Special Communication

# 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

## Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

Hypertension is the most common condition seen in primary care and leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately. Patients want to be assured that blood pressure (BP) treatment will reduce their disease burden, while clinicians want guidance on hypertension management using the best scientific evidence. This report takes a rigorous, evidence-based approach to recommend treatment thresholds, goals, and medications in the management of hypertension in adults. Evidence was drawn from randomized controlled trials, which represent the gold standard for determining efficacy and effectiveness. Evidence quality and recommendations were graded based on their effect on important outcomes.

There is strong evidence to support treating hypertensive persons aged 60 years or older to a BP goal of less than 150/90 mm Hg and hypertensive persons 30 through 59 years of age to a diastolic goal of less than 90 mm Hg; however, there is insufficient evidence in hypertensive persons younger than 60 years for a systolic goal, or in those younger than 30 years for a diastolic goal, so the panel recommends a BP of less than 140/90 mm Hg for those groups based on expert opinion. The same thresholds and goals are recommended for hypertensive adults with diabetes or nondiabetic chronic kidney disease (CKD) as for the general hypertensive population younger than 60 years. There is moderate evidence to support initiating drug treatment with an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker, or thiazide-type diuretic in the nonblack hypertensive population, including those with diabetes. In the black hypertensive population, including those with diabetes, a calcium channel blocker or thiazide-type diuretic is recommended as initial therapy. There is moderate evidence to support initial or add-on antihypertensive therapy with an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in persons with CKD to improve kidney outcomes.

Although this guideline provides evidence-based recommendations for the management of high BP and should meet the clinical needs of most patients, these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.

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**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Paul A. James, MD, University of Iowa, 200 Hawkins Dr, 01286-D PFP, Iowa City, IA 52242-1097 (paul-james@uiowa.edu).

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Hypertension remains one of the most important preventable contributors to disease and death. Abundant evidence from randomized controlled trials (RCTs) has shown benefit of antihypertensive drug treatment in reducing important health outcomes in persons with hypertension.[1-3] Clinical guidelines are at the intersection between research evidence and clinical actions that can improve patient outcomes. The Institute of Medicine Report *Clinical Practice Guidelines We Can Trust* outlined a pathway to guideline development and is the approach that this panel aspired to in the creation of this report.[4]

The panel members appointed to the Eighth Joint National Committee (JNC 8) used rigorous evidence-based methods, developing Evidence Statements and recommendations for blood pressure (BP) treatment based on a systematic review of the literature to meet user needs, especially the needs of the primary care clinician. This report is an executive summary of the evidence and is designed to provide clear recommendations for all clinicians. Major differences from the previous JNC report are summarized in **Table 1**. The complete evidence summary and detailed description of the evidence review and methods are provided online (see Supplement).

**ACEI** *angiotensin-converting enzyme inhibitor*

**ARB** *angiotensin receptor blocker*

**BP** *blood pressure*

**CCB** *calcium channel blocker*

**CKD** *chronic kidney disease*

**CVD** *cardiovascular disease*

**ESRD** *end-stage renal disease*

**GFR** *glomerular filtration rate*

**HF** *heart failure*

## The Process

The panel members appointed to JNC 8 were selected from more than 400 nominees based on expertise in hypertension (n = 14), primary care (n = 6), including geriatrics (n = 2), cardiology (n = 2), nephrology (n = 3), nursing (n = 1), pharmacology (n = 2), clinical trials (n = 6), evidence-based medicine (n = 3), epidemiology (n = 1), informatics (n = 4), and the development and implementation of clinical guidelines in systems of care (n = 4).

The panel also included a senior scientist from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a senior medical officer from the National Heart, Lung, and Blood Institute (NHLBI), and a senior scientist from NHLBI, who withdrew from authorship prior to publication. Two members left the panel early in the process before the evidence review because of new job commitments that prevented them from continuing to serve. Panel members disclosed any potential conflicts of interest including studies evaluated in this report and relationships with industry. Those with conflicts were allowed to participate in discussions as long as they declared their relationships, but they recused themselves from voting on evidence statements and recommendations relevant to their relationships or conflicts. Four panel members (24%) had relationships with industry or potential conflicts to disclose at the outset of the process.

In January 2013, the guideline was submitted for external peer review by NHLBI to 20 reviewers, all of whom had expertise in hypertension, and to 16 federal agencies. Reviewers also had expertise in cardiology, nephrology, primary care, pharmacology, research (including clinical trials), biostatistics, and other important related fields. Sixteen individual reviewers and 5 federal agencies responded. Reviewers' comments were collected, collated, and anonymized. Comments were reviewed and discussed by the panel from March through June 2013 and incorporated into a revised document. (Reviewers' comments and suggestions, and responses and disposition by the panel are available on request from the authors.)

## Questions Guiding the Evidence Review

This evidence-based hypertension guideline focuses on the panel's 3 highest-ranked questions related to high BP management identified through a modified Delphi technique.[5] Nine recommendations are made reflecting these questions. These questions address thresholds and goals for pharmacologic treatment of hypertension and whether particular antihypertensive drugs or drug classes improve important health outcomes compared with other drug classes.

1. In adults with hypertension, does initiating antihypertensive pharmacologic therapy at specific BP thresholds improve health outcomes?
2. In adults with hypertension, does treatment with antihypertensive pharmacologic therapy to a specified BP goal lead to improvements in health outcomes?
3. In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?

## The Evidence Review

The evidence review focused on adults aged 18 years or older with hypertension and included studies with the following prespecified subgroups: diabetes, coronary artery disease, peripheral artery disease, heart failure, previous stroke, chronic kidney disease (CKD), proteinuria, older adults, men and women, racial and ethnic groups, and smokers. Studies with sample sizes smaller than 100 were excluded, as were studies with a follow-up period of less than 1 year, because small studies of brief duration are unlikely to yield enough health-related outcome information to permit interpretation of treatment effects. Studies were included in the evidence review only if they reported the effects of the studied interventions on any of these important health outcomes:

- Overall mortality, cardiovascular disease (CVD)–related mortality, CKD-related mortality
- Myocardial infarction, heart failure, hospitalization for heart failure, stroke
- Coronary revascularization (includes coronary artery bypass surgery, coronary angioplasty and coronary stent placement), other revascularization (includes carotid, renal, and lower extremity revascularization)
- End-stage renal disease (ESRD) (ie, kidney failure resulting in dialysis or transplantation), doubling of creatinine level, halving of glomerular filtration rate (GFR).

