griswold ME, et al. Systematic review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical practice guidelines. *Hypertension.* 2018;71:E116–E135.
- SPRINT Research Group. Final report of a trial of intensive versus standard blood-pressure control. *N Engl J Med.* 2021;384:1921–1930.
- Kitagawa K, Yamamoto Y, Arima H, et al. Effect of standard vs intensive blood pressure control on the risk of recurrent stroke: a randomized clinical trial and meta-analysis. *JAMA Neurol.* 2019;76:1309–1318.
- Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: effects of various classes of antihypertensive drugs-overview and meta-analyses. *J Hypertens.* 2015;33:195–211.
- Blood Pressure Lowering Treatment Trialists Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet.* 2021;397:1625–1636.
- Bundy JD, Li C, Stuchlik P, et al. Systolic blood pressure reduction and risk of cardiovascular disease and mortality: a systematic review and network meta-analysis. *JAMA Cardiol.* 2017;2:775–781.
- Verdecchia P, Angeli F, Gentile G, et al. More versus less intensive blood pressure-lowering strategy: cumulative evidence and trial sequential analysis. *Hypertension.* 2016;68:642–653.
- Bangalore S, Toklu B, Gianos E, et al. Optimal systolic blood pressure target after SPRINT: insights from a network meta-analysis of randomized trials. *Am J Med.* 2017;130:707–719.e708.
- Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet.* 2016;387:957–967.
- Beddhu S, Chertow GM, Cheung AK, et al. Influence of baseline diastolic blood pressure on effects of intensive compared with standard blood pressure control. *Circulation.* 2018;137:134–143.

- Jones DW, Whelton PK, Allen N, et al. Management of stage 1 hypertension in adults with a low 10-year risk for cardiovascular disease: filling a guidance gap: a scientific statement from the American Heart Association. *Hypertension.* 2021;77:e58–e67.

5.2.8. Electrolyte Imbalances

- Fried LF, Emanuele N, Zhang JH, et al. Combined angiotensin inhibition for the treatment of diabetic nephropathy. *N Engl J Med.* 2013;369:1892–1903.
- Investigators O, Yusuf S, Teo KK, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med.* 2008;358:1547–1559.
- Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med.* 2003;349:1893–1906.
- Agiro A, An A, Cook EE, et al. Real-world modifications of renin-angiotensin-aldosterone system inhibitors in patients with hyperkalemia initiating sodium zirconium cyclosilicate therapy: the OPTIMIZE I study. *Adv Ther.* 2023;40:2886–2901.
- Spinowitz BS, Fishbane S, Pergola PE, et al. Sodium zirconium cyclosilicate among individuals with hyperkalemia: a 12-month phase 3 study. *Clin J Am Soc Nephrol.* 2019;14:798–809.

5.2.9. Kidney Dysfunction/Injury

- Vaduganathan M, Ferreira JP, Rossignol P, et al. Effects of steroidal mineralocorticoid receptor antagonists on acute and chronic estimated glomerular filtration rate slopes in patients with chronic heart failure. *Eur J Heart Fail.* 2022;24:1586–1590.
- Chen X, Li X, Zhang K, et al. The role of a novel mineralocorticoid receptor antagonist, finerenone, in chronic kidney disease: mechanisms and clinical advances. *Clin Exp Nephrol.* 2024;28:125–135.
- Fu Y, Hall JE, Lu D, et al. Aldosterone blunts tubuloglomerular feedback by activating macula densa mineralocorticoid receptors. *Hypertension.* 2012;59:599–606.
- Holtkamp FA, de Zeeuw D, Thomas MC, et al. An acute fall in estimated glomerular filtration rate during treatment with losartan predicts a slower decrease in long-term renal function. *Kidney Int.* 2011;80:282–287.
- Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? *Arch Intern Med.* 2000;160:685–693.
- Apperloo AJ, de Zeeuw D, de Jong PE. A short-term antihypertensive treatment-induced fall in glomerular filtration rate predicts long-term stability of renal function. *Kidney Int.* 1997;51:793–797.
- Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med.* 2001;345:861–869.
- Ruggenenti P, Perna A, Gherardi G, et al. Renal function and requirement for dialysis in chronic nephropathy patients on long-term ramipril: REIN follow-up trial. *Lancet.* 1998;352:1252–1256.
- Damman K, Gori M, Claggett B, et al. Renal effects and associated outcomes during angiotensin-nepriylsin inhibition in heart failure. *J Am Coll Cardiol.* 2018;6:489–498.
- Mullens W, Damman K, Testani JM, et al. Evaluation of kidney function throughout the heart failure trajectory—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2020;22:584–603.

5.3. Comorbidities

- Vasan RS, Song RJ, Xanthakis V, et al. Hypertension-mediated organ damage: prevalence, correlates, and prognosis in the community. *Hypertension.* 2022;79:505–515.
- Cuspidi C, Sala C, Tadic M, et al. High-normal blood pressure and abnormal left ventricular geometric patterns: a meta-analysis. *J Hypertens.* 2019;37:1312–1319.
- Perrone-Filardi P, Coca A, Galderisi M, et al. Non-invasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients: a consensus paper from the European Association of Cardiovascular Imaging (EACVI), the European Society of Cardiology Council on Hypertension, and the European Society of Hypertension (ESH). *Eur Heart J Cardiovasc Imaging.* 2017;18:945–960.
- Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet.* 2014;383:1899–1911.
- Rutan GH, Kuller LH, Neaton JD, et al. Mortality associated with diastolic hypertension and isolated systolic hypertension among men screened for the Multiple Risk Factor Intervention Trial. *Circulation.* 1988;77:504–514.

6. Persu A, De Plaen JF. Recent insights in the development of organ damage caused by hypertension. *Acta Cardiol*. 2004;59:369–381.
7. Allen NB, Siddique J, Wilkins JT, et al. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. *JAMA*. 2014;311:490–497.
8. Pletcher MJ, Bibbins-Domingo K, Lewis CE, et al. Prehypertension during young adulthood and coronary calcium later in life. *Ann Intern Med*. 2008;149:91–99.
9. Juhola J, Magnussen CG, Berenson GS, et al. Combined effects of child and adult elevated blood pressure on subclinical atherosclerosis: the International Childhood Cardiovascular Cohort Consortium. *Circulation*. 2013;128:217–224.
10. Cuspidi C, Sala C, Tadic M, et al. Pre-hypertension and subclinical carotid damage: a meta-analysis. *J Hum Hypertens*. 2019;33:34–40.
11. Lembo M, Pacella D, Manzi MV, et al. Hypertension-mediated organ damage involving multiple sites is an independent risk factor for cardiovascular events. *Eur Heart J Open*. 2023;3:oead102.
12. Suvisa K, Niiranen TJ. Interrelations between high blood pressure, organ damage, and cardiovascular disease: no more room for doubt. *Hypertension*. 2022;79:516–517.
13. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.

5.3.1. Diabetes

1. Rahman F, McEvoy JW, Ohkuma T, et al. Effects of blood pressure lowering on clinical outcomes according to baseline blood pressure and cardiovascular risk in patients with type 2 diabetes mellitus. *Hypertension*. 2019;73:1291–1299.
2. Emdin CA, Rahimi K, Neal B, et al. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2015;313:603–615.
3. Arguedas JA, Leiva V, Wright JM. Blood pressure targets for hypertension in people with diabetes mellitus. *Cochrane Database Syst Rev*. 2013;CD008277.
4. Yang Q, Zheng R, Wang S, et al. Systolic blood pressure control targets to prevent major cardiovascular events and death in patients with type 2 diabetes: a systematic review and network meta-analysis. *Hypertension*. 2023;80:1640–1653.
5. Bi Y, Li M, Liu Y, et al. Intensive blood-pressure control in patients with type 2 diabetes (BPROAD). *N Engl J Med*. 2025;392:1155–1167.
6. Hansson L, Zanchetti A, Carruthers SG, et al. HOT Study Group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *Lancet*. 1998;351:1755–1762.
7. Whelton PK, Barzilay J, Cushman WC, et al. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Arch Intern Med*. 2005;165:1401–1409.
8. Keane WF, Brenner BM, de Zeeuw D, et al. The risk of developing end-stage renal disease in patients with type 2 diabetes and nephropathy: the RENAAL study. *Kidney Int*. 2003;63:1499–1507.
9. Strippoli GF, Bonifati C, Craig M, et al. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. *Cochrane Database Syst Rev*. 2006;2006:CD006257.
10. Palmer SC, Mavridis D, Navarese E, et al. Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis. *Lancet*. 2015;385:2047–2056.
11. Schmieder RE, Hilgers KF, Schlaich MP, et al. Renin-angiotensin system and cardiovascular risk. *Lancet*. 2007;369:1208–1219.
12. Mann JF, Gerstein HC, Yi QL, et al. Progression of renal insufficiency in type 2 diabetes with and without microalbuminuria: results of the Heart Outcomes and Prevention Evaluation (HOPE) randomized study. *Am J Kidney Dis*. 2003;42:936–942.
13. Kannel WB, Wilson PW, Zhang TJ. The epidemiology of impaired glucose tolerance and hypertension. *Am Heart J*. 1991;121:1268–1273.
14. Stamler J, Vaccaro O, Neaton JD, et al. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care*. 1993;16:434–444.
15. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.
16. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362:1575–1585.
17. Wu W, Tong HM, Li YS, et al. The effect of semaglutide on blood pressure in patients with type-2 diabetes: a systematic review and meta-analysis. *Endocrine*. 2024;83:571–584.
18. Solomon SD, Rice MM, K AJ, et al. Renal function and effectiveness of angiotensin-converting enzyme inhibitor therapy in patients with chronic stable coronary disease in the Prevention of Events with ACE inhibition (PEACE) trial. *Circulation*. 2006;114:26–31.

5.3.2. Obesity and Metabolic Syndrome

1. Wilding JP, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384:989–1002.
2. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389:2221–2232.
3. Rubino DM, Greenway FL, Khalid U, et al. Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: the STEP 8 randomized clinical trial. *JAMA*. 2022;327:138–150.
4. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. *JAMA*. 2021;325:1403–1413.
5. de Lemos JA, Linetzkyy B, le Roux CW, et al. Tirzepatide reduces 24-hour ambulatory blood pressure in adults with body mass index ≥ 27 kg/m²: SURMOUNT-1 ambulatory blood pressure monitoring substudy. *Hypertension*. 2024;81:e41–e43.
6. Schiavon CA, Cavalcanti AB, Oliveira JD, et al. Randomized trial of effect of bariatric surgery on blood pressure after 5 years. *J Am Coll Cardiol*. 2024;83:637–648.
7. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2010;56:1113–1132.
8. Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1636–1664.
9. Ndumele CE, Rangaswami J, Chow SE, et al. Cardiovascular-kidney-metabolic health: a presidential advisory from the American Heart Association. *Circulation*. 2023;148:1606–1635.
10. Martin SS, Aday AW, Almarazoo ZI, et al. 2024 Heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913.
11. Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. *JAMA*. 2021;325:1414–1425.
12. King WC, Hinerman AS, Belle SH, et al. Comparison of the performance of common measures of weight regain after bariatric surgery for association with clinical outcomes. *JAMA*. 2018;320:1560–1569.
13. Kennedy C, Hayes P, Salama S, et al. The effect of semaglutide on blood pressure in patients without diabetes: a systematic review and meta-analysis. *J Hypertens*. 2023;41:e11.
14. Liu D, Huang Y, Huang C, et al. Calorie restriction with or without time-restricted eating in weight loss. *N Engl J Med*. 2022;386:1495–1504.
15. Adams TD, Davidson LE, Litwin SE, et al. Weight and metabolic outcomes 12 years after gastric bypass. *N Engl J Med*. 2017;377:1143–1155.

