The 2013 ACC/AHA Cholesterol Guidelines: Impact and Future Directions

MN - ACP
November 6th, 2015
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Disclosures

• None
Objectives

• Why the need for change in the guidelines?
• What is the potential impact of these guidelines?
• Where do we go from here?
Factors of Risk in the Development of Coronary Heart Disease—Six-Year Follow-up Experience

The Framingham Study


Framingham, Massachusetts

Figure 1. Six year incidence of coronary heart disease according to serum cholesterol level.
A General Cardiovascular Risk Profile: The Framingham Study

Persons at high risk of cardiovascular disease can be effectively identified from a measurement of their serum cholesterol and blood pressure, a smoking history, an electrocardiogram and a determination of glucose intolerance. One general function for identifying persons at high risk of cardiovascular disease is also effective in identifying persons at risk for each of the specific diseases, coronary heart disease, atherothrombotic brain infarction, hypertensive heart disease and intermittent claudication, even though the variables used have a different impact on each particular disease.

The 10 percent of persons identified with use of this function as at highest risk accounted for about one fifth of the 8 year incidence of coronary heart disease and about one third of the 8 year incidence of atherothrombotic brain infarction, hypertensive heart disease and intermittent claudication. Hence the function provides an economic and efficient method of identifying persons at high cardiovascular risk who need preventive treatment and persons at low risk who need not be alarmed about one moderately elevated risk characteristic.
### TABLE IV

Coefficients for Calculating Risk of Cardiovascular Disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.3743307</td>
<td>0.2665693</td>
</tr>
<tr>
<td>Age X age</td>
<td>-0.0021165</td>
<td>-0.0012655</td>
</tr>
<tr>
<td>Serum cholesterol (mg/ml)</td>
<td>0.0258102</td>
<td>0.0180593</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>0.0156953</td>
<td>0.0144265</td>
</tr>
<tr>
<td>Cigarette smoking*</td>
<td>0.5583013</td>
<td>0.0395348</td>
</tr>
<tr>
<td>LVH by ECG*</td>
<td>1.0529656</td>
<td>0.8745090</td>
</tr>
<tr>
<td>Glucose intolerance*</td>
<td>0.6020336</td>
<td>0.6821258</td>
</tr>
<tr>
<td>Cholesterol X age</td>
<td>-0.0003619</td>
<td>-0.0002157</td>
</tr>
<tr>
<td>Intercept</td>
<td>-19.7709560</td>
<td>-16.4588427</td>
</tr>
</tbody>
</table>

*Yes = 1, no = 0 (for definitions see Shurtleff et al.*).

To obtain the probability that cardiovascular disease will occur in 8 years to a man or woman initially free of cardiovascular disease multiply the value of the characteristic in the units specified by the coefficient for the variable, sum these products and add the intercept. This provides the coefficient (C) to calculate the probability, \( P = 1/(1 + e^{-C}) \).

ECG = electrocardiogram; LVH = left ventricular hypertrophy.

### TABLE V

Incidence of Cardiovascular Disease per 1,000 in 8 Years According to Decile of Cardiovascular Risk

