The History: Old JNCs

Development of clinical practice guidelines was a key role for NHLBI in those years

Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure (JNC)

- JNC 7: 2003
- JNC 6: 1997
- JNC 5: 1992
- JNC 4: 1988
- JNC 3: 1984
- JNC 2: 1990
- JNC 1: 1976

Clinical Guidelines on the Identification, Evaluation, & Treatment of Overweight and Obesity

- Obesity 1: 1998
- ATP III Update: 2004
- ATP III: 2002
- ATP II: 1993
- ATP I: 1988

Hypertension: A Moving Target

JNC BP Classifications: DBP

- JNC II: Arch Intern Med. 1980;140:1280-1285
- JNC III: Arch Intern Med. 1984;144:1045;1057
- JNC IV: Arch Intern Med. 1993;153:154-183
- JNC VI: Arch Intern Med. 2005;165;2413-2446
- JNC VII: Arch Intern Med. 2014;174:1046;1097
- JNC IX: Arch Intern Med. 2015;175;174-192

Hyper-tension: A Moving Target

Hypertension: A Moving Target

Hypertension: A Moving Target

Hypertension: A Moving Target
New U.S. Approach to Hypertension Guideline Development

- Evidence-based
- Standardized coordinated guideline updates
- Evidence-based approach to implementation; emphasize user needs and implementability
  Primary care, specialists, and patients/consumers
  User friendly with clear focused messages
How the Process Has Evolved

- Strictly evidence-based
- Focus only on randomized controlled trials assessing important health outcomes (no use of intermediate/surrogate measures)
- Every included study is rated for quality by two independent reviewers using standardized tools
- Evidence statements graded for quality using prespecified criteria
- Separate grading for recommendations
- Independent methodology team to ensure objectivity of the review
- Initial set of recommendations focused on 3 key questions

Critical Questions Identified by the Panel

This 2014 HTN evidence-based guideline focuses on the panel's 3 highest ranked questions related to HTN management

1. In adults with HTN, does initiating antihypertensive pharmacologic therapy at specific BP thresholds improve health outcomes?
2. In adults with HTN, does treatment with antihypertensive pharmacologic therapy to a specified BP goal lead to improvements in health outcomes?
3. In adults with HTN, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?
Evidence Quality Grading and Recommendation Strength

<table>
<thead>
<tr>
<th>Evidence Quality For each ES</th>
<th>Strength Of each Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>A – Strong</td>
</tr>
<tr>
<td>Well-designed and conducted RCTs</td>
<td>B – Moderate</td>
</tr>
<tr>
<td>Moderate</td>
<td>C – Weak</td>
</tr>
<tr>
<td>RCTs with minor limitations</td>
<td>D – Against</td>
</tr>
<tr>
<td>Well-conducted observational studies</td>
<td>E – Expert Opinion</td>
</tr>
<tr>
<td>Low</td>
<td>N – No Recommendation</td>
</tr>
<tr>
<td>RCTs with major limitations</td>
<td></td>
</tr>
<tr>
<td>Observational studies with major limitations</td>
<td></td>
</tr>
</tbody>
</table>

Evidence-Based Clinical Practice Guidelines for CVD Prevention

The Most Important Clinical Questions in Hypertension

- Does evidence from RCTs of antihypertensive treatment support (or refute) 140/90 mm Hg as a treatment threshold or goal?
- Should the threshold or goal be lower or higher in persons with diabetes or CKD, the elderly or those with other co-morbidities or special characteristics?
- Is there RCT evidence that BP lowering treatment with a particular drug or drug class improves outcomes compared to any other drug/drug class?


