Making Sense of the US Hypertension Guideline in 2018

William J. Elliott, M.D., Ph.D.

04 MAY 18

Presenter Disclosure Information

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DISCLOSURE INFORMATION:
Dr. Elliott has received research funding, honoraria, and/or travel expenses from essentially every pharmaceutical company that makes, markets, or distributes antihypertensive drugs in the United States. A former full-time employee of RUSH Medical College, he was prohibited from (and still does not) own individual stocks or financial instruments related to healthcare.

Affidavit of Originality

• The following material is based exclusively on the speaker’s own opinion, knowledge and expertise.
• There is no organization, company, or entity that has exercised any control or influence over the content of this presentation, nor has any other person or organization had any part in drafting, scripting or designing its content.
• The information presented is based on the principles of “Evidence-Based Medicine,” and is intended to avoid promotion of any specific commercial interest, product, or company.
WARNING!
During this discussion, attempts will be made to avoid discussion of “off-label” or investigational uses of medicines or devices not yet approved by the US FDA, but very few antihypertensive medicines or devices have been specifically approved to reduce the risk of cardiovascular or renal disease, or to reduce the incidence or severity of adverse effects.

DISCLAIMER:
The audience member should interpret each example and every statement in the context of the “local standard of care” regarding medical practice, and judge each allegation regarding drug therapy within the standards approved by the most current product information for each marketed agent, as reflected in the most recent FDA-approved package insert. The speaker assumes no liability for any erroneous interpretation of the information contained herein, stated or implied.

More Disclaimers
• The speaker has participated (with known experts in the field) in writing a “Scientific Statement” from the American Heart Association on the topic of “Treatment of Hypertension in Patients with Coronary Heart Disease.
• The speaker served as the Chair of the Continuing Education Committee and on the Education Committee of the American Society of Hypertension, which was involved in generating the 2017 ACC/AHA 2017 hypertension guideline.
• This presentation does NOT reflect opinion, consensus, or recommendations from the American Heart Association, or the American Society of Hypertension.

Making Sense of the US Hypertension Guideline in 2018

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Educational Objectives

At the end of this 50-minute session, the awake audience member should be able to:

1. Name at least one advantage and at least one disadvantage for the most current US hypertension guideline(s) promulgated by:
   b. The panel members appointed to JNC 8,
   c. The American Society of Hypertension and the International Society of Hypertension,
   d. The American Diabetes Association,
   e. The National Kidney Foundation, and
   f. The American College of Cardiology and The American Heart Association.

2. Interpret the results of the recent Systolic blood Pressure Intervention Trial (SPRINT), and summarize their impact on the 2017 ACC/AHA Evidence-Based US Hypertension Guideline.

3. Explain why, using clinical trial evidence, the recommended initial drug therapy for hypertension depends on the patient’s race/ethnicity, in all guidelines since JNC 7.

“Current” US HTN Guideline(s)

2. The panel members appointed to JNC 8 (2013),
3. The American Society of Hypertension and the International Society of Hypertension (2013),
4. The American Diabetes Association (2018),
5. The National Kidney Foundation (2012), and
Advantages:
• The last set of governmentally-issued, comprehensive clinical practice guidelines on hypertension.
• Relatively short, easy-to-implement recommendations.
• Summarized in one side of one-third of a sheet of paper.
• Focused on issues relevant to hypertension in the USA.

Disadvantages:
• Now 15 years old.
• Could not take into account recent information.
• NHLBI dissolved the NHBPEP program shortly after JNC 7 was released, and folded the NHBPEP’s endowment into discretionary funds, making it impossible to use the framework of the first 7 JNCs in the future.
Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

Executive Committee

George L. Bakris, M.D.
Department of Preventive Medicine
Rush-Presbyterian-St. Luke’s Medical Center

Harry B. Black, M.D.
Department of Preventive Medicine
Rush-Presbyterian-St. Luke’s Medical Center

William C. Cushman, M.D.
Preventive Medicine Section
Veterans Affairs Medical Center

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University of Michigan

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University of Mississippi Medical Center

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Suzanne Oparil, M.D.
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University of Alabama

Jackson T. Wright, Jr., M.D.
University Hospitals of Cleveland
Case Western Reserve University

Executive Secretary
Edward J. Roccella, Ph.D., M.P.H.
National Heart, Lung, and Blood Institute

Advantages:
• All but one of the physician members were well-recognized national figures in clinical hypertension.
• All physician members were nominated by constituent societies or groups that made up the NHBPEP.
• All members were appointed by the Director of the NHLBI.

