Management of Hypertension

2015 Georgia Chapter ACP Scientific Meeting
John J. White, MD FASN
Disclosures

• Co-I NHLBI
  – “Stress Related Mechanisms of Hypertension”
• Co-I NIDDK
  – “Red Blood Cell Pathology in Hemodialysis”
Goals & Objectives

At the end of presentation, learners should be able to:

• Describe the basic epidemiology and importance of hypertension
• Discuss current evidence-based management guidelines including limitations
• Apply evidence-based guidelines into practice
• Give High Value Care to their patients
ARS Q1. Which of the following is associated with the highest Global Burden of Disease?

A. Air Pollution
B. Low Child Birthweight
C. HIV
D. Hypertension
E. Smoking

![Bar chart showing percentages]
Global DALYs Attributable to the 25 Leading Risk Factors in 1990 and 2010.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>2010 Rank</th>
<th>DALYs (95% UI) in thousands</th>
<th>1990 Rank</th>
<th>DALYs (95% UI) in thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure</td>
<td>1</td>
<td>173,556 (155,939–189,025)</td>
<td>4</td>
<td>137,017 (124,360–149,366)</td>
</tr>
<tr>
<td>Tobacco smoking, including exposure to second-hand smoke</td>
<td>2</td>
<td>156,838 (136,543–173,057)</td>
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<td>Household air pollution from solid fuels</td>
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<tr>
<td>Diet low in fruit</td>
<td>4</td>
<td>104,095 (81,833–124,169)</td>
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<td>80,453 (63,298–95,763)</td>
</tr>
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<td>Alcohol use</td>
<td>5</td>
<td>97,237 (87,087–107,658)</td>
<td>8</td>
<td>73,715 (66,090–82,089)</td>
</tr>
<tr>
<td>High body-mass index</td>
<td>6</td>
<td>93,609 (77,107–110,600)</td>
<td>10</td>
<td>51,565 (40,786–62,557)</td>
</tr>
<tr>
<td>High fasting plasma glucose level</td>
<td>7</td>
<td>89,012 (77,743–101,390)</td>
<td>9</td>
<td>56,358 (48,720–65,030)</td>
</tr>
<tr>
<td>Childhood underweight</td>
<td>8</td>
<td>77,316 (64,497–91,943)</td>
<td>1</td>
<td>197,741 (169,224–238,276)</td>
</tr>
<tr>
<td>Exposure to ambient particulate-matter pollution</td>
<td>9</td>
<td>76,163 (68,086–85,171)</td>
<td>6</td>
<td>81,699 (71,012–92,859)</td>
</tr>
<tr>
<td>Physical inactivity or low level of activity</td>
<td>10</td>
<td>69,318 (58,646–80,182)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Diet high in sodium</td>
<td>11</td>
<td>61,231 (40,124–80,342)</td>
<td>12</td>
<td>46,183 (30,363–60,604)</td>
</tr>
<tr>
<td>Diet low in nuts and seeds</td>
<td>12</td>
<td>51,289 (33,482–65,959)</td>
<td>13</td>
<td>40,525 (26,308–51,741)</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>13</td>
<td>48,225 (33,769–67,592)</td>
<td>11</td>
<td>51,841 (37,477–71,202)</td>
</tr>
<tr>
<td>Suboptimal breast-feeding</td>
<td>14</td>
<td>47,537 (29,868–67,518)</td>
<td>5</td>
<td>110,261 (69,615–153,539)</td>
</tr>
<tr>
<td>High total cholesterol level</td>
<td>15</td>
<td>40,900 (31,662–50,484)</td>
<td>14</td>
<td>39,526 (32,704–47,202)</td>
</tr>
<tr>
<td>Diet low in whole grains</td>
<td>16</td>
<td>40,762 (32,112–48,486)</td>
<td>18</td>
<td>29,404 (23,097–35,134)</td>
</tr>
<tr>
<td>Diet low in vegetables</td>
<td>17</td>
<td>38,559 (26,006–51,658)</td>
<td>16</td>
<td>31,558 (21,349–41,921)</td>
</tr>
<tr>
<td>Diet low in seafood n-3 fatty acids</td>
<td>18</td>
<td>28,199 (20,624–35,974)</td>
<td>20</td>
<td>21,740 (15,869–27,537)</td>
</tr>
<tr>
<td>Drug use</td>
<td>19</td>
<td>23,810 (18,780–29,246)</td>
<td>25</td>
<td>15,171 (11,714–19,369)</td>
</tr>
<tr>
<td>Occupational risk factors for injuries</td>
<td>20</td>
<td>23,444 (17,736–30,904)</td>
<td>21</td>
<td>21,265 (16,644–26,702)</td>
</tr>
<tr>
<td>Occupation-related low back pain</td>
<td>21</td>
<td>21,750 (14,492–30,533)</td>
<td>23</td>
<td>17,841 (11,846–24,945)</td>
</tr>
<tr>
<td>Diet high in processed meat</td>
<td>22</td>
<td>20,939 (6982–33,468)</td>
<td>24</td>
<td>17,359 (5137–27,949)</td>
</tr>
<tr>
<td>Intimate-partner violence</td>
<td>23</td>
<td>16,794 (11,373–23,087)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Diet low in fiber</td>
<td>24</td>
<td>16,452 (7401–25,783)</td>
<td>26</td>
<td>13,347 (5970–20,751)</td>
</tr>
<tr>
<td>Lead exposure</td>
<td>25</td>
<td>13,936 (11,750–16,327)</td>
<td>31</td>
<td>5,365 (4534–6279)</td>
</tr>
</tbody>
</table>

