Blood Pressure Control in the Elderly – How High Should You Go?

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Learning Objectives

1. Summarize the epidemiology, pathophysiology and treatment of hypertension.
2. Explain recent updates to clinical practice guidelines for the management of hypertension in the elderly.
3. Compare the major differences of geriatric hypertension recommendations between guidelines.
4. Evaluate the evidence for a blood pressure goal < 150/90 mmHg in patients over age 60.
I. Introduction
   A. Epidemiology \(^1,^2\)
      1. United States
         a. 77.9 million adults have hypertension (HTN)
         b. 33% of the adult population in 2013 had HTN (1 out of every 3 adults)
         c. Adults ≥ 20 years old
            i. Non-Hispanic, whites: 33.4% of men; 30.7% of women
            ii. Non-Hispanic, African Americans: 42.6% of men; 47% of women
            iii. Hispanics: 30.1% of men; 28.8% of women

   Figure 1. Prevalence of High Blood Pressure in Adults\(^1,^2\)

   2. National Health and Nutrition Examination Survey (NHANES) 2007-2010 data on patients with HTN
      a. 81.5% of patients aware
      b. 74.9% treated
      c. 52.5% controlled; 47.5% uncontrolled
   3. Estimated by 2030, 41.4% of the adult population will have HTN (an increase of 8.4% from 2013)

B. Economic costs \(^3\)
   1. 2010 HTN data
      a. Indirect and direct cost to the U.S. $47.5 billion
      b. Annual expenditures for those treated averaged $733 per adult

C. Complications \(^4\)
   1. Cardiovascular
      a. Angina/myocardial infarction (MI)
         i. Approximately 69% of those who have a first heart attack have a BP > 140/90 mm Hg
      b. Heart failure
         i. Approximately 74% of patients with heart failure have a BP > 140/90 mmHg
      c. Ventricular arrhythmias
2. Cerebrovascular  
   a. Stroke  
      i. Approximately 77% of patients who have a first stroke have a BP > 140/90 mmHg  
      ii. For each 10 mmHg increase of SBP  
          - 8% increase of stroke risk in whites  
          - 24% increase of stroke risk in African Americans  
   b. Transient ischemic attack (TIA)

3. Chronic Kidney Disease (CKD)

4. Peripheral vascular system  
   a. Peripheral artery disease  
   b. Abdominal aortic aneurysm

5. Eyes  
   a. Retinopathy  
   b. Arteriovenous (AV) nicking

6. HTN is associated with shorter life expectancy  
   i. Normotensive men at age 50 live 5.1 years longer than males with HTN  
   ii. Normotensive women at age 50 live 4.9 years longer than females with HTN

II. Hypertension

A. Causes  
   1. Primary HTN  
      a. Also called essential HTN  
      b. 95% of HTN cases  
      c. Unknown cause  
   2. Secondary HTN  
      a. Chronic kidney disease  
      b. Renal artery stenosis  
      c. Excess aldosterone secretion  
      d. Pheochromocytoma  
      e. Sleep apnea

B. Risk factors  
   1. African American  
   2. Family history  
   3. Advanced age  
   4. Gender  
      a. Higher percentage of men before age 45  
      b. Similar rates age 45-64  
      c. Higher percentage of women vs. men age 65 or older  
   5. Lack of physical activity  
   6. Overweight and obesity  
   7. Diet  
      a. Excessive sodium intake  
      b. Insufficient potassium intake  
   8. Alcohol  
   9. Smoking (first-hand and second-hand)

C. Pathophysiology  
   1. Blood pressure: generated when the heart contracts against the resistance of the blood vessels  
      (primarily arteries). See Appendix A (page 17) for more information  
   2. Hypertension results from an increase in cardiac output (CO) and/or total peripheral resistance (TPR)  
      a. Often the TPR is increased and CO is normal or slightly increased  
         i. Typical pattern of primary hypertension, primary aldosteronism, pheochromocytoma,  
            renovascular disease and renal parenchymal disease  
      b. Other patients CO is increased and TPR eventually increases due to autoregulation.  
         i. Typically seen in thyrotoxicosis, aortic regurgitation and the elderly
Table 1. Potential Mechanisms of HTN Pathogenesis

<table>
<thead>
<tr>
<th>Increased Cardiac Output</th>
<th>Increased cardiac preload:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Increased fluid volume from excess sodium intake or renal sodium retention</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Venous constriction:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Renin-angiotensin-aldosterone system (RAAS) excess stimulation</td>
</tr>
<tr>
<td>• Sympathetic nervous system overactivity</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Increased TPR</th>
<th>Vascular constriction:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• RAAS excess stimulation</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic nervous system overactivity</td>
</tr>
<tr>
<td></td>
<td>• Genetic alterations of cell membranes</td>
</tr>
<tr>
<td></td>
<td>• Endothelial-derived factors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Structural vascular hypertrophy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• RAAS excess stimulation</td>
</tr>
<tr>
<td>• Sympathetic nervous system overactivity</td>
</tr>
<tr>
<td>• Genetic alterations of cell membranes</td>
</tr>
<tr>
<td>• Endothelial-derived factors</td>
</tr>
<tr>
<td>• Hyperinsulinemia</td>
</tr>
</tbody>
</table>

D. Diagnosis

1. Diagnosed by sphygmomanometry but history & physical (H&P) examination and other tests may help determine etiology and if target organ damage has occurred

2. Signs/Symptoms
   a. Usually asymptomatic
   b. Dizziness
   c. Headache
   d. Fatigue
   e. Nervousness
   f. Flushing of the face
   g. Retinal changes (arteriolar narrowing, hemorrhages, exudates)
   h. S4 (fourth heart sound)
      i. A rare heart sound heard before the normal S1 and S2 ("lub-dub") heart sounds
      ii. Indicative of hypertensive heart disease

