VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING

Department of Veterans Affairs
Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 4.0 – 2020

Prepared by:

The Diagnosis and Management of Hypertension in the Primary Care Setting Work Group

With support from:

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&

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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the Health Executive Committee (HEC) "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with hypertension (HTN), thereby leading to improved clinical outcomes.

In 2014, the VA and DoD published a CPG for the Diagnosis and Management of Hypertension in the Primary Care Setting (2014 VA/DoD HTN CPG), which was based on evidence reviewed through April 2014. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of HTN. Consequently, a recommendation to update the 2020 VA/DoD HTN CPG was initiated in 2018. The updated 2020 VA/DoD HTN CPG includes objective, evidence-based information on the diagnosis and management of HTN. It is intended to assist healthcare providers in all aspects of patient care, including, but not limited to, screening, diagnosis, and management. The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being by guiding health providers who are caring for patients with HTN along management pathways that are supported by the evidence. The expected outcome of successful implementation of this guideline is to:

- Assess the individual's condition and determine the best treatment method, in collaboration with the patient
- Optimize health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care (PCC)

II. Background

This guideline, developed under the auspices of the VHA and the DoD pursuant to directives from the VA, is an update to the 2014 VA/DoD Clinical Practice Guideline for Diagnosis and Management of Hypertension in the Primary Care Setting.

The definition of HTN continues to evolve and an international consensus does not exist. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), published in 2003, defined HTN as a systolic blood pressure (SBP) ≥140 mm Hg or a diastolic blood pressure (DBP) ≥90 mm Hg. This definition was not changed in the 2014 Evidence Based Guideline for the Management of High Blood Pressure in Adults.[2] Prehypertension was classified as SBP 120-139 or DBP 80-89.[3] The 2017 American College of Cardiology/American Heart Association (ACC/AHA) defines HTN as an SBP ≥130 mm Hg, a DBP ≥80 mm Hg, or both.[4] Prehypertension was removed as a clinical term; however, elevated blood pressure was added and defined as an SBP of 120-129 with a DBP <80 mm Hg. For the purposes of this CPG, the Work Group, based on our review of the literature, defines HTN as an SBP ≥130 mm Hg, a DBP ≥90 mm Hg, or both, assuming proper measurement technique.

The reason for the evolution over time in the definition of HTN is because the evidence base supporting the benefits of treatment continue to change. While the relationship between systemic arterial pressure and cardiovascular morbidity or mortality appears to be linear above 115/75 mm Hg based on epidemiologic data, the evidence supporting benefit from treatment of elevated blood pressure starts at a higher threshold.[5] Kaplan and Victor suggests the definition of HTN should be the point at which the benefit of treatment of elevated blood pressure outweighs the risks and cost.[6] Treatment of HTN has long been associated with benefit, but this treatment benefit has not been proven for lowering slightly elevated blood pressures to a "normal" blood pressure of 115/75 mm Hg. In this CPG, the Work Group specifically investigated the point of proven benefit for HTN treatment (see Recommendation 9); based on this evidence, the Work Group defines HTN as SBP and/or DBP at or above 130/90 mm Hg, assuming proper measurement technique. For those with a blood pressure above "normal" but not in the hypertensive range, there is no evidence to date that there is a benefit from treatment; however, their cardiovascular risk remains elevated.

HTN is described as either primary or secondary HTN. Primary, or essential, HTN accounts for about 95% of cases and is a heterogeneous disorder in which different causal factors, including genetic predisposition, central adiposity, sedentary lifestyle, and dietary choices, can lead to high blood pressure.[7] Secondary HTN is high blood pressure that results from an underlying and identifiable cause.[8] Main causes of secondary HTN include adverse effects (AEs) of medications (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], corticosteroids, decongestants, hormonal contraception, erythropoietin, amphetamines – prescription or illicit) or illegal drugs, renovascular disease, chronic kidney disease (CKD), obstructive sleep apnea (OSA), hyperaldosteronism, pheochromocytoma, aortic coarctation, and others.

Complications of HTN include damage to the large arteries (macrovascular complications) that can lead to stroke, myocardial infarction (MI), or peripheral arterial disease, as well as damage to the smaller arteries (microvascular complications) that can lead to CKD, lacunar infarcts, multi-infarct dementia, or

retinopathy. In addition to these arterial complications, HTN itself can lead to cardiac complications including diastolic dysfunction, left ventricular hypertrophy (LVH) and chronic heart failure (CHF) with preserved or reduced ejection fraction. Treatment of HTN reduces the risk of these complications.

A. Epidemiology and Impact in the General Population

Blood pressure is a continuous variable that increases with advancing age similar to the increase in associated comorbid conditions like coronary artery disease, heart failure, stroke, peripheral vascular disease, and CKD.[5] This hypertensive risk is elevated in persons with diabetes and/or CKD. Over 66% of both men and women 65 years of age and over have HTN compared to <15% of men and women between 20 and 44 years of age.[9] HTN is more common in older adults; in 2016, a higher percentage of men 20-44 versus >64 years old (33% versus 16%) were unaware they had HTN. The asymptomatic nature of HTN can lead to challenges with detection; therefore, routine screening is important in order to diagnose the condition. Also, the asymptomatic nature of HTN can lead to challenges with adherence to treatment. In African Americans, HTN develops at a younger age and may present with a higher prevalence of complications at the time of diagnosis, including stroke and end-stage kidney disease, when compared with other ethnic groups.[10]

The definition of HTN has evolved over the past five decades as clinical trials have progressively lowered the level of blood pressure at which the benefits of treatment outweigh the risks. Based on National Health and Nutrition Examination Survey (NHANES) data from 9,623 participants studied between 2011 and 2014, it is estimated that 72 million (or about one in three adult Americans) have HTN using the definition of SBP ≥140 and DBP ≥90 mm Hg published in the JNC 7 guidelines in 2003.[3,11] By the eighth decade of life, over 75% meet the aforementioned criteria, most commonly based on systolic elevation. In 2017, the AHA/ACC high blood pressure guideline recommended that the definition of HTN be lowered to 130/80 mm Hg or higher based on new clinical trial evidence of cardiovascular benefit from treatment to lower targets.[11] The implication of this recommendation is that an additional 14% of the adult United States (U.S.) population (or 31 million Americans) now meet the blood pressure criteria for HTN.[4]

B. Hypertension in the Department of Defense and the Department of Veterans Affairs Populations

Estimates of HTN prevalence among active duty military are limited and undoubtedly skewed by policies that exclude recruitment of individuals who already have cardiovascular risk factors such as HTN, obesity, and diabetes. However, it was reported in 2008 that 13% of active duty military had HTN,[12] similar to the percentage in the general population 20-44 years of age.[9] As in the civilian population, increased age, increased body mass index (BMI), male sex, and African American race were all independently associated with HTN. Compared to active duty military not deployed, exposure to multiple stressful deployments was also associated with a new diagnosis of HTN.[13] In the first study to directly compare cardiovascular health metrics of active duty Army men and women with those of NHANES participants evaluated between 2011 and 2012, NHANES participants had a higher prevalence of ideal blood pressure defined as <120/80 mm Hg (46% versus 27% for men, 63% versus 52% for women) compared to active duty Army personnel, even though NHANES participants were considerably older than the Army personnel (only 50% of NHANES participants <40 years old versus 86% of Army personnel <40 years old).[14]

The prevalence of HTN among Veterans was 37% in 2011.[15] Although more recently published data on prevalence of HTN among Veterans is lacking, this prevalence is lower than the 46% reported for the U.S. general population, which was based on data accumulated between 2013 and 2016.[16] The reported blood pressure control rate, based on a treatment goal of <140/90 mm Hg, was 76.3% in 2010, which shows that blood pressure control among Veterans is better than that reported in the general population.[9]

This CPG on the management of HTN in the primary care setting is intended to promote evidence-based management of HTN and thereby improve patients' clinical outcomes. It can assist primary care providers in the screening and diagnosis of HTN, determination of appropriate treatment, and delivery of individualized interventions. Although it was developed for a broad range of clinical settings, it should be applied with enough flexibility to accommodate local practice and individual situations.

III. About this Clinical Practice Guideline

This updated guideline represents a significant effort toward improving the screening, diagnosis, and management of HTN among patients who are eligible to receive care in the VA and/or DoD healthcare systems. As with other CPGs, however, challenges remain. These include evidence gaps, as well as ongoing needs to develop effective strategies for guideline implementation and to evaluate the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD healthcare primary care practitioners including physicians, nurse practitioners, physician assistants, nurses, dietitians, pharmacists, social workers, and others involved in the team caring for patients with HTN. Additionally, this guideline is intended for those in community practice involved in the care of Service Members or Veterans with HTN.

As elaborated in the qualifying statement on page one, this CPG is not intended to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. This CPG is based on information available through March 25, 2019 and is intended to provide a general guide to best practices. The guideline can assist care providers, but the use of a CPG must always be considered as a recommendation within the context of a variety of factors such as providers' clinical judgment, patient values and preferences, state and federal legal statutes, ethical guidelines, professional standards, and healthcare system policies.

A. Methods

The current document is an update to the 2014 VA/DoD HTN CPG. The methodology used in developing the 2020 VA/DoD HTN CPG follows the *Guideline for Guidelines*, an internal document of the VA and DoD EBPWG that was updated in January 2019.[17] The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts (SMEs) from within the VA and DoD (known as the Work Group) and the development and submission of an updated HTN CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by primary care

providers within the VA/DoD healthcare systems as well as those within the community who treat individuals within the VA and DoD. Specifically, the Champions and Work Group members for this guideline were responsible for identifying the key questions (KQs) of the most clinical relevance, importance, and interest for the diagnosis and management of patients with HTN. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified four clinical leaders, William Cushman, MD and Dan Berlowitz, MD, MPH from the VA and CDR Travis E. Harrell, MD, FACC, FACP and CDR Mark P. Tschanz, DO, MACM, FACP from the DoD, as Champions for the 2020 VA/DoD HTN CPG.

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI Institute, Sigma Health Consulting, and Anjali Jain Research & Consulting, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The first conference call was held in October 2018, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review (SR) about the diagnosis and management of HTN. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of HTN, from which Work Group members were recruited. The specialties and clinical areas of interest included: internal medicine, family medicine, nephrology, cardiology, nutrition, nursing, and pharmacy.

The guideline development process for the 2020 VA/DoD HTN CPG update consisted of the following steps:

1. Formulating and prioritizing KQs and defining critical outcomes
2. Convening a patient focus group
3. Conducting the systematic evidence review
4. Convening a face-to-face meeting with the CPG Champions and Work Group members to develop recommendations
5. Drafting and submitting a final CPG on the management of HTN to the VA/DoD EBPWG

Appendix A provides a detailed description of each of these tasks.

a. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a strength for each

recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[18]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

Additional information regarding these domains can be found in Appendix A.

Using these four domains, the Work Group determined the relative strength of each recommendation ("Strong" or "Weak"). Generally, a "Strong" recommendation indicates a high confidence in the quality of the available scientific evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient or provider values and preferences, and understood influence of other implications (e.g., resource use, feasibility). Generally, if the Work Group has less confidence after the assessment across these domains and believes that additional evidence may change the recommendation, it assigns a "Weak" recommendation. It is important to note that the GRADE terminology used to indicate the assessment across the four domains (i.e., "Strong" versus "Weak") should not be confused with the clinical importance of the recommendation. A "Weak" recommendation may still be important to the clinical care of a patient with HTN.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met the evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The grade of each recommendation made in the 2020 VA/DoD HTN CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in Appendix A.

b. Reconciling 2014 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence or as scheduled and subject to time-based expirations.[19] For example, the U.S. Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[20]

The HTN CPG Work Group largely focused on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Work Group considered, without complete review of the relevant evidence, the current applicability of other recommendations that were included in the 2014 VA/DoD HTN CPG, subject to evolving practice in today's environment.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[21,22] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories considered whether or not the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current care environment and within the scope of the CPG. Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The categories for the recommendations included in the 2020 version of the guideline can be found in the section on Recommendations. The categories for the recommendations carried forward from the 2014 VA/DoD HTN CPG are noted in Appendix D.

c. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business days.

The peer reviewers comprised individuals working within the VA and DoD healthcare systems as well as experts from relevant outside organizations designated by the Work Group members. Organizations that were designated by the Work Group to participate in the peer review and provided feedback included the following:

- American Association of Nurse Practitioners
- Mayo Clinic
- Scripps Clinic
- Tulane University of Medicine

The VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were made in accordance with the evidence.

B. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values of those most affected by the recommendations: patients. Patients bring perspectives, values, and preferences into their healthcare experience that can vary from those of clinicians. These differences can affect decision making in various situations and should be highlighted and made explicit due to their potential to influence a recommendation's implementation.[23,24] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the HTN CPG Work Group, held a patient focus group. The patient focus group was held on January 23, 2019 at the Naval Medical Center in San Diego, CA. The aim of the focus group was to further understand and incorporate the perspective of patients with HTN and who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus group lasted for approximately three hours and delved into the patients' perspectives on a set of topics related to their HTN management, including their priorities, the challenges they have experienced, the information they received regarding their care, and the impacts of their care on their lives.

The focus group comprised a convenience sample, and the Work Group recognizes the lack of generalizability and other limitations inherent in the small sample size. A total of three patients and one caregiver were included in the focus group to be consistent with the requirements of the Federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample included in this focus group is not representative of all patients within the VA and DoD healthcare systems. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to HTN management in the VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus groups. These limitations, as well as others, were considered during guideline development as the information collected from the discussion was being used. Recruitment for participation in the focus groups was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facilities at which the focus groups took place.

The following ideas and suggestions about aspects of care that are important to patients with HTN emerged as recurring themes during the discussions (Table 1). These concepts were important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives. Additional details regarding the patient focus group methods and findings can be found in Appendix B.

Table 1. Hypertension CPG Focus Group Concepts

Patient Focus Group Themes
A. Provide comprehensive information and education to patients regarding their condition, management strategies, and self-management, including expanding available information on complementary and alternative therapies.
B. Improve the method of measuring blood pressure in the office.
C. Education around home monitoring devices and strategies for measurement and management, including frequency of measurement, is important.
D. Improve communication between providers and patients, considering patient preferences regarding frequency of communication and mode of communication.
E. All patients understood the importance of lifestyle modifications to lower their blood pressure.

C. Conflicts of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in the past 24 months. The project team followed the guidance on COI management from the VA/DoD EBPWG. Verbal affirmations of no COI were used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., Centers for Medicare and Medicaid Services [CMS] open payments or ProPublica).

If a project team member reported a COI (actual or potential), then it was reported to the VA and DoD program offices. It was also discussed with the HTN CPG Champions in tandem with their review of the evidence and development of recommendations. The VA and DoD program offices and the HTN CPG Champions determined whether or not action, such as restricting participation or voting on sections related to the conflict or removal from the Work Group, was necessary. If it was deemed necessary, action to mitigate the COI was taken by the Champions and VA and DoD program offices, based on the level and extent of involvement. No COIs were identified for the HTN CPG Work Group members or Champions. Disclosure forms are on file with the VA Office of Quality, Safety and Value and available upon request.

D. Scope of this Clinical Practice Guideline

Regardless of setting, any patient in the VA and DoD healthcare systems should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to be patient centered. Thus, treatment and care should consider a patient's needs and preferences. Effective, open communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. Use of an empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnic, and other considerations. The information that patients are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. Treatment information should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family and caregiver involvement should be considered, if appropriate.

This CPG is designed to assist in managing or co-managing patients with HTN. Moreover, the patient population of interest for this CPG is patients with HTN who are eligible for care in the VA and DoD

healthcare delivery systems and those who are in the community receiving care from community-based clinicians. It includes Veterans as well as deployed and non-deployed active duty Service, Guard, and Reserve Members and their dependents.

E. Highlighted Features of this Clinical Practice Guideline

The 2020 edition of the VA/DoD HTN CPG is the third update to the original CPG. It provides practice recommendations for the care of individuals with HTN as well as guidance for treatment. A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians engaged in the diagnosis and management of HTN.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of the intervention, the potential for variation in patient values and preferences, and other considerations (e.g., resource use, subgroup considerations) as appropriate. Applicability of the evidence to VA/DoD populations was also taken into consideration. An algorithm accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and to assist with training providers (see Algorithm section). The algorithm may be used to help facilitate translation of guideline recommendations into practice.

F. Patient-centered Care

VA/DoD CPGs encourage providers to use a PCC approach that is individualized based on patient needs, characteristics, and preferences. Regardless of setting, all patients in the healthcare system should be able to access evidence-based care appropriate to their specific needs or condition. When properly executed, PCC may decrease patient anxiety, increase trust in clinicians, and improve treatment adherence.[25,26] Improved patient-clinician communication and a PCC approach conveys openness and supports disclosure of current and future concerns. As part of the PCC approach, providers should ask each patient about any concerns he or she has or barriers to high quality care he or she has experienced.

G. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on shared decision making (SDM). The SDM model was introduced in *Crossing the Quality Chasm*, an Institute of Medicine (IOM) (now called the National Academy of Medicine [NAM]) report, in 2001.[27] It is readily apparent that patients, together with their clinicians, make decisions regarding their plan of care and management options. Patients with HTN require sufficient information and time to be able to make informed decisions. Clinicians must be adept at presenting information to their patients regarding treatments, expected outcomes, and levels and/or locations of care. Clinicians are encouraged to use SDM to individualize treatment goals and plans based on patient capabilities, needs, goals, and preferences.

H. Co-occurring Conditions

Co-occurring health conditions are important to recognize because they can modify the degree of risk and trajectory of an individual's lifestyle, impact the diagnosis and management of HTN, influence patient or provider treatment priorities and clinical decisions, and affect the overall provider approach to the management of HTN. Providers should expect that many Veterans, Service Members, and their families will have one or more co-occurring health conditions. Because of the nature of HTN management, which sometimes takes place in parallel with ongoing care for co-occurring conditions, it is often best to manage

HTN collaboratively with other care providers. Some co-occurring conditions may require early specialist consultation in order to discuss any necessary changes in treatment or to establish a common understanding of how care will be coordinated and delivered. VA/DoD CPGs exist for CKD,[1] diabetes,[2] obesity and overweight,[3] and pregnancy.[4]

I. Implementation

This CPG and algorithm are designed to be adapted by individual healthcare providers with consideration of local needs and resources. The algorithms serve as tools to prompt providers to consider key decision points during an episode of care.

Although this CPG represents the recommended practices on the date of its publication, medical practice is evolving and requires ongoing awareness by providers of newly published information. New technology and additional research will improve patient care in the future. The CPG can assist in identifying priority areas for research and informing optimal allocation of resources. Future studies examining the results of CPG implementation may lead to the development of new evidence particularly relevant to clinical practice.

[1] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

[2] See the VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/CD/diabetes/

[3] See the VA/DoD Clinical Practice Guideline for Screening and Management of Obesity and Overweight. Available at: https://www.healthquality.va.gov/guidelines/CD/obesity/

[4] See the VA/DoD Clinical Practice Guideline for the Management of Pregnancy. Available at: https://www.healthquality.va.gov/guidelines/WH/up/

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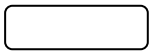
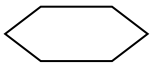
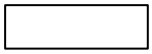
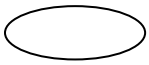
V. Algorithm

This CPG includes an algorithm that is designed to facilitate understanding of the clinical pathways and decision-making processes used in managing patients with HTN. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making; it also has potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted through the algorithm and its format allows the provider to assess the critical information needed at the major decision points in the clinical process. It includes:

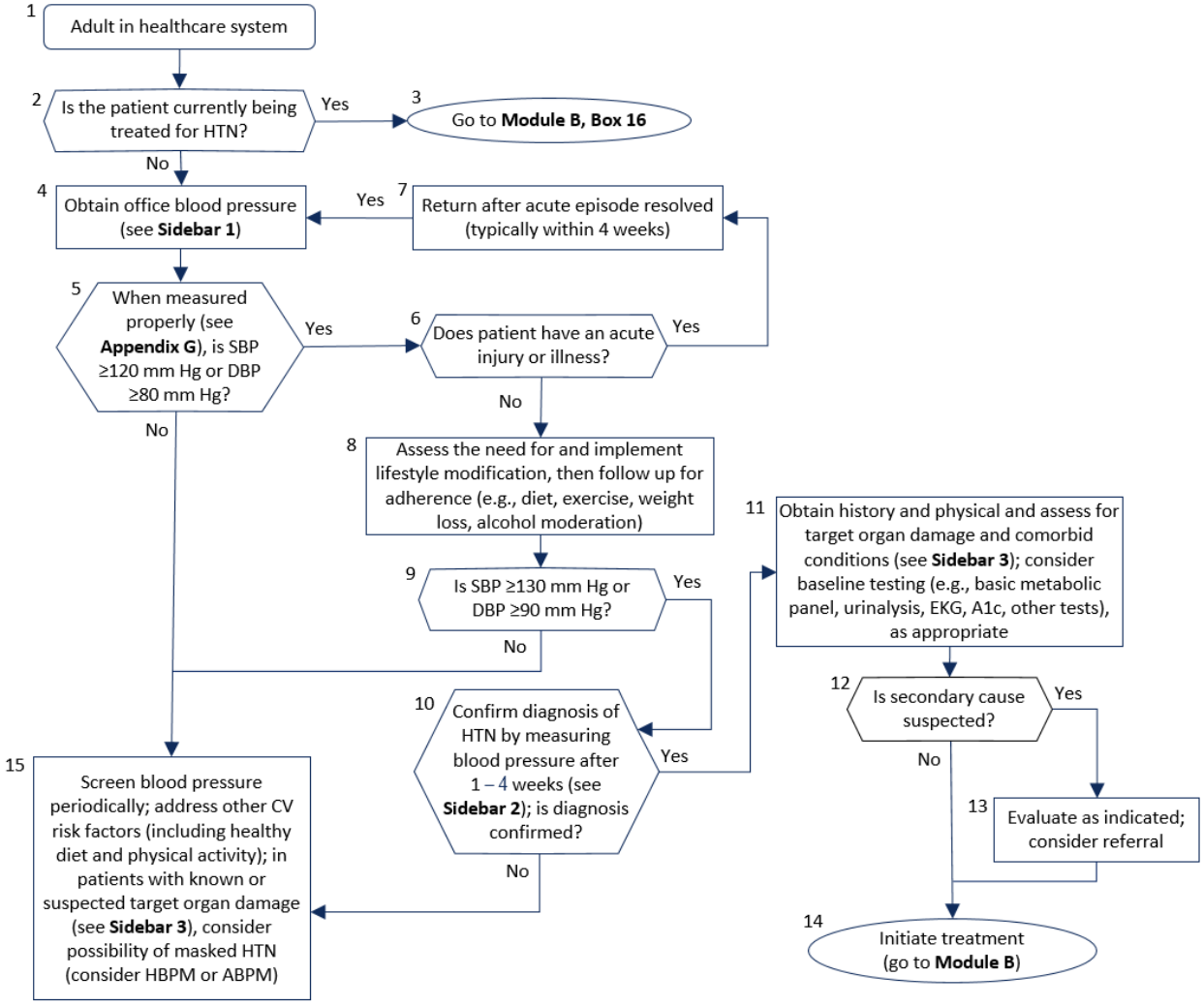
- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each VA/DoD CPG, there is a corresponding clinical algorithm that is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[28]

Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the guideline

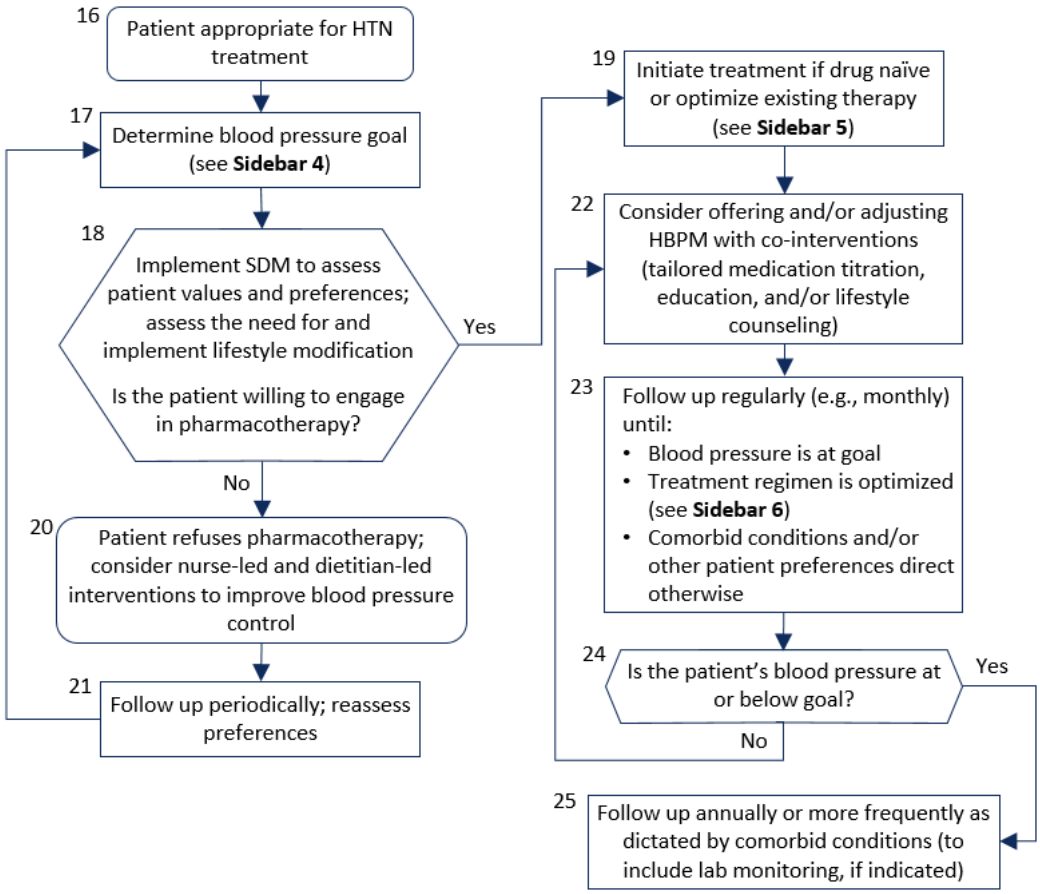
Appendix K contains alternative text descriptions of Module A and Module B.

A. Module A: Screening and Diagnosis



Abbreviations: ABPM: ambulatory blood pressure monitoring; CV: cardiovascular; DBP: diastolic blood pressure; EKG: electrocardiogram; HBPM: home blood pressure monitoring; HTN: hypertension; SBP: systolic blood pressure

B. Module B: Treatment



Abbreviations: HBPM: home blood pressure monitoring; HTN: hypertension; SDM: shared decision making

Sidebar 1: Office Blood Pressure Measurement

See Appendix G of the full HTN CPG for appropriate blood pressure cuff selection, patient preparation, and proper technique

AOBP (preferred)

- Fully automated machine programmed to wait five minutes and record the average of three measurements separated by at least 30 seconds

Standard Technique (alternative)

- Use a properly calibrated and validated sphygmomanometer
- Use an average of ≥2 readings

Abbreviations: AOBP: automated office blood pressure; CPG: clinical practice guideline; HTN: hypertension

Sidebar 2: Confirm Diagnosis

- If the follow-up clinic blood pressure value is ≥130 mm Hg SBP or ≥90 mm Hg DBP, make diagnosis of HTN without further testing
- Consider HBPM or ABPM to inform the diagnosis in select patients (see Recommendation 4)
- If blood pressure is <130 mm Hg SBP and <90 mm Hg DBP, yet there is evidence of target organ damage, which may suggest the presence of masked HTN, consider HBPM or ABPM to inform the diagnosis (see Recommendation 4)

Abbreviations: ABPM: ambulatory blood pressure monitoring; DBP: diastolic blood pressure; HBPM: home blood pressure monitoring; HTN: hypertension; SBP: systolic blood pressure

Sidebar 3: Examples of Target Organ Damage and Comorbid Conditions*

- Target organ damage: stroke, MI, peripheral arterial diseases, LVH, CHF, CKD, and retinopathy
- Comorbid conditions: CKD, dyslipidemia, diabetes, obesity/overweight, OSA, and tobacco dependence

*If patient has comorbid conditions, engage relevant VA/DoD CPGs, when available (e.g., CKD[5], lipids[6], diabetes[7], obesity[8])

Abbreviations: CHF: chronic heart failure; CKD: chronic kidney disease; CPGs: clinical practice guidelines; LVH: left ventricular hypertrophy; MI: myocardial infarction; OSA: obstructive sleep apnea

Sidebar 4: Goals for Blood Pressure

Systolic Goal (see Recommendations 6 – 8)

<130 mm Hg

- If less stringent goal is desired per clinical judgment and/or patient preferences, aim for at least:
  - <150 mm Hg for patients age 60 and over
  - <140 mm Hg for patients age 60 and over with type 2 diabetes

Diastolic Goal (see Recommendation 9)

<90 mm Hg for patients age 30 and over

[5] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

[6] See the VA/DoD Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction. Available at: https://www.healthquality.va.gov/guidelines/CD/lipids/

[7] See the VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care. Available at: https://www.healthquality.va.gov/guidelines/CD/diabetes/

[8] See the VA/DoD Clinical Practice Guideline for Screening and Management of Obesity and Overweight. Available at: https://www.healthquality.va.gov/guidelines/CD/obesity/

Sidebar 5: Initiate Drug Therapy

General Population:

- Recommend one or more of the following:
  - Thiazide-type diuretics
  - ACEIs or ARBs*
  - Long-acting CCBs
- For patients unlikely to achieve goal with monotherapy (e.g., patients with SBP/DBP of >20/10 mm Hg above goal), consider initiating treatment with combination therapy or monotherapy with close follow-up for titration and/or addition of medications based on blood pressure response

Specific Populations:

- For patients age 65 and over, we suggest a thiazide-type diuretic for reduction in composite cardiovascular outcomes
- For African American patients, we recommend against using ACEIs or ARBs as monotherapy
- For patients with CKD, see the VA/DoD CKD CPG[9]

*We recommend against more than one of the following three drug classes together in the same patient: ACEIs, ARBs, or direct renin inhibitors

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; CCB: calcium channel blocker; CKD: chronic kidney disease; CPG: clinical practice guideline

Sidebar 6: Optimize Treatment

- Assess adherence
- Consider evaluating for interfering substances (some prescription medications, NSAIDs, alcohol, recreational drugs)
- Consider evaluating and addressing contributing lifestyle factors
- Optimize treatment (refer to Appendix F, Table F-1)
  - Titrate initial drug
  - Add another agent from a different class
- Reevaluate diagnosis (resistant HTN, secondary causes of HTN)
- Consider specialty consultation for patients with resistant HTN
- Consider co-interventions to enhance management of HTN and improve blood pressure:
  - Pharmacist-led
  - Nurse-led
  - Dietitian-led

