

Hypertension Diagnosis and Treatment Guideline

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Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Major Changes as of August 2014

New	Previous
Blood pressure goals	
<p>The blood pressure (BP) goal for the general population aged 80 or older has been raised to < 150/90 mm Hg. The BP goal for the general population up to age 80 remains at < 140/90 mm Hg. (Note: this is different from the JNC 8 panel guideline; see Evidence Summary for rationale.)</p>	<p>The BP goal for the general population was 140/90 for patients of all ages.</p>
<p>Diabetes and atherosclerotic cardiovascular disease (ASCVD) patients no longer have a lower BP goal than the general population. The BP goal for these populations has been raised to < 140/90 mm Hg.</p>	<p>The BP goal for patients with diabetes or ASCVD was < 140/80 mm Hg.</p>
<p>There are now two separate BP goals for patients with chronic kidney disease (CKD): < 140/90 mm Hg for those without albuminuria, and < 130/80 mm Hg for those with albuminuria.</p>	<p>The BP goal for all patients with CKD was < 140/80 mm Hg.</p>
Drug treatment and monitoring	
<p>Diuretics, ACE inhibitors/angiotensin receptor blockers (ARBs), and calcium channel blockers are now listed as equivalent first-line choices for the general population.</p>	<p>ACE inhibitors and diuretics were first-line choices for patients with no history of ASCVD; ACE inhibitors and beta-blockers were first-line choices for patients with a history of ASCVD; and ACE inhibitors/ARBs were listed as the first-line choice for patients with heart failure.</p>
<p>Beta-blockers are no longer a first-line recommendation for hypertension for the general population.</p>	<p>Beta-blockers were listed as first-line for patients with history of ASCVD, second-line for patients with heart failure, and fourth-line for patients with no history of ASCVD.</p>
<p>Lisinopril/ hydrochlorothiazide (HCTZ) is now recommended as the starting medication in most clinical cases, with amlodipine as the next medication.</p>	<p>Lisinopril/HCTZ was recommended as the starting medication only for patients with no history of ASCVD.</p>
<p>A default, incremental medication pathway is recommended for most cases:</p> <ul style="list-style-type: none"> ▪ Lisinopril/HCTZ 20/12.5 mg x ½ tab daily ▪ Lisinopril/HCTZ 20/12.5 mg x 1 tab daily ▪ Lisinopril/HCTZ 20/12.5 mg x 2 tabs daily ▪ Amlodipine 5 mg x ½ tab daily ▪ Amlodipine 5 mg x 1 tab daily ▪ Amlodipine 5 mg x 2 tabs daily 	<p>There was previously no routine recommended medication pathway.</p>
<p>For frail patients or those aged 60 years or older, there is now a recommendation to consider checking sodium level in addition to potassium and creatinine.</p>	<p>Monitoring sodium levels was recommended optionally as well, but not as prominently.</p>

Preface

In December 2013, the 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (<http://jama.jamanetwork.com/article.aspx?articleid=1791497>) was released by “the Panel Members Appointed to the Eighth Joint National Committee (JNC 8).” This group had initially been sponsored by the National Heart, Lung, and Blood Institute (NHLBI) to write the guideline based on an evidence review sponsored by the NHLBI. However, during that process the NHLBI changed its focus, and the JNC 8 group partnered instead with the American College of Cardiology (ACC) and the American Heart Association (AHA) to jointly publish a guideline. That partnership fell through as well, so when the JNC 8 panel members’ guideline was published in the *Journal of the American Medical Association*, it was without the support of any sponsoring organization.

The “JNC 8” guideline itself has been quite controversial. The most hotly debated recommendation is one to loosen the blood pressure goal for healthy patients from 140/90 mm Hg to 150/90 mm Hg starting at age 60. Five of the 17 panel members opposed this recommendation strongly enough that, in a highly unusual move, they published a special “minority view” article (<http://annals.org/article.aspx?articleid=1813288&resultClick=3>) in the January 14, 2014 *Annals of Internal Medicine*. They argued that the blood pressure goal should be loosened to 150/90 mm Hg only starting at age 80. The later age cutoff is more consistent with other international guidelines, and, in their view, more consistent with the available evidence as well.

The ACC and AHA are currently working on a hypertension guideline using the evidence review provided by the NHLBI, and they intend to release their own guideline, probably sometime in 2015.

Please keep all of this in mind when reviewing the guideline that follows. We attempt to match national guidelines whenever possible, but we do have some key differences from “JNC 8”—in particular, that we support the minority view of relaxing blood pressure goals starting at age 80 rather than at age 60. We have adapted much of the rest of their recommendations, but as always, our guideline is a mixture of all available major, trusted guidelines, combined with our own interpretation of the evidence. Please see the Evidence Summary section (p. 12) for a more detailed explanation of how we arrived at various decisions, including the question of the age at which the blood pressure goal should be relaxed.

