Hypertension guidelines: Evidence-based treatments for maintaining blood pressure control

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Abstract:

Approximately one in three adults in the United States has hypertension. This article provides an update on the latest JNC-8 guideline for treating hypertension in adults. Emphasis is placed on new and updated information and implications for primary care clinicians to help patients achieve and maintain better blood pressure control.

Keywords: hypertension | JNC 8 guideline | primary care | treatment guidelines | uncontrolled BP

Article:

Approximately 78 million Americans have hypertension (HTN), which equates to about one in three adults ages 18 years and older.[1] Men have a higher prevalence until about the age of 45 years; then there is similar prevalence between men and women at ages 45 to 64 years.[1] After the age of 64, HTN is more prevalent in women. Almost half (47.5%) of adults with HTN in the United States have uncontrolled blood pressure (BP).[1] Furthermore, Black males and Mexican American males have a higher likelihood of uncontrolled BP (approximately 60% and 65%, respectively).[1]

In addition, younger adults (20 to 39 years) with HTN are more likely to have uncontrolled BP (~62%) compared with those age 40 and above (~46%).[1] Thus, there remains an opportunity to improve control rates for those not meeting treatment goals. This article will review key points from the *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)*.[2] Emphasis will be placed on what has changed since the last report and what the implications are for primary care clinicians to help their patients achieve and maintain better BP control.

Overview of the JNC-8 Guideline

The JNC-8 writing group was charged with developing an updated, more focused guideline based primarily on the best evidence. The guideline focuses on critical questions, which were identified and prioritized by the writing group. The guideline is no longer a document that covers a broad spectrum from diagnosis through management of HTN. The evidence included data from randomized controlled trials (RCTs) of adults with HTN that studied at least 100 subjects and reported outcomes for at least 1 year of follow up.

Evidence from observational studies, systematic reviews, or meta-analyses was not included, as the original RCTs are considered the “gold-standard” for evidence. Initially, the search for the evidence included studies from 1966 to 2009 with an updated search in 2013 prior to finalizing the guideline recommendations. The National Heart, Lung, and Blood Institute quality rating tool was used to evaluate the studies retrieved as high, moderate, or low quality. The strength of each recommendation was then rated as strong (A), moderate (B), weak (C), recommendation against (D), expert opinion (E), or as no recommendation for or against (No).[2]

Definition of HTN

The JNC-8 writing group did not address the definition of HTN that was defined in the JNC-7 guideline.[3] There was no evidence to support changing the threshold to define HTN as systolic BP (SBP) of 140 mm Hg or greater and/or diastolic BP (DBP) of 90 mm Hg or greater. This threshold is consistent with other national guidelines published in the last few years, specifically the National Institute for Health and Care Excellence (NICE) guideline from the United Kingdom and the European Society of Hypertension/European Society of Cardiology (ESH/ESC).[4,5] However, unlike JNC-8, the NICE and ESH/ESC guidelines use out of office readings (obtained by ambulatory BP monitoring or home BP monitoring) to confirm the elevated readings noted by clinicians to make the diagnosis of HTN.

Three critical questions addressed by JNC-8

The JNC-8 panelists selected the three highest-ranking critical questions to answer in the guideline: What is the right time to start a medication in order to improve outcomes; how low do you go for treatment goals to improve the outcomes; and which specific drug classes should be used to improve outcomes without undue harmful outcomes? In answering these three questions, the panelist included a total of nine recommendations. The first five recommendations addressed questions 1 and 2; recommendations six to eight answered question 3; and the ninth recommendation summarized expert opinion related to other questions that were important for the panelist to address, including best strategies to achieve and maintain controlled BP based on RCTs.

First two critical questions

The first two critical questions (when to start medications and what the treatment goal should be) conveniently use the same threshold to guide clinicians' treatment decisions. This helps simplify the guideline recommendations to facilitate better management of BP.

BP threshold and goal for the general population.

