Current Hypertension Management Guidelines: How Low Should We Go?

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Disclosure Statement – no financial relationships to disclose

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• Statement of Disclosure

- I have no relevant financial relationships with commercial interests pertaining to the content presented in this program.

Learning Objectives

• List goal BP values based on recommendations for patients with hypertension according to national guidelines and other expert consensus recommendations
• Explain results of the SPRINT trial and how they may influence treatment of patients with hypertension
• Create treatment plans for patients with resistant hypertension
Case SR

- 65-year-old African American man with a past history of obesity, hypertension, GERD and dyslipidemia
- Social History: 2-3 beers/day, no particular diet, 1 ppd smoker (x 40 years), exercise limited to walking his dog
- Meds: Atorvastatin 20 mg daily, omeprazole 20 mg daily
- Vital Signs
  - BP 164/102, 162/104 mm Hg; HR 80 bpm
- Other parameters
  - BMI 32.7 kg/m²
  - Serum creatinine 1.2 mg/dL; eGFR 73 mL/min/1.73m²
  - Urine Alb:Cr = 17 mg/g
  - All other labs are normal
Which of the following is the most appropriate goal BP for SR?

A. <150/90
B. <140/90
C. <130/80
D. <120/80

Goal BP Recommendations

**ASH/ISH Guidelines**

- **Age < 80 years:**
  - <140/90 mm Hg
- **Age ≥ 80 years:**
  - <150/90 mm Hg
  - <140/90 mm Hg if diabetes or CKD

**JNC 8 Report**

- **Age < 60 years:**
  - <140/90 mm Hg
- **Age ≥ 60 years:**
  - <150/90 mm Hg
  - <140/90 mm Hg if diabetes or CKD

*If pharmacologic treatment results in lower achieved SBP (e.g., <140 mm Hg) and is well tolerated and without adverse effects, treatment does not need to be adjusted.

ADA Standards of Medical Care in Diabetes 2016

**Hypertension/Blood Pressure**

- **Goals**
  - <140/90 mmHg (A)
  - Systolic BP <130 mm Hg (C) or diastolic BP <80 mm Hg (B), may be appropriate for certain individuals, such as younger patients, those with albuminuria and/or those with one or more additional atherosclerotic cardiovascular disease risk factors if they can be achieved without undue treatment burden
Kidney Disease: Improving Global Outcomes Clinical Practice Guideline

- Management of BP in CKD
  - Non-dialysis patients

<table>
<thead>
<tr>
<th>Urine Albumin Excretion per 24 hrs</th>
<th>BP Goal (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 mg</td>
<td>≤ 140/90</td>
<td>Not specified</td>
</tr>
<tr>
<td>30 to 300 mg</td>
<td>≤ 130/80</td>
<td>ACEi or ARB</td>
</tr>
<tr>
<td>&gt; 300 mg</td>
<td>≤ 130/80</td>
<td>ACEi or ARB</td>
</tr>
</tbody>
</table>

- Same recommendations for patients with and without diabetes, but different levels of evidence

Systolic Blood Pressure Intervention Trial (SPRINT)
Sponsored by NHLBI
- 9361 patients ≥ 50 yrs with SBP ≥ 130 mm Hg and one or more additional CV risk factors
- Serious comorbidities were exclusions (e.g., diabetes, prior stroke, left ventricular dysfunction)
- Randomized, open-label to:
  - Intensive treatment: SBP < 120 mm Hg
  - Standard treatment: SBP < 140 mm Hg
- Primary outcome: First occurrence of MI, acute coronary syndrome, stroke, heart failure, or CVD death
- Prespecified subgroups: CKD, sex, race, elderly (≥75 yr), baseline SBP

SPRINT: Population
- Trial stopped early after a median of 3.26 yr

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP (mm Hg)</td>
<td>139.7/78.2</td>
<td>139.7/77.0</td>
</tr>
<tr>
<td>Women (%)</td>
<td>36.0</td>
<td>35.2</td>
</tr>
<tr>
<td>Mean Age (yr)</td>
<td>67.9</td>
<td>67.9</td>
</tr>
<tr>
<td>Age ≥75 yr (%)</td>
<td>28.2</td>
<td>28.2</td>
</tr>
<tr>
<td>CKD (%)</td>
<td>28.4</td>
<td>28.1</td>
</tr>
<tr>
<td>Black (%)</td>
<td>31.1</td>
<td>31.9</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10.8</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Results:
- Mean SBP at one year (mm Hg) 121.4 136.2
- Mean number of antihypertensive 2.8 1.8
SPRINT: Primary Endpoint