Exclusions

This guideline does not apply to women who are pregnant or anticipating pregnancy. These patients should be referred to Obstetrics for blood pressure management.

Prevention

Efforts should be made to minimize hypertension risk factors: obesity, physical inactivity, moderate to high alcohol intake, high sodium intake, and high saturated fat intake. See Lifestyle Modifications (p. 5) for more details.

Screening

Table 1. Screening for hypertension		
Population eligible for screening	Test(s)	Frequency
Adults aged 18 and older	Blood pressure (BP) measurement using optimal technique. ¹ If the first reading is elevated, repeat measurement and document both readings.	Every visit ²
¹ See Proper Technique for Obtaining and Recording BP Measurement (staff intranet).		
² Measure BP at every Primary Care and Specialty visit, with the exception of eye care and dermatology.		

Diagnosis

Assess the patient for hypertension using the BP measure at initial visit and repeated measurements taken at home or at office visits.

Prehypertension: 120–139 mm Hg systolic or 80–89 mm Hg diastolic

Stage 1 hypertension: 140–159 mm Hg systolic or 90–99 mm Hg diastolic

Stage 2 hypertension: \geq 160 mm Hg systolic or \geq 100 mm Hg diastolic

Hypertensive urgency

If **any** BP measurement is greater than **180/110 mm Hg**, treat the patient either immediately or within days, depending on the clinical situation and any complications present. If it is greater than **210/120 mm Hg**, immediate treatment is warranted.

Home BP measurement

Measuring blood pressure at home is an effective strategy to help establish a hypertension diagnosis and help patients achieve their blood pressure target.

Some patients' BP may be slightly elevated when measured in office settings compared to when it is measured at home. To adjust for this, the standard practice for all patients is to use a slightly lower threshold for diagnosing hypertension using home blood pressure measurements: 135/85 mm Hg instead of 140/90 mm Hg.

A pamphlet for patients, "[Measuring Your Blood Pressure at Home](#)" is available. Information about home BP measurement is also available in the AVS SmartPhrase .avsbpselfreport.

Medications, substances and conditions that may affect blood pressure

When making a diagnosis of hypertension, it is important to consider medications and other causes that may be increasing the patient's blood pressure. Examples include:

- Medications such as adrenal steroids, estrogen, sympathomimetics, NSAIDs, and appetite suppressants. Consider eliminating, switching to another medication, or decreasing the dose.
- Alcohol, illicit drugs (e.g., cocaine and other stimulants), and smoking. Consider screening (see the Unhealthy Drinking in Adults Guideline, Detox Manual [staff intranet], and Tobacco Use Guideline).
- Sodium. See "Diet" under Lifestyle Modifications (p. 5) for recommended limits.
- Obstructive sleep apnea (OSA). Consider this as a potential cause of elevated blood pressure if symptoms consistent with OSA are present.

Initial lab workup

- EKG.
- Cholesterol screening.
- Diabetes screening.
- Potassium and creatinine.
- Sodium. (Consider for frail patients or those aged 60 years or older.)

Additional workup may be needed if the patient has a comorbidity (e.g., diabetes, ASCVD).

The following are **generally not necessary** for routine follow-up of a hypertension diagnosis: urinalysis, blood chemistry, hematocrit, general electrolytes, BUN, and liver function tests.

If the patient has an abrupt increase in BP measurement, consider lab workup for secondary hypertension.

Treatment Goals

Note: In the JNC 8 panel guideline, the goal BP changes from < 140/90 mm Hg to < 150/90 mm Hg starting at age 60. In this guideline, the goal BP makes the same change but not until age 80. Please see the Evidence Summary (p. 12) for an explanation of the rationale behind this decision.

Eligible population	Goal
General population through age 79	BP lower than 140/90 mm Hg
General population aged 80 and older ¹	BP lower than 150/90 mm Hg
Patients with diabetes	BP lower than 140/90 mm Hg
Patients with ASCVD	BP lower than 140/90 mm Hg
Patients with chronic kidney disease (CKD)	
with albuminuria ²	BP lower than 130/80 mm Hg
without albuminuria ²	BP lower than 140/90 mm Hg
¹ Consider using this goal for frail elderly patients and patients under age 80 who are not tolerating pharmacologic treatment. ² Whether moderately increased (30–300 mcg/mg, previously called “microalbuminuria”) or severely increased (> 300 mcg/mg, previously called “macroalbuminuria”).	

