Calculating the CVD Risk Score: Which Tool for Which Patient?

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Disclosures

• No relevant RWI
• Dr. Lloyd-Jones has received grant funding from the NHLBI and NCATS Institute
Question 1

Almost 50% of people who have an acute MI have no identifiable traditional risk factor.

1. False
2. True
A 45 yo non-smoking, non-diabetic man has total cholesterol of 240, HDL-c 50, and untreated SBP of 160. His Framingham risk estimate for hard CHD is:

1. 5%
2. 15%
3. 25%
4. 35%
5. 45%
A 45 yo non-smoking, non-diabetic man has total cholesterol of 240, HDL-c 50, and untreated SBP of 160. **His lifetime risk estimate for CVD is:**

1. 26%
2. 42%
3. 50%
4. 69%
5. 98%
Question 3

A 45 yo woman comes to your office complaining of 2 months of progressive exertional chest pressure with dyspnea. Her total cholesterol is 200, HDL-c 50, SBP 130, she is a non-smoker, and non-diabetic. Her Framingham risk estimate for hard CHD is:

1. <1%
2. 2%
3. 5%
4. 7%
5. 12%
Question 4

Which of the following is true?

1. Clinicians tend to **overestimate** CVD risk
2. Clinicians tend to **underestimate** CVD risk
3. Patients tend to **overestimate** CVD risk
4. Patients tend to **underestimate** CVD risk
Question 5

How often do you use a CVD risk estimator (FRS, ATP-III, HeartScore, Reynolds) in your practice?

1. Very often
2. Often
3. Rarely
4. Never
Topics

• Perceived vs actual risk
• Effect of risk assessment in clinical practice
• What is the right score?
• What is the right endpoint?
• Pitfalls of short-term risk assessment
• Potential utility of long-term risk assessment
Why Do We Estimate Absolute Risk?

• Cornerstone of “high-risk strategy”
  ▪ Relative risk is poorly understood by clinicians and patients
    - Problem of the referent group
  ▪ Patients and clinicians very poor at intuiting true risk
    - Understand absolute risk for prognosis
  ▪ Improve communication and motivate lifestyle change/adherence to therapy
  ▪ Identify treatment-eligible individuals at sufficiently high risk to merit treatment and expect net cost-effective benefit
  ▪ Directly compare benefits and harms of therapy
Current Paradigm for Risk Estimation and Treatment: ATP-III

“Intensity of prevention efforts should match the absolute risk of the patient”

Estimate 10-year risk (FRS)

- <10%
- 10-20%
- >20% or DM

Further testing

Lifestyle modification

Lifestyle and drug therapy
Patients substantially overestimate and underestimate risk

- 1557 primary care patients asked to estimate risk on a continuous scale of 0% to 100%

- Mean absolute differences between perceived and actual predicted 10-year risk were:
  - 22.9% (95% CI 21.8–24.0%) for MI
  - 24.6% (23.4–25.8%) for stroke

| 1–20% lower | 28.2 | 21.9 |
| >20% lower | 2.0 | 0.4 |
Physicians overestimate and underestimate risk

- 79 physicians at all levels at 3 university hospitals
- Surveyed re: 12 primary prevention scenarios
  - Overestimation (MD estimate >1.5x actual risk)
  - Underestimation (MD estimate <0.67x actual risk)
- Only 24% of physicians' risk estimates were accurate
  - Physicians overestimated absolute risk 32% to 92% of the time
  - Physicians made larger errors in patient scenarios involving patients with high total or LDL-c levels
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“...global CHD risk information alone or with accompanying education increased the accuracy of perceived risk and probably increased intent to start therapy. Studies with repeated risk information or risk information and repeated doses of counseling showed small significant reductions in predicted CHD risk (absolute differences, -0.2% to -2% over 10 years in studies using risk estimates derived from Framingham equations). Studies providing global risk information at only 1 point in time seemed ineffective.
• 11 studies (6 examining benefits, 5 harms)
• When MDs presented with risk, tendency to prescribe lipid and BP meds more often and appropriately
• Modest improvements in intermediate outcomes; no harms identified
• Outcomes data needed

Sheridan, BMC Health Svcs Res 2008
Topics

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A Couple of Risk Scores to Help You Assess Risk in Your Patients

