NEW HYPERTENSION GUIDELINES (JNC 8)

FOCUS ON HIGHER BLOOD PRESSURE GOALS, EASE UP ON DRUG CHOICES

- Introduction – Summary of Changes from JNC-7 to JNC-8
- What are the New Blood Pressure Goals?
- Randomized Controlled Trial Evidence for New Blood Pressure Thresholds
- Pharmacological Management: Four First Line Antihypertensive Classes based on population
- Evidence Based Dosing for Antihypertensive Drugs
- What are the recommended strategies to Initiate/Dose Antihypertensive Therapy?
- List of Later Line Antihypertensive Therapies
- Summary of Recommendations
- References

Highlights: The Quick Read Information

1. JNC-8 defined stage 1 hypertension as a blood pressure of:
   a. ≥ 140/90 mmHg  b. ≥ 130/80 mmHg  c. ≥ 160/100 mmHg  d. Did not define/address
2. What is the JNC-8 recommended blood pressure goal for a 55 yo white male without diabetes or CKD?
   a. < 120/80 mmHg  b. < 130/80 mmHg  c. < 140/90 mmHg  d. <150/90 mmHg
3. What is the JNC-8 recommended blood pressure goal for a 70 yo African American male without diabetes or CKD?
   a. < 120/80 mmHg  b. < 150/90 mmHg  c. < 140/80 mmHg  d. None of the above
4. What is the JNC-8 recommended blood pressure goal for a 55 yo white male with diabetes?
   a. < 120/80 mmHg  b. <130/80 mmHg  c. < 140/90 mmHg  d. <150/90 mmHg
5. Which of the following antihypertensives is recommended as an initial therapy for patient in #4?
   a. ACEI  b. Thiazide diuretic  c. CCB  d. Any of the above
6. Which of the following antihypertensives is recommended as an initial therapy for a 50 yo white male with CKD?
   a. ACEI  b. Renin Inhibitor  c. Thiazide diuretics  d. ACEI + ARB (combo therapy)
7. Which of the following are considered later-line antihypertensive agents?
   a. Clonidine  b. Furosemide  c. Metoprolol tartrate  d. All of the above

QUIZ ANSWERS
**Introduction:**

Essential hypertension is a major risk factor for cardiovascular disease, stroke and renal failure and is one of the most frequently identified and treated conditions in the primary care setting. The aim of early detection and treatment is to lower blood pressure to a threshold which improves health outcomes while limiting undue treatment adverse effects.

The last revised blood pressure guidelines, the Seventh Joint National Committee (JNC 7), were published in 2003 thus the emphasis on updating these clinical recommendations based on most recent available scientific evidence. The new Joint National Committee (JNC 8) adult hypertension guidelines were published in the Journal of American Medicine on December 18th 2013.

**Link to Guidelines:** [2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults](http://www.nhlbi.nih.gov/health-professionals/guidelines/)

The New guidelines focused on **3 primary questions** in guiding the Evidence Review:

1. Does initiating antihypertensive therapy at specific BP thresholds improve health outcomes?
2. Does treatment with antihypertensive therapy to a specific BP goal lead to improved health outcomes?
3. Do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?

### Summary of Changes

<table>
<thead>
<tr>
<th>Topic</th>
<th>JNC 7</th>
<th>JNC 8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methodology</strong></td>
<td>• Non-systemic literature review</td>
<td>• Expert panel defined critical questions &amp; review criteria</td>
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<td></td>
<td>• Recommendations based on expert panel consensus</td>
<td>• Initial systemic review restricted to RCT evidence with subsequent review by expert panel</td>
</tr>
<tr>
<td><strong>Definitions</strong></td>
<td>• Defined hypertension &amp; prehypertension</td>
<td>• Did not define prehypertension &amp; hypertension</td>
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<tr>
<td></td>
<td></td>
<td>• Thresholds for pharmacologic treatment defined</td>
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<tr>
<td><strong>Treatment Goals</strong></td>
<td>• Separate treatment goals for:</td>
<td>• Similar treatment goals defined for all populations except when evidence supports different goals</td>
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<tr>
<td></td>
<td>✓ “Uncomplicated” hypertension</td>
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<td></td>
<td>✓ Various comorbid conditions (CKD, DM)</td>
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<td><strong>Lifestyle</strong></td>
<td>• Based on literature review &amp; expert opinion</td>
<td>• Endorsed lifestyle workgroup recommendations</td>
</tr>
<tr>
<td><strong>Drug Therapy</strong></td>
<td>• Recommended 5 classes as initial therapy (ACEI or ARB, CCB, thiazide diuretic, B-Blocker)</td>
<td>• Recommended 4 classes as initial therapy (ACEI or ARB, CCB, thiazide diuretics)</td>
</tr>
<tr>
<td></td>
<td>✓ Thiazides typically recommended without compelling indication for another class</td>
<td>✓ Doses based on RCT evidence (see table of drugs/doses)</td>
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<td></td>
<td>✓ Specific drug classes for patients with compelling indications (ex. Diabetes, CKD, heart failure, MI, stroke)</td>
<td>✓ Specific drug classes based on evidence review for racial, CKD, and diabetic subgroups only</td>
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<tr>
<td></td>
<td></td>
<td>✓ Did not address compelling indications (ex. MI)</td>
</tr>
<tr>
<td><strong>Scope of Topics</strong></td>
<td>• Addressed multiple issues (BP measurement methods, patient evaluation, secondary hypertension, adherence, resistant hypertension, special populations)</td>
<td>• Addressed limited number of critical questions (see 3 primary questions above)</td>
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**JNC 8**