Initiating Treatment

Diagnosis	Lifestyle modifications	Drug treatment ¹
Prehypertension	At diagnosis	Drug treatment not recommended
Stage 1 hypertension	At diagnosis	Consider at or before 6 months of lifestyle modifications if BP goals unmet
Stage 2 hypertension	At diagnosis	At diagnosis
¹ For frail elderly patients, standing blood pressure measurements should be considered before initiating drug treatment. If patient is hypotensive when standing but has mild hypertension when seated, pharmacologic treatment may cause more harm than good.		

Lifestyle Modifications

Lifestyle modifications should be encouraged for all patients, regardless of stage of hypertension.

Tobacco cessation

Quitting smoking, a primary risk factor for cardiac disease, has immediate as well as long-term benefits for patients with hypertension and the people with whom they live. See the Tobacco Use Screening and Intervention Guideline for recommendations.

Weight management

The risk of serious health conditions—such as diabetes, heart disease, arthritis, and stroke, as well as high blood pressure—increases with a body mass index (BMI) of 25 or higher. (BMI = weight in kilograms divided by height in meters squared [kg/m^2].) *Overweight* is defined as a BMI of 25 to 29.9, *obesity* as a BMI of 30 or higher. While most overweight or obese adults can lose weight by eating a healthy diet or increasing physical activity, doing both is most effective. See the Adult Weight Management Screening and Intervention Guideline for recommendations and further information.

Diet

Patients with hypertension should be advised to reduce their dietary sodium intake to no more than 2,400 mg per day; further reduction to 1,500 mg/day is desirable as it leads to even greater decreases in BP. If the desired sodium level is not achieved, consider an alternative goal of reducing current sodium intake by 1,000 mg/day.

Additionally, all patients should strive to:

- Make smart choices from every food group to meet their caloric needs.
- Get the most and best nutrition from the calories consumed.

The DASH eating plan provides the following key elements: an abundance of plant foods (fruits, vegetables, whole-grain breads or other forms of cereals, beans, nuts, and seeds), minimally processed foods, lean meats, poultry, and fish, and seasonally fresh foods. Use the AVS SmartPhrases .avsdash and .avsnutrition.

Physical activity

Advise adults to engage in aerobic physical activity 3 to 4 sessions per week. Each session should be of moderate-to-vigorous intensity and last an average of 40 minutes.

For patients who have been inactive for a while, recommend starting slowly and working up, at a comfortable pace, to at least 30 minutes per day. If a patient is unable to be active for 30 minutes at one time, suggest accumulating activity over the course of the day in 10- to 15-minute sessions.

Moderation of alcohol consumption

Because alcohol use can raise blood pressure, patients with hypertension should use alcohol in moderation, if at all. Screen patients using the AUDIT-C Alcohol Questionnaire, and provide brief guidance when appropriate. See the Adult Unhealthy Drinking Screening and Intervention Guideline for more detailed recommendations.

Pharmacologic Options

Table 4. Initial antihypertensive medication recommendations by patient subgroup

Note: A suggested default pathway for medication treatment is on p. 8.

Patient subgroup	Drug class for initial therapy (Bold type indicates a preferred drug class. See also “Prescribing notes” following this table.)
General population	Alone or in combination: ACE inhibitor (or ARB if intolerant) Thiazide diuretic Calcium channel blocker
Chronic kidney disease (CKD)	Alone or in combination: ACE inhibitor (or ARB if intolerant) Thiazide diuretic Calcium channel blocker
Diabetes	Alone or in combination: ACE inhibitor (or ARB if intolerant) Thiazide diuretic Calcium channel blocker
Atherosclerotic cardiovascular disease (ASCVD)	Alone or in combination: ACE inhibitor (or ARB if intolerant) Beta-blocker (preferred for patients with recent angina or myocardial infarction) Thiazide diuretic Calcium channel blocker
Congestive heart failure (CHF)	Treat per standard CHF guidelines. Given the blood pressure–lowering effect of many first-line CHF medications, it is rarely necessary to add medications specifically for the hypertension. Consult Cardiology if questions.

Prescribing notes: Table 4

ACE inhibitors and ARBs

- ACE inhibitors and ARBs should not be used in combination.
- ACE inhibitors and ARBs are somewhat less efficacious in black patients, and therefore are not a preferred first-line choice for blacks, unless they have a clinical condition where these medications are recommended (e.g., CKD, diabetes, ASCVD).
- ACE inhibitors and ARBs are teratogenic. If a patient is pregnant or anticipating pregnancy, consider consultation with Obstetrics for BP management.
- ACE inhibitors should generally be chosen first-line above ARBs. ACE inhibitors are less expensive, and while some studies show similar clinical outcomes, others still show ACE inhibitors as superior. However, if a dry, persistent cough develops (normally within about 2 weeks, but potentially at up to 6 months) and appears to be caused by the ACE inhibitor, consider switching directly to an ARB. In a meta-analysis of 125 studies, the pooled incidence of ACE inhibitor–induced cough was reported to be 10.6% (Bangalore 2010).

