Plasma Lipids and Global Cardiovascular Risk

Ian Graham
Chair JTF4 on the Prevention of CVD and PIC
Member ESC/EAS Lipid Guidelines

with special thanks to
Željko Reiner,
Trinity College Dublin- and Zagreb
Lipids and total CVD risk

- Guideline development
- Why estimate total risk?
- Which system to use?
- Mortality ot total events
- BMI and HDL cholesterol - very different effects
- Re-classification of risk with HDL cholesterol
- Risk in the young
- The continuum of risk
Recent developments in CVD prevention in Europe

- 1994: First Joint Task Force Recommendations
- 1995-96: Joint European Societies Implementation Group on Coronary Prevention
- 1998: EUROASPIRE I
- 1999-2000: EUROASPIRE II
- 2000: Joint European Societies CVD Prevention Committee
- 2003: Third Joint Task Force Recommendations
- 2006-2007: EUROASPIRE III
- 2007: Fourth Joint Task Force Recommendations
- 2012: Fifth Joint Task Force Recommendations

www.escardio.org
ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation†

Authors/Task Force Members: Željko Reiner* (ESC Chairperson) (Croatia), Alberico L. Catapano* (EAS Chairperson)* (Italy), Guy De Backer (Belgium), Ian Graham (Ireland), Marja-Riitta Taskinen (Finland), Olov Wiklund (Sweden), Stefan Agewall (Norway), Eduardo Alegria (Spain), M. John Chapman (France), Paul Durrington (UK), Serap Erdine (Turkey), Julian Halcox (UK), Richard Hobbs (UK), John Kjekshus (Norway), Pasquale Perrone Filardi (Italy), Gabriele Riccardi (Italy), Robert F. Storey (UK), David Wood (UK).
Dyslipidaemia guidelines – how should they look?

• Simple, user-friendly guidelines with most recent data and details concerning lipids

• Increase cardiologist’s, GP’s, other healthcare professionals & also patient’s knowledge and awareness

• Clear recommendations – what to do

• The next 5th Joint CVD prevention guidelines (2012), diabetes (2013) and hypertension guidelines (2014) should be consistent and compatible – we have to speak with one voice, always allowing for developments in knowledge
Why assess total cardiovascular risk?

- CVD is usually the result of multiple interacting risk factors
- It is not easy to assess the combined effects clinically
- Therefore a risk assessment system is recommended
- ESC recommends SCORE
- We re-looked at Framingham, Q-risk, Assign, Procam, WHO and Reynolds & undertook two systematic reviews
SCORE

- Representative- 205,000 subjects from 11 European countries
- High and low risk versions available + 15 country-specific versions
- Can be re-calibrated if up-to-date mortality and risk factor data available
- Electronic, interactive version available on-and off-line – HeartScore- with Guideline advice for physicians and patients- www.heartscore.org
- New functions- HDL, BMI, risk age
Risk levels - mortality or morbidity?

- Physicians intuitively want total events
- Issue examined exhaustively
- Non-fatal events variable and unstable - vary with time, definition, diagnostic tests, methods of ascertainment
- Term “20%” CHD/CVD is *meaningless* unless derivation is explicitly known
- Mortality allows easy re-calibration for other countries in Europe or elsewhere
SCORE total events- can a multiplier be derived?

- Finrisk is the biggest contributor to SCORE high risk and used well-defined, MONICA end-points
- Using HARD CVD end points, the multiplier from mortality to total events is 3, so that a 5% mortality risk equates to a 15% hard total event risk
SCORE chart: 10 year risk of fatal cardiovascular disease (CVD) in populations at high CVD risk
SCORE chart: 10 year risk of fatal cardiovascular disease (CVD) in populations at low CVD risk
BMI & HDL - important but very different effects

- BMI relates strongly to CVD mortality, especially in younger persons, but loses significance when adjusted for other risk factors.
- This is because it works through effects on BP, total and HDL cholesterol and does not reduce its public health importance.
- HDL is strongly related to risk and remains independent after adjustment for all other factors.
- HDL relates to risk at all ages, in both genders, and at all levels of baseline risk.
SCORE & HDL Cholesterol

- The original SCORE charts used cholesterol and HDL/cholesterol ratio
- They looked almost identical, in part because the ratio is dominated by cholesterol which has a wider spread than HDL
- More useful information when HDL is entered into the model separately
- HDL does not improve the AUROC greatly
- But re-classifies subjects close to the 5% threshold- 4% overall and up to 17% of women in high risk countries
Risk function without high-density lipoprotein-cholesterol (HDL-C) for men in populations at high cardiovascular disease risk
Risk in the young

- A low absolute risk may conceal a high relative risk
- Options include relative risk chart, risk age, lifetime risk and risk advancement periods
This chart may be used to show younger people at low absolute risk that, relative to others in their age group, their risk may be many times higher than necessary. This may help to motivate decisions about avoidance of smoking, healthy nutrition and exercise, as well as flagging those who may become candidates for medication.

Please note that this chart shows RELATIVE not absolute risk. The risks are RELATIVE to 1 in the bottom left. Thus a person in the top right hand box has a risk that is 12 times higher than a person in the bottom left.
• Total CVD risk estimate is part of a continuum - the cut points that are used to define high risk are in part arbitrary.

• Previous guidelines - a split up of the asymptomatic population into 2 groups: high risk (SCORE > 5%) in whom preventive action should be maximized (interpreted by many physicians strongly influenced by drug industry as "all on lipid-lowering drugs and/or all on antihypertensives") and SCORE < 5% in whom nothing was done.

• Not only high risk subjects should be identified and managed but also those at moderate risk (the large majority) professional advice regarding lifestyle changes and in some of them drug therapy.
### Intervention strategies as a function of total CV risk and LDL-C level

<table>
<thead>
<tr>
<th>Total CV risk (SCORE) %</th>
<th>LDL-C levels</th>
<th>&lt;70 mg/dL &lt;1.8 mmol/L</th>
<th>70 to &lt;100 mg/dL 1.8 to &lt;2.5 mmol/L</th>
<th>100 to &lt;155 mg/dL 2.5 to &lt;4.0 mmol/L</th>
<th>155 to &lt;190 mg/dL 4.0 to &lt;4.9 mmol/L</th>
<th>&gt;190 mg/dL &gt;4.9 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>No lipid intervention</td>
<td>No lipid intervention</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td></td>
</tr>
<tr>
<td>≥1 to &lt;5</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td></td>
</tr>
<tr>
<td>≥5 to &lt;10, or high risk</td>
<td>Lifestyle intervention, consider drug*</td>
<td>Lifestyle intervention, consider drug*</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td></td>
</tr>
<tr>
<td>≥10 or very high risk</td>
<td>Lifestyle intervention, consider drug*</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td></td>
</tr>
</tbody>
</table>

www.escardio.org
Lipids and total CVD risk

- Guideline development
- Why estimate total risk?
- Which system to use?
- Mortality vs total events
- BMI and HDL cholesterol - very different effects
- Re-classification of risk with HDL cholesterol
- Risk in the young
- The continuum of risk
Guidelines are nothing without implementation

Guidelines alone are good for the vanity of the authors and bad for rain forests; they are a waste of time without a defined implementation strategy

(Ian Graham)
Thank you