REVIEW ARTICLE

The JNC 8 Guidelines: A Clinical Review

Gary Rivard, DO; Erik Seth Kramer, DO, MPH; Sean Tyler O'Sullivan, DO
Central Maine Family Medicine Residency Program

KEYWORDS:
Hypertension
Review
Diagnosis
Treatment
Guidelines

Hypertension remains a significant cause of mortality and morbidity in the United States and is seen routinely in the primary care setting. Family physicians are frequently encountering individuals with hypertension and are primarily responsible for the initial diagnosis and initiation of treatment. The last review of this condition with a summary of definitions and recommendations for both diagnostic criteria and treatment came in the form of the guideline by Seventh Joint National Committee on the management of hypertension (JNC 7) in 2003. In the last decade research has placed direct questioning of the recommendations put forth in that document. Now the Eighth Joint National Commission (JNC 8) review has been made available with changes in diagnostic criteria and treatment options.

Three questions guiding the most recent review of literature were put forth. 1) Does initiating treatment at a particular threshold improve outcomes, 2) Does treatment to a particular systolic or diastolic goal improve outcomes, and 3) Do the various classes of medication confer different benefits and harms relative to specific outcomes. Key changes from JNC 7 include an increase in the systolic threshold to 150mmHg prior to initiation of pharmacologic treatment in those aged 60 and older and specific pharmacologic options based on racial differences and the presence of diabetes and/or chronic kidney disease.

INTRODUCTION

The National Lung, Heart, and Blood Institute (NHLBI) has long been the administrating organization for the National High Blood Pressure Education Program (NHBPEP) Coordinating Committee and subsequently the organization responsible for the formation of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. This group is charged with evaluating the evidence and submitting periodic reports with recommendations for the evaluation and management of hypertension.

In 2003, the JNC 7 was released. It was the first review of this topic since the JNC 6 report in 1997. When released, it was the most comprehensive review of the management of hypertension to date and was universally adopted as a reference. The goal was to synthesize the evidence available at the time and put forth patient centered recommendations for the management of hypertension. Examples of these recommendations include the formal adoption of the "DASH" diet and the use of concise resources for both patients and clinicians for use to educate and guide both groups in evaluation and treatment in the form of pocket cards and electronic resources. Key messages included systolic blood pressure goals and a summary of both non-pharmacologic and medication options for the treatment of hypertension.[1]

In 2013, an updated review of current literature was performed by the Eighth Joint National Committee (JNC8). A multi-disciplinary team assembled to review all recent literature on this topic. The 50-plus member team consisted of those from primary care; geriatrics, cardiology, nephrology, pharmacology, nursing, epidemiology, informatics, as well as specialists in review of evidence based medicine and the development and implementation of clinical guidelines. The guideline was then submitted through a peer review process between January and June of 2013. The reviewers were those with expertise in the treatment of hypertension. The guideline was also sent for review by federal agencies and those with primary interests to include primary care physicians, cardiologists, nephrologists, and pharmacologists. At the completion of this vigorous process the JNC 8 report was released in December 2013.

Only randomized controlled trials (RCT's) were included in the most recent literature review. This was a departure from the prior processes used to form the recommendations. In the JNC 7 report, a "less than systematic" approach to a review of the literature was used. Therefore, the choice to use only RCT's was based on a "true" evidence review and led to a more systematic approach.[2] A database search spanning 1966-1996 was done initially with an ongoing literature search performed as the document was being drafted.

Address correspondence to: Gary Rivard, DO, Central Maine Family Medicine Residency Program, 76 High Street, Lewiston, Maine 04240, Email: rivardga@cmhc.org

Four criteria were used to determine the adequacy of data and overall study selection for review to include in the summary of recommendations. These were 1) The primary focus of the study was hypertension; 2) the study had at least 2,000 participants, 3) multicentered, and 4) met other inclusion/exclusion criteria. The data were synthesized into tables of evidenced based "statements" that were then voted on. The panel was also asked to assign a grade based on the quality of evidence for each statement. For recommendations and statements based on reviewed evidence, a 2/3-majority vote was necessary for inclusion into the guideline. For those recommendations based on expert opinion only, at 75% majority agreement was required.

In stark contrast to the JNC 7 document, this review and its recommendations are based largely on expert opinion and are not endorsed by any public or professional organization. The JNC 7 report had been reviewed by multiple professional organizations to include federal agencies and the NHBPEP which was a primarily driver for the formation of the JNC 7 as noted above.