Global DALYs Attributable to the 25 Leading Risk Factors in 1990 and 2010.

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Iron deficiency, Suboptimal breast-feeding, High total cholesterol level, Diet low in whole grains, Diet low in vegetables, Diet low in seafood n-3 fatty acids, Drug use, Occupational risk factors for injuries, Occupation-related low back pain, Diet high in processed meat, Intimate-partner violence, Diet low in fiber, Lead exposure.
CV Mortality Risk Doubles with Each 20/10 mm Hg BP Increment*

CV mortality risk

SBP/DBP (mm Hg)

115/75
135/85
155/95
175/105

CV: Cardiovascular
Lancet. 2002; 60:1903-1913.
JNC VII. JAMA. 2003.
Every Millimeter of Blood Pressure Reduction Counts

Each 10-14 mm Hg

Each 5-6 mm Hg

17%

33%

40%

J HTN 1999;17:151-183
Hypertension Statistics 2013

• Prevalence: 74,500,000 (1:3)
• Controlled ~ 50% (JAMA 2010;303:2043)
• Resistant HTN ~ 30%
• $ 46 Billion/yr
• Mortality data 2013
  • HTN contributed to 360,000 deaths
  • 1,000/day

www.CDC.gov
ICD-10 Codes

- R14.3 Flatulence causing injury
- V97.33XD Sucked into jet engine, sub encounter
- V91.07XA Burn due to water-skis on fire, initial encounter
- W61.62XD Stuck by duck, sub encounter
- W22.02XD Walked into lamppost, sub encounter
- Z6311 Problems in relationship with in-laws
Accurate Diagnosis Requires Correct Measurement

- Office BP inaccurate
- White coat HTN
  - 15-30% of patients
- Masked HTN
  - 10% of patients
- US Preventive Services Task Force 2015
  - Proposes out-of-office BP measurements (ABPM or standardized home BP measurements) to confirm office findings
# BP Measurement: Key Techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest ≥ 5 min, quiet</td>
<td>↑ 12/6</td>
</tr>
<tr>
<td>Seated, back supported</td>
<td>↑ 6/8</td>
</tr>
<tr>
<td>Cuff at midsternal level</td>
<td>↑ ↓ 2/inch</td>
</tr>
<tr>
<td>Correct cuff size</td>
<td>↑ 6-18/4-13 if too small</td>
</tr>
<tr>
<td>Bladder center over artery</td>
<td>↓ 7/5 if too large</td>
</tr>
<tr>
<td>Deflate 2 mm Hg/sec</td>
<td>↑ 3-5/2-3</td>
</tr>
<tr>
<td>No talking during measurement</td>
<td>↓ SBP/↑ DBP</td>
</tr>
<tr>
<td>If initial BP &gt; goal BP:</td>
<td></td>
</tr>
<tr>
<td>3 readings, 1 min apart</td>
<td>1st reading higher</td>
</tr>
<tr>
<td>Discard 1st, average last 2</td>
<td>• “Alerting response”</td>
</tr>
<tr>
<td></td>
<td>• Reclassify 18-34% as normotensive</td>
</tr>
<tr>
<td></td>
<td>• Requires 8-11 minutes!</td>
</tr>
</tbody>
</table>

References:
- J Clin Hypertens 2012;14:751
- Hypertension 2005; 45:142
- J Gen Int Med 2012; 27:623
- J Hypertens 2005; 23:697
- Can J Card 2014; 30:485
Although home blood pressure monitors are usually not reimbursed by insurers, their relatively low cost (usually less than $100) and reasonable accuracy have made them attractive components to the management of hypertension.
# Lifestyle Modifications to Manage Hypertension

<table>
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<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>SBP Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5-24.9)</td>
<td>5-20 mm Hg/10-kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8-14 mm Hg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)</td>
<td>2-8 mm Hg</td>
</tr>
</tbody>
</table>