5.3.3. Chronic Coronary Disease

1. Carrick D, Haig C, Maznyczka AM, et al. Hypertension, microvascular pathology, and prognosis after an acute myocardial infarction. *Hypertension*. 2018;72:720–730.
2. Wright JT Jr, Williamson JD, Whelton PK, et al. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.
3. Bundy JD, Li C, Stuchlik P, et al. Systolic blood pressure reduction and risk of cardiovascular disease and mortality: a systematic review and network meta-analysis. *JAMA Cardiol*. 2017;2:775–781.
4. Lewis CE, Fine LJ, Beddhu S, et al. SPRINT Research Group. Final report of a trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2021;384:1921–1930.
5. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023;148:e9–e119.

- Bohm M, Schumacher H, Teo KK, et al. Achieved diastolic blood pressure and pulse pressure at target systolic blood pressure (120–140 mm Hg) and cardiovascular outcomes in high-risk patients: results from ONTARGET and TRANSCEND trials. *Eur Heart J*. 2018;39:3105–3114.
- Law MR, Morris JK, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009;338:b1665.
- Yndegegn T, Lindahl B, Mars K, et al. Beta-blockers after myocardial infarction and preserved ejection fraction (REDUCE-AMI). *N Engl J Med*. 2024;390:1372–1381.
- Jeffers BW, Robbins J, Bhambhani R. Efficacy of calcium channel blockers versus other classes of antihypertensive medication in the treatment of hypertensive patients with previous stroke and/or coronary artery disease: a systematic review and meta-analysis. *Am J Ther*. 2017;24:e68–e80.
- Lubsen J, Wagener G, Kirwan BA, et al. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with symptomatic stable angina and hypertension: the ACTION trial. *J Hypertens*. 2005;23:641–648.

5.3.4. Prevention of HF in Adults With Hypertension

- Lv J, Ehteshami P, Sarnak MJ, et al. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. *CMAJ*. 2013;185:949–957.
- Reboldi G, Angeli F, Gentile G, et al. Benefits of more intensive versus less intensive blood pressure control. Updated trial sequential analysis. *Eur J Intern Med*. 2022;101:49–55.
- Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels - updated overview and meta-analyses of randomized trials. *J Hypertens*. 2016;34:613–622.
- Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet*. 2016;387:435–443.
- Siddiqi TJ, Usman MS, Siddiqui A, et al. Association of low diastolic blood pressure with cardiovascular outcomes and all-cause mortality: a meta-analysis. *Curr Probl Cardiol*. 2024;49:102131.
- Baffour PK, Jahangir L, Jain S, et al. Blood pressure, hypertension, and the risk of heart failure: a systematic review and meta-analysis of cohort studies. *Eur J Prev Cardiol*. 2024;31:529–556.
- Bibbins-Domingo K, Pletcher MJ, Lin F, et al. Racial differences in incident heart failure among young adults. *N Engl J Med*. 2009;360:1179–1190.
- Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. *JAMA*. 1970;213:1143–1152.
- Kostis JB, Davis BR, Cutler J, et al, SHEP Cooperative Research Group. Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. *JAMA*. 1997;278:212–216.
- Law MR, Morris JK, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009;338:b1665.
- Thomopoulos C, Bazoukis G, Tsioufis C, et al. Beta-blockers in hypertension: overview and meta-analysis of randomized outcome trials. *J Hypertens*. 2020;38:1669–1681.
- Wright JT Jr, Williamson JD, Whelton PK, et al. Sprint Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.

5.3.4.1. HF With Reduced Ejection

- Khan SU, Khan MZ, Alkhouli M. Trends of clinical outcomes and health care resource use in heart failure in the United States. *J Am Heart Assoc*. 2020;9:e016782.
- Drazner MH. The progression of hypertensive heart disease. *Circulation*. 2011;123:327–334.
- Multicenter Diltiazem Postinfarction Trial Research Group. The effect of diltiazem on mortality and reinfarction after myocardial infarction. *N Engl J Med*. 1988;319:385–392.
- Goldstein RE, Boccuzzi SJ, Cruess D, et al, The Adverse Experience Committee; and the Multicenter Diltiazem Postinfarction Research

Group. Diltiazem increases late-onset congestive heart failure in postinfarction patients with early reduction in ejection fraction. *Circulation*. 1991;83:52–60.

- Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e895–e1032.

5.3.4.2. HF With Preserved Ejection Fraction

- Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e895–e1032.
- Kittleson MM, Panjath GS, Amancherla K, et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81:1835–1878.
- Solomon SD, McMurray JJV, Anand IS, et al. Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. *N Engl J Med*. 2019;381:1609–1620.
- Anker SD, Butler J, Filippatos G, et al. Empagliflozin in heart failure with a preserved ejection fraction. *N Engl J Med*. 2021;385:1451–1461.
- Kario K, Ferdinand KC, O'Keefe JH. Control of 24-hour blood pressure with SGLT2 inhibitors to prevent cardiovascular disease. *Prog Cardiovasc Dis*. 2020;63:249–262.
- Zhang Q, Zhou S, Liu L. Efficacy and safety evaluation of SGLT2i on blood pressure control in patients with type 2 diabetes and hypertension: a new meta-analysis. *Diabetol Metab Syndr*. 2023;15:118.

5.3.5. Atrial Fibrillation

- Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149:e1–e156.
- Huxley RR, Lopez FL, Folsom AR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study. *Circulation*. 2011;123:1501–1508.
- Verdecchia P, Angeli F, Reboldi G. Hypertension and atrial fibrillation: doubts and certainties from basic and clinical studies. *Circ Res*. 2018;122:352–368.
- Kornej J, Borschel CS, Benjamin EJ, et al. Epidemiology of atrial fibrillation in the 21st century: novel methods and new insights. *Circ Res*. 2020;127:4–20.
- Soliman EZ, Rahman AF, Zhang ZM, et al. Effect of intensive blood pressure lowering on the risk of atrial fibrillation. *Hypertension*. 2020;75:1491–1496.
- Emdin CA, Callender T, Cao J, et al. Effect of antihypertensive agents on risk of atrial fibrillation: a meta-analysis of large-scale randomized trials. *Europace*. 2015;17:701–710.
- Pinho-Gomes AC, Azevedo L, Copland E, et al. Blood pressure-lowering treatment for the prevention of cardiovascular events in patients with atrial fibrillation: an individual participant data meta-analysis. *PLoS Med*. 2021;18:e1003599.
- Gawalko M, Linz D. Atrial fibrillation detection and management in hypertension. *Hypertension*. 2023;80:523–533.
- Neefs J, van den Berg NW, Limpens J, et al. Aldosterone pathway blockade to prevent atrial fibrillation: a systematic review and meta-analysis. *Int J Cardiol*. 2017;231:155–161.

5.3.6. Valvular Heart Disease

- Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e72–e227.
- Antonini-Canterin F, Huang G, Cervesato E, et al. Symptomatic aortic stenosis: does systemic hypertension play an additional role? *Hypertension*. 2003;41:1268–1272.
- Rieck AE, Cramariuc D, Staal EM, et al. Impact of hypertension on left ventricular structure in patients with asymptomatic aortic valve stenosis (a SEAS substudy). *J Hypertens*. 2010;28:377–383.

4. Bull S, Loudon M, Francis JM, et al. A prospective, double-blind, randomized controlled trial of the angiotensin-converting enzyme inhibitor Ramipril In Aortic Stenosis (RIAS trial). *Eur Heart J Cardiovasc Imaging*. 2015;16:834–841.
5. Yang LT, Pellikka PA, Enriquez-Sarano M, et al. Diastolic blood pressure and heart rate are independently associated with mortality in chronic aortic regurgitation. *J Am Coll Cardiol*. 2020;75:29–39.
6. Ochiai T, Saito S, Yamanaka F, et al. Renin-angiotensin system blockade therapy after transcatheter aortic valve implantation. *Heart*. 2018;104:644–651.
7. Otto CM. Heartbeat: beta-blockers for aortic regurgitation. *Heart*. 2016;102:165–167.
8. Aronow WS. Hypertension, aortic stenosis, and aortic regurgitation. *Ann Transl Med*. 2018;6:43.
9. Elder DH, Wei L, Swzjekowski BR, et al. The impact of renin-angiotensin-aldosterone system blockade on heart failure outcomes and mortality in patients identified to have aortic regurgitation: a large population cohort study. *J Am Coll Cardiol*. 2011;58:2084–2091.
9. Wright J, Jackson T, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA*. 2002;288:2421–2431.
10. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med*. 2001;345:861–869.
11. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med*. 2001;345:851–860.
12. Yusuf S, Teo KK, Pogue J, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med*. 2008;358:1547–1559.
13. Holtkamp FA, de Zeeuw D, Thomas MC, et al. An acute fall in estimated glomerular filtration rate during treatment with losartan predicts a slower decrease in long-term renal function. *Kidney Int*. 2011;80:282–287.
14. Clase CM, Barzilay J, Gao P, et al. Acute change in glomerular filtration rate with inhibition of the renin-angiotensin system does not predict subsequent renal and cardiovascular outcomes. *Kidney Int*. 2017;91:683–690.
15. McCallum W, Tighiouart H, Ku E, et al. Acute declines in estimated glomerular filtration rate on enalapril and mortality and cardiovascular outcomes in patients with heart failure with reduced ejection fraction. *Kidney Int*. 2019;96:1185–1194.
16. Bhandari S, Mehta S, Khwaja A, et al. Renin-angiotensin system inhibition in advanced chronic kidney disease. *N Engl J Med*. 2022;387:2021–2032.
17. Fried LF, Emanuele N, Zhang JH, et al. Combined angiotensin inhibition for the treatment of diabetic nephropathy. *N Engl J Med*. 2013;369:1892–1903.
18. Mann JF, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. *Lancet*. 2008;372:547–553.

5.3.7. Aortic Disease

1. Rooprai J, Boodhwani M, Beauchesne L, et al. Central hypertension in patients with thoracic aortic aneurysms: prevalence and association with aneurysm size and growth. *Am J Hypertens*. 2022;35:79–86.
2. Altobelli E, Rapacchietta L, Profeta VF, et al. Risk factors for abdominal aortic aneurysm in population-based studies: a systematic review and meta-analysis. *Int J Environ Res Public Health*. 2018;15:2805.
3. Kobeissi E, Hibino M, Pan H, et al. Blood pressure, hypertension and the risk of abdominal aortic aneurysms: a systematic review and meta-analysis of cohort studies. *Eur J Epidemiol*. 2019;34:547–555.
4. Hibino M, Otaki Y, Kobeissi E, et al. Blood pressure, hypertension, and the risk of aortic dissection incidence and mortality: results from the J-SCH Study, the UK Biobank Study, and a meta-analysis of cohort studies. *Circulation*. 2022;145:633–644.
5. Otaki Y, Watanabe T, Konta T, et al. Effect of hypertension on aortic artery disease-related mortality; 3.8-year nationwide community-based prospective cohort study. *Circ J*. 2018;82:2776–2782.
6. Howard DP, Banerjee A, Fairhead JF, et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *Br J Surg*. 2015;102:907–915.
7. Jaeger BC, Bress AP, Bundy JD, et al. Longer-term all-cause and cardiovascular mortality with intensive blood pressure control: a secondary analysis of a randomized clinical trial. *JAMA Cardiol*. 2022;7:1138–1146.
8. Sweeting MJ, Thompson SG, Brown LC, et al. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg*. 2012;99:655–665.
9. Isselbacher EM, Preventza O, Black JH 3rd, et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;146:e334–e482.