3. Diagnosis is based on the average of ≥ 2 seated BP readings (properly measured) at ≥ 2 office visits

4. Obtain H&P
   a. History of coronary events, renal dysfunction, dyslipidemia, gout, diabetes
   b. Family history of any coronary disease and above conditions
   c. Diet
   d. Physical Exam

5. Testing
   a. The more severe the hypertension and the younger the patient the more extensive testing required
   b. Determine target organ damage and identify cardiovascular risk factors
      i. Urinalysis (including urine albumin: creatinine ratio)
      ii. Basic metabolic panel
      iii. Thyroid function tests
      iv. Fasting lipid profile
      v. Depending on initial results of the tests and examination other tests may be warranted: electrocardiogram, renal ultrasound, chest x-ray, echocardiogram, etc.
Table 2. Blood Pressure Classifications

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥ 160</td>
<td>≥ 100</td>
</tr>
</tbody>
</table>

E. **Lifestyle recommendations**

1. **Diet**
   a. High intake: vegetables, fruits, whole grains, low-fat dairy products, poultry, fish, non-tropical vegetable oils, legumes and nuts
   b. Limit: sweets, sugar-sweetened beverages and red meats
   c. Achievable through the Dietary Approaches to Stop Hypertension (DASH) diet, USDA Food Pattern or the American Heart Association Diet
   d. Low sodium intake
      i. ≤ 2,400 mg per day
      ii. ≤ 1,500 mg per day can result in even greater BP reduction
      iii. Even without reaching these goals, decreasing sodium intake by 1,000 mg per day lowers BP

2. **Physical Activity**
   a. Moderate to vigorous activity for 40 minutes/session and 3-4 sessions/week (approximately 150 minutes/week)
      i. Brisk walking
      ii. Bicycling
      iii. Jogging

3. **Weight reduction**
   a. Weight loss of 5.1 kg has shown to reduce SBP 4.4 mmHg and DBP 3.6 mmHg

4. **Smoking cessation**

5. **Moderate alcohol consumption** (2 drinks for men per day, 1 drink for women per day)

F. **Anti-hypertensive agents**

1. **Focus on 4 classes recommended in the JNC 8 Guidelines. See Appendices A & B (pages 17-18) for additional agents**

2. **Thiazide-type diuretics**
   a. Mechanism of action (MOA): Inhibit Na⁺ reabsorption in the distal tubules of the kidney, increasing Na⁺ and water secretion, as well as H⁺ and K⁺ ions
   b. Side effects: fatigue, frequent urination, thirst, muscle cramps, diarrhea or constipation, increased sensitivity to sunlight, hyperglycemia, hypercalcemia and potassium depletion

3. **Angiotensin-converting enzyme inhibitors (ACEI)**
   a. MOA: ACE inhibition prevents conversion of angiotensin I and angiotensin II thus reducing aldosterone secretion
   b. Side effects: cough, dizziness, rash, increased potassium, fainting

4. **Angiotensin II receptor blockers (ARBs)**
   a. MOA: Direct antagonism of angiotensin II receptors leads to reduced aldosterone secretion
   b. Side effects: muscle cramps, dizziness, increased potassium

5. **Calcium channel blockers (CCBs)**
   a. 2 classes
      i. Dihydropyridine (DHPs)
         • MOA: Inhibits Ca²⁺ from entering the smooth muscle, causing relaxation of vascular smooth muscle and peripheral vasodilation
         • Side effects: peripheral edema, dizziness, drowsiness, nausea, pulmonary edema
      ii. Phenylalkylamines (also known as non-DHPs)
         • MOA: Inhibits Ca²⁺ from entering smooth muscle and myocardium producing coronary vasodilation
         • Side effects: edema, headache, bradycardia, dizziness, constipation, diarrhea

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Table 3. Evidence-Based Dosing for Anti-Hypertensive Agents

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose (mg)</th>
<th>Target Dose*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thiazide-type Diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>12.5 mg daily</td>
<td>12.5-25 mg daily</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12.5-25 mg daily</td>
<td>25-50 mg daily (divided 1-2 doses)**</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25 mg daily</td>
<td>1.25-2.5 mg daily</td>
</tr>
<tr>
<td><strong>ACEI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>50 mg BID</td>
<td>150-200 mg BID</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5 mg daily</td>
<td>20 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 mg daily</td>
<td>40 mg daily</td>
</tr>
<tr>
<td><strong>ARBs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eprosartan</td>
<td>400 mg daily</td>
<td>600-800 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 mg daily</td>
<td>12-32 mg daily</td>
</tr>
<tr>
<td>Losartan</td>
<td>50 mg daily</td>
<td>100 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td>Valsartan</td>
<td>40-80 mg daily</td>
<td>160-320 mg daily</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>75 mg daily</td>
<td>300 mg daily</td>
</tr>
<tr>
<td><strong>CCBs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5 mg daily</td>
<td>10 mg daily</td>
</tr>
<tr>
<td>Diltiazem (extended release)</td>
<td>120-180 mg daily</td>
<td>360 mg daily</td>
</tr>
</tbody>
</table>

*Target doses achieved in randomized controlled trials (RCTs)
**Recommended evidence-based dose balancing efficacy and safety is 25-50mg daily, minimal increase in response when doses > 50 mg/day.

