

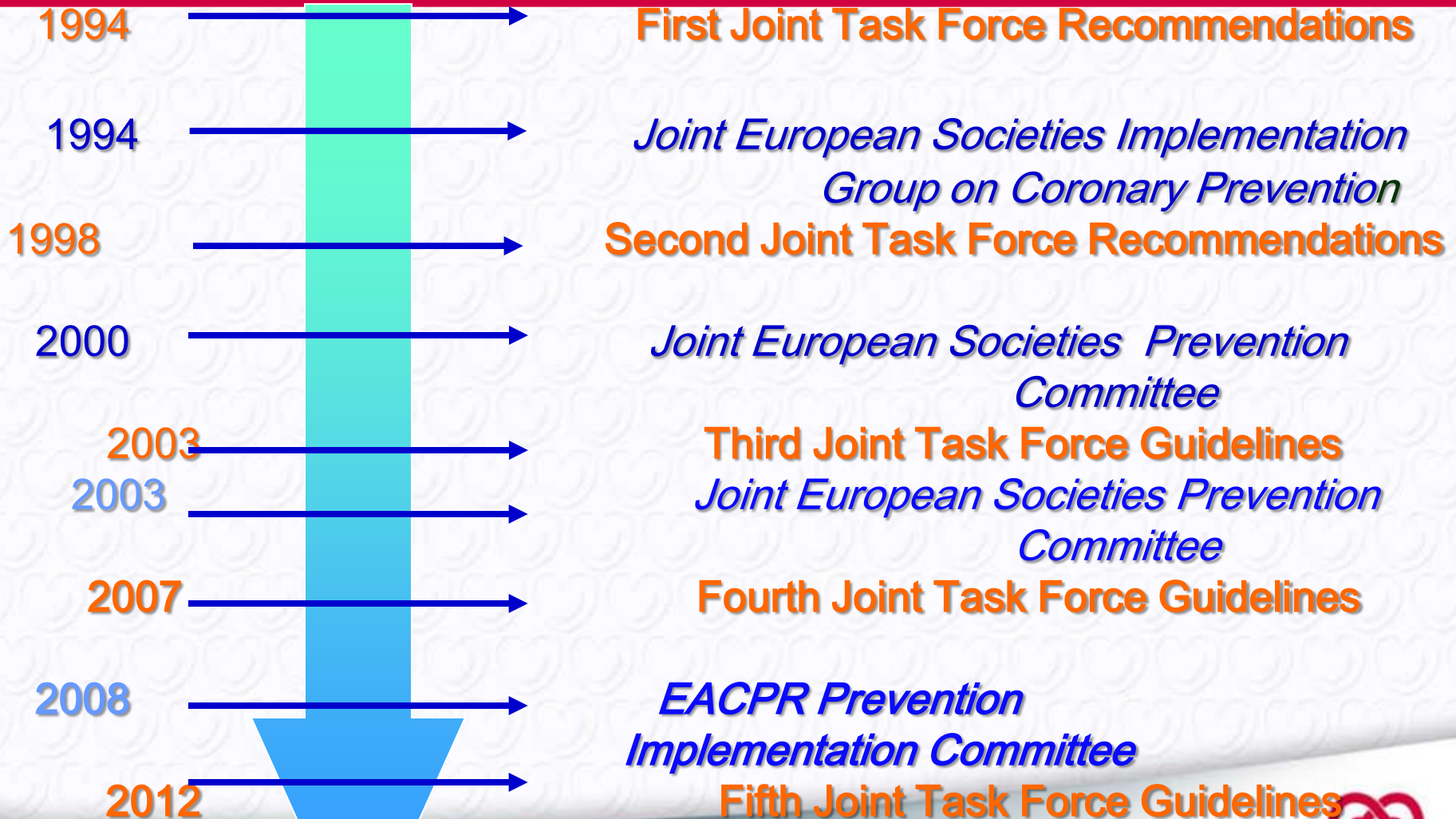
# Present state and future trends of prevention guidelines

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# History of European guidelines on CVD prevention



# Partner Societies

## The 5th Joint European Societies' Task Force on Cardiovascular Disease Prevention in Clinical Practice

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European Society of  
Cardiology (ESC)



European Society of General Practice/  
Family Medicine (ESGP/FM/Wonca)



European Association for  
Cardiovascular Prevention &  
Rehabilitation (EACPR)



European Atherosclerosis Society  
(EAS)



European Society of  
Hypertension (ESH)



European Association for the Study  
of Diabetes (EASD)



International Society of  
Behavioural Medicine (ISBM)



International Diabetes Federation  
Europe (IDF-Europe)



European Heart Network (EHN)



European Stroke Organization (ESO)

# Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
<b>Class I</b>	<b>Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.</b>	<b>Is recommended/ is indicated.</b>
<b>Class II</b>	<b>Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.</b>	
<b><i>Class IIa</i></b>	<b><i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i></b>	<b><i>Should be considered.</i></b>
<b><i>Class IIb</i></b>	<b><i>Usefulness/efficacy is less well established by evidence/opinion.</i></b>	<b>May be considered.</b>
<b>Class III</b>	<b>Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.</b>	<b>Is not recommended.</b>

# Levels of evidence

<b>Level of Evidence A</b>	<b>Data derived from multiple randomized clinical trials or meta-analyses.</b>
<b>Level of Evidence B</b>	<b>Data derived from a single randomized clinical trial or large non-randomized studies.</b>
<b>Level of Evidence C</b>	<b>Consensus of opinion of the experts and/or small studies, retrospective studies, registries.</b>