The first recommendation addresses the threshold to start BP medication for adults age 60 and above (considered the "general population"). For this group (based on the strongest recommendation level [Grade A]), the threshold is 150/90 mm Hg. Furthermore, based on moderate-to-high-quality evidence from RCTs, having a goal of less than 150/90 mm Hg improved outcomes, specifically lower rates of stroke, heart failure (HF), and coronary heart disease. While having a BP of 140/90 mm Hg or greater meets the definition of having HTN for all adults, according to the evidence (albeit low quality) from RCTs, there is no additional benefit related to outcomes associated with having a goal of less than 140 mm Hg in this general population group. If an SBP of less than 140 mm Hg can be achieved in the general population without adverse reactions or a reduced quality of life, then treatment does not need to be adjusted (expert opinion—Grade E). However, if clinicians can only get patients in this group less than 150 mm Hg, there is no need to add medications to get the SBP less than 140 mm Hg.[2]

The panelists acknowledged that there was insufficient evidence (Level N) to raise the BP target for those in high-risk groups (Black individuals, those with cardiovascular disease [including stroke], or those with multiple cardiovascular risk factors). Thus, for those high-risk groups, the panelists recommended keeping the prior treatment goals (less than 140/90), which helped simplify the guideline to facilitate implementation.

BP threshold and goal for adults less than age 60.

The second and third recommendations address what the SBP and DBP should be for adults below the age of 60. Based on the highest level of evidence (Grade A) for adults age 30 to 59, the threshold to start medication is a DBP of 90 mm Hg and above. The treatment goal (based on high-quality evidence) is therefore DBP less than 90 mm Hg for this group to reduce cerebrovascular events, HF, and overall mortality. According to the evidence, lowering the DBP less than 85 or less than 80 mm Hg offers no additional benefit compared with a DBP less than 90 mm Hg. Since there was no evidence available for determining what the BP goal should be for those less than age 30, based on expert opinion (Grade E), the panelists concluded to keep the DBP threshold the same (less than 90 mm Hg) in an effort to simplify the guideline to facilitate implementation into practice.

In regard to SBP, there was no evidence to support a specific threshold or goal for adults less than 60 years of age. Thus, based on expert opinion (Grade E), the panel recommended an SBP threshold of 140 mm Hg or greater to start medications with a treatment goal of less than 140 mm Hg. Keeping the same threshold for this group also helps simplify the guideline for ease of implementation.

BP threshold and goal for adults with chronic kidney disease or diabetes mellitus.

The fourth recommendation by panelists identified the threshold and treatment goal for adults with chronic kidney disease (CKD). Based on expert opinion (Grade E), the panelists recommended using an SBP threshold of 140 mm Hg to start medications with an SBP treatment

goal of less than 140 mm Hg. There was insufficient evidence (Grade N) to support lowering the threshold below 140 mm Hg based on mortality or cerebrovascular outcomes. According to moderate-level evidence, there was no benefit in slowing the progression of kidney disease with a lower SBP threshold. While this less stringent SBP threshold and treatment goal represents a change in practice for clinicians, using 140 mm Hg as the threshold helps simplify the guideline for ease of implementation.

Similarly, the fifth recommendation addresses what the threshold and treatment goal should be for adults with diabetes. Based on expert opinion (Grade E), the panelists recommended a threshold to start medications as 140/90 mm Hg, with a treatment goal of less than 140/90 mm Hg. There was insufficient evidence to support a lower threshold or treatment goal (including a prior recommendation by the American Diabetes Association to use less than 140/80) based on outcomes. Keeping the threshold and treatment goal of 140/90 mm Hg for those with diabetes helps simplify the guideline.

Third critical question

The third critical question answered by JNC-8 addressed which specific drug classes should be used to manage HTN in order to improve outcomes for patients without causing undue harm. Recommendations 6 to 8 were made to answer this question.

Priority drug classes for general population.

The sixth recommendation addresses choice of antihypertensive medication class to use for the “general population” (defined in the JNC-8 guideline as non-Blacks, with or without diabetes). This group includes those with diabetes because the outcomes for the general population did not differ based on the presence or absence of diabetes. For this group, Grade B (moderate amount) evidence supported the use of either an angiotensin-converting enzyme inhibitor (ACE-I), an angiotensin II receptor blocker (ARB), a calcium channel blocker (CCB), or a thiazide-like diuretic (for example, thiazide diuretic, chlorthalidone, or indapamide) as first-line therapy to decrease mortality and improve cardiovascular, cerebrovascular, and kidney outcomes. According to the evidence, the use of a thiazide-like diuretic as first-line therapy is associated with better outcomes compared to using an ACE-I or a CCB as the initial treatment.

