A Practical Approach to the Management of Hypertension: 2013 Update

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University of Iowa
Disclosure of Relationships

Over the past 5 years

• Grant Support: NIH, AHRQ, VA HSR&D.

• Member of the JNC 5, 6, 7 and 8 committees

• I have had NONE of the following: Consultant, Speakers Bureau, Major Stock Shareholder, or Other Support from Industry.
Learning Objectives

At the completion of the presentation, participants will be able to:

1. Describe the evidence quality grading and recommendation strength process used by JNC-8 which will be used to formulate the guidelines.

2. Compare and contrast the JNC-8 systematic review and guideline development process with other hypertension guidelines.

3. Discuss recent NICE, ADA and CKD guidelines and how they could relate to JNC-8.
# NHLBI-sponsored Adult CVD Prevention Guidelines

<table>
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<tbody>
<tr>
<td>JNC 2: 1980</td>
<td></td>
<td>ATP II: 1993</td>
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<td>JNC 1: 1976</td>
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Evidence-Based Clinical Practice Guidelines for CVD Prevention
National Heart, Lung, and Blood Institute
National High Blood Pressure Education Program

Seventh Report of the Joint National Committee Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) EXPRESS
My Observations About Previous Structure and Process

- **JNC- V (1993):** Chairman – Ray Gifford, Jr. MD
  - Subcommittee on Pharmacologic TX: Edward D. Frohlich, MD chair
  - Started June 1991, published January 1993

- **JNC- VI (1997):** Chairman – Sheldon Sheps, MD
  - Prevention and Treatment Chair: Norman Kaplan, MD

- **JNC-7 (2003):** Chairman: Aram Chobanian, MD
  - Started December 2002, published May 2003

- **JNC- 8 (pending):** Co-Chairs: Paul James, MD, Suzanne Oparil, MD
  - Prevention and Treatment Chairs: William Cushman, MD, Jackson Wright, MD
NHLBI Evidence Quality Grading and Recommendation Strength

**Evidence Quality**
- **High**
  - Well-designed and conducted RCTs
- **Moderate**
  - RCTs with minor limitations
  - Well-conducted observational studies
- **Low**
  - RCTs with major limitations
  - Observational studies with major limitations

**Recommendation Strength**
- **A – Strong**
- **B – Moderate**
- **C – Weak**
- **D – Against**
- **E – Expert Opinion**
- **N – No Recommendation**
NHLBI Systematic Review and Guideline Development Process

1. Critical Questions & Study Eligibility Criteria Identified
2. Literature Searched; Eligible Studies Identified
3. Studies Quality Rated; Data Abstracted
4. Evidence Tables Developed; Body of Evidence Summarized
5. Graded Evidence Statements & Recommendations Developed
6. External Review of Guideline Drafts; Revised as Needed
7. Guidelines Disseminated & Implemented

Evidence-Based Clinical Practice Guidelines for CVD Prevention
Expertise Represented

- Hypertension, primary care, cardiology, nephrology, clinical trials, research methodology, evidence-based medicine, epidemiology, guideline development and implementation, nutrition/lifestyle, nursing, pharmacy, systems of care, and informatics

- Panel also includes senior scientists from NHLBI and NIDDK with expertise in hypertension, clinical trials, translational research, nephrology, guideline development, and evidence-based methodology
JNC 8 Committee Members

Co-Chair: Suzanne Oparil MD
Jackson T. Wright, Jr. MD, PhD
Sandra J. Taler, MD
Joel Handler, MD
Barry L. Carter, PharmD
Daniel T. Lackland, DrPH
Sidney C. Smith, Jr., MD
Olugbenga Ogedegbe, MD, MPH, MS
Cheryl Dennison Himmelfarb, RN, ANP, PhD

Co-Chair: Paul A. James MD
Laura Svetkey, MD, MHS
Michael L. LeFevre, MD, MSPH
Raymond R. Townsend, MD
William C. Cushman, MD
Thomas D. MacKenzie, MD, MSPH
Andrew S. Narva, MD (Ex-Officio)
Lawrence J. Fine, MD, DrPH (Ex-Officio)
Eduardo Ortiz, MD, MPH, NHLBI Lead, Ex-Officio, Non-Voting Member

* 4 members had relationships to disclose; 13 had no relationships to disclose. Panel members disclose their relationships and recuse themselves from voting on evidence statements and recommendations relevant to their relationships.
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

Evidence-Based Clinical Practice Guidelines for CVD Prevention
How Were Questions Selected?