The panel limited its evidence review to RCTs because they are less subject to bias than other study designs and represent the gold standard for determining efficacy and effectiveness.[6] The studies



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Table 1. Comparison of Current Recommendations With JNC 7 Guidelines

| Topic | JNC 7 | 2014 Hypertension Guideline |
|---|---|---|
| Methodology | Nonsystematic literature review by expert committee including a range of study designs<br>Recommendations based on consensus | Critical questions and review criteria defined by expert panel with input from methodology team<br>Initial systematic review by methodologists restricted to RCT evidence<br>Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol |
| Definitions | Defined hypertension and prehypertension | Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined |
| Treatment goals | Separate treatment goals defined for "uncomplicated" hypertension and for subsets with various comorbid conditions (diabetes and CKD) | Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particular subpopulation |
| Lifestyle recommendations | Recommended lifestyle modifications based on literature review and expert opinion | Lifestyle modifications recommended by endorsing the evidence-based Recommendations of the Lifestyle Work Group |
| Drug therapy | Recommended 5 classes to be considered as initial therapy but recommended thiazide-type diuretics as initial therapy for most patients without compelling indication for another class<br>Specified particular antihypertensive medication classes for patients with compelling indications, ie, diabetes, CKD, heart failure, myocardial infarction, stroke, and high CVD risk<br>Included a comprehensive table of oral antihypertensive drugs including names and usual dose ranges | Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence<br>Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups<br>Panel created a table of drugs and doses used in the outcome trials |
| Scope of topics | Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion | Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority. |
| Review process prior to publication | Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies | Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred |

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; CVD, cardiovascular disease; JNC, Joint National Committee; RCT, randomized controlled trial

in the evidence review were from original publications of eligible RCTs. These studies were used to create evidence tables and summary tables that were used by the panel for their deliberations (see Supplement). Because the panel conducted its own systematic review using original studies, systematic reviews and meta-analyses of RCTs conducted and published by other groups were not included in the formal evidence review.

Initial search dates for the literature review were January 1, 1966, through December 31, 2009. The search strategy and PRISMA diagram for each question is in the online Supplement. To ensure that no major relevant studies published after December 31, 2009, were excluded from consideration, 2 independent searches of PubMed and CINAHL between December 2009 and August 2013 were conducted with the same MeSH terms as the original search. Three panel members reviewed the results. The panel limited the inclusion criteria of this second search to the following. (1) The study was a major study in hypertension (eg, ACCORD-BP, SPS3; however, SPS3 did not meet strict inclusion criteria because it included nonhypertensive participants. SPS3 would not have changed our conclusions/recommendations because the only significant finding supporting a lower goal for BP occurred in an infrequent secondary outcome).[7,8] (2) The study had at least 2000 participants. (3) The study was multicentered. (4) The study met all the other inclusion/exclusion criteria. The relatively high threshold of 2000 participants was used because of the markedly lower event rates observed in recent RCTs such as ACCORD, suggesting that larger study populations are needed to obtain interpretable results. Additionally, all panel members were asked to identify newly published studies for consideration if they met the above criteria. No additional clinical trials met the previously described inclusion criteria. Studies selected were rated for quality using NHLBI's standardized quality rating tool (see Supplement) and were only included if rated as good or fair.

An external methodology team performed the literature review, summarized data from selected papers into evidence tables, and provided a summary of the evidence. From this evidence review, the panel crafted evidence statements and voted on agreement or disagreement with each statement. For approved evidence statements, the panel then voted on the quality of the evidence (**Table 2**). Once all evidence statements for each critical question were identified, the panel reviewed the evidence statements to craft the clinical recommendations, voting on each recommendation and on the strength of the recommendation (**Table 3**). For both evidence statements and recommendations, a record of the vote count (for, against, or recusal) was made without attribution. The panel attempted to achieve 100% consensus whenever possible, but a two-thirds majority was considered acceptable, with the exception of recommendations based on expert opinion, which required a 75% majority agreement to approve.

## Results (Recommendations)

The following recommendations are based on the systematic evidence review described above (**Box**). Recommendations 1 through 5 address questions 1 and 2 concerning thresholds and goals for BP treatment. Recommendations 6, 7, and 8 address question 3 concerning selection of antihypertensive drugs. Recommendation 9 is a summary of strategies based on expert opinion for starting and adding antihypertensive drugs. The evidence statements supporting the recommendations are in the online Supplement.



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Table 2. Evidence Quality Rating

| Type of Evidence | Quality Rating[a] |
|---|---|
| Well-designed, well-executed RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes<br>Well-conducted meta-analyses of such studies<br>Highly certain about the estimate of effect; further research is unlikely to change our confidence in the estimate of effect | High |
| RCTs with minor limitations affecting confidence in, or applicability of, the results<br>Well-designed, well-executed non-randomized controlled studies and well-designed, well-executed observational studies<br>Well-conducted meta-analyses of such studies<br>Moderately certain about the estimate of effect; further research may have an impact on our confidence in the estimate of effect and may change the estimate | Moderate |
| RCTs with major limitations<br>Non-randomized controlled studies and observational studies with major limitations affecting confidence in, or applicability of, the results<br>Uncontrolled clinical observations without an appropriate comparison group (eg, case series, case reports)<br>Physiological studies in humans<br>Meta-analyses of such studies<br>Low certainty about the estimate of effect; further research is likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate. | Low |

Abbreviations: RCT, randomized controlled trial

[a]The evidence quality rating system used in this guideline was developed by the National Heart, Lung, and Blood Institute's (NHLBI's) Evidence-Based Methodology Lead (with input from NHLBI staff, external methodology team, and guideline panels and work groups) for use by all the NHLBI CVD guideline panels and work groups during this project. As a result, it includes the evidence quality rating for many types of studies, including studies that were not used in this guideline. Additional details regarding the evidence quality rating system are available in the online Supplement.

Table 3. Strength of Recommendation

| Grade | Strength of Recommendation |
|---|---|
| A | Strong Recommendation<br>There is high certainty based on evidence that the net benefit[a] is substantial. |
| B | Moderate Recommendation<br>There is moderate certainty based on evidence that the net benefit is moderate to substantial or there is high certainty that the net benefit is moderate. |
| C | Weak Recommendation<br>There is at least moderate certainty based on evidence that there is a small net benefit. |
| D | Recommendation against<br>There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits. |
| E | Expert Opinion ("There is insufficient evidence or evidence is unclear or conflicting, but this is what the committee recommends.")<br>Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the committee thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area. |
| N | No Recommendation for or against ("There is insufficient evidence or evidence is unclear or conflicting.")<br>Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the committee thought no recommendation should be made. Further research is recommended in this area. |

The strength of recommendation grading system used in this guideline was developed by the National Heart, Lung, and Blood Institute's (NHLBI's) Evidence-Based Methodology Lead (with input from NHLBI staff, external methodology team, and guideline panels and work groups) for use by all the NHLBI CVD guideline panels and work groups during this project. Additional details regarding the strength of recommendation grading system are available in the online Supplement.

[a]Net benefit is defined as benefits minus the risks/harms of the service/intervention.

