Prevention of Heart Disease: The New Guidelines

Nisha I. Parikh MD MPH
Assistant Professor of Medicine
Division of Cardiology
Department of Medicine
University of California San Francisco
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Disclosures

• No relevant disclosures
Summary of Talk

• Introduction
• 2013 ACC/AHA Guidelines on Treatment of Cholesterol
• 2013 ACC/AHA Guideline on Assessment of CVD Risk
• Conclusions

Four guidelines

• 2013 ACC/AHA Guidelines on Treatment of Cholesterol
• 2013 ACC/AHA Guideline on Assessment of CVD Risk
• 2013 ACC/AHA Guideline on Lifestyle Management to Reduce CVD Risk
• 2013 ACC/AHA Guideline on Management of Overweight and Obesity in Adults
Age-Adjusted Prevalence of Cardiovascular Disease Risk Factors in Adults, U.S. 1961-2011

Deaths From Cardiovascular Diseases, U.S. 1900–2010

Vital Statistics of the United States, NCHS. NHLBI Factbook 2012
Background: NCEP ATP 3: 2001 and update in 2004

- NCEP ATP 3, 2001
  - <10, 10-20, >20% 10 yr. CHD Risk Categories (based on Framingham Risk Score)
  - “Risk Equivalents”: DM, AAA, PVD
  - High Risk LDL goal < 100 mg/dL, institute diet, lifestyle changes if LDL between 100-129 mg/dL

- ATP 3 Update, 2004
  - Additional Goal LDL of <70 mg/dL for very high risk CVD
  - Initiate diet/medical therapy for all persons over LDL goal
  - Target LDL reduction of 30-40%

Deaths From Cardiovascular Diseases, U.S. 1900–2010

Vital Statistics of the United States, NCHS. NHLBI Factbook 2012

2013 AHA/ACC Prevention Guidelines

- Focused on evidence
- Statin-Based Randomized Controlled Trials (RCTs)
  - These were designed with fixed statin dosages
  - RCTs either compared fixed doses of statins with placebo or untreated controls,
  - or RCTs compared fixed doses of higher-intensity statins with moderate-intensity statins.
  - RCTs not focused on LDL and non-HDL treatment targets
- These guidelines were thus a departure from prior NCEP ATP 3 guidelines

* Not age-adjusted, † CLRD= COPD and asthma
Vital Statistics of the United States, NCHS. NHLBI Factbook 2012
Statin Trials of CVD Prevention: LDL level and risk of CHD

Association between LDL lowering/CHD risk reduction
* All LDL levels
* Less at lower LDL levels

Recommendation and Level of Evidence: Size of Treatment Effect

- Class I: Benefit >>> Risk, SHOULD DO
- Class IIa: Benefit >> Risk (+ studies needed) IT IS REASONABLE TO DO
- Class IIb: Benefit ≥ Risk, (++) studies needed) MAY BE CONSIDERED
- Class III: No Benefit or There is Harm
Recommendation and Level of Evidence: Certainty of Treatment Effect

- LEVEL A: Multiple populations, multiple RCTs or meta-analyses
- LEVEL B: Limited populations, single RCT or nonrandomized trial
- LEVEL C: Very limited populations, consensus opinion, expert opinion, case studies

ASCVD Definition

- ASCVD
  - Atherosclerotic cardiovascular disease
  - Includes coronary heart disease (CHD), stroke, and peripheral arterial disease
Definitions of Statin Intensity

**Table 5.**

High-, Moderate-, and Low-Intensity Statin Therapy (Used in the RCTs Reviewed by the Expert Panel)*

