Hypertension Update 2014:
JNC 8 and more

Karol E. Watson, MD, PhD, FACC
Associate Professor of Medicine/Cardiology
Co-director, UCLA Program in Preventive Cardiology

Disclosures
- Research Grants:
  - NHLBI
  - NIDDK
- Clinical Trials Adjudication Committee:
  - Merck and Company

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)

JAMA. Published online December 18, 2013. doi:10.1001/jama.2013.284427

Important to Note...
- JNC 7 was "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure"
- JNC 8 is the “2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults"
- In JNC 8 they give 9 Evidence-based Recommendations
- “… these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”

Strength of Recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strong recommendation: There is high certainty based on evidence that the net benefit is substantial.</td>
<td>2</td>
</tr>
<tr>
<td>B</td>
<td>Moderate recommendation: There is moderate to high certainty based on evidence that the net benefit is moderate to substantial.</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>Weak recommendation: There is at least moderate certainty based on evidence that there is a small net benefit.</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Recommendation against: There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits.</td>
<td>0</td>
</tr>
<tr>
<td>E</td>
<td>Expert opinion: (There is insufficient evidence or evidence is unclear or conflicting.) Net benefit is unclear. Balances of benefits and harms cannot be determined because of no evidence, insufficient evidence, or conflicting evidence. The Panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area.</td>
<td>5</td>
</tr>
<tr>
<td>N</td>
<td>No recommendation for or against: (There is insufficient evidence or evidence is unclear or conflicting.) Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, or conflicting evidence. The Panel thought no recommendation should be made. Further research is recommended in this area.</td>
<td>0</td>
</tr>
</tbody>
</table>

Recommendation #1

1. In patients aged ≥60 years, initiate pharmacologic treatment in systolic BP ≥150mmHg or diastolic BP ≥90mmHg and treat to a goal systolic BP <150mmHg and goal diastolic BP <90mmHg. (Strong Recommendation – Grade A)

In other words: Ease up on Hypertension Treatment in Older Adults (60 years of age or older)
BP goal <150/90
HYVET Trial: Study Design

Prospective. Randomized. Double Blinded. Placebo-Controlled. Mean follow-up 1.8 yrs
3845 patients ≥ 80 years with HTN and systolic blood pressure ≥ 160 mmHg

Inclusion Criteria:
- Aged 80 or more
- Systolic BP: 160-199 mmHg
- Diastolic BP: <110 mmHg

Exclusion Criteria:
- Standing SBP < 140 mmHg
- Dementia, need for daily nursing care
- Stroke in last 6 months

Active Treatment
- 1.5 mg Indapamide SR (± perindopril)
- n=1933

Placebo Matching Dose
- n=1912

Target blood pressure
150/80 mmHg

Primary Endpoint: fatal and non-fatal strokes
Secondary Endpoints: death from: stroke, cardiovascular causes, cardiac causes and any cause

What??? You mean treating SBP ≥ 140 mmHg is only "Expert Opinion"

- Prior guidelines relied on epidemiologic evidence and observational studies that noted that the risks for cardiovascular events in untreated adults increased rapidly as SBP increased above 140 mm Hg
- Older trials actually used a DBP goal rather than a SBP goal
- The older trials that did use a SBP goal, targeted < 160
- So, direct RCT evidence to support this threshold is limited.

JNC 8 acknowledges this limitation

Recommendations #2 and #3

2. In patients aged <60 years, initiate pharmacologic treatment at DIASTOLIC BP ≥ 90mmHg and treat to a goal <90mmHg.
For ages 30–59 years, Strong Recommendation–Grade A
For ages 18–29 years, Expert Opinion–Grade E

3. In patients aged <60 years, initiate pharmacologic treatment at SYSTOLIC BP ≥ 140mmHg and treat to a goal <140mmHg.
Expert Opinion–Grade E

For Adults under 60 years of age
BP goal <140/90

There's strong evidence for treating high diastolic BP in patients 30–59 years of age. Everything else is "Expert Opinion"

