Lipid Panel Management
Refresher Course for the Family Physician

Kevin T. Schleich, Pharm.D., BCACP
Clinical Pharmacy Specialist, Department of Family Medicine
University of Iowa Hospitals and Clinics

Objectives
• Understand the evidence that was evaluated to develop the 2013 ACC/AHA guidelines
• Discuss the utility and “accuracy” of the new ASCVD Risk Calculator
• Be familiar with non-statin drugs and their place in therapy based on the new guidelines
• Utilize patient cases to highlight practical scenarios related to lipid management

History
• The National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults
  • ATP-I: 1985
  • ATP-II: 1993
  • ATP-III: 2003
• In response to the 2011 IOM report on the development of trustworthy guidelines, the National Heart, Lung, and Blood Institute (NHLBI) decided to partner with the American College of Cardiology (ACC) and the American Heart Association (AHA)

Scope of the Guidelines
• “The Expert Panel was charged with updating the clinical practice recommendations for the treatment of blood cholesterol levels to reduce atherosclerotic cardiovascular disease (ASCVD) risk...”
  • ASCVD = coronary heart disease (CHD), stroke, and peripheral arterial disease (PAD), all of presumed atherosclerotic origin
  • “…intended to address the treatment of adults (> 21 years of age)...”
  • “…these guidelines were never intended to be a comprehensive approach to lipid management for purposes other than ASCVD risk reduction.”

Evidence for 3 Critical Questions
1. What is the evidence for LDL-C and non-HDL goals for the secondary prevention of ASCVD?
   • Expert Panel reviewed 19 RCTs
2. What is the evidence for LDL-C and non-HDL goals for the primary prevention of ASCVD?
   • Expert Panel reviewed 6 RCTs
3. For primary and secondary prevention, what is the impact on lipid levels, effectiveness, and safety of specific cholesterol-modifying drugs for lipid management?
   • Unclear how many RCTs were evaluated for this specific question

Statin Benefit Groups

4 Statin Benefit Groups
Primary Prevention Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Results</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Prevention of Acute Coronary Events: a randomized controlled trial</td>
<td>• R, DL, PC; n=18,000 with LDL-C 70-189 mg/dL or placebo</td>
<td>• First occurrence of CHD was significantly reduced in patients on R (OR 0.67, 95% CI [0.60; 0.75])</td>
<td>Published by Merck</td>
</tr>
<tr>
<td>Primary prevention of CV events in men and women with high cholesterol not treated with statins</td>
<td>• R, DL, B</td>
<td>• First occurrence of CV events was significantly reduced in patients on DL (RRR 30%, 95% CI [5%; 50%])</td>
<td></td>
</tr>
<tr>
<td>Primary prevention of CV events in men and women with high cholesterol not treated with statins</td>
<td>• R, DL, B; n=6800 with high sensitivity LDL-C (≥ 200 mg/dL)</td>
<td>• Risk reduction in the incidence of major coronary events 30% (95% CI [20; 39%])</td>
<td></td>
</tr>
</tbody>
</table>

How Intense is Your Statin?

<table>
<thead>
<tr>
<th>High-intensity Statin</th>
<th>Moderate-intensity Statin</th>
<th>Low-intensity Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovastatin 40-80 mg</td>
<td>lovastatin 10-20 mg</td>
<td>lovastatin 10 mg</td>
</tr>
<tr>
<td>Pravastatin 40 mg</td>
<td>pravastatin 20 mg</td>
<td>pravastatin 10 mg</td>
</tr>
<tr>
<td>Simvastatin 40 mg</td>
<td>simvastatin 20 mg</td>
<td>simvastatin 10 mg</td>
</tr>
<tr>
<td>Fluvastatin 40 mg</td>
<td>fluvastatin 20 mg</td>
<td>fluvastatin 10 mg</td>
</tr>
<tr>
<td>Pitavastatin 40 mg</td>
<td>pitavastatin 20 mg</td>
<td>pitavastatin 10 mg</td>
</tr>
<tr>
<td>Rosuvastatin 80 mg</td>
<td>rosuvastatin 40 mg</td>
<td>rosuvastatin 20 mg</td>
</tr>
<tr>
<td>Atorvastatin 80 mg</td>
<td>atorvastatin 40 mg</td>
<td>atorvastatin 20 mg</td>
</tr>
<tr>
<td>Ezetimibe 10 mg</td>
<td>ezetimibe 5 mg</td>
<td>ezetimibe 2.5 mg</td>
</tr>
</tbody>
</table>

ASCVD Risk Estimator

- **What was wrong with the Framingham?**
  - Risk estimates were derived from exclusively white populations
  - Only estimated risk of coronary heart disease
  - Did not include risk estimates of stroke

- **The ASCVD Risk Estimator estimates the 10-year risk of:**
  - Nonfatal myocardial infarction
  - Coronary heart disease death
  - Fatal or nonfatal stroke

Can We Trust New Calculator?

- **What literature was evaluated for risk estimates?**
  - ARIC Study
  - Cardiovascular Health Study
  - CARDIA Study
  - Framingham Original Study
  - Framingham Offspring Study

- **What patients were included in the “pooled cohort”?**
  - African American and white men/women
  - Age 40-79 years
  - Patients with established cardiovascular disease were excluded
  - Majority of patients were not on statin therapy
Risk Factors

• **How to modify the modifiable**
  • Smoking

• 44 year-old African American male (TC: 195 mg/dL; HDL 50 mg/dL) who has controlled hypertension on chlorthalidone and amlodipine (SBP 135 mmHg) and smokes 2 ppd.

