Identification of subjects at high risk for cardiovascular disease
Introductory remarks
Why detect

To prevent premature development of cardiovascular disease
Cardiovascular Disease Prevention
Impact of prevention vs. treatment - the landmark Finnish example

Proportionate reduction

Observed Mortality

Enhanced by therapeutic success

Predicted by the three factors combined

Cardiovascular Disease Prevention
Impact prevention vs. treatment - CHD deaths in the US 1980 - 2000

341,745 fewer deaths in 2000 →

Risk Factors worse +17%
- Obesity (increase) +7%
- Diabetes (increase) +10%

Risk Factors better -65%
- Population BP fall -20%
- Smoking -12%
- Cholesterol (diet) -24%
- Physical activity -5%

Treatments -47%
- AMI treatments -10%
- Secondary prevention -11%
- Heart failure -9%
- Angina: CABG & PTCA -5%
- Hypertension therapies -7%
- Statins (primary prevention) -5%

Unexplained -9%

Cardiovascular Disease Prevention
Four pillars for success

**Epidemiological information**
- Population based, trustworthy and updated
- Mortality not enough, morbidity important
Epidemiology on Cardiovascular Disease
Information from the ESC and EHN collaborating on the European Heart Health Charter
Epidemiology of Cardiovascular Disease
Trends in mortality and morbidity

[Graphs showing trends in hospital discharges and cardiovascular mortality over time for men and women in different regions.]
Epidemiology of Cardiovascular Disease
Cardiovascular mortality across Europe (<65 years)

CVD the major contributor to an almost 20 year difference in life expectancy across Europe
Diabetes in Europe
Actual in 2007

Million with diabetes 48 and IGT 63

Diabetes in Europe
Prognosis for 2026


Million with diabetes 56 and IGT 71
Diabetes
Hospital days spent and costs of complications

Total 736 mill €
4.5% of health care expenditures

Annual costs/patient (€)

- Cardiovascular disease
- Vascular complications
- Eye disease
- Kidney disease
- Other complications
- Neuropathy

UK

(Original: IDF 1999)
(Henriksson et al. 2000 J Intern Med; 248:387)
Cardiovascular Disease Prevention (CVD)
Four pillars for success

Epidemiological information
- Population based, trustworthy and updated
- Mortality not enough, morbidity important

Risk assessment tools
- Considering total risk
- Risk engines
- Risk assessment tools
Cardiovascular Disease Prevention (CVD)
Three strategies

Population distribution of cardiovascular (CV) risk

- **Primary**
  - Low risk: Covering most of those falling ill
- **High risk**
  - High risk: Covering a few at high risk falling ill

Proportion of Population

10-year risk

### Guidelines for CVD

#### The European version

<table>
<thead>
<tr>
<th>Year</th>
<th>Joint Task Force Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>First Joint Task Force recommendations</td>
</tr>
<tr>
<td>1998</td>
<td>Second Joint Task Force recommendations</td>
</tr>
<tr>
<td>2003</td>
<td>Third Joint Task Force guidelines</td>
</tr>
<tr>
<td>2007</td>
<td>Fourth Joint Task Force guidelines</td>
</tr>
<tr>
<td>2011</td>
<td>Fifth under way</td>
</tr>
</tbody>
</table>
Assessment of CV Risk
Classic and Emerging Methods

- ID of (vulnerable) plaques
- MR/MSCRT

Lab examinations
- Lipids
- Glucose

Case history
- Length/weight
- Waist circumference
- Blood pressure

ECG
- Stress test
- Echocardiogram
The Concept of Total Risk Assessment

Cornerstone in Cardiovascular Disease Prevention

- CVD is multifactorial in origin
- Risk factors interact synergistically
- Physicians see people, not isolated risk factors

About diabetes and cardiovascular risk

INTERHEART

(Yusuf et al. Lancet 2004; 364:937)

Of importance
… the rapid increase in Odds Ratio by a combination of risk factors…
Common in diabetes