Beta-blockers

- Beta-blockers are no longer a first-line recommendation for hypertension unless the patient has a comorbidity for which beta-blockers are preferred (e.g., angina, recent myocardial infarction, systolic heart failure, atrial fibrillation, or thoracic aneurysm). Consider beta-blockers if blood pressure has still not been controlled with the medications in Table 4.
- If the patient is already on beta-blockers for hypertension, use shared decision making to consider whether to continue with beta-blockers or switch to one of the preferred classes.

Consultative specialty service referral

Patients should be referred to consultative specialty services in the following situations:

- Blood pressure remains uncontrolled despite aggressive therapy with a minimum trial of 3 or 4 medications listed in Table 4.
- The patient has shown a dramatic failure to respond to medications.
- The patient is under age 25 years.

Refer patients to:

- Consultative Internal Medicine, unless there is a clear element of renal failure.
- Nephrology if there is a clear element of renal failure (creatinine > 2 mg/dL or rising creatinine with proteinuria).
- Cardiology only if the patient is currently under the active management of a cardiologist.

The following workup should be ordered and completed prior to the patient being seen by the consultative specialty service:

- CXR.
- Urinalysis.
- CBC and fasting lipid.
- Creatinine, sodium, potassium, fasting glucose, and EKG.
- Evaluate the patient for a high-salt diet or NSAID use, and correct these factors prior to referral.
- Consider obtaining a 24-hour urine for creatinine, sodium, and creatinine clearance (helpful but not required).

Default medication pathway

Below is a suggested default pathway for initiating and advancing blood pressure medication treatment. Following this pathway has several advantages:

- It works in each patient subgroup noted above (Table 4).
- By starting at ½ tab, we use resources effectively, and patients are more willing to make a dose adjustment (to 1 full tab) as needed to reach goal.
- A second dose adjustment (to 2 full tabs) can be made without requiring a new prescription.

Step 1	Combination ACE inhibitor and thiazide diuretic (lisinopril/HCTZ) 20/12.5 mg tabs Initiate at: ½ tab daily Advance every 2–4 weeks, as needed, to: 1 tab daily 2 tabs daily Throughout: Lab monitoring as needed (see Table 7)
Step 2	<i>If BP remains uncontrolled, add:</i> Calcium channel blocker (amlodipine) 5 mg tabs Initiate at: ½ tab daily Advance every 2–4 weeks, as needed, to: 1 tab daily 2 tabs daily Throughout: Lab monitoring as needed (see Table 7)
¹ Frail elderly patients may require lower initial doses and slower titration schedules. Frail elderly patients may require lower therapeutic doses as well.	

Medication dosing

Table 6. Antihypertensive medications: initial and recommended maximum dosing ¹		
Antihypertensive medication	Initial dose	Recommended maximum dose
Thiazide diuretics		
Hydrochlorothiazide (HCTZ)	12.5 mg daily	25 mg daily
Chlorthalidone	12.5 mg daily	25 mg daily
ACE inhibitors		
Lisinopril	10 mg daily	40 mg daily
Combination lisinopril/HCTZ	20/12.5 mg x ½ tab daily	20/12.5 mg x 2 tabs daily
Angiotensin receptor blockers		
Losartan	25 mg/day in 1–2 doses	100 mg/day in 1–2 doses
Calcium channel blockers		
Amlodipine	2.5 mg daily	10 mg daily
Beta-blockers		
Metoprolol IR (tartrate)	25 mg twice daily	100 mg twice daily
Metoprolol LA (succinate)	50 mg daily	200 mg daily
Atenolol ²	25 mg/day in 1–2 doses	100 mg/day in 1–2 doses
¹ Frail elderly patients may require lower initial doses and slower titration schedules. Frail elderly patients may require lower therapeutic doses as well. ² Not preferred in frail elderly patients or those with CKD.		

Drug timing strategies

- QHS (“bedtime”) dosing: There is some evidence to support using BP medications in the evening instead of the morning (except in patients with glaucoma or vascular ischemic disorders). (See Evidence Summary, p. 14.)
- BID (twice-daily) dosing: When dosing reads “in 1–2 doses,” this means the package insert states that QDAY (once-daily) dosing is acceptable. However, better clinical results are often achieved with BID dosing of these medications. Consider BID dosing more strongly as the dose increases.
- When considering either of these strategies, use shared decision making. For some patients, compliance is more difficult if they have to take medications twice per day instead of once. Also note that QHS diuretic dosing may result in poor tolerance/adherence in some patients. Be sure to discuss this with patients and ask how compliant they feel they would be with a more complicated medication regimen.

