Epidemiology and Control of Cardiovascular Disease

Jaroslav Kotulán

History

In the 19th century, infectious diseases dominated the public health scene

In the 20th century, CVD have come to overshadow all others as a cause of death in industrialized populations

Causes - decline in major infectious diseases
- increase in the incidence rates of CVD (absolute as well as relative)
→ changes in lifestyle, origin in social and economic development

Cardiovascular diseases (CVD)

five main conditions:

- hypertension
- atherosclerosis
- cardiovascular heart disease (CHD)
  - myocardial infarction (heart attack)
  - angina pectoris
- stroke
- heart failure

Other important vascular conditions (less frequent): atherosclerotic peripheral arterial disease, aortic aneurysm, cardiomyopathies, rheumatic heart disease, congenital heart disease, deep vein thrombosis, pulmonary embolism etc.

Two main categories of CVD

1. **Coronary disease - the main cause of the death. Related to affluence (not inevitably)**

2. **Strokes - also kill, but mainly cause chronic disability their incidence largely reflects hypertension**

CHD and stroke have been the first and second leading causes worldwide since 1990 and are two major contributors to disability worldwide

They have been under extensive epidemiologic investigations over the past half-century. As a result, understanding of the causes of and means to prevent CHD and stroke have become well established

Epidemiologic Methods in Cardiovascular Diseases

Examples of studies:

Population surveys (cross-sectional surveys)

The **INTERSALT Study** demonstrated association between the slope of increasing blood pressure with age and urinary electrolyte excretion in adults among 52 study centers in 32 countries (1986)

The case-control study

WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception (1996).

Increased risk of venous thromboebolism, CHD and stroke
- rises with other risk factors, smoking etc.
- rises with age
- differences among different preparations.

Cohort studies

The Framingam Heart Study is a long-term, ongoing cardiovascular study on residents of the US town of Framingham (Ma).

Goal: to identify the common factors that contribute to CVD by following its development over long of time in a large group of participants.

The study began in 1948 with 5,209 adult subjects from Framingham, and is now on its third generation of participants

The intensive biennial examination schedule (physical characteristics, life conditions) over its decades-long history have made this a uniquely rich source of data on individual risks of CVD events.

Prior to it almost nothing was known about the epidemiology of hypertensive or arteriosclerotic cardiovascular disease.

A landmark report of the Framinham Study, based on the first 6 years of follow-up, identified serum cholesterol concentration, blood pressure, and electrocardiographic evidence of left ventricular hypertrophy as predictors of CHD development

Much of the now-common knowledge concerning heart disease, such as the effects of diet, exercise, and common medications such as aspirin, is based on this longitudinal study.

It was in this report that the Framingham Study investigators introduced the term “risk factor” to describe such predictive characteristics.

Many other studies were performed in U.S and Europe with designs and methods similar to those of the Framingam Study.

Epidemiological Features of CVD

- CVD is pervasive throughout the world recognized as a public health problem of global importance, not only of rich, but also of low- and middle-income countries

- Atherosclerosis: Early life-onset and lifelong progression
  → prevention required as early as childhood and adolescence

- A strong age gradient in degree of atherosclerosis:
  from a range of 0-25 percent of initial surface involvement with fibrous plaques at age 20, the percentage approximately doubled by age 30 and continued to increase, although less steeply, to later ages at death

Mortality, morbidity

Of an estimated 58 million deaths globally from all causes in 2005, cardiovascular disease (CVD) accounted for 30%.

A substantial proportion of these deaths (46%) were of people under 70 years of age, in the more productive period of life.

A significant proportion of this morbidity and mortality could be prevented.

Basic documents

WHO: **Global Strategy for the Prevention and Control of Noncommunicable Diseases (2000).**

Convention on Tobacco Control, Global Strategy for Diet, Physical Activity and Health

These activities target common risk factors that are shared by CVD, cancer, diabetes and chronic respiratory disease

CVD Mortality Rate - MALES

Nr	State	Year	Mort, *)
1	France	2004	190,6
2	Spain	2004	210,8
3	Switzerland	2004	216,0
4	Iceland	2005	220,4
5	Netherlands	2004	252,7
6	Norway	2004	254,7
7	Portugal	2004	271,1
8	Luxembourg	2005	271,6
9	Ireland	2005	277,3
10	Sweden	2004	277,6
11	Italy	2001	280,0
12	United Kingdom	2004	280,1
13	Austria	2005	287,3
14	Germany	2004	315,2
15	Malta	2005	317,5
16	Finland	2005	321,1
17	Greece	2005	321,3
18	Denmark	2001	321,4
19	Slovenia	2005	360,4
20	Poland	2005	492,8
21	Czechia	2005	508,1
22	Croatia	2005	525,8
23	Slovakia	2005	634,9
24	Hungary	2005	643,9
25	Estonia	2005	692,0
26	Lithuania	2005	750,5
27	Romania	2004	762,0
28	Latvia	2005	804,2
29	Bulgaria	2004	840,5
30	Belarus	2005	995,7
31	Ukraine	2005	1094,1
32	Russia	2005	1145,1

