HYPERTENSION GUIDELINES:
WHERE ARE WE NOW?

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ANNUAL MEETING
OCTOBER 27, 2018

DISCLOSURES

- I have no relevant relationships to disclose
- Other relationships:
  - Advisor to the Centers for Disease Prevention and Control
  - Advisor to the Pan American Health Organization

HYPERTENSION GUIDELINES:
Questions to consider

- What are the major changes in the new guidelines?
- What is the evidence behind the guidelines?
- What are the major implications of the new guidelines?
- Should the new guidelines be adopted? All, in part, not at all?

WHERE ARE WE NOW AND HOW DID WE GET HERE?

OR

You can see a lot by just looking!
(Yogi Berra)
Question: What is the appropriate BP treatment threshold and target goal?

It is important to consider **two groups:**

* The general population younger than 60-65 years of age.
* Those 60-65 years and older, at high cardiovascular risk, or with diabetes, or with chronic kidney disease.

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HOT Study: Risk of a Major CV Event Reduced by 30% (DBP)

Optimal DBP reduction -83 mmHg

![HOT Study Chart](chart1.png)

Framingham Heart Study

“High-normal” BP Is Not Benign

![Framingham Heart Study Chart](chart2.png)

TROPHY – study design

![TROPHY Study Design Chart](chart3.png)

TROPHY: Risk of hypertension after two years with candesartan vs placebo, followed by two years of placebo vs placebo

![TROPHY Risk Chart](chart4.png)
Treatment of Mild Hypertension Study (TOMHS): JAMA 1993

- 6 groups of patients with baseline DBP <100 mmHg were studied for five years:
  - 1 group: placebo plus intensive life-style modification (sodium reduction, smoking cessation, and exercise)
  - 5 groups: intensive life-style modification plus either
    - Chlorthalidone: thiazide diuretic
    - Acebutolol: beta blocker with intrinsic sympathomimetic activity
    - Doxazosin: alpha blocker
    - Amlodipine: calcium channel blocker
    - Enalapril: angiotensin converting enzyme inhibitor

Treatment of Mild Hypertension Study: Results

- SBP: significantly less in drug treatment groups vs placebo group (-15.9 vs -9.1 mmHg)
- DBP: significantly less in drug treatment groups vs placebo group (-12.3 vs -8.6 mmHg)
- No difference in either SBP or DBP reduction between drug treatment groups
- Clinical events: significantly less in drug treatment groups vs placebo group (-11.1 vs 16.2 %; p=0.03)

JNC-7 Report (2003): BP treatment threshold and target goal?

- In the general population at any age, the treatment threshold is 140/90 mmHg and the target is <140/90 mmHg.
- In those with diabetes or chronic kidney disease, the treatment threshold is 140/90 mmHg and the target is <130/80 mmHg.
- Cardiovascular risk was not specifically addressed.

JNC-8 Committee (2013): BP treatment threshold and target goal?

- In the general population younger than 60 years of age, and those with diabetes or chronic kidney disease, the treatment threshold is 140/90 mmHg and the target is <140/90 mmHg.
- In those 60 years of age or older, the treatment threshold is 150/90 mmHg and the target is <150/90 mmHg. Cardiovascular risk not specifically addressed.
- What happened between JNC-7 and the JNC-8 report? Greater use of evidence-based medicine.

SPRINT Research Question

Examine effect of more intensive high blood pressure treatment than is currently recommended

Randomized Controlled Trial
Target Systolic BP

Intensive Treatment
Goal SBP < 120 mm Hg

Standard Treatment
Goal SBP < 140 mm Hg

SPRINT design details available at:
- ClinicalTrials.gov (NCT01206062)
**Major Inclusion Criteria**

- ≥50 years old
- Systolic blood pressure: 130 – 180 mm Hg (treated or untreated)
- Additional cardiovascular disease (CVD) risk
  - Clinical or subclinical CVD (including stroke)
  - Chronic kidney disease (CKD), defined as eGFR 20 – <60 ml/min/1.73m²
  - Framingham Risk Score for 10-year CVD risk ≥15%
  - Age ≥75 years