G. Geriatric Hypertension

1. Geriatric definition
   a. The United Nations defined an older population as > 60 years old
   b. According to the World Health Organization, most developed countries accept > 65 years old as the definition of elderly or older person
   c. Definition varies among countries

2. Prevalence
   a. Among people 40-59 years old 30.4% of the population has HTN
   b. Among those ≥ 60 years old 66.7% of the population has HTN
   c. U.S. adults ≥ 65 years old
      i. Prevalence was 70.8%
      ii. Awareness of HTN 75.9% of those with HTN
      iii. Treatment of HTN 69.3% of those with HTN
      iv. Of those treated control of HTN was 48.8%

3. Pathophysiology of HTN in the elderly
   a. Increased SBP due to arterial stiffness caused by decreased vascular smooth muscle cells and increased collagen content in the vessel wall, calcium deposition and disruption of elastic fibers
   b. Limited recoil of the vessels may lead to a decline in DBP

4. Stroke in the elderly
   a. Prevalence of stroke by age and sex
      i. Men and women aged 40-59: 2.1%
      ii. Men aged 60-79: 6.2%
      iii. Women aged 60-79: 6.9%
      iv. Men aged >80: 13.9%
      v. Women aged >80: 13.8%
b. Over the next forty years, the number of strokes is expected to double, with the majority of the increase among patients 75 years of age or older.

**Figure 2. Mortality within 5 years After First Stroke**

5. Cardiovascular disease (CVD)
   a. 42.2 million adults ≥ 60 years old have CVD
   b. Most common cause of death in the U.S.
      i. 32% of all deaths in the U.S. during 2010
      ii. Average of 1 death every 40 seconds due to CVD

**Figure 3. Prevalence of Cardiovascular Disease in Adults**

6. Leading causes of death in patients ≥ 65 years old
   a. Women number one cause is heart disease, and number three cause is stroke
   b. Men number one cause is heart disease, and number four cause is stroke
7. Antihypertensive agents in the elderly
   a. Large meta-analysis found the benefit of reducing BP is similar in magnitude and independent of anti-hypertensive agent
   b. Common adverse effects of all agents: hypotension, dizziness
   c. Adverse effects in the elderly based on drug class
      i. Thiazide-type diuretics
         - More prone to thiazide-induced dehydration and orthostatic changes
      ii. CCBs
         - Orthostatic hypotension, edema
         - Verapamil induced constipation
      iii. ACEIs/ARBs
         - Elevate blood urea nitrogen (BUN) and serum creatinine (SCr) if patient has renal insufficiency, dehydration or heart failure, which these conditions are more common in the elderly
      iv. B-blockers
         - Bradycardia and conduction abnormalities

8. Risks of treating HTN in the elderly
   a. Increased risk of falls
      i. Risk factors for falls in the elderly include gait impairment, postural hypotension, dizziness
      ii. A meta-analysis of observational studies showed a 24% increased risk of falls while on anti-hypertensive agents
      iii. Serious fall injuries decrease functionality and increase the risk of mortality

III. Guidelines
   A. JNC 8
      1. Published online December 2013, 10 years after JNC 7 publication
      2. See Appendix C (page 19) for differences between JNC 7 and JNC 8
      3. Studies were included only if the interventions addressed overall mortality, CV-related mortality, CKD-related mortality, MI, heart failure (HF), hospitalization for HF or stroke, coronary revascularization, ESRD, doubling of creatinine level, halving of GFR
      4. Three main questions the expert panel wanted to address in JNC 8
         a. What BP level to start medications?
         b. What are the appropriate BP treatment goals?
         c. Which medications for HTN are best?
      5. See Appendix D (page 20) for JNC 8 Algorithm

Table 5. Strength of Recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strong (high certainty of significant benefit)</td>
</tr>
<tr>
<td>B</td>
<td>Moderate (moderate certainty of moderate or significant benefit)</td>
</tr>
<tr>
<td>C</td>
<td>Weak (moderate certainty of little benefit)</td>
</tr>
<tr>
<td>D</td>
<td>Against (moderate certainty of no benefit)</td>
</tr>
<tr>
<td>E</td>
<td>Expert Opinion (insufficient evidence or unclear evidence)</td>
</tr>
<tr>
<td>N</td>
<td>No recommendation for or against</td>
</tr>
</tbody>
</table>

Table 6. Nine Recommendations

<table>
<thead>
<tr>
<th>Population</th>
<th>Initiate Drug Therapy (mmHg)</th>
<th>Goal BP (mmHg)</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 years old</td>
<td>SBP ≥ 150 or DBP ≥ 90</td>
<td>&lt; 150/90</td>
<td>SBP: A</td>
</tr>
<tr>
<td>&lt; 60 years old</td>
<td>SBP ≥ 140 or DBP ≥ 90</td>
<td>&lt; 140/90</td>
<td>SBP: E DBP: E</td>
</tr>
<tr>
<td>≥ 18 years old + CKD</td>
<td>SBP ≥ 140 or DBP ≥ 90</td>
<td>&lt; 140/90</td>
<td>E</td>
</tr>
<tr>
<td>≥ 18 years old + Diabetes</td>
<td>SBP ≥ 140 or DBP ≥ 90</td>
<td>&lt; 140/90</td>
<td>E</td>
</tr>
<tr>
<td>Guideline</td>
<td>Population</td>
<td>Goal BP (mmHg)</td>
<td>Initial Drug Therapy</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------</td>
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<td>-------------------------------------------</td>
</tr>
<tr>
<td>JNC 8</td>
<td>General, non-black &lt; 60 years</td>
<td>&lt; 140/90</td>
<td>CCB, ACEI or ARB, Thiazide</td>
</tr>
<tr>
<td></td>
<td>General, non-black ≥ 60 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General, black &lt; 60 years</td>
<td>&lt; 140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General, black ≥ 60 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td>ESH/ESC</td>
<td>General &lt; 65 years</td>
<td>&lt; 140/90</td>
<td>Diuretic, β-blocker, CCB, ACEI, ARB</td>
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<tr>
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<td>General ≥ 65 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td>CHEP</td>
<td>General &lt; 80 years</td>
<td>&lt; 140/90</td>
<td>Thiazide, ACEI (if non-black), ARB, β-blocker (if &lt;60 years)</td>
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<tr>
<td></td>
<td>General ≥ 80 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td>ASH/ISH</td>
<td>General, non-black &lt; 60 years</td>
<td>&lt; 140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General, non-black 60-79 years</td>
<td>&lt;140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General, non-black ≥ 80 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General, black &lt; 80 years</td>
<td>&lt; 140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General black ≥ 80 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
<tr>
<td>ACC/AHA /CDC</td>
<td>Stage 1 HTN*</td>
<td>≤ 139/89</td>
<td>Lifestyle modifications +/- thiazide</td>
</tr>
<tr>
<td></td>
<td>Stage 2 HTN**</td>
<td>≤ 139/89</td>
<td>Thiazide + (ACEI or ARB) or CCB</td>
</tr>
<tr>
<td>NICE</td>
<td>General &lt; 80 years</td>
<td>&lt; 140/90</td>
<td>CCB</td>
</tr>
<tr>
<td></td>
<td>General ≥ 80 years</td>
<td>&lt; 150/90</td>
<td></td>
</tr>
</tbody>
</table>