(Yusuf et al. Lancet 2004; 364:937)
Why stress assessment of total CVD risk

- Usually multiple risk factors behind atherosclerosis causing CVD
- These risk factors interact, sometimes multiplicatively
- The aim is to reduce total risk
- If a target cannot be reached with one risk factor, total risk can still be reduced by trying harder with other
Objectives with CVD prevention

1. To assist people at low risk of CVD to maintain this state lifelong and help those at increased risk to reduce it.

2. To achieve the “healthy characteristics”
   - No smoking
   - Healthy food choices
   - Physical activity: 30 min of moderate activity/day
   - BMI <25 kg/m² + avoidance of central obesity
   - BP <140/90 mmHg
   - Total cholesterol <5 mmol/L
   - LDL cholesterol <3 mmol/L
   - Blood glucose <6mmo/L
Objectives with CVD prevention

3 To achieve rigorous risk factor control in high risk subjects, especially in known CVD or diabetes
   - Blood pressure under 130/80 mmHg if feasible
   - Total cholesterol <4.5 mmol/L; option <4 mmol/L
   - LDL cholesterol <2.5 mmol/L; option <2 mmol/L
   - Fasting blood glucose <6 mmol/L and HbA1c <6.5%

4 To consider cardioprotective drug therapy in high risk subjects especially those with atherosclerotic CVD
Consider Total CV Risk
A Need to Adapt Prevention to Total Individual Cardiovascular Risk

Randomized trials show that statins cause a RR reduction of $-30\%$ (outcome when applied to 2 different risk patterns)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total CV risk during 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute risk (%)</td>
<td>1</td>
</tr>
<tr>
<td>Adj RR (%)</td>
<td>30</td>
</tr>
<tr>
<td>NNT (n)</td>
<td>333</td>
</tr>
<tr>
<td>NNT to side effects</td>
<td>!!!</td>
</tr>
</tbody>
</table>
Assessment of Total CV Risk

General rule according to European Guidelines

Total CV risk is high or very high in subjects with:

- Established CVD
- DM
- Markedly elevated single risk factors
  - Total cholesterol $\geq 8$ mmol/L, LDL cholesterol $\geq 6$ mmol/L
  - SBP $\geq 180$ mm Hg and/or DBP $\geq 110$ mm Hg
- Pronounced family history of CVD at young age

In all other subjects, total CV risk should be estimated with a risk score model.

LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic BP.
Identification of people at risk
Risk assessment tools used in Western populations

- Framingham-based risk equation (USA)\(^1\)
- Systematic Coronary Risk Evaluation (SCORE; Europe)\(^2\)
- PREDICT\(^TM\) (New Zealand)\(^3\)
- Joint British Societies’ coronary risk prediction\(^4\)
- HeartScore (Europe)\(^5\)

Assessment of Total CV Risk
Framingham Heart Disease Risk Calculator

Kannel WB, McGee D, Gordon T
A general cardiovascular risk profile: the Framingham Study
*Am J Cardiol.* 1976;38:46

An updated coronary risk profile. A statement for health professionals
KM Anderson, PW Wilson, PM Odell and WB Kannel
*Circulation* 1991;83:356-362
### Assessment of Total CV Risk

**Framingham Heart Disease Risk Calculator**

**Characteristics**

A rather small US population for fatal/nonfatal CHD includes:

- Sex and age
- Total & HDL cholesterol
- Smoking
- Systolic blood pressure

---

**Step 1: Age**

<table>
<thead>
<tr>
<th>Years</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>-9</td>
</tr>
<tr>
<td>35-39</td>
<td>-4</td>
</tr>
<tr>
<td>40-44</td>
<td>0</td>
</tr>
<tr>
<td>45-49</td>
<td>3</td>
</tr>
<tr>
<td>50-54</td>
<td>6</td>
</tr>
<tr>
<td>55-59</td>
<td>8</td>
</tr>
<tr>
<td>60-64</td>
<td>10</td>
</tr>
<tr>
<td>65-69</td>
<td>11</td>
</tr>
<tr>
<td>70-74</td>
<td>12</td>
</tr>
<tr>
<td>75-79</td>
<td>13</td>
</tr>
</tbody>
</table>