**What are the New Blood Pressure Goals?**

New JNC-8 blood pressure thresholds were based on a systemic review of *randomized controlled trials*. Based on this evidence, JNC 8 recommendations have shifted to focus more on a evidence based diastolic blood pressure goal of <90 mmHg. New recommendations also focus on less strict systolic blood pressure goals, mostly due to insufficient evidence to support lower thresholds. JNC-8 does not provide definitions for pre-hypertension & hypertension as did JNC-7, but only thresholds to which therapy should be initiated and maintained.

Changes to these BP thresholds are anticipated to still lead to improved health outcomes while minimizing adverse effects from low blood pressure or overtreatment. Subsequently, this may limit the number of prescribed antihypertensive medications as well as increase medication adherence among patients.

**New JNC -8 Blood Pressure Threshold Recommendations**

| Age 18-59 years (without major comorbidities) OR Age ≥ 18 years (with Diabetes or CKD) | BP goal < 140/<90 mmHg |
| Age ≥ 60 years old (without diabetes or CKD) | BP goal < 150/<90 mmHg |

BP goal < 140/<90 mmHg

Note: SBP < 140 mmHg is reasonable if not associated with adverse effects

**RCT Evidence Results for Blood Pressure Thresholds**

**General Population:**

- **BP goal <150/<90mmHg (patients ≥ 60 years old)**
  - Moderate-high quality evidence: BP <150/90 mmHg reduces stroke, heart failure, & CHD
  - Low quality evidence: No additional benefit of SBP < 140mmHg compared with SBP 140-160 or 140-149 mmHg
  - Expert opinion: If SBP <140 mmHg(& therapy is well tolerated)it is not necessary to adjust medications to allow for BP to increase

- **SBP goal < 140 mmHg (patients < 60 years old)**
  - Insufficient evidence: No good or fair quality RCT evidence to support SBP threshold for patients < 60 years
  - Expert Opinion: No available evidence to change current recommendations–recommend goal SBP <140mmHg
• **DBP goal <90 mmHg**
  - **High quality Evidence (age 30-69):** DBP <90 mmHg reduces cerebrovascular events, heart failure, & overall mortality. Evidence supports no benefit in treating to DBP < 80 mmHg or < 85 mmHg compared to < 90 mmHg
  - **Expert Opinion (Age <30):** No good evidence exists - recommend goal DBP < 90mmHg
  - Elevated DBP is a more important cardiovascular risk factor than elevated SBP in younger patients without major comorbidities. In patients ≥ 60 years of age SBP control remains the most important factor (see above for goal <150/90 mmHg)

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**Patients with Diabetes:**

• **Goal BP <140/<90 mmHg (**Patients ≥18 years**)**
  - **Moderate Quality Evidence:** SBP goal < 150 mmHg improves cardiovascular and cerebrovascular health outcomes and lowers mortality in adults with diabetes & hypertension
  - **Insufficient Evidence:** No RCT addressed whether treatment to an SBP goal <140 mmHg compared with a higher goal (<150 mmHg) improves health outcomes in adults with diabetes & hypertension.
  - **Limited/No Evidence:** No RCT evidence to support SBP <130 mmHg in adults with diabetes and hypertension.
  - **Expert Opinion:** Recommend BP goal <140/90mmHg for all adults with diabetes (≥18 years) and hypertension consistent with the BP goals of the general population age < 60 years

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**Patients with Kidney Disease:**

• **Goal BP <140/<90 mmHg (**Patients ≥18-70 years, GFR < 60ml/min OR albuminuria > 30 mg/g at any GFR**)**
  - **Insufficient Evidence/Expert Opinion:** (CKD age 18-70 years) Insufficient evidence to determine benefit of lower BP goal (ex. <130/80mmHg) compared to <140/90 mmHg on mortality, cardiovascular or cerebrovascular health. Recommend BP goal <140/90mmHg.
  - **Moderate quality evidence:** No benefit in slowing progression of kidney disease with a lower BP goal (<130/80mmHg) compared to <140/90mmHg
  - **Limited available evidence:** (CKD age >70) recommendations could not be made by panel. BP goal should be individualized –taking into account factors such as frailty, comorbidities and albuminuria.