## Recommendation 1

In the general population aged 60 years or older, initiate pharmacologic treatment to lower BP at systolic blood pressure (SBP) of 150 mm Hg or higher or diastolic blood pressure (DBP) of 90 mm Hg or higher and treat to a goal SBP lower than 150 mm Hg and goal DBP lower than 90 mm Hg.
*Strong Recommendation – Grade A*

### Corollary Recommendation

In the general population aged 60 years or older, if pharmacologic treatment for high BP results in lower achieved SBP (for example, <140 mm Hg) and treatment is not associated with adverse effects on health or quality of life, treatment does not need to be adjusted.
*Expert Opinion – Grade E*

Recommendation 1 is based on evidence statements 1 through 3 from question 2 in which there is moderate- to high-quality evidence from RCTs that in the general population aged 60 years or older, treating high BP to a goal of lower than 150/90 mm Hg reduces stroke, heart failure, and coronary heart disease (CHD). There is also evidence (albeit low quality) from evidence statement 6, question 2 that setting a goal SBP of lower than 140 mm Hg in this age group provides no additional benefit compared with a higher goal SBP of 140 to 160 mm Hg or 140 to 149 mm Hg.[9,10]

To answer question 2 about goal BP, the panel reviewed all RCTs that met the eligibility criteria and that either compared treatment with a particular goal vs no treatment or placebo or compared treatment with one BP goal with treatment to another BP goal. The trials on which these evidence statements and this recommendation are based include HYVET, Syst-Eur, SHEP, JATOS, VALISH, and CARDIO-SIS.[1-3,9-11] Strengths, limitations, and other considerations related to this evidence review are presented in the evidence statement narratives and clearly support the benefit of treating to a BP lower than 150 mm Hg.

The corollary to recommendation 1 reflects that there are many treated hypertensive patients aged 60 years or older in whom SBP is currently lower than 140 mm Hg, based on implementation of previous guideline recommendations.[12] The panel's opinion is that in these patients, it is not necessary to adjust medication to allow BP



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**Box. Recommendations for Management of Hypertension**

**Recommendation 1**
In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥150 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg. (Strong Recommendation – Grade A)

**Corollary Recommendation**
In the general population aged ≥60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg, <140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)

**Recommendation 2**
In the general population <60 years, initiate pharmacologic treatment to lower BP at DBP ≥90 mm Hg and treat to a goal DBP <90 mm Hg. (For ages 30-59 years, Strong Recommendation – Grade A; For ages 18-29 years, Expert Opinion – Grade E)

**Recommendation 3**
In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg and treat to a goal SBP <140 mm Hg. (Expert Opinion – Grade E)

**Recommendation 4**
In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

**Recommendation 5**
In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

**Recommendation 6**
In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB). (Moderate Recommendation – Grade B)

**Recommendation 7**
In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB. (For general black population: Moderate Recommendation – Grade B; for black patients with diabetes: Weak Recommendation – Grade C)

**Recommendation 8**
In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status. (Moderate Recommendation – Grade B)

**Recommendation 9**
The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed. (Expert Opinion – Grade E)

to increase. In 2 of the trials that provide evidence supporting an SBP goal lower than 150 mm Hg, the average treated SBP was 143 to 144 mm Hg.[2,3] Many participants in those studies achieved an SBP lower than 140 mm Hg with treatment that was generally well tolerated. Two other trials[9,10] suggest there was no benefit for an SBP goal lower than 140 mm Hg, but the confidence intervals around the effect sizes were wide and did not exclude the possibility of a clinically important benefit. Therefore, the panel included a corollary recommendation based on expert opinion that treatment for hypertension does not need to be adjusted if treatment results in SBP lower than 140 mm Hg and is not associated with adverse effects on health or quality of life.

While all panel members agreed that the evidence supporting recommendation 1 is very strong, the panel was unable to reach unanimity on the recommendation of a goal SBP of lower than 150 mm Hg. Some members recommended continuing the JNC 7 SBP goal of lower than 140 mm Hg for individuals older than 60 years based on expert opinion.[12] These members concluded that the evidence was insufficient to raise the SBP target from lower than 140 to lower than 150 mm Hg in high-risk groups, such as black persons, those with CVD including stroke, and those with multiple risk factors. The panel agreed that more research is needed to identify optimal goals of SBP for patients with high BP.

## Recommendation 2

In the general population younger than 60 years, initiate pharmacologic treatment to lower BP at DBP of 90 mm Hg or higher and treat to a goal DBP of lower than 90 mm Hg.
*For ages 30 through 59 years, Strong Recommendation – Grade A*
*For ages 18 through 29 years, Expert Opinion – Grade E*

Recommendation 2 is based on high-quality evidence from 5 DBP trials (HDFP, Hypertension-Stroke Cooperative, MRC, ANBP, and VA Cooperative) that demonstrate improvements in health outcomes among adults aged 30 through 69 years with elevated BP.[13-18] Initiation of antihypertensive treatment at a DBP threshold of 90 mm Hg or higher and treatment to a DBP goal of lower than 90 mm Hg reduces cerebrovascular events, heart failure, and overall mortality (question 1, evidence statements 10, 11, 13; question 2, evidence statement 10). In further support for a DBP goal of lower than 90 mm Hg, the panel found evidence that there is no benefit in treating patients to a goal of either 80 mm Hg or lower or 85 mm Hg or lower compared with 90 mm Hg or lower based on the HOT trial, in which patients were randomized to these 3 goals without statistically significant differences between treatment groups in the primary or secondary outcomes (question 2, evidence statement 14).[19]

In adults younger than 30 years, there are no good- or fair-quality RCTs that assessed the benefits of treating elevated DBP on health outcomes (question 1, evidence statement 14). In the absence of such evidence, it is the panel's opinion that in adults younger than 30 years, the DBP threshold and goal should be the same as in adults 30 through 59 years of age.

## Recommendation 3

In the general population younger than 60 years, initiate pharmacologic treatment to lower BP at SBP of 140 mm Hg or higher and treat to a goal SBP of lower than 140 mm Hg.
*Expert Opinion – Grade E*



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Recommendation 3 is based on expert opinion. While there is high-quality evidence to support a specific SBP threshold and goal for persons aged 60 years or older (See recommendation 1), the panel found insufficient evidence from good- or fair-quality RCTs to support a specific SBP threshold or goal for persons younger than 60 years. In the absence of such evidence, the panel recommends an SBP treatment threshold of 140 mm Hg or higher and an SBP treatment goal of lower than 140 mm Hg based on several factors.

First, in the absence of any RCTs that compared the current SBP standard of 140 mm Hg with another higher or lower standard in this age group, there was no compelling reason to change current recommendations. Second, in the DBP trials that demonstrated the benefit of treating DBP to lower than 90 mm Hg, many of the study participants who achieved DBP of lower than 90 mm Hg were also likely to have achieved SBPs of lower than 140 mm Hg with treatment. It is not possible to determine whether the outcome benefits in these trials were due to lowering DBP, SBP, or both. Third, given the recommended SBP goal of lower than 140 mm Hg in adults with diabetes or CKD (recommendations 4 and 5), a similar SBP goal for the general population younger than 60 years may facilitate guideline implementation.