Controversy?

• Dr. John Ioannidis, MD published a viewpoint in JAMA in December 2013
  • "Statinization" of the world population
    • Guidelines developed for US population, but extrapolations to world population will occur
    • 33 million Americans are expected to have a 10-year risk ≥ 7.5%
    • 13 million Americans are expected to have risk between 3% and 7.4%

• Dr. Paul Ridker, M.D. and Dr. Nancy Cook, M.D. published a perspective in JAMA in November 2013
  • "...it is possible that as many as 40-50% of the 33 million middle-aged Americans targeted by the new ACC/AHA guidelines for statin therapy do not actually have risk thresholds that exceed the 7.5% threshold suggested for treatment."

What About Everything Else?
No Evidence for Preventing ASCVD Risk

Safety of Non-Statins

- **Fibrates**
  - Gemfibrozil should NOT be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis.
  - Fenofibrate may be considered in those with a low- or moderate-intensity statin ONLY.
  - Avoid all fibrates in patients with high-intensity statins.
  - Avoid fibrates in patients with compromised renal function (GFR < 30 mL/min).

- **Omega 3**
  - When used for severe hypertriglyceridemia (TG ≥ 500 mg/dL), main ADRs are GI disturbances, skin changes and bleeding.

Safety of Non-Statins

- **Niacin**
  - Avoid with hepatic dysfunction (ALT > 2-3 times ULN).
  - Avoid if new-onset atrial fibrillation or weight loss occurs.
  - Start at a low dose and titrate very slowly.
  - ER: start at 500 mg/d and increase up to 2000 mg/d over 4 to 8 weeks.
  - IR: start at 100 mg daily to 310 and increase slowly up to 3 g/d.

- **BAS**
  - Avoid in patients with fasting TG ≥ 300 mg/dL.
  - Discontinue if TG exceed 400 mg/dL during therapy.

- **Ezetimibe**
  - Do not initiate, or discontinue of ALT elevations > 3 times ULN occur.

Case #1

- LI is a 47-year-old white male with controlled hypertension (130/85 mmHg), and type 2 diabetes mellitus (A1c = 7.1%).
  - He smoked for 10 years, but quit over 2 years ago.
  - **Current medications:**
    - Aspirin 81 mg daily, chlorthalidone 25 mg daily, glipizide XL 10 mg daily, lisinopril 40 mg daily, metformin 1000 mg twice daily.
  - He wants to transfer care to you, so you obtain lab work:

<table>
<thead>
<tr>
<th>Lab Value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>215 mg/dL</td>
</tr>
<tr>
<td>HDL</td>
<td>33 mg/dL</td>
</tr>
<tr>
<td>LDL-c</td>
<td>147 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>165 mg/dL</td>
</tr>
<tr>
<td>ALT</td>
<td>20 U/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>50 U/L</td>
</tr>
</tbody>
</table>

Case #2

- HM is a 70-year-old healthy white male with no significant past medical history. He presents for his yearly physical. He only takes aspirin 81 mg daily. He has no significant family history for early cardiovascular disease. He partakes in cardiovascular exercise 60 to 90 minutes every day. His lipid panel today demonstrates the following:

<table>
<thead>
<tr>
<th>Lab Value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>100 mg/dL</td>
</tr>
<tr>
<td>HDL</td>
<td>75 mg/dL</td>
</tr>
<tr>
<td>LDL-c</td>
<td>165 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>100 mg/dL</td>
</tr>
</tbody>
</table>
Case #2

• BC is a 67 year-old white female who presents to your clinic for follow-up. She has a past medical history significant for MI, s/p CABG (2005), hypertension (139/89 mmHg treated), peripheral artery disease, type 2 diabetes mellitus (A1c 9.5%), and hypothyroidism.

• She returns after being tried on atorvastatin 40 mg daily 3 months ago. She stopped using it after 2 weeks due to severe myopathy. She has previously been intolerant to lovastatin, simvastatin, and now most recently pravastatin. Her lipid panel 3 months ago was:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>225 mg/dL</td>
</tr>
<tr>
<td>HDL</td>
<td>25 mg/dL</td>
</tr>
<tr>
<td>LDL</td>
<td>170 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>250 mg/dL</td>
</tr>
<tr>
<td>ALT</td>
<td>23 U/L</td>
</tr>
</tbody>
</table>

Conclusions

- The 2013 ACC/AHA Lipid Guidelines were developed to help manage 10-year ASCVD risk
- Robust evidence is lacking for the use of statins for primary prevention
- The ASCVD Risk Calculator should act as a tool to help stratify risk and help guide decision-making for optimal treatment of patients
- The ASCVD Risk Calculator is more encompassing than the Framingham Risk Calculator, but still has controversies surrounding the ability to accurately predict risk

Questions/Discussion

- Non-statin drugs do not have the evidence to reduce ASCVD outcomes, so ensure they are being utilized safely if they are being used
- It is appropriate to focus on risk factor modification to help improve ASCVD risk as opposed to simply starting statins
- Consider alternate statin options for patients who have previously been intolerant to statins
  - Every-other-day rosvastatin
  - Pravastatin or fluvastatin
- Utilize the new guidelines to have discussions with your patients about risks vs. benefits of starting lipid-lowering therapy