If patient is not meeting BP goal

Determine whether the patient is taking prescribed medications according to instructions. Using open-ended questions, talk with the patient about any barriers to adherence and check their understanding of their condition and the treatment(s) they’ve been prescribed. See [“Medication Adherence Counseling”](#) (staff intranet) for more detailed information.

If patient also has ASCVD or diabetes, consider a referral to Pharmacy. To see the exact referral criteria, consult the text of the Pharmacy referral order in Epic.

ASCVD Prevention

See the atherosclerotic cardiovascular disease (ASCVD) guidelines, Primary Prevention and Secondary Prevention, as appropriate.

Follow-up/Monitoring

Note: If the patient has an abrupt increase in BP measurement, consider secondary hypertension.

Medication monitoring

Medication	Test(s)	Frequency
ACE inhibitors or ARBs ¹	Potassium and Creatinine	Before initiating therapy and 2 weeks after initiating therapy and
Diuretics and/or aldosterone antagonists ²	Potassium and Creatinine	With each increase in dose and Annually
	Sodium ³	Before initiating therapy and consider at the time periods listed above.
Beta-blockers and/or Calcium channel blockers	No routine lab monitoring is required.	Not applicable

¹ For patients on ACE inhibitors or ARBs, renal function (creatinine) should be checked because treatment may be associated with deterioration of renal function and/or increases in serum creatinine, particularly in patients dependent on renin-angiotensin-aldosterone system; potassium should be checked because 2–5% of patients develop hyperkalemia.

² For patients on diuretics or aldosterone antagonists, potassium should be checked at least once a year, and perhaps twice a year and with any change of dose because excessive dosages can lead to profound diuresis with fluid and electrolyte loss; renal function (creatinine) should be checked because use of diuretics may cause oliguria, azotemia, and reversible increases in creatinine.

³ For patients who are > 60 years, on multiple medications, or who have heart failure, consider checking sodium levels as well.

Evidence Summary

Methods and sources

To develop the Hypertension Guideline, the guideline team:

- Considered recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards.
- Reviewed additional literature using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

Externally developed guidelines considered

- 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) (James 2014)
- 2014 Kaiser National Clinical Practice Guideline: Hypertension, adopting JNC 8
- 2013 North California and Southern California Permanente Medical Group Hypertension Guideline
- 2013 Guidelines for the Management of Arterial Hypertension. European Society of Hypertension/ European Society of Cardiology
- 2013 and 2014 Canadian Hypertension Education Program: Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension (Hackam 2013, Canadian Hypertension Education Program 2014)
- 2012 ICSI Hypertension Diagnosis and Treatment (Luehr 2012)
- 2011 NICE Hypertension: Clinical Management of Primary Hypertension in Adults

Additional evidence review

The guideline team reviewed additional evidence in the following areas:

- Screening for hypertension
- Blood pressure target and intensity of control
- Antihypertensive pharmacological therapies
- Antihypertensive therapy in the elderly
- Chronotherapy (timing of medication) for hypertension
- Lifestyle modification
- Home monitoring of blood pressure

Screening for hypertension

The U.S. Preventive Services Task Force (2007) strongly recommends screening adults aged 18 years and older for high blood pressure. This is based on indirect evidence that blood pressure measurement can identify adults who are at increased risk for cardiovascular disease due to hypertension, and good direct evidence that treatment of hypertension substantially decreases the incidence of cardiovascular disease and causes few major harms.

Blood pressure target and intensity of control

- All the reviewed U.S., Canadian and European guidelines on the management of hypertension—with the exceptions of JNC 8 2014 and Kaiser 2014, which adopted JNC 8—recommend a goal of < 140/90 mm Hg for the general population under 80 years of age, and a goal of < 150/90 mm Hg for the very elderly (80 years of age or older). JNC 8 recommends a goal of < 140/90 mm Hg for the general population under 60 years of age, and a goal of < 150/90 mm Hg for those aged 60 years and older.
- The HYVET trial (Beckett 2008) used a BP target of 150/80 mm Hg for elderly patients at least 80 years old with hypertension. This was achieved among 48% of the patients randomized to the active treatment.
- There is evidence from the JATOS (JATOS Study Group 2008) and VALISH (Ogihara 2010) trials that strict BP control among elderly hypertensive patients lowers BP significantly versus moderate control, but strict control does not have a significant benefit in reducing morbidity or mortality.