### Recommendation 4

In the population aged 18 years or older with CKD, initiate pharmacologic treatment to lower BP at SBP of 140 mm Hg or higher or DBP of 90 mm Hg or higher and treat to goal SBP of lower than 140 mm Hg and goal DBP lower than 90 mm Hg.
*Expert Opinion – Grade E*

Based on the inclusion criteria used in the RCTs reviewed by the panel, this recommendation applies to individuals younger than 70 years with an estimated GFR or measured GFR less than 60 mL/min/1.73 $m^2$ and in people of any age with albuminuria defined as greater than 30 mg of albumin/g of creatinine at any level of GFR.

Recommendation 4 is based on evidence statements 15-17 from question 2. In adults younger than 70 years with CKD, the evidence is insufficient to determine if there is a benefit in mortality, or cardiovascular or cerebrovascular health outcomes with antihypertensive drug therapy to a lower BP goal (for example, <130/80 mm Hg) compared with a goal of lower than 140/90 mm Hg (question 2, evidence statement 15). There is evidence of moderate quality demonstrating no benefit in slowing the progression of kidney disease from treatment with antihypertensive drug therapy to a lower BP goal (for example, <130/80 mm Hg) compared with a goal of lower than 140/90 mm Hg (question 2, evidence statement 16).

Three trials that met our criteria for review addressed the effect of antihypertensive drug therapy on change in GFR or time to development of ESRD, but only one trial addressed cardiovascular disease end points. Blood pressure goals differed across the trials, with 2 trials (AASK and MDRD) using mean arterial pressure and different targets by age, and 1 trial (REIN-2) using only DBP goals.[20-22] None of the trials showed that treatment to a lower BP goal (for example, <130/80 mm Hg) significantly lowered kidney or cardiovascular disease end points compared with a goal of lower than 140/90 mm Hg.

For patients with proteinuria (>3 g/24 hours), post hoc analysis from only 1 study (MDRD) indicated benefit from treatment to a lower BP goal (<130/80 mm Hg), and this related to kidney outcomes only.[22] Although post hoc observational analyses of data from this trial and others suggested benefit from the lower goal at lower levels of proteinuria, this result was not seen in the primary analyses or in AASK or REIN-2 (question 2, evidence statement 17).[20,21]

Based on available evidence the panel cannot make a recommendation for a BP goal for people aged 70 years or older with GFR less than 60 mL/min/1.73$m^2$. The commonly used estimating equations for GFR were not developed in populations with significant numbers of people older than 70 years and have not been validated in older adults. No outcome trials reviewed by the panel included large numbers of adults older than 70 years with CKD. Further, the diagnostic criteria for CKD do not consider age-related decline in kidney function as reflected in estimated GFR. Thus, when weighing the risks and benefits of a lower BP goal for people aged 70 years or older with estimated GFR less than 60 mL/min/1.73$m^2$, antihypertensive treatment should be individualized, taking into consideration factors such as frailty, comorbidities, and albuminuria.

### Recommendation 5

In the population aged 18 years or older with diabetes, initiate pharmacologic treatment to lower BP at SBP of 140 mm Hg or higher or DBP of 90 mm Hg or higher and treat to a goal SBP of lower than 140 mm Hg and goal DBP lower than 90 mm Hg.
*Expert Opinion – Grade E*

Recommendation 5 is based on evidence statements 18-21 from question 2, which address BP goals in adults with both diabetes and hypertension. There is moderate-quality evidence from 3 trials (SHEP, Syst-Eur, and UKPDS) that treatment to an SBP goal of lower than 150 mm Hg improves cardiovascular and cerebrovascular health outcomes and lowers mortality (see question 2, evidence statement 18) in adults with diabetes and hypertension.[23-25] No RCTs addressed whether treatment to an SBP goal of lower than 140 mm Hg compared with a higher goal (for example, <150 mm Hg) improves health outcomes in adults with diabetes and hypertension. In the absence of such evidence, the panel recommends an SBP goal of lower than 140 mm Hg and a DBP goal lower than 90 mm Hg in this population based on expert opinion, consistent with the BP goals in recommendation 3 for the general population younger than 60 years with hypertension. Use of a consistent BP goal in the general population younger than 60 years and in adults with diabetes of any age may facilitate guideline implementation. This recommendation for an SBP goal of lower than 140 mm Hg in patients with diabetes is also supported by the ACCORD-BP trial, in which the control group used this goal and had similar outcomes compared with a lower goal.[7]

The panel recognizes that the ADVANCE trial tested the effects of treatment to lower BP on major macrovascular and microvascular events in adults with diabetes who were at increased risk of CVD, but the study did not meet the panel's inclusion criteria because participants were eligible irrespective of baseline BP, and there were no randomized BP treatment thresholds or goals.[26]

The panel also recognizes that an SBP goal of lower than 130 mm Hg is commonly recommended for adults with diabetes and hypertension. However, this lower SBP goal is not supported by any RCT that randomized participants into 2 or more groups in which



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treatment was initiated at a lower SBP threshold than 140 mm Hg or into treatment groups in which the SBP goal was lower than 140 mm Hg and that assessed the effects of a lower SBP threshold or goal on important health outcomes. The only RCT that compared an SBP treatment goal of lower than 140 mm Hg with a lower SBP goal and assessed the effects on important health outcomes is ACCORD-BP, which compared an SBP treatment goal of lower than 120 mm Hg with a goal lower than 140 mm Hg.[7] There was no difference in the primary outcome, a composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. There were also no differences in any of the secondary outcomes except for a reduction in stroke. However, the incidence of stroke in the group treated to lower than 140 mm Hg was much lower than expected, so the absolute difference in fatal and nonfatal stroke between the 2 groups was only 0.21% per year. The panel concluded that the results from ACCORD-BP did not provide sufficient evidence to recommend an SBP goal of lower than 120 mm Hg in adults with diabetes and hypertension.

The panel similarly recommends the same goal DBP in adults with diabetes and hypertension as in the general population (<90 mm Hg). Despite some existing recommendations that adults with diabetes and hypertension should be treated to a DBP goal of lower than 80 mm Hg, the panel did not find sufficient evidence to support such a recommendation. For example, there are no good- or fair-quality RCTs with mortality as a primary or secondary prespecified outcome that compared a DBP goal of lower than 90 mm Hg with a lower goal (evidence statement 21).

In the HOT trial, which is frequently cited to support a lower DBP goal, investigators compared a DBP goal of 90 mm Hg or lower vs a goal of 80 mm Hg or lower.[19] The lower goal was associated with a reduction in a composite CVD outcome (question 2, evidence statement 20), but this was a post hoc analysis of a small subgroup (8%) of the study population that was not prespecified. As a result, the evidence was graded as low quality.