- PROCAM
- FRS CVD 2008
- FRS 1998
- Reynolds for Women
- QRISK
- SCORE - N. Europe
- ARIC Genetic RS
- SCORE
- SCORE - S. Europe
- SCORE - Greece
- FRS/ATP-III
- Reynolds for Men
- FRS 1991
- Cuore
- Cuore
A Brief History and a Matter of Inputs

<table>
<thead>
<tr>
<th>Risk Score, Year</th>
<th>Covariates</th>
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</thead>
<tbody>
<tr>
<td>FRS, 1991</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, DM, ECG-LVH</td>
</tr>
<tr>
<td>FRS, 1998</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, DM</td>
</tr>
<tr>
<td>ATP-III, 2001</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, anti-HTN Rx</td>
</tr>
<tr>
<td>PROCAM, 2002</td>
<td>Age, Sex, LDL-c, HDL-c, TG, SBP, Smoking, DM, Family Hx</td>
</tr>
<tr>
<td>SCORE, 2003 +</td>
<td>Age, Sex, TC, SBP, Smoking</td>
</tr>
<tr>
<td>QRISK, 2007</td>
<td>Age, Sex, TC/HDL, SBP, Smoking, BMI, Family Hx, antiHTN Rx, Townsend deprivation</td>
</tr>
<tr>
<td>Reynolds (women), 2007</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, HbA1c with DM, hs-CRP, Parental Hx &lt;60</td>
</tr>
<tr>
<td>Reynolds (men), 2008</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, hs-CRP, Parental Hx &lt;60</td>
</tr>
<tr>
<td>FRS Global CVD, 2008</td>
<td>Age, Sex, TC, HDL-c, SBP, Smoking, DM, anti-HTN Rx</td>
</tr>
</tbody>
</table>
Topics

• Perceived vs actual risk
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• What is the right score?
• What is the right endpoint?
• Pitfalls of short-term risk assessment
• Potential utility of long-term risk assessment
<table>
<thead>
<tr>
<th>Risk Score, Year</th>
<th>Endpoint</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRS, 1991</td>
<td>All CHD</td>
<td>CHD death, MI, unstable angina, angina pectoris</td>
</tr>
<tr>
<td>FRS, 1998</td>
<td>All CHD, Hard CHD</td>
<td>CHD death, MI, unstable angina, angina pectoris</td>
</tr>
<tr>
<td>ATP-III, 2001</td>
<td>Hard CHD</td>
<td>CHD death, non-fatal MI</td>
</tr>
<tr>
<td>PROCAM, 2002</td>
<td>Hard CHD</td>
<td>CHD death, nonfatal MI</td>
</tr>
<tr>
<td>SCORE, 2003 and after</td>
<td>CVD death</td>
<td>CVD death only; Multiple region-and country-specific versions</td>
</tr>
<tr>
<td>QRISK, 2007</td>
<td>CVD</td>
<td>CHD, stroke, TIA</td>
</tr>
<tr>
<td>Reynolds (women), 2007</td>
<td>Global CVD</td>
<td>CVD death, MI, stroke, revascularization</td>
</tr>
<tr>
<td>Reynolds (men), 2008</td>
<td>Global CVD</td>
<td>CVD death, MI, stroke, revascularization</td>
</tr>
<tr>
<td>FRS Global CVD, 2008</td>
<td>Global CVD</td>
<td>CVD death, all CHD, stroke, heart failure, claudication</td>
</tr>
</tbody>
</table>
Should We Care about CHD vs. CVD as our Endpoint?

• YES!
• Captures more events of interest
  ▪ Debate about revascularization
• Women at risk for stroke and HF before CHD
• Common underlying risk factors
• Captures more young people at risk
• Scaleable
  ▪ D-Agostino multiplier FRS 2008
The Trouble with Revascularization

• US 2009
  ▪ 600,000 patients underwent PCI
  ▪ 240,000 patients underwent CABG

Ko, JACC 2012
The Trouble with Revascularization

• US 2007 PCI rates
The Trouble with Heart Failure

• Difficult to define/measure consistently in different populations
• Racial disparities
• Overwhelmingly a disease of older people
• Different underlying risk coefficients
• Solution: Focus on estimating risk for atherosclerotic CVD; assume all older adults with HTN potentially at risk for HF
What happens if we use a CVD risk score rather than a CHD risk score?