# New GRADE, focus on population studies

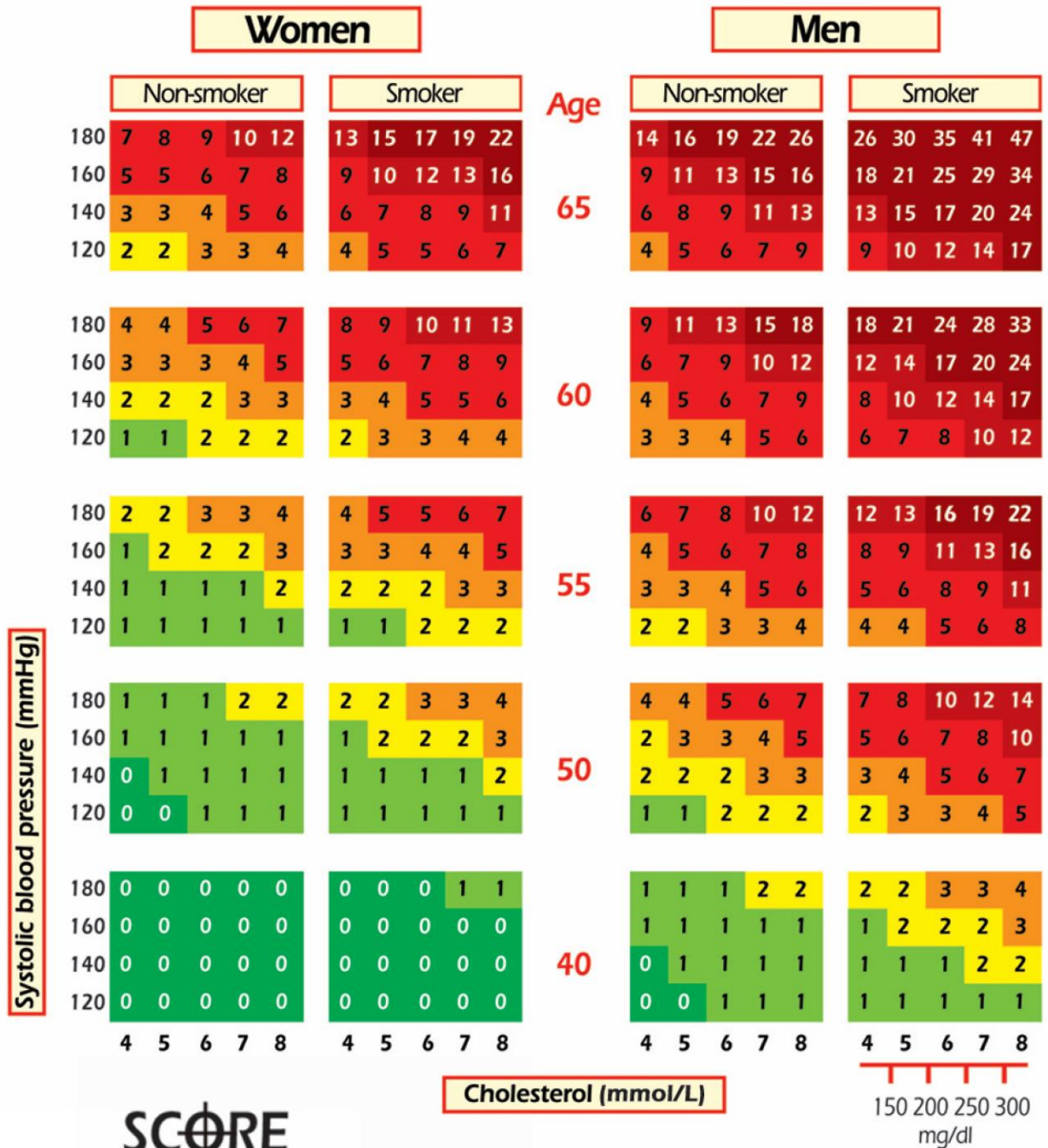
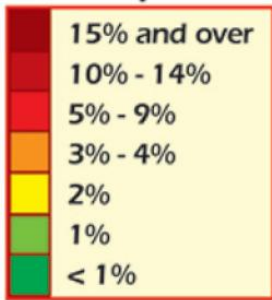
- **Conventional ESC method:**
  - Evidence levels: A, B and C,
  - Recommendation: I, IIa, IIb or III,
  - RCT greatest weight,
  - Population studies undervalued.
- **GRADE:**
  - **Recommendation: strong or weak:**
    - **Strong:** one should offer this treatment,
    - **Weak:** one might wish to consider other options.