*JAMA* 2003; 289:2560-2572.
## Lifestyle Modifications to Manage Hypertension

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<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>SBP Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 min/d)</td>
<td>4-9 mm Hg</td>
</tr>
<tr>
<td>Moderation of Alcohol Consumption</td>
<td>Limit consumption to no more than 2 drinks/d in most men and no more than 1 drink/d in women and lighter-weight persons</td>
<td>2-4 mm Hg</td>
</tr>
</tbody>
</table>

*JAMA 2003; 289:2560-2572.*
Lifestyle modifications, including weight loss, reduction of dietary sodium intake, aerobic physical activity of at least 30 minutes a day at least three times a week, and a reduction in alcohol consumption, are a relatively cost-effective way to reduce high blood pressure.
Level of Evidence for Alternative Tx

<table>
<thead>
<tr>
<th>Alternative Treatments</th>
<th>Level of Evidence</th>
<th>Class of Evidence Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral therapies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transcendental meditation</td>
<td>B</td>
<td>II B</td>
</tr>
<tr>
<td>Other meditation techniques</td>
<td>C</td>
<td>III (no benefit)</td>
</tr>
<tr>
<td>Biofeedback approaches</td>
<td>B</td>
<td>II B</td>
</tr>
<tr>
<td>Yoga</td>
<td>C</td>
<td>III (no benefit)</td>
</tr>
<tr>
<td>Other relaxation techniques</td>
<td>B</td>
<td>III (no benefit)</td>
</tr>
<tr>
<td>Noninvasive procedures or devices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acupuncture</td>
<td>B</td>
<td>III (no benefit)</td>
</tr>
<tr>
<td>Device-guided breathing</td>
<td>B</td>
<td>II A</td>
</tr>
<tr>
<td>Exercise-based regimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamic aerobic exercise</td>
<td>A</td>
<td>I</td>
</tr>
<tr>
<td>Dynamic resistance exercise</td>
<td>B</td>
<td>II A</td>
</tr>
<tr>
<td>Isometric handgrip exercise</td>
<td>C</td>
<td>II B</td>
</tr>
</tbody>
</table>

Hypertension 2013;61:1360
Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

JAMA 2014;311:507
Recommendation #1

1. “General population” >= 60 years, initiate treatment to lower BP at >= 150/90 mmHg

If treatment for high BP results in lower SBP (i.e. < 140 mmHg) and treatment is well-tolerated and without adverse effects on health or quality of life, treatments does not need to be adjusted
Recommendation #2/3

2. “General Population” < 60 years, initiate treatment to lower BP at DBP > 90 mmHg

3. “General Population” < 60 years, initiate treatment to lower SBP < 140 mmHg
The Elderly

- HTN as high as 60 to 80%
- ISH = BP > 160/90
- CV events increases with increased SBP & PP
  - Problem of J curve
- SHEP trial
- Syst-Eur trial
- MRC trial
- HYVET
HYVET

• 3845 pts > 80 (84) BP 173/91
• Indapamide (+perindopril) vs placebo
• BP target 150/80
  – 143/78 vs 158/84
• Stroke (12.4 vs 17.7% p < 0.06)
• Fatal stroke (6.5 vs 10.7%)
• Death (47.2 vs 59.6%)
Recommendation #4/5

• 4. Population with **CKD** initiate and treat to lower BP at 140/90 mmHg

• 5. Population with **diabetes** initiate and treat to lower BP at 140/90 mmHg
BP and Mortality in US Veterans with CKD

SBP 130-160 & Diastolic BP 70-90 associated with lowest mortality risk
Strict vs Conventional BP Control in CKD Associate with Worse Survival
ESRD

- Up to 85% with HTN
- Dialysis BP misleading
  - Post SBP may reflect interdialytic BP
  - Home BP > 150 more accurate
  - Best prognosis SBP 125-145
- Targets controversial
  - Mortality increases < 110 and > 180
<table>
<thead>
<tr>
<th>Pre-SBP &lt; 140</th>
<th>Frequency %</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>18.4</td>
<td>1.0</td>
</tr>
<tr>
<td>0-25%</td>
<td>41.9</td>
<td>1.20 [1.09-1.32]</td>
</tr>
<tr>
<td>25-75%</td>
<td>21.5</td>
<td>1.40 [1.26-1.54]</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>18.2</td>
<td>1.90 [1.73-2.10]</td>
</tr>
</tbody>
</table>

N = 13,792

*J Am Soc Nephrol 2007;18:2377*
6. General **non-black population (including diabetes)**—initial treatment should include a thiazide diuretic, calcium channel blocker, ACE-inhibitor, or ARB

7. General **black population (including diabetes)**—initial treatment should include a thiazide diuretic or calcium channel blocker

