Controversial High Impact Publications in Hypertension: SPRINTing Toward the Goal

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University of Colorado School of Pharmacy
Denver, Colorado
Disclosure

• Faculty have nothing to disclose.
Learning Objectives

• Compare and contrast guidelines and consensus recommendations for the treatment of patients with hypertension.

• Explain the findings from and strengths and weaknesses of the SPRINT trial, and discuss the implications for establishing the blood pressure goal for a patient with hypertension.

• Design patient-centered antihypertensive treatment plans in complex patients with hypertension.
The Landscape of Hypertension

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University of Colorado School of Pharmacy
Denver, Colorado
American Heart Association (AHA)
Heart Disease and Stroke Statistics—2016 Update

85.6 Million patients in the United States have Cardiovascular Disease (CVD)


*Includes diagnosed and undiagnosed patients
Hypertension in the United States

Patients (%)

Years

Aware
Treatment
Control/Treated
Control
Prevalence

Control Blood Pressure (BP):
<140/90 mm Hg

Time for a Poll
How to vote via the web or text messaging

From any browser

From a text message
How to vote via text message

How's my presentation so far?

- Respond at PollEv.com/ashp
- Text a KEYWORD to 22333

<table>
<thead>
<tr>
<th>Comment</th>
<th>Votes</th>
</tr>
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<tbody>
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<td>It's amazing.</td>
<td>152964</td>
</tr>
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From any browser
Question 1: 65-year-old African American man with obesity, hypertension, type 2 diabetes and dyslipidemia. Drinks 2-3 beers/day, follows no particular diet, 1 ppd smoker (x 40 years), limited exercise. Current medications are: atorvastatin 20 mg daily, hydrochlorothiazide 25 mg daily. BP is 154/92 mm Hg, HR 80 bpm, SCr 1.2 mg/dL (eGFR 73 mL/min/1.73m²), urine Alb:Cr = 10 mg/g.

Which of the following is the most appropriate goal BP for him?

A. < 140/90 mm Hg
B. < 150/90 mm Hg
C. < 130/80 mm Hg
D. < 120/80 mm Hg
Your poll will show here

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Lifestyle Management to Reduce BP

**Dietary Pattern**
- Emphasize vegetables, fruits, and whole grains; low-fat dairy, poultry, fish, legumes, nontropical vegetable oils, and nuts; limit sweets, sugar-sweetened beverages, and red meats (e.g., DASH)
- Lower sodium intake (max 2400 mg/day; 1500 mg/day better; at least reduce by 1000 mg/day)
- Limit alcohol (2 drinks/day, men; 1 drink/day, women)

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

# 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

ASH/ISH = American Society of Hypertension/International Society of Hypertension; JNC = Joint National Committee; CKD = chronic kidney disease

BP Goals: Other Organizations

• American Diabetes Association (ADA) 2016:
  – <140/90 mm Hg (A)
  – Systolic BP <130 mm Hg (C) or diastolic BP < 80 mm Hg (B) may be appropriate for some patients

• Kidney Disease: Improving Global Outcomes (KDIGO) 2012:
  – ≤ 130/80 mm Hg in CKD patients with persistent albuminuria

Antihypertensive Agents

**First-Line**
- Angiotensin Converting Enzyme Inhibitor (ACEi)
- Angiotensin Receptor Blocker (ARB)
- Calcium Channel Blocker (CCB)
- Thiazide Diuretic

**Alternatives**
- Aldosterone Antagonist (e.g., spironolactone)
- Alpha Antagonist (e.g., terazosin)
- Centrally Acting Alpha Agonist (e.g., clonidine)
- Direct Arterial Vasodilator (e.g., hydralazine)
- Direct Renin Inhibitor (i.e., Aliskiren)
- Reserpine

**Add-on or First-Line in Compelling Indications**
- Beta-Blocker

Compelling Indications (Special Cases)

First-Line Regimen

- **Diabetes**
  - ACEi or ARB
    - (In Black patients CCB or Thiazide may be acceptable)

- **CKD**
  - ACEi or ARB

- **CHD**
  - Beta-blocker plus ACEi or ARB

- **Prior Stroke**
  - ACEi or ARB

- **Heart Failure with Reduced Ejection Fraction**
  - ACEi (or ARB) plus beta-blocker plus diuretic plus spironolactone

ACCOMPLISH Trial

- Randomized, double-blind, controlled trial*
  - Benazepril/Hydrochlorothiazide 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, hydrochlorothiazide 25 mg/day, amlodipine 10 mg/day

Question 2: Which of the following is true regarding the antihypertensive effects of hydrochlorothiazide 25 mg daily and chlorthalidone 25 mg daily?

A. Hydrochlorothiazide is more potent
B. Chlorthalidone is more potent
C. They are equal in potency
D. I do not know
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C. They are equal in potency
D. I do not know
Resistant Hypertension

Patients not at goal BP with $\geq 3$ medications (ideally, at full doses), one of which is a diuretic; or requiring 4 or more medications, even if at goal BP

**Pharmacotherapy Options:**
- Assure appropriate diuretic therapy
  - Switch hydrochlorothiazide to chlorthalidone
  - Add an aldosterone antagonist (e.g., spironolactone)
  - Use a loop diuretic (if stage 4 or 5 CKD) as needed
- Switch typical beta-blocker (e.g., metoprolol, atenolol) to carvedilol or labetalol
- Use an alternative agent(s), combination CCB therapy

# A Tale of Two Thiazides

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

CardioBrief: Can 50 Million Prescriptions Be Wrong?
—Innovative trial to determine actual benefit of hydrochlorothiazide

• Diuretic Comparison Project:
  – Hydrochlorothiazide vs. chlorthalidone
  – 13,500 veterans, age ≥ 65 years with hypertension
  – Primary endpoint: CV events over multiple years
  – Will use a new, efficient, and less expensive study design known as “point of care”

http://www.medpagetoday.com/Cardiology/CardioBrief/59702?xid=nl_mpt_DHE_2016-08-17&eun=g379325d0r&pos=1

https://clinicaltrials.gov/ct2/show/NCT02185417?term=VA+diuretic+comparative+study&rank=1
Key Takeaways