Disadvantages:
• All but one of the physician members had been financially involved in some way with the US pharmaceutical industry.
• No physician member was disqualified because of such involvement.
• No representation from allied health personnel or interested lay persons.

National High Blood Pressure Education Program

Coordinating Committee

American Academy of Family Physicians
American Academy of Neurology
American Academy of Ophthalmology
American Academy of Physician Assistants
American Association of Occupational Health Nurses
American College of Cardiology
American College of Chest Physicians
American College of Occupational and Environmental Medicine
American College of Physicians
American College of Preventive Medicine
American Dental Association
American Diabetes Association
American Dietetic Association
American Heart Association
American Hospital Association
American Nurses Association
American Optometric Association
American Osteopathic Association
American Pharmaceutical Association
American Podiatric Medical Association
American Public Health Association
American Red Cross
American Society for Health System Pharmacists
American Society for Hypertension
American Society of Hypertension Association of Black Cardiologists
Citizens for Public Action on High Blood Pressure and Cholesterol, Inc.
Hypertension Education Foundation, Inc.
International Society on Hypertension in Blacks
National Black Nurses Association, Inc.
National Kidney Foundations, Inc.
National Medical Association
National Organ Transplantation Association
National Stroke Association
National Public Health Association
National Society for Children’s Hunger
National Center for Health Statistics
National Heart, Lung, and Blood Institute
National Institute of Diabetes and Digestive and Kidney Diseases
For persons over age 50, SBP is more important than DBP as a CVD risk factor.

Starting at 115/75 mmHg, CVD risk doubles with each increment of 20/10 mmHg throughout the BP range.

Persons who are normotensive at age 55 have a 90% lifetime risk for developing HTN.

Those with SBP 120–139 mmHg or DBP 80–89 mmHg should be considered “pre-hypertensive;” they require health-promoting lifestyle modifications to prevent CVD.

Thiazide-type diuretics should be the initial drug therapy for most patients, either alone or combined with other drug classes.

Certain high-risk conditions are compelling indications for other drug classes.

Most patients will require two or more antihypertensive drugs to achieve goal BP.

If BP is >20/10 mmHg above goal, consideration should be given to initiating therapy with two agents, one of which usually should be a thiazide-type diuretic.

The most effective therapy prescribed by the careful clinician will control HTN only if patients are motivated.

Motivation improves when patients have positive experiences with, and trust in, the clinician.

Empathy builds trust and is a potent motivator.

The responsible physician’s judgment remains paramount.
• In 2007, the Director of the National Heart, Lung, and Blood Institute (NHLBI) authorized selection of the members of JNC 8 (the NHBPEP had been dissolved in 2006).
• More than 400 people were nominated; 17 were selected; 4 had relationships with industry.
• After nearly two years of face-to-face and telephone meetings, they decided to address, using techniques recommended by the Institute of Medicine (and evidence from 54 high-quality clinical trials alone), only 3 questions.

**Updating JNC 7: The Process**

• In adults with hypertension, does initiating antihypertensive pharmacologic therapy at specific blood pressure thresholds improve health outcomes?
• In adults with hypertension, does treatment with antihypertensive pharmacologic therapy to a specified blood pressure goal lead to improvements in health outcomes?
• In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?

**JNC 8: The Questions**

• Randomized clinical trials enrolling adults (≥ 18 years of age) with hypertension were excluded if:
  – Trial was carried out at a single center
  – Sample size < 100 (later 2000)
  – Duration of follow-up < 1 year
  – Reported outcomes did not include overall mortality, cardiovascular mortality, myocardial infarction, heart failure, heart failure hospitalization, stroke, coronary revascularization, other revascularization, end-stage renal disease, doubling of serum creatinine, or halving of glomerular filtration rate.
  – Lower than “fair” quality using the NHLBI’s standardized quality rating tool.
JNC 8: The Delays

- Two teams of statistical consultants were unable to complete their work on time, and were replaced.
- Adjustments to the initial inclusion criteria for evidence review were made.
- Criteria for both strength and grading of recommendations were changed by the Institute of Medicine.
- On 19 JUN 13, the Director of the NHLBI announced a decision to “get out of the guideline business,” and to work with others (ACCF/AHA, etc.) to formalize guidelines.
- ACCF/AHA desired a different standardized process; the JNC 8 panel decided to publish their recommendations independently (i.e., without the formal backing of any organization, governmental body, or other entity).

US HTN Guidelines: Confusion?