8. Population with **CKD**, initial or add-on therapy should include and ACEI or ARB to improve kidney outcomes regardless of race or diabetes.
Proportion of US Adults Affected by the 2014 Hypertension Guideline

![Bar chart showing the proportion of US adults affected by the 2014 hypertension guideline for different categories: Treatment Eligible and BP at Goal for all adults, adults 18-59 y, and adults ≥60 y. The chart includes the number of NHANES participants and total participants for each category.](chart.png)
Cost-Effectiveness of HTN Therapy According to 2014 Guidelines

**Groups without Prior Cardiovascular Disease**

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 2 hypertension</td>
<td>Stage 2 hypertension, diabetes or CKD</td>
</tr>
<tr>
<td></td>
<td>Stage 1 hypertension, no diabetes or CKD</td>
<td>Stage 1 hypertension, diabetes or CKD</td>
</tr>
<tr>
<td>33–44 Yr</td>
<td>Cost-saving</td>
<td>Cost-saving</td>
</tr>
<tr>
<td></td>
<td>$13,000</td>
<td>$26,000</td>
</tr>
<tr>
<td>45–59 Yr</td>
<td>Cost-saving</td>
<td>Cost-saving</td>
</tr>
<tr>
<td></td>
<td>$40,000</td>
<td>$125,000</td>
</tr>
<tr>
<td>60–74 Yr</td>
<td>Cost-saving</td>
<td>Cost-saving</td>
</tr>
<tr>
<td></td>
<td>$3,000</td>
<td>$7,000</td>
</tr>
</tbody>
</table>

**NEJM 2015;372:447**
# Comparison of HTN Guidelines 2011-2014

<table>
<thead>
<tr>
<th></th>
<th>NICE’11</th>
<th>ESH/ESC ’13</th>
<th>ASH/ISH ’14</th>
<th>AHA/ACC/ CDC ’13</th>
<th>JNC 8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>&gt;140/90</td>
<td>&gt;140/90</td>
<td>&gt;140/90</td>
<td>&gt;140/90</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Start Tx</strong></td>
<td>&gt;160/100</td>
<td>&gt;140/90</td>
<td>&gt;140/90</td>
<td>&gt;140/90</td>
<td>&lt;60 y &gt;140/90 &gt;60 y &gt;150/90</td>
</tr>
<tr>
<td><strong>B-blockers</strong></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Diuretic</strong></td>
<td>CLTD Indapamide</td>
<td>Thiazides,CLTD, Indapamide</td>
<td>Thiazides,CLTD, Indapamide</td>
<td>Thiazides</td>
<td>Thiazides,CLTD, Indapamide</td>
</tr>
<tr>
<td><strong>Start 2 Drugs</strong></td>
<td>NA</td>
<td>Marked HTN</td>
<td>&gt;160/100</td>
<td>&gt;160/100</td>
<td>&gt;160/100</td>
</tr>
<tr>
<td><strong>BP targets</strong></td>
<td>&lt;140/90 &gt;80 y &lt;150/90&lt;150 systolic in fragile elderly &gt;80 y &lt;150/90 Consider &lt;130/80 if tolerated</td>
<td>&lt;140/90 &gt;80 y &lt;150/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90 &gt;60 y &lt;140/90 &gt;60 y &lt;150/90</td>
<td></td>
</tr>
<tr>
<td><strong>DM/CKD</strong></td>
<td>NA</td>
<td>&lt;140/85</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
</tr>
</tbody>
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*KDIGO ‘12 – BP < 130/80 with proteinuria; ADA ‘13 - BP < 140/80, consider < 130
Beta-blockers

• Use after MI or rate control with atrial fibrillation (afib)
• SHOULD NOT BE 1st line drug for BP control
  – higher risk of CVA in smokers
  – higher risk of CAD and all CV events
  – higher risk of mortality with atenolol
  – Impaired glucose tolerance
• Vasodilating beta-blockers carvedilol and nebivolol probably OK
ICD-10 Codes cont.

- R46.0 Very low level personal hygiene
- R46.1 Bizarre personal appearance
- T505x6A Underdosing of appetite depressants, initial encounter
- W56.22XA Struck by orca, initial encounter
- W55.41XA Bitten by pig, initial encounter
- W60.XXXS Contact with Sharp Leaves
Effects of Dietary Sodium Reduction on Blood Pressure in Subjects With Resistant Hypertension: Results From a Randomized Trial
Eduardo Pimenta, Krishna K. Gaddam, Suzanne Oparil, Inmaculada Aban, Saima Husain, Louis J. Dell'Italia and David A. Calhoun
Δ20/10 mmHg