• Key Takeaway #1
  – A BP goal of < 140/90 mm Hg is recommended by most guidelines/experts for most patients with hypertension, with lower goals (e.g., <130/80 mm Hg) an option in certain patients

• Key Takeaway #2
  – First-line medications consist of an ACEi, ARB, CCB, or thiazide; recommendations for specific medications provided for compelling indications
Joseph Saseen, Pharm.D., BCACP, BCPS
Professor of Clinical Pharmacy and Family Medicine
University of Colorado School of Pharmacy
Denver, Colorado
Systolic Blood Pressure Intervention Trial (SPRINT)

• Multicenter, randomized, controlled trial in 9,361 patients with hypertension randomized open-label to:
  – Intensive treatment: SBP <120 mm Hg
  – Standard treatment: SBP <140 mm Hg

• Primary outcome: first the occurrence of a myocardial infarction (MI), acute coronary syndrome, stroke, heart failure, or cardiovascular disease death

• Hypothesis: Intensive treatment compared with standard treatment will reduce the primary outcome

• Prespecified subgroups: CKD, CVD, elderly (≥75 yr)

SPRINT Inclusion Criteria

• ≥ 50 years old
• Systolic blood pressure
  – 130–180 mm Hg on 0 or 1 medication
  – 130–170 mm Hg on up to 2 medications
  – 130–160 mm Hg on up to 3 medications
  – 130–150 mm Hg on up to 4 medications
• At increased risk for atherosclerotic cardiovascular disease (various criteria)

SPRINT Exclusion Criteria

• Secondary hypertension
• Diabetes mellitus
• Previous stroke
• CV event within 3 months
• Symptomatic HF w/in 6 months or ejection fraction < 35%
• Proteinuria (> 1 g/day), polycystic kidney disease, glomerulonephritis, estimated glomerular filtration rate < 20 ml/min/1.73m² or end-stage renal disease

SPRINT: Consolidated standards of reporting trials (CONSORT)

*Screened (n=14,692)*

- Eligible (n=10,601)
  - Randomized (n=9,361)
    - Standard Treatment (n=4,683)
    - Intensive Treatment (n=4,678)
  - Not eligible (n=4,091):
    - Age (n=34)
    - Low standing BP (n=352)
    - BP/medications (n=2,284)
    - Not at increased risk (n=718)
    - Other (n=703)

SPRINT Protocol Procedures

• Medication choice:
  – ACEi, ARB, CCB, thiazide first-line; beta-blocker in CHD
  – Chlorthalidone encouraged as the primary thiazide-type diuretic and amlodipine as the preferred CCB

• Titration of medications was based on:
  – Mean of three office BP measurements obtained in the seated position using an automated device
  – BP measured 1 min after standing at screening, baseline, 1 month, 6 months, 12 months, and annually thereafter; screening for hypotension while standing

# SPRINT: Patient Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean SBP (mm Hg)</td>
<td>139.7</td>
<td>139.7</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>28.5</td>
<td>28.1</td>
</tr>
<tr>
<td>Black</td>
<td>29.5</td>
<td>30.4</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10.8</td>
<td>10.3</td>
</tr>
</tbody>
</table>

## Results:

- Mean SBP at 1 year (mm Hg): 121.4 (Intensive) vs. 136.2 (Standard)
- Mean no. BP medications: 2.8 (Intensive) vs. 1.8 (Standard)

## SPRINT: Medication Utilization

<table>
<thead>
<tr>
<th></th>
<th>Intensive Treatment (%)</th>
<th>Standard Treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean number of agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 0</td>
<td>2.7</td>
<td>11.3</td>
</tr>
<tr>
<td>• 1</td>
<td>10.5</td>
<td>31.1</td>
</tr>
<tr>
<td>• 2</td>
<td>30.5</td>
<td>33.3</td>
</tr>
<tr>
<td>• 3</td>
<td>31.8</td>
<td>17.2</td>
</tr>
<tr>
<td>• 4+</td>
<td>24.3</td>
<td>6.9</td>
</tr>
<tr>
<td><strong>ACEi or ARB</strong></td>
<td>76.7</td>
<td>55.2</td>
</tr>
<tr>
<td><strong>Thiazide</strong></td>
<td>54.9</td>
<td>33.3</td>
</tr>
<tr>
<td><strong>CCB</strong></td>
<td>57.1</td>
<td>35.4</td>
</tr>
<tr>
<td><strong>Beta-blocker</strong></td>
<td>41.1</td>
<td>30.8</td>
</tr>
<tr>
<td><strong>Aldosterone antagonist</strong></td>
<td>8.7</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Alpha-blocker/alpha agonist/arterial vasodilator</strong></td>
<td>10.3/2.3/7.3</td>
<td>5.5/0.9/2.4</td>
</tr>
</tbody>
</table>

SPRINT: Primary Endpoint

Hazard Ratio

Year

Standard
(319 events)

Intensive
(243 events)

HR = 0.75 (95% CI: 0.64 to 0.89)

## SPRINT Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment N=4678; no. (%)</th>
<th>Standard Treatment N=4683; no. (%)</th>
<th>HR* (P-Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome‡</strong></td>
<td>243 (5.2)</td>
<td>319 (6.8)</td>
<td>0.75 (&lt;0.001)</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>116 (2.5)</td>
<td>0.83 (0.19)</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>40 (0.9)</td>
<td>1.00 (0.99)</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>70 (1.5)</td>
<td>0.89 (0.50)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.62 (0.002)</td>
</tr>
<tr>
<td>Death from CV causes</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.57 (0.005)</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>0.73 (0.003)</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>423 (9.0)</td>
<td>0.78 (&lt;0.001)</td>
</tr>
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</table>

* Hazard ratio
‡First occurrence of MI, acute coronary syndrome (ACS), stroke, heart failure, or death from CV causes