Abbreviations: HTN: hypertension; NSAIDs: nonsteroidal anti-inflammatory drugs

[9] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

VII. Recommendations

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Screening, Diagnosis, and Monitoring	*a. Screening*	1.	We recommend screening adults for elevated blood pressure periodically.	Strong for	Not Reviewed, Amended
	b. Measurement Techniques	2.	We suggest using attended or unattended, fully automated office blood pressure measurement (programmed to wait five minutes and record the average of three measurements separated by at least 30 seconds).	Weak for	Reviewed, New-added
		3.	When fully automated blood pressure measurement is not available, we suggest measurement of blood pressure using standard technique and a properly calibrated and validated sphygmomanometer.	Weak for	Reviewed, New-replaced
		4.	We suggest using out-of-office blood pressure monitoring methods (ambulatory 24-hour monitoring or home blood pressure measurements) to inform the diagnosis and management of hypertension.	Weak for	Reviewed, New-replaced
	c. Monitoring	5.	Among patients treated for hypertension, we suggest offering home blood pressure self-monitoring with co-interventions for lowering systolic and diastolic blood pressure.	Weak for	Reviewed, New-added
Treatment Goals and General Approaches to Hypertension Management	*a. Blood Pressure Goals*	6.	For all patients, including those with type 2 diabetes, we suggest treating to a systolic blood pressure goal of <130 mm Hg.	Weak for	Reviewed, New-added
		7.	For patients 60 years and over, we recommend treating to a systolic blood pressure goal of <150 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 150 mm Hg.	Strong for	Reviewed, Amended
		8.	For patients 60 years and over with type 2 diabetes, we recommend treating to a systolic blood pressure goal of <140 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 140 mm Hg.	Strong for	Reviewed, Amended
		9.	For patients 30 years and over, we recommend treating to a diastolic blood pressure goal of <90 mm Hg.	Strong for	Reviewed, Amended

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment Goals and General Approaches to Hypertension Management (cont.)	***b. General Approaches to HTN Management***	10.	We recommend offering pharmacist-led medication management as an option for patients with hypertension.	Strong for	Reviewed, New-replaced
		11.	We suggest offering nurse-led interventions as an option for patients treated for hypertension.	Weak for	Reviewed, New-replaced
		12.	We suggest offering registered dietitian-led nutrition interventions as an option for patients with hypertension who are or are not on medication.	Weak for	Reviewed, New-replaced
		13.	We suggest technology-based interventions (e.g., e-counseling, electronic transmission of data, telemonitoring, mobile applications) for improving control of hypertension.	Weak for	Reviewed, New-replaced
Non-Pharmacological Treatment	***a. Weight Reduction***	14.	We suggest advising patients with hypertension and overweight/obesity to lose weight to improve blood pressure.	Weak for	Reviewed, Amended
		15.	For patients with hypertension and overweight/obesity, we suggest offering a diet directed at weight loss for the treatment of hypertension.	Weak for	Reviewed, New-added
		16.	For the treatment of hypertension, there is insufficient evidence for or against offering weight loss medications for patients with obesity and hypertension.	Neither for nor against	Reviewed, New-added
		17.	For the treatment of hypertension, there is insufficient evidence to suggest for or against bariatric surgery for patients with obesity and hypertension.	Neither for nor against	Reviewed, New-added
	b. Exercise/ Physical Activity	18.	We suggest offering individual or group-based exercise for the treatment of hypertension to reduce blood pressure.	Weak for	Reviewed, Amended
		19.	We recommend a target for aerobic exercise of at least 120 minutes per week for reduction in blood pressure.	Strong for	Not Reviewed, Amended
	c. Dietary Modifications	20.	We recommend a dietitian-led Dietary Approaches to Stop Hypertension Diet for the treatment or prevention of hypertension for patients with hypertension or interested patients with other cardiovascular risk factors.	Strong for	Not Reviewed, Amended
		21.	In patients with hypertension, we recommend that sodium intake be limited to no more than 2,300 mg/day (100 mmol/day), with referral to a dietitian or other support as appropriate.	Strong for	Not Reviewed, Not Changed
		22.	In patients with additional cardiovascular risk factors, such as dyslipidemia, we suggest considering a dietitian-led Mediterranean Diet as an alternative to the Dietary Approaches to Stop Hypertension Diet.	Weak for	Not Reviewed, Not Changed

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Pharmacological Treatment	*a. For Hypertension*	23.	We recommend offering a thiazide-type diuretic, calcium channel blocker, or either an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker as primary pharmacologic therapy for hypertension for reduction in composite cardiovascular outcomes.	Strong for	Reviewed, New-replaced
		24.	In African American patients with hypertension, we recommend against using an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker as monotherapy.	Strong against	Not Reviewed, Not Changed
		25.	In hypertensive patients 65 years and over, we suggest a thiazide-type diuretic for reduction in composite cardiovascular outcomes.	Weak for	Reviewed, New-added
		26.	We recommend against more than one of the following three drug classes together in the same patient: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or direct renin inhibitors.	Strong against	Not Reviewed, Not Changed
		27.	For the treatment of hypertension, there is insufficient evidence to recommend for or against initiating combination therapy over initiating monotherapy with the sequential addition of another medication.	Neither for nor against	Reviewed, New-replaced
	b. For Resistant Hypertension	28.	For patients with resistant hypertension (defined as those who are not adequately controlled with maximally tolerated dose of triple therapy [i.e., a thiazide-type diuretic, calcium channel blockers, and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker]), we suggest adding spironolactone in those patients without contraindications.	Weak for	Reviewed, New-replaced

[a] For additional information, please refer to Grading Recommendations.

[b] For additional information, please refer to Recommendation Categorization and Appendix D.

A. Screening, Diagnosis, and Monitoring

a. Screening

Recommendation

1. We recommend screening adults for elevated blood pressure periodically.
   (Strong for | Not Reviewed, Amended)

Discussion

A 2007 review of the evidence for the USPSTF describes the rationale for blood pressure screening.[29] Based on their review, the USPSTF concluded that the benefits of blood pressure screening far outweigh any risks. The risk for cardiovascular events and the potential benefit from screening and subsequent treatment of HTN depend on both the degree and duration of blood pressure elevation and the presence of other cardiovascular risk factors, such as age, gender, lipid disorders, smoking, and diabetes. Because the degree and duration of blood pressure elevation are unknown before screening, selective screening to identify individuals who would benefit most from detection and treatment of HTN would need to target individuals with other cardiovascular risk factors. The 2015 update from the USPSTF concluded that, given the strong evidence base for the previous recommendations, the indirect evidence path for HTN screening did not need updating.[30]

For patients who are screened, estimates of the potential benefit of treatment can be improved both by carefully measuring the degree of blood pressure elevation and by assessing the contribution of other risk factors to global cardiovascular risk.[31-33] Since increasing age is related to greater incidence of HTN, and because lifetime risk of developing HTN is so high (reaching approximately 90% for octogenarians), it is sensible to screen periodically.[34]

Multiple separate guidelines make recommendations for rescreening intervals, but none are evidence based. Although not included in the systematic evidence review conducted as part of this guideline update, and thus not considered in determining the strength of recommendation, a 2015 SR by the USPSTF identified 40 studies addressing rescreening interval and hypertensive incidence in screened normotensive persons (defined as blood pressure <140/90 mm Hg using office blood pressure measurements).[35] There were highly variable estimates of incident HTN ranging from 2.2-4.4% at one-year interval and 2.1-28.4% at five-year intervals. This confirms the recommendation that there is value to screening normotensive adults, but the evidence remains unclear as to what the optimal interval should be.

As this is a *Not Reviewed, Amended* recommendation, the Work Group did not systematically review evidence related to this recommendation. Based on the assessment of the quality of the evidence put forth in the 2014 VA/DoD HTN CPG,[29,31-34] the Work Group's confidence in the quality of the evidence is moderate. The body of evidence had some limitations including different treatment goals/targets and confounders in the analysis. Other considerations regarding this recommendation included the benefits, including improved outcomes in cardiovascular events and mortality, outweighing the potential harm of adverse events (e.g., false positive screening, missed diagnosis), which was small. Patient values and preferences were similar, as blood pressure screening is a routine part of almost all outpatient medical care. Thus, the Work Group decided that a "Strong for" recommendation was warranted.

More research is needed on the best screening method for HTN as well as the best interval between screenings in both the general population and those at-risk for HTN.

b. Measurement Techniques

Recommendation

2. We suggest using attended or unattended, fully automated office blood pressure measurement (programmed to wait five minutes and record the average of three measurements separated by at least 30 seconds).
   (Weak for | Reviewed, New-added)

3. When fully automated blood pressure measurement is not available, we suggest measurement of blood pressure using standard technique and a properly calibrated and validated sphygmomanometer.
   (Weak for | Reviewed, New-replaced)

Discussion

The diagnosis and management of HTN has been based primarily on measurement of blood pressure in a medical clinic or office. Office measurements were used by most observational studies and all randomized controlled trials (RCTs) defining both the risk of various blood pressure levels and the goal blood pressures that have reduced cardiovascular outcomes or mortality. To obtain the values most representative of the patient's office blood pressure, evidence supports that at least two readings be taken on each of two occasions, at least one day apart. Blood pressure was measured by standard technique in all critical studies that have been used to develop recommendations for both the blood pressure levels at which to begin drug treatment as well as the blood pressure goals of treatment. Therefore, in order to make appropriate decisions in clinical practice, blood pressure should be measured with a properly calibrated and validated sphygmomanometer and with a standard technique similar to what has been used in studies.[36] Older studies used manual blood pressure determinations, such as with a mercury sphygmomanometer, while more recent studies have used fully automated oscillometric sphygmomanometers. A fully automated oscillometric manometer can be set to wait a specified rest time and take an average of several blood pressure readings with one activation. A semi-automated oscillometric device takes a single reading without a rest period after activation.

SRs and meta-analyses have reported that blood pressure readings were similar when comparing fully automated oscillometric sphygmomanometer with daytime average ambulatory blood pressure readings, but routine office readings without standard technique averaged 7.0 to 14.5 mm Hg higher than fully automated readings.[37,38] In one SR, SBP readings using research quality manual or oscillometric technique averaged 7 mm Hg higher than fully automated oscillometric technique; however, in the one study included in the SR in which the order was randomized, there was very little difference between these two techniques, suggesting the others may have been biased by regression to the mean.[38] In addition, another SR/meta-analysis concluded that, when fully automated oscillometric readings were obtained, there was not a significant difference in blood pressure levels when an observer was in the room (attended) or the patient was alone in the room (unattended).[39]

As a good summary of standard measurement technique used in research studies, the 2019 AHA recommendations for blood pressure measurement include the following key steps about proper seated blood pressure measurement in the office (adapted).[36]

Table 2. Key Steps for Proper Blood Pressure Measurements

Key Steps	Specific Instructions
Step 1: Properly prepare the patient	1. Have the patient relax, sitting in a chair with feet flat on floor and back supported. The patient should be seated for 3-5 min without talking or moving around before recording the first blood pressure reading. 2. The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement. 3. Ensure that the patient has emptied his/her bladder. 4. Neither the patient nor the observer should talk during the rest period or during the measurement. 5. Remove clothing covering the location of cuff placement. 6. Measurements made while the patient is sitting on an examining table do not fulfill these criteria.
Step 2: Use proper technique for blood pressure measurements	1. Use an upper-arm cuff blood pressure measurement device that has been validated and ensure that the device is calibrated periodically. 2. Support the patient's arm (e.g., resting on a desk) at heart level; the patient should not be holding his/her arm because isometric exercise will affect the blood pressure levels. 3. Position the middle of the cuff on the patient's upper arm at the level of the right atrium (midpoint of the sternum). 4. Use the correct cuff size such that the bladder encircles 75%-100% of the arm. 5. Use either the stethoscope diaphragm or bell for auscultatory readings.
Step 3: Take the proper measurements needed for diagnosis and treatment of elevated blood pressure/HTN	1. At the first visit, record blood pressure in both arms. Use the arm that gives the higher reading for subsequent readings (if consistently ≥10-15 mm Hg higher). 2. Separate repeated measurements by at least 30 seconds. 3. For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20-30 mm Hg above this level for an auscultatory determination of the blood pressure level.
Step 4: Properly document accurate blood pressure readings	1. Record SBP and DBP; if using the auscultatory technique, record SBP and DBP as the onset of the first of at least 2 consecutive beats and the last audible sound, respectively. 2. If using the auscultatory technique, record SBP and DBP to the nearest even number; if oscillometric, record reading displayed (or average displayed). 3. Note the time that the most recent blood pressure medication was taken before measurements.
Step 5: Average the readings	Use an average of ≥2 readings obtained on ≥2 occasions to estimate the patient's blood pressure. If fully automated oscillometric technique, manometer should display average of 2-3 readings.
Step 6: Provide blood pressure readings to patient	Provide the patient with his or her SBP/DBP readings both verbally and in writing. Assist the patient interpret the results.

Abbreviations: DBP: diastolic blood pressure; HTN: hypertension; SBP: systolic blood pressure

The 2019 AHA guidelines on measurement of blood pressure also provide a table of proper blood pressure cuff sizes.[36] Miscuffing can provide erroneous values.

Table 3. Proper Blood Pressure Cuff Sizes

Cuff Size	Arm Circumference (cm)	Bladder Dimension (width x length, cm)
Small adult	22-26	12×22
Adult	27-34	16×30
Large adult	35-44	16×36
Extra-large adult	45-52	16×42

Abbreviation: cm: centimeter

Although SRs and meta-analyses have reported the mean differences (MD) in intra-arterial compared with cuff blood pressure measurements and arm compared with leg blood pressure measurements, whenever possible, decisions concerning diagnosis and management of HTN should be made with brachial cuff determinations.[40,41] Previous evidence suggested that automated blood pressure monitors are accurate for SBP but not DBP measurement in the presence of atrial fibrillation. A recent SR and meta-analysis provided additional support by concluding that, although some monitors have been shown to be accurate with atrial fibrillation, there is considerable heterogeneity between devices, particularly for DBP measurement; accuracy for devices untested in atrial fibrillation cannot be assumed.[42]

Although standard blood pressure measurement technique in the office is critical to making correct decisions about the diagnosis and management of HTN, there is widespread failure to use proper technique in clinical practice settings.[43] The reasons for this include lack of knowledge of proper technique, lack of appreciation of the importance of many aspects of proper technique, and resistance to change, especially taking the extra time needed for quiet during the rest and measurement periods. There also may be resistance to incorporating fully automated blood pressure technique in practice, since it requires time not speaking with the patient and allowing for rest and several measurements (approximately seven to eight minutes on average when accounting for five minutes of rest and time to take measurements). The main concern is the time required for busy clinic staff to incorporate this technique. However, using automated office blood pressure (AOBP) allows staff to attend to other patients or tasks during this time.

In the patient focus group carried out as part of this guideline update, patients described the following (see Appendix B):

1. Patients noted that when their blood pressure was measured by machine in the office setting, they experienced pain and uncomfortable pressure.
2. Some of the patients noted that their blood pressure had to be taken twice when in the office setting, as the first reading was rarely accurate.
3. Patients felt the office blood pressure readings were inaccurate; they trusted the devices they use at home more.
4. There were noticeable differences between blood pressure readings when it was taken manually versus with a machine.

The Work Group believed these perspectives from patients generally support use of fully automated oscillometric manometers in clinical practice. Although there is some expense to fully automated oscillometric manometers and concern over pain of measurements, the Work Group believed these issues were minor compared with the benefits of reducing observer error and providing more accurate blood pressure data.

As Recommendations 2 and 3 are *Reviewed, New-added* and *Reviewed, New-replaced* recommendations, respectively, the Work Group systematically reviewed evidence related to these recommendations in the evidence review conducted as part of this guideline update.[37-42] The Work Group's confidence in the quality of the evidence is very low; however, standard blood pressure measurement technique was used in all major observational studies and RCTs which provide evidence for risk of blood pressure levels and goal blood pressure levels shown to reduce cardiovascular outcomes with treatment. Two SRs showed that fully automated blood pressure measurement accuracy is closer to daytime ambulatory blood pressure measurement accuracy but that "research quality" (i.e., "standard") measurement could also be acceptable.[37,38] Another SR showed that fully automated readings were similar whether staff were present in the room (attended) or the patient was left alone during the rest and measurements (unattended).[39] Other considerations regarding this recommendation included the benefits of accurate blood pressure data outweighing the potential harm of any adverse events or inconvenience, which was small. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" for these recommendations.

Recommendation

4. We suggest using out-of-office blood pressure monitoring methods (ambulatory 24-hour monitoring or home blood pressure measurements) to inform the diagnosis and management of hypertension.
   (Weak for |Reviewed, New-replaced)

Discussion

Out-of-office blood pressure monitoring methods comprise: (a) 24-hour and daytime/awake ambulatory blood pressure monitoring (ABPM) and (b) home blood pressure monitoring (HBPM). The 2014 VA/DoD HTN CPG included recommendations on ABPM and HBPM to assist in the diagnosis of HTN prior to initiation of drug therapy. The current recommendation is based on very low quality evidence from the 2014 VA/DoD HTN CPG literature review,[44-48] which found that ABPM and HBPM are better predictors of cardiovascular events compared with routine (not AOBP) office blood pressure measurements. However, ABPM and HBPM were not used as entry criteria or as treatment goals in cardiovascular outcome clinical trials. Moreover, with accumulating evidence that AOBP may be equivalent to ABPM and HBPM (see Recommendation 2 and the evidence in the next paragraph), the role of ABPM and HBPM may no longer be as important in confirming the diagnosis of HTN using out-of-office blood pressure measurements as was thought to be the case in 2014. Furthermore, because no studies comparing ABPM versus HBPM on clinical outcomes were identified in the present systematic evidence review, two separate recommendations on ABPM and HBPM from the 2014 VA/DoD HTN CPG were combined into a single "Weak for" recommendation.

Evidence from two SRs demonstrated that fully automated office blood pressure measurements were similar to SBP and DBP obtained with day-time/awake ABPM and HBPM. Pappaccogli et al. (2019) showed no significant difference for both SBP (-1.85 mm Hg) and DBP (0.12 mm Hg) in the pooled analysis of 16 studies comparing AOBP with daytime ABPM.[37] The same SR compared AOBP and HPBM using pooled data from seven studies and also found no statistically significant difference in SBP and DBP between the two methods. Similar findings from 19 studies were reported in another SR by Roerecke et al. (2019), which demonstrated a non-significant pooled mean difference in SBP of 0.3 mm Hg (95% CI -1.1 to 1.7 mm Hg) between AOBP and awake ABPM in patients who had an office SBP >130 mm Hg.[38] The Work Group did not find any evidence comparing the predictive value of AOBP versus out-of-office blood pressure on clinical outcomes.

Another key reason for the recommendation to preferentially use ABPM and HBPM in the 2014 VA/DoD HTN CPG was the ability of out-of-office blood pressure to assist in the identification of white coat and masked HTN in untreated individuals, as well as uncontrolled white coat and uncontrolled masked HTN in patients receiving antihypertensive medications. The 2014 VA/DoD HTN CPG, 2015 USPSTF,[20] and 2017 AHA/ACC [4] guidelines all recommended ruling out white coat HTN in individuals with newly diagnosed elevated office blood pressure to avoid unnecessary initiation of drug therapy. Since the evidence review and HTN outcome trials in general did not identify or exclude patients with white coat HTN as distinct from other forms of HTN, it is possible that white coat HTN is not a totally benign condition. Accordingly, it is unknown whether patients with white coat HTN benefit or do not benefit from treatment. Therefore, the Work Group concluded there was very low quality evidence supporting the utility of out-of-office blood pressure measurements in confirming diagnosis of HTN prior to the initiation of drug therapy. Nevertheless, ABPM and HBPM are valuable methods in identifying masked HTN, which is diagnosed with elevated out-of-office blood pressure in the setting of normal or controlled office blood pressure. Masked HTN should be suspected in individuals with normal or controlled office blood pressure if they report higher home blood pressure values, in the presence of target organ damage and certain chronic conditions, such as CKD. We did not find any evidence of harm associated with ABPM and HBPM; however, patient training is required for both methods, and there could be some differences in patient preferences due to increased burden of out-of-office blood pressure monitoring. Overall, the equipment used for HBPM is more readily available than for ABPM. Some patients may not be willing to wear a 24-hour ABPM on multiple occasions.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update [37,38] as well as the evidence from the 2014 VA/DoD HTN CPG.[44-48] The Work Group's confidence in the quality of the evidence is very low. The body of evidence had some limitations, such as observational study design, small sample sizes, selection and attrition bias in individual studies, and a lack of consistent reporting of blood pressure measurement methods. New considerations regarding this recommendation included evidence that AOBP provides similar blood pressure values as day-time ambulatory and home blood pressure, and that there are no outcome trials that have used out-of-office blood pressures as either entry criteria or as treatment goals. While we did not identify head-to-head comparison studies between HBPM and ABPM, both approaches seem to be of similar value for making a decision in patients in whom the diagnosis or control of HTN remains uncertain (e.g., when AOBP is not available, when there is significant discrepancy between self-monitored home blood pressure and office blood pressure, and if

masked HTN is suspected). HBPM is more readily available than ABPM and requires fewer resources; however, careful patient education on proper blood pressure measurement technique and the frequency and use of validated HBPM are recommended.

More research is needed to evaluate the effectiveness of using out-of-office blood pressure to manage HTN and whether treating to ABPM or HBPM guided blood pressure goals would improve cardiovascular morbidity and mortality in hypertensive individuals.

c. Monitoring

Recommendation

5. Among patients treated for hypertension, we suggest offering home blood pressure self-monitoring with co-interventions for lowering systolic and diastolic blood pressure. **(Weak for | Reviewed, New-added)**

Discussion

When compared with usual care, home blood pressure self-monitoring has been shown to improve SBP and DBP control when paired with a co-intervention. Our evidence review found two SRs of RCTs comparing blood pressure self-monitoring or HBPM with usual care.[49,50] One SR of 29 RCTs showed improved blood pressure control compared to usual care (adjusted MD in SBP 2.7 mm Hg).[49] Another SR and meta-analysis comparing blood pressure self-monitoring alone to usual care found that self-monitoring was not associated with lower blood pressure. However, when paired with co-interventions (including tailored medication titration and education or lifestyle counseling) blood pressure self-monitoring was associated with a lower blood pressure (MD in SBP -6.1 mm Hg).[50]

Three additional RCTs had results consistent with the SRs, finding self-monitoring more effective than usual care when accompanied by a co-intervention involving medication titration in response to self-monitoring data.[51-53] Studies in which medication adherence was examined revealed no difference in medication adherence between self-monitoring of blood pressure and usual care.

Despite general consistency in the evidence supporting home blood pressure monitoring and self-monitoring and ease of implementation, there is some variability in provider and patient preferences regarding this treatment. There was some question among the Work Group members whether a 2-4 mm Hg reduction in blood pressure was clinically significant. Some patient focus group participants expressed a desire for additional education on the use of home blood pressure management and additional interventions that they could institute on their own. However, some patients may not want the extra burden of monitoring their own blood pressure at home. Other considerations include the added cost of a home blood pressure monitor if not provided by the institution, patients in whom HBPM is not feasible, and the additional time patients would have to devote to the co-intervention. An informational video for patients on how to use a home blood pressure monitor is available on the VA/DoD Clinical Practice Guidelines page.[10]

[10] Home blood pressure monitoring video is available on the VA/DoD Clinical Practice Guidelines page at https://www.healthquality.va.gov/guidelines/cd/htn/index.asp; or directly at https://www.youtube.com/watch?v=IHY5MJc4Z_M&feature=youtu.be.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[49-53] The Work Group's confidence in the quality of the evidence is very low due to the subjective outcome assessment, incomplete outcome data, selective reporting, lack of blinding, and recruitment bias. The body of evidence had some limitations including confounders in the analysis.[49-51,53] Other considerations regarding this recommendation included the benefits of improved blood pressure and increased participation in care, which outweigh the potential harms (none identified). Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

More research is needed on the specific co-intervention paired with HBPM to identify the most effective intervention.

B. Treatment Goals and General Approaches to Hypertension Management

a. Blood Pressure Goals

Recommendation

6. For all patients, including those with type 2 diabetes, we suggest treating to a systolic blood pressure goal of <130 mm Hg.
   (Weak for | Reviewed, New-added)

Discussion

Pharmacologic treatment of HTN has been demonstrated to decrease the risk of major adverse cardiovascular events (MACE) such as CHD, stroke, heart failure, and overall mortality in patients with HTN, including patients with both HTN and diabetes.[54] Treatment of SBP to a goal of less than 130 mm Hg may lead to a reduction in cardiovascular events when compared to higher thresholds. The SR and meta-analysis by Ettehad et al. (2016) provides evidence in support of this recommendation.[54] This review included 78 RCTs comparing HTN treatment to placebo and 14 RCTs comparing intensive HTN treatment to standard treatment. The effect of a 10 mm Hg reduction on the relative risk of major cardiovascular events was estimated as a function of different baseline SBPs. Across a broad range of initial SBPs starting at greater than 130 mm Hg, a 10 mm Hg lowering in SBP was associated with improvements in the composite cardiovascular outcome. For people with diabetes, the SR and meta-analysis by Ettehad et al. (2016) showed pharmacologic treatment of HTN was associated with a 12% relative risk reduction for major adverse cardiovascular events (MACE) per 10 mm Hg reduction in SBP.[54] While this relative reduction in MACE is less than that observed in the non-diabetic population, the difference in impact between the diabetic and the non-diabetic population is neither statistically nor clinically significant.

However, SRs limited to studies comparing a standard SBP threshold to a more intensive blood pressure threshold in HTN patients have arrived at contradicting conclusions, likely based on differences in inclusion criteria. The SR by Saiz et al. (2018) found no benefit of targeting an SBP threshold of 130 mm Hg when compared to a higher SBP threshold of 150 mm Hg.[55] This mirrors the findings from the SR by Weiss et al. (2017) that looks at studies targeting a lower threshold.[56] In contrast, the SR by Reboussin et al. (2018) found significant reductions in the risk of major cardiovascular events associated with an SBP target of less than 130 mm Hg.[57] The largest individual study to date examining SBP targets, the Systolic Blood Pressure Intervention Trial (SPRINT), included HTN patients age 50 and over and demonstrated a 25% reduction in cardiovascular events in the intensive treatment group targeting an SBP of 120 mm Hg.[58]

Only a small proportion of SPRINT participants (those with known CVD) would have been included in the SR by Saiz et al. (2018),[55] which could perhaps explain why Saiz et al. (2018) did not find benefits for reducing SBP below 150 mm Hg. Specifically for HTN patients with diabetes, the SR and meta-analysis by Brunstrom et al. (2017) suggests that benefit of treatment in patients with diabetes may be limited to those with a baseline SBP of >140 mm Hg or to an achieved SBP of 130-140 mm Hg.[59] Overall, the available evidence was primarily for patients with type 2 diabetes with very limited evidence for those with type 1 diabetes.

As shown by the SR by Ettehad et al. (2016), the proportional reduction in the rates of cardiovascular outcomes resulting from a 10 mm Hg reduction in blood pressure did not differ among people with prior cardiovascular disease (CVD) events, coronary heart disease (CHD), CHF, or cerebrovascular disease.[54] Two other SRs specifically examined the risk of stroke recurrence among patients receiving more intensive HTN therapy.[60,61] These SRs also suggested a reduction in stroke recurrence based on additional HTN therapy.

For many patients, benefits of intensive therapy seem to outweigh harms.[58,62] Yet, targeting an SBP goal of <130 does not mean that it must always be achieved; if older or particularly frail people develop side effects while titrating therapy to achieve this lower threshold, they may wish to have medications tapered back or changed.

The patient focus group revealed that some patients do not want to take medications for treatment of HTN. This may limit the ability to achieve lower targets of SBP with intensive treatment, as this often requires multiple medications and may require frequent visits.

Despite the conflicting evidence supporting an SBP goal of 130 mm Hg or less, the results from the SR by Ettehad et al. (2016) do demonstrate benefit in lowering SBP for those between 130 and 150 mm Hg.[54] Thus, there is strong evidence from one SR suggesting that lowering SBP by 10 mm Hg among people with an SBP above 130 mm Hg reduces the risk of cardiovascular events.[54] However, there are inconsistencies among other studies comparing a standard threshold with more intensive therapy. The evidence reviewed included very few adults under the age of 60, which, based on the GRADE methodology, resulted in a weaker recommendation. More intensive therapy often requires additional medications, which require further resources and which some people might prefer not to take.

These results are in contrast to stronger evidence for the older population of age 60 who have hypertension, with or without diabetes (see Recommendation 7 and Recommendation 8). The research supporting the goal of SBP <130 mm Hg in the general HTN population, with or without diabetes, is less robust than higher thresholds, which, according to our methodology, resulted in a weaker recommendation for this SBP goal.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation to treat hypertensive adults, including those with type 2 diabetes, to an SBP goal of less than 130 mm Hg. [54-57,59-61] The Work Group's confidence in the quality of the evidence is moderate. For people with an SBP above 130 mm Hg, a further 10 mm Hg reduction in SBP was associated with improved cardiovascular outcomes. There is some inconsistency in the data, as SRs that only compared a standard threshold to a more intensive threshold reached contradictory conclusions.

However, there were different inclusion criteria and methods across the SRs. The benefit of improved cardiovascular outcomes outweighs the potential harm of AEs; however, patients may or may not be accepting of HTN medication therapy.[63] Some patients are concerned over AEs of medication and may indicate that they want to avoid or limit use of medications, when possible. Patients, however, may be more likely to accept medications with SDM and careful titration. Based on the above, the Work Group decided upon a "Weak for" recommendation.

Additional RCTs would be needed to definitively recommend an SBP target of less than 130 mm Hg. Given the results of SPRINT, such a large clinical trial is unlikely to be performed in the U.S. in a general (lower risk) hypertensive population. Ongoing clinical trials from other countries that mirror the SPRINT protocol, or conducted among hypertensive patients excluded from or not robustly represented in SPRINT, could provide additional evidence. In hypertension patients with diabetes, additional data from RCTs may be available in the next few years as two large trials, Blood Pressure Control Target in Diabetes (BPROAD) and Intervention for High-normal or Borderline-elevated Blood Pressure in Adults with Type 2 Diabetes (IPAD) are currently enrolling in China. These trials should provide further evidence for the benefit of specific SBP thresholds and goals in patients with diabetes.

Recommendation

7. For patients 60 years and over, we recommend treating to a systolic blood pressure goal of <150 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 150 mm Hg.
   (Strong for | Reviewed, Amended)

Discussion

Among people age 60 and over with moderate to severe HTN, there is evidence that treating to an SBP goal of 150 mm Hg or less reduces cardiovascular morbidity and mortality. This strong recommendation is based on evidence from RCTs that compared a more intensive HTN strategy with placebo or a standard or less intensive strategy. The SR by Weiss et al. (2017) considered adults age 60 and over from 21 RCTs, nine of which specifically included individuals with an SBP of 160 mm Hg or higher.[56] Improved cardiovascular outcomes were seen among those given more intensive therapy targeting an SBP less than 150 mm Hg.

Among people 60 years and over, there was also evidence of further benefit in lowering systolic blood pressure to levels between 130 and 150 mm Hg.[56] The SR by Ettehad et al. (2016) included 78 studies comparing HTN treatment to placebo and 14 studies comparing intensive HTN therapy to standard treatment. Across a broad range of initial baseline SBPs greater than 130 mm Hg, a 10 mm Hg lowering in SBP was associated with improvements in the composite cardiovascular outcome.[54] Thus, there is likely benefit to further reductions of SBP for those patients with a baseline SBP between 130 and 150 mm Hg.