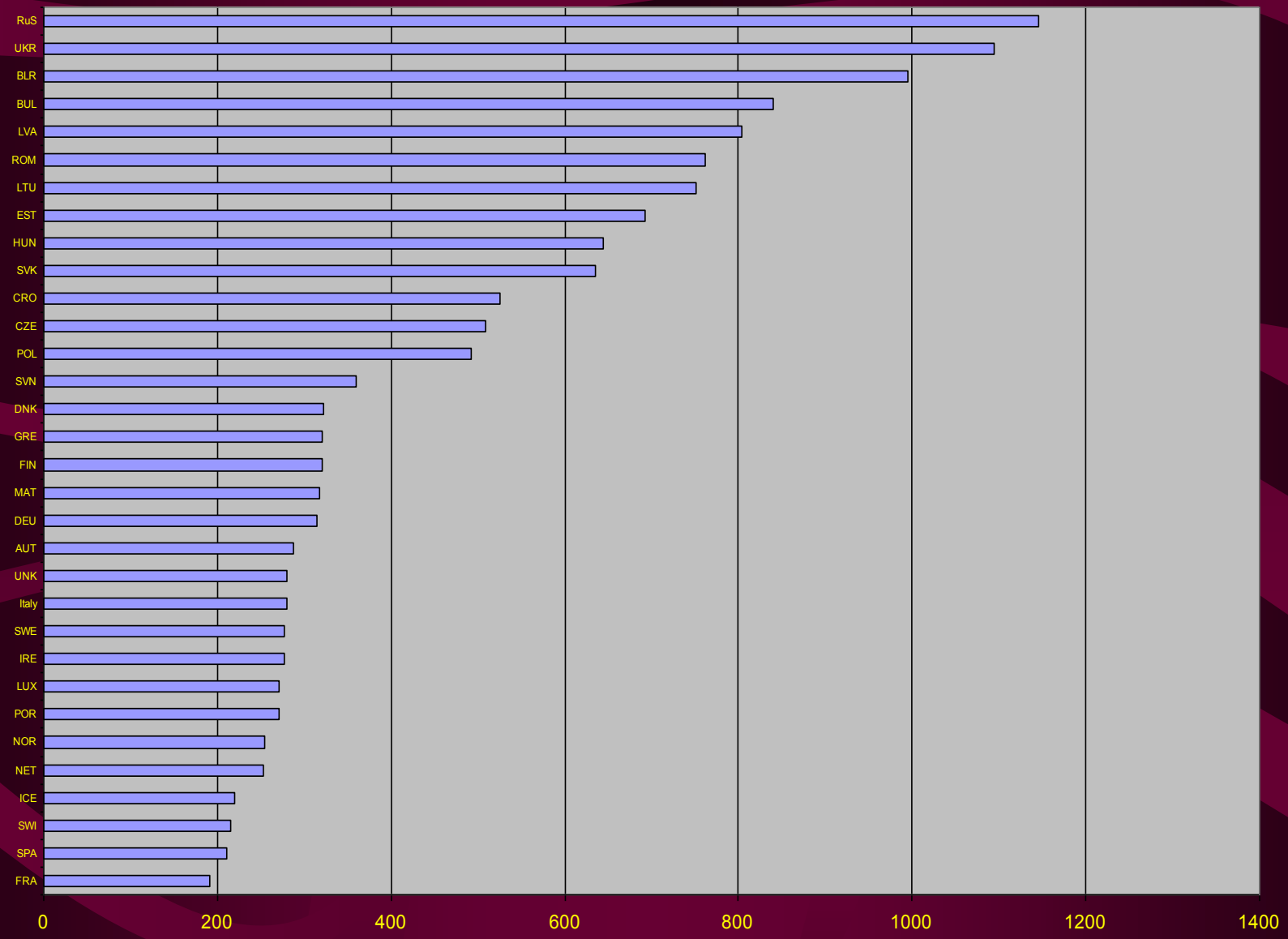
***) Standardized mortality rates per 100 000 European standard population**

