Applying the Intricacies of the New Hypertension and Lipid Guidelines to Your Patients

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OBJECTIVES

• Discuss the current hypertension guidelines
• Discuss the current lipid guidelines
• Given a clinical scenario, utilize the new guidelines to recommend appropriate therapy
Hypertension Guidelines

JOINT NATIONAL COMMITTEE (JNC)

- Federally funded program to produce hypertension guidelines
  - Latest iteration was JNC 7 published in 2003

- NHLBI announced in June 2013 that it is withdrawing from guideline development, which would then be performed by “partner organizations”

- In August 2013, NHLBI established a “partnership” with AHA and ACC to develop hypertension, cholesterol, and obesity guidelines.
  - While the cholesterol and obesity guidelines were released in November 2013, the hypertension guidelines were never developed.
SO WHERE ARE OUR HYPERTENSION GUIDELINES GOING TO COME FROM?

- JNC panel wasn’t comfortable with shopping guidelines around for endorsements, so they published their work (unendorsed) in JAMA on-line in December 2013 (JAMA 2014;311:507-520) as the document we now call JNC 8
- Once it became clear that AHA and ACC could not reach an agreement with the JNC panel, the former felt compelled to release some form of updated guideline for hypertension management, leading to an AHA-ACC Scientific Advisory Report released on-line November 15, 2013 (J Am Coll Cardiol 2014;63:1230-1238.)
  - This document is NOT a guideline, however, but more of a treatment algorithm which doesn’t really differ much from the 2003 JNC-7 recommendations
  - The AHA-ACC Task Force on Practice Guidelines intends to continue to work with NHLBI on producing hypertension guidelines with a goal of 2015 dissemination.
- Further complicating matters is the release of hypertension guidelines by the American Society of Hypertension & International Society of Hypertension in December 2013 (Available at: http://www.ash-us.org/documents/ASH_ISH-Guidelines_2013.pdf)

2013 HTN GUIDELINES
MAJOR CHANGE #1: BP GOALS

<table>
<thead>
<tr>
<th>Age Group</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>JNC-7 or ADA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 yrs. old, no comorbidities</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>60-79 yrs. old, no comorbidities</td>
<td>&lt;150/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>&gt; 80 yrs. old, no comorbidities</td>
<td>&lt;150/90 mmHg</td>
<td>&lt;150/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Diabetes</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/80 mmHg*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;130/80 mmHg optional goal*</td>
</tr>
</tbody>
</table>
**2013 HTN GUIDELINES**

**MAJOR CHANGE #2: DRUG OF CHOICE FOR TREATING UNCOMPLICATED HTN**

<table>
<thead>
<tr>
<th></th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>JNC-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 yrs. old</td>
<td>Thiazide, CCB, or ACEI/ARB</td>
<td>ACEI/ARB</td>
<td>Thiazide</td>
</tr>
<tr>
<td>&gt; 60 yrs. old</td>
<td>Thiazide, CCB, or ACEI/ARB</td>
<td>Thiazide or CCB</td>
<td>Thiazide</td>
</tr>
</tbody>
</table>

“A consensus means that everyone agrees to say collectively what no one believes individually.”

- Abba Eban, Israeli diplomat and politician

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**2013 HTN GUIDELINES**

**MAJOR CHANGE #3: DRUG OF CHOICE FOR TREATING HTN IN A PATIENT WITH DIABETES (AND NO KIDNEY DISEASE)**

<table>
<thead>
<tr>
<th></th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>JNC-7</th>
<th>ADA 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-African-American</td>
<td>Thiazide, CCB, or ACEI/ARB</td>
<td>ACEI/ARB</td>
<td>ACEI/ARB or Thiazide</td>
<td>ACEI/ARB</td>
</tr>
<tr>
<td>African-American</td>
<td>Thiazide or CCB</td>
<td>ACEI/ARB or Thiazide or CCB</td>
<td>ACEI/ARB or Thiazide</td>
<td>ACEI/ARB</td>
</tr>
</tbody>
</table>

“A consensus means that everyone agrees to say collectively what no one believes individually.”

- Abba Eban, Israeli diplomat and politician
R.M. is a 48 yo White male with no other chronic medical conditions. At a medical appointment he is noted to have an average BP of 156/88 mmHg. Two weeks later, his average BP was 152/92 mmHg. The preferred antihypertensive regimen for R.M. would be which one of the following?