Thresholds

The panel decided that, although some trials had higher thresholds for eligibility than the goals tested, translation into practice should make the threshold for initiating antihypertensive treatment the same as the BP treatment goal.
**Major Trials Testing SBP Goals in General Populations**

<table>
<thead>
<tr>
<th></th>
<th>SHEP</th>
<th>Syst-Eur</th>
<th>HYVET</th>
<th>JATOS</th>
<th>VALISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≥ 60</td>
<td>&gt; 60</td>
<td>≥ 80</td>
<td>65-85</td>
<td>&gt;70, &lt;85</td>
</tr>
<tr>
<td>Number</td>
<td>4,736</td>
<td>4,695</td>
<td>3,845</td>
<td>4,418</td>
<td>3,260</td>
</tr>
<tr>
<td>Entry SBP</td>
<td>160-219</td>
<td>160-219</td>
<td>160-199</td>
<td>≥160</td>
<td>≥160</td>
</tr>
<tr>
<td>Goal SBP</td>
<td>&lt;148</td>
<td>&lt;150</td>
<td>&lt;150</td>
<td>&lt;140</td>
<td>&lt;140</td>
</tr>
<tr>
<td>Achieved SBP</td>
<td>142</td>
<td>151</td>
<td>144</td>
<td>136</td>
<td>137</td>
</tr>
<tr>
<td>Stroke</td>
<td>36%</td>
<td>42%</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>CVD</td>
<td>32%</td>
<td>31%</td>
<td>34%</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Mortality</td>
<td>ns</td>
<td>ns</td>
<td>21%</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure  CVD = cardiovascular disease

**Diastolic BP Goal Trials**

Several trials used DBP goal <90 mm Hg and demonstrated consistent reduction of CVD events, e.g., VA morbidity trial, HDFP, MRC trial, ...

**Recommendation 1**

- In the general population ≥60 years of age, initiate pharmacologic treatment to lower BP at SBP ≥150 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.
  - Strong Recommendation – Grade A
- Corollary Recommendation: In the general population ≥60 years of age, if pharmacological treatment for high BP results in lower achieved SBPs (for example, <140 mm Hg) and treatment is not associated with adverse effects on health or quality of life, treatment does not need to be adjusted.
  - Expert Opinion – Grade E
**Why is it important not to recommend intensifying medications to reduce BP below the level proven in trials?**

- Lower thresholds/goals identify a much larger population as having "HTN" and presumably needing drug therapy. (e.g., reducing definition of HTN from 140/90 to 120/80 mm Hg doubles those with "HTN")
- Millions classified as "HTN" based on higher BP goals require more drugs to achieve lower BP goals.
- Treating to lower BP levels may be harmful (J-curve?).
- If neither beneficial nor harmful, resources would be wasted and patient adherence may suffer.

**Recommendation 2**

- In the general population <60 years of age, initiate pharmacologic treatment to lower BP at DBP ≥90 mm Hg and treat to a goal DBP <90 mm Hg.
  - For ages 30-59 years, Strong Recommendation – Grade A
  - For ages 18-29 years, Expert Opinion – Grade E

**Recommendation 3**

- In the general population <60 years of age, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg and treat to a goal SBP <140 mm Hg.
  - Expert Opinion – Grade E

**The Most Important Clinical Questions in Hypertension**

- Does evidence from RCTs of antihypertensive treatment support (or refute) 140/90 mm Hg as a treatment threshold or goal?

- Should the threshold or goal be lower or higher in persons with diabetes or CKD, the elderly or those with other co-morbidities or special characteristics?

- Is there RCT evidence that BP lowering treatment with a particular drug or drug class improves outcomes compared to any other drug/drug class?
BP Targets in Chronic Kidney Disease (CKD)

- 3 RCTs (8 reports), total of 2272 participants:
  - MDRD (Modification of Diet in Renal Disease) Study
  - AASK (African American Study of Kidney Disease and Hypertension) Trial
  - REIN-2 (Ramipril Efficacy in Nephropathy 2) trial

- No conclusive evidence favoring a BP target of <125/75 to 130/80 mm Hg rather than <140/90 mm Hg.