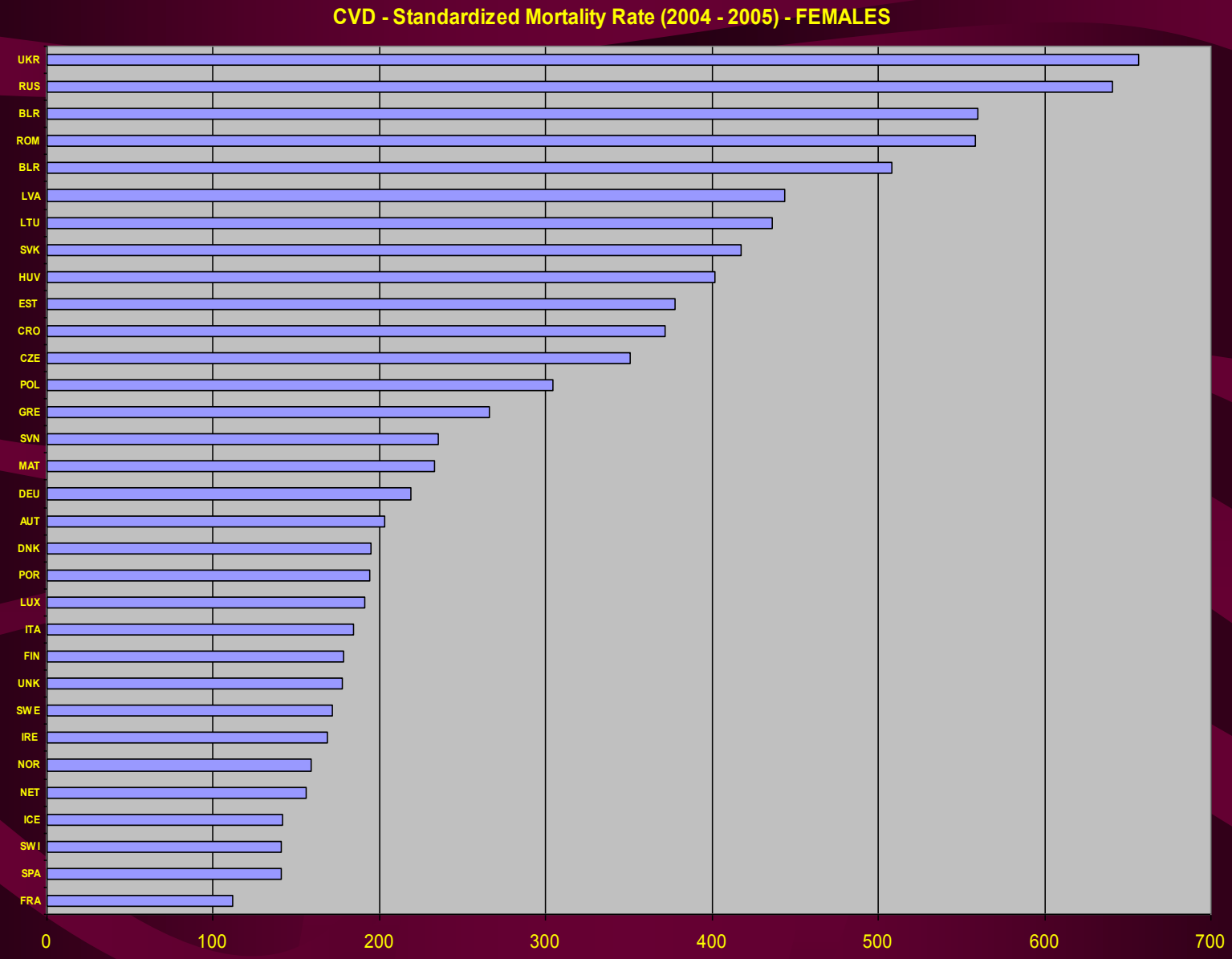
CVD Mortality Rate - FEMALES

Nr	State	Year	Mort, *)
1	France	2004	111,5
2	Spain	2004	140,9
3	Switzerland	2004	141,1
4	Iceland	2005	141,6
5	Netherlands	2004	155,8
6	Norway	2004	159,2
7	Ireland	2005	168,3
8	Sweden	2004	171,7
9	United Kingdom	2004	177,4
10	Finland	2005	178,0
11	Italy	2001	184,0
12	Luxembourg	2005	191,4
13	Portugal	2004	194,1
14	Denmark	2001	195,0
15	Austria	2005	203,0
16	Germany	2004	218,6
17	Malta	2005	232,9
18	Slovenia	2005	235,1
19	Greece	2005	265,7
20	Poland	2005	304,1
21	Czechia	2005	351,1
22	Croatia	2005	371,7
23	Estonia	2005	377,4
24	Hungary	2005	401,4
25	Slovakia	2005	417,5
26	Lithuania	2005	436,1
27	Latvia	2004	443,7
28	Belarus	2005	508,5
29	Romania	2004	558,1
30	Bulgaria	2004	560,0
31	Russia	2005	640,5
32	Ukraine	2005	656,3

