PREVENTION OF CARDIOVASCULAR DISEASE IN WOMEN:
Implications of the New Guidelines for Hypertension and Lipids

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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
**Prevention Of CVD in Women**

- Overwhelming majority of recommendations are the same for women and for men
- But...there are gender differences in the magnitude of the absolute potential benefits

**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

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**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>
<th>Statin better</th>
<th>Statin worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>285</td>
<td>360</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥100 &lt;130</td>
<td>670</td>
<td>881</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥130</td>
<td>1087</td>
<td>1365</td>
<td></td>
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</tr>
<tr>
<td>ALL PATIENTS</td>
<td>2042 (19.9%)</td>
<td>2606 (25.4%)</td>
<td></td>
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</tr>
</tbody>
</table>

24% reduction (p<0.00001)

**2013 ACC/AHA Guidelines**

**Four Groups of Patients Who Benefit From Statins**

- Individuals with clinical ASCVD
- Individuals with primary elevations of LDL ≥190
- Individuals age 40-75 with diabetes and LDL ≥70
- Individuals without ASCVD or diabetes, age 40-75, with LDL ≥70, and 10 year risk 7.5% or higher
2013 ACC/AHA Guidelines
Importance of Lifestyle Recommendations

- Heart healthy diet
- Regular aerobic exercise
- Desirable body weight
- Avoidance of tobacco

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 ≥190:
  - Treat with: high intensity statin

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?

Old Issues
- Hard vs. hard + soft CHD end points (angina)
- CHD or CVD
- Include diabetes or not
- Include peripheral vascular disease or not
- Race/ethnicity (usually not)
- Include family history and hs-CRP (Reynolds)
- Ranges vs. exact numbers
- Paper vs. computer vs. phone

How Best To Calculate 10 Year Risk?

New

Pooled Cohort Risk Assessment Equations: hard CHD events and stroke

- Insufficient shared decision making

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)

http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
Do the Pooled Cohort Risk Assessment Equations Overestimate Risk?

Ridker PM, Cook NR. Lancet. Nov 19, 2013

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 December 2014

- Use both CHD (hard end points) calculator and new CV risk calculator
- Include both in shared decision-making discussion

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: new study (IMPROVE-IT) presented as abstract November 2014

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)

63 yo woman, no traditional risk factors

LDL 155
HDL 55
TG 160
SBP 120
No BP meds
No DM
Nonsmoker

The best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)
2. Begin atorvastatin 40
3. Begin atorvastatin 10
4. Begin simvastatin 20
5. Begin sustained release niacin
6. Begin red yeast rice

2013 ACC/AHA Guidelines

What Statin for Each Group?

- 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
63 yo woman, no risks

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

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

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 controversial
- 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

NSAIDs and CVD: Meta-analysis

31 RCTs, 116,429 patients

MI: No increase naproxen, diclofenac
Ibuprofen 1.61; celecoxib 1.35

Stroke: All drugs increased
Naproxen 1.76, Ibuprofen 3.36, Diclofenac 2.86

CV death: No increase naproxen
Ibuprofen 2.39, diclofenac 3.98, celecoxib 2.07

Total death: All drugs increased
Naproxen 1.23, Ibuprofen 1.77, Diclofenac 2.31, celecoxib 1.50

Trelle S. BMJ 2011
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 women 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%; Blacks 33.5%
About 72.5% treated; 53.5% uncontrolled (>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
The next best step is:

1. Continue current therapy
2. Begin hydrochlorothiazide
3. Begin Ace Inhibitor
4. Begin Calcium Channel Blocker
5. Begin beta blocker

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)

Evidence from 6 studies of patients over age 60, treated to goal ≤150/90: HYVET, Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS

Some evidence (lower quality) comparing ≤160 to ≤140 and ≤150 to ≤140 showing no additional benefit

Hypertension in the Very Elderly Trial (HYVET)

3845 patients ≥ 80 y, 2 years

>160 mm Hg – goal of 150/80 mm Hg
BP=173/91
Indapamide SR 1.5 mg vs. placebo
Added perindopril if needed

Beckett NS, NEJM 2008; 358: 1887-1898
**HYVET Study Results**

<table>
<thead>
<tr>
<th>End Point</th>
<th>Meds</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>12.4</td>
<td>17.7</td>
<td>0.64 (0.46 - 0.95)</td>
</tr>
<tr>
<td>CVA Death</td>
<td>6.5</td>
<td>10.7</td>
<td>0.55 (0.33 - 0.93)</td>
</tr>
<tr>
<td>CHF</td>
<td>5.3</td>
<td>14.8</td>
<td>0.28 (0.17 - 0.48)</td>
</tr>
<tr>
<td>CV Death</td>
<td>23.9</td>
<td>30.7</td>
<td>0.73 (0.55 - 0.97)</td>
</tr>
<tr>
<td>Any Death</td>
<td>47.2</td>
<td>59.6</td>
<td>0.72 (0.59 - 0.88)</td>
</tr>
</tbody>
</table>

**HYVET Conclusions and Implications**

Benefits appear at 1 year of Rx

- NNT = 20 to prevent one stroke
- NNT = 10 to prevent one CHF

Never too old to treat SBP > 160

Goal does not have to be < 140

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**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**

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**73 yo woman. BP=148/88. No DM. Creat 1.1. Otherwise well. On non-drug therapy. The next best step is:**

1. **Continue current therapy**
2. Begin hydrochlorothiazide
3. Begin Ace Inhibitor
4. Begin Calcium Channel Blocker
5. Begin beta blocker
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

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

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
Intensive BP Control in Type 2 DM: ACCORD

- RCT of 4733 patients with type 2 DM
- Compare BP less than 120 mm Hg vs 140

<table>
<thead>
<tr>
<th>BP</th>
<th>120</th>
<th>140</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV events plus death</td>
<td>1.87%</td>
<td>2.09%</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.28%</td>
<td>1.19%</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.32%</td>
<td>0.53%</td>
</tr>
<tr>
<td>Adverse events</td>
<td>3.3%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

In type 2 DM: treating to 120 mm Hg did not reduce the rate of composite fatal and non-fatal CV events

Recommendations for Management of Hypertension

Recommendation 6
Nonblack population, including diabetes:

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

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

53 yo African-American man, BP=148/88. + DM Type 2, Creatinine 1.1. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker
53 yo African-American man, BP=148/88. + DM Type 2, Creatinine 1.1. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker

Recommendations for Management of Hypertension

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 and 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

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

**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

**One Other Key Point**
Take the BP accurately yourself, and record it in the medical record.