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**Pharmacological Management**

• JNC-8 recommends 1st-line therapy to be limited to *4 Drug classes* based on evidence from 4 populations.
The guideline noted that evidence reviewed for non-hypertensive populations (ex: heart failure, coronary artery disease) were limited. Therefore, therapy recommendations should be applied with caution.

### 1st Line Antihypertensive Therapy Classes:

1. Thiazide-type diuretics
2. Calcium channel blockers (CCBs)
3. Angiotensin-Converting Enzyme Inhibitor (ACEIs)
4. Angiotensin Receptor Blockers (ARBs)

<table>
<thead>
<tr>
<th>Population</th>
<th>Evidence</th>
<th>1st Line Therapy</th>
</tr>
</thead>
</table>
| General Population  | Each of the 4 drug classes yielded comparable effects on cardiovascular, cerebrovascular & kidney outcomes as well as overall mortality
                  | ✓ Exception of heart failure (however evidence was not compelling to guide therapy)          | Thiazide Diuretic        |
|                     | **B-Blocker not recommended as 1st line therapy:**                                           |                          |
|                     | ✓ LIFE study showed b-blocker vs. ARB had higher rate of primary endpoint                    | CCB                      |
|                     | ✓ Other studies comparing B-blocker to 4 initial drug classes showed similar outcomes         | ACEI or ARB              |
|                     | or evidence was insufficient                                                                  |                          |
|                     | **No RCT evidence of good/fair quality for the following:** Central alpha-2 agonists (ex. clonidine), direct vasodilators (ex. hydralazine), aldosterone receptor antagonists and loop diuretics |                          |
| Diabetes            | Trials including participants with diabetes showed no differences than those in the general population (non-black) | Thiazide Diuretic        |
| (Non Black)         |                                                                                            |                          |
| Black Population    | Recommendations stem from pre-specified black subgroup (46% diabetic) analysis from a single large trial (ALLHAT): | Thiazide Diuretic        |
| (General & Diabetes)| ✓ Thiazide more effective than ACEI in improving cerebrovascular, heart failure & combined cardiovascular outcomes | CCB                      |
|                     | ✓ ACEI showed 51% higher rate of stroke compared to CCB                                      | ACEI or ARB              |
|                     | ✓ ACEI less effective at reducing BP compared to CCB                                        |                          |
|                     | ✓ CCB was less effective than diuretic in preventing heart failure but there were no differences in CHD, cerebrovascular & kidney outcomes or overall mortality |                          |
|                     | **No outcome studies for B-blocker, ARBs, renin-angiotensin system inhibitors**               |                          |
| CKD (Regardless of race or Diabetes) | Moderate Evidence: Treatment with ACEI or ARB improves kidney outcomes for patients with CKD (with or without proteinuria) |
|                     | ✓ Recommendation based primarily on kidney outcomes as there is less evidence for cardiovascular outcomes | CKD (+/- proteinuria): ACEI or ARB |
|                     | **In Black Population (*CKD AND proteinuria)*- ACE or ARB recommended as initial therapy because of higher likelihood of progression of ESRD | Black Population (CKD + proteinuria): ACE or ARB |
|                     | **In Black Population (CKD without proteinuria)*- Choice is less clear- Initial therapy may include Thiazide, CCB, ACEI or ARB | Black Population (CKD without proteinuria): Thiazide, CCB, ACEI or ARB |
|                     | Direct renin inhibitors not recommended due to lack of studies demonstrating benefits on kidney or cardiovascular outcomes | Evidence Based Dosing for Antihypertensive Drugs |
JNC-8 noted that when initializing a first line antihypertensive drug, it is important to also have this therapy appropriately dosed to aid in achieving similar outcomes as seen in randomized controlled trials. The new guidelines also addressed three equally acceptable pharmacological treatment strategies that can be tailored based on the individual circumstances, clinician and patient preferences, and drug tolerability.