EPIDEMIOLOGY

Hypertension remains an important risk factor for cardiovascular disease including stroke, the development of arrhythmia, and myocardial infarction. The prevalence of hypertension has seen little change from 2000 to 2010, remaining at approximately 30%.[3] In the 2007–2010 Morbidity and Mortality Weekly Report Supplement, the prevalence of hypertension was found to be higher in persons aged 65 and older (71.6%) and among non-Hispanic blacks (41.3%).[3] These two groups remain an important focus of the new JNC 8 guidelines.

Healthy People 2020, a science-based 10-year national objectives initiative, set goals to both reduce the prevalence of hypertension among adults to 26.9% and to increase the prevalence of blood pressure control among adults "with" hypertension to 61.2%.[4] According to the National Health Examination Surveys (NHANES) 2011-2012 study, the age adjusted total percentage of adults aged 20 and over with hypertension has decreased from 32.1% in 2003-2004 since the JNC 7 report was first published to 30.0% in 2011-2012[5] (Figure 1). While the percentage of uncontrolled hypertension (defined as an average systolic blood pressure of 140 mm Hg or higher, or an average diastolic pressure of 90 mm Hg or higher among those with hypertension) has decreased for all age groups with high blood pressure, nearly 54.6% of adults continue to have uncontrolled high blood pressure in 2011-2012.[5] The age-specific prevalence was 11.2% in males (22-44 years old). This rate has increased to 41.2% in the group ages 45-64 old; further increasing to 61.7% in the group aged 65-74 years old, and 75.1% in the group aged 75 years and over.

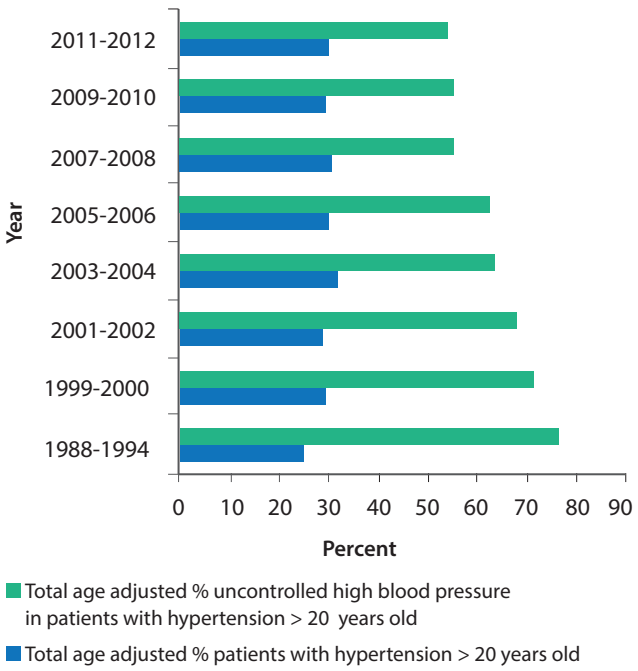
Prevalence of Hypertension by Race and Ethnicity

Black individuals have shown a higher prevalence and incidence of hypertension than white persons[5] with rates, 38.8% (male) and 42.8% (female). In addition to higher prevalence, this population has experienced a much lower awareness of hypertension, affecting control of resultant comorbidities such as stroke, coronary heart disease, and chronic renal failure.[6] These increases are likely due to the increased incidence of hypertension and diabetes in this population. In general, Mexican Americans are similar to or lower than those in non-Hispanic whites[5] with rates of 27.3% (male) and 29.3% (female), showing a lower prevalence than black individuals.

Cardiovascular Risk

The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), the older population greater than 50 years, SBP > 140 was a more important cardiovascular disease risk factor than DBP. The risk doubled with each increment of 20/10 mm Hg.[1] Limited control of blood pressure has led to increased morbidity and mortality, primarily in cardiovascular disease and stroke. From 2000-2010, the age-adjusted mortality rate among males decreased by 37% and females by 32% for stroke, and 30% and 12% for heart disease.[5]

Figure 1: Total Hypertension and Uncontrolled Hypertension in > 20 years old.



Source: CDC/NCHS, National Health and Nutrition Examination Survey, 2013.