**SPRINT: Subgroup Analyses of the Primary Endpoint**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.75 (0.64, 0.89)</td>
<td></td>
</tr>
<tr>
<td>No Prior CKD</td>
<td>0.70 (0.56, 0.87)</td>
<td>0.36</td>
</tr>
<tr>
<td>Prior CKD</td>
<td>0.82 (0.63, 1.07)</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 75</td>
<td>0.80 (0.64, 1.00)</td>
<td>0.32</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>0.67 (0.51, 0.86)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.84 (0.62, 1.14)</td>
<td>0.45</td>
</tr>
<tr>
<td>Male</td>
<td>0.72 (0.59, 0.88)</td>
<td></td>
</tr>
<tr>
<td>African–American</td>
<td>0.77 (0.55, 1.06)</td>
<td>0.83</td>
</tr>
<tr>
<td>Non African–American</td>
<td>0.74 (0.61, 0.90)</td>
<td></td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.71 (0.57, 0.88)</td>
<td>0.39</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.83 (0.62, 1.09)</td>
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<tr>
<td>SBP ≤ 132</td>
<td>0.70 (0.51, 0.95)</td>
<td>0.77</td>
</tr>
<tr>
<td>132 &lt; SBP &lt; 145</td>
<td>0.77 (0.57, 1.03)</td>
<td></td>
</tr>
<tr>
<td>SBP ≥ 145</td>
<td>0.83 (0.63, 1.09)</td>
<td></td>
</tr>
</tbody>
</table>

*Unadjusted for multiplicity

Key Takeaways

• Key Takeaway #3
  – SPRINT provides robust evidence that treating to lower BP goals (SBP < 120 mm Hg) is better than standard BP goals (SBP <140 mm Hg) in reducing CV events for certain high-risk patients
Lower BP Goals are Better

Eric J. MacLaughlin, Pharm.D., BCPS, FASHP, FCCP
Professor and Chair
Texas Tech University Health Science Center
Amarillo, Texas
Relationship between BP and ASCVD

- Meta-analysis of patients with no baseline ASCVD
  - >1 million patients from 61 prospective studies
- As SBP ↑ >115 mm Hg
  - Mortality due to ischemic heart disease and stroke ↑
- Risk increases in all age groups
  - Older patients at greater baseline risk

## SPRINT Outcomes and NNT

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<td>70 (1.5)</td>
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<td>-</td>
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<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.62 (0.002)</td>
<td>123</td>
</tr>
<tr>
<td>Death from CV causes</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.57 (0.005)</td>
<td>172</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>0.73 (0.003)</td>
<td>90</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
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<td>0.78 (&lt;0.001)</td>
<td>52</td>
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* Hazard ratio
† Number needed to treat
‡First occurrence of MI, acute coronary syndrome (ACS), stroke, heart failure, or death from CV causes

Does SPRINT apply to older patients?
Question 3: An 83 year-old patient presents to clinic for follow-up of elevated BP. At his last visit 3 weeks ago, his mean BP was 162/74 mm Hg. The readings today are unchanged, and consistent with home BP monitoring readings. The patient’s PMH is significant for osteoarthritis and gout. Which of the following BP goals is the MOST appropriate for this patient?

A. <150/90 mm Hg
B. <140/90 mm Hg
C. <130/80 mm Hg
D. <120/80 mm Hg
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A. <150/90 mm Hg
B. <140/90 mm Hg
C. <130/80 mm Hg
D. <120/80 mm Hg
Goal BPs in Older Patients per Current Guidelines

• 60-80 years of age
  – <140/90 mm Hg
    – ASH/ISH
    – CHEP
    – ESH/ESC
    – NICE
  – <150/90 mm Hg
    – JNC 8

• ≥ 80 years of age
  – <150/90 mm Hg
    – ASH/ISH
    – JNC 8
    – ESH/ESC
    – CHEP
    – NICE

ASH/ISH: American Society of Hypertension/International Society of Hypertension
CHEP: Canadian Hypertension Education Program
ESH/ESC: European Society of Hypertension/European Society of Cardiology
JNC: Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
NICE: National Institute for Health and Care Excellence
SPRINT-Senior

- **Objective**: Evaluate effects of intensive (<120 mm Hg) compared with standard (<140 mm Hg) SBP in persons ≥75 yr with HTN
- **Setting**: Pre-planned subgroup analysis of SPRINT participants
- **Patients**:  
  - Intensive group: N=1317  
  - Standard group: N=1319
- **Outcomes**:  
  - Primary: composite of MI, ACS not resulting in MI, nonfatal stroke, nonfatal acute decompensated HF, death from CV causes  
  - Secondary: All-cause mortality

SPRINT-Senior

• Funded to enhance recruitment of older patients
• Included measures of functional status and frailty
• Exclusion criteria:
  – Diagnosis of or treatment of dementia
  – Expected survival <3 years
  – Unintentional weight loss >10% during preceding 6 mos.
  – SBP <110 mm Hg after 1 min of standing
  – Nursing home resident

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intensive Treatment (n=1317)</th>
<th>Standard Treatment (n=1310)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), yr</td>
<td>79.8 (3.9)</td>
<td>79.9 (4.1)</td>
</tr>
<tr>
<td>Female sex</td>
<td>37.9%</td>
<td>38%</td>
</tr>
<tr>
<td>Seated SBP, mean (SD), mm Hg</td>
<td>141.6 (15.7)</td>
<td>141.6 (15.8)</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>9.6%</td>
<td>9.4%</td>
</tr>
<tr>
<td>History of CVD</td>
<td>25.7%</td>
<td>23.4%</td>
</tr>
<tr>
<td>1-yr Framingham CVD risk, median</td>
<td>27.8%</td>
<td>25.0%</td>
</tr>
<tr>
<td>No. BP meds at baseline, mean (SD)</td>
<td>1.9 (1.0)</td>
<td>1.9 (1.0)</td>
</tr>
<tr>
<td>Gait speed, median (IQR), m/s</td>
<td>0.90 (0.77-1.05)</td>
<td>0.92 (0.77-1.06)</td>
</tr>
<tr>
<td>Frailty status*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit (FI ≤ 0.10)</td>
<td>12.1%</td>
<td>14.4%</td>
</tr>
<tr>
<td>Less fit (FI &gt;0.10 to ≤0.21)</td>
<td>54.0%</td>
<td>56.5%</td>
</tr>
<tr>
<td>Frail (FI &gt;0.21)</td>
<td>33.4%</td>
<td>28.4%</td>
</tr>
</tbody>
</table>