<table>
<thead>
<tr>
<th>Decile</th>
<th>Men 45–54 Years</th>
<th>Men 55–64 Years</th>
<th>Men 65–74 Years</th>
<th>Women 45–54 Years</th>
<th>Women 55–64 Years</th>
<th>Women 65–74 Years</th>
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<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>102</td>
<td>128</td>
<td>21</td>
<td>62</td>
<td>144</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>121</td>
<td>146</td>
<td>26</td>
<td>74</td>
<td>128</td>
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<tr>
<td>3</td>
<td>77</td>
<td>140</td>
<td>173</td>
<td>31</td>
<td>85</td>
<td>144</td>
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<tr>
<td>4</td>
<td>89</td>
<td>157</td>
<td>184</td>
<td>36</td>
<td>95</td>
<td>160</td>
</tr>
<tr>
<td>5</td>
<td>104</td>
<td>175</td>
<td>204</td>
<td>42</td>
<td>106</td>
<td>173</td>
</tr>
<tr>
<td>6</td>
<td>120</td>
<td>197</td>
<td>224</td>
<td>48</td>
<td>117</td>
<td>190</td>
</tr>
<tr>
<td>7</td>
<td>141</td>
<td>221</td>
<td>252</td>
<td>56</td>
<td>131</td>
<td>211</td>
</tr>
<tr>
<td>8</td>
<td>168</td>
<td>256</td>
<td>296</td>
<td>66</td>
<td>152</td>
<td>234</td>
</tr>
<tr>
<td>9</td>
<td>214</td>
<td>316</td>
<td>387</td>
<td>87</td>
<td>191</td>
<td>294</td>
</tr>
</tbody>
</table>
The relationship between Cholesterol and CHD is Linear
Sick Individuals and Sick Populations

GEOFFREY ROSE

Rose G (Department of Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK). Sick individuals and sick populations. International Journal of Epidemiology 1985, 14: 32–38. Aetiology confronts two distinct issues: the determinants of individual cases, and the determinants of incidence rate. If exposure to a necessary agent is homogeneous within a population, then case/control and cohort methods will fail to detect it: they will only identify markers of susceptibility. The corresponding strategies in control are the ‘high-risk’ approach, which seeks to protect susceptible individuals, and the population approach, which seeks to control the causes of incidence. The two approaches are not usually in competition, but the prior concern should always be to discover and control the causes of incidence.
Distributions of cholesterol levels and age-adjusted CHD deaths.

Psaty B M Circulation 2010;121:940-945
The Benefit of Statin Therapy is Independent of Baseline LDL Cholesterol

Heart Protection Study (HPS)

<table>
<thead>
<tr>
<th>Baseline LDL-C (mg/dL)</th>
<th>Statin (n = 10,269)</th>
<th>Placebo (n = 10,267)</th>
<th>Event Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>282 (16.4%)</td>
<td>358 (21.0%)</td>
<td>Statin Better</td>
</tr>
<tr>
<td>100–129</td>
<td>668 (18.9%)</td>
<td>871 (24.7%)</td>
<td></td>
</tr>
<tr>
<td>≥130</td>
<td>1083 (21.6%)</td>
<td>1356 (26.9%)</td>
<td>Statin Worse</td>
</tr>
<tr>
<td>All patients</td>
<td>2033 (19.8%)</td>
<td>2585 (25.2%)</td>
<td>0.76 (0.72–0.81)</td>
</tr>
</tbody>
</table>

Can you go to low?

Figure 1: Cardiovascular Events and All-Cause Mortality by Baseline LDL-C Level

Numbers of patients with baseline low-density lipoprotein cholesterol (LDL-C) in each category, hazard ratios, and 95% confidence intervals for time to occurrence of the primary endpoint, the primary endpoint or death, and the composite of the primary endpoint, venous thromboembolism (VTE), or death are shown by baseline LDL-C level.

Hsia et al. JACC 2011
Statin Good - More Statin Better

Cholesterol Treatment Trialists’ (CTT) Collaboration
Meta-analysis of 169,138 patients randomized to at least 2 years of statin therapy

Five year risk of a major vascular event, %

LDL cholesterol level (mmol/L)

Control

Statin

More statin

21% relative risk reduction per mmol/L

16% relative risk reduction per 0.5 mmol/L
Statin Therapy in Hypertensive Individuals
Reduced CHD Events

Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA)

10,305 patients with HTN randomized to atorvastatin (10 mg) or placebo for 5 years

Cumulative incidence of MI and fatal CHD (%)

- Atorvastatin 90 mg/dl*
- Placebo 126 mg/dl*

Statin Therapy in Individuals with Diabetes
Reduced CHD Events

- LDL <160mg/dl
- Atorvastatin 10mg
- Stopped early

**CARDS Trial**

**Figure 4:** Cumulative hazard of primary endpoint, all-cause mortality, and any cardiovascular endpoint
New Cholesterol Guidelines – Overall Theme