# Total CVD risk

- **Total risk estimation is a crucial tool to guide patient management because clinicians treat whole people (and not individual risk factors), whose CVD risk usually reflects the combined effects of several risk factors.**
- **Multiple risk factors usually contribute to the atherosclerosis that causes CVD.**
- **The aim should be to reduce total risk; if a target cannot be reached with one risk factor, total risk can still be reduced by trying harder with others - if perfect control of a risk factor is difficult (for example, blood pressure control), total CVD risk can still be reduced by reducing other risk factors such as smoking or blood cholesterol.**

# SCORE: 10 year risk of fatal CVD in high risk regions of Europe

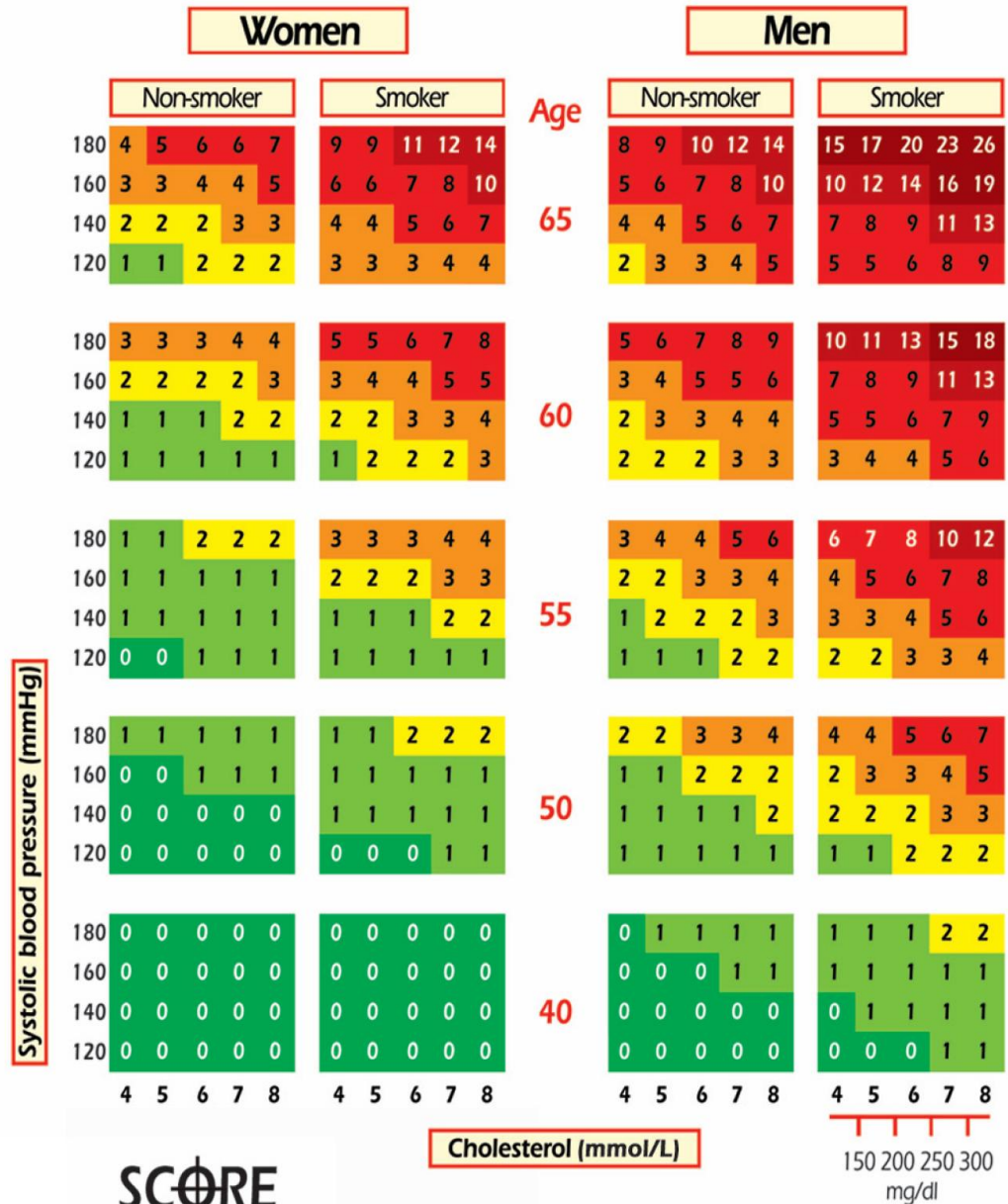
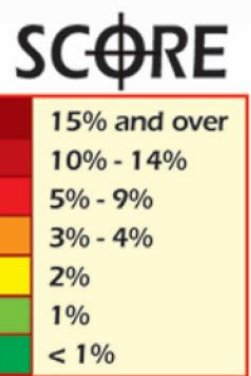
## SCORE







# SCORE: 10 year risk of fatal CVD in low risk regions of Europe



# Risk regions in Europe

## **Countries at low CVD risk** (use *SCORE low risk chart*\*)

Based on age, sex, smoking, systolic blood pressure, total cholesterol:

Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, The Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.

**High CVD risk countries** are all those not listed under the low risk chart (use *SCORE high risk chart*)  
**CROATIA IS IN THIS GROUP !**