<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, on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL-C, on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL-C, on average, by &lt;30%</td>
</tr>
<tr>
<td><strong>Atorvastatin (40†)–80 mg</strong></td>
<td><strong>Atorvastatin 10 (20) mg</strong></td>
<td><strong>Simvastatin 10 mg</strong></td>
</tr>
<tr>
<td><strong>Rosuvastatin 20 (40) mg</strong></td>
<td><strong>Rosuvastatin (5) 10 mg</strong></td>
<td><strong>Pravastatin 10–20 mg</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Simvastatin 20–40 mg‡</strong></td>
<td><strong>Lovastatin 20 mg</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Pravastatin 40 (80) mg</strong></td>
<td><strong>Fluvastatin XL 80 mg</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Lovastatin 40 mg</strong></td>
<td><strong>Fluvastatin 40 mg BID</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Fluvastatin 40 mg BID</strong></td>
<td><strong>Pitavastatin 2–4 mg</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Pitavastatin 2–4 mg</strong></td>
<td><em>Simvastatin 10 mg</em>*</td>
</tr>
</tbody>
</table>

ACC/AHA Guidelines: Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults

**KEY RECOMMENDATIONS**
Summary of Key Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults

Secondary Prevention/Clinical ASCVD (I,A)
1. ≤ Age 75: High Intensity Statin
2. > Age 75: Moderate Intensity Statin

Primary Prevention, LDL ≥ 190 mg/dL
1. Rule out underlying cause (I,B)
2. Age ≥ 21 years, start High Intensity Statin (I,B)
3. Want to achieve ≥ 50% LDL reduction (IIa, B)
4. Non-statin can be added on as needed (IIb, C)
Common secondary causes of hyperlipidemia

<table>
<thead>
<tr>
<th>Secondary Cause</th>
<th>Elevated LDL-C</th>
<th>Elevated Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Saturated or trans fats, weight gain, anorexia nervosa</td>
<td>Weight gain, very-low-fat diets, high intake of refined carbohydrates, excessive alcohol intake</td>
</tr>
<tr>
<td>Drugs</td>
<td>Diuretics, cyclosporine, glucocorticoids, amiodarone</td>
<td>Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sevelamer, ranolazine, tamoxifen, beta blockers (not carvedilol), thiazides</td>
</tr>
<tr>
<td>Diseases</td>
<td>Biliary obstruction, nephrotic syndrome</td>
<td>Nephrotic syndrome, chronic renal failure, lipodystrophies</td>
</tr>
<tr>
<td>Disorders and altered states of metabolism</td>
<td>Hypothyroidism, obesity, pregnancy*</td>
<td>Diabetes (poorly controlled), hypothyroidism, obesity, pregnancy*</td>
</tr>
</tbody>
</table>

Summary of Key Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults

Primary Prevention, Diabetes, ages 40-75, LDL 70-190 mg/dL

1. Moderate Intensity Statin (I,A)
2. High Intensity Statin if 10 yr ASCVD risk ≥ 7.5% (IIa,B)
Summary of Key Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults

Primary Prevention, No DM, ages 40-75, LDL 70-190 mg/dL

* 10 year calculation of ASCVD risk Q 4-6 yrs
  1. ≥ 7.5%: High intensity statin (I,B)
  2. 5 to < 7.5: Moderate intensity statin (IIa,B)
  3. Can consider other factors: CAC ≥ 300 AU, ABI < 0.9, FH CAD, HS-CRP > 2, LDL-C > 160, Lifetime ASCVD risk (IIb, C)

Summary of Key Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults

Primary Prevention

1. When LDL < 190 mg/dL or age < 40 or >75, and ASCVD risk < 5%
   A. Statin therapy may be considered in selected individuals (IIb,C)
   B. Measure hs-CRP, lifetime risk, FH premature CAD, ABI, CAC etc. (IIb,C)
Populations in which statins not shown to be effective

• Hemodialysis
• Heart Failure

Statin Adherence and Safety: Highlights

1. Measure a fasting lipid panel 4-6 weeks after initiation or dose change
2. Do not measure ALT or CK unless symptomatic
Muscle Symptoms and CK measurement

• The incidence of myopathy, defined as unexplained muscle symptoms including weakness and muscle fatigue, in combination with CK >10 times ULN or rhabdomyolysis, defined as CK >40 times ULN, was extremely low in clinical trials

• Rhabdomyolysis - common in simvastatin 80 mg - limit the use of this dosage to those already on this dosage