*Measured using a 37-item frailty index (FI)

SBP Results: SPRINT-Senior

Least-Square Means for Post-randomization SBP Achieved

Selected Outcomes: SPRINT-Senior

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment 1317; no. (%)</th>
<th>Standard Treatment N=1319; no. (%)</th>
<th>HR (95% CI)*</th>
<th>NNT†</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD Primary Outcome‡</td>
<td>102 (7.7)</td>
<td>148 (11.2)</td>
<td>0.66 (0.51-0.85)</td>
<td>27</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>37 (2.8)</td>
<td>53 (4.0)</td>
<td>0.69 (0.45-1.05)</td>
<td>-</td>
</tr>
<tr>
<td>ACS not resulting in MI</td>
<td>17 (1.3)</td>
<td>17 (1.3)</td>
<td>1.03 (0.52-2.04)</td>
<td>-</td>
</tr>
<tr>
<td>Stroke</td>
<td>27 (2.1)</td>
<td>34 (2.6)</td>
<td>0.72 (0.43-1.21)</td>
<td>-</td>
</tr>
<tr>
<td>Heart failure</td>
<td>35 (2.7)</td>
<td>56 (4.2)</td>
<td>0.62 (0.40-0.95)</td>
<td>67</td>
</tr>
<tr>
<td>CVD Death</td>
<td>18 (1.4)</td>
<td>29 (2.2)</td>
<td>0.60 (0.33-1.09)</td>
<td>-</td>
</tr>
<tr>
<td>Nonfatal heart failure</td>
<td>35 (2.7)</td>
<td>55 (4.2)</td>
<td>0.63 (0.40-0.96)</td>
<td>67</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>73 (5.5)</td>
<td>107 (8.1)</td>
<td>0.67 (0.49-0.91)</td>
<td>41</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>144 (10.9)</td>
<td>205 (15.5)</td>
<td>0.68 (0.54-0.84)</td>
<td>22</td>
</tr>
</tbody>
</table>

*Hazard ratio and 95% confidence Interval
†NNT over mean of 3.41 years; reported CVD Primary Outcome and all-cause mortality indicated
‡Nonfatal MI, ACS not resulting in MI, nonfatal stroke, nonfatal acute decompensated HF, and death from CV causes

### Primary Outcome by Frailty and Gait Speed

<table>
<thead>
<tr>
<th>Frailty*</th>
<th>Intensive Treatment No./Total with Outcome Events</th>
<th>Standard Treatment No./Total with Outcome Events</th>
<th>HR (95% CI)</th>
<th>P-Value</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fit</td>
<td>4/159</td>
<td>10/190</td>
<td>0.47 (0.13-1.39)</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Less Fit</td>
<td>48/711</td>
<td>77/745</td>
<td>0.63 (0.43-0.91)</td>
<td>0.01</td>
<td>0.84</td>
</tr>
<tr>
<td>Frail</td>
<td>50/440</td>
<td>61/375</td>
<td>0.68 (0.45-1.01)</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gait Speed</th>
<th>Intensive Treatment No./Total with Outcome Events</th>
<th>Standard Treatment No./Total with Outcome Events</th>
<th>HR (95% CI)</th>
<th>P-Value</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥0.8 m/s</td>
<td>59/880</td>
<td>86/893</td>
<td>0.67 (0.47-0.94)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>&lt;0.8 m/s</td>
<td>34/371</td>
<td>54/369</td>
<td>0.63 (0.40-0.99)</td>
<td>0.05</td>
<td>0.85</td>
</tr>
<tr>
<td>Missing</td>
<td>9/66</td>
<td>8/57</td>
<td>0.86 (0.33-2.29)</td>
<td>0.75</td>
<td></td>
</tr>
</tbody>
</table>

*Classified using 37-item Frailty index (FI): fit (FI≤0.10), less fit (FI >0.10-0.21), or frail (FI >0.21).

Bottom line: SPRINT-Senior

- SBP Goal <120 mm Hg in patients >75 yr result in:
  - ↓ CVD by 33% (NNT=27)
  - ↓ Total mortality by 32% (NNT=41)
- *Greater* benefit estimates in seniors due to greater risk and higher event rates
- Exploratory analysis showed consistent benefits in *frail* and *reduced gait speed*
- Serious adverse events comparable, including by frailty level
- Raise serious concerns about higher BP goals for elderly advocated in current guidelines
Additional data that lower BP may be better?
Effects of Intensive BP lowering on CV and renal outcomes

• **Objective:** Assess safety and efficacy of intensive BP-lowering

• **Methods:**
  – Updated systematic review and meta-analysis
  – More intensive vs. less intensive BP lowering compared

• **Trials and Patients:**
  – 19 trials including 44,989 participants; no age restrictions
  – 2,496 CV events recorded during mean follow-up of 3.8 yr.
  – Studies ≥6 mos. follow-up

• **Outcomes:**
  – Major CV events, non-vascular and all-cause mortality, stroke, HF, end-stage renal disease (ESRD), adverse events, albuminuria, progression of retinopathy

