Management of Lipid Disorders and Hypertension: Implications of the New Guidelines

Robert B. Baron MD MS
Professor and Associate Dean
UCSF School of Medicine

Disclosure

No relevant financial relationships
EXPLAINING THE DECREASE IN DEATHS FROM CVD

1980 to 2000: death rate fell by approximately 50% in both men and women

2000 to 2010: Death still falling: down 31%

- About 1/2 from acute treatments, 1/2 from risk factor modification:
  - Predominantly cholesterol (1/4), BP, smoking

New Lipid Guidelines

ACC/AHA December 2013
Management of Lipid Disorders and Hypertension

2013 ACC/AHA Guidelines
What is New?

- 4 groups of patients who benefit from statins
- Identifies high and moderate intensity statins
- No LDL treatment targets
- Non-statin therapies no not provide acceptable risk reduction
- Estimate 10-year ASCVD risk with new equation

Heart Protection Study: Vascular Events by Baseline LDL-C

<table>
<thead>
<tr>
<th>Baseline Feature</th>
<th>Statin (10,269)</th>
<th>Placebo (10,267)</th>
<th>Risk Ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>285</td>
<td>360</td>
<td>Statin better</td>
</tr>
<tr>
<td>≥100 &lt;130</td>
<td>670</td>
<td>881</td>
<td>Statin worse</td>
</tr>
<tr>
<td>≥130</td>
<td>1087</td>
<td>1365</td>
<td></td>
</tr>
<tr>
<td>ALL PATIENTS</td>
<td>2042 (19.9%)</td>
<td>2606 (25.4%)</td>
<td>24% reduction (p&lt;0.00001)</td>
</tr>
</tbody>
</table>
2013 ACC/AHA Guidelines
Four Groups of Patients Who Benefit From Statins

- Individuals with clinical ASCVD
- Individuals with primary elevations of LDL \( \geq 190 \)
- Individuals age 40-75 with diabetes and LDL \( \geq 70 \)
- Individuals without ASCVD or diabetes, age 40-75, with LDL \( \geq 70 \), and 10 year risk 7.5% or higher

Stone, Circulation 2013

2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals with clinical ASCVD:
  - Treat with: high intensity statin, or moderate intensity statin if > age 75
- Individuals with primary elevations of LDL \( \geq 190 \):
  - Treat with: high intensity statin

Stone, Circulation 2013
2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals 40-75 with diabetes and LDL ≥ 70:
  - Treat with: moderate intensity statin, or high intensity statin if risk over 7.5%

- Individuals without ASCVD or diabetes, 40-75, with LDL ≥ 70, and 10 year risk 7.5% or higher:
  - Treat with: moderate-to-high intensity statin

2013 ACC/AHA Guidelines
High Intensity vs. Moderate Intensity Statin

- High Intensity: lowers LDL by >50%
  - Atorvastatin 40 - 80
  - Rosuvastatin 20 - 40

- Moderate Intensity: lowers LDL by 30-50%
  - Atorvastatin 10 - 20
  - Rosuvastatin 5 – 10
  - Simvastatin 20 - 40
  - Pravastatin 40 – 80
  - Lovastatin 40
How Best To Calculate 10 Year Risk?

Pooled Cohort Risk Assessment Equations: hard CHD events and stroke

- http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp

Pooled Cohort Risk Assessment Equations

- Age
- Gender
- Race (White/African American)
- Total cholesterol (170 mg/dl)
- HDL cholesterol (50 mg/dl)
- Systolic BP (110 mmHg)
- Yes/no meds for BP
- Yes/no DM
- Yes/no cigs
- Outcome: 10-year risk of total CVD (fatal and non-fatal MI and stroke)
Management of Lipid Disorders and Hypertension

**Do the Pooled Cohort Risk Assessment Equations Overestimate Risk?**

Predicted rate of heart attack or stroke over 10 years

Actual rate observed in study

Percent of U.S. Adults Who Would Be Eligible for Statin Therapy for Primary Prevention, According to Set of Guidelines and Age Group.

How Best To Calculate 10 Year Risk?
Baron Approach

• Use both CHD (hard end points) calculator and new CV risk calculator

• Include both in shared decision-making discussion

How Best To Calculate 10 Year Risk?
Mayo Clinic Statin Choice Decision Aid:

• http://statindecisionaid.mayoclinic.org/index.php/statin/index?
PHPSESSID=0khk8nm14h9vubjm3423e6h6b2
Summary Lipid-Lowering Drugs

- Statins are treatment of choice based on RCT to decrease risk

- No evidence to support adding niacin or fibrates to statins

- If completely statin-intolerant, niacin may reduce CVD risk (weak evidence)

- Fibrates appear to lower MI risk, but no other CVD endpoints

Summary Lipid-Lowering Drugs

- Ezetimibe study: (IMPROVE-IT)

18,000 ACS patients (40% from North America)

RCT: Simvastatin vs simvastatin + ezetimibe. Took 7 years. Death, MI, Stroke

Simvastatin: 34.7% vs Simva/ezetimibe 32.7% (270 fewer events over 7 years)
PCSK9 Inhibitors