The SR by Ettehad et al. (2016) demonstrated benefit from a 10 mm Hg reduction in SBP but did not evaluate a specific target or threshold.[54] Different SRs have come to different conclusions in recommending a specific target for SBP less than 150 mm Hg with conclusions that are highly sensitive to inclusion criteria of studies in the SRs. The SR by Saiz et al. (2018) considered six RCTs in hypertensive patients with a history of CVD (MI, angina, stroke, and/or peripheral vascular occlusive disease), targeting a blood pressure less than or equal to 135/85 mm Hg when compared to standard therapy and found no

benefit for the more intensive approach.[55] This mirrors the findings from the SR by Weiss et al. (2017) that looked at studies targeting a lower threshold.[56] In contrast, the SR by Reboussin et al. (2018) found significant reductions in the risk of major cardiovascular events associated with an SBP target of less than 130 mm Hg.[57] The largest individual study to date examining SBP targets, the Systolic Blood Pressure Intervention Trial (SPRINT), included HTN patients age 50 and over and demonstrated a 25% reduction in cardiovascular events in the intensive treatment group targeting an SBP of 120 mm Hg.[58] Only a small proportion of SPRINT participants (those with known CVD) would have been included in the SR by Saiz et al. (2018),[55] which could perhaps explain why Saiz et al. (2018) did not find benefits for reducing SBP below 150 mm Hg.

Treating to a lower SBP goal of <130 mm Hg for older adults is also supported by evidence, but the research support this lower goal is weaker than the evidence for treating to a SBP goal of <150 mm Hg in patients 60 years and older. Thus, the current recommendation is specific to HTN in patients age 60 and over, which is supported by the large number of clinical trials that mostly included older people.

Based on the SR by Weiss et al. (2017), there is strong and consistent evidence supporting lowering SBP to a target of 150 mm Hg.[56] Benefits clearly outweigh harms and burdens associated with this therapy. There is less consistency in the evidence supporting additional blood pressure reductions for patients with an SBP between 130 and 150 mm Hg. This more intensive or aggressive approach often requires additional medications which, in turn, require further resources and which some people might not prefer.

Benefits of intensive therapy seem to outweigh harms.[58,62] Attempts at lowering systolic blood pressure further for those between 130 mm Hg and 150 mm Hg in order to achieve lower threshold goals is not always feasible; if older or particularly frail people develop side effects while titrating therapy to achieve lower blood pressures, they may wish to have medications tapered back or changed.

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence identified in the evidence review conducted as part of this guideline update.[54-58] For people with an SBP between 130 and 150 mm Hg, there is high confidence in the quality of evidence that additional reductions in blood pressure are beneficial. This is supported by the SR by Ettehad et al. (2016) which found that a 10 mm Hg reduction in SBP was associated with improved cardiovascular outcomes [54] and by the findings of the SR by Reboussin et al. (2018).[57] There is some inconsistency in the data, as not all SRs support further lowering of SBP across all patient groups. The benefit of improved cardiovascular outcomes outweighs the potential harm of adverse events, and patients are generally accepting of HTN therapy. Some patients, though, are concerned about the AEs of medication and may indicate that they want to avoid or limit use of medications, when possible.

Recommendation

8. For patients 60 years and over with type 2 diabetes, we recommend treating to a systolic blood pressure goal of <140 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 140 mm Hg.
   (Strong for | Reviewed, Amended)

Discussion

As previously stated, pharmacologic treatment of HTN has been demonstrated to decrease the risk of major adverse cardiovascular events (MACE) such as CHD, stroke, heart failure, and overall mortality in patients with HTN, including patients with both HTN and diabetes.[54] Based on the SR and meta-analysis by Ettehad et al. (2016), pharmacologic treatment of HTN is associated with a 12% relative risk reduction for MACE in patients with diabetes per 10 mm Hg reduction in SBP.[54] This review demonstrated broad reduction in MACE regardless of baseline blood pressure down to an SBP of <130 mm Hg.

Brunström et al. (2017) performed an SR of SRs with the purpose of determining the optimal blood pressure level and choice of antihypertensive agent in people with diabetes.[59] This study included 11 SRs (three SRs stratified according to baseline SBP, four SRs stratified by attained SBP, and eight SRs addressed choice of antihypertensive agent) and did not report the duration of follow-up for included studies. In these reviews, the mean age for patients was around 60 years. Evidence from Brunström et al. (2017) favored intensive blood pressure lowering in a general diabetic population when baseline SBP was >140 mm Hg. Achieving an SBP in the range of 130 to 140 mm Hg was associated with reduced CV events. A lower target of <130 mm Hg or treatment when the baseline SBP was <140 mm Hg was not, however, associated with statistically significantly improved cardiovascular outcomes or mortality. This led to conclusions that achieving an SBP in the range of 130-140 mm Hg is associated with reduced cardiovascular events.

There was some evidence for a reduced risk of stroke when patients were treated with antihypertensive therapy when the baseline SBP was <140 mm Hg, though benefits on other cardiovascular outcomes were not seen. Furthermore, there was a non-significant trend towards increased cardiovascular mortality in this group.[59] The SR performed by Ettehad el al. (2016) [54] focused on the general population with HTN but did have a subgroup analysis for patients with diabetes, which provided evidence for the recommendation suggesting treating to the lower target SBP of <130 mm Hg for patients with type 2 diabetes. This is in contrast to the SR by Brunström et al. (2017) [59] which provides strong evidence for the older population with type 2 diabetes, including patients with a history of CVD, for a target SBP of 130-140 mm Hg.

The 2014 VA/DoD HTN CPG recommended treatment to an SBP of <150 mm Hg in patients 60 years and over with type 2 diabetes, primarily based on the results of general HTN studies which had sub-populations with diabetes [64,65] and the HTN arm of the UK Prospective Diabetes Study Group.[66] In the 2014 VA/DoD HTN CPG, there was an additional suggestion to treat to an SBP of <140 mm Hg for those patients who tolerate pharmacologic antihypertensive treatment based on evidence from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) and Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trials;[67,68] however, this evidence was only moderate, which led to the “Weak for” recommendation in 2014. The SR by Brunström et al. (2017) strengthened the evidence providing support for the amended “Strong for” recommendation to treat to target SBP of <140 mm Hg and to consider additional blood pressure lowering when the SBP is between 130-140 mm Hg.[59]

The patient focus group revealed that some patients do not want to take medications for treatment of HTN. This may limit the ability to achieve target SBP.

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update,[54,59] as well as considered evidence from the 2014 VA/DoD HTN CPG.[64-68] The Work Group determined the confidence in the quality of the evidence was high in support of intensive treatment of HTN in a general population of patients with diabetes. The benefits of treatment clearly outweigh the harms, though we do note that there is variance in acceptance of intensive treatment from providers and patients and many patients may not be willing to take multiple medications to achieve target SBP levels.

The evidence included in the SR conducted as part of this guideline update is primarily from patients with diabetes type 2 who are already on pharmacologic antihypertensive treatment. These patients typically are middle-aged or elderly (but under the age of 80 years). There is little evidence for pharmacologic treatment to a target SBP in patients with type 1 diabetes, adults under the age of 50, or the very old (over 80 years). Future research on any of these subgroups may provide additional evidence regarding appropriate blood pressure goals.

Recommendation

9. For patients 30 years and over, we recommend treating to a diastolic blood pressure goal of <90 mm Hg.
   (Strong for | Reviewed, Amended)

Discussion

This recommendation is supported by strong clinical trial evidence demonstrating the benefits of treating HTN to a DBP goal of less than 90 mm Hg and was carried forward from the 2014 VA/DoD HTN CPG. Landmark studies, such as the Veterans Administration Cooperative Study Group on Antihypertensive Agents, the Hypertension Detection and Follow-up Program (HDFP), and the Medical Research Council (MRC) trial of treatment of mild HTN, all demonstrated substantial benefits in terms of reduced cardiovascular events by treating to a target DBP of less than 90 mm Hg.[69-73] Eligibility for these studies differed slightly, but all included patients 30 years of age or older. Based on the SR and meta-analysis by Saiz et al. (2018), lower target DBP goals showed no treatment benefit in mortality or cardiovascular morbidity.[55]

This recommendation may or may not apply to patients aged 18 to 29 as clinical trials did not include patients younger than 30. However, it is unlikely that clinical trials will address HTN treatment and optimal DBP targets in younger adults given the low prevalence of primary HTN in younger adults. The Work Group believes that younger adults with elevated DBP may also benefit from treatment.

The patient focus group revealed that some patients are resistant to taking medications, and lower targets generally require more medications and more clinical follow-up. Therefore, patients should find this recommendation acceptable. However, providers may note this recommendation differs from other recent HTN guidelines; therefore, our guidance may be confusing. The Work Group feels it is important to highlight for providers that there are no new RCTs providing evidence to lower the DBP target to less than 90 mm Hg (e.g., 80 mm Hg), and recommendations for a lower DBP target in other HTN guidelines are based on expert opinion. Both of these should give providers reassurance in this recommendation when

considering treatment. The Work Group, however, did not believe it likely that there would be harm for DBPs treated to lower levels, especially when treating SBP to the appropriate goal.[74]

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update,[55] as well as considered evidence from the 2014 VA/DoD HTN CPG.[69-73] The Work Group's confidence in the quality of the evidence is moderate. Other considerations regarding this recommendation included the lack of data in patients under 30 years, thus the specified age range. Patient values and preferences should be compatible with keeping the higher DBP target. Thus, the Work Group decided upon a "Strong for" recommendation.

b. General Approaches to Hypertension Management

Recommendation

10. We recommend offering pharmacist-led medication management as an option for patients with hypertension.
    (Strong for | Reviewed, New-replaced)

Discussion

Pharmacist-led interventions have been effective in improving critical outcomes in hypertensive patients. Interventions which have been evaluated include medication initiation, titration and monitoring, blood pressure measurement, reminder systems, patient education regarding both medications and long-term consequences of HTN, and physician feedback. Two SRs with large effect sizes provided much of the basis for this recommendation.[75,76] In the SR of seven RCTs by Greer et al. (2016), pharmacist-led care significantly increased the proportion of patients achieving goal blood pressure of 140/90 mm Hg versus usual care over a median period of 39 weeks (risk ratio 1.45, 95% CI 1.24-1.70). Care was provided by the pharmacist either in person, remotely, or a combination of the two, and some of the included studies granted prescriptive authority.[75] The SR by Santschi et al. (2014) included 39 RCTs and compared pharmacist-led care to usual or collaborative care in over 14,000 patients with HTN. Compared with usual care, pharmacist-led interventions resulted in significantly greater improvements in both SBP (-8.5 mm Hg) and DBP (-4.6 mm Hg) over the mean follow-up period of eight months.[76]

Four additional RCTs in the evidence base also evaluated blood pressure reduction via various pharmacist interventions and practice sites.[77-80] The study by Victor et al. (2019) reported a marked reduction in blood pressure when pharmacists provided care in barbershops catering to African American men. Significant and sustained reductions in mean SBP of approximately 20 mm Hg and mean DBP approaching 19 mm Hg were seen after 12 months in over 300 hypertensive patients versus control.[80] The lack of blinding is a limitation to this study. The study by Cheema et al. (2018), using community pharmacists who provided education and lifestyle and adherence advice, reported significant differences versus baseline for reductions in both SBP and DBP.[78]

Interventions are not required to be face-to-face to show benefit. The SR by Santschi et al. (2014) included a trial of home blood pressure telemonitoring and pharmacist management intervention in which the interventions stopped after 12 months.[76] In the long-term follow-up of this study, benefits were seen beyond the 12 month intervention period, as Margolis et al. (2018) found that there were significantly

greater reductions in SBP in the intervention group than in the usual care group at 6, 12, and 18 months (reductions of 10.7, 9.7, and 6.6 mm Hg, respectively). However, the results were not significant when evaluated at 53 months.[79] In contrast, no differences in blood pressure were noted in a small study that compared pharmacists with an education control.[77] However, results may have been influenced by study limitations related to low patient enrollment.

Statistically significant improvements in both medication adherence and medication use with pharmacist-led interventions were reported in the SR by Greer et al. (2016).[75] The barbershop study by Victor et al. (2018) showed an increase in the number of blood pressure medications per participant.[80] Improved adherence in favor of a pharmacist-led intervention was shown in one study conducted in Pakistan in which the intervention involved education.[81] There was also some evidence of improved medication use (in terms of either the numbers of antihypertensive medications used or adherence) in the referenced studies.

The Work Group determined that, in addition to providing education, there was a significant role for pharmacists in actively titrating antihypertensive drugs and managing AEs. This conclusion was based on findings from two SRs of RCTs in which pharmacists performed these higher level interventions.[75,76] Ensuring pharmacists are appropriately qualified to provide these services is also important. The study conducted by Cheema et al. (2018) utilized community pharmacists.[78] However, in both the VA and DoD, this recommendation is intended for pharmacists in the clinic setting, and not dispensing pharmacists.

Some variation was noted in patient values and preferences. The patient focus group did not discuss pharmacist-led interventions; however, in the evidence base, patients enjoyed the flexibility and ease of access to pharmacists and appreciated the improved access to care.[75,80] The benefits of pharmacist-led care outweighed the harms due to the low number of adverse events reported with the interventions in the barbershop trial.[80] The SR by Greer et al. (2016) had only limited information regarding patient satisfaction or drug-related problems.[75] This strong recommendation will have implications for resource use, as utilization of pharmacist-led interventions for the treatment of HTN could have significant system implications.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to blood pressure management using pharmacist-led care either through in-person interactions, via telehealth, or a combination of the two, and that specifically discussed studies related to pharmacist-led interventions.[75-81] The evidence reviewed included two SRs and five RCTs. The confidence in the quality of evidence was moderate. The recommendation focuses on clinical pharmacists, in contrast to the recommendation in the 2014 VA/DoD HTN CPG, which grouped nurses, pharmacists, and social workers together and centered on adherence in addition to blood pressure control. Although there were variations in the quality of the evidence for the five RCTs, the moderate quality SRs by Greer et al. (2016) and Santschi et al. (2014) with the large effect sizes and the evidence for improved adherence led to the overall confidence in the quality of evidence to be assessed as moderate. Other factors considered by the Work Group for this recommendation included the improved outcomes of blood pressure reduction and blood pressure goal attainment, which outweighed the small risk of adverse events. There was some variation in patient values and preferences. Overall, the strength of the evidence and substantial effect sizes within the two SRs contributed to the “Strong for” recommendation.[75,76]

Recommendation

11. We suggest offering nurse-led interventions as an option for patients treated for hypertension. **(Weak for | Reviewed, New-replaced)**

Discussion

Nurse-led interventions for the management of HTN encompass a wide variety of treatment approaches including cardiovascular risk assessment, education, counseling on lifestyle modification, goal setting, action planning, and the initiation and titration of antihypertensive medications using established protocols. When compared with usual care, nurse-led interventions have been found to reduce SBP and DBP, improve adherence to medication therapy, and improve quality of life metrics in patients with HTN.[82-88] All studies reviewed by the Work Group contained multiple components of nurse-led intervention, some paired with other co-interventions.

Our evidence review found one SR, by Parappilly et al. (2018), that compared nurse-led interventions to usual care.[88] It was based on 16 RCTS and enrolled a total of 3,568 participants diagnosed with a previous stroke or transient ischemic attack. The researchers observed no statistically significant difference in SBP and DBP changes between nurse-led interventions and usual care. However, the authors indicated that one RCT was found to be an outlier. After removing this study from the meta-analysis, the models demonstrated a statistically significant effect on reducing SBP and DBP in favor of nurse-led interventions when compared to usual care. The authors reported a mean difference in SBP reduction of 2.84 mm Hg and a MD in DBP reduction of 2 mm Hg, favoring nurse-led intervention. All studies included in the SR contained multiple nurse-led components including education, lifestyle changes, providing feedback, appointment scheduling, and medication review and compliance.[88] The Work Group identified two additional RCTs that had results consistent with the SR by Parappilly et al. (2018) (i.e., favoring the nurse-led intervention group).[82,84] One found a reduction in DBP similar to the SR by Parappilly et al. (2018) (i.e., favoring the nurse-led intervention).[82] Three additional RCTs reported more frequent "hypertension control" or achieving a blood pressure goal of <140/90 mm Hg in the nurse-led intervention group when compared to the usual care control group.[83,85,87] No significant harms were found with nurse-led interventions in studies that reported on the outcome.

Medication adherence is a critical component in chronic disease management for HTN. The SR by Parappilly et al. (2018) reported a statistically significant difference between nurse-led intervention and usual care in the change in medication adherence at follow-up.[88] Our evidence review found one RCT reporting a statistically significant difference in medication adherence in favor of nurse-led intervention.[87] Another RCT, by Zhu et al. (2018), found no statistically significant difference between nurse-led intervention and usual care in the change in medication adherence at follow-up.[82] Two additional RCTs found no statistically significant difference between nurse-led intervention and usual care when coupled with co-interventions such as electronic health record (EHR) tools and mobile health technologies.[83,85] These two RCTs had small sample sizes and may have been underpowered to detect the true intervention effect.

Two RCTs found a statistically significant change in quality of life metrics favoring the nurse-led intervention group versus usual care.[82,87] However, a third RCT, by Persell et al. (2018), found no quality

of life impact when using EHR tools alone or EHR tools plus nurse-led education with usual care or when interventions were compared with one another.[83]

Despite general consistency in the evidence supporting the notion that nurse-led interventions inform the management of HTN, there is some variability in provider and patient preferences. The patient focus group revealed that some patients did not feel that their providers offered the full range of management strategies available and prioritized pharmacologic interventions. This highlights an opportunity to utilize nurse-led interventions for lifestyle modification. Additionally, the patient focus group found that patients would like to be offered verbal education as well as educational materials, such as pamphlets. Some patients reported that they did not receive information on the sequelae of high blood pressure and that their providers did not consider individual patient characteristics that could impact their high blood pressure and management strategies. A common theme highlighted in the patient focus group was the desire for ongoing communication and education from providers to patients. This is a potential area in which nurse-led intervention can fill current gaps in care. In general, nurse-led intervention is well received by patients and most providers. Patients often appreciate nurse-led intervention due to increased accessibility to care and time efficiency.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[82-88] The Work Group's confidence in the quality of the evidence is very low for all included studies due to the lack of objectivity of outcome assessment, incomplete outcome data, selective reporting, small sample size, lack of blinding, and recruitment bias. The body of evidence had some limitations including confounders in the analysis.[82-88] Other considerations regarding this recommendation included the benefits of improved blood pressure and medication adherence outweighing the potential harms (none identified). Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

More research is needed to evaluate the effectiveness of nurse-led intervention to manage HTN in specific subgroups (e.g., age, ethnicity, comorbidities). Additionally, more research is needed to evaluate the effectiveness of nurse-led intervention, such as evaluating initiation and titration of antihypertensive medications using established protocols.

Recommendation

12. We suggest offering registered dietitian-led nutrition interventions as an option for patients with hypertension who are or are not on medication.
    (Weak for | Reviewed, New-replaced)

Discussion

Registered dietitian-led nutrition interventions, such as education about low sodium diets, weight loss, and increasing consumption of fresh fruits and vegetables, have been found to result in modest but statistically significant lowering of SBP and DBP in treated and untreated hypertensive individuals.[89] The current recommendation is based on low quality evidence from an SR by Reigel et al. (2018), which included 4,491 patients across 13 studies, in which nutrition-based interventions resulted in lower SBP (MD -2.82 mm Hg) and lower DBP (MD -1.37 mm Hg), as compared with the usual care.[89] However,

when studies were grouped based on whether the nutrition intervention was delivered by a registered dietitian versus other practitioners, significant reductions in SBP (MD -3.5 mm Hg) and DBP (MD -1.37 mm Hg) were only seen in the registered dietitian-led nutrition intervention group. In addition, blood pressure reductions were more pronounced with interventions longer than six months. No significant harms were found with nutrition interventions.

Focus group participants highlighted that patients and caregivers strongly valued dietary interventions to lower blood pressure. Although not systematically reviewed in this guideline update, it is generally accepted that comprehensive dietitian-led intervention can positively impact other aspects of cardiovascular health, such as blood lipid and glucose levels, weight loss, and alcohol cessation. However, there may be barriers in obtaining healthy food choices for some patients. Service Members frequently do not get a choice regarding where they are going, what they are doing, or where they will eat in a deployed/training environment. Food sources may vary (e.g., Meals Ready to Eat (MREs), items received in care packages, training area or forward operating base (FOB)/central operating base (COB) dining facilities). Depending on what area of responsibility the Service Member is deployed to/training in, these rations may be high in sodium and fat. These nutritional factors may impact HTN management and necessitate counseling related to diet.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed the relevant evidence identified in the evidence review conducted as part of this guideline update.[89] The Work Group's confidence in the quality of the evidence is low. The body of evidence showed overall modest effect size, although statistically significant, and had some limitations including small size, inadequate allocation concealment and blinding, and inclusion of dietary approach as a part of multidisciplinary intervention in some individual studies. Other considerations regarding this recommendation included patients' preferences. The potential benefit of nutritional intervention to improve global cardiovascular health outweighs potential adverse events and burden, which were not found. Thus, the Work Group decided upon a "Weak for" recommendation.

More research is needed to evaluate intensity and duration of dietitian-led interventions to improve blood pressure control and effectiveness of registered dietitian-led nutritional intervention to manage HTN in specific subgroups (e.g., different ages, ethnicities).

Recommendation

13. We suggest technology-based interventions (e.g., e-counseling, electronic transmission of data, telemonitoring, mobile applications) for improving control of hypertension.
    (Weak for | Reviewed, New-replaced)

Discussion

Several key words are defined to better understand this recommendation and its impact. Telehealth refers to data communicated between the patient and provider in ways other than face-to-face interactions. This is accomplished through a variety of methods to include use of computers, mobile devices, or mobile applications. In contrast, telemonitoring is the use of information and communication technologies to monitor and transmit items related to patient health status between geographically separated individuals, which permits home monitoring of patients to include nursing or residential care homes using external

electronic devices. Methods may include e-counseling, real-time consults, electronic transmission of data and interventions, mobile interventions, and/or interactive digital interventions. Additionally, mHealth is defined as mobile health. The World Health Organization defines it as the use of mobile applications and wireless technology to support the achievement of health goals.[90]

In the development of this recommendation, the Work Group considered whether concurrent treatment impacted outcomes. The Work Group considered whether the intervention of interest was provided instead of, or in addition to, usual care (in-person visits). Some of the possible interventions may include mobile applications, telehealth monitoring, telehealth visits with primary care or a subspecialty. The impact of the intervention of interest and any concurrent treatment on the following outcomes was considered: reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals and adherence to therapy, and percentage of patients taking medication.

In examining "instead of or in addition to usual care (in-person visits)", two RCTs, Liu et al. (2018) [91] and Nolan et al. (2018),[92] compared an e-counseling intervention with usual care or control. Liu et al. observed a not statistically significant difference in SBP change between user-driven e-counseling and control, while a statistically significant change was noted with expert-driven e-counseling.[91] Nolan et al. (2018) reported a not statistically significant difference between e-counseling plus usual care for SBP and DBP at four months.[92]

Two SRs compared mobile applications or mobile health technology with usual care or control. Alessa et al. (2018) indicated that applications had either a positive or statistically significant positive effect on SBP and DBP as compared to usual care or control.[93] Four of the 12 RCTS in Xiong et al. (2018) reported a statistically significant change in either SBP or DBP in favor of mHealth interventions as compared to usual care.[94] Marquez Contreras et al. (2018) reported a statistically significant difference in SBP change in favor of the mobile application as compared to usual care.[95] Twelve of 21 RCTs in Xiong et al. 2018) reported a significant improvement in medication adherence in the intervention group compared to controls.[94]

In looking at telehealth monitoring, one SR by McLean et al. (2016) included seven RCTs comparing interactive digital interventions with usual care. McLean et al. (2016) observed statistically significant changes in SBP and DBP in favor of interactive digital interventions compared to usual care.[96]

This recommendation looked at a variety of topics that include web-based interventions and telemonitoring. Two SRs [97,98] and two RCTs [99,100] compared telehealth visits with usual care or control. Chen et al. (2019) and Beishuizen et al. (2016) reported statistically significant differences in favor of web-based interventions for changes in SBP and DBP.[99,100] In contrast, one RCT included in Vargas et al. (2017) reported a not statistically significant difference in SBP change at three months.[98] Similarly, an additional RCT (not included in one of the above four SRs) by McManus et al. (2018) observed no statistically significant differences in SBP or DBP at six months.[52] One RCT included in Vargas et al. examined medication adherence and found no statistically significant difference in medication adherence between short message service (SMS) and control.[98] However, an additional RCT (not included in one of the above four SRs) by Pan et al. compared home telemonitoring with usual care and observed statistically significant differences in favor of home telemonitoring for SBP and DBP.[101] Given these conflicting results, additional studies need to examine possible effectiveness of mHealth.[90]

Additional considerations include the confidentiality and security of all Health Insurance Portability and Accountability Act (HIPAA)-related health information, variation in use between age population groups, and variation in access to internet or technologies due to financial considerations.

Primary HTN continues to be a concern. Emerging technologies should be considered as a possible additional intervention between the provider and patient to address HTN, thereby giving the provider additional tools to teach and evaluate the patient's progress. This recommendation's strength is "Weak for." As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed the relevant evidence for this recommendation identified in the evidence review conducted as part of this guideline update.[52,91-101] The overall confidence in the quality of the evidence is very low to low. While the balance of desirable and undesirable outcomes shows that benefits slightly outweigh harms/burden, there is a large variation of patient values and preferences. It cannot be understated that this recommendation has a broad scope with general findings that may show a modest benefit for those patients and providers who choose to utilize this medium.

Technologies continue to evolve at a rapid pace and new capabilities are continually emerging. Additional studies should consider the effectiveness, safety, adherence, and overall quality of life impact on decreasing blood pressure.

C. Non-pharmacological Management

a. Weight Reduction

The following recommendations are directed towards patients with HTN and overweight/obesity. There are benefits to weight reduction outside of treating for HTN. The various interventions may be more or less effective for other outcomes than for the treatment of HTN. Providers may refer to the VA/DoD Clinical Practice Guideline for Screening and Management of Obesity and Overweight for further discussion of treatment methods for patients with overweight/obesity.[11]

Recommendation

14. We suggest advising patients with hypertension and overweight/obesity to lose weight to improve blood pressure.
    (Weak for | Reviewed, Amended)

Discussion

As part of lifestyle modification, weight loss has been found to improve blood pressure in patients with HTN and overweight/obesity. Overall, reduction in weight or BMI had a positive effect on blood pressure.[102-109]

Therefore, the Work Group suggests advising patients with HTN and overweight/obesity to lose weight to reduce blood pressure. Although the confidence in the quality of the evidence is very low,[102-109] the Work Group believes the benefits outweigh the harms. As far as specific interventions for weight loss, the Work Group suggests offering diet directed at weight loss for treatment of HTN

[11] See the VA/DoD Clinical Practice Guideline for Screening and Management of Obesity and Overweight. Available at: https://www.healthquality.va.gov/guidelines/CD/obesity/.

(see Recommendation 15).[106-108] Additionally, the Work Group recommends neither for nor against weight loss medications for the treatment of HTN (see Recommendation 16).[103] Lastly, there is insufficient evidence to recommend for or against bariatric surgery for the treatment of HTN in patients with obesity and HTN (see Recommendation 17).[104,105]

As Recommendation 14 is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[102-109] The confidence in the quality of the evidence supporting dietary and lifestyle interventions for blood pressure reduction through weight loss was low to very low. The Work Group believes that the benefits of diet and lifestyle modifications outweigh the harms. There will be variability in patient values and preferences, as not all patients will want to lose the weight or be accepting of a lifestyle modification. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

15. For patients with hypertension and overweight/obesity, we suggest offering a diet directed at weight loss for the treatment of hypertension.
    (Weak for | Reviewed, New-added)

Discussion

The Work Group reviewed evidence on the effects of various weight loss interventions, including diet directed at weight loss which has been found to improve blood pressure in patients with HTN. One SR [108] and two RCTs [106,107] comprised the evidence base for diets directed at weight loss therapy.

One SR, by Semlitsch et al. (2016), assessed the long-term effects of weight-reducing diets in people with HTN.[108] Three of the studies included in the SR by Semlitsch et al. (2016) examined the impact of diet versus no diet on SBP and DBP reduction (n=731);[108] there was further blood pressure reduction in the diet intervention group. One study included in the SR by Semlitsch et al. (2016) demonstrated significantly reduced cardiovascular morbidity in the diet intervention group. While the study was small, there was a large effect.[110] An RCT, by Kucharska et al. (2018), found that the Dietary Approaches to Stop Hypertension (DASH) diet reduced blood pressure in patients with overweight/obesity and HTN.[107] Another RCT, by Tay et al. (2014), studied the effects of a low-carbohydrate, high-unsaturated/low-saturated fat diet (LC) versus a high–unrefined carbohydrate, low-fat diet (HC) on blood pressure reduction in patients with type 2 diabetes; results were inconclusive.[106] Confidence in the quality of the evidence is very low due to serious study limitations and imprecision. While SBP and DBP did decrease in the intervention groups for several studies, it was not clear whether it was a clinically meaningful reduction in blood pressure.[107,108]

As the recommendation on a diet directed at weight loss is *Reviewed, New-added*, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[106-108] The Work Group had very low confidence in the quality of evidence supporting dietary interventions for weight loss for the treatment of HTN; there were serious limitations and a high risk of bias. While the data was somewhat limited, the effect sizes in the evidence were reasonably large. The benefits outweigh the harms, as only a few harms were associated with the interventions. There is a large variation in patient preferences as there are various

versions of diet, and providers would need to get the patient to agree to participate in the dietary intervention. Some patients would not accept the intervention. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

16. For the treatment of hypertension, there is insufficient evidence for or against offering weight loss medications for patients with obesity and hypertension.
    (Neither for nor against | Reviewed, New-added)

Discussion

The Work Group also looked at the evidence for offering weight loss medications for patients with obesity and HTN. There was insufficient evidence in the studies reviewed by the Work Group to recommend for or against offering weight loss medications for the treatment of HTN.

An SR by Siebenhofer et al. (2016) compared weight loss medications (orlistat and phentermine/topiramate) to placebo in patients with HTN.[103] There were statistically significant improvements in SBP and DBP for individuals taking either orlistat (four studies with 2,058 patients) or phentermine/topiramate (one study with 1,305 patients) compared to placebo. The study that compared phentermine/topiramate to placebo found a high rate of low-severity side effects with use of phentermine/topiramate (85.4% for low-dose, 88.8% for high-dose) compared to placebo (77.3%), but a low rate of serious adverse events with use of phentermine/topiramate (3.4% for low-dose and 3.7% for high-dose) compared to placebo (4.2%).[103] The harms slightly outweighed the benefits. Evidence on other medications was not found and therefore not reviewed.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[103] The confidence in the quality of the evidence was low due to risk of bias concerns and the small effect size. The harms slightly outweigh the benefits; there were gastrointestinal (GI) and musculoskeletal side effects with orlistat and relatively modest benefits. There is large variation in patient preferences regarding this medication because of the side effects. Patients may not want to take the medication, and there is the potential for taking the medication for life. Therefore, the Work Group decided upon a "Neither for nor against" recommendation.