Table 1: Recommendations

1	For individuals aged 60 or older, goal systolic blood pressure is >=150mmHg and diastolic blood pressure is >=90MmmHg. These values should be used as the threshold for diagnosis and goals for treatment. Do not change treatment in those aged greater than 60 if current treatment is adequate for prior goals and the individual is not experiencing adverse side effects.	Strong Recommendation – Grade A evidence
2	For individuals aged 30-59 use a diastolic blood pressure goal of <90mmHg for diagnosis and initiation of treatment.	Strong Recommendation – Grade A evidence
2a	The diastolic goal of <90mmHg is also reasonable in those aged of 18-29	Expert Opinion – Grade E evidence
3	Start medication treatment of hypertension in those <60 to achieve a systolic blood pressure of less than 140mmHg	Expert Opinion – Grade E evidence
4	For individuals with chronic kidney disease older than 18, start medication with a goal of less than 140mmHg/90mmHg	Expert Opinion – Grade E evidence
5	For individuals with diabetes disease older than 18, start medication with a goal of less than 140mmHg/90mmHg	Expert Opinion – Grade E evidence
6	For the nonblack individuals, including those with diabetes, initiation of medication treatment of hypertension should begin with either a thiazide diuretic, calcium channel blocker (CCB), angiotensin converting enzyme inhibitor (ACE-I), or angiotensin receptor blocker (ARB).	Moderate Recommendations – Grade B evidence
7	For black individuals, including those with diabetes, initiation f medication treatment of hypertension should begin with either a thiazide diuretic or CCB*	Weak Recommendation – Grade C evidence
8	For all individuals diagnosed with chronic kidney disease over the age of 18, the initial choice or add-on treatment should include an ACE-I or ARB	Moderate Recommendation – Grade B evidence
9	• Evaluate effectiveness of treatment after one month • Titrate to a maximum dose or consider "add on" treatment with additional first line agents • Do not use an ACE-I and ARB together • If unable to achieve optimal control with a combination of 3 first line agents, consider other classes loop diuretics, alpha blocking agents, aldosterone agonists, combination alpha and beta blocker agents (ie. carvedilol or labetalol)	Expert Opinion – Grade E evidence

JNC 8 REPORT RECOMMENDATIONS

A summary of the literature review answering the questions facing the JNC 8 panel comes in the form of 9 recommendations. These are listed in Table 1. The first set of recommendations address the questions of what threshold to use for the diagnosis of hypertension and the subsequent goals in treatment and the remaining recommendations provide a concise framework for the choice of pharmacologic agents in the treatment of hypertension.

DIAGNOSIS OF HYPERTENSION AND WHEN TO INITIATE TREATMENT

The first set of recommendations address the issue of what threshold to use for the diagnosis of hypertension and the subsequent goals in treatment for older individuals and those with diabetes, chronic kidney disease, or both. In patients aged 60 years old or greater, a systolic threshold of 150mmHg and diastolic threshold of 90 mmHg is recommended. This is as a result of literature review suggesting improved outcomes in stroke and coronary heart disease.[7-9] However, if an individual is optimized on current treatment and not experiencing adverse side effects, their medication should not be changed despite having a more tightly controlled blood pressure.

In those aged 30-59, a diastolic threshold for initiation of treatment and subsequent goal of less than 90mmHg is supported by grade A evidence (strong recommendation). The recommended systolic goal, however, of 140mmHg in all persons >18 years of age has been proposed but the evidence supporting this is a less robust and based on expert opinion.[10-13]

In all persons aged 18 years and older with a diagnosis of diabetes or chronic kidney disease the recommendation is a systolic threshold for treatment initiation and subsequent goal of 140mmHg and a diastolic value of 90mmHg. There is no evidence suggesting improved preservation of renal function with blood pressure goals less than 140/90.[14,15] There are conflicting recommendations however with the last comprehensive guideline established by the American College of Clinical Endocrinologists suggesting 130/80 remain the goal and threshold for treatment.[16]

PHARMACOLOGIC MANAGEMENT

In addition to the diagnostic changes, a major focus of the current update involves how to approach the initiation of anti-hypertensive pharmacologic treatment.