- Panel Chairs and NHLBI staff developed questions based on their expertise, brief literature review, and speaking with colleagues.

- These questions were sent to panel members to review, revise, and add or delete questions.

- Resulted in 23 questions, which were sent to all panel members.
  - Panel members discussed these questions on conference calls, then independently ranked the 3-5 questions felt to be of highest priority.

- The five highest ranked questions discussed further and prioritized.
Rationale for the Questions

- Interest in assessing the evidence to support 140/90 mm Hg as a treatment threshold or goal.
- Should the treatment threshold / goal be lower in populations with diabetes, chronic kidney disease, coronary artery disease, stroke, and other co-morbidities or characteristics?
- Should the treatment threshold / goal be different in older adults?
- Use of different treatment thresholds and goals is confusing.
- Is there evidence that treatment to lower BP with a particular drug or drug class improves outcomes compared to another?
Critical Questions and I/E Criteria

- Critical Question (CQ) in PICO format
  - Population
  - Intervention/Exposure
  - Control/Comparator
  - Outcomes

- Study Inclusion/Exclusion criteria:
  - Types of studies (e.g., RCTs, epidemiology, systematic reviews)
  - Subgroups (e.g., elderly, diabetes)
  - Specific outcomes (e.g., CVD mortality, MI, stroke, HF)
Executive Committee
Sidney Smith Jr. MD

BP Panel
Paul James MD
Suzanne Oparil MD

Cholesterol Panel
Neil Stone MD
Alice Lichtenstein DSc
Jennifer Robinson MD

Obesity Panel
Michael Jensen MD
Donna Ryan MD

Lifestyle WG
Robert Eckel MD
John Jakicic PhD

Risk Assessment WG
David Goff Jr. MD, PhD
Donald M. Lloyd-Jones MD, ScD

Implementation WG
Thomas Pearson MD, PhD
Wiley Chan MD

Expert Panel Composition
- Diversity and balance of expertise
- Diversity of demographics
- Conflict of interest management
Question 1

- Among adults with hypertension, does initiating antihypertensive pharmacological therapy at specific BP thresholds improve health outcomes?
  - When to initiate drug treatment?
Question 2

Among adults, does treatment with antihypertensive pharmacological therapy to a specified BP goal lead to improvements in health outcomes?

- How low should you go?
In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?

- How do you get there?
Inclusion/Exclusion Criteria

- Randomized Controlled Trials
  - RCTs are subject to less bias and represent the gold standard for determining efficacy and effectiveness\(^1\)
- Search dates: 1966 to present
- Minimum one-year follow-up period
- Studies with sample sizes less than 100 excluded

Populations Included

- Adults 18 years of age and older
- Prespecified subgroups including:
  - Diabetes
  - Chronic kidney disease
  - Proteinuria
  - Coronary artery disease
  - Peripheral artery disease
  - Previous stroke
  - Heart Failure
  - Older Adults
  - Men and women
  - Racial and ethnic groups
  - Smoking
Outcomes

- Overall mortality, CVD-related mortality, CKD-related mortality, myocardial infarction, heart failure, hospitalization for heart failure, stroke

- Coronary revascularization (includes coronary artery bypass surgery, coronary angioplasty and coronary stent placement), peripheral revascularization (includes carotid, renal, and lower extremity revascularization)