Another commonly cited study to support a lower DBP goal is UKPDS,[25] which had a BP goal of lower than 150/85 mm Hg in the more-intensively treated group compared with a goal of lower than 180/105 mm Hg in the less-intensively treated group. UKPDS did show that treatment in the lower goal BP group was associated with a significantly lower rate of stroke, heart failure, diabetes-related end points, and deaths related to diabetes. However, the comparison in UKPDS was a DBP goal of lower than 85 mm Hg vs lower than105 mm Hg; therefore, it is not possible to determine whether treatment to a DBP goal of lower than 85 mm Hg improves outcomes compared with treatment to a DBP goal of lower than 90 mm Hg. In addition, UKPDS was a mixed systolic and diastolic BP goal study (combined SBP and DBP goals), so it cannot be determined if the benefits were due to lowering SBP, DBP, or both.

## Recommendation 6

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).
*Moderate Recommendation – Grade B*

For this recommendation, only RCTs that compared one class of antihypertensive medication to another and assessed the effects on health outcomes were reviewed; placebo-controlled RCTs were not included. However, the evidence review was informed by major placebo-controlled hypertension trials, including 3 federally funded trials (VA Cooperative Trial, HDFP, and SHEP), that were pivotal in demonstrating that treatment of hypertension with antihypertensive medications reduces cardiovascular or cerebrovascular events and/or mortality.[3,13,18] These trials all used thiazide-type diuretics compared with placebo or usual care as the basis of therapy. Additional evidence that BP lowering reduces risk comes from trials of β-blocker vs placebo[16,27] and CCB vs placebo.[1]

Each of the 4 drug classes recommended by the panel in recommendation 6 yielded comparable effects on overall mortality and cardiovascular, cerebrovascular, and kidney outcomes, with one exception: heart failure. Initial treatment with a thiazide-type diuretic was more effective than a CCB or ACEI (question 3, evidence statements 14 and 15), and an ACEI was more effective than a CCB (question 3, evidence statement 1) in improving heart failure outcomes. While the panel recognized that improved heart failure outcomes was an important finding that should be considered when selecting a drug for initial therapy for hypertension, the panel did not conclude that it was compelling enough within the context of the overall body of evidence to preclude the use of the other drug classes for initial therapy. The panel also acknowledged that the evidence supported BP control, rather than a specific agent used to achieve that control, as the most relevant consideration for this recommendation.

The panel did not recommend β-blockers for the initial treatment of hypertension because in one study use of β-blockers resulted in a higher rate of the primary composite outcome of cardiovascular death, myocardial infarction, or stroke compared to use of an ARB, a finding that was driven largely by an increase in stroke (question 3, evidence statement 22).[28] In the other studies that compared a β-blocker to the 4 recommended drug classes, the β-blocker performed similarly to the other drugs (question 3, evidence statement 8) or the evidence was insufficient to make a determination (question 3, evidence statements 7, 12, 21, 23, and 24).

α-Blockers were not recommended as first-line therapy because in one study initial treatment with an α-blocker resulted in worse cerebrovascular, heart failure, and combined cardiovascular outcomes than initial treatment with a diuretic (question 3, evidence statement 13).[29] There were no RCTs of good or fair quality comparing the following drug classes to the 4 recommended classes: dual $\alpha_1$- + β-blocking agents (eg, carvedilol), vasodilating β-blockers (eg, nebivolol), central $\alpha_2$-adrenergic agonists (eg, clonidine), direct vasodilators (eg, hydralazine), aldosterone receptor antagonists (eg, spironolactone), adrenergic neuronal depleting agents (reserpine), and loop diuretics (eg, furosemide) (question 3, evidence statement 30). Therefore, these drug classes are not recommended as first-line therapy. In addition, no eligible RCTs were identified that compared a diuretic vs an ARB, or an ACEI vs an ARB. ONTARGET was not eligible because hypertension was not required for inclusion in the study.[30]

Similar to those for the general population, this recommendation applies to those with diabetes because trials including participants with diabetes showed no differences in major cardiovascular or cerebrovascular outcomes from those in the general population (question 3, evidence statements 36-48).



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Table 4. Evidence-Based Dosing for Antihypertensive Drugs

| Antihypertensive Medication | Initial Daily Dose, mg | Target Dose in RCTs Reviewed, mg | No. of Doses per Day |
|---|---|---|---|
| ACE inhibitors | | | |
| Captopril | 50 | 150-200 | 2 |
| Enalapril | 5 | 20 | 1-2 |
| Lisinopril | 10 | 40 | 1 |
| Angiotensin receptor blockers | | | |
| Eprosartan | 400 | 600-800 | 1-2 |
| Candesartan | 4 | 12-32 | 1 |
| Losartan | 50 | 100 | 1-2 |
| Valsartan | 40-80 | 160-320 | 1 |
| Irbesartan | 75 | 300 | 1 |
| β-Blockers | | | |
| Atenolol | 25-50 | 100 | 1 |
| Metoprolol | 50 | 100-200 | 1-2 |
| Calcium channel blockers | | | |
| Amlodipine | 2.5 | 10 | 1 |
| Diltiazem extended release | 120-180 | 360 | 1 |
| Nitrendipine | 10 | 20 | 1-2 |
| Thiazide-type diuretics | | | |
| Bendroflumethiazide | 5 | 10 | 1 |
| Chlorthalidone | 12.5 | 12.5-25 | 1 |
| Hydrochlorothiazide | 12.5-25 | 25-100[a] | 1-2 |
| Indapamide | 1.25 | 1.25-2.5 | 1 |

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.

[a]Current recommended evidence-based dose that balances efficacy and safety is 25-50 mg daily.

The following important points should be noted. First, many people will require treatment with more than one antihypertensive drug to achieve BP control. While this recommendation applies only to the choice of the initial antihypertensive drug, the panel suggests that any of these 4 classes would be good choices as add-on agents (recommendation 9). Second, this recommendation is specific for thiazide-type diuretics, which include thiazide diuretics, chlorthalidone, and indapamide; it does not include loop or potassium-sparing diuretics. Third, it is important that medications be dosed adequately to achieve results similar to those seen in the RCTs (**Table 4**). Fourth, RCTs that were limited to specific nonhypertensive populations, such as those with coronary artery disease or heart failure, were not reviewed for this recommendation. Therefore, recommendation 6 should be applied with caution to these populations. Recommendations for those with CKD are addressed in recommendation 8.

## Recommendation 7

In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.

*For general black population: Moderate Recommendation – Grade B*
*For black patients with diabetes: Weak Recommendation – Grade C*

Recommendation 7 is based on evidence statements from question 3. In cases for which evidence for the black population was the same as for the general population, the evidence statements for the general population apply to the black population. However, there are some cases for which the results for black persons were different from the results for the general population (question 3, evidence statements 2, 10, and 17). In those cases, separate evidence statements were developed.