Effects of Intensive vs. Less Intensive BP Lowering

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Trials (n)</th>
<th>BP Difference (mm Hg)</th>
<th>RR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major CV events†</td>
<td>14</td>
<td>−6.8/−3.5</td>
<td>0.86 (0.78–0.96)</td>
</tr>
<tr>
<td>MI</td>
<td>13</td>
<td>−6.6/−3.4</td>
<td>0.87 (0.76–1.00)</td>
</tr>
<tr>
<td>Stroke</td>
<td>14</td>
<td>−6.8/−3.5</td>
<td>0.78 (0.68–0.90)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>10</td>
<td>−7.2/−4.0</td>
<td>0.85 (0.66–1.11)</td>
</tr>
<tr>
<td>ESRD</td>
<td>8</td>
<td>−9.4/−5.1</td>
<td>0.90 (0.77–1.06)</td>
</tr>
<tr>
<td>CV Death</td>
<td>13</td>
<td>−6.9/−3.5</td>
<td>0.91 (0.74–1.11)</td>
</tr>
<tr>
<td>Non-CV Death</td>
<td>12</td>
<td>−6.9/−3.6</td>
<td>0.98 (0.86–1.13)</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>19</td>
<td>−6.8/−3.5</td>
<td>0.91 (0.81–1.03)</td>
</tr>
</tbody>
</table>

* Confidence Interval
† Composite of MI, stroke, HF, or CV death

If lower BP goals are better, what cutoff values should be used?
Effects of more vs. less intensive BP lowering and different achieved BP levels – updated meta-analysis

- **Objective:** Identify ideal target BPs in antihypertensive treatment
- **Methods:**
  - Updated meta-analysis that includes SPRINT
  - More intensive vs. less intensive BP lowering
- **Trials and Patients:**
  - 16 hypertension trials including 52,235 participants
  - Studies ≥6 mos. follow-up
- **Outcomes:** Fatal and non-fatal events

## Effects of BP lowering in trials of active treatment vs. placebo and more vs. less intense treatment*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Achieved SBP cutoff (mm Hg)</th>
<th>Trials (n)</th>
<th>Standardized RR† (95% CI)</th>
<th>Absolute RR 1000 pts/5 yr</th>
<th>P-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>140–149 vs. ≥150</td>
<td>8</td>
<td>0.68 (0.60–0.79)</td>
<td>-20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130–139 vs. ≥140</td>
<td>15</td>
<td>0.62 (0.51–0.76)</td>
<td>-16</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130 vs. ≥130</td>
<td>7</td>
<td>0.71 (0.61–0.84)</td>
<td>-8</td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>140–149 vs. ≥150</td>
<td>8</td>
<td>0.81 (0.68–0.95)</td>
<td>-6</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>130–139 vs. ≥140</td>
<td>16</td>
<td>0.77 (0.70–0.86)</td>
<td>-8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130 vs. ≥130</td>
<td>8</td>
<td>0.86 (0.76–0.97)</td>
<td>-8</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>140–149 vs. ≥150</td>
<td>7</td>
<td>0.52 (0.41–0.65)</td>
<td>-21</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>130–139 vs. ≥140</td>
<td>10</td>
<td>0.75 (0.35–1.59)</td>
<td>-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130 vs. ≥130</td>
<td>5</td>
<td>0.81 (0.51–1.30)</td>
<td>-6</td>
<td></td>
</tr>
<tr>
<td>All-Cause Death</td>
<td>140–149 vs. ≥150</td>
<td>8</td>
<td>0.89 (0.82–0.96)</td>
<td>-16</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>130–139 vs. ≥140</td>
<td>16</td>
<td>0.83 (0.72–0.96)</td>
<td>-10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130 vs. ≥130</td>
<td>9</td>
<td>0.84 (0.73–0.95)</td>
<td>-10</td>
<td></td>
</tr>
</tbody>
</table>

* SBP stratification by active or more intensive treatment vs. mean SBP achieved in placebo or less intense treatment
† Standardized RR is to a SBP/DBP difference of -10/-5 mmHg

Key Takeaways

• Key Takeaway #4
  – Higher BP goals for older patients in current guidelines not supported by contemporary evidence

• Key Takeaway #5
  – Newer, updated meta-analyses support lower BP goals
Standard BP Goals should be Used

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Associate Professor
University of Colorado Skaggs School of Pharmacy
Aurora, Colorado
Is it safe to lower BP using more intensive goals vs standard goals?
### SPRINT Safety Outcomes and NNH

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment N=4678; no. (%)</th>
<th>Standard Treatment N=4683; no. (%)</th>
<th>HR* (P-Value)</th>
<th>NNH†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Adverse Event (SAE)‡</td>
<td>1793 (38.3)</td>
<td>1736 (37.1)</td>
<td>1.04 (0.25)</td>
<td>--</td>
</tr>
<tr>
<td>Individual SAEs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>110 (2.4)</td>
<td>66 (1.4)</td>
<td>1.67 (0.001)</td>
<td>100</td>
</tr>
<tr>
<td>Syncope</td>
<td>107 (2.3)</td>
<td>80 (1.7)</td>
<td>1.33 (0.05)</td>
<td>-</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>87 (1.9)</td>
<td>73 (1.6)</td>
<td>1.19 (0.28)</td>
<td>--</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>144 (3.1)</td>
<td>107 (2.3)</td>
<td>1.35 (0.02)</td>
<td>125</td>
</tr>
<tr>
<td>Injurious fall</td>
<td>105 (2.2)</td>
<td>110 (2.3)</td>
<td>0.95 (0.71)</td>
<td>--</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure</td>
<td>191 (4.3)</td>
<td>117 (2.5)</td>
<td>1.66 (&lt;0.001)</td>
<td>56</td>
</tr>
</tbody>
</table>

* Hazard ratio  
† Number needed to harm/3.3 years  
‡A serious adverse event was defined as an event that was fatal or life-threatening or that resulted in clinically significant or persistent disability

## SPRINT Safety Outcomes and NNH

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment N=4678; no. (%)</th>
<th>Standard Treatment N=4683; no. (%)</th>
<th>HR* (P-Value)</th>
<th>NNH†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency department visit or SAE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>158 (3.4)</td>
<td>93 (2.0)</td>
<td>1.70 (&lt;0.001)</td>
<td>72</td>
</tr>
<tr>
<td>Syncope</td>
<td>163 (3.5)</td>
<td>113 (2.4)</td>
<td>1.44 (0.003)</td>
<td>91</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>104 (2.2)</td>
<td>83 (1.8)</td>
<td>1.25 (0.13)</td>
<td>--</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>177 (3.8)</td>
<td>129 (2.8)</td>
<td>1.38 (0.006)</td>
<td>100</td>
</tr>
<tr>
<td>Injurious fall</td>
<td>334 (7.1)</td>
<td>332 (7.1)</td>
<td>1.00 (0.97)</td>
<td>--</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure</td>
<td>204 (4.4)</td>
<td>120 (2.6)</td>
<td>1.71 (&lt;0.001)</td>
<td>56</td>
</tr>
</tbody>
</table>