- End stage renal disease (i.e., kidney failure resulting in dialysis or transplant), doubling of creatinine, halving of eGFR
### NHLBI Study Assessment Tool: Controlled Intervention Studies

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Yes</th>
<th>No</th>
<th>Other</th>
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<tbody>
<tr>
<td>1. Was the study described as randomized, a randomized trial, a</td>
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<tr>
<td>randomized clinical trial, or an RCT?</td>
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<tr>
<td>5. Were the people assessing the outcomes blinded to the participants’</td>
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<td>group assignments?</td>
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<tr>
<td>7. Was the overall drop-out rate from the study at its endpoint 20%</td>
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<tr>
<td>or less than the number originally allocated to treatment?</td>
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<tr>
<td>14. Were all randomized participants analyzed in the group to which they</td>
<td></td>
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<tr>
<td>were originally assigned (i.e., did they use an intention-to-treat</td>
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<td></td>
<td></td>
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<tr>
<td>analysis)?</td>
<td></td>
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**Quality Rating (Good, Fair, Poor) (see guidance)**

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<thead>
<tr>
<th>Rater #1 initials:</th>
<th>Rater #2 initials:</th>
</tr>
</thead>
</table>

**Additional Comments (If POOR, please state why):**
Data Abstraction and Evidence Tables

- Information from individual studies
  - Key data abstracted into a database
  - Evidence table for each study/paper: subjects, sample size, intervention, comparison, results

- Evidence summaries by Critical Question
  - Tables and text of major elements relevant to the CQ

- Graded evidence statements
  - Multiple ESs for each CQ

- Graded recommendations based on the evidence
  - Multiple ESs could result in a single recommendation
Question 1: Among adults with hypertension, does initiating antihypertensive pharmacological therapy at specific BP thresholds improve health outcomes?

Articles Screened = 1496

Included = 44

Good = 8
Fair = 18
Poor = 18

Excluded = 1452
(Did not meet prespecified inclusion criteria)

Total Abstracted = 26
Question 2: Among adults, does treatment with antihypertensive pharmacological therapy to a specified BP goal lead to improvements in health outcomes?

Articles Screened = 1978

Included = 92

Good = 17  Fair = 39  Poor = 36

Excluded = 1886 (Did not meet prespecified inclusion criteria)

Total Abstracted = 56
Question 3: In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?

Articles Screened = 2662

Included = 101

Excluded = 2561 (Did not meet prespecified inclusion criteria)

Good = 15

Fair = 51

Poor = 35

Total Abstracted = 66
New reports vs Previous reports

- The new guideline reports will not look like the previous guidelines!
  - Recommendations are based on systematic reviews of RCTs
  - Restricted to a few critical questions
  - More depth, less breadth (More rigor, less comprehensive)

- The new guideline reports will look more similar to each other than in the past
  - Previous reports used different methods and structure
  - New reports are using the same methods and structure
Next Steps

- Evidence statements and recommendations (completed)
- Draft report (completed February 2013)
- Review of the draft report by (completed March 2013):
  - Other federal agencies (CDC, CMS, AHRQ, HRSA, VA, etc.)
  - Invited organizations and individuals
  - Public
- Revisions based on comments received (In process)
- Final report (fall 2013)
Question 1 Compared to NICE: When?

- Recommended ambulatory BP monitoring for all.
- Lifestyle modifications for all with hypertension
- Drug therapy for those <80 years with Stage 1 (140-159/90-99) if they have target organ damage (TOD), CV disease, DM, 10 yr CV risk ≥20%
- Drug therapy for any age with Stage 2 (≥160/100) of TOD, CVD, DM, 10 yr CV risk ≥20%
- For those <40 yrs with Stage 1 and no risk of CV disease, consider detailed assessment for TOD.

Question 1 Compared to ADA and KDIGO Guidelines: When?