ESH/ESC = European Society of Hypertension/European Society of Cardiology  
CHEP = Canadian Hypertension Education Program  
ASH/ISH = American Society of Hypertension/International Society of Hypertension  
ACC/AHA/CDC = American College of Cardiology/American Heart Association/Centers for Disease Control  
NICE= National Institute for Health and Clinical Excellence  
*Stage 1 HTN defined as SBP 140-159 or DBP 90-99mmHg  
**Stage 2 HTN defined as SBP >160 or DBP > 100mmHg

B. Similarities between the guidelines
1. All patients with BP ≥ 160/100  
   a. Initiate 2 drug therapy  
2. Diuretics of choice  
   a. Thiazides  
   b. Chlorthalidone  
   c. Indapamide  
3. B-blockers not a 1st line agent in patients without compelling indications  
   a. Exception: ESH/ESC  
4. Treat patients > 80 years old less aggressively (BP goal < 150/90)
C. Controversy with JNC 8 20-21
   1. Evidence review did not include observational studies, systematic reviews or meta-analyses.
   2. BP control in patients 60-79 years of age
      a. Increasing the blood pressure goal in patients over 60 years old may reduce the intensity of antihypertensive treatment in a population at risk for CVD
      b. Insufficient evidence supporting the decision to increase the target from 140 to 150 mmHg in these patients
      c. May reverse the declining rate of CVD from the last few decades
      d. The decision to raise the BP goal <150/90 mmHg in patients over 60 years was not unanimous agreement among the JNC 8 panel
         i. Five panel members submitted a commentary in January 2014 expressing the above concerns over the recommendation changes

IV. Clinical Question
   A. What is the appropriate blood pressure goal for patients over 60 years of age with essential hypertension and without any compelling indications?

V. Clinical trials regarding hypertension treatment in the elderly
   A. Selection of trials
      1. Mentioned or referenced in any of the guidelines
      2. Randomized trials
         a. Large study population (over 2000 patients)
         b. Multi-center
         c. Patient population 60 years or older

Systolic Hypertension in the Elderly Program (SHEP) Trial

## Objective
Determine the efficacy of antihypertensive agents to reduce the total risk of fatal and non-fatal stroke in patients 60 years or older with systolic hypertension.

## Trial Design
Double-blind, placebo controlled trial at 16 tertiary clinics in the United States

### Patient Selection

#### Inclusion
- Patients ≥ 60 years old
- Average of four seated BP measurements, at two separate visits, SBP 160-219 mmHg and DBP < 90 mmHg

#### Exclusion
- Cancer
- Alcoholic liver disease
- Renal dysfunction
- Heart failure

### Methods
- Patients followed monthly until SBP at goal, then quarterly.
- Patients with SBP > 180 mmHg at baseline, goal SBP < 160 mmHg.
- Patients with SBP 160-179 mmHg at baseline, goal decrease SBP at least 20 mmHg.
- Chlorthalidone 12.5 mg/day or matching placebo as initial therapy.
- At first follow-up (1 month after randomization), if SBP not at goal, dose was doubled.
- If goal could not be reached by the next visit, atenolol 25mg/day or matching placebo was added.
- If goal not achieved with this addition, atenolol dose could be doubled.

### Outcomes

#### Primary
- Incidence of non-fatal and fatal stroke

#### Secondary
- Cardiovascular and coronary morbidity and mortality
- All-cause mortality

### Results

#### Baseline characteristics
- N= 4736 (Active N=2365 vs. Placebo N=2371)
- Average age, years: Active 71.6±6.7 vs. Placebo 71.5±6.7

#### Outcomes: (Significance set at 1%)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Active</th>
<th>Placebo</th>
<th>RR (95% CI)</th>
<th>NNT/NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average SBP, mmHg</td>
<td>144±19.3</td>
<td>155.11±20.9</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Non-fatal stroke, patients (%)</td>
<td>96 (4.1%)</td>
<td>149 (6.3%)</td>
<td>0.63 (0.49-0.82)</td>
<td>45</td>
</tr>
<tr>
<td>Fatal stroke, patients (%)</td>
<td>10 (0.4%)</td>
<td>14 (0.6%)</td>
<td>0.71 (0.31-1.59)</td>
<td>--</td>
</tr>
<tr>
<td>All-cause mortality, patients (%)</td>
<td>213 (9%)</td>
<td>242 (10.2%)</td>
<td>0.87 (0.73-1.05)</td>
<td>--</td>
</tr>
<tr>
<td>Fatal MI, patients (%)</td>
<td>15 (0.6%)</td>
<td>25 (1.1%)</td>
<td>0.57 (0.30-1.08)</td>
<td>--</td>
</tr>
<tr>
<td>Non-fatal MI, patients (%)</td>
<td>50 (2.1%)</td>
<td>74 (3.1%)</td>
<td>0.67 (0.47-0.96)</td>
<td>100</td>
</tr>
<tr>
<td>Feeling of imbalance</td>
<td>797 (33.7%)</td>
<td>780 (32.9%)</td>
<td>--</td>
<td>125</td>
</tr>
<tr>
<td>Falls, events (%)</td>
<td>303 (12.8%)</td>
<td>247 (10.4%)</td>
<td>--</td>
<td>42</td>
</tr>
</tbody>
</table>

### Author's Conclusion
Antihypertensive agents in patients ≥ 60 years old with isolated systolic hypertension reduces the risk of non-fatal and fatal stroke.