- On the same day that The *JAMA* released the final report from the JNC 8 panel, the American Society of Hypertension and International Society of Hypertension (ASH/ISH) released their “2013 Guidelines for Management of Hypertension in the Community.”
- These were intended to have a broader range, and differed somewhat from JNC 8, particularly regarding BP targets for hypertensive people 60-79 years of age.

US HTN Guidelines: Confusion?

- JNC 8 and the ASH/ISH guidelines agreed on the new drug treatment algorithm (2 shared members!), but not the BP target for people who have had 60-79 birthdays.
- The ADA releases guidelines about [Diabetes](#) annually; drug therapy was usually ACE-I or ARB first; BP goals were < 140/90 mm Hg for all, but < 130/80 mm Hg for some.
- The NKF releases guidelines about [CKD](#) less frequently; drug therapy was ACE-I or ARB first; BP goals were < 140/90 mm Hg for all, but < 130/80 mm Hg for some.
Blood Pressure Classification?

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>JNC I-8</th>
<th>ACC/AHA 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 120/&lt; 80</td>
<td>“Normal”</td>
<td>“Normal”</td>
</tr>
<tr>
<td>120-129/&lt;80</td>
<td>“Pre-hypertension”</td>
<td>“Elevated”</td>
</tr>
<tr>
<td>130-139/80-89</td>
<td>Stage 1 HTN*</td>
<td>Stage 2 HTN</td>
</tr>
<tr>
<td>140-159/90-99</td>
<td>Stage 1 HTN</td>
<td>Stage 2 HTN</td>
</tr>
<tr>
<td>≥160/≥ 100</td>
<td>Stage 2 HTN</td>
<td>Stage 2 HTN</td>
</tr>
</tbody>
</table>

*BP drugs recommended only if 10-year CV risk is > 10%.

Implications for US Population

- Hypertension: 31.5% (JNC 7), 45.6% (ACC/AHA)
- Recommend Drug Rx: 26.2% (JNC 7), 31.9% (ACC/AHA)
- BP > Goal: 39.0% (JNC 7), 53.4% (ACC/AHA)

Prevalence in US Adults, NHANES 2011-14 (%)

- Hypertension: 72.2% (JNC 7), 103.3% (ACC/AHA)
- Recommend Drug Rx: 77.1% (JNC 7), 81.9% (ACC/AHA)
- BP > Goal: 21.2% (JNC 7), 29.2% (ACC/AHA)

Millions of US Adults, per NHANES 2011-14
BP Targets for the USA—2018

<table>
<thead>
<tr>
<th>Population</th>
<th>JNC 8</th>
<th>ACC/AHA</th>
<th>ADA</th>
<th>NKF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60 years</td>
<td>&lt; 150/90</td>
<td>&lt; 130/80</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80*</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>Diabetics</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80</td>
<td>&lt; 140/80, &lt; 130/80 for some</td>
<td>N.A.</td>
</tr>
<tr>
<td>With CKD</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80</td>
<td>N.A.</td>
<td>&lt; 140/90, &lt; 130/80 &quot;suggested&quot;</td>
</tr>
<tr>
<td>With CVD</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

*If 10-year CV risk is > 10%; otherwise < 140/90 mm Hg.

Friday, 11 SEP 15, 10:30 EDT

SPRINT: Trial Design

- Designed by Steering Committee, appointed by NHLBI
- Coordinated by Wake Forest University/Baptist Hospital & Medical Center, Winston-Salem, NC.
- Funded by NHLBI, NIDDK, NINDS, and NIA.
- Randomized, single-blind (outcomes assessment panel only!), parallel-group, prospective multicenter clinical trial.
- Comparison: Systolic BP Target < 120 mm Hg vs. Systolic BP Target < 140 mm Hg.
- Primary outcome: MI, acute coronary syndrome, stroke, heart failure, or cardiovascular death.
- Planned Duration: 2 years (recruitment) + 6 years (follow-up).
SPRINT: Subject Population

- 9361 Male or female volunteers
- Aged 50 years and older
- Systolic blood pressure ≥ 130 mm Hg and at least one other cardiovascular risk factor:
  - Presence of clinical or subclinical cardiovascular disease other than stroke
  - Estimated glomerular filtration rate between 20-59 mL/min/1.73 m²
  - A Framingham 10-year cardiovascular risk score ≥ 15%
  - Age ≥ 75 years

SPRINT Broadly Excluded:

- Diabetics (ACCORD-BP: No significant benefit)
- Prior stroke (SPS3: No significant benefit overall of < 130 mm Hg vs. 130-149 mm Hg [but there was a benefit on intracerebral hemorrhage])
- Polycystic kidney disease (MDRD substudy: No significant benefit of MAP < 92 vs. 102 mm Hg)


SPRINT: Exclusion Criteria 1:

- Indication for a specific type of blood pressure medication;
- Known cause of secondary hypertension;
- Standing systolic blood pressure < 110 mm Hg;
- Proteinuria in the previous 6 months (≥ 1 gm/day or albumin/creatinine ratio > 600 mg/gm),
- Arm circumference too large or small;
- Diabetes;
- History of stroke (but carotid endarterectomy or stenting is acceptable),
- Polycystic kidney disease;
- Glomerulonephritis requiring immunosuppressive therapy;
SPRINT: Exclusion Criteria 2:
• Estimated glomerular filtration rate < 20 mL/min/1.73 m²;
• Cardiovascular event, procedure or hospitalization for unstable angina (within the past 3 months);
• Symptomatic heart failure in the prior 6 months or known left ventricular ejection fraction < 35 %;
• Any medical condition likely to limit survival to < 3 years,
• Known malignancy other than non-melanoma skin cancer in the last 2 years;
• Limited adherence to interventions;
• Failure to provide written, informed consent;

SPRINT: Exclusion Criteria 3:
• Currently participating in another clinical trial;
• Living in the same household as an already-randomized SPRINT participant;
• Any organ transplant;
• Unintentional weight loss > 10% in the past 6 months;
• Pregnancy (or attempting pregnancy), or of child-bearing potential and not using birth control.

Some authors have suggested that these criteria exclude 89% of the age-eligible US hypertensive population

SPRINT: Interventions
• No particular antihypertensive regimen was specified or randomized, but it was expected that most patients would require a thiazide or thiazide-like diuretic (chlorothalidone was “preferred”), an ACE-inhibitor (or an ARB), and a calcium antagonist.
• Pills provided by the study included:
  – ACE-inhibitors
  – ARBs
  – Direct vasodilators
  – Thiazide-type diuretics
  – Loop diuretics
  – Potassium-sparing diuretics
  – Beta-blockers
  – Sustained-release CCBs
  – Alpha-1 blockers
  – Sympatholytics
SPRINT: Interventions

- In the lower BP (< 120 mm Hg) arm, additional pills were “required” if SBP ≥ 120 mm Hg.
- In the standard BP (< 140 mm Hg) arm, doses were to be down-titrated if SBP < 130 mm Hg at 1 visit, or < 135 mm Hg at 2 consecutive visits!

SPRINT: Stopped Early!

- Interim analyses at a regularly-scheduled DSMB meeting on 09 SEP 15 disclosed a significant difference between the two (still blinded) randomized groups in both the primary endpoint and total mortality.
- The Steering Committee (Drs. Reboussin, Wright, Cheung, Oparil, Rocco, and Cushman) met by conference call on 10 SEP 15, and recommended to Dr. Gary Gibbons, Director of the NHLBI, that the trial be stopped for cause.
- Only after the decision to stop the trial was formalized were the Steering Committee informed of which randomized group had the higher event rates.

SPRINT: Subject Flow
SPRINT: Randomization Worked!

N Engl J Med. 2015;373:2103-16

SPRINT: In-Trial SBPs

Mean = 136.2 mmHg
Mean = 121.4 mmHg

SPRINT Office BP Measurements

- All SPRINT in-office BPs were measured in triplicate, using an automated Omron® 907-XL.
- The patient was seated, in a quiet, low-light, warm room, the appropriate BP cuff attached, and the healthcare team member punched the “START” button, and left the patient alone in the room.
- After a 5-minute rest, 3 BPs were recorded at 1 minute intervals; the last 2 were averaged and used as the BP for that visit.
- Some suggest that this procedure results in a 10-20/5-10 mm Hg LOWER BP than traditional readings taken by a healthcare team member.
SPRINT: 3.26-Year Number Needed to Treat to Prevent One:

- **1° Composite endpoint: 62**
  - Myocardial Infarction: 248
  - Acute Coronary Syndrome: -109,536
  - Stroke: 591
  - Heart failure: 124
  - Cardiovascular Death: 167
  - Death: 86
  - **1° Outcome or Death: 52**

- **BUT**, in subjects without CKD at baseline, 1 in 37 treated to a BP < 120 mm Hg will experience a ≥30% drop in eGFR to < 60 mL/min/1.73 m²