***) Standardized mortality rates per 100 000 European standard population**

CVD - Standardized Mortality Rate (2004 - 2005) - MALES




CVD - Standardized Mortality Rate (2004 - 2005) - FEMALES
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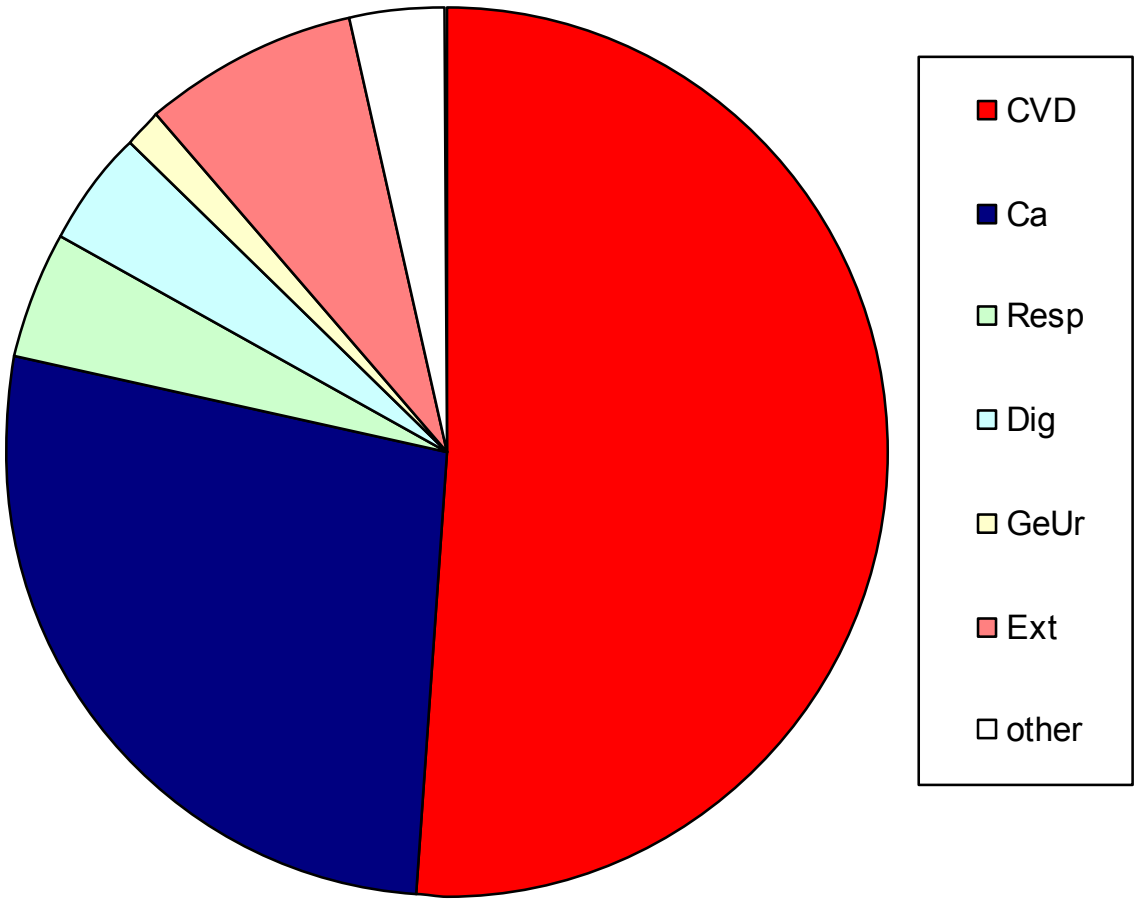
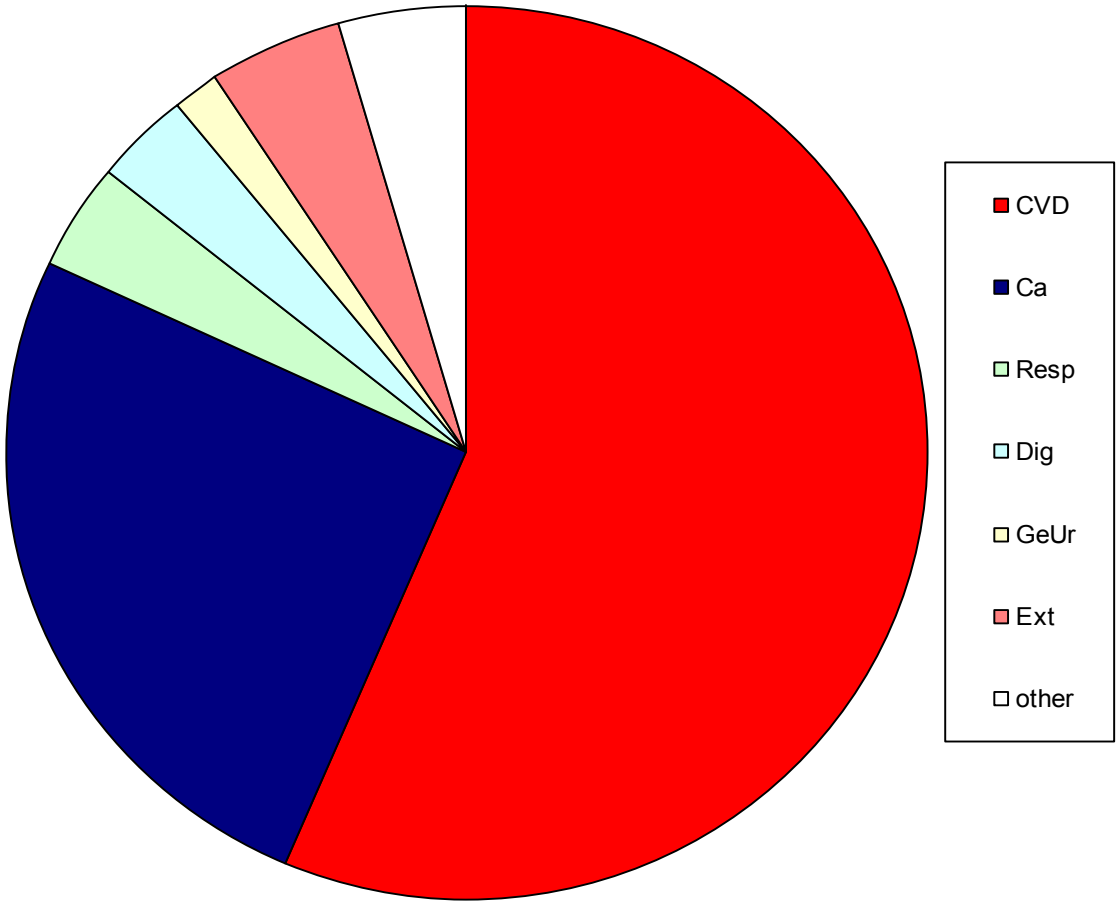
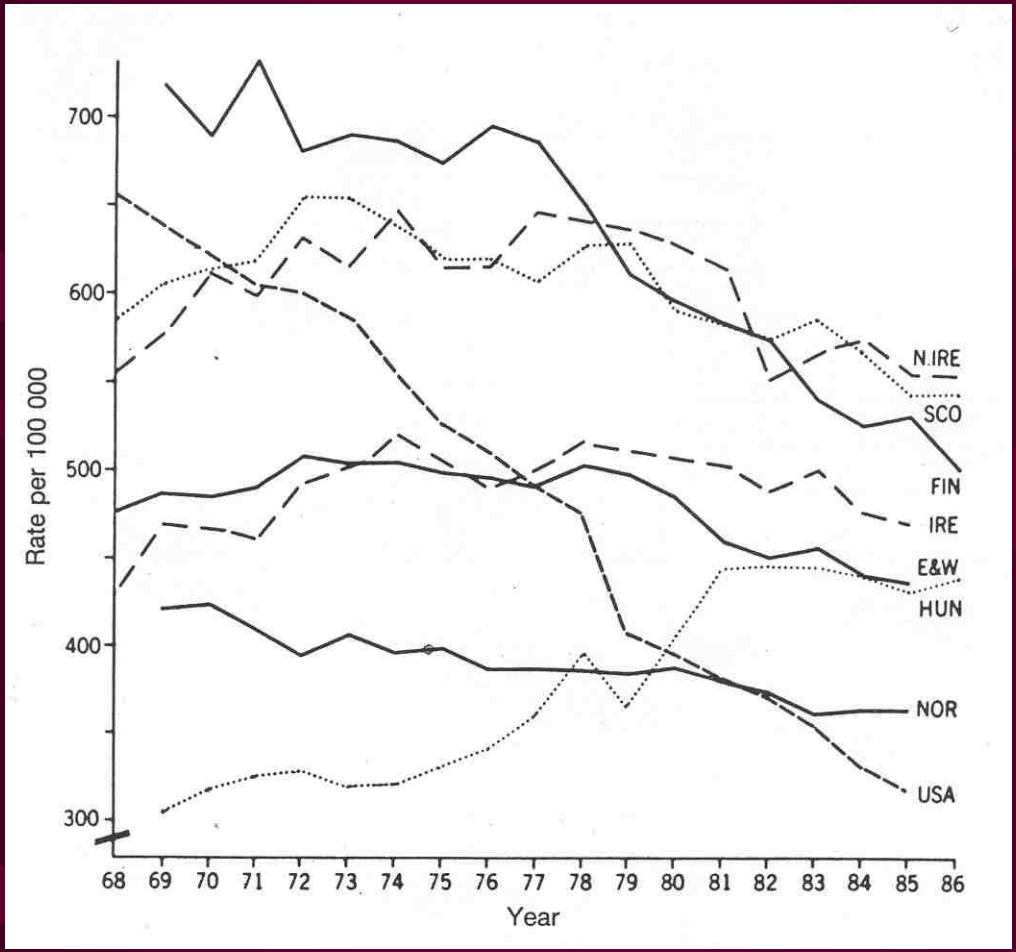
Standardized mortality rate by causes (MALES, ČR, 1999)