A. Amlodipine  
B. Atenolol  
C. Doxazosin  
D. Lisinopril  
E. HCTZ
GUIDELINE DISCORD

• JNC-8 stance: Evidence-based medicine

• ASH stance:
  • JNC report relied almost entirely on RCT results; did not include all available evidence
  • Other guidelines do not consider medication adverse effects
    • Greatest number of side effects is with thiazides, incl. impotence and questionable issue of increasing sudden cardiac death
    • ACEI/ARBs considered the safest

• ESH stance: Getting BP to goal is what’s important, regardless of how one gets there

Rationale for DBP < 80 mmHg in Diabetics

* all p-values are for < 90 mmHg vs. ≤ 80 mmHg.

## SBP GOALS FOR ELDERLY

### JNC-8 PERSPECTIVE

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (yrs.)</th>
<th>Treatment (placebo control)</th>
<th>Mean treatment SBP</th>
<th>Primary Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP</td>
<td>≥ 60</td>
<td>Chlorthalidone +/- atenolol</td>
<td>143 mmHg</td>
<td>36% reduction in stroke</td>
</tr>
<tr>
<td>Syst-Eur</td>
<td>≥ 60</td>
<td>Nitrendipine +/- Enalapril +/- HCTZ</td>
<td>151 mmHg</td>
<td>42% reduction in stroke</td>
</tr>
<tr>
<td>HYVET</td>
<td>≥ 80</td>
<td>Indapamide +/- perindopril</td>
<td>144 mmHg</td>
<td>30% stroke reduction</td>
</tr>
</tbody>
</table>

There is *no compelling* evidence that patients over 60 years old benefit from SBP lowered below 140 mmHg.

## SBP GOALS FOR ELDERLY

### ASH/ISH PERSPECTIVE

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (yrs.)</th>
<th>Treatments</th>
<th>Treatment SBP (mean)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALLHAT</td>
<td>≥ 55</td>
<td>Chlorthalidone vs. amlodipine vs. lisinopril</td>
<td>134-136 mmHg</td>
<td>In 19,173 patients ≥ 65 yo: Lower risk of HF with thiazide vs. CCB &amp; Lower risk of HF, CVD, CHD with thiazide vs. ACEI</td>
</tr>
<tr>
<td>VALUE</td>
<td>≥ 50</td>
<td>Valsartan vs. amlodipine</td>
<td>138-139 mmHg</td>
<td>In 9566 patients ≥ 65 yo: No difference between ARB &amp; CCB</td>
</tr>
<tr>
<td>ACCOMPLISH</td>
<td>≥ 55</td>
<td>Benazepril + amlodipine vs. Benazepril + HCTZ</td>
<td>132 mmHg</td>
<td>In 7640 patients ≥ 65 yo: 19% reduction in CV events with ACEI+CCB</td>
</tr>
</tbody>
</table>

There is *enough* evidence to suggest that patients between 60-79 years old benefit from SBP lowered below 140 mmHg.
GUIDELINE DISCORD

INITIAL THERAPY FOR PATIENTS >60
UNCOMPPLICATED HTN

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (yrs.)</th>
<th>Treatment (placebo control)</th>
<th>% of patients receiving step 1 therapy ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP (1991)</td>
<td>≥ 60</td>
<td>Step 1: Chlorthalidone Step 2: Atenolol</td>
<td>46%</td>
</tr>
<tr>
<td>Syst-Eur (1997)</td>
<td>≥ 60</td>
<td>Step 1: Nitrendipine Step 2: Enalapril Step 3: HCTZ</td>
<td>46%</td>
</tr>
<tr>
<td>HYVET (2008)</td>
<td>≥ 80</td>
<td>Step 1: Indapamide Step 2: Perindopril</td>
<td>26%</td>
</tr>
</tbody>
</table>

While most antihypertensive trials in the elderly utilized thiazide and CCB-based initial regimens, ACEIs were frequently used as add on therapy.
R.W. is a 68 yo White male with no chronic medical conditions. At his annual physical, he is noted to have a BP of 156/88 mmHg. A follow-up visit 2 weeks later yields the same BP readings. The decision is made to start R.W. on antihypertensive medication. Which of the following is the best initial therapy for R.W.?