1st Line Medications & Dosages Studied in RCT (currently available)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Daily Dose</th>
<th>Target Dose in RCT</th>
<th># Doses per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>50 mg</td>
<td>150-200mg</td>
<td>2</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5 mg</td>
<td>20mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 mg</td>
<td>40mg</td>
<td>1</td>
</tr>
<tr>
<td>Angiotensin Receptor Blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eprosartan</td>
<td>400 mg</td>
<td>600-800 mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 mg</td>
<td>12-32 mg</td>
<td>1</td>
</tr>
<tr>
<td>Losartan</td>
<td>50 mg</td>
<td>100 mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Valsartan</td>
<td>40-80 mg</td>
<td>160-320 mg</td>
<td>1</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>75 mg</td>
<td>300 mg</td>
<td>1</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5 mg</td>
<td>10 mg</td>
<td>1</td>
</tr>
<tr>
<td>Diltiazem Extended Release</td>
<td>120-180 mg</td>
<td>360 mg</td>
<td>1</td>
</tr>
<tr>
<td>Thiazide-Type Diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothizide</td>
<td>12.5-25 mg</td>
<td>25-50 mg</td>
<td>1-2</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>12.5 mg</td>
<td>12.5-25 mg</td>
<td>1</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25 mg</td>
<td>1.25-2.5 mg</td>
<td>1</td>
</tr>
</tbody>
</table>

Strategies to Dose Antihypertensive Drugs

<table>
<thead>
<tr>
<th></th>
<th>Start 1 Drug → Titrate to Maximum Dose → Add second drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Start 1 Drug → Add 2nd drug before achieving max dose of initial drug</td>
</tr>
<tr>
<td>C</td>
<td><strong>Start 2 Drugs simultaneously (either as separate pills or comb)</strong></td>
</tr>
</tbody>
</table>

**More preferable if SBP >160mmHg +/or DBP >90mmHg +/or SBP > 20mmHg above goal +/or DBP >10mmHg above goal

Several medications are now designated as later-line alternatives, including the following:

- Beta-blockers
- Alpha-blockers
- Alpha1/beta-blockers (eg, carvedilol)
- Vasodilating beta-blockers (eg, nebivolol)
- Central alpha2-adrenergic agonists (eg, clonidine)
- Direct vasodilators (eg, hydralazine)
- Loop diuretics (eg, furosemide)
- Aldosterone antagonists (eg, spironolactone)
- Peripherally acting adrenergic antagonists (eg, reserpine)
Clinical Pearls

❖ Titration or addition should be performed when not able to achieve target BP within \textit{1 month} of initiation date
❖ Antihypertensive may be replaced with alternate if it is perceived to be ineffective or if there are adverse effects. If BP goal cannot be reached with 1\textsuperscript{st} line therapies (3 drugs) or contraindications exist other later line therapies may be considered.
❖ ACE and ARB therapies should NOT be used together in the same patient due to risk of adverse events

Summary of Recommendations
Adult aged ≥18 years with hypertension

Implement lifestyle interventions (continue throughout management).

Set blood pressure goal and initiate blood pressure lowering-medication based on age, diabetes, and chronic kidney disease (CKD).

General population (no diabetes or CKD) vs Diabetes or CKD present

Age ≥60 years

- Blood pressure goal:
  - SBP <150 mm Hg
  - DBP <90 mm Hg

  Nonblack
  - 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.

Age <60 years

- Blood pressure goal:
  - SBP <140 mm Hg
  - DBP <90 mm Hg

  All ages Diabetes present
  - No CKD
  - Blood pressure goal:
    - SBP <140 mm Hg
    - DBP <90 mm Hg
    - Initiate ACEI or ARB, alone or in combination with other drug class.

  All ages CKD present with or without diabetes

All races

Select a drug treatment titration strategy
A. Maximize first medication before adding second or
B. Add second medication before reaching maximum dose of first medication or
C. Start with 2 medication classes separately or as fixed-dose combination.

At goal blood pressure?
Yes
Reinforce medication and lifestyle adherence.
For strategies A and B, add and titrate thiazide-type diuretic or ACEI or ARB or CCB (use medication class not previously selected and avoid combined use of ACEI and ARB).
For strategy C, titrate doses of initial medications to maximum.

At goal blood pressure?
Yes
Reinforce medication and lifestyle adherence.
Add and titrate thiazide-type diuretic or ACEI or ARB or CCB (use medication class not previously selected and avoid combined use of ACEI and ARB).

At goal blood pressure?
Yes
Reinforce medication and lifestyle adherence.
Add additional medication class (eg, β-blocker, aldosterone antagonist, or others) and/or refer to physician with expertise in hypertension management.

No
Continue current treatment and monitoring.
References


Quiz Answers:

1.) d
2.) c
3.) b
4.) c
5.) d
6.) a
7.) d