Previously, the JNC 7 proposed thiazide diuretics as initial therapy for nearly all patients. The JNC 8 report still recognizes thiazide diuretics as useful first-line agents, however angiotensin converting enzyme or ACE inhibitors,

angiotensin receptor blocker agents or ARBs, and calcium channel blockers or CCBs are also reasonable first line choices. The JNC 8 makes treatment plans more flexible by allowing providers to choose from three or four broad classes of medications. In essence, there is not a single class of medications that are considered first-line, but most classes are considered reasonable choices.[17]

JNC 7 also supported ACE inhibitors, ARBs, and CCBs in addition to thiazide-diuretics, but numerous other medications were utilized early, such as beta-blockers, alpha-blockers, loop diuretics, and many more. It is no longer recommended that beta-blockers or alpha-blockers be used as first-line therapy as beta-blockers were associated with higher rate of adverse cardiovascular events and alpha-blockers showed inferior cardiovascular outcomes respectively.[18,19] Using combination treatment strategies with a thiazide diuretic, CCB, and either an ACE inhibitor or ARB is preferred before initiation of a beta-blocker, alpha-blocker, aldosterone agonist, or loop diuretics.[17]

Patients already demonstrating adequate control, regardless of therapy, need not have their treatment regimen changed.. For example, if a patient is well controlled on beta-blocker therapy, this should be continued.

African-American individuals should not be started on ACE inhibitors or an ARB as initial therapy due to worse cardiovascular outcomes based on the ALLHAT trial, however comorbidities must be taken into account.[20] If an African-American patient has underlying renal disease or diabetes, ACE-inhibitors or ARBs are beneficial for renal protection and may be an acceptable initial option.[15,17]

CHOICE OF PHARMACOLOGIC AGENT

Thiazide Diuretics

Thiazide Diuretics work at the distal tubule of the nephron to inhibit sodium and chloride reabsorption creating diuresis. Thiazide diuretics are not as effective as loop diuretics for edema, but can be very effective in hypertension. They are appropriate for initial therapy in all ethnicities, however as discussed in the ALLHAT trial, potassium should be carefully monitored with use of thiazide diuretics due to risk of inducing new-onset diabetes. Chlorthalidone carries a higher risk for subclinical hypokalemia[21] but has been shown to produce a more effective decrease in systolic blood pressure and has a longer lasting effects on blood pressure than hydrochlorothiazide.[20]

Calcium Channel Blockers (CCB)

Calcium channel blockers act in lowering blood pressure by lowering contractility of vascular smooth muscle thus leading to systemic vasodilation. The most studied and effective of these is amlodipine. It is generally well tolerated, effective for managing hypertension, and has good compliance with once daily dosing.[20]

Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Angiotensin Receptor Blockers (ARBs)

Both ACEIs and ARBs act on the renin-angiotensin system to promote vasodilation and decrease vascular resistance to promote lowered blood pressure. Both ACEIs and ARBs are generally well tolerated and are recommended in diabetics due to renal protective effect.[15] Also of note, ACEIs and ARBs are indicated in patients with chronic heart failure and history of myocardial infarction.[1]

Table 2: Pharmacologic options for the treatment of hypertension in certain populations

Population	Initial Therapy	Add On Therapy	Other Considerations
18-75	Thiazide, CCB, or ACE-I/ARB	Triple therapy before other agents	
>75 years old	Thiazide or CCB	Thiazide or CCB	Do not use ACE-I or ARB
Diabetics	Thiazide, ACE/ ARB, or CCB	Triple therapy before other agents	
Chronic Kidney Disease	ACE-I/ARB	Thiazide or CCB	ACE-I or ARB first-line for CKD regardless of race or diabetes status
African-American	Thiazide or CCB	Thiazide or CCB	ACE/ARB contraindicated

Table 3: Comparison of potential "first line" medication classes for the treatment of hypertension

Medication Class	Benefits	Risks	Other Considerations
Thiazide Diuretics	May also improve edema	May cause hypokalemia or hypomagnesemia	
CCB	May also control irregular heart rate	Lightheadedness/ dizziness -> possible gait instability	
ACE-I/ARB	Renal protection	Worse cardiovascular outcomes in African-American patients	Do not combine ACE-I and ARB. No benefit from combination therapy.

CONCERNS REGARDING THE UPDATED RECOMMENDATIONS:

This is not an official updated guideline sanctioned by the NHLBI, as was the case in the prior JNC reports. There is

no plan to further release JNC type guidelines. This updated set of recommendations was designed to help the practicing clinician and to offer the most recent review of the literature with several key questions to be addressed. Only randomized clinical trials were included in this review. Other organizations have produced evidence based guidelines as well, particularly those from specialty organizations reviewing the clinical impact of hypertension on cardiovascular outcomes to include those individuals with diabetes and chronic kidney disease.

Issues surrounding the validity of these current recommendations as "stand alone" points should be questioned. Much of what is discussed in this update is reflective of evidence-based discussion from other groups who have the support of more extensive research for the basis of their recommendations.