Recommendation 4

- In the population ≥18 years of age with CKD, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.
  - Expert Opinion – Grade E

RCTs Testing BP Goals In Hypertensive Diabetic Patients

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Duration (years)</th>
<th>SBP goal, mmHg</th>
<th>DBP goal, mmHg</th>
<th>Mean BP, less intense, mmHg</th>
<th>Mean BP, more intense, mmHg</th>
<th>Outcome</th>
<th>Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP</td>
<td>503</td>
<td>5</td>
<td>&lt;140</td>
<td>none</td>
<td>155/72</td>
<td>146/69</td>
<td>Stroke CVD CHD</td>
<td>22% (ns) 34% 25%</td>
</tr>
<tr>
<td>Syst-Eur</td>
<td>492</td>
<td>2</td>
<td>&lt;150</td>
<td>none</td>
<td>162/82</td>
<td>153/75</td>
<td>Stroke CVD</td>
<td>69% 62%</td>
</tr>
<tr>
<td>HOT</td>
<td>1,951</td>
<td>3</td>
<td>none</td>
<td>&lt;80</td>
<td>146/65</td>
<td>144/63</td>
<td>CVD 51%</td>
<td>58% (ns) 35%</td>
</tr>
<tr>
<td>UKPDS</td>
<td>1,148</td>
<td>8.4</td>
<td>&lt;150</td>
<td>&lt;85</td>
<td>154/87</td>
<td>144/62</td>
<td>CVD (stroke, MI, death, MI-related deaths, stroke) 43%</td>
<td>44% 45% 38%</td>
</tr>
<tr>
<td>ACCO</td>
<td>470</td>
<td>5.3</td>
<td>none</td>
<td>&lt;75</td>
<td>138/66</td>
<td>132/70</td>
<td>Microvascular (retinopathy, nephropathy) 37%</td>
<td>nc 40% (ns)</td>
</tr>
<tr>
<td>ACCORD</td>
<td>4,733</td>
<td>4.7</td>
<td>&lt;130</td>
<td>none</td>
<td>134</td>
<td>119</td>
<td>CVD (stroke) 12%  (ns)</td>
<td>41%</td>
</tr>
</tbody>
</table>

**Recommendation 5**

- In the population ≥18 years of age with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

**Updated HEDIS® Quality Measures**

The National Committee for Quality Assurance (NCQA) released the 2015 edition of the Healthcare Effectiveness Data and Information Set (HEDIS®), the gold standard in healthcare performance measurement. The 2015 HEDIS included changes to several existing measures.

**Controlling High BP:** NCQA added age and condition-specific treatment goals that align with the Eighth Joint National Committee (JNC 8) hypertension guidelines:

- 18–59 years (<140/90 mm Hg)
- 60–85 years with diabetes (<140/90 mm Hg)
- 60–85 years without diabetes (<150/90 mm Hg)

**Background**

On the basis of the 2014 guidelines for hypertension therapy in the U.S., many eligible adults remain untreated. We projected the cost-effectiveness of treating hypertension in U.S. adults according to the 2014 guidelines.
Conclusions
The implementation of the 2014 hypertension guidelines for U.S. adults between the ages of 35 and 74 years could potentially prevent about 56,000 CV events and 13,000 deaths annually, while saving costs. Controlling hypertension in all patients with CVD or stage 2 hypertension could be effective and cost-saving. (Funded by the NHLBI and others.)

The Most Important Clinical Questions in Hypertension

- Does evidence from RCTs of antihypertensive treatment support (or refute) 140/90 mm Hg as a treatment threshold or goal?
- Should the threshold or goal be lower or higher in persons with diabetes or CKD, the elderly or those with other co-morbidities or special characteristics?
- Is there RCT evidence that BP lowering treatment with a particular drug or drug class improves outcomes compared to any other drug/drug class?