* Hazard ratio
† Number needed to harm/3.3 years
‡ A serious adverse event was defined as an event that was fatal or life-threatening, that resulted in clinically significant or persistent disability

Is standard BP lowering safer than intensive BP lowering in the elderly?
## SPRINT-Senior Safety Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment N=1317; no. (%)</th>
<th>Standard Treatment N=1319; no. (%)</th>
<th>HR* (P-Value)</th>
<th>NNH†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Adverse Event (SAE)‡</td>
<td>637 (48.4)</td>
<td>637 (48.3)</td>
<td>0.99 (0.895)</td>
<td>--</td>
</tr>
<tr>
<td>Individual SAEs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>32 (2.4)</td>
<td>19 (1.4)</td>
<td>1.71 (0.066)</td>
<td>--</td>
</tr>
<tr>
<td>Syncope</td>
<td>39 (3.0)</td>
<td>32 (2.4)</td>
<td>1.23 (0.401)</td>
<td>--</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>38 (2.9)</td>
<td>40 (3.0)</td>
<td>0.89 (0.610)</td>
<td>--</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>53 (4.0)</td>
<td>36 (2.7)</td>
<td>1.51 (0.058)</td>
<td>--</td>
</tr>
<tr>
<td>Injurious fall</td>
<td>65 (4.9)</td>
<td>73 (5.5)</td>
<td>0.91 (0.605)</td>
<td>--</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure</td>
<td>72 (5.5)</td>
<td>53 (4.0)</td>
<td>1.41 (0.061)</td>
<td>--</td>
</tr>
</tbody>
</table>

* Hazard ratio  
† Number needed to harm/3.3 years  
‡A serious adverse event was defined as an event that was fatal or life-threatening or that resulted in clinically significant or persistent disability

## Trials Evaluating BP Treatment Goals in Elderly

<table>
<thead>
<tr>
<th>Trial</th>
<th>Mean Age (yr)</th>
<th>Age Range (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYVET</td>
<td>83</td>
<td>80-105</td>
</tr>
<tr>
<td>Syst-Eur</td>
<td>70</td>
<td>60+</td>
</tr>
<tr>
<td>SHEP</td>
<td>72</td>
<td>60+</td>
</tr>
<tr>
<td>JATOS</td>
<td>73</td>
<td>65-85</td>
</tr>
<tr>
<td>VALISH</td>
<td>75</td>
<td>70-84</td>
</tr>
<tr>
<td>SPRINT (pre-specified subgroup)</td>
<td>79</td>
<td>75-84</td>
</tr>
</tbody>
</table>


Hypertension in the Very Elderly Trial (HYVET)

- 3845 patients ≥80 yr with hypertension
- Randomized, double-blind to:
  - Placebo or
  - Perindopril +/- Indapamide
- Stopped early after 1.8 years

Primary Endpoint: Stroke
- Placebo: 17.7%
- Drug Therapy: 12.4%
  \[ P = 0.06 \]

Secondary Endpoint: Mortality
- Placebo: 59.6%
- Drug Therapy: 47.2%
  \[ P = 0.02 \]

Question #4

A 65 year-old male with chronic hypertension presents to the clinic for follow-up on his blood pressure. The patient’s PMH is significant for gout, diabetes mellitus, stage 3 CKD, and an MI 3 years ago. His current BP is 146/80 mm Hg and he takes amlodipine 10 mg daily and lisinopril 40 mg daily.

Which of the following would exclude him from meeting the SPRINT Trial Criteria?

A. Stage 3 CKD
B. Diabetes mellitus
C. MI 3 years ago
D. Gout
Question #4

Your poll will show here

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2. Make sure you are in Slide Show mode

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Open poll in your web browser
Question #4
A 65 year-old male with chronic hypertension presents to the clinic for follow-up on his blood pressure. The patient’s PMH is significant for gout, diabetes mellitus, stage 3 CKD, and an MI 3 years ago. His current BP is 146/80 mm Hg and he takes amlodipine 10 mg daily and lisinopril 40 mg daily.

Which of the following would exclude him from meeting the SPRINT Trial Criteria?

- A Stage 3 CKD
- B Diabetes mellitus
- C MI 3 years ago
- D Gout
Who do the SPRINT results not apply to?
SPRINT Exclusion Criteria

• Secondary HTN
• Proteinuria (≥ 1 g/day)
• Diabetes mellitus
• History of stroke
• CV event within 3 months
• Symptomatic HF within 6 months or EF < 35%
• Polycystic kidney disease
• Glomerulonephritis
• eGFR < 20 mL/min/1.73m² or ESRD
How does automated office blood pressure (AOBP) compare to manual auscultatory blood pressure measurement?
Automated Office Blood Pressure (AOBP) Measurement

- **AOBP**
  - More accurate than manual office BP measurement
  - More closely related to awake ambulatory and home BP

- **Omron HEM-907 (used in ONTARGET, ACCORD, and SPRINT)**
  - In SPRINT patients resting alone in an examining room
  - Protocol included a 5-min rest period before the device was activated to record three BP readings automatically, at 1-min intervals.
  - AOBP measurement used in SPRINT is similar to AOBP as performed in other studies using BpTRU

AOBP vs. Manual BP

• Systolic/diastolic BP measured in research studies was on average 10/7 mm Hg lower than BP measured in routine clinical practice

• If standard office BP measurement used without a resting period and without automatic cycling of measurements
  – Adjust SBP goal 5-10 mmHg higher than the BP trials using AOBP