**NHANES 30 to 74 year-olds**

<table>
<thead>
<tr>
<th>FRS, mil (%)</th>
<th>&lt;6%</th>
<th>6-&lt;10%</th>
<th>10-20%</th>
<th>&gt;20%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6%</td>
<td>91.5 (72%)</td>
<td>25.2 (20%)</td>
<td>10.0 (8%)</td>
<td>0.3 (0.2%)</td>
<td>127.0 (76%)</td>
</tr>
<tr>
<td>6-&lt;10%</td>
<td>0.2 (1%)</td>
<td>5.5 (34%)</td>
<td>9.3 (57%)</td>
<td>1.3 (8%)</td>
<td>16.4 (10%)</td>
</tr>
<tr>
<td>10-20%</td>
<td>0</td>
<td>0.6 (3%)</td>
<td>10.2 (46%)</td>
<td>11.1 (51%)</td>
<td>22.0 (13%)</td>
</tr>
<tr>
<td>&gt;20%</td>
<td>0</td>
<td>0</td>
<td>0.4 (15%)</td>
<td>2.2 (85%)</td>
<td>2.6 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>91.7 (55%)</td>
<td>31.5 (19%)</td>
<td>29.9 (18%)</td>
<td>15.0 (9%)</td>
<td>168.0</td>
</tr>
</tbody>
</table>

15% 27%
How many move?

NHANES: Age 30 to 74 years

U.S. Adults (millions)

>20%  
10 - 20%  
6 - <10%  
0 - <6%

FRS

UFRP
Who moves?

Millions of Men and Women Upstaged from <10% (FRS) to ≥10% (UFRP)

30-49 years: 0.2
50-59 years: 3.3
60-74 years: 7.3

3.3
4.5
1.1
Summary

- **Numerical impact:**
  - 20 million upstaged to cross 10% risk threshold
  - 12 million upstaged by 2+ levels of risk

- **Upstaged individuals:**
  - Younger men
  - Women
  - Elevated SBP, SBP Rx

- **UFRP changes more people than RRS**
  - UFRP upstages 20 million to cross 10%
  - RRS upstages 8 million to cross 10%
Topics

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10-Year Predicted Risks in ATP Risk Assessment Tool: Woman, Age 55

Pitfalls of Short-Term Risk Estimates

• Vast majority of younger adults are considered to be at “low risk”
  ▪ Weight of age
  ▪ 10-year risk window
  ▪ Clinical treatment thresholds imposed
• BUT low risk ≠ “no risk”
• Additional means for risk estimation and communication needed to help men age <45 and women age <65
  ▪ Importance of addressing multiple moderate or single elevated risk factors for long-term CHD prevention
Topics

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• What is the right score?
• What is the right endpoint?
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• Potential utility of long-term risk assessment
Rationale: Lifetime Risk Estimation

• Lifetime risk
  ▪ The absolute cumulative risk of an individual developing a given disease before death
  ▪ Accounts for risk of disease of interest, remaining life expectancy, and competing causes of death
  ▪ Reflects real-life risks better than Kaplan-Meier cumulative incidence
  ▪ Dispenses with age dominance of 10-year risk models
Lifetime Risks of Cardiovascular Disease

Jarett D. Berry, M.D., Alan Dyer, Ph.D., Xuan Cai, M.S., Daniel B. Garside, B.S., Hongyan Ning, M.D., Avis Thomas, M.S., Philip Greenland, M.D., Linda Van Horn, R.D., Ph.D., Russell P. Tracy, Ph.D., and Donald M. Lloyd-Jones, M.D.
## Aggregate Risk Factor Burden

<table>
<thead>
<tr>
<th></th>
<th>All Optimal</th>
<th>Not Optimal</th>
<th>Elevated</th>
<th>1 Major</th>
<th>≥2 Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP/DBP</td>
<td>&lt;120 and &lt;80</td>
<td>120-139 or 80-89</td>
<td>140-159 or 90-99</td>
<td>≥160 or</td>
<td>≥100 or</td>
</tr>
<tr>
<td>TC</td>
<td>&lt;180</td>
<td>180-199</td>
<td>200-239</td>
<td>≥240 or</td>
<td>Rx</td>
</tr>
<tr>
<td>DM</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Lloyd-Jones, *Circulation* 2006; 113: 791-798
Lifetime Risks for All ASCVD
Cardiovascular Lifetime Risk Pooling Project