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**Serious Adverse Events**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Treatment (N=936)</th>
<th>Standard Treatment (N=936)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse event only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>138 (13.6)</td>
<td>99 (10.6)</td>
<td>1.87</td>
<td>0.084</td>
</tr>
<tr>
<td>Eosinopenia</td>
<td>107 (11.3)</td>
<td>80 (8.6)</td>
<td>2.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Embolic phenomena</td>
<td>26 (2.8)</td>
<td>15 (1.6)</td>
<td>2.11</td>
<td>0.01</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>144 (15.3)</td>
<td>130 (14.0)</td>
<td>1.55</td>
<td>0.35</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>148 (16.0)</td>
<td>123 (13.3)</td>
<td>1.37</td>
<td>0.07</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure</td>
<td>159 (16.5)</td>
<td>127 (13.6)</td>
<td>1.86</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Emergent department visit or serious adverse event

- Hypertension: 358 (12.0) vs 257 (11.8)
- Eosinopenia: 154 (16.6) vs 107 (11.3)
- Embolic phenomena: 278 (19.3) vs 157 (16.9)
- Diastolic dysfunction: 143 (15.3) vs 124 (13.3)
- Hypoglycemia: 126 (13.3) vs 103 (11.2)
- Acute kidney injury: 170 (18.0) vs 132 (14.1)

**SPRINT: Conclusion**

- "Among patients at high risk for cardiovascular events but without diabetes, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events were observed in the intensive-treatment group."

N Engl J Med. 2015;373:2103-16
**Policymakers’ Summary: SPRINT**

- Treating 10,000 hypertensive people to a SBP < 120 (rather than < 140) mm Hg will save 162 people from 1° composite endpoints, and:
  - 40 myocardial infarctions,
  - 17 strokes,
  - 81 heart failure episodes,
  - 60 cardiovascular deaths,
  - 118 deaths, 
  - 194 deaths or 1° composite endpoints,

- At the expense of:
  - Uncalculable cost of extra meds & blood tests, office/ED visits for hypotension, syncope, electrolyte abnormalities
  - 191 people who suffer a ≥ 30% decline in eGFR.

**Achieved SBP & Risk of CVD, Death**

- 42 Randomized clinical trials involving 144,220 subjects had their CVD and mortality outcomes subjected to network meta-analysis, based on their mean achieved SBP.

*JAMA Cardiol. 2017;2:775-81.*

**Achieved SBP & Risk of CVD**

*JAMA Cardiol 2017;2:775-81.*
Achieved SBP & Death Risk

The BP Target Is Now < 130/80
- Because SPRINT showed CV event and death prevention at SBP < 120 (using BP measurement technology that is probably 10 mm Hg LOWER than usual clinic measurements).
- Because a meta-analysis showed the best CV event and death prevention at SBP between 120-124 mm Hg.
- Because simulation analyses showed more absolute CV event and death prevention among individuals at higher absolute risk.

OK, Maybe. But Which Drug Should Be Used for Initial Therapy?
Algorithm for Treatment of Hypertension

Not at Goal Blood Pressure (<140/90 mmHg)
(<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Drug(s) for the compelling indications

Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

Stage 1 Hypertension (SBP 140–159 or DBP 90–99 mmHg)
Thiazide-type diuretics for most. May consider ACEI, ARB, BB, or CCB as alternatives.

Stage 2 Hypertension (SBP ≥160 or DBP ≥100 mmHg)
2-drug combination for most (thiazide-type diuretic and ACEI, ARB, BB, or CCB).

JNC 8 Treatment Algorithm

Lifestyle Modifications

Without Compelling indications

Drugs for the compelling indications

Consider consultation with hypertension specialist.

Not at Goal Blood Pressure

Optimize dosages or add additional drugs until goal blood pressure is achieved.

Stage 2 Hypertension

Stage 1 Hypertension

Optimize dosages or add additional drugs until goal blood pressure is achieved.
Why Other Initial Drugs (besides the traditional diuretic)?

• Numerous meta-analyses (including my own) show no significant differences between an initial diuretic, ACE-inhibitor, or calcium antagonist for most cardiovascular endpoints (heart failure excepted; a diuretic is best).
• Multiple drugs from each of these four classes of antihypertensive drugs are now available generically.
• Essentially all analyses show that achieving and maintaining goal BP is more important than which drug class is used to start the process.

“Default” Initial HTN Therapy Differs by Race/Ethnicity?