### Strengths & Limitations

#### Strengths
- Large sample size
- Average follow-up 4.5 years
- Baseline characteristics similar

#### Limitations
- Both groups received additional, anti-hypertensives in the last year of the trial
- Due to sample size unable to power study for significance (needed 4800 patients for 90% power)

### Conclusion
Treatment with chlorthalidone and atenolol decreased SBP to less than < 150/90. Both agents reduced the rate of non-fatal stroke and MI in comparison to placebo. However, the two agents did not reduce fatal stroke or all-cause mortality in comparison to the placebo group.

Hypertension in the Very Elderly Trial (HYVET)

**Objective**
Evaluate the safety and efficacy of targeting a blood pressure < 150/80 mmHg in patients 80 years or older

**Trial Design**
HYVET study: Double-blind, placebo-controlled trial at 195 centers in 13 countries

**Patient Selection**

**Inclusion criteria:**
- ≥ 80 years old
- Persistent HTN defined as sustained SBP ≥ 160 mmHg
- DBP ≤ 110 mmHg

**Exclusion criteria:**
- Secondary HTN
- Heart failure
- SCr > 1.7 mg/dL
- Serum K+ < 3.5 mmol/L or > 5.5 mmol/L
- Gout
- Hemorrhagic stroke in the last 6 months

**Methods**
- Patients stopped all antihypertensive medications and started taking a placebo tablet daily for 2 months prior to starting the study
- If the average of SBPs taken at 2 separate visits was 160-199 mmHg, patients were randomized.
- Randomized to receive indapamide 1.5 mg sustained release or placebo
- At each visit, perindopril (2 or 4 mg) or placebo, were added if patient was not at goal BP
- Patients were withdrawn if they received maximum doses of drugs and still had SBP ≥ 220 mmHg or DBP ≥ 110 mmHg.

**Outcomes**

**Primary**
- Any fatal or nonfatal stroke (not including TIA)

**Secondary**
- All-cause mortality
- Cardiac-related death (MI, sudden death, fatal heart failure)
- Fatal stroke

**Results**

**Baseline characteristics**
- N = 3845 (Active group N = 1933 and Placebo group N = 1912)
- Mean age, yr: Active 83.6 ± 3.2 vs. Placebo 83.5 ± 3.1

**Outcomes:** *(Significance set at 1%)*
- Target BP attained at 2 years: Active 48% vs. Placebo 19.9% (p<0.001)

**Endpoint**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Active (N)</th>
<th>Placebo (N)</th>
<th>p-value</th>
<th>NNT/NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke, patients (%)</td>
<td>51 (2.6%)</td>
<td>69 (3.6%)</td>
<td>0.06</td>
<td>--</td>
</tr>
<tr>
<td>Fatal stroke, patients (%)</td>
<td>27 (1.3%)</td>
<td>42 (2.2%)</td>
<td>0.046</td>
<td>--</td>
</tr>
<tr>
<td>All-cause mortality, patients (%)</td>
<td>196 (10.1%)</td>
<td>235 (12.3%)</td>
<td>0.02</td>
<td>--</td>
</tr>
<tr>
<td>CV death, patients (%)</td>
<td>99 (5.1%)</td>
<td>121 (6.3%)</td>
<td>0.06</td>
<td>--</td>
</tr>
<tr>
<td>Adverse events</td>
<td>358 (18.5%)</td>
<td>448 (23.4%)</td>
<td>0.001</td>
<td>20</td>
</tr>
</tbody>
</table>

**Author’s Conclusions**

Indapamide alone or in conjunction with perindopril (2 or 4 mg) significantly reduced the risk of death from any cause and death from stroke. Results support a target BP of < 150/80 mmHg.

**Strengths and Limitations**

**Strengths**
- Large sample size
- Randomized, double-blind
- Similar baseline characteristics

**Limitations**
- Patients on BP agents were off medication for 2 months, which may increase risk of having a stroke or coronary event
- Required follow-up for only 3 months, however, median duration was 1.8 years.
- Achieved 8,123 patient years of follow-up (needed 10,500 patient years for 90% power)

**Conclusion**
The HYVET trial showed a reduced rate of all endpoints in the active treatment group, but these were not statistically significant. The majority of patients were on dual treatment in the active group, which may account for the reduction in fatal and non-fatal endpoints.
Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS)

**Objective**  
Evaluate the efficacy of 2 years treatment to maintain a SBP < 140 mmHg versus maintaining a SBP >140 and <160 mmHg in an elderly population.