Standardized mortality rate by causes (FEMALES, ČR, 1999)



CVD age-adjusted mortality (men aged 40-69 years)



CORONARY HEART DISEASE (ischaemic heart disease)

In western countries responsible for
about 30 per cent of deaths in men
25 per cent death in women
= 3/4 of all CV deaths

All-ages case fatality is much higher in women than in men

Most men in western populations develop ischaemic myocardial scarring
perhaps only 10 % will escape significant atherosclerosis

Distribution in the world

Association with the affluence is no longer apparent

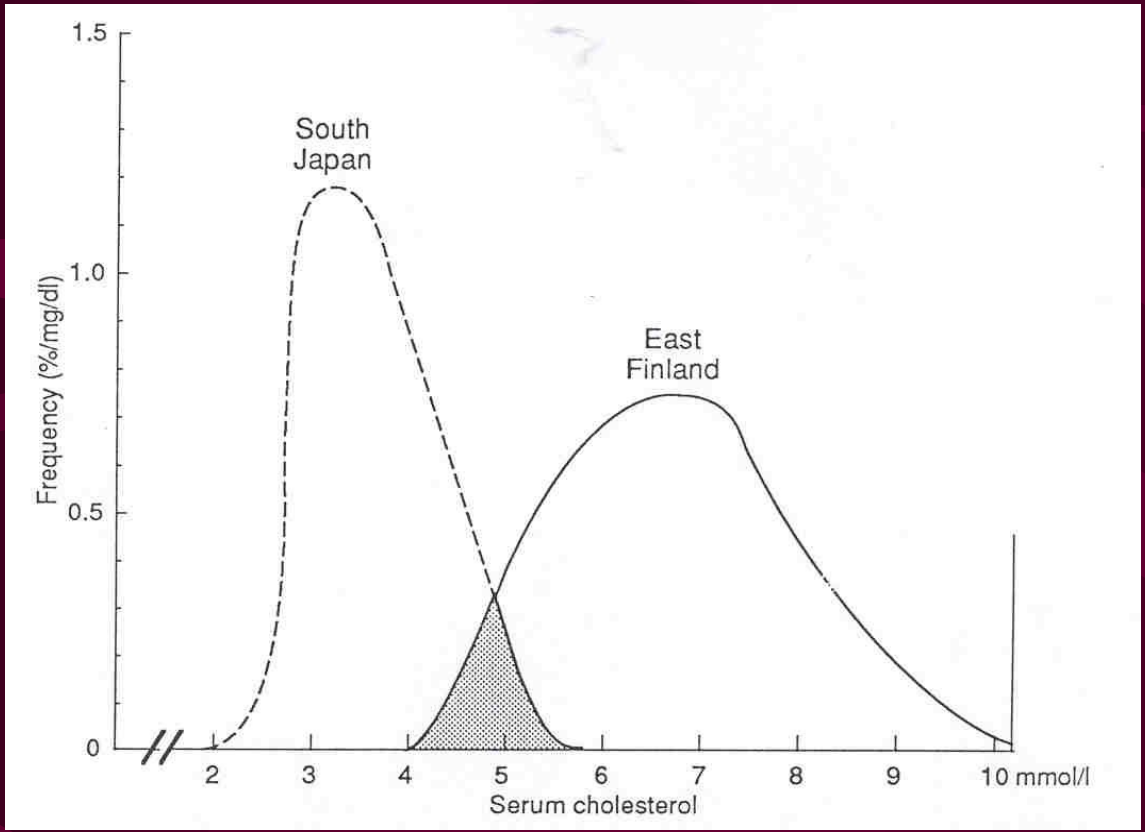
Japan is heavily industrialized but rates are low and are actually falling

North Karelia in Finland had until recently the highest rates in the world
strenuous rural life is an insufficient protection

International differences can be explained partly by differences in the major risk factors

but there are many exceptions

Distribution of cholesterol levels in Japan and Finland



Time trends

Coronary heart disease (CHD) is not new, is known as early as in the antiquity
new is its occurrence as a mass disease

The epidemic began at different times in different countries
rates started to rise in the early 1920s in the US
a few years later in the UK

but in the Netherlands and Norway there was no major rise until 1950
still later in Eastern Europe

In the US the plateau has been reached in the 1960s
around 1968, there began a steady decline in coronary mortality

amounting by 1985 to 40 per cent fall

Substantial declines in coronary mortality are also **occurring elsewhere**:
Canada, Austria, New Zealand, Belgium, The Netherlands, Scandinavia etc.
since 1990 also in the CR

Aetiology

The main determinants of population incidence are now known but much remains unknown concerning individual susceptibility

= rates can be predicted much better then cases

Concepts of prevention

Two broad approaches – the individual (or high-risk) approach and the population-wide approach. These two approaches are complementary

The North Carelia Project - a great example of intervention studies, with broad implications for prevention policy.

Finish men experienced exceptionally high CHD mortality that had increased sharply in the 1950s

Concern about this led to implementation in 1972 of a multifaceted community-based prevention project in which North Carelia (population 210,000) and Kuopio (population 250,000), both in Eastern Finland, would be intervention and control communities, respectively.

Among the many components of the project were programs targeting high blood cholesterol concentration, high blood pressure, and smoking. Extensive community involvement and engagement with health services were major aspects of these programs.

Twenty-year changes in risk factors for men included reductions in cholesterol concentrations by 13% and in diastolic blood pressure by 9%, while smoking decreased from 53 to 37%.

Observed decrease in mortality: by 68% for women and 55% for men.