SPRINT: Subgroup Analyses

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>248/2768 (9.2)</td>
<td>277/3081 (8.6)</td>
<td>0.75 (0.64–0.89)</td>
</tr>
<tr>
<td>Yes</td>
<td>205/2399 (8.8)</td>
<td>233/2640 (8.8)</td>
<td>0.70 (0.57–0.87)</td>
</tr>
<tr>
<td>No</td>
<td>43/2785 (1.5)</td>
<td>44/441 (1.5)</td>
<td>0.87 (0.70–1.10)</td>
</tr>
<tr>
<td>Age ≤ 55</td>
<td>423/4998 (8.4)</td>
<td>473/5384 (8.6)</td>
<td>0.90 (0.74–1.10)</td>
</tr>
<tr>
<td>Age &gt; 54</td>
<td>265/2770 (9.6)</td>
<td>204/3427 (8.8)</td>
<td>0.90 (0.75–1.10)</td>
</tr>
<tr>
<td>Male</td>
<td>127/1361 (9.4)</td>
<td>151/1655 (9.2)</td>
<td>0.92 (0.76–1.12)</td>
</tr>
<tr>
<td>Female</td>
<td>121/1407 (8.6)</td>
<td>153/1772 (8.3)</td>
<td>0.91 (0.73–1.13)</td>
</tr>
<tr>
<td>Black</td>
<td>423/4998 (8.4)</td>
<td>473/5384 (8.6)</td>
<td>0.90 (0.74–1.10)</td>
</tr>
<tr>
<td>Nonblack</td>
<td>265/2770 (9.6)</td>
<td>204/3427 (8.8)</td>
<td>0.90 (0.75–1.10)</td>
</tr>
<tr>
<td>Previous cardiovascular disease</td>
<td>248/2768 (9.2)</td>
<td>277/3081 (8.6)</td>
<td>0.75 (0.64–0.89)</td>
</tr>
<tr>
<td>No</td>
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<td>44/441 (1.5)</td>
<td>0.87 (0.70–1.10)</td>
</tr>
<tr>
<td>Proteinuria in urine (mg/dL)</td>
<td>99/1155 (8.5)</td>
<td>115/1291 (8.9)</td>
<td>0.79 (0.60–1.10)</td>
</tr>
<tr>
<td>&lt;150 mg/dL</td>
<td>233/2640 (8.8)</td>
<td>205/2399 (8.8)</td>
<td>0.70 (0.57–0.87)</td>
</tr>
<tr>
<td>≥150 mg/dL</td>
<td>43/2785 (1.5)</td>
<td>44/441 (1.5)</td>
<td>0.87 (0.70–1.10)</td>
</tr>
</tbody>
</table>

Case SR

Should SR be treated with antihypertensive therapy?
ACC/AHA Guideline:
Lifestyle Management to Reduce BP

Dietary Pattern

• Emphasize vegetables, fruits, whole grains; low-fat dairy, poultry, fish, legumes, nontropical vegetable oils, and nuts; limit sweets, sugar-sweetened beverages, red meats (e.g., DASH)
• Lower sodium intake (max 2400 mg/day; 1500 mg/day better; at least reduce by 1000 mg/day)

Physical Activity

• Aerobic physical activity 3–4 sessions/week, 40-minute sessions, moderate-to-vigorous-intensity

Antihypertensive Agents

First-Line

• Angiotensin Converting Enzyme Inhibitor (ACEi)
• Angiotensin Receptor Blocker (ARB)
• Calcium Channel Blocker (CCB)
• Thiazide Diuretic

Add-on or First-Line in Compelling Indications

• Beta-Blocker

Alternatives

• Aldosterone Antagonist (e.g., spironolactone)
• Alpha Antagonist (e.g., terazosin)
• Centrally Acting Alpha Agonist (e.g., clonidine)
• Direct Arterial Vasodilator (e.g., hydralazine)
• Aliskiren
• Reserpine

Drug Therapy Recommendations

Most Patients (without a Compelling Indication)

1. Stage 1 (BP ≥140-159/90-99 mm Hg)
   – Black: CCB or thiazide
   – Non-Black: CCB or thiazide if ≥60 yr
               ACEi or ARB if <60 yr

2. Stage 2 (BP ≥160/100 mm Hg)
   – Start with two: CCB or thiazide with
               ACEi or ARB


### Compelling Indications

(aka, Special Cases)

**First-Line Regimen**

- **Diabetes Mellitus**
  - ACEi or ARB
    - (In Black patients, CCB or Thiazide is acceptable)
- **Chronic Kidney Disease**
  - ACEi or ARB
    - (In Black patients, good evidence with ACEI)
- **Coronary Artery Disease**
  - Beta-blocker plus ACEi or ARB
- **Prior Stroke**
  - ACEi or ARB
- **Heart Failure with Reduced EF**
  - ACEi (or ARB) plus beta-blocker plus diuretic plus spironolactone
  - Regardless of blood pressure if symptomatic

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**Which combination regimen is proven to be the most efficacious in lowering risk of CV events in patients like SR?**

A. ACEi with CCB
B. ACEi with Thiazide
C. ACEi with ARB
D. Thiazide with triamterene

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**ACCOMPLISH Trial**

- Randomized, double-blind, controlled trial*
  - Benazepril/HCTZ vs. Benazepril/Amlodipine
- 11,506 patients with hypertension and:
  - Age ≥ 60 yr; or 55-59 yr if multiple CV risk factors
  - SBP ≥ 160 mm Hg or on BP medication
- Primary endpoint: CV events