Hypertension 2009;54:375
Efficacy of BP Meds

White

Black
<table>
<thead>
<tr>
<th>Comparison</th>
<th>No of events/patients</th>
<th>Difference in SBP/DBP (mm Hg)</th>
<th>Risk ratio (95% CI)</th>
<th>Risk ratio (95% CI)</th>
<th>P for homogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angiotensin converting enzyme inhibitor v</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diuretic or β blocker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;65</td>
<td>819/9448</td>
<td>1066/12 012 1.3/0.1</td>
<td>1.05 (0.96 to 1.14)</td>
<td></td>
<td>0.44</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>1795/10 783</td>
<td>2525/14 429 2.0/0.5</td>
<td>1.01 (0.95 to 1.06)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Calcium antagonist v diuretic or β blocker</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;65</td>
<td>1165/20 358</td>
<td>1430/23 236 1.1/-0.2</td>
<td>1.06 (0.98 to 1.14)</td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>2653/21 204</td>
<td>3363/24 981 0.5/-0.4</td>
<td>1.02 (0.97 to 1.06)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Angiotensin converting enzyme inhibitor v</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>calcium antagonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;65</td>
<td>548/5130</td>
<td>568/4919 0.9/0.6</td>
<td>0.91 (0.78 to 1.06)</td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>1583/8170</td>
<td>1608/8140 1.0/1.0</td>
<td>0.98 (0.92 to 1.05)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ALLHAT

• 41,000 participants BP 146/84
• CLTD vs amlodipine vs lisinopril vs doxasosin
  – Doxasosin arm d/c’d re: CHF
• Mean f/u 4.9 years
• BP similar though slightly lower CLTD
• No difference in primary end point
• CLTD lower rate of CHF
• CLTD less CVD events compared to lisinopril
Thiazide vs Thiazide Like Diuretics

• Thiazides
  – HCTZ, chlorothiazide, trichlormethiazide, bendrofluazide

• Thiazide-Like
  – indapamide, chlorthalidone, metolazone
    • Longer half-life
    • Better 24 hour BP
    • Experiments reduce platelet aggregation and vascular permeability
Meta-Analysis Highlights Superiority of Thiazide-Like Diuretics

A. Cardiovascular events
- Thiazide-type, $R^2 = 0.59$
- Thiazide-like, $R^2 = 0.57$

B. Heart failure
- Thiazide-type, $R^2 = 0.40$
- Thiazide-like, $R^2 = 0.39$

12%RR
21%RR

Hypertension 2015;65:1033
ICD-10 Codes Cont.

- W56.52 Struck by other fish
- Y92241 Hurt at the library
- Y92146 Hurt at swimming pool of prison as the place of occurrence
- Y92.022 Bathroom in mobile home as place of injury
- W5803XA Crushed by alligator, initial encounter
Systemic Based Strategies Improve Hypertension Control Rates

• Kaiser Permanente Southern California
  – Comprehensive hypertension program in 2000
  – Captured hypertensive members using hypertension registry
  – Standardized blood pressure measurements
  – Drafted & disseminated a treatment algorithm
  – Multidisciplinary approach utilizing medical assistants, nurses, and pharmacists
ACE-Inhibitor^2 / Thiazide Diuretic

Lisinopril / HCTZ
(Advance as needed)
20 / 25 mg X ½ daily
20 / 25 mg X 1 daily
20 / 25 mg X 2 daily

Pregnancy Potential: Avoid ACE-Inhibitors^2

If not in control

Calcium Channel Blocker
Add amlodipine 5 mg X ½ daily → 5 mg X 1 daily → 10 mg daily

If not in control

Beta-Blocker OR Spironolactone
Add atenolol 25 mg daily → 50 mg daily (Keep heart rate > 55)
OR
IF on thiazide AND eGFR ≥ 60 mL/min/1.73m^2 AND K < 4.5
Add spironolactone 12.5 mg daily → 25 mg daily

Thiazide Diuretic
Chlorthalidone 12.5 mg → 25 mg
OR
HCTZ 25 mg → 50 mg
Marked Improvement in BP Control Rates Over Short Period of Time!

- 2004: 54% controlled, 46% uncontrolled
- 2005: 64% controlled, 36% uncontrolled
- 2006: 71% controlled, 29% uncontrolled
- 2007: 97% controlled, 3% uncontrolled
- 2008: 75% controlled, 25% uncontrolled
- 2009: 66% controlled, 34% uncontrolled
- 2010: 61% controlled, 39% uncontrolled
ARS Q2. 52 yo WF in follow-up for continued adjustment of BP meds. She has stable CAD and quit smoking 4 years ago. You started lisinopril two visits ago. Last visit, you increased lisinopril to 40 mg daily. BMI is 23.2 kg/m2. BP is 151/86 mmHg.
ARS Q2. Which of the following is the most appropriate next step in treating this patient’s hypertension?