A. Chlorthalidone  
B. HCTZ  
C. Lisinopril  
D. Benazepril + HCTZ  
E. Losartan + amlodipine

Chlorthalidone vs. HCTZ
Office BP measurements

![Bar chart showing change in SBP (mm Hg) over weeks after starting treatment with HCTZ and Chlorthalidone.](Hypertension 2006:47:352-8.)
Antihypertensive Efficacy of HCTZ monotherapy as assessed by 24-hr ABPM

HCTZ dose 12.5-25 mg; p < 0.001 vs. other antihypertensives.
N = number of studies

J Am Coll Cardiol 2011;590-600.

CHLORTHALIDONE VS. HCTZ
RELATIVE RISK OF CV EVENTS

Hypertension 2012;59:1110-1117.
Not All Thiazides Are Equal

25 mg HCTZ ≈ 8.0 mg chlorthalidone ≈ 1.5 mg bendroflumethiazide

Thiazides
Balancing Risks and benefits

Hypertension 2012;59:1104-1109.
There are over 30 commercially available single-tablet antihypertensive combinations which incorporate HCTZ compared to only 4 which contain chlorthalidone and zero which contain indapamide. The products which contain chlorthalidone incorporate it with one of the following:

- Atenolol
- Azilsartan
- Clonidine
- Reserpine

HTN CONTROL DURING THE FIRST YEAR
Lipid Guidelines


Circulation. 2014;129:S1-S45; originally published online November 12, 2013;
doi: 10.1161/01.cir.0000437738.63853.7a

- Joint guideline between the American College of Cardiology (ACC) & the American Heart Association (AHA)
- Expert Panel
  - 23 experts
  - Included all members of NHLBI ATP-IV Panel (n=16)
- NHLBI charge to the Expert Panel
  - Evaluate higher quality randomized controlled trial (RCT) evidence for cholesterol-lowering drug therapy to reduce atherosclerotic cardiovascular disease (ASCVD) risk
CONCOMITANT ACC/AHA GUIDELINES

• Guideline on Assessment of Cardiovascular (CV) risk
• Guideline on Lifestyle Management to Reduce CV risk
• Guideline on Management of Overweight and Obesity in Adults


2013 AHA/ACC CHOLESTEROL TREATMENT GUIDELINES: CRITICAL QUESTIONS (CQ)

• CQ 1: What evidence supports LDL-C and non-HDL-C goals for secondary prevention of ASCVD?
• CQ 2: What evidence supports LDL-C and non-HDL-C goals for primary prevention?
• CQ 3: What is the impact of the major cholesterol modifying drugs on efficacy and safety?

MAJOR CHANGES FROM NCEP

• New risk assessment calculator for primary prevention
  ▪ Pooled Cohort Equations estimate 10-year risk of atherosclerotic cardiovascular disease (ASCVD)
  ▪ Equations based on modern, more diverse cohort
  ▪ ASCVD risk includes non-fatal and fatal myocardial infarction (MI) and non-fatal and fatal stroke
• Elimination of LDL & non-HDL treatment goals

MAJOR CHANGES FROM NCEP

• Identification of 4 statin benefit groups
  ▪ Treatment selection is based on intensity of LDL-lowering
• Safety recommendations
  ▪ Provide expert guidance on management of statin-associated adverse effects
• Deemphasize non-statin therapy
• No recommendations for triglycerides
GUIDELINES EMPHASIZE HEART HEALTHY LIFESTYLE

- Heart-healthy diet
  - Increased vegetables, fruits, whole grains, low-fat dairy, poultry, fish, legumes, nuts
  - Limit sweets, sugar-sweetened beverages, red meats
  - Utilize plans such as DASH, USDA food pattern or AHA diet
  - Reduce sodium intake (< 2,400 mg/day)
- Exercise
  - 150 minutes/week of moderate-intensity exercise, or
  - 75 minutes/week of vigorous-intensity exercise
- Achieve and maintain a healthy weight
- Smoking cessation

2013 AHA/ACC CHOLESTEROL TREATMENT GUIDELINES

Group 1
- Clinical ASCVD
- High-intensity statin therapy

Group 3
- DM (Type 1 or 2) & age 40 – 75 yrs & LDL-C < 189 mg/dL
- Calculate 10-yr risk of ASCVD*

Group 4
- No DM and age 40 – 75 yrs and LDL-C 70 – 189 mg/dL
- Calculate 10-yr risk of ASCVD*

Group 2
- LDL-C > 190 mg/dL
- High-intensity statin therapy

*The 10-year risk of ASCVD is calculated with the use of the new risk calculator available at http://my.americanheart.org/cvriskcalculator.