• Population-based, age-adjusted, hypertension-related cardiovascular and renal risks differ by race/ethnicity:
  – Stroke
  – Heart disease
  – End-stage renal disease (dialysis or transplant).
• Outcomes in ALLHAT differed by race/ethnicity (and drug selected):
  – Stroke
  – Combined cardiovascular disease endpoint.
• Cough and angioedema with ACE-inhibitors are more common in blacks.
• Dr. John Laragh said this all happens because plasma renin activity differs by race/ethnicity…

Age-Adjusted Black:White Ratios Related to HTN, USA 2010-15

• Hypertension Prevalence Rates: 1.50
• Hypertension-related Death Rates: 2.43
• Stroke Death Rates: 1.40
• Heart Disease Death Rates: 1.27
• Kidney Disease Death Rates: 2.09
• Crude ESRD Incidence Rates: 2.46
• Crude ESRD Prevalence Rates: 3.05
• Gender-Adjusted ESRD Incidence: 3.36
• Gender-Adjusted ESRD Prevalence: 4.00
Outcomes in Treated Hypertensive Subjects Differ With Different Therapies in Different Racial/Ethnic Groups
cf. ALLHAT

Cumulative Event Rates for Combined CVD by ALLHAT Treatment Group

"Combined CVD" = fatal or nonfatal MI, CABG, PCTA, hospitalized angina, stroke, HF, PVD procedure

JAMA. 2002;288:2981-2997

Combined CVD – Subgroup Comparisons – RR (95% CI)

JAMA. 2002;288:2981-2997
Cumulative Event Rates for Stroke by ALLHAT Treatment Group

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>RR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/C</td>
<td>0.93 (0.81-1.06)</td>
<td>0.28</td>
</tr>
<tr>
<td>L/C</td>
<td>1.15 (1.02-1.30)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Number at risk:
- Chlor: 15,255 14,515 13,934 13,309 11,570 6,385 3,217 567
- Amlo: 9,048 8,617 8,271 7,949 6,937 3,845 1,813 506
- Lisin: 9,054 8,543 8,172 7,784 6,765 3,891 1,828 949

Cumulative Event Rates for Stroke by ALLHAT Treatment Group

<table>
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<tr>
<th>ALLHAT Treatment Group</th>
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<tr>
<td>L/C</td>
<td>1.15 (1.02-1.30)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Adverse Effects: ACE-Inhibitors

- Discontinuation due to cough is 2-4 times more common in blacks and Asians than in whites.
- Angioedema is about 2-5 times more common in blacks compared to whites.

In ALLHAT:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Blacks</th>
<th>Non-blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorothalidone</td>
<td>2 / 5,369 (&lt;0.1%)</td>
<td>6 / 9,886 (0.1%)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>23 / 3,210 (0.7%)</td>
<td>15 / 5,844 (0.3%)</td>
</tr>
</tbody>
</table>

p<.001 p=.002

BP Drugs & Race/Ethnicity

- African Americans (as a group) have a very high risk of hypertension, and suffer more of its consequences.
- In ALLHAT, the largest clinical trial ever done in African Americans, those given initial lisinopril had worse outcomes (combined CV events, stroke) than those given chlorthalidone.
- African Americans given chlorthalidone had similar outcomes as nonblacks given chlorthalidone.
- Nonblacks given lisinopril had similar outcomes to nonblacks given chlorthalidone or amlodipine.
- ARBs are assumed to have a similar profile as ACE-Is.
- ACE-inhibitors have a higher risk of angioedema or cough in African Americans and Asians than in whites.


Conclusions

- JNC 7 was the last federally-supported set of US hypertension guidelines, but it was issued in 2003.
- JNC 8 used rigorous methods to answer only 3 questions, and its recommendations were not supported by any organization or entity.
- The ADA guidelines pertain only to diabetics.
- The NKF guidelines pertain only to those with chronic kidney disease, and is influenced by studies that provide reduced rates of CKD.

Conclusions

- The ACC/AHA 2017 US Hypertension Guideline breaks new ground:
  - Threshold for diagnosis of hypertension is lower.
  - Classification of BP is different (more aggressive).
  - Lifestyle modifications are emphasized; only about 2% more people will need drug therapy.
  - Drug treatment decision for Stage 1 hypertension is now based on the 10-year CV risk score.
  - Goal BP is different (and lower) for many people.
- The ACC/AHA 2017 US Hypertension Guideline is controversial; some groups (ABFP, ACP) have stated that they will not support it.