Recommendation

17. For the treatment of hypertension, there is insufficient evidence to suggest for or against bariatric surgery for patients with obesity and hypertension.
    (Neither for nor against | Reviewed, New-added)

Discussion

The Work Group also looked at the evidence for offering bariatric surgery for the treatment of HTN for patients with obesity and HTN. There was insufficient evidence in the studies reviewed by the Work Group to recommend for or against offering bariatric surgery for the treatment of HTN.

The evidence for this recommendation was based on one SR [105] and one RCT.[104] In the RCT, by Schiavon et al. (2018), patients with a BMI of 30 to 39.9 kg/m^2 were followed for 12 months after surgical

intervention and demonstrated a greater reduction in anti-hypertensive medication usage as compared to patients treated with medications (from an average of three medications to zero to one). There were adverse events reported when patients were medically or surgically treated.[104] Schiavon et al. (2018) reported no differences in reduction of SBP and DBP between medical or surgical treatment groups.[104] The SR by Yan et al. (2016) followed the patients receiving medical treatment or bariatric surgery for 12 to 60 months; the highest BMI was 43 kg/m^2.[105] Yan et al. (2016) found only a statistically significant decrease in SBP in the bariatric surgery treatment group.[105] The confidence of the quality of the evidence is very low, and benefits and harms were balanced.

As this is a *Reviewed, New-added*, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[104,105] The confidence in the quality of the evidence was very low. The benefit and harms of bariatric surgery are balanced. The potential for positive outcomes was balanced with the risk of adverse events from surgery. There was large variation in the patient values and preferences regarding whether to have the surgery or avoiding surgery and committing to a lifestyle change. Not everyone would or should accept surgery as an intervention due to personal values and the inherent risks of any surgery, including bariatric surgery. The necessary medications and cost of surgery also need to be considered. Most of the evidence focused on patients with comorbid HTN and diabetes. Based on all these considerations, the Work Group determined that there was insufficient evidence for or against recommending bariatric surgery to treat HTN.

b. Exercise/Physical Activity

Recommendation

18. We suggest offering individual or group-based exercise for the treatment of hypertension to reduce blood pressure.
    (Weak for | Reviewed, Amended)

Discussion

The evidence in support of this recommendation was strongest for combined aerobic and resistance exercise interventions and for group/team-based sports. Other interventions reviewed included aerobic dance training, water-based exercise, yoga, traditional Chinese exercises such as Tai Chi and Qigong, and digital interventions to reduce sedentary time.

Aerobic and resistance exercise interventions, both individually and in combination, have been shown to reduce blood pressure. Herrod et al. (2018) conducted an SR of RCTs comparing non-pharmacologic strategies to non-intervention controls.[111] The included studies had mean participant ages of at least 65; intervention duration ranged from four weeks to one year. The researchers found statistically significant improvements favoring each type of exercise intervention for both SBP and DBP. MDs in SBP and DBP for combined aerobic/resistance exercise versus control were -5.9 mm Hg and -3.5 mm Hg, respectively. A 2016 meta-analysis by Corso et al. (2016) also examined the efficacy of combining aerobic and resistance exercise interventions of similar duration for blood pressure reduction in slightly younger (mean age across studies 56 years) prehypertensive adults.[112] Statistically significant reductions of -3.2 mm Hg (SBP) and -2.5 mm Hg (DBP) were seen for concurrent aerobic and resistance training versus control.

Herrod et al. (2018) also reported data favoring separate aerobic, resistance, and isometric exercise interventions over control.[111] MDs in SBP and DBP for aerobic exercise versus control were -5.1 mm Hg and -2.2 mm Hg, respectively, while MDs in SBP and DBP for resistance exercise versus control were -5.5 mm Hg and -2.0 mm Hg, respectively. Only two studies included in the SR looked at isometric exercise versus control; MDs of -9.1 mm Hg (SBP) and -3.0 mm Hg (DBP) were reported. Additional data on aerobic exercise comes from a 2016 RCT comparing aerobic dance training to non-exercise controls in participants on two antihypertensive agents.[113] Statistically significant differences in both SBP and DBP favored dance training. A larger proportion of participants in the dance group were able to reduce their number of blood pressure medications; however, control participants were older and had a higher BMI at baseline.

Recreational group sports may offer similar blood pressure reductions as combination aerobic/resistance exercise, as well as improving other cardiovascular risk factors. Bellissimo et al. (2018) conducted an SR and meta-analysis to estimate the pooled effects of community-based, recreational-level group sports on cardiometabolic risk factors and fitness parameters in adults.[114] Included trials compared group sports interventions against exercise and/or non-exercise controls; the majority used soccer as the group sports intervention. Intervention groups averaged 134 min/week of physical activity; the average intervention duration was roughly six months. Statistically significant differences favored recreational group sports for both SBP (MD -5.7 mm Hg) and DBP (MD -3.4 mm Hg). Improvements in total cholesterol, low-density lipoprotein (LDL) cholesterol, and BMI were also seen with intervention groups; statistically significant differences favored recreational group sports.

An SR by Reichert et al. (2018) examined the blood pressure effects of aquatic-based exercise versus land training or non-exercise controls in adults and elderly individuals.[115] Aquatic interventions included aerobic, resistance, or combined aerobic/resistance training, but were limited to exercise performed in an upright position due to potentially beneficial physiological changes associated with hydrostatic pressure from immersion. Improvements in blood pressure for aquatic-based exercise versus control reached statistical significance only with sensitivity analyses for individuals with HTN (SBP and DBP) or for individuals with prehypertension (DBP only).

Evidence reviewed did not suggest meaningful differences between higher and lower intensities of exercise or digital interventions to reduce sedentary time versus control. The strength of evidence reviewed for yoga and traditional Chinese exercise was rated low or very low quality and showed either no benefit for intervention versus control or inconsistent findings for critical outcomes.[116-119]

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified in the evidence review conducted as part of this guideline update.[111-119] Quality of the evidence reviewed was affected by the inherent difficulty of blinding participants to exercise interventions. Some studies also lacked blinding (or reporting of blinding) of assessors to interventions or had meaningful differences in baseline characteristic between intervention groups. The Work Group's confidence in the quality of the evidence for exercise overall is low, but varied across types of interventions, with the strongest evidence (moderate quality) found for combined aerobic/resistance exercise and for recreational group sports.

Patient preferences regarding exercise may vary considerably; some may dislike exercise, while others may value it as a means to potentially limit pill burden. Preferences for different types of exercise may also

vary. Patients who dislike traditional exercise may be more likely to engage in group sports due to social or competitive aspects. The benefits of exercise outweigh the harms, particularly given the wide range of other health parameters positively affected by physical activity.

Recommendation

19. We recommend a target for aerobic exercise of at least 120 minutes per week for reduction in blood pressure.
    (Strong for | Not Reviewed, Amended)

Discussion

As this is a *Not Reviewed, Amended* recommendation, the Work Group did not systematically review new evidence related to this recommendation. Two meta-analyses of RCTs studying the effects of aerobic exercise on blood pressure were reviewed during the 2014 VA/DoD HTN CPG update and provide evidence that the quantity of aerobic exercise influences its efficacy in blood pressure reduction.[120,121] Whelton et al. (2002) showed statistically significant improvements in blood pressure for interventions involving at least 120 minutes/week of aerobic exercise; magnitude of effect was clinically meaningful for SBP and DBP.[121] Kelley et al. (2001) also showed statistically significant improvements in blood pressure; furthermore, a meta-regression showed that increased minutes of exercise per session were associated with greater reductions in blood pressure.[120] Based on the assessment of the quality of the evidence put forth in the 2014 VA/DoD HTN CPG,[120,121] the Work Group determined the confidence in the quality of evidence is moderate for SBP and low for DBP. Benefits clearly outweigh the harms, although some patients may dislike, or have limited ability to, exercise.

c. Dietary Modifications

Recommendation

20. We recommend a dietitian-led Dietary Approaches to Stop Hypertension Diet for the treatment or prevention of hypertension for patients with hypertension or interested patients with other cardiovascular risk factors.
    (Strong for | Not Reviewed, Amended)

Discussion

Clinical trials on supplements frequently produce different or even opposite results than those expected based on epidemiologic data showing associations between food constituents and health outcomes. As individuals consume whole foods rather than isolated nutrients, it is more useful to confirm that a pattern of whole foods confers benefit, rather than that a micro/macronutrient is beneficial dependent on context.

Fiber and various micronutrients such as potassium, magnesium, and calcium are thought to improve blood pressure based on epidemiologic data. The DASH trial represents the first major clinical trial to test a dietary pattern for the prevention and/or management of HTN. The DASH trial emphasized inclusion of these nutrients via commonly consumed foods rather than supplements.[122] This approach allows for the detection of potential additive and/or synergistic effects of these nutrients which might individually be too small to detect. The DASH diet has been shown to reduce SBP and DBP in both hypertensive and normotensive adults, whether at dietary sodium intakes similar to the average daily consumption [123] or

in combination with varying degrees of sodium restriction.[122] Combining the DASH diet with sodium restriction consistently produces larger decreases in blood pressure than either intervention alone across diverse subgroups.[124]

As this is a *Not Reviewed, Not Changed* recommendation, the Work Group did not systematically review new evidence related to this recommendation. However, confidence in the quality of the evidence systematically reviewed for the 2014 VA/DoD HTN CPG is high.[122-124] Benefits outweigh harms, though patient preferences regarding dietary modification may vary. Some patients may be resistant to changing eating patterns or face geographical or financial barriers to accessing certain types of healthy foods. Others may have high levels of motivation to improve diet quality in an effort to reduce pill burden. Patient focus group participants indicated that initial referral to a dietitian is common but expressed the desire for spouses/caregivers to be included in nutrition interventions when possible. The current guideline continues to recommend the DASH diet based on the existing body of evidence to support its use in lowering blood pressure.

Recommendation

21. In patients with hypertension, we recommend that sodium intake be limited to no more than 2,300 mg/day (100 mmol/day), with referral to a dietitian or other support as appropriate. **(Strong for | Not Reviewed, Not Changed)**

Discussion

Many national and international organizations recommend reducing sodium intake for the prevention and management of HTN, with the ultimate goal of reducing associated morbidity and mortality. New evidence was not reviewed as part of this CPG update; evidence reviewed during the 2014 VA/DoD HTN CPG update is summarized below.

There is a strong body of evidence from animal studies and human observational and experimental studies noting a dose-dependent relationship between dietary sodium intake and blood pressure in both normotensive and hypertensive individuals, though there is known variation in "salt sensitivity" both within and across populations.

It should be noted that recommendations for dietary sodium reduction to reduce cardiovascular risk generally rely on surrogate markers (e.g., blood pressure) rather than clinical outcomes. The current guideline recommends a reduction to 2300 mg/day. There is strong clinical evidence from the DASH sodium trial that a reduction from 3400 mg (average daily intake of U.S. adults) to 2300 mg (the previously defined tolerable upper intake level [UL] [125])[12] improves blood pressure in the short term.[126] Limited observational research suggests that CVD event rates also decrease with reductions in sodium intake down to 2300 mg.[127]

Two relevant RCTs addressing blood pressure and/or mortality outcomes for reducing sodium intake were reviewed during the 2014 VA/DoD HTN CPG update. The Trials of Hypertension Prevention Phase II (TOHP II)

[12] There is no longer a defined UL for sodium, as there is no toxicological indicator specific to excessive sodium intake. The 2019 Dietary Reference Intakes now include a new category, the Chronic Disease Risk Reduction Intake (CDRR), or intake above which intake reduction is expected to reduce chronic disease risk in an apparently healthy population. The value of the new CDRR for adults (2300 mg) is the same as the previous UL for sodium.

study compared counseling on sodium reduction to usual care in overweight adults.[128] The intervention group achieved greater mean net decreases in SBP and DBP at both 18 and 36 months. The effect was statistically significant when compared with controls for SBP at both times and for DBP at 18 months only. Shea et al. (2011) presented mortality outcome data from a post-hoc analysis of the Trial of Non-pharmacologic Interventions in the Elderly (TONE).[129] Despite the TONE trial achieving clinically and statistically significant improvements in blood pressure,[110] no change in all-cause mortality was found for the intervention group when compared to usual care.[129]

Both TOHP II and TONE were lifestyle interventions in free-living cohorts rather than controlled feeding trials. Thus, the low percentage of intervention group participants who met the studies' goal of <80 mmol/day (1840 mg) average sodium intake (21% in TOHP II, roughly 40% in TONE) represents the inherent difficulty of lifestyle modification compounded by the ubiquity of sodium in the present U.S. food supply. The studies support reducing sodium intake as a means to lower blood pressure, but do not justify a lower goal than 2300 mg or confirm that clinical outcomes are improved. It is possible that an effect on mortality would have been detected had TONE intervention participants been more successful in lowering sodium intake.

Several organizations recommend or suggest lower targets for daily sodium intake. The 2017 ACC/AHA CPG recommends sodium reduction for adults with elevated blood pressure and lists <1500 mg as an "optimal goal."[4] The 2015-2020 Dietary Guidelines for Americans recommends daily sodium intake <2300 mg for adults, but note that those with HTN or prehypertension may benefit from further reduction to 1500 mg.[130]

The average daily sodium intake in the U.S. is over 3400 mg/day excluding table salt, well above this guideline's recommendation of 2300 mg/day.[131] Disagreement regarding the exact cut-point at which risks outweigh benefits should not distract from a unified public health message that a reduction in sodium intake from current levels is desirable.

As this is a *Not Reviewed, Not Changed* recommendation, the Work Group did not systematically review new evidence related to this recommendation. The Work Group's confidence in the quality of the evidence remains high based on evidence reviewed during the 2014 VA/DoD HTN CPG update.[126,128,129] The benefits of reducing daily dietary sodium intake to 2300 mg outweigh the harms. As dietary sodium recommendations rely heavily on research on surrogate markers, additional research is warranted to confirm that reducing blood pressure via reducing sodium intake has the predicted effect on morbidity and mortality. Future research is also needed to determine the efficacy and safety of lower sodium targets. Since the majority of sodium consumed by Americans comes from processed and prepared foods (versus added table salt), recommended intake levels would be attained most feasibly with changes to the food supply in addition to individual dietary modification. The U.S. Food and Drug Administration (FDA) has solicited comments on, but has not yet released, voluntary sodium reduction targets for food manufacturers and restaurants. Patients' desire and ability to reduce sodium intake may vary; some may find low sodium diets unpalatable, and others, such as deployed military, may have limited access to fresh/unprocessed foods. Referral to a dietitian can help interested patients incorporate this recommendation into the broader context of a healthful diet. Per the patient focus group, inclusion of spouses/caregivers in nutrition interventions may provide additional benefit, as they may be responsible for household food shopping and/or preparation.

Recommendation

22. In patients with additional cardiovascular risk factors, such as dyslipidemia, we suggest considering a dietitian-led Mediterranean Diet as an alternative to the Dietary Approaches to Stop Hypertension Diet.
    (Weak for | Not Reviewed, Not Changed)

Discussion

Epidemiologic data has long suggested a cardio-protective effect of a Mediterranean-style diet. Despite known variation in the cuisine of Mediterranean countries, certain characteristic features are commonly used to describe a traditional Mediterranean diet: high intake of vegetables, fruits, nuts, unrefined grains, and olive oil; moderate intake of fish and poultry; low or moderate intake of wine; and low intake of red meat, processed meat, dairy, and sweets. New evidence was not reviewed as part of the current CPG update. Evidence reviewed during the 2014 VA/DoD HTN CPG update is summarized below.

Toledo et al. evaluated the effects of a Mediterranean diet on blood pressure in the PREDIMED (PREvención con DIeta MEDiterránea) trial in Spain, which included a large cohort of men and women at high cardiovascular risk.[132] The two intervention groups received individual and group education on an energy-unrestricted Mediterranean diet from registered dietitians, as well as regular supplies of either extra-virgin olive oil or mixed nuts. The control group received a similar format of education on a low-fat diet. Statistically significant improvements in DBP, but not SBP, were found for both intervention groups when compared to controls at four years.[132] Furthermore, the two groups randomized to the Mediterranean diet experienced a significant 28-30% reduction in major cardiovascular events (MI, stroke, or death from cardiovascular causes).[133]

The PREDIMED trial was subsequently retracted and republished in 2018 due to issues with the randomization process.[134] One site enrolled household members without randomization. Another assigned entire clinics to an intervention group rather than individual participants. A third site reported inconsistent use of randomization tables. In the republished paper, data was reanalyzed to account for correlations within families or clinics. The authors also reported a reanalysis of data after exclusion of participants known or suspected to have been improperly randomized. Reported results were similar after these corrections.

As this is a *Not Reviewed, Not Changed* recommendation, the Work Group did not systematically review new evidence related to this recommendation as part of this guideline update. Confidence in the quality of evidence is low based on evidence put forth in the 2014 VA/DoD HTN CPG.[132] Issues with the randomization process of the PREDIMED trial were reported, but the corrected results were similar to those initially published.[134] Additional research is warranted to confirm these results, as well as to test the Mediterranean diet in RCTs of more diverse populations and against controls with more dissimilar baseline characteristics and intervention dietary patterns. Based on the available evidence, the benefits of this intervention outweigh the harms. Patient preferences vary regarding dietary modification; interested patients may prefer one dietary pattern over another. A Mediterranean-style dietary pattern may be beneficial to patients with HTN. It presents a viable alternative to the DASH diet for those who find lower fat diets unpalatable, have additional cardiovascular risk factors, or otherwise

prefer the Mediterranean dietary pattern. Referral to a registered dietitian, when available, may help patients achieve the desired changes.

D. Pharmacological Treatment

a. For Hypertension

Recommendation

23. We recommend offering a thiazide-type diuretic, calcium channel blocker, or either an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker as primary pharmacologic therapy for hypertension for reduction in composite cardiovascular outcomes. **(Strong for | Reviewed, New-replaced)**

Discussion

The effects of the various antihypertensive drug classes on reducing composite cardiovascular outcomes, and not just differences in blood pressure lowering effect, were the focus for the recommendation. The SR and meta-analysis of 50 RCTs by Thomopoulos et al. (2015) was the key body of evidence reviewed to recommend these four main drug classes as initial therapy for HTN.[135] Head-to-head comparisons of different antihypertensive drug classes were made for the critical and important outcomes. The components of the critical outcome from the SR included the composite of fatal or nonfatal stroke and CHD events (coronary death and nonfatal MI), both with and without hospitalizations for heart failure. In patients with HTN, the SR found that angiotensin-converting enzyme inhibitors (ACEIs) were equivalent to angiotensin II receptor blockers (ARBs); ACEIs were equivalent to thiazide-type diuretics; and calcium channel blockers (CCBs) were equivalent to thiazide-type diuretics for composite cardiovascular outcomes. No significant differences in the critical outcome were found for the comparisons of ACEIs and CCBs or ARBs and CCBs. This does not imply equivalency, only that a conclusion could not be determined. No critical outcomes were noted for ARBs versus thiazide-type diuretics.[135]

The Work Group did not make a formal recommendation for other outcomes such as stroke or heart failure reduction alone. However, there were an extensive number of comparisons that addressed other outcomes. Notable findings were that thiazide-type diuretics were superior to the other drug classes for preventing CHF outcomes, CCBs were superior to the other drug classes for reducing all-cause mortality, and CCBs were inferior to other drug classes at preventing CHF outcomes.[135] ACEIs and ARBs are not used concomitantly, due to well-recognized safety risks, as discussed in Recommendation 26.

Although the evidence was not supportive of a recommendation, providers can consider beta blockers as an alternative to the four main antihypertensive classes for patients with compelling indications, including those with underlying CAD, following MI, and in heart failure with reduced ejection fraction. Patients who are intolerant to the four main antihypertensive drug classes may also consider a beta blocker. The SR found beta blockers were equivalent to ARBs for the composite cardiovascular outcomes and reported no significant difference between beta blockers and CCBs or thiazide-type diuretics. There were no critical outcomes reported for beta blockers compared to ACEIs. Some important outcomes showed beta blockers were inferior to the other drugs classes, particularly for stroke reduction.[135] Beta blockers are not recommended as initial antihypertensive therapy, as the evidence is mixed as to whether there is a clear benefit in reducing cardiovascular events.

Thomopoulos et al. (2015) did not evaluate differences in adverse events.[135] However, the Work Group determined that the benefits of the reduction in composite cardiovascular outcomes outweighed the harms, including both the AEs associated with pharmacologic therapy (e.g., orthostatic hypotension, increases in serum creatinine, hyperkalemia, other metabolic concerns) and the alternative of not receiving drug treatment.

Although the four main drug classes for initial therapy were supported by the evidence base, there is still some variation, as individual patients may show differences in personal choices, including tablet burden and frequency of medication administration. Additionally, patient-to-patient variation in tolerability of AEs can be a factor when choosing a particular antihypertensive drug class. This variability was also supported by the patient focus group, during which some of the patients indicated that providers focused on pharmacological therapies, rather than providing information and education on non-pharmacologic treatments.

An important implication in terms of resource use is cost. Drug copayments for VA and TRICARE beneficiaries vary depending on factors such as dispensing venue (e.g., military treatment facilities [MTF] versus mail order) and whether a generic versus branded formulation is dispensed. Cost may be less of an issue for active duty personnel, who receive their medications at no cost.

The Work Group agreed on a "Strong for" recommendation due to the robust and extensive body of evidence from RCTs, meta-analyses, and SRs supporting use of the four main antihypertensive drug classes.[135] This is considered a *Reviewed, New-replaced* recommendation, as new evidence from the SR focused on composite cardiovascular outcomes, in contrast to the 2014 VA/DoD HTN CPG recommendation for which the primary literature was evaluated to recommend thiazide-type diuretics as first-line.

The confidence in the quality of evidence was moderate, as the authors of the SR adjusted outcomes so that the blood pressure reductions in each drug class were similar.[135] This led to the conclusion that antihypertensive drugs from the same classes have the same blood pressure lowering effect, which may or may not be true.

Thomopoulos et al. (2015) did not include the same individual components of the critical outcome in the SR as the guideline-defined composite cardiovascular outcome (which was comprised of cardiovascular and all-cause mortality, stroke, CHF, kidney function, safety and blood-pressure lowering).[135] However, overall, the consensus of the Work Group was that the critical outcome results supported that the four antihypertensive drug classes produced similar effects on reducing composite cardiovascular events.

Recommendation

24. In African American patients with hypertension, we recommend against using an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker as monotherapy.
    (Strong against | Not Reviewed, Not Changed)

Discussion

In addition to being recommended as primary pharmacologic therapy for HTN for reduction in composite cardiovascular outcomes in this CPG (see Recommendation 23), a thiazide-type diuretic or CCB are

appropriate initial choices for African Americans with HTN.[136] Of the 33,357 participants in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) trial, 35% were African American.[137] A subgroup analysis of this patient population found that the ACEI (lisinopril) was less effective in lowering blood pressure than the thiazide-type diuretic (chlorthalidone) or the long-acting dihydropyridine (LA DHP) CCB (amlodipine).[136] Although there was no significant difference between an ACEI or thiazide-type diuretic in the primary outcome of combined fatal CHD or nonfatal MI, the subgroup analysis of African American patients found that those participants randomized to the ACEI versus the thiazide-type diuretic were at a 40% greater risk of stroke, 30% greater risk of heart failure, 19% greater risk of CVD, and 15% greater risk of combined CHD.[136] There was no difference in major CVD outcomes between the thiazide-type diuretic and the LA DHP CCB in the subgroup of African American patients, other than a higher incidence of heart failure with the CCB.[136] The ALLHAT study also found that African American patients randomized to the LA DHP CCB (amlodipine) had greater adherence to treatment and required fewer medications to reach the blood pressure goal than those randomly assigned to the ACEI (lisinopril).[138] Additionally, the Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study reported that African Americans prescribed a beta-blocker (atenolol) had better cardiovascular outcomes than those prescribed an ARB (losartan).[139]

In the African American Study of Kidney Disease and Hypertension (AASK), ACEIs were found to be more effective than beta-blockers or LA DHP CCBs in slowing glomerular filtration rate (GFR) decline among African American patients with proteinuria.[140] The AASK trial would suggest that African Americans with CKD should be placed on an ACEI, but the ALLHAT study reported that chlorthalidone was superior to lisinopril for CVD outcomes in African Americans.[141] Therefore, for African American patients with CKD on monotherapy with an ACEI or an ARB, the addition of a thiazide-type diuretic would be appropriate as additional therapy to augment the cardiovascular protection of diuretics to the kidney protection of ACEIs or ARBs. Providers may refer to the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease[13] for further discussion of use of an ACEI or ARB in patients with CKD.

In addition, the potential for increased risk of AEs with blood pressure medication was a concern noted among the participants in the patient focus group. Although not included in the previous evidence review, the Work Group noted the potential for harm with an ACEI in African American patients due to an increased risk for angioedema reported to be up to five times greater than in white patients. Of the patients randomized to an ACEI in ALLHAT, angioedema was reported as a serious adverse event more frequently in the subgroup of African American patients (0.72%) compared to non-African American patients (0.31%), and more frequently than African American patients receiving treatment with a thiazide-type diuretic (0.04%) or a LA DHP CCB (0.06%).[136] Per FDA product information, angioedema has been reported rarely in patients treated with an ARB. Additional research is needed to determine the risk in African American patients and/or patients who have previously experienced angioedema while on an ACEI. Additional considerations include potential compelling indications for use of an ACEI or ARB in patients with HTN and comorbidities.

As this is a *Not Reviewed, Not Changed* recommendation, the Work Group did not systematically review evidence related to this recommendation. Based on the evidence review from the 2014 VA/DoD HTN CPG,

[13] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/cd/ckd/index.asp

the Work Group's confidence in the quality of the evidence is high.[136-141] Other considerations regarding this recommendation include the potential for harm (from a rare but serious adverse event) as well as reduced benefit in this patient population (i.e., reduced outcome benefit and less blood pressure reduction compared to alternative treatments). Patient values and preferences were considered to be similar. Thus, the Work Group decided to carry forward the "Strong for" recommendation against use of an ACEI or ARB as monotherapy in African American patients with HTN. It is appropriate to add an ACEI or ARB to a thiazide-type diuretic and/or a CCB for this population.

Recommendation

25. In hypertensive patients 65 years and over, we suggest a thiazide-type diuretic for reduction in composite cardiovascular outcomes.
    (Weak for | Reviewed, New-added)

Discussion

In hypertensive patients over the age of 65, treatment with a thiazide-type diuretic compared to other treatment options has been shown to reduce a composite cardiovascular outcome which included heart failure and stroke.[142] In this same meta-analysis, beta-blockers performed worse than all other therapies and CCBs, ACEIs, and ARBs had no significant difference in the composite outcome for patients over the age of 65 compared to other therapies. It is important to note that the age of 65 is an arbitrary cut-off that was used in this single meta-analysis. Individual trials have used various age cut-offs for enrollment. Furthermore, this meta-analysis reported similar outcomes with an age cut-off of 60, as compared to 65. Large RCTs are consistent with this recommendation, specifically ALLHAT which is especially pertinent to VA/DoD providers due to the more than 7,000 Veterans included in the study.[137] Of note, ALLHAT enrolled patients age 55 and over and demonstrated improved CVD outcomes with chlorthalidone compared to amlodipine or lisinopril. Harms of thiazide-type diuretics versus other therapies were considered, but a meta-analysis of adverse events did not demonstrate any significant difference between thiazide-type diuretics and other therapies.[142] In general, the evidence supports the use of thiazide-type diuretics in older patients with HTN over other classes of medication.

While there is strong evidence that thiazide-type diuretics in general reduce a composite cardiovascular outcome, there is significant variability between agents in the thiazide-type diuretic class. The strongest trial evidence for improved CVD outcomes with thiazide-type diuretics involves chlorthalidone and indapamide, from ALLHAT and the Hypertension in the Very Elderly Trial (HYVET), respectively.[137,143] In Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH), ACEI/CCB combination was favored over an ACEI/thiazide-type diuretic combination.[144] The dose and type of the thiazide-type diuretic in ACCOMPLISH (hydrochlorothiazide [HCTZ] 12.5-25 mg/day) was lower than equipotent doses of chlorthalidone or indapamide. For initial or add-on treatment of HTN, chlorthalidone and indapamide result in greater decreases of blood pressure compared to low doses (12.5-25 mg/day) of HCTZ. For these reasons, chlorthalidone or indapamide is preferred over HCTZ when choosing a thiazide-type diuretic. Patient preferences may vary based on the requirement for laboratory monitoring with thiazide-type medications.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[137,142-144] The Work Group's confidence in the quality of the

evidence is moderate. The body of evidence had some limitations including an assumption of class effect between all thiazide-type diuretics, inconsistent results across different composite outcomes, and an age cut-off that did not match the primary study evidence.[137,142-144] Other considerations regarding this recommendation included the benefits, primarily in the composite cardiovascular outcome, outweighing the potential harm of adverse events, which was insignificant compared to other therapies. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

More research is needed into the comparative effectiveness of different medications in the thiazide-type diuretic class.

Recommendation

26. We recommend against more than one of the following three drug classes together in the same patient: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or direct renin inhibitors.
    (Strong against | Not Reviewed, Not Changed)

Discussion

Despite the potential for additional blood pressure reduction with combination therapy of agents that act at the renin-angiotensin system (ACEIs, ARBs, and direct renin inhibitors [DRIs]), data from clinical trials have reported an increased risk for harm (including hypotensive symptoms, kidney dysfunction or acute kidney injury events, or hyperkalemia) without long-term cardiovascular or kidney outcome benefit in patients treated with combination therapy with any two of these three classes compared to monotherapy.[145-147] Although these trials primarily studied high-risk patients (those with at least one of the following conditions: vascular disease, diabetes, CKD, or diabetic nephropathy), the majority of patients either had a diagnosis of HTN or were being treated with antihypertensive medications.[145-147]

As this is a *Not Reviewed, Not Changed* recommendation, the Work Group did not systematically review evidence related to this recommendation. Based on the evidence reviewed during the 2014 VA/DoD HTN CPG update, the Work Group's confidence in the quality of the evidence was moderate.[147] Two additional studies that were not part of the 2014 VA/DoD HTN CPG evidence review, but were included in the previous discussion, provide support for the lack of benefit and potential harm with combination therapy.[145,146] Other considerations regarding this recommendation include the potential harm of adverse events, which was significant, and lack of outcome benefit, outweighing the minimal potential benefit of additional blood pressure reduction. Patient values and preferences were considered to be similar. The Work Group decided to carry forward the "Strong against" recommendation against use of combination therapy with an ACEI, ARB, or DRI, so as to inform providers of the rationale against this practice.