The project began to influence policy nationwide after its first five years. The mortality change in Finland as a whole has continued to the present

North Karelia Project is a powerful demonstration of the potential for an integrated, coordinated, and sustained public health effort to affect the major cardiovascular conditions of our time, CHD and stroke.

Deteminants, risk factors:

- Unmodifiable: Age, sex, race or ethnicity, and heredity
- Modifiable: dietary inbalance
  - unfavorable macronutrient composition:
    types and amounts of animal fats (especially saturated), relative to fruits, vegetables, and legumes
  - excessive sodium intake
  - excessive energy intake relative to energy expenditure.

Physical inactivity:

= reduced physical work (locomotion, occupation, leisure time)

- failure of matching energy expenditure with energy intake
- numerous biological mechanisms related to cardiac metabolism and physiology

Dietary imbalance contributes directly to the development of adverse blood lipid profiles (high concentration of LDL-cholesterol

Smoking of tobacco: established major risk factor for CVD and for other chronic diseases

Prevention: New guidelines (WHO) (two publications)

Prevention of Cardiovascular Disease

Guidelines for assessment and management of cardiovascular risk

World Health Organization, Geneva 2007, 92 pp.

Prevention of Cardiovascular Disease

Pocket Guidelines for Assessment and Management of Cardiovascular Risk, Europe.

(WHO/ISH Cardiovascular Risk Prediction Charts for the European Region)

IHS = International Society of Hypertension

World Health Organization, Geneva 2007, 20 pp.

Edited for 14 regions of the world)

http://www.who.int/bookorders/

CVD prevention: Basis of recommendations

(the best available evidence)

1. Modification of behaviour
   - 1.1 Tobacco
   - 1.2 Diet
   - 1.3 Physical activity
   - 1.4 Body weight
   - 1.5 Alcohol
2. Multiple risk factor interventions
3. Blood pressure lowering
4. Lipid lowering
5. Control of glycaemia
6. Aspirin therapy

Tobacco

There is a large body of evidence regarding the beneficial effect of smoking cessation on coronary heart disease mortality

The age of quitting has a major impact on survival prospects;

those who quit between 35 and 44 years of age had the same survival rates as those who had never smoked

Recent evidence from the Interheart study has highlighted the adverse effects of use of any tobacco product and, importantly, the harm caused by even very low consumption (1–5 cigarettes a day).

Passive cigarette smoking produces a small increase in cardio vascular risk.

Bans on advertising of tobacco products in public places and on sales of tobacco to young people are essential components of any primary prevention programme

Also ban on smoking in restaurants etc.

Diet

Saturated fats as a whole have been shown to raise LDL-cholesterol levels

Saturated fatty acids: (palmitic $C_{16:0}$, stearic $C_{18:0}$, myristic $C_{14:0}$)

Monounsaturated acids (oleic a. C18:1) (abundant in olive oil)
and polyunsaturated acids
n-6 (omega 6) – (double bond at the sixth carbon atom of the end CH_3)
linoleic $C_{18:2}$, arachidonic $C_{20:4}$,
(abundant in soybean and sunflower oil)
They lower total cholesterol, LDL cholesterol and triglyceride concentrations

n-3 (omega 3) polyunsaturated acids
linolenic $C_{18:3}$, eicosapentaenoic $C_{20:5}$ (EPA), docosahexaenoic $C_{22:6}$ (DHA)
The main dietary sources: fish and fish oils
Significant benefit on cardiovascular morbidity and mortality
in patients with coronary heart disease

We need both n-6 an n-3: production of two types of prostaglandins and leukotrienes (= tisue hormones)

Diet (continued)

Trans-fatty acids (margarine) increase LDL-cholesterol and, at high intakes, lower HDL cholesterol and increase the risk of coronary heart disease

Current guidelines recommend a diet that provides less than

30% of calories from dietary fat, less than 10% of calories from saturated fats,

up to 10% from polyunsaturated fats, and about 15% from monounsaturated fats

Dietary cholesterol seems to have a relatively small effect on serum lipids, compared with dietary saturated and trans-fatty acids

Reducing or modifying dietary fat reduces the incidence of combined cardiovascular events by 16% and cardiovascular mortality by 9%

Diet (continued)

Dietary sodium

High salt intake is associated with an increased risk of high blood pressure

Within the daily intake range of 3 to 12 g, the lower the salt intake achieved, the lower the blood pressure

Recommendations on salt intake: < 5 g (90 mmol) per day

Fruits and vegetables

may promote cardiovascular health through a variety of micronutrients, antioxidants, phytochemicals, flavonoids, fibre and potassium

On the basis of the available evidence, a daily intake of at least 400 g of fruit and vegetables is recommended

Physical activity

The evidence points to the benefit of continued regular moderate physical activity

Physical activity improves endothelial function, which enhances vasodilatation and vasomotor function in the blood vessels. In addition, physical activity contributes to weight loss, glycaemic control, improved blood pressure, lipid profile and insulin sensitivity

Body weight

Relationship between overweight or obesity and cardiovascular morbidity, CVD mortality and total mortality

Obesity is strongly related to major cardiovascular risk factors, such as raised blood pressure, glucose intolerance, type 2 diabetes, and dyslipidaemia.

Significant weight loss: reduces total cholesterol and LDL-cholesterol, increases HDL-cholesterol, improves control of blood pressure and diabetes

The ideal weight : BMI > 25 kg/m^2

Alcohol

Many studies have shown a U- or J-shaped association between mortality and alcohol consumption

A recent meta-analysis of 54 published studies: there is no level of alcohol consumption that is beneficial with respect to coronary heart disease

From both the public health and clinical viewpoints, there is no merit in promoting alcohol consumption as a preventive strategy.