• Application of the SPRINT intensive BP targets
  – Correspond to a SBP target range of 125-135 mmHg to be similar to the level of BP control achieved in the SPRINT intensive BP group

How about intensive vs. standard BP lowering in other subpopulations?
The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Blood Pressure Trial

- Randomized, open-label, multicenter trial
- Intensive (SBP <120 mm Hg) vs. standard (SBP < 140 mm Hg) BP lowering
- 4733 patients with hypertension and:
  - Stable type 2 diabetes and high CVD risk
  - 40-79 years if established clinical CVD, or 55-79 years if ≥ 2 CV risks or subclinical CVD
- Primary Outcome:
  - Nonfatal MI, nonfatal stroke, or CV death

ACCORD: Results at year 1

## ACCORD: Primary & Secondary Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Intensive Events (%/yr)</th>
<th>Standard Events (%/yr)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>208 (1.87)</td>
<td>237 (2.09)</td>
<td>0.88 (0.73-1.06)</td>
<td>0.20</td>
</tr>
<tr>
<td>Total Mortality</td>
<td>150 (1.28)</td>
<td>144 (1.19)</td>
<td>1.07 (0.85-1.35)</td>
<td>0.55</td>
</tr>
<tr>
<td>CV Death</td>
<td>60 (0.52)</td>
<td>58 (0.49)</td>
<td>1.06 (0.74-1.52)</td>
<td>0.74</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>126 (1.13)</td>
<td>146 (1.28)</td>
<td>0.87 (0.68-1.10)</td>
<td>0.25</td>
</tr>
<tr>
<td>Nonfatal Stroke</td>
<td>34 (0.30)</td>
<td>55 (0.47)</td>
<td>0.63 (0.41-0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>Total Stroke</td>
<td>36 (0.32)</td>
<td>62 (0.53)</td>
<td>0.59 (0.39-0.89)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

NNT for nonfatal stroke = 589/year  
NNT for total stroke = 477/year

## ACCORD-BP vs. SPRINT

<table>
<thead>
<tr>
<th></th>
<th>ACCORD-BP</th>
<th>SPRINT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SBP Target (mm Hg)</strong></td>
<td>&lt; 120 vs. &lt; 140</td>
<td>&lt; 120 vs. &lt; 140</td>
</tr>
<tr>
<td><strong>Inclusion</strong></td>
<td>Diabetes&lt;br&gt;SBP 130-180 mm Hg</td>
<td>No Diabetes&lt;br&gt;SBP 130-180 mm Hg</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Age ≥ 40 with CVD&lt;br&gt;Age ≥ 55 + one of the following:&lt;br&gt;• Atherosclerosis&lt;br&gt;• Albuminuria&lt;br&gt;• Left ventricular hypertrophy&lt;br&gt;• &gt; 2 risk factors</td>
<td>Age ≥ 50 + one of the following:&lt;br&gt;• CVD&lt;br&gt;• CKD&lt;br&gt;• Framingham risk score ≥ 15%&lt;br&gt;Age ≥ 75</td>
</tr>
<tr>
<td><strong>Key Exclusion</strong></td>
<td></td>
<td>Stroke and HF</td>
</tr>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>MI, Stroke, CV death*</td>
<td>MI, ACS, Stroke, HF, CV Death</td>
</tr>
<tr>
<td><strong>Prespecified Secondary Outcomes</strong></td>
<td>Primary + Revascularization or HF HF&lt;br&gt;Individual Major CV Events</td>
<td>Primary + All-Cause Death&lt;br&gt;Individual Major CV Events</td>
</tr>
</tbody>
</table>

*Underpowered to detect a different in primary CV outcome

People with diabetes and hypertension should be treated to a systolic blood pressure goal of $<140 \text{ mm Hg}$ and diastolic blood pressure goal of $<90 \text{ mm Hg}$.” (A)

"Lower systolic targets, such as $<130 \text{ mm Hg}$, may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden.” (C)

“Patients with diabetes should be treated to a DBP of $<80 \text{ mm Hg}$.” (B)
Cardiovascular Events and Mortality Relative to Average BP in CAD Patients

• Prospective observational study
• Stable CAD + HTN (N=22,672)
• Primary Outcome: CV death, MI, or stroke
• SBP: (< 120 mm Hg) vs (120-129 mm Hg)
  – HR = 1.56 (95% CI: 1.36 - 1.81)
• DBP: (< 60 mm Hg) vs (70-79 mm Hg)
  – HR = 2.01 (95% CI: 1.50 - 2.70)
• DBP: (60-69 mm Hg) vs (70-79 mm Hg)
  – HR = 1.41 (95% CI: 1.24 - 1.61)

### 2015 AHA/ACC/ASH Scientific Statement: HTN in Patients With CAD

<table>
<thead>
<tr>
<th>BP Goal (mm Hg)</th>
<th>Condition</th>
<th>Class/LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 140/90</td>
<td>CAD, ACS, HF</td>
<td>IIa/B, IIa/B, IIa/B</td>
</tr>
<tr>
<td>&lt;130/80</td>
<td>CAD, Clinical ASCVD</td>
<td>IIb/B, IIb/B</td>
</tr>
</tbody>
</table>

ACC = American College of Cardiology  
LOE = Level of Evidence  
Key Takeaways

• Key Takeaway #6
  – BP goal of < 140/90 mm Hg still appropriate for most patients with hypertension

• Key Takeaway #7
  – If using standard office BP measurement without a resting period or automatic cycling of measurements, use target SBP 5-10 mmHg higher than clinical trials (e.g., SPRINT)
Complex Case Discussion

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Case 1

- RP is a 57-year-old African-American man with a history of type 2 diabetes that is treated with metformin 1000 mg po twice daily. His current A1C is 6.8%. His BP is 156/90 mm Hg, which is similar to his previous values. He is a smoker (1 ppd), is obese, and drinks 2 alcoholic beverages weekly.