Recommendations #4

4. In patients aged ≥ 60 years with chronic kidney disease, initiate pharmacologic treatment at systolic BP ≥ 140mmHg or diastolic BP ≥ 90mmHg and treat to goal systolic BP <140mmHg and goal diastolic BP <90mmHg.
(Expert Opinion–Grade E)

For Adults with CKD aim for the same BP goals as in the general population
BP goal <140/90

Treatment goals set by former Guidelines
JNC 7 / ADA / NKF / ISHIB

- General Population <140/90 mm Hg
- DM <130/80 mm Hg
- Chronic renal disease <130/80 mm Hg

Hypertension in CKD

Modification of Diet in Renal Disease (MDRD)
- Randomized to a MAP < 93 (120/80) vs MAP < 107 (140/90)
- RESULT: No CV or renal benefit

African American Study of Kidney Disease
- randomized to a MAP < 93 vs MAP 102-107; Achieved BP 130/78 vs 141/86
- RESULT: No CV or renal benefit

Flack JM et al. Hypertension 2010;56:780.
Recommendation #5

5. In patients aged ≥18 years with diabetes, initiate pharmacologic treatment at systolic BP ≥140mmHg or diastolic BP ≥90mmHg and treat to a goal systolic BP <140mmHg and goal diastolic BP <90mmHg. (Expert Opinion–Grade E)

For Adults with diabetes aim for the same BP goals as in the general population

BP goal <140/90

Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial

- NHLBI 10,251 Type 2 diabetics
- Three Trial arms
  - Glycemic control
  - BP
  - Lipids
- BP arm 4,773 randomized to SBP<120 or <140


ACCORD Trial: Blood Pressures

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean N Meds</td>
<td>3.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Intensive</td>
<td>3.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Standard</td>
<td>3.4</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Average after 1st year: 133.5 Standard vs. 119.3 Intensive, Delta = 14.2

ACCORD Trial: Outcomes

Primary Outcome: Nonfatal MI, Nonfatal Stroke or CVD Death

Total Stroke

HR = 0.88
95% CI (0.73-1.06)

HR = 0.59
95% CI (0.39-0.89)

NNT for 5 years = 89

ACCORD Trial: Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Intensive (%)</th>
<th>Standard (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious AE</td>
<td>77 (3.3)</td>
<td>30 (1.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypotension</td>
<td>17 (0.7)</td>
<td>1 (0.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Syncope</td>
<td>12 (0.5)</td>
<td>5 (0.2)</td>
<td>0.10</td>
</tr>
<tr>
<td>Bradycardia or Arrhythmia</td>
<td>12 (0.5)</td>
<td>3 (0.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>9 (0.4)</td>
<td>1 (0.04)</td>
<td>0.01</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>5 (0.2)</td>
<td>1 (0.04)</td>
<td>0.12</td>
</tr>
<tr>
<td>eGFR &lt;30 mL/min/1.73m²</td>
<td>99 (4.2)</td>
<td>52 (2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any Dialysis or ESRD</td>
<td>59 (2.5)</td>
<td>58 (2.4)</td>
<td>0.93</td>
</tr>
<tr>
<td>Dizziness on Standing</td>
<td>217 (44)</td>
<td>188 (40)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

NOTE: βblockers are OUT

Recommendations #6

6. In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, CCB, ACE inhibitor, or ARB. (Moderate Recommendation–Grade B) This recommendation is different from the JNC 7 in which the panel recommended thiazide-type diuretics as initial therapy for most patients.

While JNC 7 recommended thiazide-type diuretics as the initial antihypertensive choice for all, JNC 8 broadens the choices to also include CCB, ACE-I, and ARBs along with thiazide-type diuretics.
Which “Thiazide”?  
- Thiazide  
  - Hydrochlorothiazide  
  - Chlorthiazide (Diuril®)  
  - Bendroflumethiazide (Naturetin®)  
  [Bendroflumethiazide / Nadolol (Corzide®)]  
- Thiazide-like  
  - Metolazone  
  - Indapamide (Lozol®)  
  - Chlorthalidone (Thalitone®, Hygroton®)

ALLHAT Hypertension Trial  
42,418 high-risk hypertensive patients  
90% previously treated  
10% untreated  