Statins and Cognition

• No evidence of cognitive decline from RCTs
  – HPS (20K Simvastatin versus Placebo)
  – Prosper (8K on Pravastatin versus Placebo)
  – Jupiter “confusional state” in 18 versus 4 on rousuvastatin (8K in each arm)

• In the resulting statin safety advisory, the FDA noted that post-marketing adverse event reports “generally described individuals over the age of 50 years who experienced notable, but ill-defined memory loss or impairment that was reversible upon discontinuation of statin therapy”
RCT of Non-LDL Targets: AIM-High

The NEW ENGLAND JOURNAL of MEDICINE

Niacin in Patients with Low HDL Cholesterol Levels Receiving Intensive Statin Therapy

The AIM-HIGH Investigators

AIM-High: Higher Side effect Profile in Niacin + Statin vs. Placebo + Statin

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo plus Statin (N = 1696)</th>
<th>Extended-Release Niacin plus Statin (N = 1718)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of study-drug dose after randomization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients requiring dose reduction — no. (%)</td>
<td>58 (3.4)</td>
<td>109 (6.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary reason for dose reduction — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flushing or itching</td>
<td>23 (1.4)</td>
<td>57 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Abnormality on liver-function test</td>
<td>0</td>
<td>1 (0.1)</td>
<td></td>
</tr>
<tr>
<td>Request by patient</td>
<td>11 (0.6)</td>
<td>13 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Request by nonstudy physician</td>
<td>3 (0.2)</td>
<td>1 (0.1)</td>
<td></td>
</tr>
<tr>
<td>Other clinical reason</td>
<td>10 (0.6)</td>
<td>21 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Increased glucose level</td>
<td>5 (0.3)</td>
<td>10 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>4 (0.2)</td>
<td>4 (0.2)</td>
<td></td>
</tr>
</tbody>
</table>
A New Perspective on LDL-C and/or Non–HDL-C Treatment Goals

- The Expert Panel was unable to find RCT evidence to support continued use of specific LDL-C or non–HDL-C treatment targets.
- The appropriate intensity of statin therapy should be used to reduce ASCVD risk in those most likely to benefit.
- Non-statin therapies, as compared with statin therapy, do not provide acceptable ASCVD risk-reduction benefits relative to their potential for adverse effects.
Role of Biomarkers and Noninvasive Tests

- Treatment decisions in selected individuals who are not included in the statin benefit groups may be informed by other factors as recommended by the Risk Assessment Work Group and Blood Cholesterol Expert Panel.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Uncertain</th>
<th>Certain</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApoB</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>albuminuria</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>glomerular filtration rate</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>cardiorespiratory fitness</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>family history</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>hs-CRP</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>CAC score</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>ABI</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
ASCVD Risk Calculator

• Population
  – Pooled cohorts:
    • ARIC (Atherosclerosis Risk in Communities) study,
    • Cardiovascular Health Study
    • CARDIA (Coronary Artery Risk Development in Young Adults) Study
    • Framingham Original and Offspring Study cohorts
  – Age range 21-74 years of age

ASCVD Risk Calculator Example:
50 year old AA Woman
Total Cholesterol 200, HDL 40
SBP 140 mmHg
on BP Medications

https://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
Future Updates to the Blood Cholesterol Guideline

- Future updates will build on this foundation to provide expert guidance on the management of complex lipid disorders and incorporate refinements in risk stratification based on critical review of emerging data.
- RCTs comparing alternative treatment strategies are needed in order to inform future evidence-based guidelines for the optimum ASCVD risk-reduction approach.
Conclusions

2013 Lipid Guidelines
- Based on available RCT data
- No longer advocate treatment targets
- Recommend treating at lower ASCVD risk level than prior guidelines
- Will likely increase % of men and women on statins as compared to NCEP ATP 3*
- Implications on ASCVD risk reduction should be studied

* Kavousi et al, JAMA 2014

THANK YOU!

“Your cholesterol levels are excellent, but you still won’t make it past February.”

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