- **ADA**: lifestyle if BP > 120/80 (B); drug therapy if ≥140/80 mm Hg (B)

- **KDIGO**: treatment if BP > 140/90 (1B) if urine albumin <30mg/24 hrs; drug therapy if ≥130/80 mm Hg if urine albumin 30-300 mg/24 hrs. (2D)


Question 2: - How low should you go?

- NICE: <140/90 if less than 80 years, <150/90 if >80 years.
- ADA: <140/80 mm Hg (B), <130/80 may be appropriate for some.
- KDIGO: <140/90 (1B) if urine albumin <30mg/24 hrs; drug therapy if ≤130/80 mm Hg if urine albumin 30-300 mg/24 hrs. (2D)

Question 3: – What should be the initial therapy? NICE Guidelines

Step 1:

- <55 years, use ACE or ARB (whites) or CCB if African American
- **DO NOT** combine ACE and ARB for hypertension
- >55 years, CCB for most but offer thiazide-like diuretic if HF or high risk of HF or intolerance to CCB.
- If thiazide-like diuretic is offered, should use chlorthalidone 12.5-25 mg once daily or indapamide 2.5 mg once daily.
- If already taking HCTZ (25-50 mg) and BP is well controlled, continue this treatment.
- BB only in younger people with intolerance to ACE or ARB, women of childbearing potential or high sympathetic drive


*Evidence-Based Clinical Practice Guidelines for CVD Prevention*
Question 3: – How do you get there?

- ADA:
  - regimen should include ACE or ARB (C)
  - 2 or more agents usually needed (B)
  - Give 1 or more meds at bedtime (A)

- KDIGO:
  - ARB or ACE-I if urine albumin 30-300 mg/24 hrs. (2D)
  - ARB or ACE-I if urine albumin >300 mg/24 hrs. (1B)
  - BP reduction more important than agent

BASE CASE RESULTS (65-YEAR-OLD, 2% CV RISK, 1.1% DIABETES RISK, 1% HF RISK)

<table>
<thead>
<tr>
<th></th>
<th>Mean Effect (QALYs Per Person, Discounted)</th>
<th>Mean Cost (2009 UK £ Per Person, Discounted)</th>
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<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No intervention</td>
<td></td>
<td>£4,800, £4,600, £4,400, £4,200, £4,000</td>
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<tr>
<td>Calcium-channel blockers</td>
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<td>£4,200, £4,400, £4,600, £4,800, £5,000</td>
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<tr>
<td>ACE inhibitors/angiotensin II receptor antagonists</td>
<td></td>
<td>£4,400, £4,600, £4,800, £5,000, £5,200</td>
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<tr>
<td><strong>Women</strong></td>
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<td></td>
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<tr>
<td>No intervention</td>
<td></td>
<td>£5,400, £5,200, £5,000</td>
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<tr>
<td>Thiazide-type diuretics</td>
<td></td>
<td>£5,000, £5,200, £5,400, £5,600, £5,800</td>
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<tr>
<td>Beta-blockers</td>
<td></td>
<td>£5,200, £5,400, £5,600, £5,800, £6,000</td>
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</tbody>
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QALYs, quality-adjusted life years


Evidence-Based Clinical Practice Guidelines for CVD Prevention
Antihypertensive Drug Treatment Algorithm
NICE 2011

Age <55 yrs

Step 1
A

Step 2
A + C†

Step 3
A + C + D

Step 4
A + C + D + further diuretic‡
Consider specialist advice

Age ≥55 yrs or black*

Step 1
C†

Step 2
A + C†

A = angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker; C = calcium channel blocker; D = thiazide-like diuretic
*Of African or Caribbean family origin
†CCB preferred but D is an alternative in people intolerant of C or at high risk of heart failure
‡Consider low-dose spironolactone or higher-dose thiazide

Conclusion

The new NHLBI-sponsored adult CV guideline reports

- Are strictly evidence based
- Will not look like the previous guidelines
- Will have more depth and rigor; will have less breadth
- Will be released in late 2013, one at a time as they are ready
- Will use evidence based strategies for Implementation
Thank You

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