MANAGEMENT OF HIGH BLOOD CHOLESTEROL: IMPLICATIONS OF THE NEW GUIDELINES

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Declaration of full disclosure: No conflict of interest

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
• Reductions in cholesterol: 1/4

Placebo-Controlled Statin Trials

Prevention Of CVD in Women

• Overwhelming majority of recommendations are the same for women and for men
• Aspirin use is a notable exception
• But…there are gender differences in the magnitude of the absolute potential benefits
A 40 year women, in good health. In for a preventive visit. BMI, BP, diet and exercise all at ideal. What blood tests will you order to screen her for a lipid disorder?

1. Total cholesterol (fasting or non-fasting)
2. Total and HDL cholesterol (fasting or non-fasting)
3. LDL and HDL cholesterol (fasting)
4. LDL, HDL, and hs-CRP
5. No screening blood tests for lipids

USPSTF: Screening Recommendations

- Men:
  - age 35 and older, regardless of risk level
  - age 20 to 35, at increased risk

- Women:
  - age 20 and older at increased risk
  - If not at increased risk, no recommendation (I)

- Increased Risk:
  - tobacco use, diabetes, hypertension, obesity, and family history of premature CV disease.

ACC/AHA Screening

- All adults age 21.

ACC/AHA CVD Risk: Ideal

- Total cholesterol <200 mg/dL (untreated)
- BP <120/<80 mm Hg (untreated)
- Fasting blood glucose <100 mg/dL (untreated)
- Body mass index <25 kg/m2
- Abstinence from smoking
- Physical activity at goal for adults >20 y of age: 150 min/wk moderate intensity, 75 min/wk vigorous intensity, or combination
- Healthy (DASH-like) diet
A 40 year woman, in good health. In for a preventive visit. BMI, BP, diet and exercise all at ideal. No prior lipid screen. What blood tests will you order to screen her for a lipid disorder?

1. Total cholesterol (fasting or non-fasting)
2. Total and HDL cholesterol (fasting or non-fasting)
3. LDL and HDL cholesterol (fasting) (MY CHOICE)
4. LDL, HDL, and hs-CRP
5. No screening blood tests for lipids

BARON TREATMENT CONCLUSIONS: OLDER

= Patients with CHD or CHD equivalent:
  • Treat aggressively with statin independent of LDL level (to LDL <70 in most cases)
  • Treat other risk factors aggressively as well, especially easy ones (HTN, Aspirin use)
  • Little evidence that adding a second drug (if on statin) adds benefit
  • Patients at high risk are undertreated. Maximize adherence and avoid clinical inertia

BARON TREATMENT CONCLUSIONS: OLDER

= Patients without CHD:
  • Use medications at thresholds based on LDL and risk:

<table>
<thead>
<tr>
<th>LDL goal</th>
<th>LDL drug threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk (&gt;20%) &lt;100 (&lt;70 optional)</td>
<td>≥100</td>
</tr>
<tr>
<td>Mod high risk (10-20%) &lt;100</td>
<td>≥130</td>
</tr>
<tr>
<td>Moderate risk (&lt;10%) &lt;100</td>
<td>≥160</td>
</tr>
<tr>
<td>Low risk (no risk factors) &lt;100</td>
<td>≥190</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>ASA</th>
<th>STATIN</th>
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<tbody>
<tr>
<td>High Risk (&gt;20%) YES</td>
<td>YES</td>
</tr>
<tr>
<td>Mod high risk (10-20%) YES</td>
<td>YES</td>
</tr>
<tr>
<td>Moderate risk (&lt;10%) NO</td>
<td>Occasional YES</td>
</tr>
<tr>
<td>Low risk (no risk factors) NO</td>
<td>Usually NO</td>
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</table>
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>
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</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></td>
</tr>
<tr>
<td>≥100 &lt;130</td>
<td>670</td>
<td>881</td>
<td></td>
</tr>
<tr>
<td>≥130</td>
<td>1087</td>
<td>1365</td>
<td></td>
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<tr>
<td>ALL PATIENTS</td>
<td>2042 (19.9%)</td>
<td>2858 (23.4%)</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 ≥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