Recommendation

27. For the treatment of hypertension, there is insufficient evidence to recommend for or against initiating combination therapy over initiating monotherapy with the sequential addition of another medication.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Combination therapy for treating HTN is common. The ACCOMPLISH study confirmed that combination therapy is safe and effective.[144] Patients in ALLHAT often utilized combination therapy,[137] with only 26% of participants reaching goal blood pressure (<140/90 mm Hg) with monotherapy.[148] Generally speaking, larger reductions of blood pressure (e.g., 20/10 mm Hg or more) often require at least two medications to achieve blood pressure control, and initiating therapy with two drugs is effective and well tolerated, apart from a slight increase in dizziness incidence for some combination dosing, in most patients.[149]

However, evidence is lacking on the effect of various treatment approaches on important primary outcomes (e.g., mortality, cardiovascular events, stroke). Specifically, additional studies are needed on initiating therapy with one drug and sequentially titrating agents compared to starting two drugs simultaneously and titrating as necessary. The systematic evidence review conducted for this CPG update did not identify any studies that met inclusion criteria. From a practical perspective, providers and patients—depending on their preferences as well as a patient's comorbid conditions and the anticipated magnitude of blood pressure lowering—may wish to consider combination therapy when selecting initial therapy. Initial combination therapy may reduce the number of titrations and visits to achieve blood pressure goal. Patients with a compelling indication for more than one class of antihypertensive agent may benefit from initial combination therapy, as well. Additionally, combination pills, when available, may reduce medication co-payments for some patients. Whether using sequential or initial combination therapy, providers should attempt to achieve dosing ranges that have been found to impact important clinical outcomes.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically searched for evidence related to this recommendation in the evidence review conducted as part of this guideline update; however, no evidence met inclusion criteria. Therefore, this recommendation is based on evidence cited in the 2014 VA/DoD HTN CPG.[137,144,149] The Work Group determined there is some variation in patient values and preferences as some patients may prefer reducing the number of pills but fixed-dose combination therapy may not always be available (e.g., in the desired drug combination or strength) or prescribed.

b. For Resistant Hypertension

Recommendation

28. For patients with resistant hypertension (defined as those who are not adequately controlled with maximally tolerated dose of triple therapy [i.e., a thiazide-type diuretic, calcium channel blockers, and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker]), we suggest adding spironolactone in those patients without contraindications.
    (Weak for | Reviewed, New-replaced)

Discussion

The mineralocorticoid receptor antagonist (MRA) spironolactone more effectively reduced SBP and DBP compared to placebo when added as the fourth agent to the treatment regimen of patients with resistant HTN (RHT).[150,151] In patients with a history of hyperkalemia and diminished renal function, spironolactone should be used cautiously and with frequent monitoring of potassium and renal function in

RHT patients, and should be avoided altogether in patients with eGFR less than 30 ml/min/1.73M^2 or a serum potassium greater than 5.0 mEq/L. Since spironolactone has both antiandrogenic and endocrine effects, it should also be used cautiously in patients with menstrual irregularities, breast pain or gynecomastia.

Two SRs that included five RCTs of 662 patients with RHT and four RCTs of 553 patients with RHT, respectively, compared spironolactone to placebo or to ramipril.[150,151] Compared to placebo, spironolactone reduced office SBP/DBP by an average of 15.73/6.21 mm Hg and 24-hour ambulatory or home SBP/DBP by 8.70/4.12 mm Hg.[150] More limited studies of another MRA, eplerenone,[152] and an epithelial sodium channel blocker, amiloride,[153] suggest that they have qualitatively similar effects on blood pressure as spironolactone in patients with RHT. Compared with clonidine or spironolactone, the addition of other antihypertensive drugs (notably candesartan, doxazosin, bisoprolol, ramipril, atenolol, or alpha methyldopa) to the three-drug regimen of patients with RHT were less effective in reducing blood pressure.[150,154] It should be noted, however, that there are no studies which directly compare either amiloride or eplerenone with spironolactone in patients with RHT. From a safety perspective, spironolactone, eplerenone, and amiloride all consistently resulted in a modest increase in serum potassium.

The longest period of evaluation of the effect of spironolactone, another antihypertensive drug, or placebo on blood pressure in these RCTs was 24 weeks. Thus, it was not possible to determine the effect of the drugs on cardiovascular outcomes. However, one RCT, the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial (TOPCAT), included patients who met the criteria for RHT.[155] A subset of 403 of the study participants from the Americas (U.S., Canada, Argentina, and Brazil) had RHT; 1,361 patients without RHT served as the comparator group. Patients were treated for an average of 2.92 years with either spironolactone or placebo in addition to their three-drug therapy. SBP in the spironolactone group was lower than in the placebo group at four weeks and remained significantly lower for at least eight months. The significantly greater reduction in the primary endpoint in spironolactone- versus placebo-treated patients was comparable in those with and without RHT.

The evidence on which this recommendation is made is derived from three SRs and two independent RCTs that were not included in the SRs.[150-152,154,155] A third open-label study documented the blood pressure lowering effect of amiloride in a subset of 146 RHT patients who had already been treated with spironolactone, placebo, bisoprolol, or doxazosin in the Pathway-2 RCT.[153] The results of this substudy were not included in the three SRs since it was published later. The Work Group did not consider this substudy in its development of the recommendation or determination of the confidence in the quality of the evidence. Among the five RCTs included in the SR by Liu et al. (2017) spironolactone consistently lowered office and ambulatory or home SBP and DBP in the pooled analysis.[150] In this analysis, spironolactone also lowered SBP by 4.5 mm Hg compared to atenolol, candesartan, or alpha methyldopa, a statistically significant effect. The strength of evidence to support the efficacy of spironolactone to lower both SBP and DBP compared to either placebo or other drugs previously listed was considered to be high with a low risk of bias. Similar conclusions were reached after review of the SR by Wang et al. (2016).[151] In contrast, the strength of the evidence represented by the 19 studies of 2,758 patients with RHT in the SR by Makai et al. (2017) was very low.[152] Studies of both spironolactone and eplerenone (MRAs) were combined for this analysis so it was impossible to determine if the efficacy of each was equivalent to the

other. Furthermore, the collective risk of bias among the studies was considered to be a serious limitation even though 24-hour SBP and DBP were significantly reduced when assessed by ABPM but not by office DBP. When Krieger et al. (2018) compared the effects of clonidine on office and 24-hour blood pressure with those of low-dose spironolactone in patients with RHT with multiple comorbidities excluded, there were no significant differences but there was considerable variability in the responses of the patients.[154] Collectively, there was sufficient concern about either imprecision or risk of bias among the SRs and RCT supporting the addition for adding spironolactone as the preferred fourth agent in patients with RHT still not controlled on three drugs to make only a "Weak for" recommendation. Although of considerable clinical interest, the findings that spironolactone reduced cardiovascular outcomes in the TOPCAT cohort with preserved ejection fraction heart failure and RHT similarly to those without RHT was not considered in the above assessment because of the serious limitations of the study design as well as serious imprecision.[155] In addition, it is likely that this population of preselected patients with heart failure are phenotypically different from other patients with RHT.

Before adding a fourth drug to the treatment regimen, medication adherence should be assessed and the benefits of non-pharmacologic therapy should be reinforced in every patient who meets the criteria for RHT. Because of the frequency with which medication non-adherence occurs in this population, the term "apparent treatment resistant hypertension" has appeared in the literature with increasing frequency. If addition of spironolactone is being considered, it should be remembered that spironolactone will interfere with the tests that are ordered as part of the evaluation for hyperaldosteronism, a secondary form of HTN. If a secondary HTN workup is planned, initiation of therapy with spironolactone should be delayed until that workup is complete.

Drugs other than spironolactone may be more appropriate for the RHT patient who has a history of hyperkalemia, has significantly impaired kidney function, sexual dysfunction, or has developed either mastodynia or gynecomastia upon exposure to this drug in the past. A number of different drugs are available for the RHT patient whose blood pressure remains uncontrolled.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed the evidence related to this recommendation. The following three SRs or meta-analyses [150-152] and two RCTs [154,155] identified in the evidence review conducted as part of this guideline update were evaluated in detail. The strengths and weakness of the data in this literature are summarized above. The benefits of taking once-daily spironolactone outweighs the potential for AEs when the RHT patient is chosen carefully and monitored closely as therapy is initiated.

Epidemiologically, patients who meet the criteria for RHT are at increased risk for fatal and non-fatal cardiovascular events. Yet there are no outcome data to guide the clinical practitioner on which fourth-line drug will have the greatest effect on cardiovascular events. Furthermore, little is known about the impact of age, gender, and comorbidities like diabetes, CKD, CAD, or prior stroke on the response to specific medications in patients with RHT.

VIII. Research Priorities

During the development of the 2020 VA/DoD HTN CPG, the Work Group identified numerous areas for future research, including areas requiring stronger evidence to support current recommendations as well as research exploring new areas to guide future CPGs.

A. Automated Office Blood Pressure and Out-of-office Blood Pressure

Out-of-office blood pressure measurements were shown to be superior to routine office blood pressure measurements in predicting cardiovascular events; therefore, future studies should focus on impact of blood pressure management based on out-of-office blood pressure measurements on clinically relevant outcomes in hypertensive individuals. Further research is also needed to evaluate whether patient-related outcomes can be improved with management of HTN in the general population based on blood pressure targets obtained with AOBP that is being increasingly recognized as equivalent to out-of-office blood pressure. Additionally, variation in appropriate management for blood pressure variation by time of day and season should be included in future studies to determine the clinical significance.

B. Self-monitoring of Blood Pressure

Areas of research include the development of protocols allowing for self-management and self-adjustment of antihypertensive medications by hypertensive individuals, based on home self-monitoring of blood pressure and provider guidance. Furthermore, it is important to identify what specific hypertensive populations (demographic characteristics and comorbidities) would benefit the most from self-monitoring of blood pressure and what outcomes (blood pressure control, adherence, cardiovascular outcomes) may be improved with self-monitoring of blood pressure.

C. New Technology

Future research on application of new technology in management of HTN should include incorporation of telemonitoring using smartphone applications and other technology to improve patients' adherence to medications and enable communication with healthcare providers to maximize access to treatment.

D. Interdisciplinary Approaches

HTN treatment requires a complex approach combining prescription drug management, implementation of a healthy lifestyle and diet, and monitoring of adherence to these interventions. Therefore, high quality randomized trials are needed to evaluate cost-effectiveness and impact on patient-related clinical outcomes of protocolized nurse-led and pharmacist-led antihypertensive medication titration programs, and the role of registered dietitian-led interventions targeting healthy lifestyle changes and diet, and adherence monitoring for improving blood pressure control and patient-centered outcomes.

E. Diet and Exercise

Most of the evidence supports modest reduction in blood pressure with low sodium diets; however, clinical trials are needed to evaluate whether long-term cardiovascular outcomes can be also affected by low sodium diets, and whether it is the low sodium diet itself or low sodium intake as a part of an overall healthy dietary pattern which leads to improved clinical end-points.

Despite general belief that a reduction in sedentary time results in lowering of blood pressure, there is a paucity of clinical data about optimal duration, frequency and specific type(s) of exercise that would result in improved patient outcomes. Clinical trials are required to address these research questions.

F. Obesity and Hypertension

Growing rates of obesity call for additional research on blood pressure lowering as well as cardiovascular benefits of weight loss interventions, including pharmacological therapy and bariatric surgery in obese hypertensive individuals. Trials with long-term follow up are especially important to evaluate sustainability and impact of weight-lowering interventions in patients with obesity and HTN.

G. Pharmacotherapy

Combination antihypertensive therapy may allow for use of lower doses of individual agents and, therefore, minimize adverse drug effects. However, clinical trials are needed to evaluate whether (and which specific) combination of antihypertensive agents and at what doses are more effective than a maximum-level dose of a single agent for blood pressure control and medication adherence. Clinical trials should also focus on comparative effectiveness of (1) equivalent doses of chlorthalidone and hydrochlorothiazide, and (2) newer antihypertensive agents, such as vasodilatory beta-blockers in essential HTN.

Management of RHT is a rapidly expanding area and future studies with long-term follow-up that would allow evaluation of clinical outcomes are needed to establish optimal fourth-line antihypertensive agents in RHT and whether variations in patient characteristics may necessitate differential approaches to a fourth-line agents for RHT.

H. Screening for Asymptomatic Hypertension-mediated Target Organ Damage

Despite clinically sound concerns about target organ damage resulting from HTN and routine screening for asymptomatic CVD and kidney disease that is done by many general practitioners, there is a paucity of evidence to support this practice. Future studies are needed to evaluate cost effectiveness and clinical impact of routine screening for asymptomatic target organ damage in hypertensive individuals. For example, coronary artery calcification (CAC) score carries prognostic value in hypertensive patients. However, additional research should address whether CAC scores can direct initiation of antihypertensive therapy and dictate individualization of blood pressure management and goals.

Appendix A: Evidence Review Methodology

A. Developing the Scope and Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying KQs to guide the systematic review of the literature on HTN. These questions, which were developed in consultation with the Lewin Team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 provides a brief overview of the PICOTS typology.

Table A-1. PICOTS [156]

PICOTS Element	Description
Population, Patients, or Problem	A description of the patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
Comparison	Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
Outcome	Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
Timing, if applicable	Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
Setting, if applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

Abbreviation: PICOTS: population, intervention, comparison, outcome, timing and setting

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. Table A-2 contains the final set of KQs used to guide the SR for this CPG.

Once the KQs were finalized, the Work Group rated and prioritized the outcomes they had defined for each KQ based on how important the Work Group judged each outcome to be. Rating outcomes by their relative importance can help focus attention on those outcomes that are considered most important for clinical decision making when making judgements regarding the overall quality of the evidence to support a recommendation.[157]

Using GRADE methodology, the Work Group rated each outcome on a 1-9 scale (7-9, critical for decision making; 4-6, important, but not critical, for decision making; and 1-3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see Outcomes); however, only outcomes judged to be critical were used to determine the overall quality of evidence (see Grading Recommendations).

a. Population(s)

- Adult patients (≥18 years of age) with (management) or without (screening, primary prevention) HTN
- Including women of childbearing age, women with a history of preeclampsia, pregnant women, deployed Service Members, and patients with comorbidities (e.g., diabetes, CKD)
    - Note: Although evidence on pregnant women was included in the search, no evidence in this population was identified in the evidence review; see the VA/DoD Clinical Practice Guideline for the Management of Pregnancy for additional information regarding HTN in pregnant women[14]
- Excluding children, adolescents, and patients with unusual causes of secondary HTN (e.g., pheochromocytoma, aldosteronism)

b. Interventions

- Key Question 1
    - Interventions to diagnose and manage HTN, including white coat HTN, masked HTN, undiagnosed masked HTN
    - Home measure (self-measure), 24-hour ambulatory monitoring (daytime, nighttime, and 24-hour), AOBP
    - Different approaches to physician office manual blood pressure measurement
- Key Question 2
    - Home measure (self-measure), 24-hour ambulatory monitoring (daytime, nighttime, and 24-hour), telemonitoring, night-time home measurement
- Key Question 3
    - Bariatric surgery
    - Obesity medications approved for chronic weight management (phentermine/topiramate, lorcaserin, orlistat, naltrexone/bupropion, liraglutide)
    - Lifestyle interventions to reduce weight (only weight loss diet studies designed to reduce HTN), including dietary changes, physical activity, decrease in sedentary activities, and including intervention using behavioral modification methods
- Key Question 4
    - Lifestyle modification that involves exercise
    - Aerobic exercise, non-aerobic exercise
    - Interventions intended to reduce sedentary time
    - Weight training/ resistance (e.g., hand grip)

[14] See the VA/DoD Clinical Practice Guideline for the Management of Pregnancy. Available at: https://www.healthquality.va.gov/guidelines/WH/up/

    - Tai Chi, Qigong, yoga
- Key Question 5
    - Antihypertensive pharmacologic therapy to a specific systolic blood pressure goal or range or with the goal of reduction in blood pressure
- Key Question 6
    - Antihypertensive pharmacologic therapy to a specific diastolic blood pressure goal or range or with the goal of blood pressure reduction
- Key Question 7
    - Initial therapy: thiazide-type diuretics, ACEIs, ARBs, CCBs, beta blockers
    - Add-on therapy: a drug/class from list above that is other than the initial therapy, or other drugs/classes (e.g., spironolactone, a MRA, aka aldosterone antagonist [AA], etc.) could be used as add-on therapy
- Key Question 8
    - Initial therapy various combinations of: thiazide-type diuretic + ACEI, thiazide-type diuretic + ARB, thiazide-type diuretic + ARB, thiazide-type diuretic + beta blocker, thiazide-type diuretic + CCB, ACEI + CCB, ARB + CCB
    - Note: Interventions were not limited to combination within one tablet
- Key Question 9
    - Addition of a fourth drug (any)
    - Initial three medications should include (all in maximum tolerated doses): long-acting dihydropyridine CCB, renin-angiotensin system blocker (ACEI or ARB), thiazide-type diuretic
- Key Question 10
    - Telehealth visit with primary care or sub-specialty
    - Telehealth monitoring
    - Mobile apps
    - Instead of or in addition to usual care (in-person visits)
- Key Question 11
    - Clinical provider other than prescribers, such as clinical pharmacists, nurses, etc. (In-person or via telehealth)
    - Instead or in addition to usual care (in-person visits)
- Key Question 12
    - Screening for asymptomatic CKD with eGFR and urine protein (albumin) measurement
    - Screening for asymptomatic CAD with electrocardiogram (ECG) and calcium score

- Screening for asymptomatic left ventricular hypertrophy (LVH) with ECG and echocardiogram (ECHO)
- Screening for asymptomatic peripheral vascular disease (PVD) with carotid ultrasound (US) and ankle-brachial index (ABI)
- At diagnosis and whether should be repeated at certain intervals

c. Comparators

- Key Question 1
  - Other method of blood pressure measurement
- Key Question 2
  - No monitoring
  - Standard of care office blood pressure
  - Other forms of monitoring listed in intervention
- Key Question 3
  - Standard care
  - No intervention
  - Wait list
  - Active intervention unrelated to weight or blood pressure
  - Other intervention listed in intervention column
  - Placebo
  - Sham surgery
  - Different frequency or amount
- Key Question 4
  - Standard of care
  - No intervention
  - Wait list
  - Active intervention unrelated to blood pressure
  - Other intervention listed in intervention column
  - Different frequency or amount
- Key Question 5
  - Comparator group has a different systolic blood pressure goal or range (i.e., study arms did not need to have the same blood pressure goal or the comparator was a placebo)
  - Usual care

  - Placebo
  - No treatment
  - No goal
- Key Question 6
  - Comparator group has a different diastolic blood pressure goal or range (i.e., study arms did not need to have the same blood pressure goal or the comparator was a placebo)
  - Usual care
  - Placebo
  - No treatment
  - No goal
- Key Question 7
  - Initial therapy (where comparator is from a different class than the Intervention): thiazide-type diuretics, ACEIs, CCBs, beta blockers
  - Add-on therapy: a drug/class from list above other than initial therapy, or other drugs/ classes (e.g., MRA) could be used as add-on therapy
- Key Question 8
  - Initial therapy: thiazide-type diuretics, ACEIs, CCBs, beta blockers
  - With second drug added in at a later time from list above
- Key Question 9
  - Placebo
  - A different fourth drug (any)
- Key Question 10
  - Usual care
  - No intervention
  - Wait list
  - Active intervention unrelated to blood pressure
  - Another telemonitoring method from intervention list with a different intensity
- Key Question 11
  - Usual care
  - No intervention
  - Wait list
  - Active intervention unrelated to blood pressure

- Another intervention from intervention list with a different intensity

- Key Question 12
  - No screening

d. Outcomes

- Key Question 1
  - Critical outcomes: specificity, sensitivity, positive predictive values (PPV), negative predictive values (NPV), area under curve (AUC), etc. to diagnose and manage HTN, including white coat HTN, masked HTN, undiagnosed masked HTN
- Key Question 2
  - Critical outcomes: Reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control; adherence to therapy, percentage of patients taking medications
  - Important outcomes: composite cardiovascular (CV) outcomes; CV and all-cause mortality; strokes; reduction in CV risks; time to blood pressure control, number of office visits to achieve control
- Key Question 3
  - Critical outcomes: Reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control
  - Important outcomes: composite CV outcomes; CV and all-cause mortality; coronary events; strokes; safety; reduction in antihypertensive medications, number of antihypertensive medications
- Key Question 4
  - Critical outcomes: Reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control
  - Important outcomes: composite CV outcomes; CV and all-cause mortality; coronary events; strokes; CHF; reduction in CV risks
- Key Questions 5 and 6
  - Critical outcomes: composite CV outcomes
  - Important outcomes: CV and all-cause mortality; coronary events; strokes; CHF; renal function; safety
- Key Question 7
  - Critical outcomes: composite CV outcomes
  - Important outcomes: CV and all-cause mortality; strokes; CHF; renal function; safety; reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control

- Key Question 8
    - Critical outcomes: reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control
    - Important outcomes: composite CV outcomes; safety; time to blood pressure control, number of office visits to achieve control; adherence to therapy, percentage of patients taking medications
- Key Question 9
    - Critical outcomes: safety; reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control
    - Important outcomes: composite CV outcomes; strokes; CHF; renal function
- Key Questions 10 and 11
    - Critical outcomes: Reduction in blood pressure, change in blood pressure from baseline, achievement of lower blood pressure goals, HTN control; adherence to therapy, percentage of patients taking medications
    - Important outcomes: patient quality of life; safety, AEs/adverse events
- Key Question 12
    - Critical outcomes: composite outcomes
    - Important outcomes: CV and all-cause mortality; strokes, renal function; reduction in CV risk; diagnosis of masked HTN; dosing and drug selection decisions for antihypertensive drugs

B. Conducting the Systematic Review

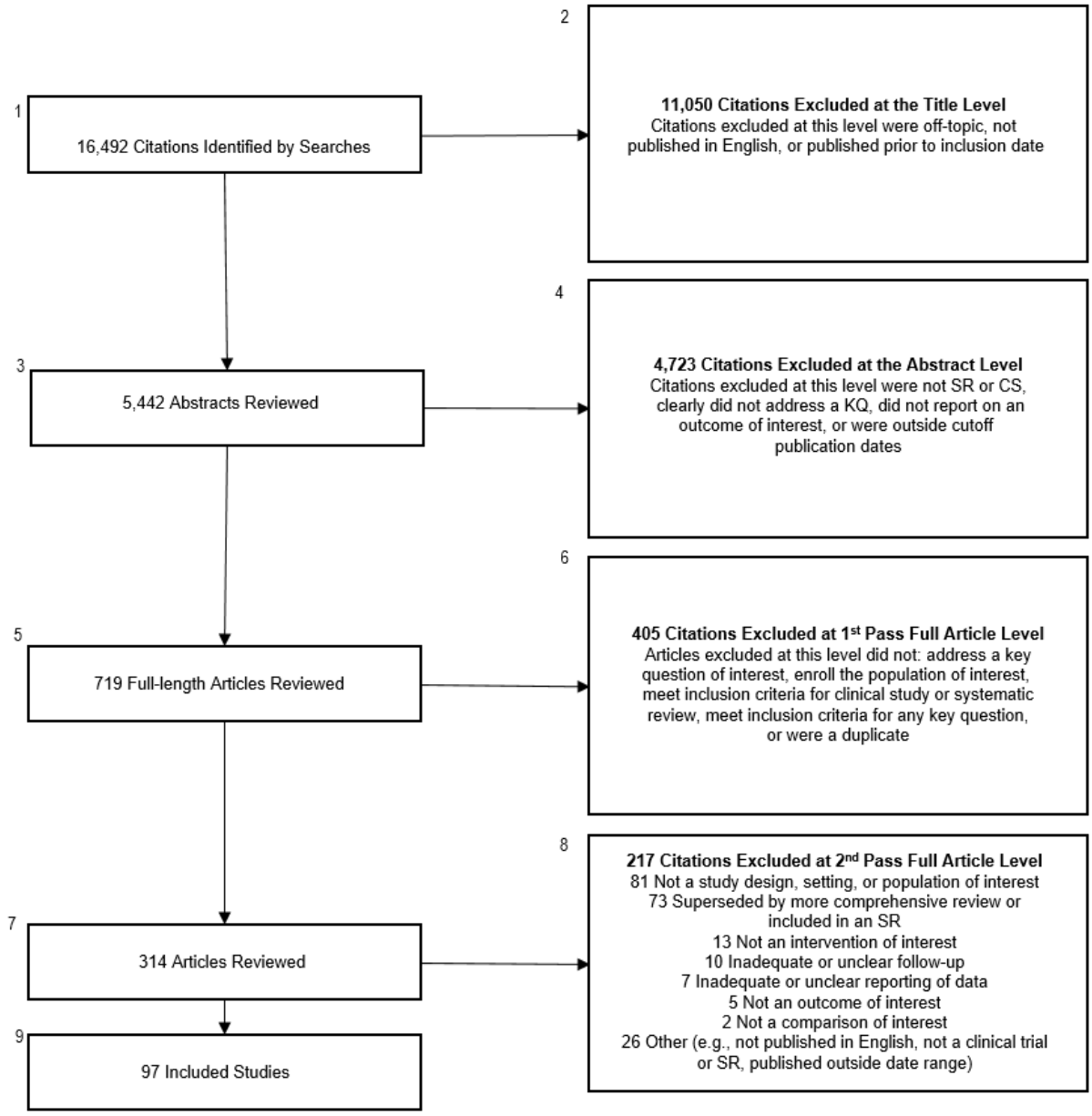
Based on the decisions made by the Champions and Work Group members regarding the scope, the KQs, and the PICOTS statements, the Lewin Team produced an SR protocol prior to conducting the review. The protocol was reviewed and approved by the Champions and Work Group members. It described in detail the final set of KQs, the methodology to be used during the SR process, and the inclusion/exclusion criteria to be applied to each potential study, including, but not limited to, study type, sample size, and PICOTS criteria.

Extensive literature searches identified 16,492 citations potentially addressing the KQs of interest to this evidence review. Of those, 11,050 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date). Overall, 5,442 abstracts were reviewed with 4,723 of those being excluded for the following reasons: not an SR or an accepted study design (see the General Criteria for Inclusion in Systematic Review and Key Question Specific Criteria), did not address a KQ of interest to this review, did not report on an outcome of interest, or published outside cut-off publication dates. A total of 719 full-length articles were reviewed. Of those, 405 were excluded at a first pass review for the following: not addressing a KQ of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or SR, not meeting inclusion criteria for any KQ, or being a duplicate publication. A total of

314 full-length articles were thought to address one or more KQs and were further reviewed. Of these, 217 were ultimately excluded and reasons for their exclusion are presented in Figure A-1.

Overall, 97 studies addressed one or more of the KQs and were considered as evidence in this review. Table A-2 indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



Abbreviations: KQ: key question; SR: systematic review

Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion/exclusion process. Arrows point down to boxes that describe the next literature

review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 16,492 citations identified by searches
    a. Right to Box 2: 11,050 citations excluded at the title level
        i. Citations excluded at this level were off-topic, not published in English, or published prior to inclusion date
    b. Down to Box 3
2. Box 3: 5,442 abstracts reviewed
    a. Right to Box 4: 4,723 citations excluded at the abstract level
        i. Citations excluded at this level were not an SR or clinical study, clearly did not address a KQ, did not report on an outcome of interest, or were outside cutoff publication dates
    b. Down to Box 5
3. Box 5: 719 full-length articles reviewed
    a. Right to Box 6: 405 citations excluded at 1st pass full article level
        i. Articles excluded at this level did not: address a key question of interest, enroll the population of interest, meet inclusion criteria for clinical study or SR, meet inclusion criteria for any key question, or were a duplicate
    b. Down to Box 7
4. Box 7: 314 articles reviewed
    a. Right to Box 8: 217 citations excluded at 2nd pass KQ level
        i. 81 not a study design, setting, or population of interest
        ii. 73 superseded by more comprehensive review or included in an SR
        iii. 13 not an intervention of interest
        iv. 10 inadequate or unclear follow-up
        v. 7 inadequate or unclear reporting of data
        vi. 5 not an outcome of interest
        vii. 2 not a comparison of interest
        viii. 26 other (e.g., not published in English, not a clinical trial or SR, published outside date range)
    b. Down to Box 9
5. Box 9: 97 included studies

Table A-2. Evidence Base for KQs

Question Number	Question	Number of Studies and Type of Studies
1	What is the optimal method for accurately measuring blood pressure?	6 SRs
2	What is the impact of blood pressure monitoring on adherence to therapy and achievement of blood pressure goals?	3 SRs 4 RCTs
3	What is the effectiveness of obesity or overweight treatment (including lifestyle modifications, medications, surgery) to prevent or treat HTN?	4 SRs 8 RCTs
4	What is the effectiveness of lifestyle modification that involves exercise (including aerobic exercise, Tai Chi or Qigong) to prevent or treat HTN? What is the optimal amount of these exercises necessary to prevent or treat HTN?	11 SRs 8 RCTs
5, 6	For adult outpatients being treated for HTN, what is the systolic (KQ5) or diastolic (KQ6) blood pressure goal that is associated with improved health outcomes?	8 SRs
7	For adult outpatients with HTN, what are the comparative effectiveness and harms of the antihypertensive drug classes thiazide-type diuretics, ACEIs, ARBs, CCBs, and beta blockers (as initial therapy, with or without add-on therapy)?	7 SRs 1 RCT
8	For adult outpatients with HTN, what is the effectiveness and comparative effectiveness and harms of initiating a combination of two or more drug classes versus initiating one drug and adding a second drug later on in selected patients?	No evidence
9	For adult patients with resistant or difficult to control HTN, what is the effectiveness and comparative effectiveness and harms of adding any antihypertensive drug to an existing drug regimen of three or more drugs?	3 SRs 2 RCTs
10	What are the effectiveness, comparative effectiveness, and harms of telehealth, mobile applications, or other new technologies to improve blood pressure control in adults with HTN?	7 SRs 5 RCTs 1 cluster RCT
11	What are the effectiveness, comparative effectiveness, and harms of less conventional forms of HTN care delivery, such as clinical pharmacists-run clinic, nurses-run clinic, using established protocols?	4 SRs 6 RCTs 5 cluster RCTs
12	For adult outpatients with HTN and prehypertension, should screening for asymptomatic HTN-mediated end-organ damage by performed?	2 SRs 2 prospective cohort studies
	Total Evidence Base	**97 studies**

Abbreviations: HTN: hypertension; RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Review

- SRs or clinical studies published on or after December 15, 2013 to March 25, 2019. If multiple SRs addressed a KQ, we selected the most recent and/or comprehensive review. SRs were supplemented with clinical studies published subsequent to the SR.
- Studies must have been published in English.
- Publication must have been a full SR or clinical study; abstracts alone were not included. Similarly, letters, editorials, and other publications that were not full-length clinical studies were not accepted as evidence.
- SRs must have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as GRADE or something compatible (e.g., the one used by the AHRQ Evidence-based Practice Centers). If an existing review did not assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of evidence. We did not use an existing review as evidence if we were not able to assess the overall quality of the evidence in the review.
- Intervention studies must have assessed pharmacological or non-pharmacological treatment and have been a prospective, RCT with an independent control group. Crossover trials were not included.
- Study must have enrolled at least 30 patients (15 per study group) unless otherwise noted (see Key Question Specific Criteria below).
- Study must have enrolled at least 85% of patients who met the study population criteria: adults aged 18 years or older who have or might be at risk for developing HTN.
- Study must have had follow-up data for at least 85% of enrolled participants.
- Study must have reported on at least one critical or important outcome of interest.

b. Key Question Specific Criteria

- For all KQs, SRs of clinical study types appropriate for the respective key question (as outlined below) were the first line of evidence
- KQ 1: RCTs and diagnostic cohort studies that reported on the diagnostic characteristics of the screening test (e.g., sensitivity, specificity, repeatability)
- KQ 2: RCTs or non-randomized, prospective comparative studies
- KQ 3, 4: RCTs, overall sample size ≥30
- KQ 5, 6, 7, 8: RCTs, total sample size ≥100
- KQ 9: RCTs or non-randomized, prospective comparative trials, total sample size ≥100; retrospective comparative trials total sample size ≥400 (minimum 200/arm)
- KQ 10, 11: RCTs
- KQ 12: RCTs, non-randomized comparative trials, and diagnostic cohort studies

c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in the table below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix J.