5.3.8. Hypertension Treatment in Patients With CKD

1. Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.
2. Aggarwal R, Petrie B, Bala W, et al. Mortality outcomes with intensive blood pressure targets in chronic kidney disease patients. *Hypertension*. 2019;73:1275–1282.
3. Malhotra R, Nguyen HA, Benavente O, et al. Association between more intensive vs less intensive blood pressure lowering and risk of mortality in chronic kidney disease stages 3 to 5: a systematic review and meta-analysis. *JAMA Intern Med*. 2017;177:1498–1505.
4. Xie X, Liu Y, Perkovic V, et al. Renin-angiotensin system inhibitors and kidney and cardiovascular outcomes in patients with CKD: a bayesian network meta-analysis of randomized clinical trials. *Am J Kidney Dis*. 2016;67:728–741.
5. Wu HY, Huang JW, Lin HJ, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: systematic review and bayesian network meta-analysis. *BMJ*. 2013;347:f6008.
6. Plantinga LC, Miller ER 3rd, Stevens LA, et al. Blood pressure control among persons without and with chronic kidney disease: US trends and risk factors 1999–2006. *Hypertension*. 2009;54:47–56.
7. Bangalore S, Toklu B, Gianos E, et al. Optimal systolic blood pressure target after SPRINT: insights from a network meta-analysis of randomized trials. *Am J Med*. 2017;130:707–719.e708.
8. Molnar MZ, Kalantar-Zadeh K, Lott EH, et al. Angiotensin-converting enzyme inhibitor, angiotensin receptor blocker use, and mortality in patients with chronic kidney disease. *J Am Coll Cardiol*. 2014;63:650–658.

5.3.8.1. Hypertension After Kidney Transplantation

1. Kasiske BL, Anjum S, Shah R, et al. Hypertension after kidney transplantation. *Am J Kidney Dis*. 2004;43:1071–1081.
2. Malhotra R, Katz R, Weiner DE, et al. Blood pressure, chronic kidney disease progression, and kidney allograft failure in kidney transplant recipients: a secondary analysis of the FAVORIT trial. *Am J Hypertens*. 2019;32:816–823.
3. Chatzikyrkou C, Schmieder RE, Schiffer M. Update on treatment of hypertension after renal transplantation. *Curr Hypertens Rep*. 2021;23:25.
4. Eleftheriadis G, Naik MG, Osmanodja B, et al. Office or home versus 24-hour blood pressure measurement in stable kidney transplant recipients. *Nephrol Dial Transplant*. 2024;28:gfae076.
5. Tutone VK, Mark PB, Stewart GA, et al. Hypertension, antihypertensive agents and outcomes following renal transplantation. *Clin Transplant*. 2005;19:181–192.
6. Natale P, Palmer SC, Jaure A, et al. Blood pressure lowering for kidney transplant recipients: systematic review with network meta-analysis. *J Hypertens*. 2024;42:848–855.
7. Mortensen LA, Jespersen B, Helligsoe ASL, et al. Effect of spironolactone on kidney function in kidney transplant recipients (the SPIREN trial): a randomized placebo-controlled clinical trial. *Clin J Am Soc Nephrol*. 2024;19:755–766.

5.3.9. Cerebrovascular Disease

1. Martin SS, Aday AW, Almarazooq ZI, et al. 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913.

5.3.9.1. Acute Intracerebral Hemorrhage

1. Anderson CS, Heeley E, Huang Y, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med*. 2013;368:2355–2365.
2. Ma L, Hu X, Song L, et al. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. *Lancet*. 2023;402:27–40.
3. Moullaali TJ, Wang X, Martin RH, et al. Blood pressure control and clinical outcomes in acute intracerebral haemorrhage: a preplanned pooled analysis of individual participant data. *Lancet Neurol*. 2019;18:857–864.
4. Manning L, Hirakawa Y, Arima H, et al. Blood pressure variability and outcome after acute intracerebral haemorrhage: a post-hoc analysis of INTERACT2, a randomised controlled trial. *Lancet Neurol*. 2014;13:364–373.
5. Arima H, Heeley E, Delcourt C, et al. Optimal achieved blood pressure in acute intracerebral hemorrhage: INTERACT2. *Neurology*. 2015;84:464–471.

6. Qureshi AI, Palesch YY, Barsan WG, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *N Engl J Med*. 2016;375:1033–1043.
7. Qureshi AI, Huang W, Lobanova I, et al. Outcomes of intensive systolic blood pressure reduction in patients with intracerebral hemorrhage and excessively high initial systolic blood pressure: post hoc analysis of a randomized clinical trial. *JAMA Neurol*. 2020;77:1355–1365.
8. Martin SS, Aday AW, Almarazq ZI, et al. 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913.
9. Boulouis G, Morotti A, Goldstein JN, et al. Intensive blood pressure lowering in patients with acute intracerebral haemorrhage: clinical outcomes and haemorrhage expansion. Systematic review and meta-analysis of randomised trials. *J Neurol Neurosurg Psychiatry*. 2017;88:339–345.
10. Bath PM, Woodhouse LJ, Krishnan K, et al. Prehospital transdermal glyceryl trinitrate for ultra-acute intracerebral hemorrhage: data from the RIGHT-2 trial. *Stroke*. 2019;50:3064–3071.

5.3.9.2. Acute Ischemic Stroke

1. Wohlfahrt P, Krajcoviechova A, Jozifova M, et al. Low blood pressure during the acute period of ischemic stroke is associated with decreased survival. *J Hypertens*. 2015;33:339–345.
2. Leonardi-Bee J, Bath PM, Phillips SJ, et al. Blood pressure and clinical outcomes in the International Stroke Trial. *Stroke*. 2002;33:1315–1320.
3. Vemmos KN, Tsvigoulis G, Spengos K, et al. U-shaped relationship between mortality and admission blood pressure in patients with acute stroke. *J Intern Med*. 2004;255:257–265.
4. National Institute of Neurological Disorders Stroke, PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333:1581–1587.
5. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. 2008;359:1317–1329.
6. Katsanos AH, Malhotra K, Ahmed N, et al. Blood pressure after endovascular thrombectomy and outcomes in patients with acute ischemic stroke: an individual patient data meta-analysis. *Neurology*. 2022;98:e291–e301.
7. Anadani M, Arthur AS, Alawieh A, et al. Blood pressure reduction and outcome after endovascular therapy with successful reperfusion: a multicenter study. *J Neurointerv Surg*. 2020;12:932–936.
8. Liu L, Xie X, Pan Y, et al. Early versus delayed antihypertensive treatment in patients with acute ischaemic stroke: multicentre, open label, randomised, controlled trial. *BMJ*. 2023;383:e076448.
9. Anderson CS, Huang Y, Lindley RJ, et al. Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial. *Lancet*. 2019;393:877–888.
10. He J, Zhang Y, Xu T, et al. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke: the CATIS randomized clinical trial. *JAMA*. 2014;311:479–489.
11. Sandset EC, Bath PM, Boysen G, et al. The angiotensin-receptor blocker candesartan for treatment of acute stroke (SCAST): a randomised, placebo-controlled, double-blind trial. *Lancet*. 2011;377:741–750.
12. Yang P, Song L, Zhang Y, et al. Intensive blood pressure control after endovascular thrombectomy for acute ischaemic stroke (ENCHANTED2/MT): a multicentre, open-label, blinded-endpoint, randomised controlled trial. *Lancet*. 2022;400:1585–1596.
13. Nam HS, Kim YD, Heo J, et al. Intensive vs conventional blood pressure lowering after endovascular thrombectomy in acute ischemic stroke: the OPTIMAL-BP randomized clinical trial. *JAMA*. 2023;330:832–842.
14. Mistry EA, Hart KW, Davis LT, et al. Blood pressure management after endovascular therapy for acute ischemic stroke: the BEST-II randomized clinical trial. *JAMA*. 2023;330:821–831.
15. Qureshi AI, Ezzeddine MA, Nasar A, et al. Prevalence of elevated blood pressure in 563 704 adult patients with stroke presenting to the ED in the United States. *Am J Emerg Med*. 2007;25:32–38.
16. Castillo J, Leira R, Garcia MM, et al. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. *Stroke*. 2004;35:520–526.
17. Enos Trial Investigators. Efficacy of nitric oxide, with or without continuing antihypertensive treatment, for management of high blood pressure in acute stroke (ENOS): a partial-factorial randomised controlled trial. *Lancet*. 2015;385:617–628.
18. Zhao R, Liu FD, Wang S, et al. Blood pressure reduction in the acute phase of an ischemic stroke does not improve short- or long-term dependency or mortality: a meta-analysis of current literature. *Medicine (Baltimore)*. 2015;94:e896.
19. Muscare A, Puddu GM, Serafini C, et al. Predictors of short-term improvement of ischemic stroke. *Neurol Res*. 2013;35:594–601.
20. Visvanathan A, Dennis M, Whiteley W. Parenteral fluid regimens for improving functional outcome in people with acute stroke. *Cochrane Database Syst Rev*. 2015;2015:CD011138.
21. Waltimo T, Haapaniemi E, Surakka IL, et al. Post-thrombolytic blood pressure and symptomatic intracerebral hemorrhage. *Eur J Neurol*. 2016;23:1757–1762.
22. Malhotra K, Ahmed N, Filippatou A, et al. Association of elevated blood pressure levels with outcomes in acute ischemic stroke patients treated with intravenous thrombolysis: a systematic review and meta-analysis. *J Stroke*. 2019;21:78–90.
23. Mistry EA, Sucharew H, Mistry AM, et al. Blood pressure after endovascular therapy for ischemic stroke (BEST): a multicenter prospective cohort study. *Stroke*. 2019;50:3449–3455.
24. Ghazy S, Mortezaei A, Elfil M, et al. Intensive vs conventional blood pressure control after thrombectomy in acute ischemic stroke: a systematic review and meta-analysis. *JAMA Netw Open*. 2024;7:e240179.

5.3.9.3. Secondary Stroke Prevention

1. Zonneveld TP, Richard E, Vergouwen MD, et al. Blood pressure-lowering treatment for preventing recurrent stroke, major vascular events, and dementia in patients with a history of stroke or transient ischaemic attack. *Cochrane Database Syst Rev*. 2018;7:CD007858.
2. Wang WT, You LK, Chiang CE, et al. Comparative effectiveness of blood pressure-lowering drugs in patients who have already suffered from stroke: traditional and Bayesian network meta-analysis of randomized trials. *Medicine (Baltimore)*. 2016;95:e3302.
3. Katsanos AH, Filippatou A, Manios E, et al. Blood pressure reduction and secondary stroke prevention: a systematic review and metaregression analysis of randomized clinical trials. *Hypertension*. 2017;69:171–179.
4. Progress Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. *Lancet*. 2001;358:1033–1041.
5. Kitagawa K, Yamamoto Y, Arima H, et al. Effect of standard vs intensive blood pressure control on the risk of recurrent stroke: a randomized clinical trial and meta-analysis. *JAMA Neurol*. 2019;76:1309–1318.
6. Mant J, McManus RJ, Roaloe A, et al. Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention After Stroke--Blood Pressure) randomised controlled trial. *BMJ*. 2016;352:708.
7. Bath PM, Scutt P, Blackburn DJ, et al. Intensive versus guideline blood pressure and lipid lowering in patients with previous stroke: main results from the pilot 'Prevention of Decline in Cognition after Stroke Trial' (PODCAST) randomised controlled trial. *PLoS One*. 2017;12:e0164608.
8. Martin SS, Aday AW, Almarazq ZI, et al. 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913.
9. Lin Q, Ye T, Ye P, et al. Hypertension in stroke survivors and associations with national premature stroke mortality: data for 2.5 million participants from multinational screening campaigns. *Lancet Glob Health*. 2022;10:e1141–e1149.
10. Zheng S, Yao B. Impact of risk factors for recurrence after the first ischemic stroke in adults: a systematic review and meta-analysis. *J Clin Neurosci*. 2019;60:24–30.
11. Biffi A, Anderson CD, Battey TW, et al. Association between blood pressure and risk of recurrent intracerebral hemorrhage. *JAMA*. 2015;314:904–912.
12. Nguyen-Huynh MN, Hills NK, Sidney S, et al. Race-ethnicity on blood pressure control after ischemic stroke: a prospective cohort study. *J Am Soc Hypertens*. 2017;11:38–44.
13. Zahuranec DB, Wing JJ, Edwards DF, et al. Poor long-term blood pressure control after intracerebral hemorrhage. *Stroke*. 2012;43:2580–2585.
14. Rodriguez-Torres A, Murphy M, Kourkoulis C, et al. Hypertension and intracerebral hemorrhage recurrence among White, Black, and Hispanic individuals. *Neurology*. 2018;91:e37–e44.
15. Liu L, Wang Z, Gong L, et al. Blood pressure reduction for the secondary prevention of stroke: a Chinese trial and a systematic review of the literature. *Hypertens Res*. 2009;32:1032–1040.
16. Schrader J, Luders S, Kulschewski A, et al. Morbidity and mortality after stroke, eprosartan compared with nitrendipine for secondary prevention: principal

results of a prospective randomized controlled study (MOSES). *Stroke*. 2005;36:1218–1226.