HF = heart failure; NYHA FC = New York Heart Association functional class; ASCVD = Atherosclerotic cardiovascular disease, LDL-C = low-density lipoprotein cholesterol; ESRD = end stage renal disease; HD = hemodialysis; DM = diabetes mellitus.

INTENSITY OF STATIN THERAPY*

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C by approximately &gt; 50%</td>
<td>Daily dose lowers LDL–C by approximately 30 to &lt; 50%</td>
<td>Daily dose lowers LDL–C by &lt; 30%</td>
</tr>
</tbody>
</table>

Atorvastatin (40†)-80 mg
Rosuvastatin 20 (40) mg

Atorvastatin 10 (20) mg
Rosuvastatin (5) 10 mg
Simvastatin 20–40 mg‡
Pravastatin 40 (80) mg
Lovastatin 40 mg
Fluvastatin 40 mg bid
Fluvastatin XL 80 mg
Pitavastatin 2–4 mg

Pravastatin 10–20 mg
Lovastatin 20 mg
Simvastatin 10 mg
Fluvastatin 20–40 mg
Pitavastatin 1 mg

*Individual responses to statin therapy varied in the RCTs. There might be a biologic basis for a less-than-average response.


INTENSITY OF STATIN THERAPY

• Moderate intensity in place of high intensity for:
  - Multiple or serious comorbidities, including impaired renal or hepatic function
  - History of previous statin intolerance or muscle disorders
  - Unexplained ALT elevations > 3 x ULN
  - Concomitant use of drugs affecting metabolism
  - > 75 years of age
  - History of hemorrhagic stroke
  - Asian ancestry
RISK ASSESSMENT FOR PRIMARY PREVENTION: GROUPS 2, 3, AND 4

• Adults, aged 20 to 79 years
  ▪ Reasonable to assess traditional ASCVD risk factors (RF) every 4 to 6 years
    - For adults aged 40 to 79 years, assess 10-year ASCVD risk every 4 to 6 years
    - Consider assessing 30-year or lifetime ASCVD risk based on ASCVD RFs for adults 20 – 59 years


RISK ASSESSMENT FOR PRIMARY PREVENTION

• Obtain complete fasting* lipoprotein profile
  ▪ total cholesterol, LDL, HDL, triglycerides
• Assess traditional ASCVD RFs
  ▪ Current cigarette smoking
  ▪ Hypertension (BP ≥140/90 mmHg or on BP medication)
  ▪ HDL-C <40 mg/dl
  ▪ Age ≥ 45 years in men or ≥ 55 years in women
  ▪ Diabetes (obtain hemoglobin A1c if status unknown)
• Calculate risk using Pooled Cohort Equations
• Discuss results with patient

* 9 to 12 hours without food or drink of any caloric value
RISK ASSESSMENT FOR PRIMARY PREVENTION

• Patient discussion
  ▪ 10-year risk and/or lifetime risk
  ▪ Patient’s risk factors (including diet and exercise)
    - Consider additional non-traditional RFs
      • Family history (1st degree relative) of premature CHD (< 55 yrs in males, < 65 yrs in females)
      • LDL-C > 160 mg/dL
      • hs-CRP ≥ 2 mg/L
      • Coronary artery calcium score: ≥ 300 agatson units or ≥ 75th percentile for age, gender, & ethnicity
      • Ankle-brachial Index (ABI): < 0.9
  ▪ Importance of lifestyle changes
  ▪ Review potential benefits and harms of statin therapy
  ▪ Ask patient their treatment preferences

PATIENTS NOT IN STATIN BENEFIT GROUPS

• No DM, between 40 and 75 years, 10-year risk 5 – 7.5%
  ▪ Lifestyle modification
  ▪ Consider non-traditional RFs
  ▪ +/- moderate intensity statin
• No DM, between 40 and 75 years, 10-year risk < 5%
  ▪ Lifestyle modification
  ▪ Consider non-traditional RFs
• No DM, < 40 or > 75 years
  ▪ < 40, consider lifetime risk, non-traditional RFs
  ▪ > 75, consider comorbidities, life expectancy, risks of therapy
Cholesterol Treatment Trialists’ (CTT) Collaborators