- The pooled results of randomized controlled trials (RCTs) in two meta-analyses (Lv 2012 and 2013) show that intensive blood pressure lowering for patients with chronic kidney disease and proteinuria reduces their risk of kidney failure. An analysis performed by the authors indicates that a 10 mm Hg reduction in BP may result in an overall reduction of 22% in the risk of kidney failure. These results may not be generalized to patients with diabetic kidney disease, as these patients were not included in the majority of the included trials.
- The pooled results of RCTs in two meta-analyses (Arguedas 2013 and Reboldi 2011) indicate that tight blood pressure control may reduce the risk of stroke in patients with diabetes. The intensive BP lowering, however, was not found to reduce the risk of fatal and nonfatal events when combined or when mortality, myocardial infarction, and heart failure were considered separately.

Why do we differ from the JNC 8 panel in their recommendation to increase the target systolic blood pressure from 140 mm Hg to 150 mm Hg in persons aged \geq 60 years without diabetes or CKD?

1. There is insufficient evidence to support raising the target systolic BP in patients aged \geq 60 years. (Note: Insufficient or no evidence of benefit is not the same as evidence of no benefit.)

The JNC 8 panel based their recommendation for raising the BP goal among patients aged \geq 60 years on the HYVET, Syst-Eur (Staessen 1997), SHEP (Curb 1996), JATOS, VALISH, and Cardio-Sis (Verdecchia 2009) trials. The panel members indicated that there is moderate- to high-quality evidence that treating the general population aged \geq 60 years with high BP to a goal $<$ 150/90 mm Hg reduces stroke, heart failure, and coronary heart disease. They also noted that low-quality evidence shows that a systolic BP goal of $<$ 140 mm Hg in this age group provides no additional benefit versus a higher goal of systolic BP 140 to $<$ 160 mm Hg (JATOS) or 140–149 mm Hg (VALISH).

The ages of the populations included in the trials the JNC 8 panel cited were \geq 80 years in HYVET, 70– $<$ 85 years in VALISH, 65–85 years in JATOS, \geq 60 years in SHEP and Syst-Eur, and \geq 55 years in Cardio-Sis. The mean BP measurements achieved in the active and/or more intensive treatment groups of these studies were 143.5/77.9 mm Hg, 136.6/74.8 mm Hg, 135.9/74.8 mm Hg, 143/68 mm Hg, 150.8/78.5 mm Hg, and 136/79.2 mm Hg, respectively. The JATOS and VALISH studies—which the JNC 8 panel referred to as showing no additional benefit with lower targets—were statistically underpowered to detect such a benefit due to the very low rates of stroke and CHD reported during follow-up. The majority of these trials suggest that a systolic BP goal of $<$ 140 mm Hg is safe in non-frail, relatively healthy older patients.

FEVER (Liu 2005)—a large trial with 9,711 Chinese patients aged 50–79 years that was not included in the JNC 8 review—indicated that a difference in systolic/diastolic BP as small as 4/2 mm Hg (induced by adding low-dose felodipine to low-dose hydrochlorothiazide in the trial) is associated with significant reductions in the incidence of stroke, all CVD, CHD, heart failure, and total mortality. The mean BP achieved at study end (60 months) with the addition of felodipine was 138.1/82.3 mm Hg versus 141.6/83.9 mm Hg with the addition of a placebo. A subgroup analysis for patients aged $>$ 65 years showed a 44% reduction in all strokes (Zhang 2011).

2. The JNC 8 panel did not disallow treatment to $<$ 140 mm Hg systolic BP. In a corollary recommendation, the panel indicated that treatment for hypertension does not need to be adjusted if the treatment results of SBP $<$ 140 mm Hg are not associated with adverse effects on health or quality of life.
3. The JNC 8 panel recommendation for raising the target BP in patients aged \geq 60 years was not based on a unanimous agreement. Some members argued that there was insufficient evidence to raise the target to 150 mm Hg in high-risk groups such as black persons, those with CVD including stroke, and those with multiple risk factors. This minority group explained that increasing the target would probably reduce the intensity of antihypertensive treatment in a large population at high risk for CVD. The panel agreed that more research is needed to identify optimal goals, yet they still raised the goal for those \geq 60 years of age.
4. The American Society of Hypertension/International Society of Hypertension 2014 (Weber 2014), Canadian CHEP 2013, European ESC/ESC Task Force 2013, ICSI 2012, and NICE 2011

guidelines all recommend a BP goal of < 140/90 mm Hg for the general population aged < 80 years, and < 150/90 mm Hg for those aged 80 years or over.

5. There is a concern that the higher SBP goal for patients aged ≥ 60 years may increase their risk of stroke.
6. The risk of cardiovascular events increases with age, and raising the BP goal for patients aged ≥ 60 years will result in inadequate treatment for some higher-risk patients and deprive others of therapy. This would reduce all the benefits gained in the last few years from reducing blood pressure.