Blood pressure lowering

Almost all clinical trials have confirmed the benefits of antihypertensive treatment at blood pressure levels of 160 mmHg (systolic) and 100 mmHg (diastolic) and above

Diuretics, beta-blockers, and calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors

For the endpoint of total cardio vascular mortality, the meta-analyses showed no strong evidence of differences between drug classes

The Hypertension Optimal Treatment (HOT) trial found maximal cardiovascular benefit when blood pressure was reduced to 139/83 mmHg

Lipid lowering

The effectiveness of statins in patients with established atherosclerotic disease (principally coronary artery disease) is well established

Risks

- **From 1987 to 2000 in the USA 30 cases of liver failure attributable to statins – about one per million person-years of use**
- **Few haemorrhagic strokes were observed in the randomized trials (only people with a very low cholesterol concentration)**

There are currently no data to suggest the superiority of one statin over others in reducing cardiovascular events

Control of glycaemia

The risk of cardiovascular events is 2–3 times higher in people with type 1 or type 2 diabetes

Treatment should aim to achieve:

- **a fasting blood glucose level of 4–7 mmol/l (72–126 mg/dl);**
- **an HbA1c level of 6.5% or less**
  =glycosylated haemoglobin

Aspirin therapy

In randomised controlled trials and meta-analyses aspirin was associated with a 32% reduction in myocardial infarction

Risks: Aspirin roughly doubles the risk of gastrointestinal haemorrhage. The excess risks attributable to aspirin are 1–2 per 1000 per year at age 60 and 7 per1000 per year at age 80

The balance of benefit and risk, therefore, needs to be clearly defined before aspirin can recommended for all elderly people

Two strategies of control

Their contributions are complementary, each is necessary

1 **1. "High risk strategy"** - screening for early disease

- A simple screening examination:

a self-administered chest pain questionnaire and electrocardiogram
can give warning of about a half of all the coronary deaths in the next 5 years
but – psychological trauma of „labelling"

Some of the main predictors of CHD can be readily identified by screening:

- **family history**
- **smoking history**
- **blood pressure**
- **serum (total) cholesterol**

(If these are known, measures of overweight do not improve the prediction.)

The value of high risk strategy for CHD prevention is limited

it concentrates preventive efforts on the small fraction of persons with highest risk
more important fraction is the large group of people where the individual risk is lower
most cases of CHD occur in this large low-risk group

Resources and organization for effective advice and follow-up is necessary
if not, the risk screening is worse than useless

2. Mass primary prevention

Primary prevention depends on mass changes – on normalizing averages
goal: not to have centred around some „ideal“ value
but to lower the whole distribution
individual variation is inevitable

Targets for population norms are thus defined in terms of desirable average values of risk factors not in desirable individual values

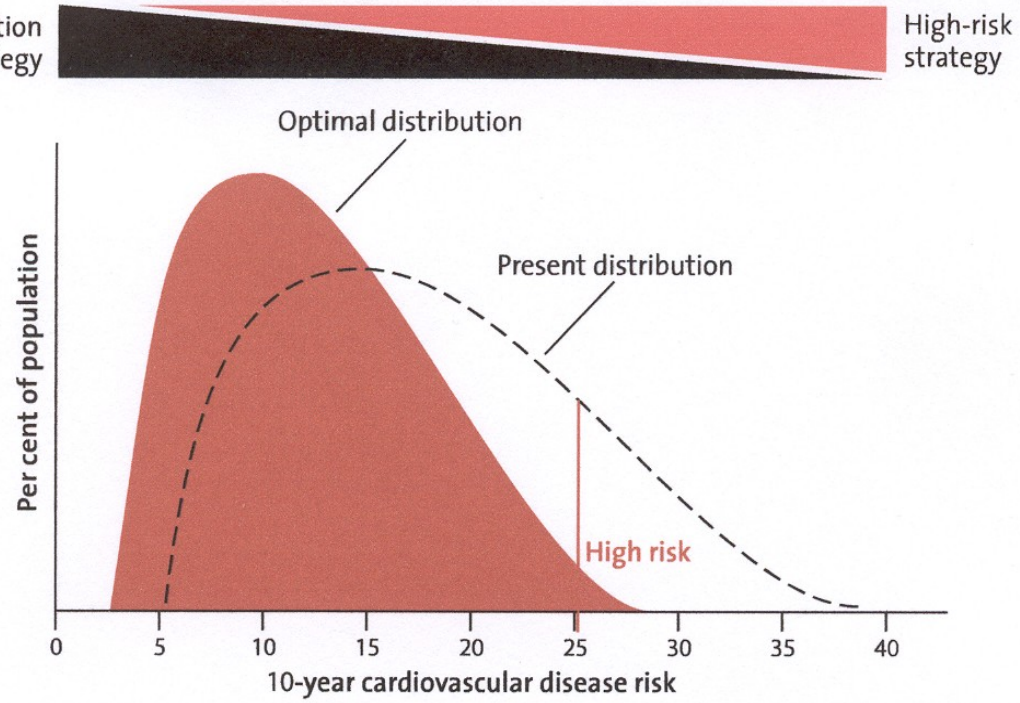


FIGURE 1

A combination of population-wide and high-risk strategies are required to reduce the cardiovascular disease risk distribution of the population (to shift the cardiovascular risk distribution to the left)
source: ref. 11

Health education – changing the behaviour
It needs a major effort of opinion formers, health professionals, community leaders, and local and national government

Recommendations of the Second Joint Task Force of European Societies on Coronary Prevention (2001)

- Stop smoking
- Make healthy food choices
- Be physically active
- Achieve ideal weight
- Achieve blood pressure <140/90

  total cholesterol < 5.0 mmol/l (190 mg/dl)

  LDL cholesterol < 3.0 mmol/l (115 mg/dl)

  when not achieved by lifestyle changes, lowering drug therapies should be used
- Aspirin (75 mg) at high CHD risk

The World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction charts

Two categories of people:

- **1.People with risk factors who had not yet developed clinically manifest cardiovascular disease (primary prevention)**
- **2. People with established CHD, CeVD or peripheral vascular disease (secondary prevention)**

The charts enable the estimation of total cardiovascular risk of people in the first category

The evidence-based recommendations

People in the second category have high cardiovascular risk and need intensive lifestyle interventions and appropriate drug therapy.
Risk stratification is not required in them.