**Major Exclusion Criteria**

- Stroke
- Diabetes mellitus
- Polycystic kidney disease
- Congestive heart failure (symptoms or EF < 35%)
- Proteinuria > 1 g/d
- CKD with eGFR < 20 ml/min/1.73m² (MDRD)
- Adherence concerns

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**Demographic and Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Total (N=9361)</th>
<th>Intensive (N=4678)</th>
<th>Standard (N=4683)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, years</td>
<td>67.9 (9.4)</td>
<td>67.9 (9.4)</td>
<td>67.9 (9.5)</td>
</tr>
<tr>
<td>% ≥75 years</td>
<td>28.2%</td>
<td>28.2%</td>
<td>28.2%</td>
</tr>
<tr>
<td>Female, %</td>
<td>35.6%</td>
<td>36.0%</td>
<td>35.2%</td>
</tr>
<tr>
<td>White, %</td>
<td>57.7%</td>
<td>57.7%</td>
<td>57.7%</td>
</tr>
<tr>
<td>African-American, %</td>
<td>29.9%</td>
<td>29.5%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Hispanic, %</td>
<td>10.5%</td>
<td>10.8%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Prior CVD, %</td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Mean 10-year Framingham CVD risk, %</td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.1%</td>
</tr>
<tr>
<td>Taking antihypertensive meds, %</td>
<td>90.6%</td>
<td>90.8%</td>
<td>90.4%</td>
</tr>
<tr>
<td>Mean (SD) number of antihypertensive meds</td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
</tr>
<tr>
<td>Mean (SD) Baseline BP, mm Hg</td>
<td>139.7 (15.6)</td>
<td>139.7 (15.6)</td>
<td>139.8 (15.4)</td>
</tr>
<tr>
<td>Systolic</td>
<td>78.1 (11.9)</td>
<td>78.2 (11.8)</td>
<td>78.0 (12.0)</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SPRINT Primary Outcome Cumulative Hazard**

- Hazard Ratio = 0.75 (95% CI: 0.64 to 0.89)

**All-cause Mortality Cumulative Hazard**

- Hazard Ratio = 0.73 (95% CI: 0.60 to 0.90)
**SPRINT Primary Outcome and its Components**

**Event Rates and Hazard Ratios**

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>243</td>
<td>319</td>
<td>0.75 (0.64, 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>All MI</strong></td>
<td>97</td>
<td>116</td>
<td>0.83 (0.64, 1.09)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Non-MI ACS</strong></td>
<td>40</td>
<td>40</td>
<td>1.00 (0.64, 1.55)</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>All Stroke</strong></td>
<td>62</td>
<td>70</td>
<td>0.89 (0.63, 1.25)</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>All HF</strong></td>
<td>62</td>
<td>100</td>
<td>0.62 (0.45, 0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>CVD Death</strong></td>
<td>37</td>
<td>65</td>
<td>0.57 (0.38, 0.85)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Serious Adverse Events* (SAE) During Follow-up**

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
<th>HR (P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All SAE reports</strong></td>
<td>1793 (38.3)</td>
<td>1736 (37.1)</td>
<td>1.04 (0.25)</td>
</tr>
</tbody>
</table>

**SAEs associated with Specific Conditions of Interest**

- Hypertension: 110 (2.4) / 66 (1.4) / 1.67 (0.001)
- Syncope: 107 (2.3) / 80 (1.7) / 1.33 (0.05)
- Deafness: 105 (2.2) / 110 (2.3) / 0.95 (0.71)
- Bradyarrhythmia: 87 (1.9) / 73 (1.6) / 1.29 (0.28)
- Electrolyte abnormality: 144 (3.1) / 107 (2.3) / 1.35 (0.020)
- Acute kidney injury or acute renal failure: 193 (4.1) / 117 (2.5) / 1.66 (<0.001)

*Fatal or life-threatening event, resulting in significant or persistent disability, requiring or prolonging hospitalization, or judged important medical event.