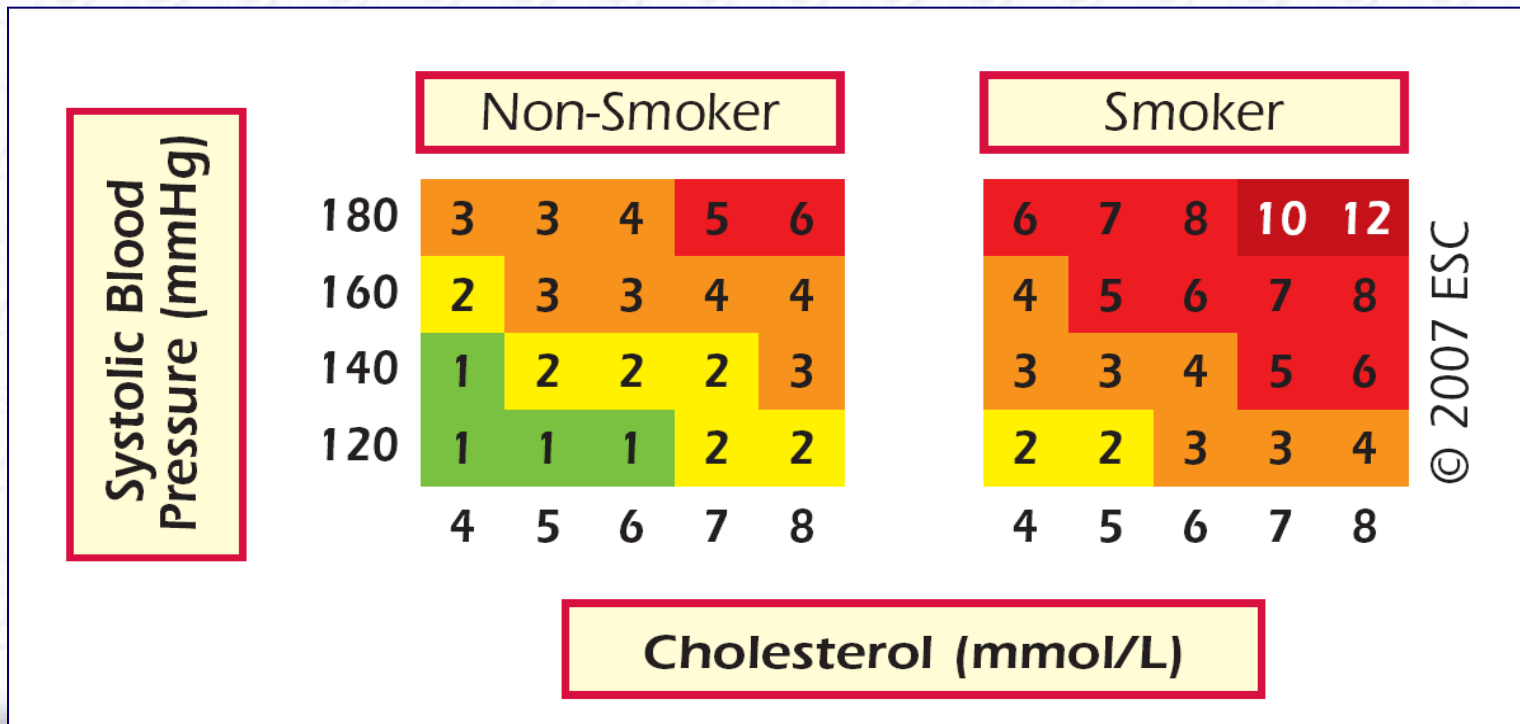
Of these, some are at **very high CVD risk**, and the high-risk chart may under-estimate risk in these: Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Macedonia FYR, Moldova, Russia, Ukraine and Uzbekistan.

\* Re-calibrated charts may be available for your country  
(see [www.heartscore.org](http://www.heartscore.org))