- He is diagnosed with hypertension and is started on lisinopril and eventually hydrochlorothiazide. After titration to lisinopril/hydrochlorothiazide 40/25 mg po daily (fixed-dose combination), his BP is 134/84 mm Hg.
Case 1:

**Question 5:** Which of the following lifestyle modifications should be recommended in him to specifically lower his BP?

- **A** Weight loss
- **B** Smoking cessation
- **C** Alcohol restriction
- **D** All of the above
Question 5 – Case 1:

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Case 1:

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A. Weight loss  
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D. All of the above
Case 1:

**Question 6:** Which of the following BP goals is the MOST appropriate for this patient?

- **A** <150/90 mm Hg
- **B** <140/90 mm Hg
- **C** <130/80 mm Hg
- **D** <120/80 mm Hg
Question 6 – Case 1:

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Case 1:

**Question 6:** Which of the following BP goals is the MOST appropriate for this patient?

A. <150/90 mm Hg
B. <140/90 mm Hg
C. <130/80 mm Hg
D. <120/80 mm Hg
Case 1:

Question 7: Which of the following is your greatest concern regarding treating this patient to a BP goal that is lower than the traditional < 140/90 mm Hg?

A. Lack of proven benefit that lower is better
B. Increased risk of orthostatic hypotension
C. Higher cost of therapy needed for intensive BP lowering
D. Risk of worsened glycemic control
Question 7 – Case 1:

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C. Higher cost of therapy needed for intensive BP lowering
D. Risk of worsened glycemic control
Case 1:

**Question 8:** Upon further investigation, this patient reports an annoying dry cough. He thinks it is from his antihypertensive medication. Which of the following is the most appropriate replacement for his current lisinopril/hydrochlorothiazide?

A. Chlorthalidone  
B. Hydrochlorothiazide with amlodipine  
C. Hydrochlorothiazide/valsartan  
D. Amlodipine/olmesartan
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- **A** Chlorthalidone
- **B** Hydrochlorothiazide with amlodipine
- **C** Hydrochlorothiazide/valsartan
- **D** Amlodipine/olmesartan
Case 2

• An 81-year-old woman with a long-standing history of hypertension is currently treated with chlorthalidone 25 mg po daily and felodipine 5 mg po daily. She feels great, and other than dyslipidemia and osteoporosis (both well controlled on atorvastatin and alendronate) she is quite healthy.

• While on her current antihypertensive regimen, her BP is 144/80 mm Hg. She follows a strict low-sodium diet, has a BMI of 20 kg/m\(^2\), and exercises 4 times a week (swimming for 30 minutes).
Case 2:

Question 9: Based on her current antihypertensive regimen, what potential drug-related side effect is she at risk for?

A. Bradycardia
B. Hyperkalemia
C. Kidney stones
D. Hyponatremia
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Case 2:

**Question 9:** Based on her current antihypertensive regimen, what potential drug-related side effect is she at risk for?

- A Bradycardia
- B Hyperkalemia
- C Kidney stones
- D Hyponatremia
Case 2:

**Question 10:** Which of the following BP goals is the MOST appropriate for this patient?

- A) <150/90 mm Hg
- B) <140/90 mm Hg
- C) <130/80 mm Hg
- D) <120/80 mm Hg
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Case 2:

**Question 10:** Which of the following BP goals is the MOST appropriate for this patient?

A. <150/90 mm Hg  
B. <140/90 mm Hg  
C. <130/80 mm Hg  
D. <120/80 mm Hg
Case 2:

**Question 11:** Which of the following is your greatest concern regarding additional BP lowering?

- **A** Lack of proven benefit that lower is better
- **B** Increased risk of orthostatic hypotension
- **C** Higher cost of therapy needed for intensive BP lowering
- **D** Risk of worsened glycemic control
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Management Case

• Assume that you are an ambulatory care clinical pharmacist working in a primary care internal medicine clinic. Your scope of practice broadly includes direct patient care services.

• The clinical pharmacy services provided include managing chronic diseases under collaborative drug therapy management (CDTM) protocols.

• You currently have CDTM protocols for hypertension, dyslipidemia, and diabetes. You are currently starting in the process of annually updating your hypertension CDTM, and it must reflect current evidence, including the SPRINT findings.
Question 12: In your CDTM protocol, which BP goals will you include assuming that your clinic sees a typical internal medicine population?

A. < 120/80 mm Hg
B. < 140/90 mm Hg
C. < 150/90 mm Hg
D. A and B
E. A, B and C
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Question 12: In your CDTM protocol, which BP goals will you include assuming that your clinic sees a typical internal medicine population?

A. < 120/80 mm Hg
B. < 140/90 mm Hg
C. < 150/90 mm Hg
D. A and B
E. A, B and C
Question 13: In your CDTM protocol, did you include preferential use of chlorthalidone instead of hydrochlorothiazide?

A Yes
B No
C Did not think about it
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Question 13: In your CDTM protocol, did you include preferential use of chlorthalidone instead of hydrochlorothiazide?

A Yes
B No
C Did not think about it
Question 14: In your CDTM protocol, did you include specific drug therapy considerations for patients with resistant hypertension?

A Yes
B No
C Did not think about it
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Question 14: In your CDTM protocol, did you include specific drug therapy considerations for patients with resistant hypertension?

- A. Yes
- B. No
- C. Did not think about it
Management Case Discussion

Think/Pair/Share:

• What BP goals will you use and in which populations will they apply?

• What criteria will you use to safely implement therapy for patients with a SBP goal of < 120 mm Hg?

• Which specific medications will you include in your CDTM protocol?
American Heart Association/American Stroke Association 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 National Heart Lung and Blood Institute
Final Takeaways

• Key Takeaway #1
  – ACEi, ARB, CCB, and thiazide are first line

• Key Takeaway #2
  – SPRINT provides robust evidence that treating to lower BP goal is better at reducing CV events than standard BP goal in certain high-risk patients

• Key Takeaway #3
  – Higher BP goals for older patients are not supported by contemporary evidence

• Key Takeaway #4
  – BP goal of < 140/90 mm Hg still appropriate for most patients and standard office BP measurement can adjust measurement
Questions?