**Primary Outcome Experience in the Six Pre-specified Subgroups of Interest**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>0.75 (0.64, 1.30)</td>
<td>0.36</td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.70 (0.50, 1.03)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.67 (0.43, 1.05)</td>
<td>0.05</td>
</tr>
<tr>
<td>Age &lt; 75</td>
<td>0.89 (0.64, 1.20)</td>
<td>0.52</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>0.97 (0.51, 1.86)</td>
<td>0.63</td>
</tr>
<tr>
<td>Female</td>
<td>0.94 (0.62, 1.43)</td>
<td>0.45</td>
</tr>
<tr>
<td>Male</td>
<td>0.72 (0.50, 1.08)</td>
<td>0.48</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 (0.58, 0.95)</td>
<td>0.06</td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.71 (0.57, 0.88)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.83 (0.63, 1.09)</td>
<td>0.03</td>
</tr>
<tr>
<td>SBP &lt; 130</td>
<td>0.70 (0.51, 1.00)</td>
<td>0.77</td>
</tr>
<tr>
<td>130 ≤ SBP &lt; 145</td>
<td>0.77 (0.57, 1.05)</td>
<td>0.04</td>
</tr>
<tr>
<td>SBP ≥ 145</td>
<td>0.83 (0.63, 1.10)</td>
<td>0.50</td>
</tr>
</tbody>
</table>

*All P values were adjusted for multiple comparisons. **HR (95% CI) = 0.95 (0.81-1.11) / P-value = 0.51**

**SPRINT: Clinically Important Caveats**

- Intensive clinical research setting with close monitoring.
- Adherent, already under treatment (90%-2 drugs), older (68 years), high cardiovascular risk patient population (20%).
- Intensive BP group: 3 agents and greater use of diuretics and RAAS inhibitors (event reduction largely heart failure).
- Relative risk reduction was only 0.5%.
- BPs determined by an automated device, mostly non-observed in a quiet room after 5 minutes of rest.
- This methodology **COULD** result in a SBP 10-12 mmHg LOWER than BP measurements in clinical practice and previous landmark hypertension trials.

**Unique Aspects of HOPE-3**

- Intermediate CV risk individuals without CVD
- Placebo controlled
- BP lowering trial with wide range of BP entry criteria
- Cholesterol lowering treatment based on risk opposed to baseline LDL or HDL measurement
- Diverse population
PATIENTS WITH HYPERTENSION AND DIABETES

Benefits of BP Reduction in HOT: Diabetic Cohort

Table 1: Primary and Secondary Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Therapy (n=2083)</th>
<th>Standard Therapy (n=2035)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>276</td>
<td>206</td>
<td>0.48 (0.41-0.56)</td>
<td>0.000</td>
</tr>
<tr>
<td>Prespecified secondary outcome</td>
<td>50%</td>
<td>47%</td>
<td>1.07 (0.86-1.33)</td>
<td>0.62</td>
</tr>
<tr>
<td>Stroke</td>
<td>36</td>
<td>32</td>
<td>0.76 (0.59-1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>24</td>
<td>25</td>
<td>0.98 (0.77-1.25)</td>
<td>1.94</td>
</tr>
<tr>
<td>Dementia</td>
<td>150</td>
<td>129</td>
<td>1.89 (1.48-2.41)</td>
<td>0.001</td>
</tr>
<tr>
<td>Kept on study during follow-up</td>
<td>955</td>
<td>936</td>
<td>0.98 (0.86-1.11)</td>
<td>0.76</td>
</tr>
<tr>
<td>Major coronary disease event</td>
<td>253</td>
<td>231</td>
<td>0.94 (0.74-1.20)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

ACCORD STUDY: Intensive Blood Pressure Control in Type 2 Diabetes

**Figure 1.** Mean Systolic Blood Pressure Levels at Each Study Visit.


ACCORD STUDY: Intensive Blood Pressure Control in Type 2 Diabetes

10/15/2018
ACCORDIAN Trial (2015): Follow-up to ACCORD

- ACCORD ended in 2009. About 4000 pts were still followed (87% of the total pts alive)
- Main result: Intensive BP reduction did not lower primary CV endpoints (similar to ACCORD) but decrease in stroke now not seen
- However, there was a significant interaction between BP and glycemic control
- In pts with standard BS control, intensive BP reduction decreased CV events (21%, p<0.08)