• Statins should be used to reduce ASCVD risk in individuals most likely to benefit
• Absolute risk is better predictor of benefit than cholesterol
• Statin therapy should be allocated based on absolute risk
Objectives

• Why the need for change in the guidelines?
• What is the potential impact of these guidelines?
• Where do we go from here?
The 4 Statin Groups

- Known Clinical CVD
- Type II Diabetes
- LDL-C >190mg/dl
- Individuals with a >7.5% 10-year CVD Risk
Implications

Statin-Eligibility in the U.S.

US Adults (40-75) in millions

Total Population

ATP III

ACC/AHA

Pencina et al, NEJM 2014
The Calculator Controversy

Women's Health Study

Physicians' Health Study

- Observed event rates
- Event rates predicted by new ACC/AHA risk prediction algorithm
The Calculator Controversy

Multi-Ethnic Study of Atherosclerosis

White women

White men

Black women

Black men

Rate

0.20

0.15

0.10

0.05

0.00

Ridker Lancet 2013
Statin Eligibility in ARIC

Miedema et al – JAMA-IM-2014
Objectives

• Why the need for change in the guidelines?
• What is the potential impact of these guidelines?
• Where do we go from here?
Coronary Artery Calcium Score

- “Mammogram” of the heart
- Quantifies the amount of plaque in the coronary arteries
- ~ .8 millisievert of Radiation
- Cost $100
Plaque Burden Strongly Correlates with CHD Risk

Figure 1. Unadjusted Kaplan–Meier Cumulative-Event Curves for Coronary Events among Participants with Coronary-Artery Calcium Scores of 0, 1 to 100, 101 to 300, and More Than 300.

Panel A shows the rates for major coronary events (myocardial infarction and death from coronary heart disease), and Panel B shows the rates for any coronary event. The differences among all curves are statistically significant (P<0.001).

Detrano et al. NEJM 2007
Mortality by CAC and age

Tota-Maharaj European Heart Journal 2013
CAC Distribution by age

MESA
Mortality by CAC and Risk Factors

Figure 3. Mortality rate (per 1000 person-years) with increasing coronary artery calcium (CAC) scores according to burden of risk factors (RFs).
CAC and CVD Events – ACC/AHA Risk Calculator

Yeboah et al. AHA 2014
CAC distribution across Statin Eligibility Groups

Nasir et al. JACC 2015
CAC distribution Across Spectrum of 10 Year Risk Score Among those >7.5% Risk Score

<table>
<thead>
<tr>
<th>CAC distribution</th>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAC = 0</td>
<td>55</td>
<td>43</td>
<td>37</td>
<td>26</td>
<td>28</td>
<td>34</td>
<td>31</td>
<td>32</td>
<td>45</td>
<td>431</td>
<td></td>
</tr>
<tr>
<td>CAC 1 - 100</td>
<td>28</td>
<td>23</td>
<td>34</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>45</td>
<td>608</td>
<td></td>
</tr>
<tr>
<td>CAC &gt; 100</td>
<td>17</td>
<td>23</td>
<td>34</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>45</td>
<td>342</td>
<td></td>
</tr>
</tbody>
</table>

N=431 N=608 N=342 N=441
CHD Event Rate Per 1000 Person Among Non Diabetics with LDL 70-189 mg/dl Across Spectrum of CAC Burden & Increasing 10 Year ASCVD Risk >7.5% Categories

Dotted line represent reference line for 10-year ASCVD risk estimate of 7.5%
ASCVD Event Rate Per 1000 Person Among Non Diabetics with LDL 70-189 mg/dl Across Spectrum of CAC Burden & Increasing 10 Year ASCVD Risk >7.5% Categories

Dotted line represent reference line for 10-year ASCVD risk estimate of 7.5%
The Prevention Paradox…Preventable?

MESA
Thank You

• Questions?