Step 1 agents titrated and atenolol, clonidine, reserpine, and/or hydralazine added as needed to achieve BP goal  

ALLHAT Treatment Group  

Comparison of Diuretics and βBlockers and Their Effects on CV Events  

Recommendations #7  
7. In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.  
For general black population: Moderate Recommendation - Grade B  
For black patients with diabetes: Weak Recommendation - Grade C  

JNC 8 recommends a thiazide-type diuretic or CCB as the initial choice in African Americans, but there’s less certainty about African Americans with diabetes due to lack of data (they were torn about not including ACE/ARB)
**ALLHAT**

**Blacks**

Lisinopril/Chlorthalidone Relative Risk and 95% Confidence Interval

<table>
<thead>
<tr>
<th>Event</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal MI + CHD Death</td>
<td>1.10</td>
<td>(0.94 - 1.28)</td>
</tr>
<tr>
<td>All-Cause Mortality</td>
<td>1.06</td>
<td>(0.95 - 1.18)</td>
</tr>
<tr>
<td>Combined CHD</td>
<td>1.15</td>
<td>(1.02 - 1.30)</td>
</tr>
<tr>
<td>Combined CVD</td>
<td>1.19</td>
<td>(1.09 - 1.30)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.40</td>
<td>(1.17 - 1.68)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>1.30</td>
<td>(1.10 - 1.54)</td>
</tr>
<tr>
<td>End Stage Renal Disease</td>
<td>1.29</td>
<td>(0.94 - 1.75)</td>
</tr>
</tbody>
</table>

Favors Lisinopril 1 2 Favors Chlorthalidone


**Recommendation # 8**

8. In the population aged ≥ 18 years with chronic kidney disease, initial (or add-on) antihypertensive treatment should include an ACE inhibitor or ARB to improve kidney outcomes. (Moderate Recommendation–Grade B)

In adult patients with CKD, make sure an ACE-I or an ARB is part of the antihypertensive regimen.

**Recommendation # 9**

9. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in Recommendation 6. If goal BP cannot be reached using only the drugs in Recommendation 6… antihypertensive drugs from other classes can be used. (Expert Opinion–Grade E)

Don’t dilly dally. If BP is not at goal within a month, use one of these 3 strategies:
1. Increase the dose of the initial drug
2. Add a 2nd, then a 3rd drug (Rec #6)
   (Not an ACE + ARB together)
3. Add a drug from other classes

**ACE-I or ARB in CKD reduces progression of kidney disease**

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts</th>
<th>Design</th>
<th>RR for kidney disease progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macchio et al 1996</td>
<td>583</td>
<td>Benazapril v. placebo</td>
<td>53%</td>
</tr>
<tr>
<td>Gent group 1997</td>
<td>166</td>
<td>Ramapril v. placebo</td>
<td>48%</td>
</tr>
<tr>
<td>Hou et al 2006</td>
<td>224</td>
<td>Benazapril v. placebo</td>
<td>43%</td>
</tr>
<tr>
<td>Brenner et al 2001</td>
<td>1513</td>
<td>Losartan v. placebo</td>
<td>22%</td>
</tr>
</tbody>
</table>

**Telmisartan vs. Telmisartan + Ramipril: Primary Outcome (MI, Stroke, CV death, CV hospitalization)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Ram</th>
<th>Ram + Tel</th>
<th>RR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (yrs)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.20</td>
<td>0.30</td>
</tr>
<tr>
<td>Concomitant Cases</td>
<td>0.00</td>
<td>0.00</td>
<td>0.20</td>
<td>0.30</td>
</tr>
</tbody>
</table>