- Evolocumab (Repatha) and alirocumab (Praluent)—monoclonal antibodies that reduce liver LDL-receptor degradation
- Reduce LDL by 50%. Injectable Q2 – 4 weeks
- Approved for FH or patients with CVD “who need additional LDL lowering.”
- Unproven cardiovascular benefits

63 yo woman, no risks

<table>
<thead>
<tr>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
<th>SBP</th>
<th>BP meds</th>
<th>Smoking</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>155</td>
<td>55</td>
<td>160</td>
<td>120</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

10 yr CHD risk (old calculator): 2%…
10 yr CV risk (new calculator): 4.5%…

Therefore no medication recommended
63 yo man, no risks

LDL  155, HDL  55, TG  160
SBP  120, No BP meds
Non smoker, No DM

10 yr CHD risk (old calculator): 10%…
10 yr CV risk (new calculator): 10.8%…
“Toss-up.”  Shared decision making. If start statin (per new guidelines), can start with moderate intensity statin
Management of Lipid Disorders and Hypertension

**The Good and The Controversial of the New Cholesterol Guidelines**

- Focus on healthy lifestyle is **good**
- Focus to use statins (and not other agents) is **good**
- Focus to treat patients at high risk is **good**
- Focus to treat all patients with LDL <190 mg/dl and treat patients with DM/existing CV disease is **good**
- Not having target LDL is **controversial**
- Adults with no DM or heart disease and 10-year calculated risk >7.5% (using new risk calculator) to be treated – **controversial**

**Competing Risks**

- Example: women with 10-year risk 10%
- Reduce risk by 30% with statins. Risk now 7%.
- Add NSAID. Increase risk by 50%
- Total risk now back to 10%.
Lipid Conclusions I

- Statins are effective and cost effective in selected groups of patients

- Screen most patients (shared decision-making) at age 21 (to identify those > LDL 190, other genetic lipid disorders)

Lipid Conclusions II

- Use statins in patients with ASCVD, LDL ≥190 and diabetes

- For those without ASCVD and diabetes, calculate 10 year risk (how best uncertain), and treat those with risk greater than 7.5% (maybe 10%). Use shared decision making.

- Use appropriate intensity statin (high and moderate)
Lipid Conclusions III

- Monitor adherence, but do not treat to specific LDL goal

- Do not treat those over age 75 (unless ASCVD), on dialysis, or moderate/severe CHF

- Do not treat with other lipid-modifying drugs in addition to statins (but may need if truly statin intolerant)

- Avoid other factors that raise risk as much as statins lower it (i.e. NSAIDS)

New Hypertension Guidelines

Joint National Committee (JNC) 8
February, 2014
Current Status of Hypertension

- Prevalence 29.1%; Blacks 42.1%
- About 75.6% treated; 51.8% controlled (<140/90)
- Risk for poor control: Latinos, Blacks, age 18-44 and ≥80, <300% poverty, < college degree
- Better control: Any insurance, ≥2 visits, and a usual source of care

Accurate BP Measurement

1) Seated for 5 minutes in chair
2) Arms bared and supported
3) No cigs, coffee; no talking
4) Correct fitting cuff for arm (small cuff results in elevated BP)
5) First appearance of sound is SBP; disappearance is DBP
6) Two or more reading in 2 minutes averaged
7) Two visits to define HTN
Joint National Commission 8 (JNC 8)

Three questions:
1) Does Rx at specific BP thresholds improve outcomes?
2) Does Rx to a specific BP goal improve outcomes?
3) Do various meds differ on outcomes?

Nine recommendations

Recommendations for Management of Hypertension

Recommendation 1
≥60 years:

- Lower BP at SBP ≥150 mm Hg or DBP ≥90 mm Hg
- Treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

Strong Recommendation – Grade A (but not unanimous)

Recommendations for Management of Hypertension

Corollary Recommendation
≥60 years:

- If treatment results in lower SBP (eg, <140 mm Hg) and is well tolerated treatment does not need to be adjusted.

Expert Opinion – Grade E

Recommendations for Management of Hypertension

Recommendation 2
<60 years:

- Treat to lower BP at DBP ≥90 mm Hg
- Treat to a goal DBP <90 mm Hg.

30-59 years, Strong Recommendation – Grade A
18-29 years, Expert Opinion – Grade E
Recommendations for Management of Hypertension

Recommendation 3
<60 years:
❖ Treat to lower BP at SBP ≥140 mm Hg
❖ Treat to a goal SBP <140 mm Hg.
(Expert Opinion – Grade E)

Recommendation 4
≥18 years with chronic kidney disease (CKD) (GFR < 60 or proteinuria >30 mg alb/g creat):
❖ Treat to lower SBP ≥140 mm Hg or DBP ≥90 mm Hg
❖ Treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.
(Expert Opinion – Grade E)
Recommendations for Management of Hypertension

Recommendation 5

- ≥18 years with diabetes, treat to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg
- Treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg.