SUMMARY

In stark contrast to the JNC 7 document, this review and its recommendations are based largely on expert opinion and are not endorsed by any public or professional organization. The JNC7 report had been reviewed by multiple professional organizations to include federal agencies and the NHBPEP, which was a primary driver for the formation of the widely accepted JNC7 as noted above. The more liberal thresholds for diagnosis and treatment should be evaluated relative to co-morbid conditions and in discussion with the patient.

There may never be another update of JNC recommendations like those seen last in the JNC 7 report. This is evidenced by the fact that no recommendations continuing to support lifestyle modification were included. The basis for those recommendations remains without question. The (Dietary Approach to Stop Hypertension) DASH diet, exercise recommendations, and smoking cessation continue to be the cornerstone of prevention.[1] In the future we will likely be offered recommendations from multiple work groups representing different organizations coming together for more "consensus" type work. This will certainly eliminate repetitive work and will decrease the degree of conflicting recommendations.

REFERENCES

1. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42(6):1206-1252.
2. Powers B, Greene L, Balfe LM. Updates on the treatment of essential hypertension: A summary of AHRQ's comparative effectiveness review of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and direct renin inhibitors. *J Manag Care Pharm*. 2011;17(8 Suppl):S1-14.
3. Gillespie CD, Hurvitz KA, Centers for Disease Control and Prevention (CDC). Prevalence of hypertension and controlled hypertension - united states, 2007-2010. *MMWR Surveill Summ*. 2013;62 Suppl 3:144-148.
4. `Heart disease and stroke." - healthy people 2020. N. p., 2 dec 2010. .
5. Health, United States, 2013. In: Hyattsville (MD): National Center for Health Statistics (US); 2014 May:Table 64.
6. Brown M. Hypertension and ethnic group. *BMJ*. 2006;332(7545):833-6.
7. Ogihara T, Saruta T, Matsuoka H, et al. Valsartan in elderly isolated systolic hypertension (VALISH) study: Rationale and design. *Hypertens Res*. 2004;27(9):657-661.
8. Ogihara T, Saruta T, Rakugi H, et al. Target blood pressure for treatment of isolated systolic hypertension in the elderly: Valsartan in elderly isolated systolic hypertension study. *Hypertension*. 2010;56(2):196-202.
9. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. final results of the systolic hypertension in the elderly program (SHEP). SHEP cooperative research group. *JAMA*. 1991;265(24):3255-3264.
10. Armario P, de la Sierra A. Blood pressure as a therapeutic target in stroke. *Curr Top Med Chem*. 2009;9(14):1278-1284.
11. Five-year findings of the hypertension detection and follow-up program. I. reduction in mortality of persons with high blood pressure, including mild hypertension. hypertension detection and follow-up program cooperative group. 1979. *JAMA*. 1997;277(2):157-166.
12. Five-year findings of the hypertension detection and follow-up program. III. reduction in stroke incidence among persons with high blood pressure. hypertension detection and follow-up program cooperative group. *JAMA*. 1982;247(5):633-638.
13. Five-year findings of the hypertension detection and follow-up program. I. reduction in mortality of persons with high blood pressure, including mild hypertension. hypertension detection and follow-up program cooperative group. *JAMA*. 1979;242(23):2562-2571.
14. Curb JD, Pressel SL, Cutler JA, et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. systolic hypertension in the elderly program cooperative research group. *JAMA*. 1996;276(23):1886-1892.
15. Wright JT,Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: Results from the AASK trial. *JAMA*. 2002;288(19):2421-2431.
16. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE comprehensive diabetes management algorithm 2013. *Endocr Pract*. 2013;19(2):327-336.
17. Page MR. The JNC 8 hypertension guidelines: An in-depth guide. *American Journal of Managed Care*. 2014(Jan-Feb).
18. Bangalore S, Steg G, Deedwania P, et al. Beta-blocker use and clinical outcomes in stable outpatients with and without coronary artery disease. *JAMA*. 2012;308(13):1340-1349.
19. Dahlof B, Devereaux R, Kjeldsen S. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension studey (LIFE): A randomised trial against atenolol. *Lancet*. 2002;359(9311):995-1003.
20. Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group. Diuretic versus alpha-blocker as first-step antihypertensive therapy: Final results from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *Hypertension*. 2003;42(3):239-246.
21. Muntner P, Levitan EB, Lynch AI, et al. Effect of chlorthalidone, amlodipine, and lisinopril on visit-to-visit variability of blood pressure: Results from the antihypertensive and lipid-lowering treatment to prevent heart attack trial. *J Clin Hypertens* (Greenwich). 2014