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

TREATING TO NEW TARGETS (TNT)

- RCT of 10,001 patients with stable CHD; 35-75 yr
- LDL <130 mg/dl
- Atorvastatin 10 vs atorvastain 80
- Followed for 4.9 years
- Research question: safety and efficacy of lowering LDL below 100 mg/dl

<table>
<thead>
<tr>
<th></th>
<th>LDL</th>
<th>Event %</th>
<th>Death %</th>
<th>↑ LFTs %</th>
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<tbody>
<tr>
<td>Atorv 10</td>
<td>101</td>
<td>10.9</td>
<td>2.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Atorv 80</td>
<td>77</td>
<td>8.7</td>
<td>2.0</td>
<td>1.2</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>0.09</td>
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</table>
### 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 Issues

- 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)**

**How Best To Calculate 10 Year Risk? New**

**Pooled Cohort Risk Assessment Equations: hard CHD events and stroke**

- [http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp](http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp)
- [http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx](http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx)
Do the Pooled Cohort Risk Assessment Equations Overestimate Risk?

How Best To Calculate 10 Year Risk?
Baron approach April 2014

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

63 yo woman; s/p MI

<table>
<thead>
<tr>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
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<tbody>
<tr>
<td>115</td>
<td>45</td>
<td>160</td>
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</table>

The best next step in lipid management is:

1. Atorvastatin 40 mg
2. Rosuvastatin 10 mg
3. Pravastatin 40 mg
4. Simvastatin 40 mg
5. Lovastatin 40 mg
6. Whatever works to get her LDL below 70 mg/dl
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

The best next step in lipid management is:

1. Atorvastatin 40 mg
2. Rosuvastatin 10 mg
3. Pravastatin 40 mg
4. Simvastatin 40 mg
5. Lovastatin 40 mg
6. Whatever works to get her LDL below 70 mg/dl

63 yo woman; s/p MI. On atorvastatin 80.

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<table>
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<tr>
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<tbody>
<tr>
<td>LDL</td>
<td>95</td>
</tr>
<tr>
<td>HDL</td>
<td>40</td>
</tr>
<tr>
<td>TG</td>
<td>200</td>
</tr>
</tbody>
</table>

The best next step in lipid management is:

1. Continue current therapy
2. Switch to rosuvastatin 40 mg
3. Add fenofibrate
4. Add fish oil
5. Add niacin
6. Add ezetimibe
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
• Ezetimibe: just say no

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

The best next step in lipid management is:

1. Continue current therapy
2. Switch to rosuvastatin 40 mg (Also potentially correct, but medication still on patent)
3. Add fenofibrate
4. Add fish oil
5. Add niacin
6. Add ezetimibe

63 yo woman, no traditional risk factors

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>LDL</td>
<td>155</td>
</tr>
<tr>
<td>HDL</td>
<td>55</td>
</tr>
<tr>
<td>TG</td>
<td>160</td>
</tr>
<tr>
<td>SBP</td>
<td>120</td>
</tr>
<tr>
<td>No BP meds</td>
<td></td>
</tr>
<tr>
<td>No DM</td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
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</tbody>
</table>
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 traditional risk factors

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

LDL  155, HDL  55, TG  160
SBP  120, No BP meds
Nonsmoker, 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 best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)- old (but toss-up)
2. Begin atorvastatin 40-new (but still close call)
3. Begin atorvastatin 10-new (but still close call)
4. Begin simvastatin 20-new (but still close call)
5. Begin sustained release niacin
6. Begin red yeast rice

Key is shared decision-making
**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 1.78, 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

**NSAIDs and CVD**

- Danish national study, 97,698 patients with prior MI. 44% received NSAIDS.

- NSAIDS associated with 42% increase in CV death (CI 1.36 – 1.49)

- Diclofenac 96% and rofecoxib 66% increase

- Ibuprofen 34% and naproxen 27% increase


**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%

**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)
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).

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).