Atherosclerotic Disease Risk Score

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2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women with Heart Disease

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New ACC/AHA guidelines

- Decide if the patient falls into one of four statin benefit groups
  - Clinical ASCVD
  - LDL > 190
  - Diabetes (age 40-75)
  - ASCVD risk score “Pooled Cohort Equation” ≥ 7.5% and age 40 to 75

### ASCVD Risk Benefit Groups

**Adults > 21 years and able to tolerate statins:**

- **YES** Clinical ASCVD
  - **YES** Age ≤ 75 years of age; High Intensity statin
  - **YES** Age > 75 years; Moderate Intensity statin
  - **NO** LDL > 190 mg/dL
    - **YES** High Intensity statin
    - **NO** Moderate intensity statin
  - **NO** Diabetes
    - **YES** ASCVD risk score is ≥ 7.5%; High intensity statin
    - **NO** Moderate to high intensity statin
  - **YES** ASCVD risk score ≥ 7.5% and age 40

**ASCVD risk benefit of statins may be less clear in other groups**
Pooled cohort equation= Risk score estimates ASCVD, defined as nonfatal MI, or CHD death, or fatal or nonfatal stroke, in 10 years

Framingham-based risk calculators

ATP III hard CHD risk score (2002)

Table III.1a. Estimates of 10-Year Risk for Men (Framingham Point Scores)

<table>
<thead>
<tr>
<th>Age Points</th>
<th>Total Cholesterol</th>
<th>Points at Ages 20–39</th>
<th>Points at Ages 40–49</th>
<th>Points at Ages 50–59</th>
<th>Points at Ages 60–69</th>
<th>Points at Ages 70–79</th>
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<td>20–34</td>
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<tr>
<td>75–79</td>
<td>13</td>
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</table>

<table>
<thead>
<tr>
<th>HDL Points</th>
<th>Systolic BP</th>
<th>If Untreated</th>
<th>If Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>120–129</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>130–139</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>140–159</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>≥160</td>
<td>2</td>
<td>2</td>
<td>3</td>
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</table>

Diabetes as a “risk equivalent”

MORTALITY FROM CORONARY HEART DISEASE IN SUBJECTS WITH TYPE 2 DIABETES AND IN NONDIABETIC SUBJECTS WITH AND WITHOUT PRIOR MYOCARDIAL INFARCTION


Framingham General CVD Risk Score (2008)

- Including endpoints of CVA, TIA, claudication, heart failure

Reynolds Risk Score (2007-2008)

- Ridker & Cook (Brigham & Women’s): analysis of the Women’s Health Study
- 24,558 participants, initially healthy women 45+yrs, followed prospectively for 10.2 yrs
- Outcomes: incident MI, CVA, coronary revascularization, CV death
- Developed the risk prediction algorithm using random 2/3 of the sample (16,400), then validated using the remaining 1/3 (8,158)


ACC/AHA Pooled Cohort Equations

- Based on pooled data from several NHLBI-sponsored cohort studies
  - Atherosclerosis Risk in Communities (ARIC)
  - Cardiovascular Health Study (CHS)
  - Coronary Artery Risk Development in Young Adults (CARDIA)
  - Framingham Original and Offspring cohort data
The Risk Score Controversy

- Differences in opinion on how to estimate risk
- First hard ASCVD events (defined as occurrence of coronary death or fatal stroke or first occurrence of nonfatal myocardial infarction [MI] or stroke) rather than CHD alone
- Created a new risk assessment algorithm using pooled cohort data from a number of longitudinal NHLBI-funded community based epidemiological cohort studies.
- Biracial, community-based population samples

- Using this data, equations created to predict 10 year risk.
- These were externally validated in the Multi-Ethnic Study of Atherosclerosis (MESA) and Reasons for Geographic and Racial Differences in Stroke study (REGARDS).
- Overprediction noted in the MESA and REGARDS groups, more pronounced in the higher risk than lower risk patients (but more important in the lower risk patients)
- Limitations to external validation- MESA low risk group, lipid-lowering and BP-lowering therapy hampers assessment- may have significantly lowered event rates
Calculated predicted 10-year risks of the same atherosclerotic events using the new ACC/AHA risk prediction algorithm and compared these estimates with observed event rates in three large-scale primary prevention cohorts, the Women's Health Study, the Physicians' Health Study, and the Women's Health Initiative Observational Study.

In all three of these primary prevention cohorts, the new ACC/AHA risk prediction algorithm systematically overestimated observed risks by 75–150%, roughly doubling the actual observed risk.

Similar overestimation of risk was observed in two external validation cohorts used by the guideline developers themselves, an issue readily acknowledged in the report.

On the basis of data from these five external validation cohorts, 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.

Miscalibration to this extent should be reconciled and addressed in additional external validation cohorts before these new prediction models are widely implemented. It is possible, for example, that the five external validation cohorts are more contemporary than the cohorts used in the risk prediction algorithm and thus reflect secular improvements in overall health and lifestyle patterns in the USA over the past 25 years.
Paul M. Ridker, Nancy R. Cook
Statins: new American guidelines for prevention of cardiovascular disease

The Lancet, Volume 382, Issue 9907, 2013, 1762 - 1765
The Rebuttal

• 1990s
• CHD and stroke
• African-Americans
• Too complex to follow inclusion and exclusion criteria
• Trial data shows higher risk $\rightarrow$ higher benefit
• Benefit extends to 5% 10 year risk
• Only 31% of Americans aged 40-75 w/o existing CVD are eligible for statins under the new guidelines, similar to if 20% 10 year risk had been dropped to 10%

• Trial data presented by Ridker and Cook had low event rates
• Overestimation in lower risk patients $\rightarrow$ why threshold set to 7.5%
The European guidelines

<table>
<thead>
<tr>
<th>Total CV risk (SCORE)</th>
<th>LDL-C levels</th>
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</thead>
<tbody>
<tr>
<td>%</td>
<td>&lt;70 mg/dL</td>
</tr>
<tr>
<td>&lt;1</td>
<td>No lipid intervention</td>
</tr>
<tr>
<td>Class I/level A</td>
<td>NC</td>
</tr>
<tr>
<td>≥1 to &lt;5</td>
<td>No lipid intervention</td>
</tr>
<tr>
<td>Class I/level B</td>
<td>NC</td>
</tr>
<tr>
<td>≥5 to &lt;10, or high-risk</td>
<td>No lipid intervention</td>
</tr>
<tr>
<td>Class II/level B</td>
<td>Is/A</td>
</tr>
<tr>
<td>≥10 or very high-risk</td>
<td>Lifestyle intervention, consider drug</td>
</tr>
</tbody>
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ACC/AHA Pooled Cohort Equations

Men with average risk factor profile exceed the threshold at 60 yrs

African American men with HTN tx exceed threshold at 50 yrs