Why do we recommend a lower BP target for patients with CKD and albuminuria?

The JNC 8 panel recommended a goal of < 140/90 mm Hg for patients aged ≥ 18 years with CKD, based on expert opinion. The guideline panel, however, suggested that patients > 70 years with CKD or albuminuria should receive treatment based on comorbidity, frailty, and other patient-specific factors. They indicated that there was insufficient evidence to support a goal BP of < 140/90 mm Hg in patients > 70 years with CKD or albuminuria.

The JNC 8 panel's evidence review did not include meta-analyses or observational studies. The initial literature search was conducted through December 31, 2009. A second search made through August 2013 was restricted to multicenter RCTs with at least 2,000 participants.

More recent evidence from meta-analyses (Lv 2012 and 2013) not reviewed by the JNC 8 panel suggests that intensive blood pressure lowering for patients with chronic kidney disease and proteinuria reduces their risk of major cardiovascular events, composite kidney failure events, and end-stage kidney disease. The most aggressive trials had an SBP target of < 120 mm Hg (in three of the trials included in the analysis) and < 130 mm Hg (in one). The DBP target was < 75 mm Hg in one trial and < 80 mm Hg in two trials.

Antihypertensive pharmacological therapies

- There is evidence from a large meta-analysis (Law 2009) that lowering systolic blood pressure by 10 mm Hg and/or diastolic blood pressure by 5 mm Hg using any of the five classes of antihypertensive drugs leads to similar risk reduction for CHD and stroke. The more recent Blood Pressure Lowering Treatment Trialists' Collaboration meta-analysis (2013) also showed that the effects of BP lowering on reducing cardiovascular risk were similar irrespective of the antihypertensive drugs or regimens used (ACE inhibitors, calcium channel blockers, or diuretics/beta-blockers).
- There is supporting evidence that: thiazides and ACE inhibitors used as first-line therapy for hypertension reduce the risk of morbidity and mortality due to CHD, stroke, and other cardiovascular events; CCBs reduce the risk of stroke but not of CHD events or mortality; and beta-blockers are inferior in benefit compared with other classes.
- There is evidence from a large meta-analysis (Wald 2009) that the BP reduction from each class of drug combined with one from another class is approximately additive. The meta-analysis also shows that combining given doses of two classes of drugs is approximately five times more effective than doubling the dose of one drug.
- There is good evidence from a large meta-analysis and subsequent validated RCTs that low-dose combination perindopril-indapamide therapy is more effective in controlling hypertension than sequential monotherapy or the stepped-care approach (Kang 2004, Mourad 2004 and 2007, Patel 2007).
- There is some evidence that fixed-dose combination therapies may be associated with higher rates of compliance and persistence with therapy in addition to better control of blood pressure.
- A Cochrane review and meta-analysis (Heran 2008 - CD003823) showed that there were no clinically meaningful BP-lowering differences between the different ACE inhibitors. Another meta-analysis by the same group (Heran 2008 - CD003822) also suggests that no one ARB is superior or inferior to others.
- The ONTARGET trial (ONTARGET Investigators 2008) provides evidence that ARBs are not

inferior to ACE inhibitors and that combining both classes does not lead to better outcomes but does lead to more harms.

- There is evidence that the use of beta-blockers (atenolol in 75% of the studies) as a first-line therapy for hypertension had a weak effect on reducing cardiovascular disease and stroke, and no effect on reducing CHD compared to placebo. When compared to other active antihypertensive therapies, it had a trend for worse outcomes and discontinuation of therapy due to side effects.
- There is some evidence that, compared to other antihypertensive drugs, atenolol used as a first-line monotherapy had a similar effect in lowering BP but was associated with higher mortality and stroke (Carlberg 2004, Lindholm 2005). This could be due to the fact that in most atenolol trials the drug was given in a once-daily dose. According to several investigators, atenolol needs to be taken more frequently, based on its pharmacodynamic and pharmacokinetic properties. Atenolol has a half-life of 6–9 hours and is usually given once daily, while carvedilol and metoprolol have half-lives of 6–10 hours and 3–7 hours respectively, and are given in at least twice-daily doses (Neutel 1990, Sarafidis 2008).
- There is evidence that calcium channel blockers slightly decrease the risk of all-cause mortality and stroke versus other treatments, but increase the risk of heart failure.
- There is insufficient evidence to determine the comparative effectiveness and safety of chlorthalidone and HCTZ in patients with hypertension. The published evidence from observational studies and meta-analyses with indirect comparisons was conflicting.
- Dhalla and colleagues' observational study (2013) suggests that chlorthalidone may be associated with higher incidence of electrolyte abnormalities in older adults.
- There is evidence from meta-analyses (Heran 2009, Chen 2010) quantifying the dose-related SBP- and DBP-lowering efficacy of the different antihypertensive agents that:
 - For ACE inhibitors, a dose of one-eighth or one-fourth of maximum recommended dose achieved a BP-lowering effect 60–70% of that attained by the maximum manufacturer-recommended dose (one-half of the maximum dose achieved BP lowering 90% of the maximum dose).
 - For ARBs, a dose of one-eighth or one-fourth of maximum recommended dose achieved a BP-lowering effect 60–70% of that attained by the maximum manufacturer-recommended dose.
 - For beta-blockers, the addition of one-fourth the recommended dose to a thiazide or calcium channel blocker was associated with BP reduction (2.9/1.4 mm Hg). Adding 1x starting dose was associated with BP reduction of 6/4 mm Hg.