17. Jeffers BW, Robbins J, Bhambhani R. Efficacy of calcium channel blockers versus other classes of antihypertensive medication in the treatment of hypertensive patients with previous stroke and/or coronary artery disease: a systematic review and meta-analysis. *Am J Ther*. 2017;24:e68–e80.
18. Benavente OR, Coffey CS, Conwit R, et al. S. P. S. Study Group. Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomized trial. *Lancet*. 2013;382:507–515.
19. Yusuf S, Diener HC, Sacco RL, et al. Telmisartan to prevent recurrent stroke and cardiovascular events. *N Engl J Med*. 2008;359:1225–1237.

5.3.9.4. Mild Cognitive Impairment and Dementia

1. Peters R, Collerton J, Granic A, et al. Antihypertensive drug use and risk of cognitive decline in the very old: an observational study - the Newcastle 85+ Study. *J Hypertens*. 2015;33:2156–2164.
2. Hughes D, Judge C, Murphy R, et al. Association of blood pressure lowering with incident dementia or cognitive impairment: a systematic review and meta-analysis. *JAMA*. 2020;323:1934–1944.
3. Williamson JD, Pajewski NM, Auchus AP, et al. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*. 2019;321:553–561.
4. Reboussin DM, Gaussoin SA, Pajewski NM, et al. Long-term effect of intensive vs standard blood pressure control on mild cognitive impairment and probable dementia in SPRINT. *Neurology*. 2025;104:e213334.
5. He J. Effectiveness of blood pressure reduction on all-cause dementia among patients with hypertension: an open-label, blinded-endpoint, cluster-randomized trial. *Nat Med*. Published online April 21, 2025. doi: 10.1038/s41591-025-03616-8.
6. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2023;19:1598–1695.
7. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:126–135.
8. Brookmeyer R, Corrada MM, Currier FC, et al. Survival following a diagnosis of Alzheimer disease. *Arch Neurol*. 2002;59:1764–1767.
9. Malone JE, Elkasaby MI, Lerner AJ. Effects of hypertension on Alzheimer's disease and related disorders. *Curr Hypertens Rep*. 2022;24:615–625.
10. Palta P, Albert MS, Gottesman RF. Heart health meets cognitive health: evidence on the role of blood pressure. *Lancet Neurol*. 2021;20:854–867.
11. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥ 75 years: a randomized clinical trial. *JAMA*. 2016;315:2673–2682.
12. Sweeney MD, Montagne A, Sagare AP, et al. Vascular dysfunction—the disregarded partner of Alzheimer's disease. *Alzheimers Dement*. 2019;15:158–167.
13. Iadecola C, Duering M, Hachinski V, et al. Vascular cognitive impairment and dementia: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019;73:3326–3344.
14. Longstreth WT Jr, Manolio TA, Arnold A, et al. Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study. *Stroke*. 1996;27:1274–1282.
15. Gronewold J, Jokisch M, Schramm S, et al. Association of regional white matter hyperintensities with hypertension and cognition in the population-based 1000BRAINS study. *Eur J Neurol*. 2023;30:1174–1190.
16. Zhao Y, Ke Z, He W, et al. Volume of white matter hyperintensities increases with blood pressure in patients with hypertension. *J Int Med Res*. 2019;47:3681–3689.
17. de Havenon A, Sheth KN, Yeatts SD, et al. White matter hyperintensity progression is associated with incident probable dementia or mild cognitive impairment. *Stroke Vasc Neurol*. 2022;7:364–366.
18. Qiu C, Winblad B, Fratiglioni L. The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol*. 2005;4:487–499.
19. Kivipelto M, Helkala EL, Hanninen T, et al. Midlife vascular risk factors and late-life mild cognitive impairment: a population-based study. *Neurology*. 2001;56:1683–1689.
20. Lennon MJ, Lam BCP, Lipnicki DM, et al. Use of antihypertensives, blood pressure, and estimated risk of dementia in late life: an individual participant data meta-analysis. *JAMA Netw Open*. 2023;6:e2333353.
21. Peters R, Xu Y, Fitzgerald O, et al. Blood pressure lowering and prevention of dementia: an individual patient data meta-analysis. *Eur Heart J*. 2022;43:4980–4990.

22. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet*. 1997;350:757–764.
23. Czerlichow S, Ninomiya T, Huxley R, et al. Impact of blood pressure lowering on cardiovascular outcomes in normal weight, overweight, and obese individuals: the Perindopril Protection Against Recurrent Stroke Study trial. *Hypertension*. 2010;55:1193–1198.
24. Williamson JD, Pajewski NM, Auchus AP, et al. SPRINT Mind investigators for the SPRINT Research Group. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*. 2019;321:553–561.

5.3.10. Peripheral Artery Disease

1. Lawes CM, Vander Hoorn S, Rodgers A, et al. Global burden of blood-pressure-related disease, 2001. *Lancet*. 2008;371:1513–1518.
2. Kennedy M, Solomon C, Manolio TA, et al. Risk factors for declining ankle-brachial index in men and women 65 years or older: the Cardiovascular Health Study. *Arch Intern Med*. 2005;165:1896–1902.
3. Piller LB, Simpson LM, Baraniuk S, et al. Characteristics and long-term follow-up of participants with peripheral arterial disease during ALLHAT. *J Gen Intern Med*. 2014;29:1475–1483.
4. Diehm P, Pittrow D, Lawall H. Effect of nebivolol vs. hydrochlorothiazide on the walking capacity in hypertensive patients with intermittent claudication. *J Hypertens*. 2011;29:1448–1456.
5. Paravastu SC, Mendonca DA, Da Silva A. Beta blockers for peripheral arterial disease. *Cochrane Database Syst Rev* 2013;2013:CD005508.
6. Espinola-Klein C, Weisser G, Jagodzinski A, et al. Beta-blockers in patients with intermittent claudication and arterial hypertension: results from the nebivolol or metoprolol in arterial occlusive disease trial. *Hypertension*. 2011;58:148–154.
7. Sleight P. The HOPE study (Heart Outcomes Prevention Evaluation). *J Renin Angiotensin Aldosterone Syst* 2000;1:18–20.
8. Investigators O, Yusuf S, Teo KK, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med*. 2008;358:1547–1559.
9. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VES guideline for the management of lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149:e1313–e1410.

5.4. Plan of Care for Hypertension

1. Ogungbe O, Cazabon D, Ajenikoko A, et al. Determining the frequency and level of task-sharing for hypertension management in LMICs: a systematic review and meta-analysis. *EClinicalMedicine*. 2022;47:101388.
2. He J, Irazola V, Mills KT, et al. Effect of a community health worker-led multicomponent intervention on blood pressure control in low-income patients in Argentina: a randomized clinical trial. *JAMA*. 2017;318:1016–1025.
3. Santschi V, Chiolerio A, Colosimo AL, et al. Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2014;3:e000718.
4. Victor RG, Lynch K, Li N, et al. A cluster-randomized trial of blood-pressure reduction in black barbershops. *N Engl J Med*. 2018;378:1291–1301.
5. Abdalla M, Bolen SD, Brettler J, et al. Implementation strategies to improve blood pressure control in the United States: a scientific statement from the American Heart Association and American Medical Association. *Hypertension*. 2023;80:e143–e157.
6. Fontil V, Gupta R, Moise N, et al. Adapting and evaluating a health system intervention from Kaiser Permanente to improve hypertension management and control in a large network of safety-net clinics. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004386.
7. Jaffe MG, Lee GA, Young JD, et al. Improved blood pressure control associated with a large-scale hypertension program. *JAMA*. 2013;310:699–705.
8. Hanlin RB, Asif IM, Wozniak G, et al. Measure accurately, Act rapidly, and Partner with patients (MAP) improves hypertension control in medically underserved patients: Care Coordination Institute and American Medical Association Hypertension control project pilot study results. *J Clin Hypertens (Greenwich)* 2018;20:79–87.
9. Behling EM, Garriss T, Blankenship V, et al. Improvement in hypertension control among adults seen in federally qualified health center clinics in the Stroke Belt: implementing a program with a dashboard and process metrics. *Health Equity*. 2023;7:89–99.