This recommendation stems from a prespecified subgroup analysis of data from a single large trial (ALLHAT) that was rated good.[31] In that study, a thiazide-type diuretic was shown to be more effective in improving cerebrovascular, heart failure, and combined cardiovascular outcomes compared to an ACEI in the black patient subgroup, which included large numbers of diabetic and nondiabetic participants (question 3, evidence statements 10, 15 and 17). Therefore, the recommendation is to choose thiazide-type diuretics over ACEI for black patients. Although a CCB was less effective than a diuretic in preventing heart failure in the black subgroup of this trial (question 3, evidence statement 14), there were no differences in other outcomes (cerebrovascular, CHD, combined cardiovascular, and kidney outcomes, or overall mortality) between a CCB and a diuretic (question 3, evidence statements 6, 8, 11, 18, and 19). Therefore, both thiazide-type diuretics and CCBs are recommended as first-line therapy for hypertension in black patients.

The panel recommended a CCB over an ACEI as first-line therapy in black patients because there was a 51% higher rate (relative risk, 1.51; 95% CI, 1.22-1.86) of stroke in black persons in ALLHAT with the use of an ACEI as initial therapy compared with use of a CCB (question 3, evidence statement 2).[32] The ACEI was also less effective in reducing BP in black individuals compared with the CCB (question 3, evidence statement 2).[32] There were no outcome studies meeting our eligibility criteria that compared diuretics or CCBs vs β-blockers, ARBs, or other renin-angiotensin system inhibitors in black patients.

The recommendation for black patients with diabetes is weaker than the recommendation for the general black population because outcomes for the comparison between initial use of a CCB compared to initial use of an ACEI in black persons with diabetes were not reported in any of the studies eligible for our evidence review.



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Therefore, this evidence was extrapolated from findings in the black participants in ALLHAT, 46% of whom had diabetes. Additional support comes from a post hoc analysis of black participants in ALLHAT that met the criteria for the metabolic syndrome, 68% of whom had diabetes.[33] However, this study did not meet the criteria for our review because it was a post hoc analysis. This recommendation also does not address black persons with CKD, who are addressed in recommendation 8.

## Recommendation 8

In the population aged 18 years or older with CKD and hypertension, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status.
*Moderate Recommendation – Grade B*

The evidence is moderate (question 3, evidence statements 31-32) that treatment with an ACEI or ARB improves kidney outcomes for patients with CKD. This recommendation applies to CKD patients with and without proteinuria, as studies using ACEIs or ARBs showed evidence of improved kidney outcomes in both groups.

This recommendation is based primarily on kidney outcomes because there is less evidence favoring ACEI or ARB for cardiovascular outcomes in patients with CKD. Neither ACEIs nor ARBs improved cardiovascular outcomes for CKD patients compared with a β-blocker or CCB (question 3, evidence statements 33-34). One trial (IDNT) did show improvement in heart failure outcomes with an ARB compared with a CCB, but this trial was restricted to a population with diabetic nephropathy and proteinuria (question 3, evidence statement 5).[34] There are no RCTs in the evidence review that directly compared ACEI to ARB for any cardiovascular outcome. However, both are renin-angiotensin system inhibitors and have been shown to have similar effects on kidney outcomes (question 3, evidence statements 31-32).

Recommendation 8 is specifically directed at those with CKD and hypertension and addresses the potential benefit of specific drugs on kidney outcomes. The AASK study showed the benefit of an ACEI on kidney outcomes in black patients with CKD and provides additional evidence that supports ACEI use in that population.[21] Additional trials that support the benefits of ACEI or ARB therapy did not meet our inclusion criteria because they were not restricted to patients with hypertension.[35,36] Direct renin inhibitors are not included in this recommendation because there were no studies demonstrating their benefits on kidney or cardiovascular outcomes.

The panel noted the potential conflict between this recommendation to use an ACEI or ARB in those with CKD and hypertension and the recommendation to use a diuretic or CCB (recommendation 7) in black persons: what if the person is black and has CKD? To answer this, the panel relied on expert opinion. In black patients with CKD and proteinuria, an ACEI or ARB is recommended as initial therapy because of the higher likelihood of progression to ESRD.[21] In black patients with CKD but without proteinuria, the choice for initial therapy is less clear and includes a thiazide-type diuretic, CCB, ACEI, or ARB. If an ACEI or ARB is not used as the initial drug, then an ACEI or ARB can be added as a second-line drug if necessary to achieve goal BP. Because the majority of patients with CKD and hypertension will require more than 1 drug to achieve goal BP, it is anticipated that an ACEI or ARB will be used either as initial therapy or as second-line therapy in addition to a diuretic or CCB in black patients with CKD.

Recommendation 8 applies to adults aged 18 years or older with CKD, but there is no evidence to support renin-angiotensin system inhibitor treatment in those older than 75 years. Although treatment with an ACEI or ARB may be beneficial in those older than 75 years, use of a thiazide-type diuretic or CCB is also an option for individuals with CKD in this age group.

Use of an ACEI or an ARB will commonly increase serum creatinine and may produce other metabolic effects such as hyperkalemia, particularly in patients with decreased kidney function. Although an increase in creatinine or potassium level does not always require adjusting medication, use of renin-angiotensin system inhibitors in the CKD population requires monitoring of electrolyte and serum creatinine levels, and in some cases, may require reduction in dose or discontinuation for safety reasons.

## Recommendation 9

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed.
*Expert Opinion – Grade E*

Recommendation 9 was developed by the panel in response to a perceived need for further guidance to assist in implementation of recommendations 1 through 8. Recommendation 9 is based on strategies used in RCTs that demonstrated improved patient outcomes and the expertise and clinical experience of panel members. This recommendation differs from the other recommendations because it was not developed in response to the 3 critical questions using a systematic review of the literature. The **Figure** is an algorithm summarizing the recommendations. However, this algorithm has not been validated with respect to achieving improved patient outcomes.

How should clinicians titrate and combine the drugs recommended in this report? There were no RCTs and thus the panel relied on expert opinion. Three strategies (**Table 5**) have been used in RCTs of high BP treatment but were not compared with each other. Based on the evidence reviewed for questions 1 through 3 and on the expert opinion of the panel members, it is not known if one of the strategies results in improved cardiovascular outcomes, cerebrovascular outcomes, kidney outcomes, or mortality compared with an alternative strategy. There is not likely to be evidence from well-designed RCTs that compare these