**Step 2: Total Cholesterol**

<table>
<thead>
<tr>
<th>TC (mg/dL)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 20-39</td>
<td>0</td>
</tr>
<tr>
<td>Age 40-49</td>
<td>0</td>
</tr>
<tr>
<td>Age 50-59</td>
<td>0</td>
</tr>
<tr>
<td>Age 60-69</td>
<td>0</td>
</tr>
<tr>
<td>Age 70-79</td>
<td>0</td>
</tr>
<tr>
<td>&lt;160</td>
<td>0</td>
</tr>
<tr>
<td>160-199</td>
<td>1</td>
</tr>
<tr>
<td>200-239</td>
<td>4</td>
</tr>
<tr>
<td>240-279</td>
<td>7</td>
</tr>
<tr>
<td>&gt;280</td>
<td>11</td>
</tr>
</tbody>
</table>

**Step 3: HDL-C**

<table>
<thead>
<tr>
<th>HDL-C (mg/dL)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>-1</td>
</tr>
<tr>
<td>50-59</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>1</td>
</tr>
<tr>
<td>&lt;40</td>
<td>2</td>
</tr>
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</table>

**Step 4: Systolic Blood Pressure**

<table>
<thead>
<tr>
<th>SBP (mm Hg)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated</td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td></td>
</tr>
<tr>
<td>&lt;120</td>
<td>0</td>
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<tr>
<td>120-129</td>
<td>0</td>
</tr>
<tr>
<td>130-139</td>
<td>1</td>
</tr>
<tr>
<td>140-159</td>
<td>2</td>
</tr>
<tr>
<td>≥160</td>
<td>2</td>
</tr>
</tbody>
</table>

**Step 5: Smoking Status**

<table>
<thead>
<tr>
<th>Points at Age</th>
<th>20-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Smoker</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Step 6: Adding Points**

<table>
<thead>
<tr>
<th>Category</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Total-C</td>
<td></td>
</tr>
<tr>
<td>HDL-C</td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
</tr>
<tr>
<td>Point Total:</td>
<td></td>
</tr>
</tbody>
</table>

**Step 7: CHD Risk**

<table>
<thead>
<tr>
<th>Point Total</th>
<th>10-Year Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>0</td>
<td>1%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>2</td>
<td>1%</td>
</tr>
<tr>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>4</td>
<td>1%</td>
</tr>
<tr>
<td>5</td>
<td>1%</td>
</tr>
<tr>
<td>6</td>
<td>2%</td>
</tr>
<tr>
<td>7</td>
<td>2%</td>
</tr>
<tr>
<td>8</td>
<td>3%</td>
</tr>
<tr>
<td>9</td>
<td>4%</td>
</tr>
<tr>
<td>10</td>
<td>5%</td>
</tr>
<tr>
<td>11</td>
<td>6%</td>
</tr>
<tr>
<td>12</td>
<td>8%</td>
</tr>
<tr>
<td>13</td>
<td>10%</td>
</tr>
<tr>
<td>14</td>
<td>12%</td>
</tr>
<tr>
<td>15</td>
<td>16%</td>
</tr>
<tr>
<td>16</td>
<td>20%</td>
</tr>
<tr>
<td>≥17</td>
<td>≥30%</td>
</tr>
</tbody>
</table>

Assessment of Total CV Risk
Framingham Heart Disease Risk Calculator: Online Access

http://www.nhlbi.nih.gov

Risk Assessment Tool for Estimating 10-year Risk of Developing Hard CHD (Myocardial Infarction and Coronary Death)
The risk assessment tool below uses recent data from the Framingham Heart Study to estimate 10-year risk for “hard” coronary heart disease outcomes (myocardial infarction and coronary death). This tool is designed to estimate risk in adults aged 20 and older who do not have heart disease or diabetes. Use the calculator below to estimate 10-year risk.