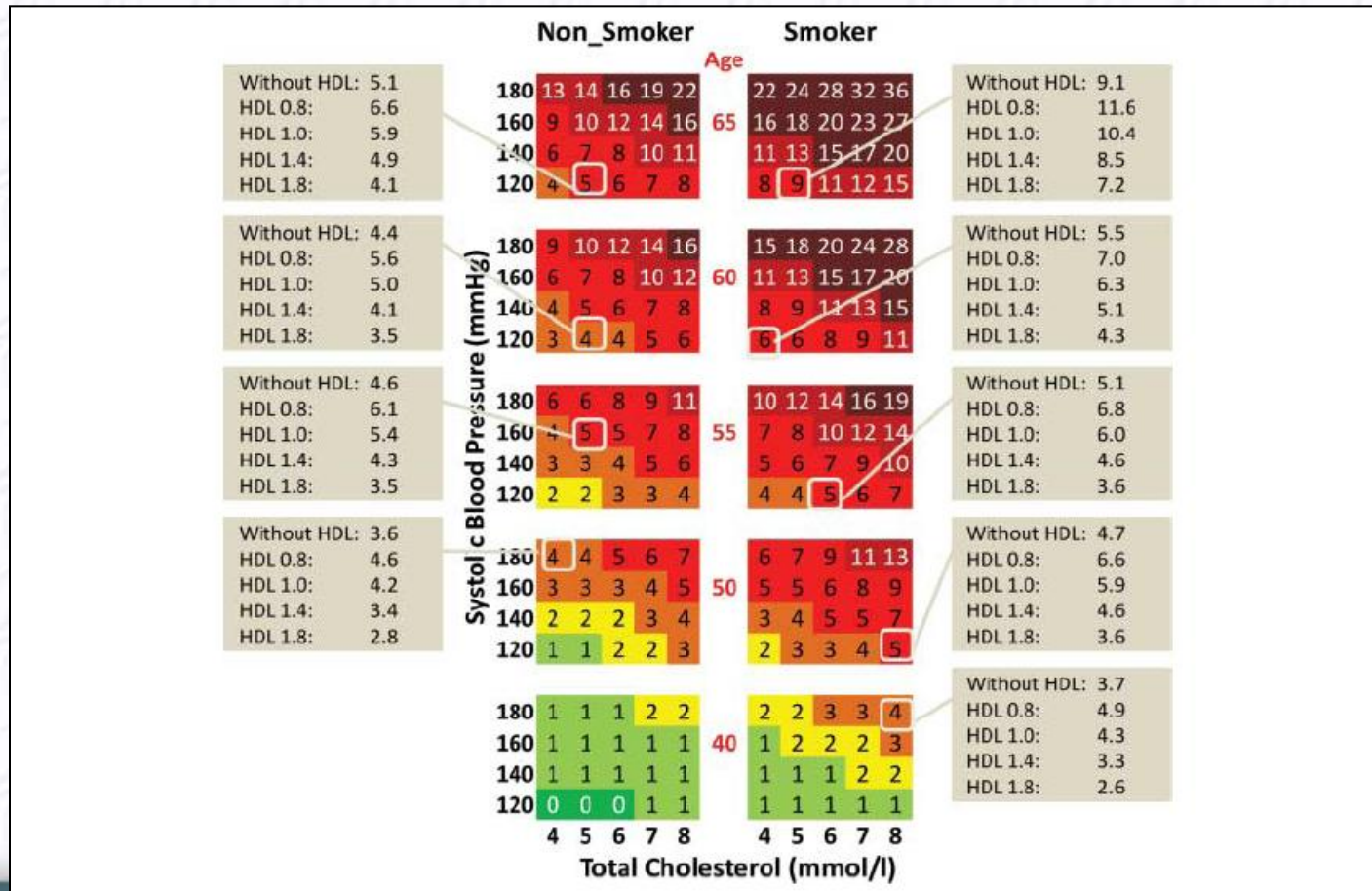
# Relative risk chart

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



# Risk function with and without HDL-cholesterol for men in populations at high cardiovascular disease risk

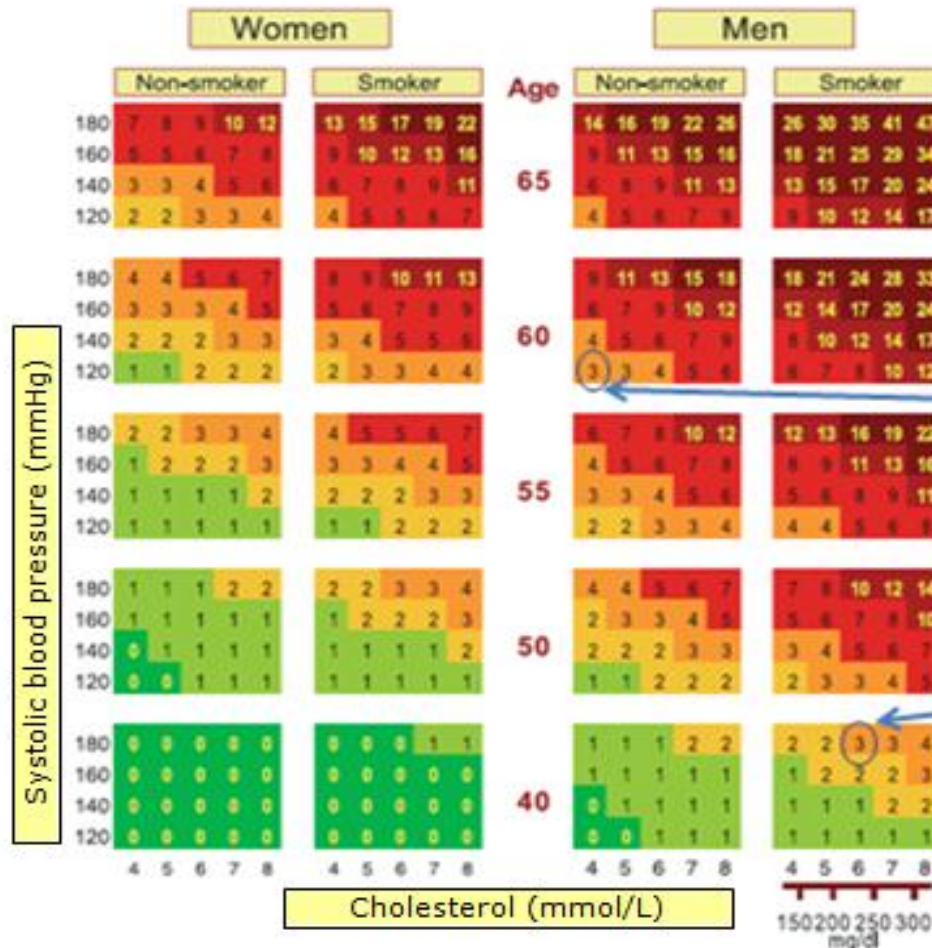


# Risk age, a new concept:

The risk age of a person with several risk factors is the same as that of a person with no risk factors, as illustrated below. This can be helpful in motivating change in risk factors to reduce risk age.

HeartScore, the interactive version of SCORE, is now available at: [www.heartscore.org](http://www.heartscore.org)

HDL cholesterol modulates risk estimates at all levels of risk and in both genders. HDL charts, an instant calculation of risk age and BMI are now included in the updated electronic risk estimation system which also provides interactive management advice.