10. Egan BM, Sutherland SE, Rakotz M, et al. Improving hypertension control in primary care with the Measure Accurately, Act Rapidly, and Partner With Patients (MAP) protocol. *Hypertension*. 2018;72:1320–1327.
11. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116.
12. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362:1575–1585.
13. Xu W, Goldberg SI, Shubina M, et al. Optimal systolic blood pressure target, time to intensification, and time to follow-up in treatment of hypertension: population based retrospective cohort study. *BMJ (Online)*. 2015;350:h158.
14. McManus RJ, Mant J, Franssen M, et al. Efficacy of self-monitored blood pressure, with or without telemonitoring, for titration of antihypertensive medication (TASMINH4): an unmasked randomised controlled trial. *Lancet*. 2018;391:949–959.
15. Ose D, Adediran E, Owens R, et al. Electronic health record-driven approaches in primary care to strengthen hypertension management among racial and ethnic minoritized groups in the United States: systematic review. *J Med Internet Res*. 2023;25:e42409.
16. Pletcher MJ, Fontil V, Modrow MF, et al. Effectiveness of standard vs enhanced self-measurement of blood pressure paired with a connected smartphone application: a randomized clinical trial. *JAMA Intern Med*. 2022;182:1025–1034.
17. Rakotz MK, Ewigman BG, Sarav M, et al. A technology-based quality innovation to identify undiagnosed hypertension among active primary care patients. *Ann Fam Med*. 2014;12:352–358.
18. Baral N, Volgman AS, Seri A, et al. Adding pharmacist-led home blood pressure telemonitoring to usual care for blood pressure control: a systematic review and meta-analysis. *Am J Cardiol*. 2023;203:161–168.
19. Verberk WJ, Kessels AG, Thien T. Telecare is a valuable tool for hypertension management, a systematic review and meta-analysis. *Blood Press Monit*. 2011;16:149–155.
20. Liu S, Dunford SD, Leung YW, et al. Reducing blood pressure with internet-based interventions: a meta-analysis. *Can J Cardiol*. 2013;29:613–621.
21. Margolis KL, Asche SE, Bergdall AR, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. *JAMA*. 2013;310:46–56.
22. McManus RJ, Little P, Stuart B, et al. Home and Online Management and Evaluation of Blood Pressure (HOME BP) using a digital intervention in poorly controlled hypertension: randomised controlled trial. *BMJ*. 2021;372:m4858.
23. Omboni S, Gazzola T, Carabelli G, et al. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring: meta-analysis of randomized controlled studies. *J Hypertens*. 2013;31:455–467; discussion 467–458.
24. Duan Y, Xie Z, Dong F, et al. Effectiveness of home blood pressure telemonitoring: a systematic review and meta-analysis of randomised controlled studies. *J Hum Hypertens*. 2017;31:427–437.
25. Acharya S, Neupane G, Seals A, et al. Self-measured blood pressure-guided pharmacotherapy: a systematic review and meta-analysis of United States-based telemedicine trials. *Hypertension*. 2024;81:648–657.
26. Margolis KL, Asche SE, Dehmer SP, et al. Long-term outcomes of the effects of home blood pressure telemonitoring and pharmacist management on blood pressure among adults with uncontrolled hypertension: follow-up of a cluster randomized clinical trial. *JAMA Netw Open*. 2018;1:e181617.
27. Community Preventive Services Task Force. Heart disease and stroke prevention: team-based care to improve blood pressure control. December 13, 2024. Accessed January 18, 2025. <https://www.cdc.gov/high-blood-pressure/php/data-research/team-basedcare/index.html>
28. Himmelfarb CR, Commodore-Mensah Y, Hill MN. Expanding the role of nurses to improve hypertension care and control globally. *Ann Glob Health*. 2016;82:243–253.
29. U.S. Department of Health and Human Services. The Surgeon General's Call to Action to Control Hypertension. U.S. Department of Health and Human Services, Office of the Surgeon General; 2020. Accessed September 20, 2024. <https://www.cdc.gov/high-blood-pressure/media/pdfs/SG-CTA-HTN-Control-Report-508.pdf>
30. World Health Organization. HEARTS Technical package for cardiovascular disease management in primary health care: team-based care. 2018. Accessed September 24, 2024. <https://www.who.int/publications/i/item/WHO-NMH-NVI-18-4>
31. Proia KK, Thota AB, Njie GJ, et al. Team-based care and improved blood pressure control: a community guide systematic review. *Am J Prev Med*. 2014;47:86–99.
32. Pasha M, Brewer LC, Sennhauser S, et al. Health care delivery interventions for hypertension management in underserved populations in the United States: a systematic review. *Hypertension*. 2021;78:955–965.
33. Islam NS, Wyatt LC, Ali SH, et al. Integrating community health workers into community-based primary care practice settings to improve blood pressure control among South Asian immigrants in New York city: results from a randomized control trial. *Circ Cardiovasc Qual Outcomes*. 2023;16:e009321.
34. Gamage DG, Riddell MA, Joshi R, et al. Effectiveness of a scalable group-based education and monitoring program, delivered by health workers, to improve control of hypertension in rural India: a cluster randomised controlled trial. *PLoS Med*. 2020;17:e1002997.
35. Bulto LN, Roseleur J, Noonan S, et al. Effectiveness of nurse-led interventions versus usual care to manage hypertension and lifestyle behaviour: a systematic review and meta-analysis. *Eur J Cardiovasc Nurs*. 2024;23:21–32.
36. Morris AA, Masoudi FA, Abdullah AR, et al. 2024 ACC/AHA key data elements and definitions for social determinants of health in cardiology: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Data Standards. *Circulation: Cardiovascular Quality and Outcomes*. 2024;17:e000133.
37. Brush JE Jr, Handberg EM, Biga C, et al. 2015 ACC health policy statement on cardiovascular team-based care and the role of advanced practice providers. *J Am Coll Cardiol*. 2015;65:2118–2136.
38. Dunn SP, Birtcher KK, Beavers CJ, et al. The role of the clinical pharmacist in the care of patients with cardiovascular disease. *J Am Coll Cardiol*. 2015;66:2129–2139.
39. Jacob V, Chattopadhyay SK, Thota AB, et al. Economics of team-based care in controlling blood pressure: a community guide systematic review. *Am J Prev Med*. 2015;49:772–783.
40. Schmieder RE, Wassmann S, Predel HG, et al. Improved persistence to medication, decreased cardiovascular events and reduced all-cause mortality in hypertensive patients with use of single-pill combinations: results from the START-Study. *Hypertension*. 2023;80:1127–1135.
41. Carey RM, Muntner P, Bosworth HB, et al. Prevention and control of hypertension: JACC health promotion series. *J Am Coll Cardiol*. 2018;72:1278–1293.
42. Parati G, Dolan E, McManus RJ, et al. Home blood pressure telemonitoring in the 21st century. *J Clin Hypertens (Greenwich)*. 2018;20:1128–1132.
43. Lau D, Ringrose J, McAlister FA, et al. Telemonitoring and protocolized case management for hypertensive community dwelling older adults (TECH-NOMED): a randomized controlled trial. *J Hypertens*. 2022;40:1702–1712.
44. Ozpincer N, Pakyuz SC, Topcu B. Hypertension management: what is the role of case management? *Rev Esc Enferm USP*. 2017;51:e03291.
45. Jaffe MG, Young JD. The Kaiser Permanente northern California story: improving hypertension control from 44% to 90% in 13 years (2000 to 2013). *J Clin Hypertens (Greenwich)*. 2016;18:260–261.
46. Omboni S, McManus RJ, Bosworth HB, et al. Evidence and recommendations on the use of telemedicine for the management of arterial hypertension: an international expert position paper. *Hypertension*. 2020;76:1368–1383.
47. Takahashi EA, Schwamm LH, Adeoye OM, et al. An overview of telehealth in the management of cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2022;146:e558–e568.
48. Shimbo D, Artinian NT, Basile JN, et al. Self-measured blood pressure monitoring at home: a joint policy statement from the American Heart Association and American Medical Association. *Circulation*. 2020;142:E42–E63.
49. Yano Y, Reis JP, Colangelo LA, et al. Association of blood pressure classification in young adults using the 2017 American College of Cardiology/American Heart Association blood pressure guideline with cardiovascular events later in life. *JAMA*. 2018;320:1774–1782.
50. Ambrosius WT, Sink KM, Foy CG, et al. The design and rationale of a multicenter clinical trial comparing two strategies for control of systolic blood pressure: the Systolic Blood Pressure Intervention Trial (SPRINT). *Clin Trials*. 2014;11:532–546.
51. He J, Ouyang N, Guo X, et al. Effectiveness of a non-physician community health-care provider-led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): an open-label, blinded-endpoint, cluster-randomised trial. *Lancet*. 2023;401:928–938.
52. Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149:430–449.
53. Anand TN, Joseph LM, Geetha AV, et al. Task sharing with non-physician health-care workers for management of blood pressure in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Glob Health*. 2019;7:e761–e771.

54. Khetan A, Zullo M, Rani A, et al. Effect of a community health worker-based approach to integrated cardiovascular risk factor control in India: a cluster randomized controlled trial. *Glob Heart*. 2019;14:355–365.
55. Neupane D, McLachlan CS, Mishra SR, et al. Effectiveness of a lifestyle intervention led by female community health volunteers versus usual care in blood pressure reduction (COBIN): an open-label, cluster-randomised trial. *Lancet Glob Health*. 2018;6:e66–e73.
56. Mills KT, Obst KM, Shen W, et al. Comparative effectiveness of implementation strategies for blood pressure control in hypertensive patients: a systematic review and meta-analysis. *Ann Intern Med*. 2018;168:110–120.
57. Stephen C, Halcomb E, Fernandez R, et al. Nurse-led interventions to manage hypertension in general practice: a systematic review and meta-analysis. *J Adv Nurs*. 2022;78:1281–1293.
58. Reeves L, Robinson K, McClelland T, et al. Pharmacist interventions in the management of blood pressure control and adherence to antihypertensive medications: a systematic review of randomized controlled trials. *J Pharm Pract*. 2021;34:480–492.
59. Agency for Healthcare Research and Quality. Comprehensive care plan template for patients and clinicians. Accessed May 1, 2024. <https://www.ahrq.gov/evidencecenter/tools/hypertension-care-plan.html>.
60. Margolis KL, Asche SE, Bergdall AR, et al. A successful multifaceted trial to improve hypertension control in primary care: why did it work? *J Gen Intern Med*. 2015;30:1665–1672.
61. Mattei da Silva AT, de Fatima Mantovani M, Castanho Moreira R, et al. Nursing case management for people with hypertension in primary health care: a randomized controlled trial. *Res Nurs Health*. 2020;43:68–78.
62. Ma Y, Cheng HY, Sit JWH, et al. The effects of a smartphone-enhanced nurse-facilitated self-care intervention for Chinese hypertensive patients: a randomised controlled trial. *Int J Nurs Stud*. 2022;134:104313.
63. Mantovani MF, Kalinke LP, da Silva A TM, et al. Effectiveness of nursing case management versus usual care for blood pressure control in adults with hypertension: a systematic review. *Invest Educ Enferm*. 2021;39:e04.
64. Boonyasai RT, Rakotz MK, Lubomski LH, et al. Measure accurately, Act rapidly, and Partner with patients: An intuitive and practical three-part framework to guide efforts to improve hypertension control. *J Clin Hypertens (Greenwich)*. 2017;19:684–694.
65. Green BB, Cook AJ, Ralston JD, et al. Effectiveness of home blood pressure monitoring, Web communication, and pharmacist care on hypertension control: a randomized controlled trial. *JAMA*. 2008;299:2857–2867.
66. Casey DE Jr, Thomas RJ, Bhalla V, et al. 2019 AHA/ACC clinical performance and quality measures for adults with high blood pressure: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *Circ Cardiovasc Qual Outcomes*. 2019;12:e000057.
67. Schorr EN, Geppner AD, Dolansky MA, et al. Harnessing mobile health technology for secondary cardiovascular disease prevention in older adults: a scientific statement from the American Heart Association. *Circ Cardiovasc Qual Outcomes*. 2021;14:e000103.
68. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. *Circulation*. 2015;132:1157–1213.
69. Commodore-Mensah Y, Loustalot F, Himmelfarb CD, et al. Proceedings from a National Heart, Lung, and Blood Institute and the Centers for Disease Control and Prevention workshop to control hypertension. *Am J Hypertens*. 2022;35:232–243.
70. Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1982–2004.
71. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
3. Ou M, Zhang F, Cui S, et al. Oral nifedipine may be a preferential option for treating acute severe hypertension during pregnancy: a meta-analysis. *Hypertens Pregnancy*. 2023;42:2209637.
4. Wu HZ, Cheng Y, Yu D, et al. Different dosage regimens of nifedipine, labetalol, and hydralazine for the treatment of severe hypertension during pregnancy: a network meta-analysis of randomized controlled trials. *Hypertens Pregnancy*. 2022;41:126–138.
5. Awaludin A, Rahayu C, Daud NAA, et al. Antihypertensive medications for severe hypertension in pregnancy: a systematic review and meta-analysis. *Healthcare (Basel)*. 2022;10:325.
6. Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222. *Obstet Gynecol*. 2020;135:e237–e260.
7. Magee LA, Cham C, Waterman EJ, et al. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. *BMJ*. 2003;327:955–960.
8. Tita AT, Szychowski JM, Boggess K, et al. Treatment for mild chronic hypertension during pregnancy. *N Engl J Med*. 2022;386:1781–1792.
9. Attar A, Hosseinpour A, Moghadami M. The impact of antihypertensive treatment of mild to moderate hypertension during pregnancy on maternal and neonatal outcomes: an updated meta-analysis of randomized controlled trials. *Clin Cardiol*. 2023;46:467–476.
10. Barr M Jr. Teratogen update: angiotensin-converting enzyme inhibitors. *Teratology*. 1994;50:399–409.
11. Bellos I, Pergialiotis V, Papapanagiotou A, et al. Comparative efficacy and safety of oral antihypertensive agents in pregnant women with chronic hypertension: a network metaanalysis. *Am J Obstet Gynecol*. 2020;223:525–537.
12. Easterling TR, Carr DB, Brateng D, et al. Treatment of hypertension in pregnancy: effect of atenolol on maternal disease, preterm delivery, and fetal growth. *Obstet Gynecol*. 2001;98:427–433.
13. Moretti ME, Caprara D, Drehtula I, et al. The fetal safety of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers. *Obstet Gynecol Int*. 2012;2012:658310.
14. Pucci M, Sarween N, Knox E, et al. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in women of childbearing age: risks versus benefits. *Expert Rev Clin Pharmacol*. 2015;8:221–231.
15. Ford ND, Cox S, Ko JY, et al. Hypertensive disorders in pregnancy and mortality at delivery hospitalization - United States, 2017-2019. *MMWR Morb Mortal Wkly Rep*. 2022;71:585–591.
16. Cameron NA, Petito LC, Shah NS, et al. Association of birth year of pregnant individuals with trends in hypertensive disorders of pregnancy in the United States, 1995-2019. *JAMA Netw Open*. 2022;5:e2228093.
17. Cameron NA, Everitt I, Seegmiller LE, et al. Trends in the incidence of new-onset hypertensive disorders of pregnancy among rural and urban areas in the United States, 2007 to 2019. *J Am Heart Assoc*. 2022;11:e023791.
18. Petersen EE, Davis NL, Goodman D, et al. Racial/ethnic disparities in pregnancy-related deaths - United States, 2007-2016. *MMWR Morb Mortal Wkly Rep*. 2019;68:762–765.
19. Wang MC, Freaney PM, Perak AM, et al. Trends in prepregnancy obesity and association with adverse pregnancy outcomes in the United States, 2013 to 2018. *J Am Heart Assoc*. 2021;10:e020717.
20. Chronic hypertension in pregnancy. ACOG practice bulletin no.203. *Obstet Gynecol*. 2019;133:215–219.
21. ACOG Practice Advisory. Clinical guidance for the integration of the findings of the Chronic Hypertension and Pregnancy (CHAP) study. American College of Obstetricians and Gynecologists. Accessed August 9, 2024. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2022/04/clinical-guidance-for-the-integration-of-the-findings-of-the-chronic-hypertension-and-pregnancy-chap-study>.
22. Oostvogels A, Busschers WB, Spierings EJM, et al. Pre-pregnancy weight status, early pregnancy lipid profile and blood pressure course during pregnancy: the ABCD study. *PLoS One*. 2017;12:e0177554.
23. Bello NA, Woolley JJ, Cleary KL, et al. Accuracy of blood pressure measurement devices in pregnancy: a systematic review of validation studies. *Hypertension*. 2018;71:326–335.
24. Ghazi L, Bello NA. Hypertension in women across the lifespan. *Curr Atheroscler Rep*. 2021;23:43.
25. Sanusi AA, Leach J, Boggess K, et al. Pregnancy outcomes of nifedipine compared with labetalol for oral treatment of mild chronic hypertension. *Obstet Gynecol*. 2024;144:126–134.
26. Mito A, Murashima A, Wada Y, et al. Safety of amlodipine in early pregnancy. *J Am Heart Assoc*. 2019;8:e012093.
27. Ahn HK, Nava-Ocampo AA, Han JY, et al. Exposure to amlodipine in the first trimester of pregnancy and during breastfeeding. *Hypertens Pregnancy*. 2007;26:179–187.