Antihypertensive therapy in the elderly

The HYVET trial (Beckett 2008) provides good evidence that antihypertensive treatment of generally healthy elderly patients is safe and effective in reducing blood pressure, total mortality, and cardiovascular events. The results of a large meta-analysis (Blood Pressure Lowering Treatment Trialists' Collaboration 2008) show that reduction of BP with various drugs is independent of the patient's age or the drug regimen used, and supports the early and aggressive management of hypertension irrespective of age.

There is fair evidence that beta-blockers, atenolol in particular, may be associated with a higher rate of stroke compared to other antihypertensive agents, especially among older patients (Carlberg 2004, Lindholm 2005, Khan 2006).

Chronotherapy (timing of medication) for hypertension

- There is fair evidence from prospective studies (Ayala 2013, Hermida 2010, Hermida 2011 [*J Am Coll Cardiol*], Hermida 2011 [*J Am Soc Nephrol*], Fan 2010) that the asleep BP mean is a better predictor of CVD risk than either the awake or 24-hour BP mean.
- There is fair evidence from a number of prospective studies conducted mainly in Spain (Ayala 2013, Hermida 2010, Hermida 2011 [*J Am Soc Nephrol*], Hermida 2013) that bedtime administration of antihypertensive medications may lead to better BP control and reduce CVD risk

among the populations studied, which were predominantly male Spanish, Caucasian, and Asian patients.

- In a review article, the authors of the Spanish studies (Smolensky 2010) recommend taking an individualized approach and considering the harms and benefits of bedtime therapy for patients with certain comorbidities. They explained that for certain conditions, such as glaucoma and advanced vascular ischemic disorders, a too-low asleep BP could be detrimental.
- The benefit of bedtime antihypertensive medication was observed for ACE inhibitors, ARBs, and diuretics, as well as other commonly prescribed antihypertensive medications and combinations (Hermida 2011 [*Am J Hypertens*], Hermida 2011 [*Chronobiol Int*], Zeng 2011).

Lifestyle modification

The literature on the effect of lifestyle change on the control of hypertension is limited. All trials were small to moderate in size and only addressed the effect of lifestyle modification on BP control, not on morbidity and mortality. The PREMIERE trial that compared three interventions among patients with pre- or mild hypertension showed that the prevalence of hypertension was significantly lower in the group that received established recommendations plus the DASH diet than in the group that received advice only (Elmer 2006). There is also fair evidence from meta-analyses of small studies with some methodological flaws that a weight-reducing diet and salt and alcohol restrictions are associated with significant reductions in blood pressure. However, it is unclear whether these short-term lifestyle changes can reduce the need for medications or improve morbidity and mortality (Horvath 2008, Dickinson 2006).

Recommendations on lifestyle modification in the current guideline were adopted from JNC 8 panel recommendations, which were based on the 2013 ACC/AHA guideline on lifestyle management to reduce cardiovascular risk.

Home monitoring of blood pressure

There is evidence from several meta-analyses that patients diagnosed with hypertension in the office who monitor their blood pressure at home are more likely to achieve their target BP value than those monitored in the office (Cappuccio 2004, Verberk 2005, Ishikawa 2008). The studies included in the meta-analyses were conducted in different settings and used different criteria for including patients, different methods for monitoring blood pressure, and different, higher targets than those currently recommended. According to the published literature and external guidelines reviewed, the goal of blood pressure < 140/90 mm Hg when BP is measured in the office is equivalent to < 135/85 mm Hg when measured at home.

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Guideline Development Process and Team

Development process

To develop the Hypertension Guideline, the guideline team adapted recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards. The guideline team reviewed additional evidence using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in August 2014.

Team

The Hypertension Guideline development team included representatives from the following specialties: cardiology, family medicine, nephrology, nursing, pharmacy, and residency.

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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Hypertension Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.