Table A-3. Bibliographic Database Information

Name	Date Limits	Platform/Provider
Cochrane Database of Systematic Reviews (Cochrane Reviews)	December 15, 2013 to March 25, 2019	Wiley
Cochrane Central Register of Controlled Trials	December 15, 2013 to March 25, 2019	Wiley
Database of Abstracts of Reviews of Effects	December 15, 2013 to March 25, 2019	Wiley
EMBASE (Excerpta Medica)	December 15, 2013 to March 25, 2019	Elsevier
Health Technology Assessment Database (HTA)	December 15, 2013 to March 25, 2019	Wiley
MEDLINE/PreMEDLINE	December 15, 2013 to March 25, 2019	Elsevier
PsycINFO	December 15, 2013 to March 25, 2019	OvidSP
PubMed (In-process and Publisher records)	December 15, 2013 to March 25, 2019	National Library of Medicine

C. Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and one half day face-to-face meeting of the CPG Champions and Work Group members on June 3 – 6, 2019. These experts were gathered to develop and draft the clinical recommendations for an update to the 2014 VA/DoD HTN CPG. The Lewin Team presented findings from the evidence review in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review and were asked to categorize and carry forward recommendations from the 2014 VA/DoD HTN CPG, modifying the recommendations as necessary. The members also developed new clinical practice recommendations not presented in the 2014 VA/DoD HTN CPG based on the evidence review conducted as part of this guideline update. The Work Group members were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

In addition to developing recommendations during the face-to-face meeting, the Work Group members also began to revise the 2014 VA/DoD HTN CPG algorithms to reflect the new and amended recommendations. They discussed the available evidence as well as changes in clinical practice since 2014, as necessary, to update the algorithms.

D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[18]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate,
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of clinicians will offer patients therapeutic or preventive measures as long as the advantages of the intervention exceed the risks and AEs. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease the strength. The evidence review used for the development of recommendations, conducted by ECRI, assessed the confidence in the quality of the evidence base using GRADE methodology and assigned a rating of "High," "Moderate," "Low," or "Very Low." The outcomes judged to be critical were used to determine the overall quality of evidence. Per GRADE, if the quality of evidence differs across the critical outcomes, the lowest quality of evidence for any of the relevant critical

outcomes determines the overall quality of the evidence for a recommendation; the overall confidence cannot be higher than the lowest confidence in effect estimates for any outcome that is determined to be critical for clinical decision making.[24,157]

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

Values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

Other implications consider the practicality of the recommendation, including resource use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example, statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and, depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practically of the recommendation.

The framework below (Table A-4) was used by the Work Group to guide discussions on each domain.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgment
Balance of desirable and undesirable outcomes	Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? Are the desirable anticipated effects large? Are the undesirable anticipated effects small? Are the desirable effects large relative to undesirable effects?	Benefits outweigh harms/burden Benefits slightly outweigh harms/ burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits
Confidence in the quality of the evidence	Is there high or moderate quality evidence that answers this question? What is the overall certainty of this evidence?	High Moderate Low Very low
Values and preferences	Are you confident about the typical values and preferences and are they similar across the target population? What are the patient's values and preferences? Are the assumed or identified relative values similar across the target population?	Similar values Some variation Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	Are the resources worth the expected net benefit from the recommendation? What are the costs per resource unit? Is this intervention generally available? Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? Is there lots of variability in resource requirements across settings?	Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains.[158] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low.[18] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh

undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a specific therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option …")
- Weak For (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak Against (or "We suggest not offering this option …")
- Strong Against (or "We recommend against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

E. Recommendation Categorization

a. Recommendation Categories and Definitions

A set of recommendation categories was adapted from those used by NICE.[21,22] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2014 VA/DoD HTN CPG. The categories and definitions can be found in Table A-5.

Table A-5. Recommendation Categories and Definitions*

Evidence Reviewed*	Recommendation Category	Definition
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) [21] and Garcia et al. (2014) [22]

Abbreviation: CPG: clinical practice guideline

b. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2014 VA/DoD HTN CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline, but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

The "Reviewed, Not Changed" category was used for recommendations carried forward to the updated CPG with review of the evidence and where no changes were deemed necessary to the recommendation language. For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the "Reviewed, Amended" recommendation category was used. This allowed for the wording of the recommendation to reflect GRADE methodology as well as for any other non-substantive (i.e., not clinically meaningful) language changes deemed necessary. The evidence used to support these recommendations was carried forward from the previous version of the CPG and/or was identified in the evidence review for the update.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

c. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without an updated SR of the evidence. Due to time and budget constraints, the update of the HTN CPG could not include a review of all available evidence on management of HTN; instead, the KQs were focused on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated SR of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," "Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the HTN CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations that were modified from the 2014 VA/DoD HTN CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, and condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2020 version of the guideline are noted in the Recommendations. The categories for the recommendations from the 2014 VA/DoD HTN CPG are noted in Appendix D.

F. Drafting and Submitting the Final Clinical Practice Guideline

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2014 VA/DoD HTN CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2014 VA/DoD HTN CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14-20 business days for internal review and comment by the

Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in the section titled Peer Review Process. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocket card, and patient summary. The final 2020 VA/DoD HTN CPG was submitted to the EBPWG in March 2020.

Appendix B: Patient Focus Group Methods and Findings

A. Methods

As part of the effort to update this CPG, VA and DoD Leadership held a patient focus group. The patient focus group was held on January 23, 2019, at the Naval Medical Center in San Diego, CA. The aim of the focus group was to further understand and incorporate the perspective of patients with HTN and who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus group delved into the patients' perspectives on a set of topics related to their HTN management, including their priorities, challenges they have experienced, the information they received regarding their care, as well as the impacts of their care on their lives.

Participants for the focus group were recruited by VA and DoD Leadership as well as by the HTN CPG Champions. Patient focus group participants were not intended to be a representative sample of VA and DoD patients. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The HTN CPG Champions and Work Group, with support from Lewin, developed a set of questions to help guide the focus group. The focus group facilitator led the discussion using the previously prepared questions as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all of the listed questions were addressed.

B. Findings

a. Provide comprehensive information and education to patients regarding their condition, management strategies, and self-management, including expanding available information on complementary and alternative therapies.

- Patients would like to be offered educational materials (e.g., pamphlets) as well as verbal communication of pertinent information related to their condition.
- Some of the patients felt that their providers did not offer the full range of management options available and seemed to prioritize pharmacologic interventions.
- Patients noted that there were many non-pharmacological management strategies that had not been offered to them and/or they were not aware of, including Tai Chi, yoga, meditation, etc.
- Some of the patients felt that their providers did not consider all of their individual, unique characteristics that could impact their high blood pressure and management strategies.
- Several patients mentioned that they did not receive information on the harms of having high blood pressure, including the increased risk of stroke, heart disease, etc. (i.e., education on the importance of treating and managing high blood pressure).
- Patients would like communication around the AEs of medication.

- Patients raised concern over AEs of medication and some noted that they wanted to avoid use of medications, when possible.

b. Improve the method of measuring blood pressure in the office.

- Patients noted that when their blood pressure was measured by machine in the office setting, they experienced pain and uncomfortable pressure.
- Some of the patients noted that their blood pressure had to be taken twice when in the office setting, the first reading rarely being accurate.
- Patients felt that the office blood pressure readings were inaccurate; they trusted the devices they use at home more.
- There were noticeable differences between blood pressure readings when it was taken manually versus a machine.

c. Education around home monitoring devices and strategies for measurement and management, including frequency of measurement, is important.

- All patients noted that they have a device to monitor their blood pressure at home, however, none of the patients had received instruction from their provider about how to use the device to measure their own blood pressure.
- None of the patients reported having learned from their provider how often to measure their blood pressure at home; the patients all reported different frequencies of self-monitoring their blood pressure.

d. Improve communication between providers and patients, considering patient preferences regarding frequency of communication and mode of communication.

- Patients felt that providers should listen actively to their patients and take into consideration the patient's other medical conditions (e.g., co-occurring diabetes, injuries/physical limitations) and needs that may affect their treatment to provide a holistic approach to managing their HTN.
- Some patients appreciated and/or felt they would benefit from additional contact with their providers in between their annual or bi-annual visits.
- All patients were interested in telehealth modalities to improve communication with their providers and were willing to engage with providers through phone calls, email, or mobile applications.

e. All patients understood the importance of lifestyle modifications to lower their blood pressure.

- All of the patients reported closely monitoring and changing their diet when they learned of their HTN diagnosis.
- All of the patients understood that they should decrease sodium and alcohol intake and should not smoke.

- Most of the patients noted that they put a strong emphasis on staying active to improve their blood pressure.
- Patients were interested in other complementary alternative therapies to improve their blood pressure, such as meditation, yoga, and acupuncture.

Appendix C: Evidence Table

Table C-1. Evidence Table[a,b,c]

Recommendation	2014 Strength of Recommendation	Evidence	2020 Strength of Recommendation	Recommendation Category
1. We recommend screening adults for elevated blood pressure periodically.	Strong for	[29,31-34] **Additional References:** [30,35]	Strong for	Not Reviewed, Amended
2. We suggest using attended or unattended, fully automated office blood pressure measurement (programmed to wait five minutes and record the average of three measurements separated by at least 30 seconds).	N/A	[37-42] **Additional References:** [36,43]	Weak for	Reviewed, New-added
3. When fully automated blood pressure measurement is not available, we suggest measurement of blood pressure using standard technique and a properly calibrated and validated sphygmomanometer.	Strong for	[37-42] **Additional References:** [36,43]	Weak for	Reviewed, New-replaced
4. We suggest using out-of-office blood pressure monitoring methods (ambulatory 24-hour monitoring or home blood pressure measurements) to inform the diagnosis and management of hypertension.	Strong for, Weak for	[37,38,44-48] **Additional References:** [4,20]	Weak for	Reviewed, New-replaced
5. Among patients treated for hypertension, we suggest offering home blood pressure self-monitoring with co-interventions for lowering systolic and diastolic blood pressure.	N/A	[49-53]	Weak for	Reviewed, New-added

[a] Strength of Recommendation columns: Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

[b] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference needed to be identified through the evidence review carried out as part of this guideline update or included in the evidence base for the 2014 VA/DoD HTN CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation, but which were not systematically identified through a literature review. These references were not included in the evidence base for the recommendation and therefore did not influence the strength and direction of the recommendation.

[c] Recommendation Categorization column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2014 Strength of Recommendation	Evidence	2020 Strength of Recommendation	Recommendation Category
6. For all patients, including those with type 2 diabetes, we suggest treating to a systolic blood pressure goal of <130 mm Hg.	N/A	[54-57,59-61] **Additional References:** [58,62,63]	Weak for	Reviewed, New-added
7. For patients 60 years and over, we recommend treating to a systolic blood pressure goal of <150 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 150 mm Hg.	Strong For, Strong for	[54-57] **Additional References:** [58,62]	Strong for	Reviewed, Amended
8. For patients 60 years and over with type 2 diabetes, we recommend treating to a systolic blood pressure goal of <140 mm Hg with added benefit to lowering systolic blood pressure further for those between 130 mm Hg and 140 mm Hg.	Weak for	[54,59,64-68]	Strong for	Reviewed, Amended
9. For patients 30 years and over, we recommend treating to a diastolic blood pressure goal of <90 mm Hg.	Strong for	[55,69-73] **Additional References:** [74]	Weak for	Reviewed, Amended
10. We recommend offering pharmacist-led medication management as an option for patients with hypertension.	Weak for	[75-81]	Strong for	Reviewed, New-replaced
11. We suggest offering nurse-led interventions as an option for patients treated for hypertension.	Weak for	[82-88]	Weak for	Reviewed, New-replaced
12. We suggest offering registered dietitian-led nutrition interventions as an option for patients with hypertension who are or are not on medication.	Weak for	[89]	Weak for	Reviewed, New-replaced
13. We suggest technology-based interventions (e.g., e-counseling, electronic transmission of data, telemonitoring, mobile applications) for improving control of hypertension.	Weak for	[52,91-101] **Additional References:** [90]	Weak for	Reviewed, New-replaced
14. We suggest advising patients with hypertension and overweight/obesity to lose weight to improve blood pressure.	Strong for	[102-109]	Weak for	Reviewed, Amended
15. For patients with hypertension and overweight/obesity, we suggest offering a diet directed at weight loss for the treatment of hypertension.	N/A	[106-108]	Weak for	Reviewed, New-added

Recommendation	2014 Strength of Recommendation	Evidence	2020 Strength of Recommendation	Recommendation Category
16. For the treatment of hypertension, there is insufficient evidence for or against offering weight loss medications for patients with obesity and hypertension.	N/A	[103]	Neither for nor against	Reviewed, New-added
17. For the treatment of hypertension, there is insufficient evidence to suggest for or against bariatric surgery for patients with obesity and hypertension.	N/A	[104,105]	Neither for nor against	Reviewed, New-added
18. We suggest offering individual or group-based exercise for the treatment of hypertension to reduce blood pressure.	Strong for	[111-119]	Weak for	Reviewed, Amended
19. We recommend a target for aerobic exercise of at least 120 minutes per week for reduction in blood pressure.	Strong for	[120,121]	Strong for	Not Reviewed, Amended
20. We recommend a dietitian-led Dietary Approaches to Stop Hypertension Diet for the treatment or prevention of hypertension for patients with hypertension or interested patients with other cardiovascular risk factors.	Strong for	[122-124]	Strong for	Not Reviewed, Amended
21. In patients with hypertension, we recommend that sodium intake be limited to no more than 2,300 mg/day (100 mmol/day), with referral to a dietitian or other support as appropriate.	Strong for	[126,128,129] **Additional References:** [4,110,125,127,130,131]	Strong for	Not Reviewed, Not Changed
22. In patients with additional cardiovascular risk factors, such as dyslipidemia, we suggest considering a dietitian-led Mediterranean Diet as an alternative to the Dietary Approaches to Stop Hypertension Diet.	Weak for	[132] **Additional References:** [133,134]	Weak for	Not Reviewed, Not Changed
23. We recommend offering a thiazide-type diuretic, calcium channel blocker, or either an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker as primary pharmacologic therapy for hypertension for reduction in composite cardiovascular outcomes.	Strong for, Strong for	[135]	Strong for	Reviewed, New-replaced
24. In African American patients with hypertension, we recommend against using an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker as monotherapy.	Strong against	[136-141]	Strong against	Reviewed, Not Changed
25. In hypertensive patients 65 years and over, we suggest a thiazide-type diuretic for reduction in composite cardiovascular outcomes.	N/A	[137,142-144]	Weak for	Reviewed, New-added

Recommendation	2014 Strength of Recommendation	Evidence	2020 Strength of Recommendation	Recommendation Category
26. We recommend against more than one of the following three drug classes together in the same patient: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or direct renin inhibitors.	Strong against	[147] **Additional References:** [145,146]	Strong against	Not Reviewed, Not Changed
27. For the treatment of hypertension, there is insufficient evidence to recommend for or against initiating combination therapy over initiating monotherapy with the sequential addition of another medication.	Weak for	[137,144] **Additional References:** [148,149]	Neither for nor against	Reviewed, New-replaced
28. For patients with resistant hypertension (defined as those who are not adequately controlled with maximally tolerated dose of triple therapy [i.e., a thiazide-type diuretic, calcium channel blockers, and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker]), we suggest adding spironolactone in those patients without contraindications.	Strong for	[150-152,154,155] **Additional References:** [153]	Weak for	Reviewed, New-replaced

Appendix D: 2014 Recommendation Categorization Table

Table D-1. 2014 Recommendation Categorization Table[a,b,c,d,e]

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
1.1	1	p. 21	We recommend screening adults for elevated blood pressure occur periodically, preferably annually. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.*)*	Strong for	Not reviewed, Amended	Recommendation 1
1.1	2	p. 21	We suggest that screening occur at the time of routine preventive care or routine health assessment. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Weak for	Not reviewed, Deleted	--
1.2	3	p. 22	We recommend the diagnosis of hypertension be determined based on at least two blood pressure readings on two separate patient visits. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Strong for	Not reviewed, Deleted	--
1.3	4	p. 26	We recommend that blood pressure be measured with a technique recommended for the measurement of blood pressure in adults using a properly calibrated and validated sphygmomanometer. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Strong for	Reviewed, New-replaced	Recommendation 3
1.3	5	p. 26	For patients whose diagnosis of hypertension remains uncertain, we recommend offering home blood pressure monitoring to confirm diagnosis prior to beginning pharmacologic treatment. (Two to three times a day for seven consecutive days, disregard the first day and take the average of measurements.)	Strong for	Reviewed, New-replaced	Recommendation 4

[a] 2014 Location columns: The first three columns indicate the location of each recommendation within the 2014 VA/DoD HTN CPG.
[b] 2014 Recommendation Text column: The 2014 Recommendation Text column contains the wording of each recommendation from the 2014 VA/DoD HTN CPG.
[c] 2014 Strength of Recommendation column: Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.
[d] Recommendation Category column: The Recommendation Category column indicates the way in which each 2014 VA/DoD HTN CPG recommendation was updated.
[e] 2020 Recommendation column: For recommendations that were carried forward to the 2020 VA/DoD HTN CPG, this column indicates the new recommendation(s) to which they correspond.

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
1.3	6	p. 26	For patients whose diagnosis of hypertension remains uncertain, we suggest offering 24-hour ambulatory blood pressure monitoring as an alternative to home blood pressure monitoring to confirm diagnosis prior to beginning pharmacologic treatment.	Weak for	Reviewed, New-replaced	Recommendation 4
2.1	7	p. 29	We suggest offering a multi-modal approach to adherence interventions, which could include telemonitoring, multi-disciplinary group medical appointments, (e.g., shared medical appointments), case management (by pharmacists, nurses, social workers), patient and provider education, behavioral therapy, etc.	Weak for	Reviewed, New-replaced	Recommendation 10 Recommendation 11 Recommendation 12 Recommendation 13
3.1	8	p. 31	We recommend offering lifestyle modification interventions for patients with prehypertension or hypertension based on patient indications and preferences as well as assessment of available local resources. (*Modified from 2004 VA/DoD HTN CPG)*	Strong for	Reviewed, Amended	Recommendation 14 Recommendation 18
3.2	9	p. 31	We recommend discussing healthy weight range and advising overweight or obese hypertensive patients to reduce their body mass index to below 25. *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Reviewed, Deleted	--
3.2	10	p. 31	If a normal body mass index (<25) cannot be achieved, we suggest advising patient that a weight reduction of at least 10 pounds can achieve a decrease in blood pressure.	Weak for	Not reviewed, Deleted	--
3.3	11	p. 32	We recommend a target for aerobic exercise of 30 to 45 minutes per session, at least four times per week. *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Not reviewed, Amended	Recommendation 19
3.3	12	p. 32	We suggest the use of a self-monitoring device (e.g., pedometer, mobile apps, etc.) to increase adherence to physical activity.	Weak for	Reviewed, Deleted	--
3.4	13	p. 33	For patients interested in complementary and alternative medicine, we suggest considering mind-body therapies such as transcendental meditation or yoga.	Weak for	Reviewed, Deleted	--
3.4	14	p. 33	We suggest not offering Tai Chi for the treatment of hypertension as there is a moderate body of evidence that shows this intervention does not reduce blood pressure.	Weak against	Reviewed, Deleted	--

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
3.5	15	p. 33	We recommend a dietitian-led Dietary Approaches to Stop Hypertension (DASH) Diet for the treatment and/or prevention of hypertension for patients with hypertension and/or interested patients with prehypertension and other cardiovascular risk factors. *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Not reviewed, Amended	Recommendation 20
3.5	16	p. 33	In patients with additional cardiovascular risk factors, such as dyslipidemia, we suggest considering a dietitian-led Mediterranean Diet as an alternative to the DASH Diet.	Weak for	Not reviewed, Not changed	Recommendation 22
3.5	17	p. 33	We recommend against the use of soy protein supplements for the treatment of hypertension.	Strong against	Not reviewed, Deleted	--
3.6	18	p. 35	In patients with hypertension or prehypertension, we recommend that sodium intake be limited to no more than 2300mg/day (100 mmol/day), with referral to a dietitian or other support as appropriate. *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Not reviewed, Not changed	Recommendation 21
3.7	19	p. 37	We recommend advising hypertensive and prehypertensive patients to limit alcohol intake to no more than 1 oz per day for men or 0.5 oz of alcohol per day for women. (This is approximately 2 drinks/day in men and 1 drink/day in women, where a drink is 1.5 oz 80-proof liquor, 12 oz beer, or 5 oz wine [all 14g]). *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Not reviewed, Deleted	--
4.1	20	p. 37	We recommend offering pharmacologic treatment for hypertensive patients 60 years and older with a systolic blood pressure ≥ 160 mmHg.	Strong for	Not reviewed, Deleted	--
4.1	21	p. 37	We suggest considering pharmacologic treatment using a shared decision-making model for hypertensive patients 60 years and older with systolic blood pressure <160 mmHg.	Weak for	Not reviewed, Deleted	--
4.1	22	p. 37	We suggest offering pharmacologic treatment to patients with a history of cerebrovascular disease (stroke, transient ischemic attack, or asymptomatic carotid artery disease) and a systolic blood pressure ≥140 mmHg.	Weak for	Not reviewed, Deleted	--
4.1	23	p. 38	We suggest pharmacologic treatment for hypertensive patients younger than 60 with a systolic blood pressure ≥160 mmHg, regardless of diastolic blood pressure.	Weak for	Not reviewed, Deleted	--

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
4.1	24	p. 39	We recommend offering pharmacologic treatment for patients 30 years and older with a diastolic blood pressure ≥90 mmHg.	Strong for	Not reviewed, Deleted	--
4.1	25	p. 39	We suggest offering pharmacologic treatment for patients age 18 to 29 with a diastolic blood pressure ≥90 mmHg.	Weak for	Not reviewed, Deleted	--
4.2	26	p. 40	For patients 60 years and over, we recommend treating to a systolic blood pressure goal of <150 mmHg.	Strong for	Reviewed, Amended	Recommendation 7
4.2	27	p. 40	For patients below 60 years of age, we suggest treating to a systolic blood pressure goal of <150 mmHg.	Weak for	Reviewed, Deleted	--
4.2	28	p. 41	We recommend treating to a diastolic blood pressure goal <90 mmHg in patients 30 years and older.	Strong for	Reviewed, Amended	Recommendation 9
4.2	29	p. 41	We suggest treating to a diastolic blood pressure goal <90 mmHg in patients age 18 to 29.	Weak for	Reviewed, Deleted	--
4.2	30	p. 42	For patients with diabetes (all age groups), we recommend treating to a systolic blood pressure goal of <150 mmHg.	Strong for	Reviewed, Amended	Recommendation 7
4.2	31	p. 42	For patients with diabetes (all age groups) who tolerate antihypertensive drugs, we suggest treating to a systolic blood pressure goal of <140 mmHg.	Weak for	Reviewed, Amended	Recommendation 8
4.2	32	p. 42	For patients with diabetes, we recommend treating to a diastolic blood pressure goal <85 mmHg.	Strong for	Reviewed, Deleted	--
4.3	33	p. 44	We suggest that patients be seen within one month of initiation of lifestyle or pharmacological therapy to determine adequacy of hypertension control, degree of patient adherence, and presence of adverse effects. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Weak for	Reviewed, Deleted	--
4.3	34	p. 44	Once the patient's blood pressure is controlled, we suggest follow-up at least annually, or more frequently as indicated, depending on patient preference. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Weak for	Reviewed, Deleted	--
4.4	35	p. 48	We suggest taking into consideration the patient's baseline blood pressure and presence of comorbidities, when deciding on either monotherapy or combination therapy (two drugs) when initiating drug therapy. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Weak for	Reviewed, New-replaced	Recommendation 27

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
4.4	36	p.48	We suggest initiating combination therapy for patients with a baseline systolic blood pressure of >20 mmHg or diastolic blood pressure of >10 mmHg above the patient's goal. *(Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)*	Weak for	Not reviewed, Deleted	--
4.5	37	p. 49	We recommend the use of thiazide-type diuretics for the treatment of hypertension.	Strong for	Reviewed, New-replaced	Recommendation 23
4.5	38	p. 49	We suggest the use of thiazide-type diuretics at recommended treatment doses as first-line therapy for drug treatment of hypertension either as monotherapy or in combination with other agents. *(Modified from 2004 VA/DoD HTN CPG)*	Weak for	Reviewed, Deleted	--
4.5	39	p. 49	To initiate treatment of hypertension with a thiazide-type diuretic, we suggest the use of chlorthalidone or indapamide over hydrochlorothiazide.	Weak for	Reviewed, Deleted	--
4.5	40	p. 49	We do not suggest switching from hydrochlorothiazide to chlorthalidone or indapamide if the patient is adequately controlled on and tolerating hydrochlorothiazide.	Weak against	Reviewed, Deleted	--
4.5	41	p. 49	We suggest considering a switch from hydrochlorothiazide to chlorthalidone for patients whose hypertension is inadequately controlled on 50mg/day of hydrochlorothiazide.	Weak for	Reviewed, Deleted	--
4.5	42	p. 50	We recommend a dosage of 12.5-25mg/day of chlorthalidone, 25-50mg/day of hydrochlorothiazide, or a dosage of 2.5mg/day immediate-release or 1.5- 2.5mg/day sustained-release (not currently available in the US) of indapamide.	Strong for	Reviewed, Deleted	--
4.6	43	p. 51	We recommend using the following as alternative therapies for patients who cannot tolerate thiazide-type diuretics, as supplementary therapies for patients who do not reach their hypertensive goals, or for those starting on combination therapy: a. Angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers (but not together) b. Long-acting dihydropyridine calcium channel blockers *(Modified from 2004 VA/DoD HTN CPG)*	Strong for	Reviewed, New-replaced	Recommendation 23

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
4.6	44	p. 52	We recommend against the use of more than one of the following three drug classes together in the same patient: angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers, or direct renin inhibitors.	Strong against	Not reviewed, Not changed	Recommendation 26
4.6	45	p. 52	We recommend additional therapy in refractory hypertension (for those who do not tolerate or are not adequately controlled with triple therapy [i.e., thiazidetype diuretics, ACEI or ARB, and CCBs] described in Recommendation 43) or as supplementary therapy in some clinical indications. Drug classes for consideration can include (not in priority order): a. Aldosterone/mineralocorticoid receptor antagonists (e.g., spironolactone, eplerenone) b. Other potassium-sparing diuretic (i.e., amiloride) c. Alpha adrenergic blockers d. Beta adrenergic blockers e. Non-dihydropyridine calcium channel blockers f. Combined alpha-beta adrenergic blockers g. Peripherally acting antiadrenergic agents (reserpine, pending availability) h. Direct acting vasodilators (e.g., hydralazine, minoxidil) i. Centrally acting antiadrenergic drugs (e.g., clonidine, methyldopa)	Strong for	Reviewed, New-replaced	Recommendation 28
4.6	46	p. 54	We recommend against the use of alpha-adrenergic blockers as monotherapy, but this class of agents may be used as supplemental therapy or if warranted by comorbid conditions (e.g., symptomatic prostatic hypertrophy). (Modified from 2004 VA/DoD HTN CPG)	Strong against	Not reviewed, Deleted	--
4.7	47	p. 54	In patients with hypertension and chronic kidney disease (reduced kidney function with albuminuria), we recommend treatment with an angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker for improving kidney outcomes. (Modified from 2004 VA/DoD HTN CPG)	Strong for	Reviewed, Deleted	--
4.7	48	p.56	In African American patients with hypertension, we recommend against using an angiotensin-converting-enzyme inhibitor or angiotensin II receptor blocker as monotherapy.	Strong against	Reviewed, Not changed	Recommendation 24

2014 Location			2014 Recommendation Text	2014 Strength of Recommendation	Recommendation Category	2020 Recommendation
Section	Number	Page				
4.7	49	p. 56	In African American patients with hypertension and stage 1-3 chronic kidney disease, we suggest a combination of a thiazide-type diuretic (for cardiovascular protection) with either an angiotensin-converting-enzyme inhibitor or angiotensin II receptor blocker (for renal protection).	Weak for	Reviewed, Deleted	--

Appendix E: Dietary Information

Table E-1: Nutrient Composition of the Dietary Approaches to Stop Hypertension (DASH) Diet[a,b] [159]

Nutrient	Recommended Intake
Saturated fat	6% of total calories
Total fat	27% of total calories
Carbohydrate	55% of total calories
Dietary fiber	30 grams/day
Protein	18% of total calories
Cholesterol	150 mg/day
Total calories (energy)	Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain

[a] Additional information on the DASH diet is available at: http://www.nhlbi.nih.gov/health/health-topics/topics/dash/.[159]

[b] The DASH diet was shown to be most effective in lowering blood pressure when combined with sodium restriction.[124]

Table E-2: Summary of Dietary Recommendations in the Mediterranean Diet[a] [132,160]

	Food	Goal
Recommended	Olive oil	≥4 tbsp per day
	Tree nuts and peanuts	≥3 servings per week
	Fresh fruits including natural fruit juices	≥3 servings per day
	Vegetables	≥2 servings per day
	Seafood (primarily fatty fish)	≥3 servings per week
	Legumes	≥3 servings per week
	Sofrito[b]	≥2 servings per week
	White meat	In place of red meat
	Wine with meals	≥7 glasses per week, for those who drink[c]
Discouraged	Soda drinks	<1 drink per day
	Commercial baked goods, sweets, pastries[d]	<3 servings per week
	Spread fats	<1 serving per day
	Red and processed meats	<1 serving per day

[a] Dietary patterns vary both within and among countries in the Mediterranean region, precluding a single standardized definition of the Mediterranean diet, though certain characteristic features are generally agreed upon by those studying its potential health effects; the table above represents the specific dietary recommendations used in the research study constituting our evidence base for this section of the guideline

[b] Sofrito is a sauce made with tomato and onion, and often includes garlic, herbs, and olive oil

[c] Recommended wine volume per glass: 100 mL for women, 150 mL for men

[d] Commercial baked goods, sweets, and pastries included cakes, cookies, biscuits, and custard, and did not include those that are homemade