Interpreting the 2017 ACC/AHA Hypertension Guidelines for Clinical Practice

**Classification of Hypertension**

<table>
<thead>
<tr>
<th>BP Category</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>&lt;80 mm Hg</td>
</tr>
<tr>
<td>Elevated</td>
<td>120–129 mm Hg</td>
<td>&lt;80 mm Hg</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Stage 1</td>
<td>or 80–89 mm Hg</td>
</tr>
<tr>
<td></td>
<td>130–139 mm Hg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage 2</td>
<td>or ≥90 mm Hg</td>
</tr>
<tr>
<td></td>
<td>≥140 mm Hg</td>
<td></td>
</tr>
</tbody>
</table>

**Goal of the Guidelines**

- Evaluate potential benefit to home or ambulatory blood pressure monitoring
- Identify the optimal target for blood pressure lowering among patients being treated for hypertension
- Identify if differences in benefit and harm exist between different antihypertensive classes
- Identify if differences in benefit and harm exist between initiating treatment with monotherapy vs. dual-therapy

**Treatment of High Blood Pressure**

**Recommendation Stage 1 HTN:**

- Use BP-lowering medications at an average BP ≥130/80 mmHg in patients with CVD or in those with a 10-year ASCVD risk of ≥10%, with a BP target of <130/80 mmHg

**Recommendation Stage 2 HTN:**

- Use BP-lowering medications at a BP ≥140/90 mmHg
  - Strong recommendation (benefit >>> risk) based on observational evidence
- For these patients, a BP target of <130/80 mmHg may be reasonable
  - Moderate recommendation (benefit > risk) based on observational evidence for SBP and expert opinion for DBP
Special Patient Groups: Older Patients

- Recommendations:
  - In non-institutionalized ambulatory community-dwelling adults (≥65 years of age), initiate treatment for an SBP ≥ 130 mmHg with a treatment goal <130 mmHg
    - Strong recommendation (benefit >> risk) based on RCT evidence
  
  - For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, it is reasonable to use clinical judgement and patient preference
    - Moderate recommendation (risk >> benefit) based on expert opinion

ACC/AHA 2017 guidelines: Broad U. S. implications (Bundy et al. JAMA Cardiology 2018)

- Compared to the 2014 guidelines, using 2016 NHANES data adopting the 2017 ACC/AHA guidelines will:
  - Increase the prevalence of HTN (32% to 45.4%)
  - Increase the number on drug Rx (31.1% to 35.9%)
  - Increase hypotensive episodes by 62,000
  - Increase AKI episodes by 79,000 BUT
  
- Decrease CV events by 340,000
- Decrease total deaths by 156,000
- Mostly from those >60 years old, high CV risk, Dm, CKD

ACC/AHA 2017 guidelines: Rapid Response

- Multiple commentaries and editorials questioning mainly the new HTN classification, treatment thresholds, and targets

- American Academy of Family Physicians, American College of Physicians, the Latin American Societies, and the European Societies of Cardiology and Hypertension did not endorse the guidelines

ECS/ESH Hypertension Guidelines 2018: Hypertension Classification and Treatment

- HTN prevalence increases and life-style modification (LSM) becomes a primary therapeutic modality.
- Given the difficulty with adherence to LSM and the lower treatment targets, an increase in the use of pharmacologic agents will likely occur.
- Significant changes in “in-office” BP measurement will be needed (SPRINT methodology).
- Out-of-office BPs (home and/or AMBP) required.
ACC/AHA Hypertension Guidelines: Patient Implications

- Increase in provider and patient education.
- Life-style modification (LSM) is difficult and expensive.
- While fixed-dose combination may help, significant increase in medications and polypharmacy is likely.
- Patient adverse events are likely to increase.
- Added complexity of home and/or ambulatory blood pressure measurements.

ACC/AHA Hypertension Guidelines: Moving forward?

- ACC/AHA guidelines are highly dependent on the SPRINT results and observational evidence
- Perhaps we should WALK before we SPRINT
- Follow the debate or better yet, call for new clinical trial driven evidence but implement what makes sense

ACC/AHA Hypertension Guidelines: What should we consider to do?

- Continue treatment threshold and control levels at 140/90 mmHg and <140/90 mmHg in all ages.
- Consider <130/80 mmHg especially in those with high CV risk, DM, or CKD.
- Aggressive life-style modification and proper office and out of office BPs.
- Use a standardized formulary and drug treatment algorithm, fixed-dose combination initial drug therapy, and team-based care.

Thank You