5.5. Hypertension and Pregnancy

1. Abalos E, Duley L, Steyn DW, et al. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. *Cochrane Database Syst Rev*. 2018;10:CD002252.
2. Henderson JT, Vesco KK, Senger CA, et al. Aspirin use to prevent preeclampsia and related morbidity and mortality: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2021;326:1192–1206.

28. Ishikawa T, Nishigori H, Akazawa M, et al. Risk of major congenital malformations associated with first-trimester antihypertensives, including amlodipine and methyldopa: a large claims database study 2010-2019. *Pregnancy Hypertens.* 2023;31:73–83.
29. Liszewski W, Boull C. Lack of evidence for feminization of males exposed to spironolactone in utero: a systematic review. *J Am Acad Dermatol.* 2019;80:1147–1148.
30. Riestler A, Reincke M. Progress in primary aldosteronism: mineralocorticoid receptor antagonists and management of primary aldosteronism in pregnancy. *Eur J Endocrinol.* 2015;172:R23–R30.
31. Forestiero V, Sconfienza E, Mulatero P, et al. Primary aldosteronism in pregnancy. *Rev Endocr Metab Disord.* 2023;24:39–48.
32. Sanga V, Rossitto G, Seccia TM, et al. Management and outcomes of primary aldosteronism in pregnancy: a systematic review. *Hypertension.* 2022;79:1912–1921.
33. National Library of Medicine. Drugs and lactation database (LactMed). National Center for Biotechnology Information. Accessed August 9, 2024. <https://www.ncbi.nlm.nih.gov/books/NBK501922/>
34. Garovic VD, Dechend R, Easterling T, et al. Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. *Hypertension.* 2022;79:e21–e41.
35. Postpartum hypertension clinic development toolkit. American College of Cardiology. Accessed August 9, 2024. <https://www.acc.org/HTNinPregnancy>

5.5.1. Gestational Hypertension

1. Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222. *Obstet Gynecol.* 2020;135:e237–e260.
2. Magee LA, von Dadelszen P, Bohun CM, et al. Serious perinatal complications of non-proteinuric hypertension: an international, multicentre, retrospective cohort study. *J Obstet Gynaecol Can.* 2003;25:372–382.
3. Magee LA, Singer J, von Dadelszen P, et al. Less-tight versus tight control of hypertension in pregnancy. *N Engl J Med.* 2015;372:2367–2368.
4. Magee LA, von Dadelszen P, Singer J, et al. The CHIPS randomized controlled trial (Control of Hypertension in Pregnancy Study): is severe hypertension just an elevated blood pressure? *Hypertension.* 2016;68:1153–1159.

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

1. Magee LA, Brown MA, Hall DR, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens.* 2022;27:148–169.
2. Low-dose aspirin use during pregnancy. ACOG committee opinion no. 743. *Obstet Gynecol.* 2018;132:e44–e52.
3. LeFevre ML, Force USPST. Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014;161:819–826.
4. Force USPST, Davidson KW, Barry MJ, et al. Aspirin use to prevent preeclampsia and related morbidity and mortality: US Preventive Services Task Force recommendation statement. *JAMA.* 2021;326:1186–1191.
5. Meszaros B, Veres DS, Nagystok L, et al. Pravastatin in preeclampsia: a meta-analysis and systematic review. *Front Med (Lausanne).* 2022;9:1076372.
6. Duhig KE, Myers J, Seed PT, et al. Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. *Lancet.* 2019;393:1807–1818.
7. Zeisler H, Llorba E, Chantraine F, et al. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. *N Engl J Med.* 2016;374:13–22.
8. Chappell LC, Duckworth S, Seed PT, et al. Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: a prospective multicenter study. *Circulation.* 2013;128:2121–2131.
9. Rana S, Salahuddin S, Mueller A, et al. Angiogenic biomarkers in triage and risk for preeclampsia with severe features. *Pregnancy Hypertens.* 2018;13:100–106.
10. Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222. *Obstet Gynecol.* 2020;135:e237–e260.

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

1. Optimizing postpartum care, practice bulletin no. 736. American College of Obstetricians and Gynecologists. Accessed August 9, 2024. <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/05/optimizing-postpartum-care>.

2. Kitt J, Krasner S, Barr L, et al. Cardiac remodeling after hypertensive pregnancy following physician-optimized blood pressure self-management: the POP-HT randomized clinical trial imaging substudy. *Circulation.* 2024;149:529–541.
3. Cairns AE, Tucker KL, Leeson P, et al. Self-management of postnatal hypertension: the SNAP-HT trial. *Hypertension.* 2018;72:425–432.
4. Steele DW, Adam GP, Saldanha JJ, et al. Postpartum home blood pressure monitoring: a systematic review. *Obstet Gynecol.* 2023;142:285–295.
5. Bellamy L, Casas JP, Hingorani AD, et al. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ.* 2007;335:974.
6. Leon LJ, McCarthy FP, Direk K, et al. Preeclampsia and cardiovascular disease in a large UK pregnancy cohort of linked electronic health records: a CALIBER study. *Circulation.* 2019;140:1050–1060.
7. Garovic VD, Dechend R, Easterling T, et al. Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. *Hypertension.* 2022;79:e21–e41.
8. Nakatsu T, Suenaga E, Kitagata Y. Extending line for minimizing air emboli between perfusion branch and left ventricular vent (ELIZABETH) circuit for minimally invasive cardiac surgery. *JTCVS Tech.* 2024;26:70–72.
9. Cho L, Davis M, Elgendy I, et al. Summary of updated recommendations for primary prevention of cardiovascular disease in women: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020;75:2602–2618.
10. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2019;140:e596–e646.
11. Cameron NA, Blyler CA, Bello NA. Oral contraceptive pills and hypertension: a review of current evidence and recommendations. *Hypertension.* 2023;80:924–935.
12. Lindley KJ, Bairey Merz CN, Davis MB, et al. Contraception and reproductive planning for women with cardiovascular disease: JACC focus seminar 5/5. *J Am Coll Cardiol.* 2021;77:1823–1834.
13. Nguyen AT, Curtis KM, Tepper NK, et al. US medical eligibility criteria for contraceptive use, 2024. *MMWR Recomm Rep.* 2024;73:1–126.

5.6. Resistant Hypertension and Renal Denervation

1. Giacona JM, Kositanurit W, Vongpatanasin W. Management of resistant hypertension—an update. *JAMA Intern Med.* 2024;184:433–434.
2. Vitarello JA, Fitzgerald CJ, Cluett JL, et al. Prevalence of medications that may raise blood pressure among adults with hypertension in the United States. *JAMA Intern Med.* 2022;182:90–93.
3. Forman JP, Stampfer MJ, Curhan GC. Non-narcotic analgesic dose and risk of incident hypertension in US women. *Hypertension.* 2005;46:500–507.
4. Fleming GA. The FDA, regulation, and the risk of stroke. *N Engl J Med.* 2000;343:1886–1887.
5. Zhu X, Wu S, Dahut WL, et al. Risks of proteinuria and hypertension with bevacizumab, an antibody against vascular endothelial growth factor: systematic review and meta-analysis. *Am J Kidney Dis.* 2007;49:186–193.
6. Williams B, MacDonald TM, Morant S, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. *Lancet.* 2015;386:2059–2068.
7. Vaclavik J, Sedlak R, Plachy M, et al. Addition of spironolactone in patients with resistant arterial hypertension (ASPIRANT): a randomized, double-blind, placebo-controlled trial. *Hypertension.* 2011;57:1069–1075.
8. Krieger EM, Drager LF, Giorgi DMA, et al. Spironolactone versus clonidine as a fourth-drug therapy for resistant hypertension the REHOT randomized study (Resistant Hypertension Optimal Treatment). *Hypertension.* 2018;71:681–690.
9. Chapman N, Chang CL, Dahlof B, et al. Effect of doxazosin gastrointestinal therapeutic system as third-line antihypertensive therapy on blood pressure and lipids in the Anglo-Scandinavian Cardiac Outcomes Trial. *Circulation.* 2008;118:42–48.
10. Hundemer GL, Knoll GA, Petrich W, et al. Kidney, cardiac, and safety outcomes associated with alpha-blockers in patients with CKD: a population-based cohort study. *Am J Kidney Dis.* 2021;77:178–189.e171.
11. Mundt HM, Matenaer M, Lammert A, et al. Minoxidil for treatment of resistant hypertension in chronic kidney disease—a retrospective cohort analysis. *J Clin Hypertens (Greenwich).* 2016;18:1162–1167.
12. Azizi M, Sharp ASP, Fisher ND, et al. Patient-level pooled analysis of endovascular ultrasound renal denervation or a sham procedure 6 months

