How good are clinical risk prediction rules?

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Disclosure statement

• No conflict of interest
Plan

• Cardiovascular risk assessment, how ? importance ?
• Do scores correctly identify events ?
  – Discrimination
• What is the accuracy of prediction ?
  – Calibration / external validation
• Risk communication
• Summary
Assessment of cardiovascular risk

• Tools to assess risk of coronary heart disease (CHD) over a 10-year period
  – Traditional cardiovascular risk factors
    • Age, gender, diabetes, blood pressure, cholesterol (HDL and LDL), smoking status
  – 1998 = Original Framingham risk score
  – 2001 = ATP III = thresholds and goals for lipid-lowering therapy based on the 10-year CHD risk


• Overestimation of risk by physician

Pignone et al. 2003 BMC Health Services Research
Risk prediction tools in Europe

- Applicability in other population questioned
  - geographically limited, white male-dominated cohort, less preventive pharmacotherapy

- Other scores than original Framingham

- Other outcomes
  - ACC/AHA 2013: stroke, all cardiovascular events
In Switzerland: Swiss Atherosclerosis Association

www.agla.ch
PROCAM risk score – IAS /AGLA guidelines

Risk period: 10 years

Outcomes
- fatal or non-fatal coronary heart disease (CHD)

= Absolute risk
- Until 10 % = low risk
- 10- 20% = intermediate risk
- 20% ou plus = high risk

www.gsla.ch
Cardiovascular risk estimation using traditional cardiovascular risk factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
<th>Score de risque du GSLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
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<tr>
<td>Familial History</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Blood Pressure</td>
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<tr>
<td>Cholesterol</td>
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</tbody>
</table>

6 traditional risk factors
primary basis for cardiovascular prevention in clinical practice
European SCORE algorithm
Recommendations ESC/EAS 2012

Risk period: 10 ans

Outcomes
- cardiovascular mortality

= Absolute risk
- <1% = low risk
- 1%-5%= Intermediate risk
- >=5% = High risk

www.escardio.org
www.heartscore.org
Importance of risk assessment to guide therapy

Therapy showing 25% relative risk reduction

Absolute Risk 40%

Number needed to treat
NNT = 10

Absolute Risk 5%

Number needed to treat
NNT = 80-100
Use in clinical practice

- National survey of physicians in the US
- n=951 responders
- 41% reported used CHD risk assessment at least occasionally

<table>
<thead>
<tr>
<th>Specialty</th>
<th>%</th>
<th>P-value*</th>
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<td>Family medicine</td>
<td>41.7</td>
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<td>Internal medicine</td>
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<td>Cardiology</td>
<td>49.4</td>
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<table>
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<tr>
<th>Years in practice</th>
<th>%</th>
<th>P-value*</th>
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<td>&gt; 20</td>
<td>38.9</td>
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<tr>
<td>10-19</td>
<td>49.7</td>
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<tr>
<td>&lt; 10</td>
<td>41.3</td>
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</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>%</th>
<th>P-value*</th>
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<tbody>
<tr>
<td>Male</td>
<td>41.6</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>41.2</td>
<td></td>
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</tbody>
</table>

Shillinglaw et al. BMC Health Services Research 2012
Do scores correctly identify adults with CHD events in Switzerland?

• 3,848 patients admitted with acute coronary syndrome between 2009 and 2013 to four university hospitals

• 10-year absolute risk using
  – the Procam risk score from Swiss AGLA guidelines 2012
  – SCORE from the European Society of Cardiology (ESC) 2012
  – American College of Cardiology/American Heart Association (ACC/AHA) guidelines 2013

SNSF 33CM30-124112, *Inflammation and acute coronary syndromes (ACS) – Novel strategies for prevention and clinical management*
Risk estimation in patient with acute coronary syndrome (n=3848)

*Pre-existing CVD, chronic kidney disease, diabetes with others risk factors

- Special categories*
- High risk
- Intermediate risk
- Low risk

Selby et al. *Preventive Medicine* 2015
Do scores correctly identify adults with cardiovascular disease?
(n=1.5 million UK participants)

Collins et al BMJ 2010; 340:c2442
Discrimination of risk scores

• C-statistics
• Area under a receiver operating characteristic curve (ROC curve)
• Probability to distinguish between those who will or those who will not have a CHD event
• Typical value 0.7
  (1 = perfect discrimination)
ROC curves for risk scores

1961 Men aged 50-74 years
In primary prevention

Calibration – External validation

- Ability to match predicted with observed events
- Accuracy of prediction
- Homser-Lemeshow test
  - Higher p-value = better calibration
Calibration – External validation in the US

1961 Men aged 50-74 years in primary prevention in the US

Calibration – External validation in a European population

Rotterdam Study, N= 4854, âge 55-75
ACC/AHA 2013 risk score

Kavousi et al. JAMA 2014
Calibration – External validation in a European population

Rotterdam Study, N= 4854, âge 55-75
Framingham ATPIII 2001 risk score

Kavousi et al. JAMA 2014
Calibration – External validation in a European population

Rotterdam Study, N= 4854, âge 55-75
SCORE from ESC guidelines 2012

Kavousi et al. JAMA 2014
Risk communication recommended in latest lipid guidelines

Integration of patients perspectives

– US ACC/AHA 2013 guidelines
  • benefits/adverse effects
  • Patient preferences  
  Stone et al. Circulation 2013

– UK NICE 2014 guidelines
  • Communicate risk assessment
  • Present individualised risk and benefits
  • Present absolute risk of events numerically
  • Use appropriate diagrams and text

Rabar et al. BMJ 2014
Risk communication

Google: type decision aid mayo

http://statindecisionaid.mayoclinic.org
Risk communication

Google: type decision aid mayo

**Current Risk**
of having a heart attack

Risk for 100 people like you who **do not**
medicate for heart problems

- **Over 10 years**
  - **7 people** will have a heart attack
  - **93 people** will have no heart attack

**Future Risk**
of having a heart attack

Risk for 100 people like you who **do take high**
dose statins

- **Over 10 years**
  - **4 people** will have a heart attack
  - **93 people** will have no heart attack
  - **3 people** will be saved from a heart attack by taking medicine

http://statindecisionaid.mayoclinic.org
Summary

• Risk assessment tools are important to guide primary prevention therapy

• Calibrated score for Switzerland should be used

• Electronic tools for risk communication can be very useful
Thank you for your attention

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Backslides
Agreement between risk scores used in Switzerland: Cross-sectional analysis

- 713 participants aged > 45 years old in primary prevention voluntary for a free check-up in 2005

- Kappa value = 0.22

Romanens et al. Cardiovasc Drugs Ther 2009
Individuals at high cardiovascular risk in Switzerland: cross-sectional analysis

Population-based study, the CoLaus Study, Lausanne

5683 participants aged 35-75 years in primary prevention between 2003-2006

Treatment threshold

Hlatky et al. Circulation 2009
Age and statin eligibility for primary prevention: population-based study in the US

Importance de l’âge pour la prescription

Pencina et al. NEJM 2014
Age and statin eligibility primary prevention population-based study in Europe

Rotterdam Study, N=4854, âge 55-75

ACC/AHA Guidelines

2013

ATP-III Guidelines

2001

Kavousi et al. JAMA 2014
Age and gender only to guide primary prevention
Primary prevention treatment based on 10-year risk and LDL-cholesterol levels

- **Very High risk:** LDL ≤ 1.8 mmol/l
- **High risk:** LDL ≤ 2.6 mmol/l
- **Intermediate risk:** LDL ≤ 3.0 mmol/l
- **Low risk:** Life style!

Recommendations Agla 2014 (www.gsla.ch)