**Adverse Events with Ramipril + Telmisartan**

<table>
<thead>
<tr>
<th>Event</th>
<th>Ram</th>
<th>Ram + Tel</th>
<th>RR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>149</td>
<td>406</td>
<td>2.75</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Syncope</td>
<td>15</td>
<td>29</td>
<td>1.95</td>
<td>0.032</td>
</tr>
<tr>
<td>Cough</td>
<td>360</td>
<td>392</td>
<td>1.10</td>
<td>0.1885</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12</td>
<td>39</td>
<td>3.28</td>
<td>0.0001</td>
</tr>
<tr>
<td>Angioedema</td>
<td>25</td>
<td>18</td>
<td>0.73</td>
<td>0.30</td>
</tr>
<tr>
<td>Renal Impairment</td>
<td>60</td>
<td>94</td>
<td>1.58</td>
<td>0.0050</td>
</tr>
<tr>
<td>Any Discontinuation</td>
<td>2099</td>
<td>2495</td>
<td>1.20</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**JNC 8 Algorithm**

Adult (age > 18 years)  
Lifestyle Interventions to be applied throughout Treatment Algorithm  
Set Blood Pressure Goal and Initiate Blood Pressure Lowering Medications  

<table>
<thead>
<tr>
<th>Age</th>
<th>Blood Pressure Goal</th>
<th>Blood Pressure Goal</th>
<th>Blood Pressure Goal</th>
<th>Blood Pressure Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 years</td>
<td>SBP &lt;150 mm Hg DBP &lt;90 mm Hg</td>
<td>SBP &lt;140 mm Hg DBP &lt;90 mm Hg</td>
<td>SBP &lt;140 mm Hg DBP &lt;90 mm Hg</td>
<td>SBP &lt;140 mm Hg DBP &lt;90 mm Hg</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>All ages with CKD</td>
<td>All ages Diabetes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NON-BLACK**  
Initiate Thiazide-type diuretic, or ACEI or ARB or CCB alone or in combination  

**BLACK**  
Initiate Thiazide-type diuretic, or CCB alone or in combination  
Initiate ACEI or ARB alone or in combination with other drug classes  

**ALL RACES**  
Select a drug titration strategy  
A. Maximize first drug  
B. Add second drug before reaching max of first  
C. Start with 2 meds  
If goal BP not reached  
A. Reinforce Adherence  
B. Add or titrate drugs above  
C. Add drugs from other classes

---

**CLINICAL PEARL # 1**  
Diastolic Hypertension is most common in young patients, but Systolic Hypertension is more common after 40 years of age

---

**CLINICAL PEARL # 2**  
Failure to use enough medication is a common cause of “resistant” hypertension

---

**Even if you make it to age 65 without HTN, you’ll likely develop it**

Even if you make it to age 65 without HTN, you’ll likely develop it

---

**“Rule of TENS for SBP”**

1 Additional Drug for Every Additional 10 mmHg Reduction in Blood Pressure

---

**Antihypertensive Drug Classes**

- β-Blockers
- ACE Inhibitors
- ARBs
- Direct renin inhibitors
- α-Blockers
- All CCBs
- Diuretics
- Sympathometics
- Vasodilators (e.g., Hydralazine)

---

**Risk of hypertension (%)**

Risk of hypertension (%)

---

**CLINICAL PEARL # 2**

Failure to use enough medication is a common cause of “resistant” hypertension
CLINICAL PEARL # 3
In many patients with HTN, adequate diuresis is ESSENTIAL for BP control.

CLINICAL PEARL # 4
Always measure BP in the standing as well as the sitting position in the very elderly as orthostatic hypotension is common.

CLINICAL PEARL # 5
Avoid lowering the diastolic blood pressure below 55-60 mm Hg as coronary perfusion may be compromised if DBP falls too much.

Diuretics and BP Control
- Most classes of antihypertensive agents lead to sodium retention, as compensation for lower BP.
- JNC 8 recommends a thiazide-type diuretic, as one of four initial antihypertensive choices in the general population.
- JNC 8 recommends a thiazide-type diuretic, as one of two initial antihypertensive choices in the Black patients.

Blood Pressure Distribution in the Population According to Age

Hypertension 2014
- Hypertension is common and will likely affect most individuals at some point in their lifetime.
- Guidelines on how best to treat hypertension are evolving and sometimes contradictory.
- For information on prevention, detection and evaluation of hypertension, international guidelines offer guidance.
- OSA and hyperaldosteronism are the most common secondary causes of resistant HTN.
- Inadequate treatment is also a common cause of resistant HTN (rule of 10s).