**Trial Design**  
Prospective, randomized, open-label trial in Japan

**Patient Selection**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
</table>
| - 65-85 years of age  
- SBP ≥ 160 mmHg during run-in period of 4 weeks while not on antihypertensive therapy or on the same antihypertensive therapy  
- Efonidipine (a long acting DHP-CCB) could be added to their current regimen | - DBP ≥ 120 mmHg  
- Secondary hypertension  
- Stroke, MI or coronary angioplasty in last 6 months  
- Heart failure NYHA class II or higher  
- Persistent arrhythmia  
- Hypertensive retinopathy  
- SCr ≥ 1.5 mg/dL |

**Methods**

- During run-in period, patients were examined at 2 visits and BP measured at least twice per visit  
- Patients received efonidipine 20-40 mg daily  
- Daily dose of efonidipine could be increased to 60mg daily  
- Physician visits every 2-4 weeks  
- Titration of other drugs allowed by physicians

**Outcomes**

**Primary**  
- Combined incidence of cerebrovascular disease (cerebral hemorrhage, cerebral infarct, TIA, subarachnoid hemorrhage), CVD (MI, heart failure, sudden death, dissecting aneurysms of the aorta) and renal failure  
- Death from any cause

**Secondary**

**Results**

**Baseline characteristics**

- N= 4,418 (Strict BP control N =2,212, Mild BP control N = 2,206)  
- Age 65-74 years old: Strict 57.7% vs Mild 57.7%  
- BP: Strict 171.6±9.7/89.1±9.5 vs. Mild 171.5±9.8/89.1±9.5  
- Prior antihypertensive therapy: Strict 55.1% vs. Mild 56.9%

**Outcomes:** *(Significance set at 5%)*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Strict</th>
<th>Mild</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP, mmHg</td>
<td>135.9±11.7/74.8±9.1</td>
<td>145.6±11.1/78.1±8.9</td>
<td>--</td>
</tr>
<tr>
<td>Combined primary endpoint, patients (%)</td>
<td>86 (3.9%)</td>
<td>86 (3.9%)</td>
<td>0.99</td>
</tr>
<tr>
<td>&lt; 75 years old and combined primary endpoint, patients (%)</td>
<td>30(1.4%)</td>
<td>44 (2%)</td>
<td>0.10</td>
</tr>
<tr>
<td>≥ 75 years old and combined primary endpoint, patients (%)</td>
<td>56 (2.5%)</td>
<td>42 (1.9%)</td>
<td>0.15</td>
</tr>
<tr>
<td>All cause mortality, patients (%)</td>
<td>54 (2.4%)</td>
<td>42 (1.9%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Adverse events*</td>
<td>550 (24.9%)</td>
<td>548 (24.9%)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

*Gastrointestinal symptoms were the most common reported adverse event.

**Author’s Conclusion**

SBP and DBP were lower at the end of treatment in the strict treatment group in comparison to the mild treatment group. However, the occurrences of the primary endpoints or secondary endpoint were similar between the two groups.

**Strengths and Limitations**

**Strengths**

- Large sample size  
- Baseline characteristics similar between the two groups  
- Ethical to keep patients on current antihypertensive regimen

**Limitations**

- Over 50% of patients in each group were already on hypertensive therapy which may have decreased their risk of the primary endpoint  
- Conducted only in Japanese patients

**Conclusion**

Trying to achieve a lower SBP in patients 65-85 years of age is not necessary to prevent cerebrovascular disease or CVD.
### Objective
Evaluate the cardiovascular morbidity and mortality of strict BP control (SBP <140 mmHg) versus moderate BP control (SBP 140-149 mmHg) in an elderly population.

### Trial Design
VALISH study: Prospective, randomized, parallel-group, open-label trial at 461 centers in Japan

### Patient Selection
**Inclusion**
- 70-85 years old
- Isolated systolic HTN defined as: SBP > 160 mmHg and DBP < 90 mmHg
- Measured at 2 visits 2-4 weeks apart.
- Not on antihypertensive medications or on one or two agents that could be converted to valsartan

**Exclusion**
- Secondary hypertension
- SBP ≥ 200 mmHg
- Cerebrovascular disorder, MI or coronary angioplasty within 6 months of enrollment
- SCr ≥ 2 mg/dL
- Severe heart failure (≥ NYHA class III)
- Severe liver dysfunction
- Atrial fibrillation, atrial flutter or arrhythmia

### Methods
- Valsartan 40-80 mg once daily as initial therapy.
- If target BP not reached in 1-2 months, valsartan dose was increased to a maximum of 160mg. Other agents could be added to therapy, except ACEIs or other ARBs.
- Patients visited the clinic every 3 months for a minimum of 2 years.

### Outcomes

#### Primary
- Composite of cardiovascular events (sudden death, fatal or nonfatal stroke, fatal or nonfatal MI, hospitalization for CVD) and renal dysfunction (doubling of SCr, SCr > 2 mg/dL or initiation of dialysis)

#### Secondary
- Overall mortality
- Individual endpoints of the composite

### Results

#### Baseline characteristics
- N=3079 (Strict control N=1545 vs. Moderate control N=1534)
- Mean age, years: Strict 76.1±4.1 vs. Moderate 76.1±4.1 (p=0.908)
- SBP, mmHg: Strict 169.5±7.9 vs. Moderate 169.6±7.9 (p=0.911)
- DBP, mmHg: Strict 81.7±6.6 vs. Moderate 81.2±6.8 (p=0.66)

#### Outcomes: (Significance set at 5%)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Strict</th>
<th>Moderate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP, mmHg</td>
<td>136.6±13.3/74.8±8.8</td>
<td>142±12.5/76.5±8.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Combined primary endpoint, patients (%)</td>
<td>47 (3.4%)</td>
<td>52 (3%)</td>
<td>0.383</td>
</tr>
<tr>
<td>≥ 75 years old and combined primary endpoint, patients (%)</td>
<td>35 (2.3%)</td>
<td>36 (2.3%)</td>
<td>0.832</td>
</tr>
<tr>
<td>All cause mortality, patients (%)</td>
<td>24 (1.6%)</td>
<td>30 (1.96%)</td>
<td>0.362</td>
</tr>
<tr>
<td>CV death, patients (%)</td>
<td>11 (0.71%)</td>
<td>11 (0.72%)</td>
<td>0.950</td>
</tr>
<tr>
<td>Any stroke, patients (%)</td>
<td>16 (1.04%)</td>
<td>16 (1.5%)</td>
<td>0.237</td>
</tr>
<tr>
<td>Rate of adverse events*</td>
<td>18.2%</td>
<td>17.9%</td>
<td>0.851</td>
</tr>
</tbody>
</table>

* Most common adverse events were gastrointestinal and respiratory symptoms.