Age: __________ years
Gender:  
○ Female  ○ Male

Total Cholesterol: __________ mg/dL
HDL Cholesterol: __________ mg/dL

Smoker:  
○ No  ○ Yes

Systolic Blood Pressure: __________ mm/Hg
Currently on any medication to treat high blood pressure.  
○ No  ○ Yes

Highest risk: >20% or a history of heart disease or DM
High risk: 10%-20% and ≥2 risk factors
Moderate risk: <10% and ≥2 risk factors
Low risk: ≤1 risk factor
Screening tools from Western populations may not be accurate in AP populations

- Background epidemiology of CVD and risk factors may differ affect risk calculations
  - NCEP ATP III criteria *underestimates* the at-risk AP population\(^1\)
  - Framingham-based CV risk calculators *overestimates* the risk in Asian populations\(^2\)

---

**AP:** Asia-Pacific; **NCEP ATP:** National Cholesterol Education Programme Adult Treatment Panel
The Framingham risk engine overestimates the CVD risk in Asian populations

Observed and predicted CV event rate according to deciles of predicted risk in Chinese patients

CV: cardiovascular
APCSC. J Epidemiol Community Health 2007;61:115–21.
Identification of people at risk
Risk assessment and ethnicity

- Development of new risk assessment equations
- Recalibration/modification of existing equations or definitions
- Resources for risk factor screening are limited in many AP countries
  - Reliable and inexpensive risk tools are needed
Identification of people at risk
Risk assessment in the Asian-Pacific region

The Asia Pacific Cohort Studies Collaboration
APCSC

Objective
To compare "low-information" equations (age, systolic blood pressure, cholesterol, smoking habits) from the Framingham Study with those derived from Asian cohorts…
Identification of people at risk
Risk assessment in the Asian-Pacific region

- Pools data from longitudinal studies with information on CVD in the Asia Pacific region
- Comprises data on >650,000 participants
  - 44 separate cohort studies in mainland China, Hong Kong, Taiwan, Japan, South Korea, Singapore, Thailand, New Zealand and Australia
- Is one of largest databases worldwide

APCSC. J Epidemiol Community Health 2007;61:115–21.
A new CVD equation for Asian populations

Observed and predicted CV event rate according to deciles of predicted risk in Chinese patients

Deciles of predicted risk based on other Asian equation

Men

Bias = +11%

Observed

Predicted

Women

Bias = +10%

Deciles of predicted risk based on other Asian equation

APCSC. J Epidemiol Community Health 2007;61:115–21.
Recalibration of the Framingham risk calculator for an Asian population

Observed and predicted CV event rate according to deciles of predicted risk in Chinese patients

Deciles of predicted risk based on the recalibrated Framingham equation

Men
Bias = −2%

Women
Bias = +4%

APCSC. J Epidemiol Community Health 2007;61:115–21.
European Cohort Studies (n = 12)
- Some with multiple sub-studies
- Mainly population based

Some figures:
- About 250,000 people
- Follow-up ≈ 3 million person years
- Cardiovascular fatalities >7000

Assessment of Total CV Risk
Systematic Coronary Risk Evaluation (SCORE)

Eur Heart J 2007; 28: 2375 – 2414
Executive summary
A 10-year risk of CVD death >5% considered as a high or at least increased risk

*Eur Heart J* 2007; 28: 2375 – 2414
Executive summary
Assessment of Total CV Risk
Systematic Coronary Risk Evaluation (SCORE)
Risk estimation using SCORE qualifiers