0% A. Increase lisinopril to 80 mg daily (max dose)
23% B. Add hydrochlorothiazide
1% C. Discontinue lisinopril and start metoprolol
15% D. Add amlodipine
60% E. Add chlorthalidone
"OPTIMAL" 2-DRUG RX: GENERAL HTN POPULATION

ASH, 2014

- Effectively ↓ BP, ↓ CVD events, ↓ side effects

\[ \downarrow \text{ACE-I (ARB) } \oplus \text{ Thiazide} \]

- ↓ BP additively, many studies
- ↓ CVD in RCTs: HYVET, PROGRESS, ADVANCE
- ↓ hypokalemia

\[ \downarrow \text{ACE-I (ARB) } \oplus \text{ CCB (amlodipine)} \]

- ↓ BP additively, many studies
- ↓ CVD in RCTS: ASCOT, ACCOMPLISH
- ↓ CCB-induced edema

ACCOMPLISH RCT, 2008: 11,056 high CVD risk pts x 36 mo

ACE-I ⊕ Thiazide vs ACE-I ⊕ Amlodipine
- ACE-I ⊕ amlodipine ↓ CVD events 20%, CKD by 48%

ACCOMPLISH trial

• 11,506 patients, 97% on 2+ drugs, BP 145/80
• Benazepril/Amlodipine vs Amlodipine/HCTZ
• DSMB stopped at 3 years
• CV composite end point
  – 9.6 vs 11.8% HR 0.8
• Doubling SCr
  – 2.0 vs 3.7%
AHA Guidelines Resistant HTN

1. Confirm Treatment Resistance
2. Exclude Pseudoresistance
3. Identify & Reverse Lifestyle Factors
4. Discontinue Interfering Substances
5. Screen for Secondary HTN
6. Pharmacological Treatment
7. Refer to Specialist

Hypertension 2008;51:1403
Low-Dose Spironolactone in Resistant Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Ouzan</th>
<th>Mahmud</th>
<th>Nishizaka</th>
<th>Chapman</th>
<th>Lane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction (mmHg)</td>
<td>-24</td>
<td>-28</td>
<td>-25</td>
<td>-22</td>
<td>-22</td>
</tr>
</tbody>
</table>

Blood pressure reduction in millimeters of mercury (mmHg)
Meta-Analysis: Aldosterone antagonists for RHTN (2640 pts)

- 3 RCTs
  - 135 pts
- 10 Observational Studies
  - 2208 pts

- Mean BP – 17/4
  - SBP – 16.5 (CI -3 to -30)
- Mean BP – 20/9
  - SBP – 19.7 (CI -16 to -23)

- Mild increase(s)
  - S Creatinine
  - S Potassium

*J Hum Hypertens 2015;29:159*
ARS Q3. A 52 yo WM with hypertension, diabetes, and OSA presents for routine follow-up. His medications are metformin, lisinopril, amlodipine, simvastatin, and HCTZ. BP is 136/82 BMI 34.5. PE and labs are otherwise unremarkable, last HbA1c 7.1%
ARS Q3. Which of the following should be considered to decrease CV risk?

A. Discontinue metformin and start insulin glargine 0.25U/kg - 4%

B. Discontinue lisinopril and add carvedilol - 16%

C. Change lisinopril dosing to bedtime - 24%

D. Change simvastatin to atorvastatin - 24%

E. Refer for bariatric surgery - 33%
Timing of Blood Pressure Dosing

• Biology of humans is rhythmic over 24 h
• BP exhibits 24 h variation
  – Circadian rhythms
    • Neural, endocrine, endothelial, ANS, RAAS
  – Cyclical Day-Night Alterations in Behavior
    • Physical activity, mental stress, posture, environment
• Net effect
  – Higher BP during day, Dip in BP at night
Circadian Dosing

Mesor values for systolic and diastolic blood pressure before and after intervention:

- **Before Intervention:**
  - Systolic: 135.8
  - Diastolic: 78.0
  - p-value for comparison of Mesor: 0.770
  - Amplitude: 0.422

- **After Intervention:**
  - Systolic: 138.4
  - Diastolic: 80.9
  - p-value for comparison of Mesor: <0.001
  - Amplitude: <0.001
MAPEC Study

- RCT 2156 HTN patients
- All meds AM vs ≥ 1 PM
- ABPM
- F/U 5.6 years
- Better BP control
- Inc Dipping Pattern
- Reduced CV Events

*Chronobiol Int* 2010;27:1629
Circadian Dosing RHTN

- RCT 776 patients
  - RHTN
  - 61 yoa
- All meds AM vs ≥ 1 PM
- 48 hr ABPM
- Mean f/u 5.4 yrs
- HR 0.38 (102 v 41 events)
- Night SBP 121 vs 113
- Control ABP 46% vs 61%