### Author’s Conclusions
There is no difference in cardiovascular events in elderly patients in which BP is maintained at < 140 mmHg compared to a BP between 140-149 mmHg. Moderate control of BP (SBP < 150 mmHg) may be appropriate to reduce cardiovascular events in elderly patients.

### Strengths and Limitations

#### Strengths
- Large sample size
- Baseline characteristics similar between the groups
- Minimal loss to follow up

#### Limitations
- Open-label
- Not a placebo-controlled trial
- Mentioned other agents patients were taking at end of treatment but not how many were on more than 2 agents

### Conclusion
The VALISH trial was unable to prove a difference in cardiovascular outcomes in elderly patients when SBP was maintained at < 140 mmHg versus 140-149 mmHg.
VI. Conclusion

A. Summary of the trials

1. SHEP
   a. Non-fatal stroke and non-fatal MI were reduced in patients (average 72 years of age) when average SBP < 150 mmHg and treating with antihypertensive agents. However, the study was not powered to detect the difference.
   b. The use of two agents did not reduce fatal stroke or all-cause mortality in comparison to placebo.

2. HYVET
   a. Maintaining a BP < 150/80 mmHg with antihypertensive agents reduced mortality and fatal stroke (versus placebo) in patients (average 83 years of age). However, the study was not powered to detect the difference.

3. JATOS
   a. There was no difference in cardiovascular or stroke outcomes in patients maintained at a SBP 145 mmHg vs. 135 mmHg.
   b. There was no difference in outcomes when age stratified (< 75 years vs. ≥ 75 years).

4. VALISH
   a. There was no difference in outcomes when patients maintained at average SBP of 137 mmHg vs. 142 mmHg.
   b. There was no difference in outcomes when age stratified (< 75 years vs. ≥ 75 years).

B. Based on the evidence from clinical trials and incidence of CV and cerebrovascular events in patients > 60 years of age, recommend:

1. In patients ≥ 60 years old maintain a BP < 160/90 mmHg
2. Interpretation of existing evidence is challenging
3. More RCTs needed to determine optimal threshold

C. All patients should be counseled on a healthy diet, weight control, and regular exercise

D. Allow for individualization of the patient

References:


**Appendix A**

**Table 8. Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>JNC</td>
<td>Joint National Convention</td>
</tr>
<tr>
<td>NHANES</td>
<td>National Health and Nutrition Survey</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean arterial blood pressure</td>
</tr>
<tr>
<td>CO</td>
<td>Cardiac output</td>
</tr>
<tr>
<td>TPR</td>
<td>Total peripheral vascular resistance</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic blood pressure</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic blood pressure</td>
</tr>
<tr>
<td>SV</td>
<td>Stroke volume</td>
</tr>
<tr>
<td>HR</td>
<td>Heart rate</td>
</tr>
<tr>
<td>DASH</td>
<td>Dietary Approaches to Stop Hypertension</td>
</tr>
<tr>
<td>MOA</td>
<td>Mechanism of action</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>CAD/CVD</td>
<td>Coronary artery disease/cardiovascular disease</td>
</tr>
<tr>
<td>NNT</td>
<td>Number needed to treat</td>
</tr>
<tr>
<td>NNH</td>
<td>Number needed to harm</td>
</tr>
</tbody>
</table>

**Blood Pressure Definition**

1. \( \text{MAP} = \text{CO} \times \text{TPR} \)
   a. \( \text{MAP} \) can be further defined as:
      i. \( \text{DBP} + (\text{SBP} - \text{DBP})/3 \)
   b. \( \text{CO} \) can be further defined as:
      i. \( \text{SV} \times \text{HR} \)
      ii. \( \text{SV} \) is dependent on pre-load, contractility, after-load