The evidence presented in the JNC-8 guideline noted that an ACE-I is more effective than a CCB for improving HF outcomes. However, despite these comparative data, the panelists emphasized that clinicians should be mindful that it is more important to get the BP down; which of these four classes to prescribe first is less important.[2] Any of the four drug classes are a good choice to initiate or use as an “add-on” agent if BP remains uncontrolled.[2] Furthermore, when selecting one of the medications, clinicians should utilize starting doses, target doses, and the number of doses per day based on the RCTs to achieve improved outcomes.[2] The JNC-8 guideline provides examples of starting doses, target doses, and the number of doses per day in the document. In addition, the use of beta-blockers, alpha-blockers, combined alpha-beta blockers, vasodilators, aldosterone antagonists, and loop diuretics are not recommended as first-line therapy based on outcomes data.[2]

Table Summary for BP goal/initial therapy based on JNC-8[2]

Population	**Goal BP mm Hg**	**Initial medication class options***
General ≥ 60 years	< 150/90	Thiazide-like diuretic, ACE-I, ARB, or CCB
General < 60 years	< 140/90	Thiazide-like diuretic, ACE-I, ARB, or CCB
Black Americans (any age; with or without DM)	< 140/90	Thiazide-like diuretic, CCB
Adults with DM (who are not Black American)	< 140/90	Thiazide-like diuretic, ACE-I, ARB, or CCB
Adults with CKD (all races)	< 140/90	ACE-I or ARB

*In no particular order of priority. Do not combine ACE-I with ARB. ACE-I= angiotensin-converting enzyme inhibitor; ARB= angiotensin II receptor blocker; CCB = calcium channel blocker; CKD = chronic kidney disease; DM = diabetes mellitus.

Priority drug classes for Black Americans

The seventh recommendation advises that clinicians use a thiazide-like diuretic or a CCB as first-line therapy for Black Americans regardless of whether or not they have diabetes. Grade B (moderate level) evidence supports the use of these two classes for those without diabetes with Grade C (weak level) evidence to support use in those with diabetes. Based on the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (or ALLHAT trial), thiazides are better than ACE-Is for improving cerebrovascular, HF, and combined cardiovascular (CV) outcomes. Overall, outcomes are best with CCB and thiazide-like diuretics, although not as effective as an ACE-I to prevent HF.[2] In particular, the use of a CCB (as opposed to an ACE-I) has been associated with better stroke outcomes. However, per the JNC-8 guideline, no studies have compared CCB to ACE-I in Black Americans with diabetes.[2] Notably, this recommendation does not address treating Black Americans with CKD.[2]

This is the first time that the treatment guideline has differentiated therapy based on race. However, this recommendation is congruent with the recommendation made in other national guidelines to treat HTN. Specifically, the 2011 NICE guideline advises using a CCB for adults less than 55 years of age who are of African or Caribbean descent to treat HTN; otherwise, an ACE-I or ARB is advised.[4] The 2013 ESH/ESC guidelines recommend using a diuretic or CCB when treating Blacks with HTN.[5]

Priority Drug Classes for CKD.

The eighth recommendation addresses which medication class should be used for adults with CKD (with or without proteinuria). Regardless of race or presence/absence of diabetes, an ACE-I or an ARB should be used to improve kidney outcomes (moderate recommendation, Grade B evidence). This recommendation is in line with the 2013 ESH/ESC guidelines, which advise clinicians to use an ACE-I or ARB for microalbuminuria, kidney dysfunction, proteinuria, or end-stage renal disease.[5]

According to JNC-8, if an ACE-I or ARB is not used as first-line therapy in patients with CKD, then either one should be used as an add-on medication. While the evidence is stronger for those with proteinuria, the choice is less clear for Black Americans with CKD who do not have proteinuria. In this case, the panelists recommended using any of the four major drug classes (thiazide-like diuretic, CCB, ACE-I, or ARB); most in this group will likely need more than one medication regardless.[2] Notably, direct renin inhibitors are not included in this recommendation, as no studies have demonstrated improved kidney or CV outcomes with this class of antihypertensive agents.[2] In addition, the JNC-8 guideline advises against combining ACE-I and ARBs to avoid dual renin-angiotensin-aldosterone-system blockade.

Importantly, the JNC-8 panelists did not issue a specific recommendation for treating adults with CKD who are age 75 and older based on lack of evidence; therefore, if clinicians are concerned about possible adverse reactions, such as hyperkalemia or worsened kidney function with use of an ACE-I or an ARB, then a thiazide-like diuretic or a CCB should be considered.[2] (See Summary for BP goal/initial therapy based on JNC-8.)