- after medication escalation: the RADIANCE clinical trial program. *Circulation*. 2024;149:747–759.
13. Azizi M, Sanghvi K, Saxena M, et al. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): a randomised, multicentre, single-blind, sham-controlled trial. *Lancet*. 2021;397:2476–2486.
 14. Kandzari DE, Weber MA, Pathak A, et al. Effect of alcohol-mediated renal denervation on blood pressure in the presence of antihypertensive medications: primary results from the TARGET BP I randomized clinical trial. *Circulation*. 2024;149:1875–1884.
 15. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. *Hypertension*. 2018;72:e53–e90.
 16. Patel KV, Li X, Kondamudi N, et al. Prevalence of apparent treatment-resistant hypertension in the United States according to the 2017 high blood pressure guideline. *Mayo Clin Proc*. 2019;94:776–782.
 17. Ebinger JE, Gluckman TJ, Magraner J, et al. Characterization of individuals with apparent resistant hypertension using contemporary guidelines: insights from CV-QUIC. *Hypertension*. 2023;80:1845–1855.
 18. Carey RM, Sakhuja S, Calhoun DA, et al. Prevalence of apparent treatment-resistant hypertension in the United States. *Hypertension*. 2019;73:424–431.
 19. Jafari E, Cooper-DeHoff RM, Effron MB, et al. Characteristics and predictors of apparent treatment resistant hypertension in real-world populations using electronic health record-based data. *Am J Hypertens*. 2024;37(1):60–68.
 20. Akinyelure OP, Jaeger BC, Oparil S, et al. Social determinants of health and uncontrolled blood pressure in a national cohort of Black and White US adults: the REGARDS study. *Hypertension*. 2023;80:1403–1413.
 21. Ebinger JE, Kauko A, FinnGen, et al. Apparent treatment-resistant hypertension associated lifetime cardiovascular risk in a longitudinal national registry. *Eur J Prev Cardiol*. 2023;30:960–968.
 22. Coccina F, Pierdomenico AM, Cuccurullo C, et al. Ambulatory resistant hypertension and risk of heart failure in the elderly. *Diagnostics*. 2023;13:1634.
 23. Kaczmarek KR, Sozio SM, Chen J, et al. Resistant hypertension and cardiovascular disease mortality in the US: results from the National Health and Nutrition Examination Survey (NHANES). *BMC Nephrol*. 2019;20:138.
 24. Narita K, Hoshida S, Kario K. Nighttime home blood pressure is associated with the cardiovascular disease events risk in treatment-resistant hypertension. *Hypertension*. 2022;79:e18–e20.
 25. Cardoso CRL, Salles GF. Prognostic impact of home blood pressures for adverse cardiovascular outcomes and mortality in patients with resistant hypertension: a prospective cohort study. *Hypertension*. 2021;78:1617–1627.
 26. Azizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomised, sham-controlled trial. *Lancet*. 2018;391:2335–2345.
 27. Azizi M, Saxena M, Wang Y, et al. Endovascular ultrasound renal denervation to treat hypertension: the RADIANCE II randomized clinical trial. *JAMA*. 2023;329:651–661.
 28. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial. *Lancet*. 2017;390:2160–2170.
 29. Kandzari DE, Townsend RR, Kario K, et al. Safety and efficacy of renal denervation in patients taking antihypertensive medications. *J Am Coll Cardiol*. 2023;82:1809–1823.
 30. Kario K, Yokoi Y, Okamura K, et al. Catheter-based ultrasound renal denervation in patients with resistant hypertension: the randomized, controlled REQUIRE trial. *Hypertens Res*. 2022;45:221–231.
 31. Schmieder RE, Ott C, Tonnes SW, et al. Phase II randomized sham-controlled study of renal denervation for individuals with uncontrolled hypertension-WAVE IV. *J Hypertens*. 2018;36:680–689.
 32. Liang W, Ma H, Cao L, et al. Comparison of thiazide-like diuretics versus thiazide-type diuretics: a meta-analysis. *J Cell Mol Med*. 2017;21:2634–2642.
 33. Peterzan MA, Hardy R, Chaturvedi N, et al. Meta-analysis of dose-response relationships for hydrochlorothiazide, chlorthalidone, and bendroflumethiazide on blood pressure, serum potassium, and urate. *Hypertension*. 2012;59:1104–1109.
 34. Ishani A, Hau C, Cushman WC, et al. Chlorthalidone vs hydrochlorothiazide for hypertension treatment after myocardial infarction or stroke: a secondary analysis of a randomized clinical trial. *JAMA Netw Open*. 2024;7:e2411081.
 35. Agarwal R, Pitt B, Palmer BF, et al. A comparative post hoc analysis of finerenone and spironolactone in resistant hypertension in moderate-to-advanced chronic kidney disease. *Clin Kidney J*. 2023;16:293–302.
 36. Agarwal R, Rossignol P, Romero A, et al. Patiromer versus placebo to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER): a phase 2, randomised, double-blind, placebo-controlled trial. *Lancet*. 2019;394:1540–1550.
 37. Chapman N, Dobson J, Wilson S, et al. Effect of spironolactone on blood pressure in subjects with resistant hypertension. *Hypertension*. 2007;49:839–845.
 38. Rosa J, Widimsky P, Tousek P, et al. Randomized comparison of renal denervation versus intensified pharmacotherapy including spironolactone in true-resistant hypertension: six-month results from the Prague-15 study. *Hypertension*. 2015;65:407–413.
 39. Eguchi K, Kabutoya T, Hoshida S, et al. Add-on use of eplerenone is effective for lowering home and ambulatory blood pressure in drug-resistant hypertension. *J Clin Hypertens (Greenwich)*. 2016;18:1250–1257.
 40. Kalizki T, Schmidt BMW, Raff U, et al. Low dose-eplerenone treatment decreases aortic stiffness in patients with resistant hypertension. *J Clin Hypertens (Greenwich)*. 2017;19:669–676.
 41. Schneider A, Schwab J, Karg MV, et al. Low-dose eplerenone decreases left ventricular mass in treatment-resistant hypertension. *J Hypertens*. 2017;23:23.
 42. Williams B, MacDonald TM, Morant SV, et al. Endocrine and haemodynamic changes in resistant hypertension, and blood pressure responses to spironolactone or amiloride: the PATHWAY-2 mechanisms substudies. *Lancet Diabetes Endocrinol*. 2018;6:464–475.
 43. Hundemer GL, Knoll GA, Petrich W, et al. Kidney, cardiac, and safety outcomes associated with alpha-blockers in patients with CKD: a population-based cohort study. *Am J Kidney Dis*. 2021;77: 178–189.e1.
 44. Gottlieb TB, Katz FH, Chidsey CA 3rd. Combined therapy with vasodilator drugs and beta-adrenergic blockade in hypertension. A comparative study of minoxidil and hydralazine. *Circulation*. 1972;45:571–582.
 45. Schlaich MP, Bellet M, Weber MA, et al. Dual endothelin antagonist apocintan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial. *Lancet*. 2022;400:1927–1937.
 46. Bohm M, Kario K, Kandzari DE, et al. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED Pivotal): a multicentre, randomised, sham-controlled trial. *Lancet*. 2020;395:1444–1451.
 47. Oliveras A, Armario P, Clara A, et al. Spironolactone versus sympathetic renal denervation to treat true resistant hypertension: results from the DENERVHTA study: a randomized controlled trial. *J Hypertens*. 2016;34:1863–1871.
 48. Townsend RR, Walton A, Hettrick DA, et al. Review and meta-analysis of renal artery damage following percutaneous renal denervation with radio-frequency renal artery ablation. *EuroIntervention*. 2020;16:89–96.
 49. Cluett JL, Blazek O, Brown AL, et al. Renal denervation for the treatment of hypertension: a scientific statement from the American Heart Association. *Hypertension*. 2024;81:e135–e148.
 50. Kirtane AJ, Sharp ASP, Mahfoud F, et al. Patient-level pooled analysis of ultrasound renal denervation in the sham-controlled RADIANCE II, RADIANCE-HTN SOLO, and RADIANCE-HTN TRIO trials. *JAMA Cardiol*. 2023;8:464–473.
 51. Ahmad Y, Francis DP, Bhatt DL, et al. Renal denervation for hypertension: a systematic review and meta-analysis of randomized, blinded, placebo-controlled trials. *JACC Cardiovasc Interv*. 2021;14:2614–2624.
 52. Ogoyama Y, Tada K, Abe M, et al. Effects of renal denervation on blood pressures in patients with hypertension: a systematic review and meta-analysis of randomized sham-controlled trials. *Hypertens Res*. 2022;45:210–220.
 53. Davis MI, Filion KB, Zhang D, et al. Effectiveness of renal denervation therapy for resistant hypertension: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2013;62:231–241.
 54. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269–1324.
 55. Calhoun DA, Jones D, Textor S, et al. Resistant hypertension: diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Hypertension*. 2008;51:1403–1419.

6.1. Management of Orthostatic Hypertension

1. Juraschek SP, Appel LJ, Miller ER 3rd, et al. Hypertension treatment effects on orthostatic hypotension and its relationship with cardiovascular disease. *Hypertension*. 2018;72:986–993.