**Figure 4. Antihypertensive Agents Mechanisms of Action**

### Appendix B

#### Table 9. Anti-hypertensive Agents

<table>
<thead>
<tr>
<th>Class</th>
<th>Agents</th>
<th>Dosing (initial to maximum)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thiazide diuretics</strong></td>
<td>Chlorothiazide</td>
<td>500-2000 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Metolazone</td>
<td>2.5-5 mg daily</td>
</tr>
<tr>
<td><strong>Loop diuretics</strong></td>
<td>Bumetanide</td>
<td>0.5-2 mg BID</td>
</tr>
<tr>
<td></td>
<td>Furosemide</td>
<td>40-80 mg BID</td>
</tr>
<tr>
<td></td>
<td>Torsemide</td>
<td>5-10 mg daily</td>
</tr>
<tr>
<td><strong>Aldosterone receptor blockers</strong></td>
<td>Spironolactone</td>
<td>25-100 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Eplerenone</td>
<td>50-100 mg/day (can be divided BID)</td>
</tr>
<tr>
<td><strong>Beta Blockers</strong></td>
<td>Atenolol</td>
<td>25-100 mg daily</td>
</tr>
<tr>
<td></td>
<td>Bisoprolol</td>
<td>2.5-20 mg daily</td>
</tr>
<tr>
<td></td>
<td>Metoprolol tartrate</td>
<td>100-450 mg daily (divided 2-3 doses)</td>
</tr>
<tr>
<td></td>
<td>Metoprolol succinate</td>
<td>25-400 mg daily</td>
</tr>
<tr>
<td></td>
<td>Nadolol</td>
<td>40-240 mg daily</td>
</tr>
<tr>
<td></td>
<td>Propranolol (IR)</td>
<td>80-640 mg daily (divided in 2-3 doses)</td>
</tr>
<tr>
<td></td>
<td>Propranolol (LA)</td>
<td>80-640 mg daily</td>
</tr>
<tr>
<td></td>
<td>Nebivolol</td>
<td>5-40 mg daily</td>
</tr>
<tr>
<td></td>
<td>Timolol</td>
<td>20-60 mg daily (divided BID)</td>
</tr>
<tr>
<td><strong>Combined alpha and beta blockers</strong></td>
<td>Carvedilol (IR)</td>
<td>6.25 -25 mg BID</td>
</tr>
<tr>
<td></td>
<td>Carvedilol (ER)</td>
<td>20-80 mg daily</td>
</tr>
<tr>
<td></td>
<td>Labetalol</td>
<td>200-2400 mg daily (divided BID)</td>
</tr>
<tr>
<td><strong>Other ACEIs</strong></td>
<td>Benazepril</td>
<td>10-80 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Quinapril</td>
<td>10-40 mg daily</td>
</tr>
<tr>
<td></td>
<td>Moexipril</td>
<td>3.75-30 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Ramipril</td>
<td>2.5-20 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Perindopril</td>
<td>4-16 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td></td>
<td>Trandolapril</td>
<td>1-8 mg daily</td>
</tr>
<tr>
<td></td>
<td>Fosinopril</td>
<td>10-80 mg daily</td>
</tr>
<tr>
<td><strong>Other ARBs</strong></td>
<td>Olmesartan</td>
<td>20-40 mg daily</td>
</tr>
<tr>
<td></td>
<td>Telmisartan</td>
<td>40-80 mg daily</td>
</tr>
<tr>
<td><strong>Other non-DHP CCBs</strong></td>
<td>Verapamil (IR)</td>
<td>240-480 mg daily (divided TID)</td>
</tr>
<tr>
<td></td>
<td>Verapamil (SR)</td>
<td>240-480 mg daily</td>
</tr>
<tr>
<td></td>
<td>Verapamil (ER)</td>
<td>Verelan PM: 100-400 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Covera HS: 180-480 mg daily</td>
</tr>
<tr>
<td><strong>Other DHP CCBs</strong></td>
<td>Felodipine</td>
<td>2.5-20 mg daily</td>
</tr>
<tr>
<td></td>
<td>Nicardipine (IR)</td>
<td>20-40 mg TID</td>
</tr>
<tr>
<td></td>
<td>Nicardipine (SR)</td>
<td>30-60 mg BID</td>
</tr>
<tr>
<td></td>
<td>Nifedipine ER</td>
<td>30-120 mg daily</td>
</tr>
<tr>
<td></td>
<td>Nisodipine ER</td>
<td>20-60 mg daily</td>
</tr>
<tr>
<td><strong>Alpha-1 blockers</strong></td>
<td>Doxazosin</td>
<td>1-16 mg daily</td>
</tr>
<tr>
<td></td>
<td>Prazosin</td>
<td>2-20 mg daily (divided 2-3 doses)</td>
</tr>
<tr>
<td></td>
<td>Terazosin</td>
<td>1-20 mg daily (divided 1-2 doses)</td>
</tr>
<tr>
<td><strong>Central alpha-2 agonists and centrally acting agents</strong></td>
<td>Clonidine</td>
<td>0.2-2.4 mg daily (divided BID)</td>
</tr>
<tr>
<td></td>
<td>Clonidine patch</td>
<td>0.1-0.3 mg weekly</td>
</tr>
<tr>
<td></td>
<td>Methylodopa</td>
<td>500-3000 mg daily (divided 2-3 doses)</td>
</tr>
<tr>
<td></td>
<td>Reserpine</td>
<td>0.1-0.5 mg daily</td>
</tr>
<tr>
<td></td>
<td>Guanfacine</td>
<td>0.5-2 mg daily</td>
</tr>
<tr>
<td><strong>Direct vasodilators</strong></td>
<td>Hydralazine</td>
<td>40-300 mg daily (divided 4 times daily)</td>
</tr>
<tr>
<td></td>
<td>Minoxidil</td>
<td>5-100 mg daily</td>
</tr>
<tr>
<td><strong>Direct renin inhibitor</strong></td>
<td>Aliskiren</td>
<td>150-300 mg daily</td>
</tr>
</tbody>
</table>
### Table 10. Differences between JNC 7 vs. JNC 8

<table>
<thead>
<tr>
<th>Topic</th>
<th>JNC 7</th>
<th>JNC 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methodology</td>
<td>Nonsystematic literature review</td>
<td>Systematic literature review of only RCTs</td>
</tr>
<tr>
<td></td>
<td>Recommendations based on consensus</td>
<td></td>
</tr>
<tr>
<td>Definitions</td>
<td>Defined hypertension and pre-hypertension</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Treatment goals</td>
<td>Various based on comorbidities</td>
<td>Similar treatment goals unless evidence supported different goal in a subpopulation</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>Based on literature review and expert opinion</td>
<td>Evidence-based recommendations of Lifestyle Work Group</td>
</tr>
<tr>
<td>Drug therapy</td>
<td>Thiazide diuretics as initial therapy w/o compelling indications</td>
<td>Recommended 4 specific classes (ACEI, ARBS, thiazides, CCBs)</td>
</tr>
<tr>
<td></td>
<td>Specified treatment based on compelling indications</td>
<td>Recommended specific classes for racial, CKD, and diabetic subgroups</td>
</tr>
<tr>
<td>Scope</td>
<td>Multiple topics including: measuring BP, adherence, patient evaluation, resistant HTN, and HTN in special populations</td>
<td>Reviewed RCTs and panel addressed high priority topics</td>
</tr>
</tbody>
</table>
**Figure 5. JNC 8 Treatment Algorithm**