Chronobiol Int 2013;30:340
Chronotherapy in Other Diseases

661 CKD patients

Composite of death, MI, CP, PCI, CHF, PAD, CVA was 1/3 of controls HR 0.31 (0.21-0.46)

JASN 2011;22:2313

448 DM type 2 patients

CV related death, MI, and CVA reduced to ¼ of controls HR 0.25 (0.10-0.61)

Diabetes Care 2011;34:1270
Effect on Sleep-time Relative BP Decline

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Awakening Rx</th>
<th>Bedtime Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-Is</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>ARBs</td>
<td>=</td>
<td>↑</td>
</tr>
<tr>
<td>CCBs</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>↓</td>
<td>=</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>=</td>
<td>↑</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>↓</td>
<td>=</td>
</tr>
</tbody>
</table>
ARS Q4. 39 yo AAF presents for eval after worksite screening examination found elevated blood pressure. She is asymptomatic and takes no medications. Serial BP measurements in office and at home average 155/96. Physical examination is normal. CBC, electrolytes, FLP, glucose, urinalysis, ECG are all normal.
ARS Q4. Which one of the following is most appropriate for management?

A. Plasma metanephrines
B. Renal Doppler US of kidneys to assess size and blood flow
C. 2D echocardiography
D. Plasma aldosterone and renin activity
E. No further diagnostic testing

2% 11% 77% 11% 0%
Only consider evaluating for secondary causes of hypertension when there is onset at a young age, no family history, no risk factors, rapid onset of significant hypertension, abrupt change in blood pressure in a patient with previously good control, or a concomitant endocrine abnormality.
### Secondary Causes of Resistant HTN

<table>
<thead>
<tr>
<th>Common</th>
<th>Uncommon</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Hyperaldosteronism</td>
<td>Cushing’s disease</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>Renal Artery Stenosis</td>
<td>Aortic coarctation</td>
</tr>
<tr>
<td></td>
<td>Intracranial tumor</td>
</tr>
</tbody>
</table>
Screening for Endocrine Hypertension

Triggers for endocrine investigation in hypertension

Family history

- Pheochromocytoma
- Neurofibromatosis
- Multiple endocrine neoplasia
- Aldosteronism

Refactory hypertension: high blood pressure resistant to 2–3 drugs

- Consider
  - Iatrogenic source
  - Noncompliance with medication
  - Renal/renovascular disease
  - Endocrine disorder
  - Measure
    - Serum electrolytes – Na+/K+
    - Urinalysis
    - Aldosterone/plasma renin activity (PRA)
    - Catecholamines
    - Consider renal angiography

Hypokalemia: persistent? K⁺ wasting? (i.e., >30 mmol/24 h excreted when plasma K⁺ <3.5 mmol/l)

- Consider
  - Iatrogenic (diuretics, licorice)
  - Accelerated primary hypertension
  - Aldosteronism
  - Pseudoaldosteronism
  - Cushing's syndrome
  - Renin-producing tumor
  - Liddle syndrome

Symptoms/signs

- ?Pheochromocytoma
  - Hyperadrenergic: sweating
- ?Thyroid
  - Change in:
    - Temperature tolerance
    - Weight
    - Skin/hair
    - Bowel habit
    - Eyes
    - Tremor
    - Sweating
- ?Acromegaly
  - Size of face/hands/feet
  - Sweating
  - ?Cushing's syndrome
  - Striae, acne, central weight gain

Hyperglycemia

- Diabetic nephropathy
- Cushing's syndrome
- Pheochromocytoma
- Acromegaly
Primary Aldosteronism is Common

Horm Met Res 2012;44:157
Update: Diagnosis of PA

- Best screening test: aldosterone-renin ratio (ARR)
- Many drugs affect results
  - No DRIs or aldosterone antagonists
  - Sertraline & escitalopram
    - Inc renin (marked) + inc aldosterone (slight) = net reduction in ARR
- High ARR
  - PA 30 to 50%
- Considerations
  - Further work-up with possible surgery
  - Trial of MRA without screening
  - Avoid biochemical and imaging tests
  - Avoid invasive adrenal vein sampling and surgery
Central arteriovenous anastomosis for the treatment of patients with uncontrolled hypertension (the ROX CONTROL HTN study): a randomised controlled trial

Creation iliac AVF lowers BP?

Lancet 2015; 385: 1634-41
• SPRINT HTN Trial
• Open-label RCT 9361 pts age 50+ with SBP > 130 & one additional CV risk factor
• Intensive SBP < 120 vs Conventional SBP < 140
• DSMB Stopped Early
  – Decreased CVEs 30%
  – Decreased Death 25%
Start Here: Begin with 2 or 3 drug therapy* using a combination of a thiazide-type diuretic**, and/or an ACEI or ARB (but not both) and/or a CCB. Include a β-blocker or other agents as appropriate for compelling indication.