Men, Age 45

- ≥2 Major RFs
- 1 Major RF
- ≥1 Elevated RF
- ≥1 Not Optimal RF
- Optimal RFs

Cumulative Risk vs. Attained Age
# Lifetime Risks* for ASCVD: Cardiovascular Lifetime Risk Pooling Project

<table>
<thead>
<tr>
<th>RF Burden</th>
<th>Index Age 45 y</th>
<th></th>
<th>Index Age 55 y</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>All Optimal</td>
<td>1.4%</td>
<td>4.1%</td>
<td>14.6%</td>
<td>10.1%</td>
</tr>
<tr>
<td></td>
<td>(0-3.4)</td>
<td>(0-8.2)</td>
<td>(1.0-28.3)</td>
<td>(0-25.0)</td>
</tr>
<tr>
<td>≥1 Not Optimal</td>
<td>31.2%</td>
<td>12.2%</td>
<td>19.7%</td>
<td>13.3%</td>
</tr>
<tr>
<td></td>
<td>(17.6-44.7)</td>
<td>(4.6-19.7)</td>
<td>(11.9-27.4)</td>
<td>(5.5-21.1)</td>
</tr>
<tr>
<td>≥1 Elevated</td>
<td>35.0%</td>
<td>15.6%</td>
<td>33.9%</td>
<td>15.3%</td>
</tr>
<tr>
<td></td>
<td>(26.8-43.2)</td>
<td>(10.3-20.9)</td>
<td>(27.9-39.8)</td>
<td>(11.3-19.3)</td>
</tr>
<tr>
<td>1 Major</td>
<td>39.6%</td>
<td>20.2%</td>
<td>32.2%</td>
<td>16.7%</td>
</tr>
<tr>
<td></td>
<td>(35.7-43.6)</td>
<td>(17.2-23.2)</td>
<td>(29.1-35.2)</td>
<td>(14.5-19.0)</td>
</tr>
<tr>
<td>≥2 Major</td>
<td>49.5%</td>
<td>30.7%</td>
<td>46.8%</td>
<td>29.2%</td>
</tr>
<tr>
<td></td>
<td>(45.0-53.9)</td>
<td>(26.3-35.0)</td>
<td>(43.0-50.7)</td>
<td>(26.2-32.3)</td>
</tr>
</tbody>
</table>

* To age 80
Distributions of 10-Year and Lifetime Risk Strata by Age and Sex
US Adults, NHANES 2003-2006

56% (87,000,000) have low short-term but high lifetime predicted risk

Marma, Circ CQO 2010
## A New Risk Estimator?

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Value</th>
<th>Endpoint</th>
<th>10-Year</th>
<th>To Age 90</th>
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</thead>
<tbody>
<tr>
<td>Gender</td>
<td>M or F</td>
<td>M</td>
<td>Hard CHD</td>
<td>1.4%</td>
<td>42%</td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>45</td>
<td>F/NF Stroke</td>
<td>0.2%</td>
<td>21%</td>
</tr>
<tr>
<td>Total Chol</td>
<td>mg/dL</td>
<td>230</td>
<td>Hard ASCVD</td>
<td>1.5%</td>
<td>46%</td>
</tr>
<tr>
<td>HDL- C</td>
<td>mg/dL</td>
<td>40</td>
<td>Alive &amp; CVD-Free</td>
<td></td>
<td>14%</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mm Hg</td>
<td>135</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment for Hypertension (if SBP &gt;120)</td>
<td>Y or N</td>
<td>N</td>
<td>Vascular Age</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>Y or N</td>
<td>N</td>
<td>Estimated Life-Years Lost</td>
<td></td>
<td>&gt;10</td>
</tr>
</tbody>
</table>
My Advice

• Unless (or until) we adopt a disease screening rather than a risk screening approach…

• **Use** a risk score when not absolutely certain

• Choose a risk score that:
  - Covers a GLOBAL endpoint you care about
    - F/NF Hard CHD, F/NF Stroke at a minimum
  - Covers a time horizon you care about
  - Is derived from a population/sample that looks like your patient
  - Is validated broadly
  - Has easily measured covariates
  - Is available online
My Advice

• Repeated risk conversations with different presentations of risk appear helpful and not harmful
  ▪ Enhance prescribing for patients at risk
  ▪ Enhance RF control rates

• In the era of generic statins
  ▪ Basis for approach to most patients should remain absolute risk estimation (10-year +/- Lifetime Risk)
  ▪ Especially if the life expectancy is >10 years