Abbreviations: mL: milliliter; tbsp: tablespoon

Appendix F: Drug Dosage Table

Table F-1. Recommended Dosage for Selected Hypertension Drug Therapy

	Drug	Usual Dose Range	Comments[a]
Thiazide-type Diuretics	Chlorthalidone[b] HCTZ[b] Indapamide	12.5-25 mg daily 25-50 mg daily[c] IR: 2.5 mg daily	• May cause hyperuricemia/ gout • Monitor K+ levels • May cause photosensitivity (rare) • May cause hyponatremia (1-2%) • May be less effective in eGFR <30 mL/minute
Angiotensin-Converting Enzyme Inhibitors (ACEI)	Benazepril Enalapril Fosinopril Lisinopril[b] Ramipril[b]	10-40 mg/day (daily or divided bid) 5-40 mg/day (daily or divided bid) 10-40 mg daily 10-40 mg daily 2.5-20 mg/day (daily or divided bid) (10 mg daily for CV risk prevention)	• Avoid in women who are planning to become pregnant or who are pregnant; when pregnancy is contemplated or detected, discontinue as soon as possible, due to potential for fetal and neonatal morbidity and death; patients of child-bearing potential should also be educated about the risks • Do not use if history of angioedema • Avoid concomitant use of ACEI with ARB or direct renin inhibitor due to increased risk of hypotension, syncope, increased K+, and changes in kidney function (see Recommendation 26) • Monitor K+ and kidney function; use caution if combined with, K+ sparing diuretic, or K+ supplement • Consider interruption or discontinuation in patients who develop clinically significant decline in kidney function after initiation of therapy, until further work-up, as indicated (e.g., kidney artery stenosis) • Compelling indications include: CKD with albuminuria (refer to VA/DoD CKD CPG[1]); HFrEF; recent MI

[1] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

	Drug	Usual Dose Range	Comments[a]
Angiotensin II Receptor Blockers (ARB)	Azilsartan[d] Candesartan[d] Eprosartan[d] Irbesartan[d] Losartan[b] Olmesartan[d] Telmisartan[d] Valsartan[b,e]	40-80 mg daily (40 mg with diuretic) 8-32 mg daily 400-800 mg/daily (daily or divided bid) 75-300 mg daily 25-100 mg/day (daily or divided bid) 20-40 mg daily 20-80 mg daily 80-320 mg daily	• Avoid in women who are planning to become pregnant or who are pregnant; when pregnancy is contemplated or detected, discontinue as soon as possible; drugs that act directly on the renin angiotensin system can cause injury and death to the developing fetus; patients of child-bearing potential should also be educated about the risks • Avoid concomitant use of ACEI with an ARB or direct renin inhibitor due to increased risk of hypotension, syncope, increased K+, and changes in kidney function (see Recommendation 26) • In general, the lower doses should be considered in patients receiving diuretics • Monitor K+ and kidney function; use caution if combined with, K+ sparing diuretic, or K+ supplement • Consider interruption or discontinuation in patients who develop clinically significant decline in kidney function after initiation of therapy, until further work-up, as indicated (e.g., kidney artery stenosis) • Compelling indications include: CKD with albuminuria (refer to VA/DoD CKD CPG[2]); HFrEF; recent MI
Long-Acting Calcium Channel Blockers (CCB)	**DHP CCBs** Amlodipine[b] Felodipine Nifedipine sustained release[b] **Non-DHP CCBs** Verapamil sustained release[b] Diltiazem sustained release[b]	 2.5-10 mg daily 2.5-10 mg daily 30-120 mg daily 120-480 mg divided daily-bid 120-540 mg daily	• Monitor AEs (DHP CCBs may cause ankle edema, dizziness, flushing, headache, constipation) • Use with caution in patients with hepatic (CCBs) or kidney (non-DHP CCBs) dysfunction • Non-DHP CCBs may be considered for rate control in supraventricular tachycardia or atrial fibrillation/flutter • Verapamil may cause constipation; verapamil is contraindicated 2nd or 3rd degree AV block, severe LV dysfunction • Diltiazem may decrease sinus rate; diltiazem is contraindicated in 2nd or 3rd degree AV block; use with caution in LV dysfunction • Verapamil or diltiazem should not usually be used with a beta-blocker due to risk of severe bradycardia or heart block

[2] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/CKD/

	Drug	Usual Dose Range	Comments[a]
Aldosterone/ Mineralocorticoid Receptor Antagonists	Eplerenone[d] Spironolactone[b]	50-100 mg/day (daily or divided bid) 25-50 mg/daily	• Avoid use if hyperkalemia or severe kidney dysfunction • Monitor K+ and kidney function; consider risk vs. benefit if combined with ACEI, ARB, K+ sparing diuretic, or K+ supplement • Higher risk of gynecomastia with spironolactone (9%) than eplerenone (≤1%) • Compelling indications include: HFrEF • Effective in resistant hypertension
Other Potassium-Sparing Diuretics	Amiloride	5-10 mg/daily	• Avoid use if hyperkalemia or severe kidney dysfunction • Helpful in reducing hypokalemia caused by thiazide diuretics • Effective in resistant hypertension
Alpha-Adrenergic Blockers	Doxazosin Prazosin Terazosin[b]	1-16 mg/daily 2-20 mg/day (divided bid or tid) 1-20 mg daily	• Initiate at low doses (1 mg) • Administer 1st dose at bedtime to avoid syncope • Avoid use as monotherapy • May be considered for use in patients with symptomatic BPH
Beta-Adrenergic Blockers	**Noncardioselective** Propranolol **Cardioselective** Atenolol[b] Metoprolol tartrate[b] Metoprolol succinate (XL)[b] **Combined alpha-beta adrenergic blockers** Carvedilol Labetalol[d]	 Immediate release: 80-160 mg/day (divided bid) Sustained release: 80-160 mg daily 25-100 mg daily (adjust dose in CKD) Immediate release: 50-300 mg/day (daily or divided bid) Sustained release: 25-200 mg/day Immediate release[b]: 12.5-50 mg/day (divided bid) Sustained release[d]: 20-80 mg/day 200-800 mg/day (divided bid)	• Discontinue with slow taper over one week • Avoid combination with non-DHP CCB due to increased risk of bradycardia or heart attack • As doses increase, cardioselectivity decreases • Beta-blockers should be used cautiously in asthma • Compelling indications include: HFrEF (evidence available for reduction in morbidity and mortality with bisoprolol, carvedilol, metoprolol succinate in HFrEF); recent MI; angina; rate control in atrial fibrillation/flutter; data available for select beta-blockers for migraine prevention

	Drug	Usual Dose Range	Comments[a]
Direct Acting Vasodilators	Minoxidil Hydralazine[b]	2.5-100 mg/day (daily or divided bid) 50-200 mg/day (divided bid)	• Monitor for hypertrichosis, volume retention, and pericardial effusions with minoxidil • Monitor for headache and SLE (dose-related) with hydralazine • Direct acting vasodilators often require concomitant use of diuretic and beta-blocker to reduce edema and reflex tachycardia
Centrally Acting Antiadrenergic Drugs	Clonidine Tablet[b] Clonidine Patch Methyldopa	0.1-0.8 mg/day (divided bid) mg patch weekly 500-2,000 mg/day (divided bid)	• Monitor for bradycardia, somnolence, and dry mouth. Taper dose to discontinue • Clonidine patches may be useful in select patients • May rarely cause bone marrow depression, positive Coombs test, hemolytic anemia and liver disorders (hepatitis, jaundice)

[a] For complete drug information, review the manufacturer's prescribing information

[b] DoD Basic Core Formulary item

[c] HCTZ 12.5 mg may be considered as an initial dose with titration recommended to 25-50 mg daily; refer to Recommendation 25 and associated discussion for further information

[d] Item not on VA National Formulary

[e] Restricted to treatment of patients with systolic heart failure in VA

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; AE: adverse effect; ARB: angiotensin II receptor blocker; AV: atrioventricular; bid: twice daily; BPH: benign prostatic hyperplasia; CCB: calcium channel blockers; CKD: chronic kidney disease; CV: cardiovascular; DHP: dihydropyridine; eGFR: estimated glomerular filtration rate; HCTZ: hydrochlorothiazide; HFrEF: heart failure with reduced ejection fraction; K+: potassium; LV: left ventricular; mL: milliliter; SLE: systemic lupus erythematosus;

Appendix G: Guidance for Conducting Office Blood Pressure Measurement

The following information has been adapted from the 2019 AHA Measurement of Blood Pressure in Humans.[36]

Properly prepare the patient

- Have the patient relax, sitting in a chair with feet flat on floor and back supported; the patient should be seated for 3-5 minutes without talking or moving around before recording the first blood pressure reading
- The patient should avoid caffeine, exercise, and smoking for at least 30 minutes before measurement
- Ensure that the patient has emptied his/her bladder
- Neither the patient nor the observer should talk during the rest period or during the measurement
- Remove clothing covering the location of cuff placement
- Measurements made while the patient is sitting on an examining table do not fulfill these criteria

Use proper technique for blood pressure measurements

- Use an upper-arm cuff blood pressure measurement device that has been validated and ensure that the device is calibrated periodically
- Support the patient's arm (e.g., resting on a desk); the patient should not be holding his/her arm because isometric exercise will affect the blood pressure levels
- Position the middle of the cuff on the patient's upper arm at the level of the right atrium (midpoint of the sternum)
- Use the correct cuff size such that the bladder encircles 75%-100% of the arm

Table G-1. Proper Blood Pressure Cuff Sizes

Cuff Size	Arm Circumference (cm)	Bladder Dimension (width x length, cm)
Small adult	22-26	12×22
Adult	27-34	16×30
Large adult	35-44	16×36
Extra-large adult	45-52	16×42

Abbreviation: cm: centimeter

Take the proper measurements needed for diagnosis and treatment of elevated blood pressure/hypertension

- At the first visit, record blood pressure in both arms; use the arm that gives the higher reading for subsequent readings (if consistently 10-15 mm Hg higher)
- Separate repeated measurements by at least 30 seconds

Properly document accurate blood pressure readings

- Record SBP and DBP
- Note the time that the most recent blood pressure medication was taken before measurements

Use average the readings

- Use an average of ≥2 readings for the visit blood pressure
- For initial documentation of the patient's blood pressure, use an average of the visit blood pressures obtained on ≥2 occasions to estimate the individual's blood pressure

Provide blood pressure readings to patient

- Provide patients their SBP/DBP readings both verbally and in writing; someone should help the patient interpret the results

What is above should be common to each appropriate standardized office blood pressure measurement technique. The following are additional guidance specific for each technique:

For fully automated office oscillometric manometer readings:

- Preprogram the manometer to wait five minutes before inflation begins and to take and average 2-3 readings at least 30 seconds apart; the most common intervals are 30 seconds, one minute, and two minutes
- Position the patient and place the proper sized cuff on the upper arm before initiating the wait time and blood pressure readings
- Turn the manometer on and set controls to take inflate to proper level (above sensed SBP) automatically and measure and average multiple readings; press the button to initiate wait period and automated readings (fully automated)
- Patient should remain quiet and not use electronic devices (e.g., phones) during the rest period and readings; person measuring the blood pressure may remain in the room (attended) or leave the patient alone in the room (unattended), but no one should interact or speak with the patient during the rest period and readings
- After the rest and measurements are completed, record the average blood pressure reading displayed; manometer should display the average of the 2-3 readings (as preset)

For standard technique with automated oscillometric device:

- Use an upper-arm cuff oscillometric device that has been validated
- Position the patient and place the proper sized cuff on the upper arm before initiating the wait time and blood pressure readings
- Turn the manometer on and set controls to take/inflate to proper level (above sensed SBP) automatically
- Patient should remain quiet and not use electronic devices (e.g., phones), and no one should speak with the patient during the rest period and readings

- After the five-minute rest period, push the button to initiate the first inflation/reading; record SBP and DBP reading
- Take the next reading(s) with at least a 30 second interval between readings and record SBP and DBP readings displayed for each reading; record the average or median SBP and average or median DBP as the patient's blood pressure

For standard auscultatory technique with manual manometer:

- Use an upper-arm cuff manual device that has been validated and recently calibrated; this includes a mercury manometer, an aneroid manometer, or an electronic manual non-oscillometric manometer for auscultatory determinations
- Position the patient and place the proper sized cuff on the upper arm before initiating the wait time and blood pressure readings
- Patient should remain quiet and not use electronic devices (e.g., phones), and no one should speak with the patient during the rest period and readings
- Use a palpated estimate of radial pulse obliteration pressure (disappearance or resumption of pulse when cuff is inflated/deflated) to estimate SBP; inflate the cuff 20-30 mm Hg above this level to perform the auscultatory determination of the blood pressure level
- Use either the stethoscope diaphragm or bell for auscultatory readings
- After the five-minute rest period, inflate the cuff and use auscultation to determine SBP and DBP; determine SBP and DBP as the onset of the first of at least two consecutive Korotkoff sounds (beats) and the last audible Korotkoff sound, respectively
- Record the SBP and DBP reading
- Take the next reading(s) with at least a 30 second interval between readings and record SBP and DBP readings for each reading; record the average or median SBP and average or median DBP as the patient's blood pressure

Appendix H: Guidance for Conducting Home Blood Pressure Measurement

The following information has been adapted from the 2019 AHA Measurement of Blood Pressure in Humans.[36]

Patient training provided by healthcare staff or providers:

- Provide information about hypertension diagnosis and treatment
- Provide information on the proper selection of a device
- Provide instruction on how patients can measure their own blood pressure (if possible, demonstrate the procedure or instruct how to access training video)
- Provide instruction that the HBPM device and blood pressure readings (log or electronic recording) should be brought to healthcare visits
- Provide education that individual blood pressure readings may vary greatly (high and low) across the monitoring period

Preferred devices and cuffs:

- Use an upper-arm cuff oscillometric device that has been validated
- Use a device that is able to automatically store all readings, if possible
- Use a device that can print results or can send blood pressure values electronically to the healthcare provider, if possible
- Use a cuff that is appropriately sized for the patient's arm circumference

Table H-1. Proper Blood Pressure Cuff Sizes

Cuff Size	Arm Circumference (cm)	Bladder Dimension (width x length, cm)
Small adult	22-26	12×22
Adult	27-34	16×30
Large adult	35-44	16×36
Extra-large adult	45-52	16×42

Abbreviation: cm: centimeter

Best practices for the patient:

- Preparation
  - Have an empty bladder
  - Rest quietly in seated position with back supported (e.g., leaning back in chair) for at least five minutes
  - Do not talk or text

- Position
    - Sit with back supported
    - Keep both feet flat on the floor
    - Legs should not be crossed
    - Blood pressure cuff should be placed on bare arm (not over clothes)
    - Blood pressure cuff should be placed directly above the antecubital fossa (bend of the arm)
    - Center of the bladder of the cuff (commonly marked on the cuff by the manufacturer) should be placed over the arterial pulsation of the patient's bare upper arm
    - Cuff should be pulled taut, with comparable tightness at the top and bottom edges of the cuff, around the bare upper arm
    - The arm with the cuff should be supported on a flat surface such as a table
- Number of readings
    - Take two readings at least one minute apart in the morning before taking any antihypertensive medications and two readings at least one min apart in the evening before going to bed; some recommend only recording the second measurement
- Duration of monitoring
    - Preferred monitoring period is ≥7 days (i.e., 28 readings or more scheduled readings); a minimum period of three days (i.e., 12 readings) may be sufficient, ideally in the period immediately before the next appointment with provider
    - Monitoring conducted over consecutive days is ideal; however, readings taken on nonconsecutive days may also provide valid data
- Analyzing readings
    - For each monitoring period, the average of all readings should be obtained
    - Some guidelines and scientific statements recommend excluding the first day of readings; if the first day of readings is excluded, the minimum and preferred periods of HBPM should be four and eight days, respectively

For a video developed for patients by the VA and DoD with instructions on measuring blood pressure at home, please visit https://www.healthquality.va.gov/guidelines/CD/htn/ and click on the "Home Blood Pressure Monitoring" video.

Appendix I: Participant List

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Appendix J: Literature Review Search Terms and Strategy

A. EMBASE and Medline Embase.com Syntax

Question	Set #	Concept	Strategy
Questions 1 and 2 – Diagnosis and Management	#1	Blood pressure	'blood pressure'/exp OR 'blood pressure monitoring'/exp OR 'diastolic blood pressure'/exp OR 'systolic blood pressure'/exp OR 'systole'/de OR 'diastole'/de
	#2		'blood pressure':ti,ab OR 'systolic pressure*':ti,ab OR 'diastolic pressure*':ti,ab OR 'arterial pressure*':ti,ab OR bp:ti,ab
	#3		(systol*:ti,ab OR diastol*:ti,ab OR arterial:ti,ab OR sbp:ti,ab OR dbp:ti,ab) AND (pressure*:ti,ab OR mmhg:ti,ab OR 'mm hg':ti,ab)
	#4		#1 OR #2 OR #3
	#5	BP measurement, screening, or monitoring	#4 AND (monitor* OR measure* OR record* OR screen* OR test* OR evaluat* OR track*):ti,ab OR 'monitoring'/exp OR 'measurement'/exp OR screening/exp)
	#6		('blood pressure'/exp AND 'hypertension'/exp/dm_dm,dm_pc,dm_th) OR 'blood pressure monitoring'/exp OR 'blood pressure monitor'/exp OR 'blood pressure measurement'/exp)
	#7	combine	#5 OR #6
	#8	Interventions/BP methods	#4 AND ('ambulatory blood pressure'/exp OR 'ambulatory blood pressure measurement'/exp OR 'ambulatory monitoring'/exp OR 'home monitoring'/exp OR 'self care'/exp OR 'self monitoring'/exp OR 'general practice'/de OR 'health center'/de)
	#9		#4 AND (routine OR office* OR clinic OR clinics OR 'general practice' OR kiosk OR 'primary care' OR auscultatory OR center OR centers OR traditional OR standard OR attended OR unattended):ti
	#10		#4 AND ((office NEAR/3 'blood pressure') OR (office NEAR/3 'BP'))
	#11		#4 AND (automated OR wake OR self-measure* OR self-record* OR self NEAR/2 monitor* OR self NEAR/2 manag* OR home OR out-of-office OR 'out of office' OR day* OR night* OR evening OR bedtime OR 'bed time' OR morning* OR '24-hour' OR 24-hour OR 'home blood pressure monitoring' OR HBPM OR 'home BP' OR ambulatory OR ABPM OR (ambulatory NEAR/3 'blood pressure') OR (ambulatory NEAR/3 BP) OR tele-monitoring OR telemonitoring)
	#12		#4 AND (sphygmomanomet* OR oscillomet* OR 'manometer'/exp OR 'sphymomanometer'/exp)
	#13		#8 OR #9 OR #10 OR #11
	#14		#7 OR #13
	#15	Test characteristics	'predictive validity'/de OR 'predictive value'/de OR 'prognosis'/de OR 'sensitivity and specificity'/de OR 'diagnostic accuracy' OR 'diagnostic test accuracy study'/exp OR 'diagnostic value'/exp OR 'hypertension'/mj/dm_di
	#16		Predict*:ti,ab OR Prognos*:ti,ab OR Sensitivity:ti,ab OR Specificity:ti,ab OR accuracy:ti,ab OR accurate:ti,ab
	#17		(sensitiv* OR accura* OR specific* OR reliab* OR predict* OR prognostic):ti,ab
	#18		#15 OR #16 OR #17

Question	Set #	Concept	Strategy
Questions 1 and 2 – Diagnosis and Management (cont.)	#19	Adherence and impact	(Adhere* OR compliance OR comply OR goal OR goals OR threshold* OR achiev* OR benef* OR impact* OR improv* OR useful* OR utility):ti
	#20		'adherence'/exp OR 'patient compliance'/exp OR 'treatment outcome'/exp
	#21		#19 OR #20
	#22	hypertension, prehypertension	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#23		hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR prehyperten*:ti,ab OR 'white coat hypertension' OR wch OR 'masked hypertension' OR ((masked:ti,ab OR 'white coat':ti,ab OR borderline:ti,ab) AND hypertension:ti,ab)
	#24		(normal OR low OR high OR elevated OR borderline) NEAR/3 'blood pressure'
	#25		#22 OR #23 OR #24
	#26	Combine BP and measure, screen, monitor, methods, accuracy	#14 AND #18
	#27	To diagnose and manage HTN	#25 AND #26
	#28	Combine BP and measure, screen, monitor, methods, adherence, and HTN	#4 AND #14 AND #21 AND #25
	#29	Combine	#27 OR #28
		Apply hedges below	
Questions 3 and 4 – Non Pharmacological Interventions	#1	hypertension	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#2		hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR (pre NEXT/1 hypertens*):ti,ab OR prehypertensi*:ti,ab OR 'white coat hypertension' OR wch OR 'masked hypertension' OR ((masked:ti,ab OR 'white coat':ti,ab OR borderline:ti,ab) AND hypertens*:ti,ab)
	#3		(high OR elevated OR borderline OR lower OR lowering) NEAR/3 'blood pressure'
	#4		1 or 2 or 3
	#5		'blood pressure'/exp OR 'diastolic blood pressure'/exp OR 'systolic blood pressure'/exp OR 'systole'/de OR 'diastole'/de
	#6		'blood pressure':ti,ab OR 'systolic pressure*':ti,ab OR 'diastolic pressure*':ti,ab OR 'arterial pressure*':ti,ab OR bp:ti,ab OR sbp:ti,ab OR dpb:ti,ab OR ((systol*:ti,ab OR diastol*:ti,ab OR arterial:ti,ab) AND (pressure*:ti,ab OR mmhg:ti,ab OR 'mm hg':ti,ab))
	#7	Combine	5 OR 6
	#8	Obesity	'obesity'/exp/mj OR 'obese patient'/exp/mj OR 'body mass'/exp OR 'body weight'/exp OR obese:ti OR obesity:ti OR overweight:ti

Question	Set #	Concept	Strategy
Questions 3 and 4 – Non Pharmacological Interventions (cont.)	#9	General treatment of overweight/obesity with the aim of preventing/ controlling hypertension	'obesity'/exp/dm_dm,dm_dt,dm_su,dm_th AND 'hypertension'/exp/dm_dm,dm_pc,dm_th
	#10	Obesity - pharma	'obesity'/exp/dm_dt OR 'tetrahydrolipstatin'/exp OR 'lorcaserin'/exp OR 'phentermine plus topiramate'/exp OR 'liraglutide'/exp OR ('obesity'/exp AND (antihypertensives OR 'anti hypertensives' OR (antihypertensive NEAR/1 drug*) OR ('anti hypertensive' NEAR/1 drug*))) OR 'antiobesity agent'/exp OR 'amfebutamone plus naltrexone'/de
	#11		phentemine OR topiramate OR qsymia OR lorcaserin OR belviq OR orlistat OR xenical OR alli OR (naltrexone NEXT/1 bupropion) OR contrave OR liraglutide OR saxenda OR victoza OR phentermine OR benzphetamine OR phendimetrazine OR diethylpropion OR (antiobesity NEXT/1 agent*) OR (antiobesity NEXT/1 drug*) OR (obesity NEXT/1 agent*) OR (obesity NEXT/1 drug*)
	#12	Combine	9 OR 10
	#13	Obesity - surgery	'bariatric surgery'/exp OR 'roux-en-y gastric bypass'/exp OR 'obesity'/exp/dm_su
	#14		(obes*:ti,ab OR bariatric:ti,ab OR gastric*:ti,ab OR stomach:ti,ab OR 'weight loss':ti,ab) AND surg*:ti,ab
	#15		obes*:ti AND (sleeve*:ti,ab OR lapband*:ti,ab OR band*:ti,ab OR 'gastric bypass':ti OR gastrectomy:ti,ab OR 'roux n y':ti,ab OR 'roux-en-y':ti,ab OR 'roux en y':ti,ab OR rygb:ti,ab)
	#16	Combine	13 OR 14 OR 15
	#17	Obesity – lifestyle modification	'body weight loss'/exp OR (('eating habit'/exp OR 'diet therapy'/exp OR 'healthy lifestyle'/exp OR 'obesity management'/exp OR 'sedentary lifestyle'/exp OR 'lifestyle modification'/exp) AND 'body weight'/exp)
	#18		(eat*:ti OR habit*:ti OR diet*:ti OR lifestyle*:ti OR sedentary:ti OR activity:ti OR active:ti OR activities:ti OR exercise:ti) AND (change*:ti OR modif*:ti OR improve*:ti OR manag*:ti)
	#19		(weight:ti OR 'body mass':ti) AND (lose:ti OR loss:ti OR lost:ti OR lowering:ti OR reduc*:ti OR manag*:ti) OR ((weight:ti OR 'body mass':ti) AND (diet*:ti OR nutrition*:ti OR food*:ti) AND (prescription:ti OR prescribed:ti)) OR (dash AND diet) OR (mediterranean AND diet) OR 'dietary approach* to stop hypertension' OR 'dash diet':ti,ab OR 'dash diet'/exp OR ((diet* OR nutrition*):ti,ab AND (sodium OR salt OR potassium):ti,ab))
	#20		(weight:ti OR 'body mass':ti) AND (lose:ti OR loss:ti OR lost:ti OR lowering:ti OR reduc*:ti OR manag*:ti)
	#21		'obesity'/exp/mj AND 'lifestyle modification'/exp OR ((diet*:ti OR nutrition*:ti) AND ('bp':ti OR 'blood pressure':ti OR 'hypertension':ti OR 'cardiovascular disease':ti OR 'cvd':ti))
	#22	Combine	17 OR 18 OR 19 OR 20 OR 21
	#23	Combine Obesity AND Obesity pharma	8 AND 12
	#24	Combine Obesity AND surgery	8 AND 16

Question	Set #	Concept	Strategy
Questions 3 and 4 – Non Pharmacological Interventions (cont.)	#25	Combine Obesity AND lifestyle mod	8 AND 22
	#26	Combine final sets of Obesity	9 OR 23 OR 24 OR 25
	#27	Physical activity	'exercise'/exp OR 'physical activity'/exp OR 'meditation'/exp OR 'transcendental meditation'/exp OR 'qigong'/exp OR 'qigong exercise'/exp OR 'tai chi'/exp OR 'yoga'/exp OR 'aerobic exercise'/exp OR 'physical activity, capacity and performance'/exp OR 'exercise intensity'/exp OR 'resistance training'/exp
	#28		exercise:ti,ab OR 'physical activity':ti,ab OR training:ti,ab OR isometric*:ti,ab OR 'weight training':ti,ab OR 'weight lift*':ti,ab OR 'resistance training':ti,ab OR walk* OR run* OR jog* OR stress*:ti,ab OR swim*:ti,ab OR aerobics OR (aerobic NEAR/3 exercis*) OR (aerobic NEAR/3 fitness) OR (aerobic NEAR/3 training)
	#29		qigong:ti,ab OR taichi:ti,ab OR 'tai chi':ti,ab OR yoga:ti,ab OR relax*:ti,ab OR meditat*:ti,ab
	#30		(exercise:ti OR ((physical NEAR/2 activity):ti)) AND (change*:ti OR improve*:ti OR modif*:ti OR increase*:ti)
	#31		sedentary:ti,ab OR 'sedentary lifestyle'/exp OR 'physical inactivity'/exp OR 'laziness'/exp
	#32	Combine final sets of physical activity	27 OR 28 OR 29 OR 30 OR 31
	#33	Combine HTN OR BP	4 OR 7
	#34	Combine HTN OR BP with final obesity set	26 AND 33
	#35	Combine HTN OR BP with final phys act set	32 AND 33
	#36	Combine	34 OR 35
		Apply hedges below	

Question	Set #	Concept	Strategy
Questions 5 and 6 – Blood pressure thresholds and goals for pharmacologic interventions	#1	hypertension, prehypertension. WCH	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#2		Hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR prehyperten*:ti,ab OR 'white coat hypertension' OR WCH OR 'masked hypertension' OR ((masked OR white-coat OR "white coat" OR borderline):ti,ab AND hypertens*:ti,ab)
	#3		(high OR elevated OR borderline OR lower OR lowering) NEAR/3 'blood pressure'
	#4		#1 OR #2 OR #3
	#5	Blood pressure	'blood pressure'/exp OR 'diastolic blood pressure'/exp OR 'systolic blood pressure'/exp OR 'systole'/de OR 'diastole'/de
	#6		'blood pressure':ti,ab OR 'systolic pressure*':ti,ab OR 'diastolic pressure*':ti,ab OR 'arterial pressure*':ti,ab OR bp:ti,ab OR sbp:ti,ab OR dpb:ti,ab OR ((systol*:ti,ab OR diastol*:ti,ab OR arterial:ti,ab) AND (pressure*:ti,ab OR mmhg:ti,ab OR 'mm hg':ti,ab))
	#7		'70 mmhg':ti,ab OR '80 mmhg':ti,ab OR '90 mmhg':ti,ab OR '100 mmhg':ti,ab OR '110 mmhg':ti,ab OR '120 mmhg':ti,ab OR '130 mmhg':ti,ab OR '140 mmhg':ti,ab OR '150 mmhg':ti,ab OR '160 mmhg':ti,ab OR '170 mmhg':ti,ab OR '180 mmhg':ti,ab
	#8	Combine	#5 OR #6 OR #7
	#9		#8 AND ((best OR goal*:ti,ab OR standard*:ti,ab OR 'standard'/exp OR optimal:ti,ab OR ideal*:ti,ab OR target*:ti,ab)
	#10		'blood pressure goal*' OR 'blood-pressure goal*' OR 'blood pressure regulation'/exp
	#11	Combine	#9 OR #10
	#12	Antihypertensive drug therapy	'hypertension'/exp/dm_dt
	#13		'antihypertensive agent'/exp/mj OR 'antihypertensive therapy'/mj OR 'antihypertensive agent'/exp/dd_dt,dd_ad,dd_cm,dd_do
	#14		(antihypertens*:ti,ab OR 'anti hypertens*':ti,ab) AND (drug*:ti,ab OR pharma*:ti,ab OR medication*:ti,ab OR medicine*:ti,ab OR prescription*:ti,ab OR dose:ti,ab OR dosage:ti,ab)
	#15	Combine	#12 OR #13 OR #14
	#16	Combine	#4 AND #11 AND #15
		Apply hedges below	
Questions 7, 8, and 9 – Pharmacologic interventions	#1	Hypertension, prehypertension. WCH	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#2		Hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR prehyperten*:ti,ab OR 'white coat hypertension' OR WCH OR 'masked hypertension' OR ((masked OR white-coat OR "white coat"):ti,ab AND hypertension:ti,ab) OR 'refractory hypertension':ti,ab OR 'resistant hypertension':ti,ab OR 'uncontrolled hypertension':ti,ab
	#3		(high OR elevated OR borderline OR low OR lowering) NEAR/3 'blood pressure'