Recommendation 6

- In the general non-Black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, CCB, ACEI or ARB.
  - Moderate Recommendation – Grade B
Initial Combinations of Medications

- β-blockers should be included in the regimen if there is a compelling indication for a β-blocker
- Diuretics
- ACE inhibitors or ARBs*
- Calcium antagonists

* Combining ACE with ARB discouraged

Drugs to Add to Initial 2-3 Drug Combinations

- spironolactone or amiloride: especially if K* low or 1* aldosteronism.
- alpha blocker: especially if LUTS
- alternative CCB: don’t combine non-DHP c BB
- beta-blocker: safe to combine (except c non-DHP CCB), but doesn’t add much efficacy to RAS blocker.
- vasodilator: hydralazine or minoxidil
- alpha-beta blocker: labetolol or carvedilol
- central agonist: most side effects frequency

ALLHAT

Only Subgroup Differences: Lisinopril vs Chlorthalidone in Blacks/Non-Blacks for CVD & Stroke

<table>
<thead>
<tr>
<th></th>
<th>Blacks</th>
<th>Non-Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.16 (1.04 - 1.28)</td>
<td>0.94 (0.85 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>1.06 (0.95 - 1.18)</td>
<td>0.97 (0.89 - 1.06)</td>
</tr>
<tr>
<td></td>
<td>Mortality</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.18 (1.09 - 1.30)</td>
<td>1.06 (1.00 - 1.13)</td>
</tr>
<tr>
<td></td>
<td>1.40 (1.17 - 1.60)</td>
<td>1.00 (0.85 - 1.17)</td>
</tr>
<tr>
<td></td>
<td>Combined CVD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.32 (1.11 - 1.58)</td>
<td>1.15 (1.01 - 1.30)</td>
</tr>
<tr>
<td></td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.28 (0.94 - 1.79)</td>
<td>0.93 (0.67 - 1.30)</td>
</tr>
<tr>
<td></td>
<td>Heart Failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>ESRD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Favors Lisinopril</td>
<td>Favors Chlorthalidone</td>
</tr>
<tr>
<td></td>
<td>Favors Lisinopril</td>
<td>Favors Chlorthalidone</td>
</tr>
<tr>
<td></td>
<td>Favors Lisinopril</td>
<td>Favors Chlorthalidone</td>
</tr>
<tr>
<td></td>
<td>Favors Lisinopril</td>
<td>Favors Chlorthalidone</td>
</tr>
</tbody>
</table>
Recommendation 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 Blacks with diabetes: Weak Recommendation – Grade C

Recommendation 8

• In the population ≥18 years of age with CKD and HTN, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with HTN regardless of race or diabetes status.
  – Moderate Recommendation – Grade B

Recommendation 9

• The main objective of HTN treatment is to attain and maintain goal BP.
• If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a 2nd drug from one of the classes in Recommendation 6 (thiazide-type diuretic, CCB, ACEI or ARB). Continue to assess BP and adjust the treatment regimen until goal BP is reached.
• If goal BP cannot be reached with 2 drugs, add and titrate a 3rd drug from the list provided. Do not use an ACEI and an ARB together in the same patient.
Recommendation 9, cont

- If goal BP cannot be reached using the drugs in Recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used.
- Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients where additional clinical consultation is needed.

— Expert Opinion – Grade E

2014 Hypertension Guideline Management Algorithm

Published online December 18, 2013.

Figure Legend:
SBP = systolic blood pressure; DBP = diastolic blood pressure; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; and CCB = calcium channel blocker.
a ACEIs and ARBs should not be used in combination.
b If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.
**Supplemental Questions**

**Question 4**

When should one start with single drug therapy and step up the dose (and how high should one go) vs. switching to a new drug vs. addition of a new drug vs. starting with 2 or more drugs vs. using fixed-dose combination drug formulations?

Do these choices depend on:

- Level of initial BP?
- Other risk factors and overall CVD risk?
- Other co-morbid conditions?
- Sex, race, or age?
Supplemental Questions

Question 5
What are the roles of home BP monitoring, office-based BP monitoring and 24-hr ABPM in the diagnosis and management of hypertension?

- Is home-based BP monitoring for patients who are well controlled + as needed office-based monitoring as good as regular office-based follow up?

- How frequently should BP be monitored for high BP in patients controlled and uncontrolled?


Thank you!