The risk of this 40 year old male smoker with risk factors is the same (3%) as that of a 60 year old man with ideal risk factor levels—therefore his risk age is 60 years

# Are raised plasma triglycerides a predictor of CVD ?

- **Fasting triglycerides relate to risk in univariate analyses but the effect is attenuated by adjustment for other factors, especially HDL-cholesterol.**
- **After adjustment for HDL-cholesterol there is no significant association between triglycerides and CVD.**

# Other biomarkers of risk

	Class	Level	GRADE
<b>Recommendations: Inflammatory markers</b>			
High-sensitivity CRP may be measured as part of refined risk assessment in patients with an unusual or moderate CVD risk profile.	IIb	B	Weak
High-sensitivity CRP should not be measured in asymptomatic low-risk individuals and high-risk patients to assess 10-year risk of CVD.	III	B	Strong
Fibrinogen may be measured as part of refined risk assessment in patients with an unusual or moderate CVD risk profile.	IIb	B	Weak
Fibrinogen should not be measured in asymptomatic low-risk individuals and high-risk patients to assess 10-year risk of CVD.	III	B	Strong
<b>Recommendations: Thrombotic markers</b>			
Homocysteine may be measured as part of a refined risk assessment in patients with an unusual or moderate CVD risk profile.	IIb	B	Weak
Homocysteine should not be measured to monitor CVD risk prevention.	III	A	Strong
LpPLA2 may be measured as part of a refined risk assessment in patients at high risk of a recurrent acute atherothrombotic event.	IIb	B	Weak

# Very high risk

**Subjects with any of the following:**

**Documented CVD by invasive or non-invasive testing (such as coronary angiography, nuclear imaging, stress echocardiography, carotid plaque on ultrasound), previous myocardial infarction, acute coronary syndrome, coronary revascularization (percutaneous coronary intervention or bypass surgery) and other arterial revascularization procedures, ischaemic stroke, peripheral artery disease**

**Diabetes mellitus (type 1 or type 2) with one or more cardiovascular riskfactors and/or target organ damage (such as microalbuminuria: 30–300 mg/24 h)**

**Severe chronic kidney disease (CKD) (glomerular filtration rate (GFR) <30 mL/min/1.73 m<sup>2</sup>).**

**A calculated SCORE ≥10%.**



# Other risk groups

## High risk

Markedly elevated single risk factors such as familial dyslipidaemias and severe hypertension.

Diabetes mellitus (type 1 or type 2) but without CV riskfactors or target organ damage.

Moderate chronic kidney disease (CKD) (glomerular filtration rate (GFR] 30-59 mL/min/1.73 m<sup>2</sup>).

A calculated SCORE of  $\geq 5\%$  and  $< 10\%$  for 10-year risk of fatal CVD.

## Moderate risk

Subjects are considered to be at moderate risk when their SCORE is  $\geq 1$  and  $< 5\%$  at 10 years. Many middle-aged subjects belong to this category.

## Low risk

The low-risk category applies to individuals with a SCORE  $< 1\%$  and free of qualifiers that would put them at moderate risk.

# Gender issues: cardiovascular disease in women

- **At any given age, risk appears lower for women than men. This is misleading since more women (55%) than men (45%) die from CVD. Compare: 3% breast cancer deaths in women.**
- **The apparent lower risk in women in SCORE reflects the fact that women develop CVD 10 years later.**
- **The evidence base for risk factor advice, especially regarding drug treatments is hampered by under-representation of women in clinical trials.**
- **Women are disadvantaged at all stages - they are less likely to be offered risk assessment, to have chest pain evaluated or investigated, and to be offered therapy and interventions.**
- **Mortality from acute coronary syndromes and after CABG is frequently higher in women.**

# Psychosocial risk factors

- **Low socioeconomic status, lack of social support, stress at work and in family life, depression, anxiety, hostility and the type D personality, contribute both to the risk of developing CVD and the worsening of clinical course and prognosis of CVD.**
- **These factors act as barriers to treatment adherence and efforts to improve lifestyle, as well as to promote health and wellbeing in patients and populations. In addition, distinct psychobiological mechanisms have been identified, which are directly involved in the pathogenesis of CVD.**

# 5 A's for Smoking Cessation

- **A – ASK:** Systematically inquire about smoking status at every opportunity.
- **A – ADVISE:** Unequivocally urge all smokers to quit.
- **A – ASSESS:** Determine the person's degree of addiction and readiness to quit
- **A – ASSIST:** Agree on a smoking-cessation strategy, including setting a quit date, behavioural counselling and pharmacological support
- **A – ARRANGE:** Arrange a schedule of follow-up

# Nutrition

**A healthy diet which is the cornerstone of CVD prevention has following characteristics:**

- **Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.**
- **Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin**
- **<5 g of salt per day.**
- **30–45 g of fibre per day, from wholegrain products, fruits and vegetables.**
- **200 g of fruit per day (2-3 servings).**
- **200 g of vegetables per day (2-3 servings).**
- **Fish at least twice a week, one of which to be oily fish.**
- **Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.**

# Physical activity

Recommendations	Class	Level	GRADE
<p>Healthy adults of all ages have to spend <b>2.5-5 hours a week on physical activity or aerobic exercise training of at least moderate intensity, or 1-2.5 hours a week on vigorous intense exercise.</b></p> <p>Sedentary subjects should be strongly encouraged to start light-intensity exercise programmes.</p>	I	A	strong
<p>Physical activity/aerobic exercise training should be performed in multiple bouts each lasting <math>\geq 10</math> minutes and evenly spread throughout the week, i.e. on 4–5 days a week</p>	IIa	A	strong
<p>Patients with previous acute myocardial infarction, CABG, PCI, stable angina pectoris or stable chronic heart failure should undergo moderate-to-vigorous intensity aerobic exercise training <math>\geq 3</math> times a week and 30 min per session. Sedentary patients should be strongly encouraged to start light-intensity exercise programmes after adequate exercise-related risk stratification</p>	I	A	strong