Question	Set #	Concept	Strategy
Questions 7, 8, and 9 – Pharmacologic interventions (cont.)	#4	Combine HTN disease	1 OR 2 OR 3
	#5	Intervention: Antihypertensive Pharma therapy	'hypertension'/exp/dm_dt OR ('hypertension'/exp/mj AND 'antihypertensive agent'/exp)
	#6		'antihypertensive agent'/exp/mj OR 'antihypertensive therapy'/mj OR 'antihypertensive agent'/exp/dd_dt,dd_ad,dd_cm,dd_do
	#7		((antihypertens* OR 'anti hypertens*') NEAR/5 (drug* OR pharma* OR medication* OR medicine* OR prescription* OR dose OR dosage)):ti,ab
	#8	Drugs (list is from workgroup members)	Thiazide* OR 'thiazide-like diuretic*' OR Chlorthalidone OR Bendroflumethiazide OR Chlorothiazide OR Hctz OR hydrochlorothiazide OR (hydrochlorothiazide NEAR/2 triamterene) OR Methyclothiazide OR Indapamide OR metolazone
	#9		'Angiotensin-converting enzyme inhibitor*' OR Benazepril OR captopril OR Enalapril OR Fosinopril OR Lisinopril OR moexipril OR Perindopril OR Quinapril OR Ramipril OR Trandolapril OR 'Angiotensin II Receptor Blocker*' OR Azilsartan OR Candesartan OR Eprosartan OR Irbesartan OR Losartan OR Olmesartan OR Telmisartan OR Valsartan
	#10		'Long-Acting Dihydropyridine Calcium Channel Blocker*' OR dihydropyridine* OR CCBs OR Amlodipine OR Felodipine OR 'Nifedipine sr' OR 'nifedipine xl' OR 'nifedipine cc' OR 'Nicardipine SR' OR 'Nisoldipine ER'
	#11		'Aldosterone NEAR/2 Antagonist*' OR 'mineralocorticoid Receptor Antagonist*' OR Eplerenone OR Spironolactone OR 'Direct Renin Inhibitor' OR Aliskiren OR 'Potassium-sparing diuretic*' OR Amiloride
	#12		Alpha-blocker* OR Doxazosin OR Prazosin OR Terazosin OR Beta-blocker* OR Propranolol OR Acebutolol OR Atenolol OR Betaxolol OR Bisoprolol OR 'Metoprolol tartrate' OR Metoprolol succinate OR Nadolol OR Nebivolol OR Penbutalol OR Pindolol OR Timolol
	#13		'Long-Acting non-DHP CCB*' OR non-dihydropyridine* OR 'Verapamil sr' OR 'Diltiazem sr' OR (alpha NEXT/2 beta NEXT/2 (antagonist* OR blocker*)) OR Carvedilol OR Labetalol OR Reserpine OR Minoxidil OR Hydralazine OR Clonidine tablet OR Clonidine patch OR Methyldopa OR Guanabenz OR Guanfacine
	#14	Combine drug sets	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
	#15	Combine HTN with drugs	#4 AND #14
		Apply hedges below	

Question	Set #	Concept	Strategy
Questions 10 and 11 – Telehealth, mobile applications, or other new technologies; alternative methods of delivering care	#1	Hypertension, prehypertension. WCH	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#2		Hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR prehyperten*:ti,ab OR 'white coat hypertension' OR WCH OR 'masked hypertension' OR ((masked OR white-coat OR "white coat"):ti,ab AND hypertension:ti,ab) OR 'refractory hypertension':ti,ab OR 'resistant hypertension':ti,ab OR 'uncontrolled hypertension':ti,ab
	#3		(high OR elevated OR borderline OR lower OR lowering) NEAR/3 'blood pressure'
	#4	Combine HTN disease	1 OR 2 OR 3
	#5	Blood Pressure	'blood pressure'/exp OR 'diastolic blood pressure'/exp OR 'systolic blood pressure'/exp OR 'systole'/de OR 'diastole'/de
	#6		'blood pressure':ti,ab OR 'systolic pressure*':ti,ab OR 'diastolic pressure*':ti,ab OR 'arterial pressure*':ti,ab OR bp:ti,ab OR sbp:ti,ab OR dpb:ti,ab OR ((systol*:ti,ab OR diastol*:ti,ab OR arterial:ti,ab) AND (pressure*:ti,ab OR mmhg:ti,ab OR 'mm hg':ti,ab))
	#7	Combine BP	#5 OR #6
	#8	Telehealth	'telehealth'/exp OR 'teleconsultation'/exp OR 'telenursing'/exp OR 'telemedicine'/exp OR 'telemonitoring'/exp OR 'videoconferencing'/exp
	#9		telemedicine:ti,ab OR teleconsult*:ti,ab OR telehealth*:ti,ab OR telenurs*:ti,ab OR telemonitor*:ti,ab OR telecare:ti,ab OR telehomecare:ti,ab OR telemanagement:ti,ab OR telemedical*:ti,ab OR telemetr*:ti,ab OR 'tele medicin*':ti,ab OR 'tele health*':ti,ab OR tele-monitor* OR 'tele nurs*':ti,ab OR ehealth:ti,ab OR 'e health':ti,ab OR bluetooth:ti,ab OR (remote NEXT/2 consult*):ti,ab OR (telephone NEXT/2 consult*):ti,ab OR telephone:ti,ab
	#10	Technology	'mobile health application'/exp OR 'mobile application'/exp OR 'mobile phone'/exp OR 'smartphone'/exp OR 'artificial intelligence'/exp OR (email OR 'e-mail' OR mhealth OR 'm-health' OR mobile OR phone OR phones OR iphone* OR remote* OR virtual OR digital OR apps OR app OR text OR texting OR texts OR "technology supported management" OR "technology based intervention*" OR 'web based' OR 'internet based' OR 'computer based' OR web):ti,ab
	#11		(device* OR monitors OR technologies OR smartwatch* OR smartphone OR watch* OR wearable OR wireless):ti,ab
	#12		'social media'/de OR ('crowd-sensing' OR facebook OR 'social media'):ti,ab
	#13	Combine telehealth and technology	#8 OR #9 OR #10 OR #11 OR #12
	#14	Combine HTN with tech	#4 AND #13
	#15	Combine BP with tech	#7 AND #13
	#16	Combine	#14 OR #15

Question	Set #	Concept	Strategy
Questions 10 and 11 – Telehealth, mobile applications, or other new technologies; alternative methods of delivering care (cont.)	#17	Other providers	(nurse* OR nutritionist OR dietitian OR dietician OR pharmacist OR pharmacy OR clinic OR clinics OR specialist* OR nephrolog* OR cardiolog*):ti,ab) OR 'health care personnel'/exp OR 'pharmacist'/exp OR ('pharmacist run' OR 'pharmacist led' OR 'nurse led' OR 'nurse run' OR clinics OR clinic OR center OR centers):ti,ab
	#18	Collaborative team	'collaborative care team'/exp OR 'collaborative care':ti,ab OR 'community care' OR 'interdisciplinary communication' OR 'multi disciplinary':ti OR multidisciplinary:ti OR collaborative:ti OR teambased:ti,ab OR 'team based':ti,ab OR integrate:ti OR integrated:ti
	#19	Combine HTN AND other providers	#4 AND #17
	#20	Combine HTN AND tech AND other providers	#13 AND #17
	#21	Combine HTN AND collaborative	#4 AND #18
	#22	Combine HTN AND collaborative AND tech	#13 AND #21
	#23	Combine	#16 OR #19 OR #20 OR #21 OR #22
		Apply hedges below	
Question 12 – Screening	#1	Hypertension, prehypertension. WCH	'hypertension'/exp OR 'hypertensive patient'/exp OR 'resistant hypertension'/exp OR 'masked hypertension'/exp OR 'white coat hypertension'/exp OR 'prehypertension'/exp
	#2		Hypertension:ti,ab OR hypertensive:ti,ab OR 'borderline hypertensive':ti,ab OR prehyperten*:ti,ab OR 'white coat hypertension' OR WCH OR 'masked hypertension' OR ((masked OR white-coat OR "white coat"):ti,ab AND hypertension:ti,ab) OR 'refractory hypertension':ti,ab OR 'resistant hypertension':ti,ab OR 'uncontrolled hypertension':ti,ab
	#3		(high OR elevated OR borderline) NEAR/3 'blood pressure'
	#4	Combine	#1 OR #2 OR #3
	#5	Disease/Conditions to screen for	'chronic kidney failure'/exp/dm_di,dm_ep,dm_et OR 'end stage renal disease'/exp/dm_di,dm_ep,dm_et OR 'estimated glomerular filtration rate'/exp OR 'proteinuria'/exp OR 'albuminuria'/exp
	#6		'chronic kidney disease':ti,ab OR 'CKD':ti,ab OR 'esrd':ti,ab OR 'egfr':ti,ab OR 'glomerular filtration rate':ti,ab
	#7		Albuminuria:ti,ab OR proteinuria:ti,ab OR (urine NEXT/1 protein):ti,ab OR (urine NEXT/1 albumin):ti,ab
	#8		'coronary artery disease'/exp/dm_di,dm_ep,dm_et OR 'coronary artery disease':ti,ab
	#9		'peripheral vascular disease'/exp/dm_di,dm_ep,dm_et OR 'peripheral vascular disease':ti,ab
	#10	Combine	#5 OR #6 OR #7 OR #8 OR #9

Question	Set #	Concept	Strategy
Question 12 – Screening (cont.)	#11	Screening	Echo*:ti,ab OR ecg:ti,ab OR urine:ti,ab OR 'urine strip':ti,ab OR urinalysis:ti,ab OR ultrasound:ti,ab OR 'ankle-brachial index':ti,ab OR Doppler:ti,ab OR 'urinalysis'/exp OR 'urine test strip'/exp OR 'echography'/exp OR 'ultrasound'/exp OR 'Doppler flowmetry'/exp
	#12		'screening'/exp OR screen:ti,ab OR screening:ti,ab
	#13		'coronary calcium scoring'/exp OR 'coronary artery calcium score'/exp OR 'coronary calcium scor*' OR 'coronary calcium scan*' OR (cac AND artery)
	#14	Combine	#11 OR #12 OR #13
	#15	Combine HTN and conditions and screening	#4 AND #10 AND #14
		Apply hedges below	
General hedges applied to each section		Date limit; Limit to English language publications; abstracts	AND [1-12-2013]/sd NOT [11-3-2019]/sd AND [English]/lim AND [abstracts]/lim
		Remove undesired age ranges	NOT (adolescen*:ti OR child*:ti OR infant*:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR youth:ti,ab)
		Remove undesired publication types (e.g., conferences, editorials)	NOT ('conference paper'/exp OR 'case report'/de OR 'book'/de OR 'editorial'/de OR 'erratum'/de OR 'letter'/de OR 'note'/de OR 'short survey'/de OR book:it OR conference:it OR editorial:it OR erratum:it OR letter:it OR note:it OR 'short survey':it OR 'a case':ti,ab OR 'a patient':ti,ab OR 'year old':ti,ab OR book:pt OR 'conference proceeding':pt OR 'case report':ti OR comment:ti)
		Remove animal studies	NOT (mouse OR mice OR rabbit* OR rat OR rats OR rodent* OR sheep OR swine OR canine* OR dog* OR porcine OR fish OR equine)
Study type hedges applied as needed		Limit to meta-analyses and systematic reviews	AND ('meta analysis'/de OR 'systematic review'/de OR 'meta analysis'/exp OR ('meta analysis' OR 'meta analytic' OR metaanaly* OR 'research synthesis' OR 'systematic review'/exp OR 'systematic review' OR pooled OR pooling OR search*):ti,ab OR ('critical review' OR 'evidence based' OR systematic*):ti OR cochrane:jt OR [Cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti)
		Limit to randomized controlled trials	AND ('random sample'/de OR 'randomized controlled trial'/exp OR randomization/de OR random*:ti,ab OR 'randomized controlled trial'/exp)
		Limit to comparative studies (used only when appropriate)	AND ('case control study'/exp OR 'cohort analysis'/de OR 'comparative study'/exp OR 'controlled study'/exp OR 'cross-sectional study'/de OR 'diagnostic test accuracy study'/de OR epidemiology/exp/mj OR 'follow up'/de OR 'longitudinal study'/de OR 'observational study'/de OR 'prospective study'/de OR 'retrospective study'/de OR ('case control' OR 'case series' OR cohort OR compar* OR 'controlled study' OR 'controlled trial' OR 'cross sectional' OR 'follow-up' OR followup OR longitudinal OR 'matched controls' OR placebo OR prospective OR retrospective):ti,ab OR (epidemiolog* OR versus OR vs):ti)

B. PsycINFO with Ovid Syntax

Question	Set #	Concept	Strategy
Questions 3 and 4 – Treatments for obesity, lifestyle modifications, physical activity	#1	Population (adults with hypertension)	Exp hypertension/ OR Hypertension.mp. OR hypertensive.mp. OR 'borderline hypertensive'.ti,ab. OR prehypertensi*.ti,ab. OR 'white coat hypertension' OR 'masked hypertension'
	#2		(high OR elevated OR borderline OR lower OR lowering) adj3 'blood pressure'
	#3	Combine sets	#1 OR #2
	#4	Obesity	Exp Obesity/ OR obese.ti. OR obesity.ti. OR overweight.ti.
	#5	Obesity surgery	Exp bariatric surgery/ OR exp weight control/ "roux en y".mp. OR "gastric bypass".mp. OR "obesity treatment".id.
	#6		(obes*.ti. OR bariatric.ti. OR gastric*.ti. OR stomach.ti. OR “weight loss”.ti. OR weight-loss.ti.) AND surg*.ti.
	#7		obes*.ti. and (sleeve or lapband or band* or "gastric bypass" or gastrectomy or "roux n y" or rygb).ti,ab.
	#8	Combine obesity surgery AND HTN	#3 AND (#5 OR #6 OR #7)
	#9	Obesity pharma	Exp obesity AND exp drug therapy
	#10		(((tetrahydrolipstatin or lorcaserin or phentermine) adj2 topiramate) or liraglutide or phentemine or topiramate or phentemine or topiramate or qsymia or lorcaserin or belviq or orlistat or xenical or alli or (naltrexone adj1 bupropion) or contrave or liraglutide or saxenda or victoza or phentermine or benzphetamine or phendimetrazine or diethylpropion or (antiobesity adj1 agent*) or (antiobesity adj1 drug*) or (obesity adj1 agent*) or (obesity adj1 drug*)).mp.
	#11		((antihypertensive* or "anti hypertensive*" or antihypertensive) adj1 drug*) or 'anti hypertensive') adj1 drug*).mp. or exp antiobesity agent/
	#12	Combine pharma	#10 OR #11
	#13	Combine obesity with pharma	#9 OR (#4 AND #12)
	#14	Obesity – lifestyle mod to control weight	Exp weight control/ OR exp weight loss/ OR weight loss.mp. OR ((weight OR body mass) AND (lose OR loss OR lost OR lowering OR reduc* OR manag*)).ti.
	#15		Exp diets/ or diet therapy.mp.
	#16		(eat* OR diet* OR food OR sedentary OR lazy OR laziness OR activity OR active OR activities OR exercise).ti. AND (habit* OR choice* OR modif* OR change* OR improve* OR manag*).ti.
	#17		(Dash adj3 diet).mp. OR (Mediterranean adj3 diet).mp. OR ((diet* OR nutrition*).ti AND (sodium OR salt OR potassium).ti.)
	#18		exp Behavior Modification/ OR exp Lifestyle Changes/ OR lifestyle modification.mp.
	#19	Combine weight control AND HTN	#3 AND #14
	#20	Combine diets AND HTN	#3 AND (#15 OR #16 OR #17 OR #18)

Question	Set #	Concept	Strategy
Questions 3 and 4 – Treatments for obesity, lifestyle modifications, physical activity (cont.)	#22		Exp meditation/ OR meditation.mp. OR exp mindfulness/ OR mindfulness.mp. OR qigong.mp. OR exp martial arts/ OR tai chi.mp. OR exp yoga/ OR yoga.mp.
	#23		Exp weightlifting/ OR resistance training.mp.
	#24		Exp running/ OR run*.ti. OR jog.ti. OR exp walking/ OR walk*.ti. OR swim*.ti. OR aerobics.ti. OR (aerobic adj2 exercise*).ti. OR (aerobic adj2 fitness).ti. OR (aerobic adj2 training).ti.
	#25		((exericse or (physical adj2 activity)) and (change* or improve* or modif* or increase*)).ti.
	#26	Combine physical activity	#21 OR #22 OR #23 OR #24 OR #25
	#27	Combine obesity AND phys activity	#4 AND #26
	#28	Combine obesity AND phys activity AND HTN	#3 AND #27
	#29		Exp sedentary behavior/ OR (sedentary OR inactive OR inactivity OR lazy OR laziness).ti,ab.
	#30	Combine with HTN	#3 AND #29
	#31	Combine final sets	#8 OR #13 OR #19 OR #20 OR #28 OR #30
	#32	Apply limits	See search hedges below
Questions 10 and 11 – Telehealth, mobile applications, or other new technologies; alternative methods of delivering care	#1	Hypertension	Exp hypertension/
	#2		Hypertension.mp. OR hypertensive.mp. OR 'borderline hypertensive'.ti,ab. OR prehypertensi*.ti,ab. OR 'white coat hypertension' OR 'masked hypertension'
	#3		(high OR elevated OR borderline) adj3 'blood pressure'
	#4	Combine HTN	#1 or #2 or #3
	#5	Blood Pressure	Exp blood pressure/ OR systolic pressure/ OR diastolic pressure/
	#6		Blood pressure.ti,ab. OR systolic*.ti,ab OR diastolic.ti,ab. OR arterial pressure.ti,ab. OR bp.ti,ab. OR sbp.ti,ab. OR dbp.ti,ab. OR ((systole* OR diastol* OR arterial).ti. AND (pressure* OR mm hg OR mmgh).ti.)
	#7	Combine BP	#5 OR #6
	#8	Technology	exp telemedicine/ or exp telenursing/ or exp remote consultation/

Question	Set #	Concept	Strategy
Questions 10 and 11 – Telehealth, mobile applications, or other new technologies; alternative methods of delivering care (cont.)	#9		exp cellular phones/ or exp mobile devices/ or exp technology/ or exp electronic communication/ or exp internet/ or exp computer applications/ or exp online therapy/ or exp social media/ or exp websites/ or exp digital computers/
	#10		((cellular OR mobile) adj2 phone).ti. OR (telemedicine OR telehealth OR telenursing OR ehealth OR e health OR remote consult* OR telephone).ti.
	#11		("personal digital assistant" OR smart phone OR cell* phone OR mobile phone OR smart watch OR androic* OR hand held OR iphone OR ipad OR webbased OR web based OR laptop OR "mobile health application" OR email OR e mail OR mhealth OR remote OR virtual OR digital OR apps OR app OR text OR texting OR texts OR "technology supported management" OR "technology based intervention" OR internet based or computer based).ti,ab.
	#12		(device* OR monitors OR technologies OR smartwatch* OR smartphone OR watch* OR wearable OR wireless OR "social media" OR facebook).ti,ab.
	#13		(telemedicine OR teleconsult* OR telehealth OR telenurs* OR telemonitor* OR telecare OR telehomecare OR telemanagement OR telemedical OR telemetr* OR ehealth OR bluetooth).ti,ab. OR (remote adj2 consult*).ti. OR (telephone adj2 consult*).ti.
	#14	Combine technology	#8 OR #9 OR #10 OR #11 OR #12 OR #13
	#15	Combine HTN AND Technology	#4 AND #14
	#16	Combine BP with Technology	#7 AND #14
	#17	Combine final technology sets	#15 OR #16
	#18	Allied health/delivery of care	(nurse* OR nutritionist OR dietitian OR dietician OR pharmacist* OR pharmacy OR health care personnel).ti. OR (pharmacist adj1 run).ti,ab. OR (pharmacist adj1 led).ti,ab. OR (nurse adj1 led).ti,ab. OR (nurse adj1 run).ti,ab. OR (clinics OR clinic OR center OR centers).ti,ab.
	#19		exp health personnel/ OR exp pharmacists/ OR exp nurses/
	#20	Combine	#18 OR #19
	#21	Combine delivery of care with HTN OR BP	(#4 OR #7) AND #20
	#22	Combine final sets	#17 OR #21
		Apply limits and hedges	See hedges below

Question	Set #	Concept	Strategy
Search hedges applied to each strategy		Limit to English language and publication year	AND (english language AND yr="2013 - 2019")
		Population	("300 adulthood <age 18 yrs and older>" or 320 young adulthood <age 18 to 29 yrs> or 340 thirties <age 30 to 39 yrs> or 360 middle age <age 40 to 64 yrs> or "380 aged <age 65 yrs and older>" or "390 very old <age 85 yrs and older>")
		Exclude conference publications, books, letters, editorials, case studies, etc..	NOT ((("column/opinion" OR "comment/reply" OR dissertation OR editorial OR letter OR book).dt. OR book.pt.) OR (letter/ or editorial/ OR news/ OR comment/ OR case report OR case reports/ OR note/ OR conference paper/) OR (letter OR editorial OR news OR comment OR case reports OR conference abstract$).pt.
		Limit to meta-analyses and systematic reviews	AND (meta analysis/ OR (systematic review OR meta analysis).mp. OR (meta-analysis OR systematic review).ti.)
		Limit to randomized controlled trials	AND (Randomized controlled trials OR random allocation OR double-blind method OR single-blind method OR placebos OR cross-over studies).de. OR placebo$.mp. OR random$.ti. OR randomized controlled trial.pt. OR crossover$.mp. OR cross over.mp. OR ((singl* OR doubl* OR tripl* OR trebl*) ADJ3 (blind* OR mask* OR sham*)).mp. OR latin square.mp. OR ISRTCN OR ACTRN* OR (NCT* not NCT) OR (clinical trials/ AND random*.ti.)
		Limit to other study types, as needed	AND (exp Cohort Analysis/ OR exp longitudinal studies/ OR exp prospective studies/ OR exp retrospective studies/ OR exp clinical trials/ OR (cohort* OR longitudinal OR prospective OR retrospective OR "case control" OR compar* OR "control group" OR "controlled study" OR "controlled trial" OR "cross over" OR crossover OR "double blind" OR "double blinded" OR "matched controls" OR placebo* OR random* OR sham OR validat*).ti,ab. OR ((versus OR vs).ti.)
		Limit to database study types	AND ("0300 clinical trial" or "0430 followup study" or "0450 longitudinal study" or "0451 prospective study" or "0453 retrospective study" or "0830 systematic review" or 1200 meta analysis or 1300 metasynthesis or 2100 treatment outcome)

Appendix K: Alternative Text Descriptions of Algorithms

A. Module A: Screening and Diagnosis

1. Module A begins with Box 1, in the shape of a rounded rectangle: "Adult in healthcare system"
2. Box 1 connects to Box 2, in the shape of a hexagon, asks the question: "Is the patient currently being treated for HTN?"
    a. If the answer is "Yes" to Box 2, then Box 3, in the shape of an oval: "Go to Module B, Box 16"
    b. If the answer is "No" to Box 2, then Box 4, in the shape of a rectangle: "Obtain office blood pressure (see Sidebar 1)"
3. Box 4 connects to Box 5, in the shape of a hexagon, asks the question: "When measured properly (see Appendix G), is SBP ≥120 mm Hg or DBP ≥80 mm Hg?"
    a. If the answer is "Yes" to Box 5, then Box 6, in the shape of a hexagon, asks the question: "Does patient have an acute injury or illness?"
        i. If the answer is "Yes" to Box 6, then Box 7, in the shape of a rectangle: "Return after acute episode resolved (typically within 4 weeks)
            1. Box 7 connects to Box 4, in the shape of a rectangle: "Obtain office blood pressure (see Sidebar 1)"
        ii. If the answer "No" to Box 6, then Box 8, in the shape of a rectangle: "Assess the need for and implement lifestyle modification, then follow up for adherence (e.g., diet, exercise, weight loss, alcohol moderation)"
    b. If the answer is "No" to Box 5, then Box 15, in the shape of a rectangle: "Screen blood pressure periodically; address other CV risk factors (including healthy diet and physical activity); in patients with known or suspected target organ damage (see Sidebar 3), consider possibility of masked HTN (consider HBPM or ABPM)"
4. Box 8 connects to Box 9, in the shape of a hexagon, asks the question: "Is SBP ≥130 mm Hg or DBP ≥90 mm Hg"
    a. If the answer is "Yes" to Box 9, then Box 10, in the shape of a hexagon, asks the question: "Confirm diagnosis of HTN by measuring blood pressure after 1-4 weeks (see Sidebar 2); is diagnosis confirmed?"
        i. If the answer is "Yes" to Box 10, then Box 11, in the shape of a rectangle: "Obtain history and physical and assess for target organ damage and comorbid conditions (see Sidebar 3); consider baseline testing (e.g., basic metabolic panel, urinalysis, EKG, A1c, other tests), as appropriate"
        ii. If the answer is "No" to Box 10, then Box 15, in the shape of a rectangle: "Screen blood pressure periodically; address other CV risk factors (including healthy diet and physical activity); in patients with known or suspected target organ damage (see Sidebar 3), consider possibility of masked HTN (consider HBPM or ABPM)"

   b. If the answer is "No" to Box 9, then Box 15, in the shape of a rectangle: "Screen blood pressure periodically; address other CV risk factors (including healthy diet and physical activity); in patients with known or suspected target organ damage (see Sidebar 3), consider possibility of masked HTN (consider HBPM or ABPM)"

5. Box 11 connects to Box 12, in the shape of a hexagon, asks the question: "Is secondary cause suspected?"
   a. If the answer is "Yes" to Box 12, then Box 13, in the shape of a rectangle: "Evaluate, as indicated; consider referral"
      i. Box 13 connects to Box 14, in the shape of an oval: "Initiate treatment (go to Module B)"
   b. If the answer is "No" to Box 12, then Box 14, in the shape of an oval: "Initiate treatment (go to Module B)"

B. Module B: Treatment

1. Module B begins with Box 16, in the shape of a rounded rectangle: "Patient appropriate for HTN treatment"
2. Box 16 connects to Box 17, in the shape of a rectangle: "Determine blood pressure goal (see Sidebar 4)"
3. Box 17 connects to Box 18, in the shape of a rectangle, asks the question: "Implement SDM to assess patient values and preferences; assess the need for and implement lifestyle modification. Is the patient willing to engage in pharmacotherapy?"
   a. If the answer is "Yes" to Box 18, then Box 19, in the shape of an rectangle: "Initiate treatment if drug naïve or optimize existing therapy (see Sidebar 5)"
   b. If the answer is "No" to Box 18, then Box 20, in the shape of a rounded rectangle: "Patient refuses pharmacotherapy; consider nurse-led and dietitian-led interventions to improve blood pressure control"
4. Box 20 connects to Box 21, in the shape of a rounded rectangle: "Follow up periodically; reassess preferences"
5. Box 21 connects to Box 17, in the shape of a rectangle: "Determine blood pressure goal (see Sidebar 4)"
6. Box 19 connects to Box 22, in the shape of a rectangle: "Consider offering and/or adjusting HBPM with co-interventions (tailored medication titration, education, and/or lifestyle counseling"
7. Box 22 connects to Box 23, in the shape of a rectangle: "Follow up regularly (e.g., monthly) until: blood pressure is at goal, treatment regimen is optimized (see Sidebar 6), comorbid conditions and/or other patient preferences direct otherwise"

8. Box 23 connects to Box 24, in the shape of a hexagon, asks the question: "Is the patient's blood pressure at or below goal?"
    a. If the answer is "Yes" to Box 24, then Box 25, in the shape of a rectangle: "Follow up annually or more frequently as dictated by comorbid conditions (to include lab monitoring, if indicated)"
    b. If the answer is "No" to Box 24, then Box 22, in the shape of a rectangle: "Consider offering and/or adjusting HBPM with co-interventions (tailored medication titration, education, and/or lifestyle counseling)"

Appendix L: Abbreviations

Abbreviation	Definition
AASK	African American Study of Kidney Disease and Hypertension
AA	aldosterone antagonist
ABI	ankle-brachial index
ABPM	ambulatory blood pressure monitoring
ACC	American College of Cardiology
ACCOMPLISH	Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension
ACCORD	Action to Control Cardiovascular Risk in Diabetes
ACEI	angiotensin-converting enzyme inhibitor
ADVANCE	Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation
AE	adverse effect
AHA	American Heart Association
AHRQ	Agency for Healthcare Research and Quality
ALLHAT	Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (
AOBP	automated office blood pressure
ARB	angiotensin II receptor blocker
AUC	area under curve
AV	atrioventricular
bid	twice daily
BMI	body mass index
BPH	benign prostatic hyperplasia
BPROAD	Blood Pressure Control Target in Diabetes
CAC	coronary artery calcification
CAD	coronary artery disease
CCB	calcium channel blocker
CHF	chronic heart failure
CKD	chronic kidney disease
cm	centimeter
CMS	Centers for Medicare and Medicaid Services
COB	central operating base
COI	conflict of interest
COR	contracting officer's representative
CPG	clinical practice guideline
CS	clinical study
CV	cardiovascular
CVD	cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DBP	diastolic blood pressure
DHP	dihydropyridines

Abbreviation	Definition
DoD	Department of Defense
DRI	direct renin inhibitors
EBPWG	Evidence-Based Practice Work Group
ECG	electrocardiogram
ECHO	echocardiogram
eGFR	estimated glomerular filtration rate
EKG	electrocardiogram
FDA	U.S. Food and Drug Administration
FOB	forward operating base
GI	gastrointestinal
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBPM	home blood pressure monitoring
HC	high-unrefined carbohydrate, low-fat diet
HCTZ	hydrochlorothiazide
HEC	Health Executive Committee
HFrEF	reduced ejection fraction
HIPAA	Health Insurance Portability and Accountability Act
HTN	hypertension
HYVET	Hypertension in the Very Elderly Trial
IPAD	Intervention for High-normal or Borderline-elevated Blood Pressure in Adults with Type 2 Diabetes
IR	immediate release
JNC 7	Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
K+	Potassium
KQ	key question
LA DHP	long-acting dihydropyridine
LC	low-carbohydrate, high-unsaturated/low-saturated fat diet
LDL	low-density lipoprotein
LIFE	Losartan Intervention For Endpoint reduction
LV	left ventricular
LVH	left ventricular hypertrophy
MACE	major adverse cardiovascular events
MD	mean difference
MHS	Military Health System
MI	myocardial infarction
mL	milliliter
MRA	mineralocorticoid receptor antagonist
MRC	Medical Research Council
MRE	Meals Ready to Eat
MTF	military treatment facilities

Abbreviation	Definition
NHANES	National Health and Nutrition Examination Survey
NICE	National Institute for Health and Care Excellence
NPV	negative predictive value
OSA	obstructive sleep apnea
PCC	patient-centered care
PICOTS	population, intervention, comparison, outcome, timing and setting
PPV	positive predictive value
PREDIMED	PREvención con DIeta MEDiterránea
PVD	perpherial vascular disease
RCT	randomized control trial
RHT	resistant hypertension
SBP	systolic blood pressure
SDM	shared decision making
SLE	systemic lupus erythematosus
SME	subject matter expert
SMS	short message service
SPRINT	Systolic Blood Pressure Intervention Trial
SR	systematic review
Tbsp	tablespoon
TOHP II	Trials of Hypertension Prevention Phase II
TONE	Trial of Non-pharmacologic Interventions in the Elderly
TOPCAT	Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial
U.S.	United States
US	ultrasound
USPSTF	U.S. Preventive Services Task Force
VA	Veterans Affairs
VHA	Veterans Health Administration

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