- To be used with knowledge and judgement
- Risk overestimated with a falling and underestimated if rising CVD mortality
- Risk appears lower for women. This is misleading - charts show that their risk is deferred by 10 years
- Risk may be higher than indicated in the chart in
  - The sedentary or obese
  - Those with a strong family history
  - The socially deprived
- Diabetes - risk x 4-5 in women and x 3 in men
For younger persons who despite a low total risk may have a several times higher risk in relation to others in the same age group.
Assessment of the Risk for Diabetes
Oral Glucose Tolerance Test (OGTT) in CAD

WHO 1999 criterion
(FPG < 6.1 mmol/l)

ADA 2003 criterion
(FPG < 5.6 mmol/l)

<table>
<thead>
<tr>
<th>% of all with OGTT</th>
<th>DM</th>
<th>IGT</th>
<th>IFG</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG&lt;WHO</td>
<td>5%</td>
<td>8%</td>
<td>27%</td>
<td>8%</td>
</tr>
<tr>
<td>FPG&lt;ADA</td>
<td>8%</td>
<td>5%</td>
<td>21%</td>
<td>5%</td>
</tr>
</tbody>
</table>

(Bartnik et al. Heart 2007; 93:72)
Finnish Diabetes Risk Score (FINDRISC) to address 10-year risk of type 2 DM (T2DM) in adults

Assessment of the Risk for Diabetes

Type 2 diabetes risk assessment form

Circle the right alternative and add up your points.

1. Age
   0 p. Under 45 years
   2 p. 45-54 years
   3 p. 55-64 years
   4 p. Over 64 years

2. Body mass Index
   0 p. Lower than 25 kg/m²
   1 p. 25-30 kg/m²
   3 p. Higher than 30 kg/m²

3. Waist circumference measured below the ribs (usually at the level of the navel)
   MEN
   0 p. Less than 94 cm
   3 p. 94-102 cm
   4 p. More than 102 cm
   WOMEN
   0 p. Less than 80 cm
   3 p. 80-88 cm
   4 p. More than 88 cm

4. Do you usually have daily at least 30 min of physical activity at work and/or during leisure time (including normal daily activity)?
   0 p. Yes
   2 p. No

5. How often do you eat vegetables, fruit, or berries?
   0 p. Every day
   1 p. Not every day

6. Have you ever taken anti-hypertensive medication regularly?
   0 p. No
   2 p. Yes

7. Have you ever been found to have high blood glucose (e.g. during an illness, during pregnancy)?
   0 p. No
   5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?
   0 p. No
   3 p. Yes: grandparent, aunt, uncle, or first cousin (but no own parent, brother, sister or child)
   5 p. Yes: parent, brother, sister, or own child

Total risk score

The risk of developing type 2 diabetes within 10 years is

Lower than 7 Low: estimated one in 100 will develop disease
7-11 Slightly elevated: estimated one in 25 will develop disease
12-14 Moderate: estimated one in 6 will develop disease
15-20 High: estimated one in three will develop disease
Higher than 20 Very High: estimated one in two will develop disease

Available at: www.diabetes
Assessment of Total CV Risk in diabetes
The UKPDS Risk engine

Risk Engine according to United Kingdom Prospective Diabetes Study (UKPDS)

Available at
www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/
From evidence to clinical practice

- Research
- Guidelines
- Surveys
- Education
Characteristics of healthy people

- 0 smoking
- 3 km of daily walking
- If high risk
- 130/80 mm Hg blood pressure
- 4.0 mmol/L total cholesterol
- 2.0 mmol/L LDL-cholesterol
- 0 diabetes

European phone number to health
0 3 5 140 90 5 3 0
Conclusions

- Prevention of CVD should be based on total CV risk rather than be split on primary and secondary prevention
- Risk calculators (ex. Framingham, SCORE UKPDS) help in assessing total risk but must be adapted to local populations
- DM is an independent risk factor for CVD
- The risk of CV events increases dramatically with concomitant risk factors
Identification of subjects at high risk for cardiovascular disease

Time for questions