Final recommendation to attain/maintain BP

Table Three strategies to use for titrating antihypertensive medications[2]

Option one: Start one drug (ACE-I, ARB, CCB or thiazide diuretic); titrate to maximum dose before adding a second agent from another class. If not to goal with the second agent; maximize the dose of the second agent before adding a third agent from a different class. **Option two:** Start one drug (ACE-I, ARB, CCB or thiazide diuretic); before titrating to the maximum dose, add a second agent from a different class if BP is not to goal. Then, up-titrate both to a maximum dose (one at a time) if BP is not to goal before adding a third agent from a different class. **Option three:** Start with two drugs at once from two different classes (ACE-I, ARB, CCB or thiazide diuretic); if BP is not to goal, then up-titrate both agents to maximum dose before adding a third drug from a different class. This strategy is typically used for those with a BP greater than 160/100 from the onset *Options are in no particular order of priority. Titrations are typically made at one month intervals if BP if not to goal. If BP is not* to *goal after the patient is* on *three drugs from three different classes, then a fourth agent from another class may be added and/or the patient should be referred to a hypertensive specialist.* ***Do not*** *combine an ACE-I with an ARB in any of the three strategies.*

ACE-I = angiotensin converting enzyme inhibitor; ARB= angiotensin II receptor blocker; CCB = calcium channel blocker.

The panelists offered a ninth recommendation, which was developed to help clinicians to more easily implement the new guideline in their mission to attain and maintain controlled BP in their patients. Under this recommendation, clinicians should increase the dose of a particular antihypertensive medication or add on another class of medications if the patient is not to goal within a month of making the last regimen change. Clinicians should also move to other classes of medications, beyond the four aforementioned medication classes, if more medications are needed, or if contraindications exist related to use of the standard classes. In addition, based on

expert opinion (Grade E evidence), patients should be referred to an HTN specialist if the desired BP goal has not be attained or for the management of complicated patients.

The ninth recommendation also included three strategies that could be used to titrate and combine drug classes based on expert opinion (Grade E evidence). Each strategy has been shown to be effective in attaining and maintaining BP goals in RCTs.[2] Notably, the three strategies have not been tested in relation to each other or compared with other strategies.[2] Yet, studies have shown that these strategies may improve BP lowering and patient adherence.[2] (See *Three strategies to use for titrating antihypertensive medications*.)

Implications for advance practice registered nurses

The intent of the simplified JNC-8 guideline is to facilitate ease in managing BP. Nurse practitioners (NPs) and other advance practice registered nurses should use the recommendations as a guide to clinical practice. This guideline, however, is not a substitute for clinical judgment. In general, treatment decisions should follow the recommendations outlined by the JNC-8 guideline, which are based on RCTs with documented improvement in cardiovascular and cerebrovascular outcomes, including death. Expert opinion was provided by the panel for recommendations in which there was either insufficient or no evidence. The guideline (based on RCTs) is felt to represent the best-available evidence with the largest number of subjects. However, clinicians treat individuals; therefore, each strategy presented in the recommendations may be tailored to the individual situation, clinician and patient preferences, cost, and drug tolerability. Substitutions may be made, especially if adverse reactions exist or if particular drug classes have shown to be ineffective for lowering BP in the individual patient.

In addition, clinicians should regularly assess BP through the use of home BP monitoring, encourage lifestyle changes, assess adherence, and adjust the treatment plan as needed in pursuit of the goals set forth by the guideline. In fact, the JNC-8 panel endorsed the 2013 American Heart Association/American College of Cardiology Guideline on Lifestyle Management to Reduce Cardiovascular Risks published 1 month prior to the JNC-8 guideline.[6] A copy of the guideline is available at:
circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437740.48606.d1.

Moving forward

NPs should be knowledgeable about the latest JNC-8 treatment guideline to attain and maintain BP control in their adult patients. The definition for HTN has not changed with the new guideline (140/90 mm Hg or greater). The treatment goal for most adults is less than 140/90 mm Hg. For the general population (adults 60 years of age or older who are not Black and who do not have diabetes or CKD), the SBP goal is less strict at less than 150 mm Hg. Antihypertensive medications should be started in conjunction with or after a trial of lifestyle changes. The four key classes of antihypertensive medications to be used for treatment include thiazide-like diuretics, ACE-I, ARB, or CCB. Most patients will require at least three to four medications from different classes to attain and maintain BP goals. Using the starting doses, target doses, and number of doses per day (as established in RCTs) will help optimize patient outcomes. NPs should combine the best-available scientific evidence, their clinical expertise/judgment, and the

individual patient preferences and tolerability for various treatments to discern the best treatment regimen to put into place.

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