Treatment Algorithm for the SPRINT Intensive Group Systolic Blood Pressure (SBP) Goal < 120 mm Hg

- Is SBP <120mm Hg at this visit?
  - No
  - A. Titrate or Add Therapy Not Already in Use**
    - AND
    - B. See patient monthly until SBP <120mm Hg
  - Yes

- Is DBP ≥100 mm Hg at this visit or is DBP ≥90 mm Hg at last 2 visits?
  - Yes
    - Titrate or Add Therapy Not Already in Use**
  - No
    - Continue Therapy^
## Results Achieved with Cheap Generics

### Table 5.1 SPRINT Formulary

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Available Strengths</th>
<th>Usual Dose Range / day</th>
<th>Usual Daily Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>Chlorthalidone</td>
<td>25mg</td>
<td>12.5-25 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Furosemide</td>
<td>20mg, 40mg, 80mg</td>
<td>20-80 mg</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Spironolactone</td>
<td>25mg</td>
<td>25-50 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Triamterene/HCTZ</td>
<td>75/50mg</td>
<td>37.5/25 mg – 75/50 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Amiloride</td>
<td>5mg</td>
<td>5-10 mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Ace Inhibitor</td>
<td>Lisinopril</td>
<td>5mg, 10mg, 20mg, 40mg</td>
<td>5-40 mg</td>
<td>1</td>
</tr>
<tr>
<td>Angiotensin Receptor Blocker</td>
<td>Losartan</td>
<td>25mg, 50mg, 100mg</td>
<td>25 – 100 mg</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Azilsartan</td>
<td>40mg, 80mg</td>
<td>40-80 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Azilsartan/chlorthalidone</td>
<td>40/12.5mg, 40/25mg</td>
<td>40/12.5 – 40/25 mg</td>
<td>1</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td>Diltiazem</td>
<td>120mg, 180mg, 240mg, 300mg</td>
<td>120-540 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Amlodipine</td>
<td>2.5mg, 5mg, 10mg</td>
<td>2.5-10 mg</td>
<td>1</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>Metoprolol Tartate</td>
<td>25mg, 50mg, 100mg</td>
<td>50-200 mg</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Atenolol</td>
<td>25mg, 50mg, 100mg</td>
<td>25-100 mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Atenolol/Chlorthalidone</td>
<td>50/25mg</td>
<td>50/25 mg</td>
<td>1</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Hydralazine</td>
<td>25mg, 50mg, 100mg</td>
<td>50-200 mg</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Minoxidil</td>
<td>2.5mg, 10mg</td>
<td>2.5-80 mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Alpha 2 Agonist</td>
<td>Guanfacine</td>
<td>1mg, 2mg</td>
<td>0.5-2 mg</td>
<td>1</td>
</tr>
<tr>
<td>Alpha Blockers</td>
<td>Doxazosin</td>
<td>1mg, 2mg, 4mg, 8mg</td>
<td>1-16 mg</td>
<td>1</td>
</tr>
<tr>
<td>Potassium Supplements</td>
<td>KCL tablets</td>
<td>20mEq</td>
<td>20-80 mEq</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>KCL oral solution (10%)</td>
<td>20mEq/15ml</td>
<td>20-80 mEq</td>
<td>1-2</td>
</tr>
</tbody>
</table>
There is wide variability in the cost of antihypertensive medications; newer and more expensive agents have not been shown to be significantly safer or more effective than many older, well-established medications that are available in generic form.

Fixed combinations of antihypertensive medications offer less dosing flexibility and are often substantially more expensive than prescribing the component medications independently.
ICD-10 Codes cont.

- V0490XA Hit by a Mack Truck
- W22.01 Walked into wall, initial encounter
- Z621 Parental overprotection
- V96.00XS Unspecified balloon accident injuring occupant, sequela
- T63.442S Toxic effect of venom of bees, intentional self harm
Evaluation

- Please take < 90 seconds to evaluate this session.
- Time permitting, speaker will take questions following evaluation.
- Responses are not displayed and are important in maintaining high quality education.
The overall performance of the speaker:

1. Poor
2. Fair
3. Average
4. Good
5. Excellent

1. 76%
2. 23%
3. 1%
4. 0%
5. 0%
How well were the learning objectives met?

1. Poor
2. Fair
3. Average
4. Good
5. Excellent

- Poor: 0%
- Fair: 0%
- Average: 1%
- Good: 22%
- Excellent: 76%
Did speaker present a balanced view of therapeutic options?

1. Yes
2. No
3. N/A
How useful will this session be in your practice?

1. Poor
2. Fair
3. Average
4. Good
5. Excellent
As a result of this program, do you intend to change your patient care?

1. Yes
2. No

- Yes: 92%
- No: 8%
Thank you!