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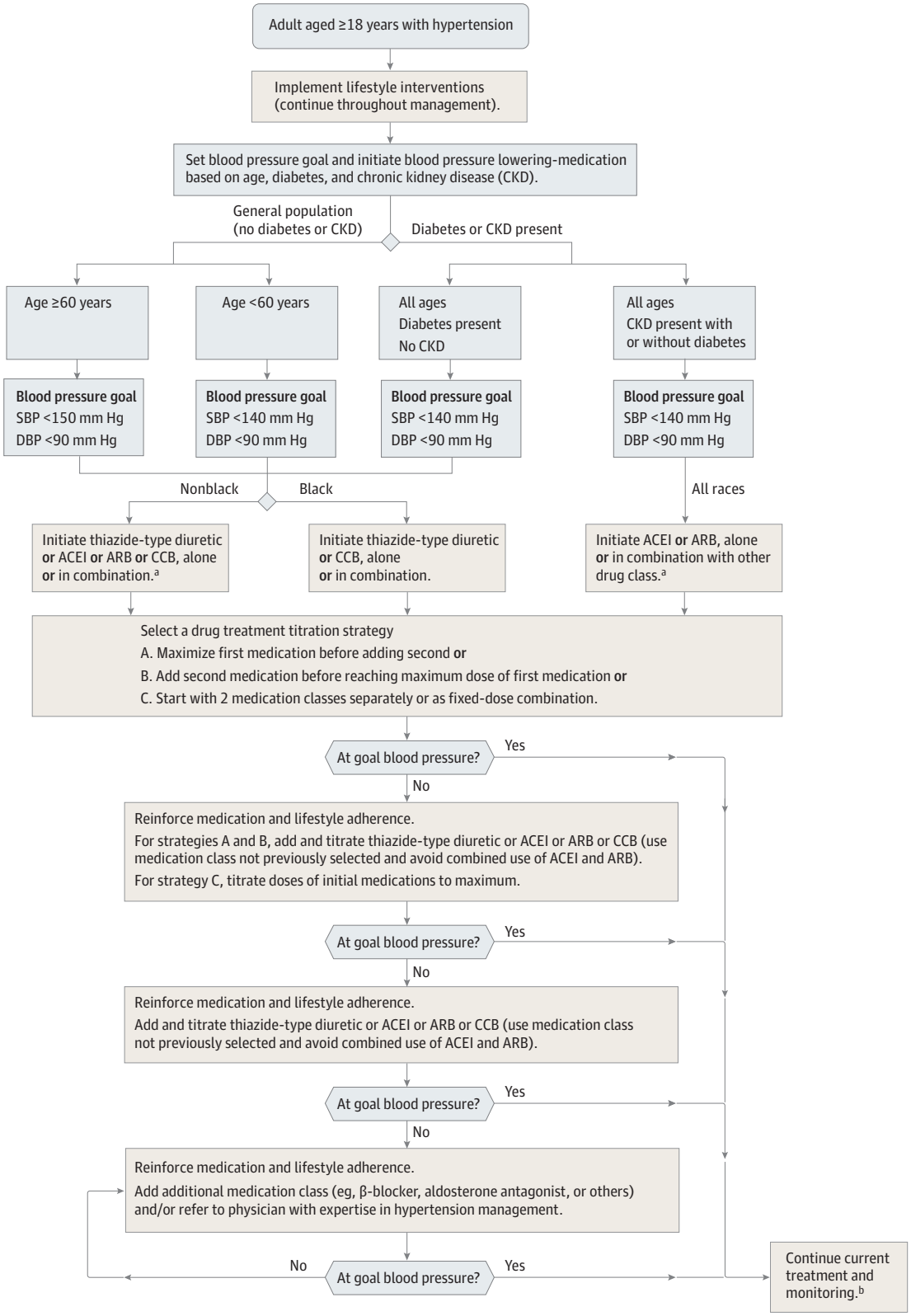
Figure. 2014 Hypertension Guideline Management Algorithm




SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; and CCB, calcium channel blocker.

[a] ACEIs and ARBs should not be used in combination.

[b] If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.



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Table 5. Strategies to Dose Antihypertensive Drugs[a]

| Strategy | Description | Details |
|---|---|---|
| A | Start one drug, titrate to maximum dose, and then add a second drug | If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP<br>If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP<br>If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP |
| B | Start one drug and then add a second drug before achieving maximum dose of the initial drug | Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP<br>If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP |
| C | Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination | Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with ≥2 drugs when SBP is >160 mm Hg and/or DBP is >100 mm Hg, or if SBP is >20 mm Hg above goal and/or DBP is >10 mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose. |

Abbreviations: ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

[a]This table is not meant to exclude other agents within the classes of antihypertensive medications that have been recommended but reflects those agents and dosing used in randomized controlled trials that demonstrated improved outcomes.

strategies and assess their effects on important health outcomes. There may be evidence that different strategies result in more rapid attainment of BP goal or in improved adherence, but those are intermediate outcomes that were not included in the evidence review. Therefore, each strategy is an acceptable pharmacologic treatment strategy that can be tailored based on individual circumstances, clinician and patient preferences, and drug tolerability. With each strategy, clinicians should regularly assess BP, encourage evidence-based lifestyle and adherence interventions, and adjust treatment until goal BP is attained and maintained. In most cases, adjusting treatment means intensifying therapy by increasing the drug dose or by adding additional drugs to the regimen. To avoid unnecessary complexity in this report, the hypertension management algorithm (Figure) does not explicitly define all potential drug treatment strategies.

Finally, panel members point out that in specific situations, one antihypertensive drug may be replaced with another if it is perceived not to be effective or if there are adverse effects.

## Limitations

This evidence-based guideline for the management of high BP in adults is not a comprehensive guideline and is limited in scope because of the focused evidence review to address the 3 specific questions (Table 1). Clinicians often provide care for patients with numerous comorbidities or other important issues related to hypertension, but the decision was made to focus on 3 questions considered to be relevant to most physicians and patients. Treatment adherence and medication costs were thought to be beyond the scope of this review, but the panel acknowledges the importance of both issues.

The evidence review did not include observational studies, systematic reviews, or meta-analyses, and the panel did not conduct its own meta-analysis based on prespecified inclusion criteria. Thus, information from these types of studies was not incorporated into the evidence statements or recommendations. Although this may be considered a limitation, the panel decided to focus only on RCTs because they represent the best scientific evidence and because there were a substantial number of studies that included large numbers of patients and met our inclusion criteria. Randomized controlled trials that included participants with normal BP were excluded from our formal analysis. In cases in which high-quality evidence was not available or the evidence was weak or absent, the panel relied on fair-quality evidence, panel members' knowledge of the published literature beyond the RCTs reviewed, and personal experience to make recommendations. The duration of the guideline development process following completion of the systematic search may have caused the panel to miss studies published after our literature review. However, a bridge search was performed through August 2013, and the panel found no additional studies that would have changed the recommendations.

Many of the reviewed studies were conducted when the overall risk of cardiovascular morbidity and mortality was substantially higher than it is today; therefore, effect sizes may have been overestimated. Further, RCTs that enrolled prehypertensive or nonhypertensive individuals were excluded. Thus, our recommendations do not apply to those without hypertension. In many studies focused on DBP, participants also had elevated SBP so it was not possible to determine whether the benefit observed in those trials arose from lowering DBP, SBP, or both. In addition, the ability to compare studies from different time periods was limited by differences in clinical trial design and analytic techniques.