Expert Opinion – Grade E

Recommendation 6

Nonblack population, including diabetes:

Initial treatment:
- Thiazide-type diuretic
- Calcium channel blocker (CCB)
- Angiotensin-converting enzyme inhibitor (ACEI)
- Angiotensin receptor blocker (ARB).

(Moderate Recommendation – Grade B)
Recommendations for Management of Hypertension

Recommendation 7
Black population, including diabetes:

Initial treatment:
✓ Thiazide-type diuretic
✓ Calcium Channel Blocker (CCB)

General black population: Moderate Rec – Grade B
Black patients with diabetes: Weak Rec – Grade C

Recommendation 8
≥18 years with CKD, initial (or add-on) treatment:

✓ ACEI or ARB to improve kidney outcomes.
✓ For all CKD patients with HTN regardless of race or diabetes

Moderate Recommendation – Grade B
Recommendations for Management of Hypertension

Recommendation 9

- If goal BP not reached within 1 month, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB).

- Assess BP and adjust the treatment regimen until goal is reached.

- If goal cannot be reached with 2 drugs, add and titrate a third drug from the list provided.

Do not use an ACE and an ARB in the same patient.

If goal cannot be reached using the drugs in rec 6 drugs from other classes can be used.

Referral to a specialist may be indicated.

Expert Opinion – Grade E
Evidence-based Medications

**ACE inhibitors**
- Captopril
- Enalapril
- Lisinopril

**Angiotensin receptor blockers**
- Eprosartan
- Candesartan
- Losartan
- Valsartan
- Irbesartan

**Beta blockers**
- Atenolol,
- Metoprolol

**Calcium channel blockers**
- Amlodipine,
- Diltiazem ER
- Nitrendipine

**Thiazide-type diuretics**
- Bendroflumethiazide,
- Chlorthalidone,
- Hydrochlorothiazide,
- Indapamide
Key Points of JNC 8

1) ≥60 yo: goal ≤150
2) Others <140/<90 (including DM, CKD, race/ethnicity)
3) Non blacks: thiazide, CCB, ACEI, ARB
4) Blacks: thiazide, CCB
5) CKD: ACEI or ARB

Are the Guidelines Already Out of Date?

- USPSTF: Screening for HTN 2015
- Begin at age 18
- Measure carefully
- Obtain measurements outside of the clinical setting before starting treatment
Measuring BP Out of the Office

• Ambulatory monitoring is the best method (the “reference standard”)
  • Independent prediction of risk of stroke and MI
  • Fewer patients will need treatment
• Home BP monitoring may also be acceptable (but there is less data)

October 13, 2015, Annals Int Med

Are the Guidelines Already Out of Date?

• SPRINT: NIH-funded RCT
• 9,361 men and women 50 and over (30% over age 75)
• SBP > 130 mm Hg
• Increased CV risk (but no DM)
• Design <120 mm Hg vs <140 mm Hg
• Actual 121.4 mm Hg vs 136.2

Nov 9, 2015; NEJM
SPRINT: Results

• Composite outcome
  • 243 events (1.65% per year) vs 319 (2.19% per year)
  • HR 0.75 (0.64 – 0.89)
  • NNT 200 per year

• All cause mortality
  • 155 (1.03% per year) vs. 210 (1.40% per year)
  • HR 0.73 (0.60 – 0.90)
  • NNT 300 per year

SPRINT: Adverse Events

• Any serious event
  • 1793 events (38.3% per year) vs 1736 (37.1% per year)
  • HR 1.04 (p=0.25)

• Conditions of interest
  • Hypotension: HR= 1.67 (p=0.001)
  • Syncope: HR 1.33 (p=0.05)
  • Electrolyte abnormality: HR 1.35 (p=0.02)
  • Acute kidney injury: HR 1.66 (p=<.001)
NNT and NNH from SPRINT

<table>
<thead>
<tr>
<th>Over 3.26 years of trial…</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary aggregate outcome</td>
<td>61</td>
<td>-</td>
</tr>
<tr>
<td>Death from any Cause</td>
<td>90</td>
<td>-</td>
</tr>
<tr>
<td>Death from CVD</td>
<td>172</td>
<td>-</td>
</tr>
<tr>
<td>Serious Adverse Event</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td>Syncope</td>
<td></td>
<td>93</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td></td>
<td>56</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td></td>
<td>97</td>
</tr>
</tbody>
</table>

SPRINT Reflections

- Generalizability: would apply 1/6 of current patients treated for HTN
- No DM, no CVD, > age 50
- Framingham risk: 20% ten year risk
- Clear benefit with relatively high NNT, but relatively high NNH
- Free care, carefully measured BP
- More meds, more combo meds, more monitoring, more frequent visits
Final Thoughts on Hypertension

- Take the BP accurately yourself and record it in the medical record
- Consider ambulatory BP monitoring before making major treatment decisions
- In 2016, treatment decisions must be individualized
- Begin to use CV risk equations for HTN decisions, too.