# Body weight

- **Both overweight and obesity are associated with a risk of death in CVD**
- **There is a positive linear association of BMI with all-cause mortality**
- **All-cause mortality is lowest with a BMI of 20 to 25 kg/m<sup>2</sup>**
- **Further weight reduction cannot be considered protective against CVD**

Recommendations	Class	Level	GRADE
Weight reduction in overweight and obese people is recommended as this is associated with favourable effects on blood pressure and dyslipidaemia, which may lead to less CVD.	I	A	strong

# Key message concerning hypertension

**Elevated blood pressure is a major risk factor for CHD, heart failure, cerebrovascular disease, renal failure and, as established more recently, for atrial fibrillation**



# Key messages concerning hypertension

- **Lifestyle measures such as weight control, increased physical activity, sodium restriction alcohol moderation, and increased consumption of fruits, vegetables, and low-fat dairy products are recommended in all patients with hypertension and in individuals with high normal BP.**

# Key messages concerning hypertension

- **Systolic BP should be lowered to <140/90 mmHg in all hypertensive patients and to <140/90 mmHg in patients with diabetes.**
- **All major antihypertensive drug classes (i.e. diuretics, ACE inhibitors, calcium antagonists, angiotensin receptor antagonists and beta-blockers) do not differ significantly in their BP-lowering efficacy and can be recommended for the initiation and maintenance of antihypertensive treatment**
- **The main benefits of antihypertensive treatment are due to lowering of BP *per se*, and are largely independent of the drugs employed.**

# Some important issues

- Promptness in the initiation of pharmacological therapy of hypertension depends on the level of total CV risk.
- A delay in achieving BP control in high-risk hypertensive patients is associated with a worse outcome.
- Initiation of antihypertensive drug therapy in patients with diabetes and high normal BP is presently **not** supported by prospective trial evidence (without subclinical organ damage, particularly microalbuminuria or proteinuria).
- Antihypertensive treatment is beneficial in patients aged  $\geq 80$  years.

# Some important issues

- **Combination therapy is needed to control BP in most patients.**
- **Trial evidence of outcome reduction has been obtained particularly for: diuretic+ACEi or diuretic+ARB or diuretic+Ca antagonist.**
- **In 15-20% patients a combination of 3 drugs is needed, the most rational appears ARB+Ca antagonist+diuretic.**

# Key messages concerning dyslipidaemias

- **Increased plasma total cholesterol and LDL cholesterol are among the main risk factors for CVD.**
- **Low HDL cholesterol is an important independent CVD risk factor and hypertriglyceridemia to a certain extent as well.**
- **Statin therapy has a beneficial effect on atherosclerotic CVD outcomes**

# Some important issues

- **Total cholesterol is recommended to be used for the estimation of total CV risk by means of the SCORE system but **not** as a target for treatment. It should be considered as treatment target only if other analyses are not available.**
- **LDL cholesterol is recommended to be used as the primary lipid analysis for screening and risk estimation and is recommended as target for treatment.**
- **HDL cholesterol is a strong risk factor and is recommended to be used for risk estimation**

# Recommendations for treatment targets for LDL cholesterol

## Target LDL-cholesterol:

**<1.8 mmol/L (< 80 mg/dL) for very high risk patients**

**<2.5 mmol/L (< 100 mg/dL) for high risk patients**

**<3.0 mmol/L (< 115 mg/dL) for for all others**

# Recommendations for the pharmacological treatment of hypercholesterolaemia

- **Statins reduce hypercholesterolaemia but also CV morbidity and mortality as well as the need for coronary artery interventions. In high doses they also seem to halt progression or even contribute to regression of coronary atherosclerosis. Therefore, they should be used as the drugs of first choice in patients with hypercholesterolaemia or combined hyperlipidaemia.**
- **Statins should be used in highest tolerable doses to reach the LDL cholesterol target level.**

Reiner Ž. Nat Rev Cardiol. 2013;10(8):453-64

European Heart Journal 2012;33:1635–1701

European Journal of Preventive Cardiology 2012;19: 4:585-667



# Recommendations for the pharmacological treatment of hypertriglyceridaemia and increasing HDL cholesterol

- Fibrates and niacin are used primarily for triglyceride lowering and increasing HDL cholesterol, while omega-3 fatty acids in doses of 2–4 g/day are used for triglyceride lowering.
- **New data on niacin !**

Reiner Ž. Nutr Metab Cardiovasc Dis. 2013;23(9):799-807

European Heart Journal 2012;33:1635–1701

European Journal of Preventive Cardiology 2012;19: 4:585-667

# Drug combinations

- Patients with dyslipidaemia, particularly those with established CVD, diabetes or metabolic syndrome, and asymptomatic high-risk individuals, may not always reach treatment targets. Therefore combination treatment may be needed.
- If LDL-C target level is not achieved with statin alone, statin + bile acid sequestrant or statin + ezetimibe can be used.
- Statin + niacin increase HDL-C and decrease triglycerides better than either of these drugs alone but flushing is the main adverse effect of niacin - affects compliance. **NEW DATA !**
- Fibrates, particularly fenofibrate + statin decrease high triglycerides and increase HDL-C and further lower LDL-C

# Diabetes

- In patients with type 2 diabetes lipid lowering therapy is recommended irrespective of their basal LDL-C.
- In patients with type 2 diabetes and CVD or CKD and in those without CVD who are over age of 40 years with one or more other CVD risk factor the recommended **goal for LDL-C is  $< 1.8$  mmol/L ( $< \sim 70$ mg/dL) and for apo B  $< 80$  mg/dL.**
- In all patients with type 2 diabetes **LDL-C  $< 2.5$  mmol/L ( $< \sim 100$  mg/dL) or apo B  $< 100$  mg/dL** are the recommended targets.

# Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of CVD in the adult – Targets based on Framingham Risk Score (FRS), modified by family history

Risk level	Initiate therapy if	Primary target LDL C	Alternate target
High FRS $\geq$ 20%	Consider treatment in all (Strong, High)	$\leq$ 2 mmol/L or $\geq$ 50% decrease in LDL-C (Strong, High)	<ul style="list-style-type: none"> <li>➤ Apo B <math>\leq</math> 0.8 g/L</li> <li>➤ Non HDL-C <math>\leq</math> 2.6 mmol/L (Strong, High)</li> </ul>
Intermediate FRS 10%-19%	<ul style="list-style-type: none"> <li>➤ LDL-C <math>\geq</math> 3.5 mmol/L (Strong, Moderate)</li> <li>➤ For LDL-C <math>&lt;</math> 3.5 consider if: Apo B <math>\geq</math> 1.2 g/L or Non-HDL-C <math>\geq</math> 4.3 mmol/L (Strong, Moderate)</li> </ul>	$\leq$ 2 mmol/L or $\geq$ 50% decrease in LDL-C (Strong, Moderate)	<ul style="list-style-type: none"> <li>➤ Apo B <math>\leq</math> 0.8 mg/L</li> <li>➤ Non HDL-C <math>\leq</math> 2.6 mmol/L (Strong, Moderate)</li> </ul>
Low FRS $<$ 10%	<ul style="list-style-type: none"> <li>➤ LDL-C <math>\geq</math> 5.0 mmol/L</li> <li>➤ Familial hypercholesterolemia (Strong, Moderate)</li> </ul>	$\geq$ 50% reduction in LDL-C (Strong, Moderate)	

# International Atherosclerosis Society position paper

- **Moving to from short-term (10-year) risk to a lifetime (long-term) risk prediction for clinical intervention using Framingham as the core estimate followed by re-calibration for individual countries.**
- **Four levels of risk up to age 80: high ( $\geq 45\%$ ), moderately high (30-44%), moderate (15-29%) and low ( $<15\%$ ). High risk also: diabetes plus other risk factors, or 2 major risk factors in men and 3 in women, or FH. Moderately high risk: diabetes without other risk factors, or chronic kidney disease, or and metabolic syndrome.**
- **Non-HDL-C is an appropriate alternative to LDL-C for lipid-lowering therapy in all patients.**

# International Atherosclerosis Society position paper

- IAS does not specifically prescribe “treatment goals’ for lipoproteins. Instead it identifies optimal levels and the intensity of lipid-lowering therapy should be adjusted to long-term risk.
- The optimal LDL-C in primary prevention: < 100 mg/dL (2.6 mmol/L).
- Since non-HDL-C can replace LDL-C, the optimal non-HDL-C for primary prevention: < 130 mg/dL (3.4 mmol/L).
- The optimal LDL-C in patients with established CVD is <70 mg/dL [1.8 mmol/L) and non-HDL-C is <90 mg/dL (2.3 mmol/L).

# Possible controversies with IAS position paper

- **LDL-C <100 mg/dL (2.6 mmol/L) as the optimal value for all the individuals and all risk levels in primary prevention is not reflecting an evidence based approach but voting of the 17 panel members.**
- **If the risk level is irrelevant for LDL-C treatment goals in primary prevention, why to bother with risk assessment?**
- **Lowering the LDL-C optimal value for all to <100 mg/dL (2.6 mmol/L) as optimal - danger: physicians might interpret it as a target - could cause medicalization of a substantial part of the population.**

# Future US guidelines - ATP IV vs. ATP III

- Stronger emphasis on evidence from clinical trials
- Clinical trials will be identified by rigorous systematic review process (study eligibility criteria will be identified; literature will be searched and all eligible studies identified; studies will be quality rated; evidence tables will be developed for each study; evidence will be summarized and graded by Panel; recommendations will be developed and graded by Panel)
- Only a limited use of expert opinion
- Focus on LDL-C
- Greatest intensity of treatment for patients at highest risk



# Future US guidelines - NHLBI's change in approach to the development of cardiovascular prevention guidelines

- The NHLBI will continue as an active partner in the evidence review required for the development of the CPGs for Hyperlipidemia, Hypertension, Cardiovascular Risk Assessment, Cardiovascular Lifestyle Interventions, and Obesity.
- The NHLBI has asked the **American Heart Association (AHA)** and **the American College of Cardiology (ACC)** to assume joint management responsibility for the CPG development process for these documents going forward.
- The AHA and the ACC are pleased to assume leadership for the CPG development process and look forward to continuing this in collaboration with other stakeholder organizations.

Gibbons GH et al. Circulation 2013; published online Aug 8

# Future development in Europe

- **At the ESC congress in Amsterdam, August 31 – September 4, new ESH/ESC Guidelines for the management of arterial hypertension (version 2013) and new ESC/EASD Guidelines on diabetes, pre-diabetes and CVD diseases (version 2013) were published**
- **The Task force for the new ESC/EAS guidelines for the management of dyslipidaemias will start working on new guidelines before the end of 2013 and they will be published in 2016**

# **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!**