While physicians use cost, adherence, and often observational data to make treatment decisions, medical interventions should whenever possible be based first and foremost on good science demonstrating benefits to patients. Randomized controlled trials are the gold standard for this assessment and thus were the basis for providing the evidence for our clinical recommendations. Although adverse effects and harms of antihypertensive treatment documented in the RCTs were considered when the panel made its decisions, the review was not designed to determine whether therapy-associated adverse effects and harms resulted in significant changes in important health outcomes. In addition, this guide-



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Table 6. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

| Guideline | Population | Goal BP, mm Hg | Initial Drug Treatment Options |
|---|---|---|---|
| 2014 Hypertension guideline | General ≥60 y | <150/90 | Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type diuretic or CCB |
| | General <60 y | <140/90 | |
| | Diabetes | <140/90 | |
| | CKD | <140/90 | ACEI or ARB |
| ESH/ESC 2013[37] | General nonelderly | <140/90 | Diuretic, β-blocker, CCB, ACEI, or ARB |
| | General elderly <80 y | <150/90 | |
| | General ≥80 y | <150/90 | |
| | Diabetes | <140/85 | ACEI or ARB |
| | CKD no proteinuria | <140/90 | ACEI or ARB |
| | CKD + proteinuria | <130/90 | |
| CHEP 2013[38] | General <80 y | <140/90 | Thiazide, β-blocker (age <60y), ACEI (nonblack), or ARB |
| | General ≥80 y | <150/90 | |
| | Diabetes | <130/80 | ACEI or ARB with additional CVD risk ACEI, ARB, thiazide, or DHPCCB without additional CVD risk |
| | CKD | <140/90 | ACEI or ARB |
| ADA 2013[39] | Diabetes | <140/80 | ACEI or ARB |
| KDIGO 2012[40] | CKD no proteinuria | ≤140/90 | ACEI or ARB |
| | CKD + proteinuria | ≤130/80 | |
| NICE 2011[41] | General <80 y | <140/90 | <55 y: ACEI or ARB |
| | General ≥80 y | <150/90 | ≥55 y or black: CCB |
| ISHIB 2010[42] | Black, lower risk | <135/85 | Diuretic or CCB |
| | Target organ damage or CVD risk | <130/80 | |

Abbreviations: ADA, American Diabetes Association; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CHEP, Canadian Hypertension Education Program; CKD, chronic kidney disease; CVD, cardiovascular disease; DHPCCB, dihydropyridine calcium channel blocker; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ISHIB, International Society for Hypertension in Blacks; JNC, Joint National Committee; KDIGO, Kidney Disease: Improving Global Outcome; NICE, National Institute for Health and Clinical Excellence.

line was not endorsed by any federal agency or professional society prior to publication and thus is a departure from previous JNC reports. The panel anticipates that an objective assessment of this report following publication will allow open dialogue among endorsing entities and encourage continued attention to rigorous methods in guideline development, thus raising the standard for future guidelines.

## Discussion

The recommendations based on RCT evidence in this guideline differ from recommendations in other currently used guidelines supported by expert consensus (**Table 6**). For example, JNC 7 and other guidelines recommended treatment to lower BP goals in patients with diabetes and CKD based on observational studies.[12] Recently, several guideline documents such as those from the American Diabetes Association have raised the systolic BP goals to values that are similar to those recommended in this evidence-based guideline.[37-42] Other guidelines such as those of the European Society of Hypertension/European Society of Cardiology also recommend a systolic BP goal of lower than 150 mm Hg, but it is not clear at what age cutoff in the general population this goal specifically applies.[37] This changing landscape is understandable given the lack of clear RCT evidence in many clinical situations.

### History of JNC 8

The panel was originally constituted as the "Eighth Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8)." In March 2008 NHLBI sent letters inviting the co-chairs and committee members to serve on JNC 8. The charge to the committee was as follows: "The JNC 8 will review and synthesize the latest available scientific evidence, update existing clinical recommendations, and provide guidance to busy primary care clinicians on the best approaches to manage and control hypertension in order to minimize patients' risk for cardiovascular and other complications." The committee was also asked to identify and prioritize the most important questions for the evidence review. In June 2013, NHLBI announced its decision to discontinue developing clinical guidelines including those in process, instead partnering with selected organizations that would develop the guidelines.[43,44] Importantly, participation in this process required that these organizations be involved in producing the final content of the report. The panel elected to pursue publication independently to bring the recommendations to the public in a timely manner while maintaining the integrity of the predefined process. This report is therefore not an NHLBI sanctioned report and does not reflect the views of NHLBI.

## Conclusions

It is important to note that this evidence-based guideline has not redefined high BP, and the panel believes that the 140/90 mm Hg definition from JNC 7 remains reasonable. The relationship between naturally occurring BP and risk is linear down to very low BP, but the benefit of treating to these lower levels with antihypertensive drugs is not established. For all persons with hypertension, the potential benefits of a healthy diet, weight control, and regular exercise cannot be overemphasized. These lifestyle treatments have the potential to improve BP control and even reduce medication needs. Al-



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though the authors of this hypertension guideline did not conduct an evidence review of lifestyle treatments in patients taking and not taking antihypertensive medication, we support the recommendations of the 2013 Lifestyle Work Group.[45]

The recommendations from this evidence-based guideline from panel members appointed to the Eighth Joint National Committee (JNC 8) offer clinicians an analysis of what is known and not known about BP treatment thresholds, goals, and drug treatment strategies to achieve those goals based on evidence from RCTs. However, these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient. We hope that the algorithm will facilitate implementation and be useful to busy clinicians. The strong evidence base of this report should inform quality measures for the treatment of patients with hypertension.

## ARTICLE INFORMATION

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**Author Affiliations:** University of Iowa, Iowa City (James, Carter); University of Alabama at Birmingham School of Medicine (Oparil); Memphis Veterans Affairs Medical Center and the University of Tennessee, Memphis (Cushman); Johns Hopkins University School of Nursing, Baltimore, Maryland (Dennison-Himmelfarb); Kaiser Permanente, Anaheim, California (Handler); Medical University of South Carolina, Charleston (Lackland); University of Missouri, Columbia (LeFevre); Denver Health and Hospital Authority and the University of Colorado School of Medicine, Denver (MacKenzie); New York University School of Medicine, New York, New York (Ogedegbe); University of North Carolina at Chapel Hill (Smith); Duke University, Durham, North Carolina (Svetkey); Mayo Clinic College of Medicine, Rochester, Minnesota (Taler); University of Pennsylvania, Philadelphia (Townsend); Case Western Reserve University, Cleveland, Ohio (Wright); National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland (Narva); at the time of the project, National Heart, Lung, and Blood Institute, Bethesda, Maryland (Ortiz); currently with ProVation Medical, Wolters Kluwer Health, Minneapolis, Minnesota (Ortiz).

**Author Contributions:** Drs James and Oparil had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
*Study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, administrative, technical, and material support,* and *study supervision:* All authors.

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