Cholesterol-Lowering Therapy in Secondary and Primary Prevention

Scott M. Grundy MD PhD
Univ of Texas Southwestern Medical Center
VA Medical Center
Dallas, Texas

COI: None
Secondary Prevention: the Lower, the Better for LDL-C

Mean LDL-C level at follow-up (mg/dL)

% with CHD event

Pl=placebo; Rx=treatment
Secondary Prevention: the Lower, the Better for LDL-C

Boekholdt et al. JACC 2014;64:485-94
What are options for intolerance to high-intensity statins?

- **Lovastatin 20 mg**
- **Lovastatin + Colestipol**
- **Simvastatin 10 mg**
- **Simvastatin + Ezetimibe**
The Future of LDL-C Lowering

LDL-C (mg/dL)

140

-50%

-50%

70

35

Atorvastatin 80 mg
Rosuvastatin 20-40 mg
+ Ezetimibe
+ PCSK9 inhibitor
• Before initiation of statin therapy for the primary prevention of ASCVD in adults with LDL-C 70–189 mg/dL without clinical ASCVD or diabetes, it is reasonable for clinicians and patients to engage in a discussion that considers the potential for ASCVD risk-reduction benefits and for adverse effects and drug–drug interactions, as well as patient preferences for treatment.
Considerations for Primary Prevention: Discussion with Patients

- The lower, the better for LDL-C
- When to start LDL lowering
- Qualitative indications for statins
- “Quantitative” global risk assessment
- Number needed to treat
- Subclinical atherosclerosis
- LDL-lowering options
Primary Prevention: The Lower the Better

Mean or Median LDL-C, mg/dL

CHD Events, Projected to 5 Years

y = 0.046x – 1.53

R² = 0.95
Primary Prevention: The Lower the Better

Multiple Risk Factor Intervention Trial (MRFIT) (N=361,662)

Age-Adjusted 6-Year CHD Mortality Per 1000 Men

Total Cholesterol (mg/dL)
Primary Prevention: the Longer, the Better for Low LDL-C

The Earlier the Better: CHD Risk Reduction and Age of Onset of LDL-Lowering (by 10%)

Law et al. BMJ. 1994 Feb 5;308:367-72
Qualitative Indications for Statins in Primary Prevention

Higher Risk Conditions

• Diabetes mellitus (CARDS)
• Metabolic syndrome (JUPITER/AFCAPS/MEGA)
• Chronic kidney disease (SHARP)

Major Risk Factors

• Hypertension (ASCOT)
• Hypercholesterolemia (WOSCOPS)
• Cigarette smoking (Multiple RCTs)
Relative Baseline Risks in Different US Cohorts

MESA = Multi-Ethnic Study of Atherosclerosis  PHS = Physicians Health Study
WHS = Women’s Health Study  WHIOS = Women’s Health Initiative Observational Study
Stroke = Reasons for Racial Differences in Stroke study

Relative Baseline Risks in Populations Worldwide

- New Zealand (1.15)
- Rural India (1.00)
- Scotland (0.91)
- Native American (0.80)
- Ireland (0.76)
- Switzerland (0.45)
- France (0.41)
- China (0.36)
- Urban India (1.86)
- Framingham (1.00)
- Australia (0.90)
- UK (0.76)
- Japan (0.50)
- Germany (0.43)
- Spain (0.37)
10-year NNT for ASCVD Morbidity/Mortality according to ACC/AHA Algorithm 2013

<table>
<thead>
<tr>
<th>Absolute 10-year Risk for ASCVD</th>
<th>NNT ASCVD Morbidity</th>
<th>NNT ASCVD Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>50/150</td>
<td></td>
</tr>
<tr>
<td>7.5%</td>
<td>33/100</td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>25/75</td>
<td></td>
</tr>
<tr>
<td>15%</td>
<td>17/51</td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>13/39</td>
<td></td>
</tr>
</tbody>
</table>
Fraction Free of CHD

- CAC 0
- CAC 1-100
- CAC >100

45-54 Years

> 75 Years

Gender-based coronary artery calcium (CAC) distribution across age groups

Primary Prevention: LDL-Lowering Options

- First-line therapy: Statins
- Second-line therapy
  - Ezetimibe
  - Bile acid sequestrants
  - Fibrates (metabolic syndrome)
- Dietary therapy
  - Low saturated fat and *trans* fat
  - Low dietary cholesterol
  - Weight reduction