- Meta-analysis of 27 statin studies
- 175,000 patients with and without vascular disease
- Relative risk per 1 mmol/L LDL-C reduction based on baseline 5-year CV risk

Patients Not in Statin Benefit Groups

- DM, < 40 or > 75 years
  - Patient discussion
    - Additional RFs
    - Potential benefits vs adverse effects
    - Patient preferences
• Measure fasting lipid profile annually
• **Statin treatment regardless of lipid levels for diabetic patients with:**
  - Overt CVD: secondary prevention
  - Primary prevention if age > 40 yrs with ≥ 1 CV RF (Fam Hx, HTN, smoking, dyslipidemia, albuminuria)
• Primary prevention goal: LDL < 100 mg/dL
  - Optional secondary prevention goal: LDL < 70 mg/dL with a high dose statin
• If drug-treated patients do not reach the above goals on maximum tolerated statin therapy, a reduction in LDL of 30–40% from baseline is an alternative goal.
• Combination therapy above statin therapy not shown to be beneficial and is not recommended

Diabetes Care 2014;37:S5-S13

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**STATIN SAFETY**

• Creatine kinase (CK)
  - Baseline CK is reasonable if at increased risk of myopathy
  - CK should not be routinely measured
  - Reasonable to measure CK in patients with muscle symptoms
  - If suspecting rhabdomyolysis, measure CK, creatinine, urinalysis for myoglobinuria
• Liver function tests (LFT), specifically ALT
  - Baseline ALT before initiating statin therapy
  - Reasonable to measure ALT in patients with symptoms suggestive of hepatotoxicity
STATIN SAFETY

• New onset diabetes
  ▪ Depends on statin intensity

  Moderate Intensity Statin Treatment
  Assumes 35% RR reduction in ASCVD.
  NNH based on 1 excess case of DM per 100 individuals txed for 10 yrs

  High Intensity Statin Treatment
  Assumes 45% RR reduction in ASCVD.
  NNH based on 3 excess cases of DM per 100 individuals txed for 10 yrs


STATIN SAFETY

• New-onset DM screening criteria
  ▪ Overweight adults (BMI > 25 kg/m²) with risk factors
    - Physical inactivity
    - DM in 1st degree relative
    - High-risk race/ethnicity
    - Females with gestational DM or birth > 9 lbs
    - HTN
    - HDL < 35 mg/dL and/or TG > 250 mg/dL
    - Polycystic ovarian syndrome
    - HbA1c > 5.7%, IGT, or IFG previously
    - Other conditions of insulin resistance (acanthosis nigricans, severe obesity)
    - History of CVD
  ▪ If risk factors are present, obtain baseline HbA1c
    - If normal repeat at minimum within 3 years

Diabetes Care 2014;37:S14-S80.
MONITORING THERAPEUTIC RESPONSE & ADHERENCE

- Repeat lipid panel 4 to 12 weeks post initiation
  - Then every 3 to 12 months as clinically indicated
- Monitor for adherence at every visit
- If insufficient response
  - Reinforce adherence
  - Attempt to use maximally tolerated intensity of statin
  - If higher risk statin group on maximally tolerated intensity of statin, consider addition of nonstatin lipid tx


Case #1:

How should Mr. Johnson be treated for his BP?

A. Amlodipine
B. Atenolol
C. Chlorothalidone
D. Hydralazine
E. Lisinopril
Case #2:

How should this patient be treated for his BP?

A. Add amlodipine
B. Add HCTZ
C. Add losartan
D. Add metoprolol
E. No other treatment is needed at this time for his BP

Case #3:

How should Mr. Kaye be treated for his BP?

A. Increase HCTZ to 25 mg once daily
B. Add amlodipine
C. Add lisinopril
D. Switch from HCTZ to chlorthalidone
E. Switch from HCTZ to lisinopril
Case #4:

How should Ms. Dulce be treated for her BP?

A. Add atenolol
B. Add HCTZ
C. Add losartan
D. Add ramipril
E. No other treatment is needed at this time for her BP