*Dosages titrated, as tolerated, to benazepril 40 mg/day, HCTZ 25 mg/day, amlodipine 10 mg/day

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**Jennerin, K et al., N Engl J Med. 2008; 359:2417-28.**
Ongoing Telmisartan Alone and in Combination With Ramipril (ONTARGET)

- 25,620 patients
- Randomized, double-blind trial
- Combination vs. ramipril:
  - Hypotension: 4.8 vs. 1.7% (p<0.001)
  - Renal dysfunction: 13.5 vs. 10.2% (p<0.001)

![Graph showing primary endpoint event rate](image_url)

AHA/ASA Newsroom: Hypertension Guideline Writing Process Underway

- Multi-disciplinary writing panel led by ACC/AHA
- Guidelines for the management of hypertension to update 12-year-old recommendations
- Nine additional medical societies are partners
- The writing process will include the use of a separate evidence review committee that will develop a systematic review on specific critical questions, which will inform recommendations in the 2016 Guideline on the Management of Hypertension
- Will update the 2003 guideline, officially the JNC 7, which was empaneled by the NHLBI

Resistant Hypertension: AHA Scientific Statement

- Definition:
  - Patients not at their goal BP on 3 or more antihypertensive agents (ideally, at full doses, one of which is a diuretic), or
  - Patient requiring 4 or more antihypertensive agents to treat hypertension, even if they are at their goal BP

- Causes may include: Improper BP measurement, volume overload, drug-induced or other causes (e.g. non-adherence), and secondary hypertension
Case - RH

- 64-year-old man with difficult to control hypertension and a past history of MI
- Hypertension Meds: atenolol 100 mg daily, amlodipine 5 mg daily (10 mg caused edema) irbesartan/HCTZ 300/25 mg daily; He is adherent
- Secondary causes of hypertension are ruled out
- He has no edema now, and no symptoms of cardiac ischemia, stroke or heart failure
- BP today:
  - 168/92, 164/90 mm Hg;
  - BP at home "150's/80's";
  - HR 58 bpm; BMI 29 kg/m^2
- Laboratory tests:
  - SCr 1.0 mg/dL, potassium 3.3 mEq/L, persistent albuminuria; all other tests are normal

Which change to this patient's antihypertensive regimen would you choose to further lower his blood pressure?

A. Switch metoprolol to carvedilol
B. Switch hydrochlorothiazide to chlorthalidone
C. Add lisinopril
D. Add spironolactone
E. Increase amlodipine and add furosemide

Resistant Hypertension: AHA Scientific Statement

Pharmacotherapy Options:
- Assure appropriate diuretic therapy
  - Chlorthalidone instead of hydrochlorothiazide
  - Aldosterone antagonist (e.g., spironolactone)
  - Loop diuretic (only if decreased renal function)
- Optimize current agents
  - Switch metoprolol to carvedilol or labetalol
- Additional pharmacotherapy options
  - Alternative antihypertensive agent
  - Dihydropyridine with non-dihydropyridine CCB
A Tale of Two Thiazides

<table>
<thead>
<tr>
<th></th>
<th>Hydrochlorothiazide</th>
<th>Chlorthalidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>Thiazide</td>
<td>Thiazide-like</td>
</tr>
<tr>
<td>Half-life (hrs)</td>
<td>9-10</td>
<td>50-60</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>25 mg</td>
<td>12.5-18.75 mg</td>
</tr>
<tr>
<td>Equivalency</td>
<td>Prescribed more</td>
<td>Preferred</td>
</tr>
<tr>
<td></td>
<td>frequently</td>
<td>agent in</td>
</tr>
<tr>
<td></td>
<td>In most combination</td>
<td>resistant</td>
</tr>
<tr>
<td></td>
<td>products</td>
<td>hypertension</td>
</tr>
<tr>
<td>Evidence-base</td>
<td>Not used in most</td>
<td>Extensive use</td>
</tr>
<tr>
<td></td>
<td>landmark trials</td>
<td>landmark clinical trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(e.g., SHEP, ALLHAT)</td>
</tr>
<tr>
<td>Hypokalemia/Hyponatremia</td>
<td>Moderate concern</td>
<td>Slightly higher in elderly patients</td>
</tr>
</tbody>
</table>

Select Recommendations

NICE: Primary Hypertension in Adults

- If diuretic treatment is to be initiated or changed, offer a thiazide-like diuretic:
  - Chlorthalidone (12.5–25.0 mg once daily) or indapamide (1.5 mg modified-release or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide
- For people who are already having treatment with bendroflumethiazide or hydrochlorothiazide and whose BP is stable and well controlled, continue treatment

Antihypertensive Prescribing in Patients with Resistant Hypertension

- Retrospective pharmacy and medical claims database analysis
- 140,126 patients with hypertension
- Prescribed ≥ 4 antihypertensive agents between May 1, 2008 and June 30, 2009
Challenges

"Drugs don't work in patients who don't take them."

- Former U.S. surgeon general C. Everett Koop