2. Juraschek SP, Hu JR, Cluett JL, et al. Effects of intensive blood pressure treatment on orthostatic hypotension: a systematic review and individual participant-based meta-analysis. *Ann Intern Med.* 2021;174:58–68.
3. Juraschek SP, Taylor AA, Wright JT Jr, et al. Orthostatic hypotension, cardiovascular outcomes, and adverse events: results from SPRINT. *Hypertension.* 2020;75:660–667.
4. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: a randomized clinical trial. *JAMA.* 2016;315:2673–2682.
5. Ogren J, Mooe T, Irewall AL. Orthostatic hypotension in stroke/TIA patients: Association with new events and the effect of the NAILED intervention. *PLoS One.* 2024;19:e0298435.
6. Kamaruzzaman S, Watt H, Carson C, et al. The association between orthostatic hypotension and medication use in the British Women's Heart and Health study. *Age Ageing.* 2010;39:51–56.
7. Townsend RR, Chang TI, Cohen DL, et al. Orthostatic changes in systolic blood pressure among SPRINT participants at baseline. *J Am Soc Hypertens.* 2016;10:847–856.
8. Rutan GH, Hermanson B, Bild DE, et al. Orthostatic hypotension in older adults. The Cardiovascular Health Study. CHS Collaborative Research Group. *Hypertension.* 1992;19:508–519.
9. Yatsuya H, Folsom AR, Alonso A, et al. Postural changes in blood pressure and incidence of ischemic stroke subtypes: the ARIC study. *Hypertension.* 2011;57:167–173.
10. Fedorowski A, Stavenow L, Hedblad B, et al. Orthostatic hypotension predicts all-cause mortality and coronary events in middle-aged individuals (The Malmo Preventive Project). *Eur Heart J.* 2010;31:85–91.
11. Di Stefano C, Milazzo V, Totaro S, et al. Orthostatic hypotension in a cohort of hypertensive patients referring to a hypertension clinic. *J Hum Hypertens.* 2015;29:599–603.
12. Svetkey L, Brobyn R, Deedwania P, et al. Double-blind comparison of doxazosin, nadolol and placebo in patients with mild-to-moderate hypertension. *Curr Ther Res.* 1988;43:969–978.
13. Heseltine D, Bramble MG. Loop diuretics cause less postural hypotension than thiazide diuretics in the frail elderly. *Curr Med Res Opin.* 1988;11:232–235.
14. Myers MG, Kearns PM, Shedletsky R, et al. Postural hypotension and mental function in the elderly. *Can Med Assoc J.* 1978;119:1061–1065.
15. Canney M OCM, Murphy CM, et al. Single agent antihypertensive therapy and orthostatic blood pressure behaviour in older adults using beat-to-beat measurements: the Irish Longitudinal Study on Ageing. *PLoS One.* 2016;11:e0146156.
16. Figueroa JJ, Basford JR, Low PA. Preventing and treating orthostatic hypotension: as easy as A, B, C. *Cleve Clin J Med.* 2010;77:298–306.
17. Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med.* 2017;166:430–437.
18. He J ZC, Zhong S, Ouyang N, Qiao L, Yang R, Zhao C, Liu H, Teng W, Liu X, Spat-Lemus J, Chen C-S, Li C, Williamson J, Sun Y. Effectiveness of blood pressure-lowering intervention on risk of total dementia among patients with hypertension: a cluster-randomized effectiveness trial. Abstract #23343. *Circulation.* 2023;148:e282-e317.
19. Sively high initial systolic blood pressure: post hoc analysis of a randomized clinical trial. *JAMA Neurol.* 2020;77:1355–1365.
20. Qureshi AI, Huang W, Lobanova I, et al. Systolic blood pressure reduction and acute kidney injury in intracerebral hemorrhage. *Stroke.* 2020;51:3030–3038.
21. Anderson TS, Herzig SJ, Jing B, et al. Clinical outcomes of intensive inpatient blood pressure management in hospitalized older adults. *JAMA Intern Med.* 2023;183:715–723.
22. Peacock FT, Varon J, Ebrahimi R, et al. Clevidipine for severe hypertension in acute heart failure: a VELOCITY trial analysis. *Congest Heart Fail.* 2010;16:55–59.
23. Garg K, Staunton MK, Peixoto AJ, et al. Correlates of spontaneous blood pressure reduction following severe inpatient hypertension development. *Am J Hypertens.* 2023;37:273–279.
24. Mohandas R, Chamarthi G, Bozorgmehr S, et al. Pro re nata antihypertensive medications and adverse outcomes in hospitalized patients: a propensity-matched cohort study. *Hypertension.* 2021;78:516–524.
25. Siddiqi TJ, Usman MS, Rashid AM, et al. Clinical outcomes in hypertensive emergency: a systematic review and meta-analysis. *J Am Heart Assoc.* 2023;12:e029355.
26. Paini A, Tarozzi L, Bertacchini F, et al. Cardiovascular prognosis in patients admitted to an emergency department with hypertensive emergencies and urgencies. *J Hypertens.* 2021;39:2514–2520.
27. Isselbacher EM, Preventza O, Hamilton Black J 3rd, et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation.* 2022;146:e334–e482.
28. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018;71:1269–1324.

6.2.1. Medications for Hypertensive Emergencies

1. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018;71:1269–1324.

6.3. Sexual Dysfunction

1. Foy CG, Newman JC, Berlowitz DR, et al. Blood pressure, sexual activity, and dysfunction in women with hypertension: baseline findings from the Systolic Blood Pressure Intervention Trial (SPRINT). *J Sex Med.* 2016;13:1333–1346.
2. Foy CG, Newman JC, Berlowitz DR, et al. Blood pressure, sexual activity, and erectile function in hypertensive men: baseline findings from the Systolic Blood Pressure Intervention Trial (SPRINT). *J Sex Med.* 2019;16:235–247.
3. Ning L, Yang L. Hypertension might be a risk factor for erectile dysfunction: a meta-analysis. *Andrologia.* 2017;49:e12644.
4. Rosen RC. Prevalence and risk factors of sexual dysfunction in men and women. *Curr Psychiatry Rep.* 2000;2:189–195.
5. Santana LM, Perin L, Lunelli R, et al. Sexual dysfunction in women with hypertension: a systematic review and meta-analysis. *Curr Hypertens Rep.* 2019;21:25.
6. Thomas HN, Evans GW, Berlowitz DR, et al. Antihypertensive medications and sexual function in women: baseline data from the SBP intervention trial (SPRINT). *J Hypertens.* 2016;34:1224–1231.
7. World Health Organization. International statistical classification of diseases and related health problems (ICD-10). Accessed July 7, 2024. <https://www.who.int/standards/classifications/classification-of-diseases>.
8. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther.* 2000;26:191–208.
9. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology.* 1997;49:822–830.
10. Viigimaa M, Vlachopoulos C, Doulas M, et al. Update of the position paper on arterial hypertension and erectile dysfunction. *J Hypertens.* 2020;38:1220–1234.

11. Doulmas M, Douma S. The effect of antihypertensive drugs on erectile function: a proposed management algorithm. *J Clin Hypertens (Greenwich)*. 2006;8:359–364.
12. Rosen RC. Sexual dysfunction as an obstacle to compliance with antihypertensive therapy. *Blood Press Suppl*. 1997;1:47–51.
13. Fogari R, Preti P, Zoppi A, et al. Effect of valsartan and atenolol on sexual behavior in hypertensive postmenopausal women. *Am J Hypertens*. 2004;17:77–81.
14. Doulmas M, Tsiodras S, Tsakiris A, et al. Female sexual dysfunction in essential hypertension: a common problem being uncovered. *J Hypertens*. 2006;24:2387–2392.

6.4. Patients Scheduled for Surgical Procedures

1. Prins KW, Neill JM, Tyler JO, et al. Effects of beta-blocker withdrawal in acute decompensated heart failure: a systematic review and meta-analysis. *JACC Heart Fail*. 2015;3:647–653.
2. Neumann A, Maura G, Weill A, et al. Clinical events after discontinuation of β -blockers in patients without heart failure optimally treated after acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004356.
3. Lindenaier PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353:349–361.
4. Shammash JB, Trost JC, Gold JM, et al. Perioperative beta-blocker withdrawal and mortality in vascular surgical patients. *Am Heart J*. 2001;141:148–153.
5. Andersson C, Merie C, Jorgensen M, et al. Association of beta-blocker therapy with risks of adverse cardiovascular events and deaths in patients with ischemic heart disease undergoing noncardiac surgery: a Danish nationwide cohort study. *JAMA Intern Med*. 2014;174:336–344.
6. Shiffermiller JF, Monson BJ, Vokoun CW, et al. Prospective randomized evaluation of preoperative angiotensin-converting enzyme inhibition (PREOP-ACEI). *J Hosp Med*. 2018;13:661–667.
7. Hollmann C, Fernandes NL, Biccari BM. A systematic review of outcomes associated with withholding or continuing angiotensin-converting enzyme inhibitors and angiotensin receptor blockers before noncardiac surgery. *Anesth Analg*. 2018;127:678–687.
8. Ackland GL, Patel A, Abbott TEF, et al. Discontinuation vs. continuation of renin-angiotensin system inhibition before non-cardiac surgery: the SPACE trial. *Eur Heart J*. 2024;45:1146–1155.
9. Marucci M, Painter TW, Conen D, et al. Hypotension-avoidance versus hypertension-avoidance strategies in noncardiac surgery: (POISE-3) an international randomized controlled trial. *Ann Intern Med*. 2023;176:605–614.
10. Roshanov PS, Rochwerf B, Patel A, et al. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before noncardiac surgery: an analysis of the vascular events in noncardiac surgery patients cohort evaluation prospective cohort. *Anesthesiology*. 2017;126:16–27.
11. Abdelmalak BB, Abd-Elsayed AA, Dalton JE, et al. The association between preinduction arterial blood pressure and postoperative cardiovascular, renal, and neurologic morbidity, and in-hospital mortality in elective noncardiac surgery: an observational study. *J Hypertens*. 2018;36:2251–2259.
12. Howell SJ, Sear JW, Foex P. Hypertension, hypertensive heart disease and perioperative cardiac risk. *Br J Anaesth*. 2004;92:570–583.
13. Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.
14. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370:1504–1513.
15. Blessberger H, Lewis SR, Pritchard MW, et al. Perioperative beta-blockers for preventing surgery-related mortality and morbidity in adults undergoing non-cardiac surgery. *Cochrane Database Syst Rev*. 2019;9:CD013438.
16. Hart GR, Anderson RJ. Withdrawal syndromes and the cessation of antihypertensive therapy. *Arch Intern Med*. 1981;141:1125–1127.
17. Charlson ME, MacKenzie CR, Gold JP, et al. The preoperative and intraoperative hemodynamic predictors of postoperative myocardial infarction or ischemia in patients undergoing noncardiac surgery. *Ann Surg*. 1989;210:637–648.
18. Cheung AT. Exploring an optimum intra/postoperative management strategy for acute hypertension in the cardiac surgery patient. *J Card Surg*. 2006;21 Suppl 1:S8–S14.
19. Dix P, Howell S. Survey of cancellation rate of hypertensive patients undergoing anaesthesia and elective surgery. *Br J Anaesth*. 2001;86:789–793.
20. Haas CE, LeBlanc JM. Acute postoperative hypertension: a review of therapeutic options. *Am J Health Syst Pharm*. 2004;61:1661–1673; quiz 1674–1665.
21. Thompson A, Fleischmann KE, Smilowitz NR, et al. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM guideline for perioperative cardiovascular management for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;150:e351–e442.
22. Wu X, Jiang Z, Ying J, et al. Optimal blood pressure decreases acute kidney injury after gastrointestinal surgery in elderly hypertensive patients: a randomized study: optimal blood pressure reduces acute kidney injury. *J Clin Anesth*. 2017;43:77–83.
23. Ling Q, Gu Y, Chen J, et al. Consequences of continuing renin angiotensin aldosterone system antagonists in the preoperative period: a systematic review and meta-analysis. *BMC Anesthesiol*. 2018;18:26.
24. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med*. 1997;157:2413–2446.
25. Wolfsthal SD. Is blood pressure control necessary before surgery? *Med Clin North Am*. 1993;77:349–363.
26. Goldman L, Caldera DL. Risks of general anesthesia and elective operation in the hypertensive patient. *Anesthesiology*. 1979;50:285–292.
27. Drummond JC, Blake JL, Patel PM, et al. An observational study of the influence of “white-coat hypertension” on day-of-surgery blood pressure determinations. *J Neurosurg Anesthesiol*. 2013;25:154–161.
28. Hopper I, Samuel R, Hayward C, et al. Can medications be safely withdrawn in patients with stable chronic heart failure? Systematic review and meta-analysis. *J Card Fail*. 2014;20:522–532.
29. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839–1847.
30. Martin PR, Ebert MH, Gordon EK, et al. Catecholamine metabolism during clonidine withdrawal. *Psychopharmacology (Berl)*. 1984;84:58–63.
31. Devereaux PJ, Beattie WS, Choi PT, et al. How strong is the evidence for the use of perioperative beta blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2005;331:313–321.

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 Alynham 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

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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 • <i>Nursing Clinics of North America</i> • PCNA • Skin, Bones, Hearts & Private Parts* • <i>The Journal for Nurse Practitioners</i> *	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 • ASPCT • 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* • <i>JAMA Cardiology</i> †	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

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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* • <i>World-views on Evidence-Based Nursing</i> (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 • <i>Stroke</i> * • <i>Stroke: Vascular and Interventional Neurology</i> • Translational Sciences†	None

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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

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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* • Pyramex • 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

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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
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† • <i>Circulation</i> • <i>Journal of Cardiac Failure</i> † • UpToDate American Heart Association	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	<i>Neurocritical Care</i> *	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.