Total CVD risk - the probability of an individual's experiencing a CVD event (e.g. myocardial infarction or stroke) over a given period of time, for example 10 years (= „10-year risk")

WHO Risk Prediction Chart

Recommendations for prevention of cardiovascular disease in people with cardiovascular risk factors (according to individual total risk) [a]

Risk <10%	Individuals in this category are at low risk. Conservative management focusing on lifestyle interventions is suggested[b]
Risk 10% to <20%	Individuals in this category are at moderate risk of fatal or non-fatal vascular events. Monitor risk profile every 6–12 months.
Risk 20% to <30%	Individuals in this category are at high risk of fatal or non-fatal vascular events. Monitor risk profile every 3–6 months
Risk ≥30%	Individuals in this category are at very high risk of fatal or non-fatal vascular events. Monitor risk profile every 3–6 months

[a] Excluding people with established CHD, CeVD and peripheral vascular disease

[b] Policy measures that create conducive environments for quitting tobacco, engaging in physical activity and consuming healthy diets are necessary to promote behavioural change. They will benefit the whole population.

SMOKING CESSATION	
All nonsmokers should be encouraged not to start smoking. All smokers should be strongly encouraged to quit smoking by a health professional and supported in their efforts to do so. (1++, A) It is suggested that those who use other forms of tobacco be advised to stop. (2+, C)	
Risk 20% to <30%	Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counselling. (1++, B)
Risk ≥30%	Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counselling. (1++, B)

Note: 1++ and the like. … levels of evidence; A, B, etc. … grades of recommendations

DIETARY CHANGES

All individuals should be strongly encouraged to reduce total fat and saturated fat intake. (1+, A)

Total fat intake should be reduced to about 30% of calories, saturated fat to less than 10% of calories, transfatty acids intake should be reduced as much as possible or eliminated and most dietary fat should be polyunsaturated (up to 10% of calories) or monounsaturated (10–15% of calories). (1+, A)

All individuals should be strongly encouraged to reduce daily salt intake by at least one third and, if possible, to <5 g or <90 mmol per day. (1+, A)

All individuals should be encouraged to eat at least 400 g a day of a range of fruits and vegetables as well as whole grains and pulses. (2+, A)

PHYSICAL ACTIVITY

All individuals should be strongly encouraged to take at least 30 minutes of moderate physical activity (e.g. brisk walking) a day, through leisure time, daily tasks and work-related physical activity. (1+, A)

WEIGHT CONTROL

All individuals who are overweight or obese should be encouraged to lose weight through a combination of a reduced-energy diet (dietary advice) and increased physical activity. (1+, A)

ALCOHOL INTAKE

Individuals who take more than 3 units of alcohol[c] per day should be advised to reduce alcohol consumption. (2++, B)

[c] One unit (drink) = half pint of beer/lager (5 % alcohol), 100 ml of wine (10 % alcohol), 25 ml spirits (40% alcohol)

BLOOD PRESSURE

Risk 10% to <20%	Individuals with persistent blood pressure ≥140/90 mmHg[e] should continue lifestyle strategies to lower blood pressure and have their blood pressure and total cardiovascular risk reassessed annually depending on clinical circumstances and resource availability.
Risk 20% to <30%	Individuals with persistent blood pressure ≥140/90 mmHg[e] who are unable to lower blood pressure through lifestyle strategies with professional assistance within 4–6 months should be considered for one of the following drugs to reduce blood pressure and risk of cardiovascular disease: thiazide-like diuretic, ACE inhibitor, calcium channel blocker, beta-blockerd. A low-dose thiazide-like diuretic, ACE inhibitor or calcium channel blocker is recommended as firstline therapy. (1++, A)
Risk ≥30%	Individuals with persistent blood pressure ≥130/80 mmHg should be given one of the following drugs to reduce blood pressure and risk of cardiovascular disease: thiazide-like diuretic, ACE inhibitor, calcium channel blocker, betablocker[d]. A low-dose thiazide-like diuretic, ACE inhibitor or calcium channel blocker is recommended as firstline therapy. (1++, A)

[d] Evidence from two recent meta-analyses indicates that for treatment of hypertension, beta-blockers are inferior to calcium-channel blockers and ACE inhibitors in reducing the frequency of hard endpoints.

[e] Reducing blood pressure by 10–15/5–8 mmHg with drug treatment reduces combined CVD mortality and morbidity by about one-third, whatever the pretreatment absolute risk.

LIPID-LOWERING DRUGS (STATINS)

All individuals with total cholesterol at or above 8 mmol/l (320 mg/dl) should be advised to follow a lipid-lowering diet and given a statin to lower the risk of cardiovascular disease. (2++, B)

All other individuals need to be managed according to the cardiovascular risk as follows
(10 year risk of cardiovascular event <10%, 10 to <20%, 20 to 30%, ≥30%)

Risk <10%	Should be advised to follow a lipid-lowering diet[g]
10 to <20%	Should be advised to follow a lipid-lowering diet[g]
Risk 20 to <30%	Adults >40 years with persistently high serum cholesterol (>5.0 mmol/l) and/or LDL cholesterol >3.0 mmol/l, despite a lipid-lowering diet, should be given a statin. (1+, A)
Risk ≥30%	Individuals in this risk category should be advised to follow a lipid-lowering diet and given a statin. (1++, A) Serum cholesterol should be reduced to less than 5.0 mmol/l (LDL cholesterol to below 3.0 mmol/l) or by 25% (30% for LDL cholesterol), whichever is greater[f].

HYPOGLYCAEMIC DRUGS

Individuals with persistent fasting blood glucose >6 mmol/l despote diet control should be given metformin. (1+, A)

f Reducing cholesterol level by 20% (approximately 1 mmol/l) with statin treatment would be expected to yield a coronary heart disease mortality benefit of 30%, whatever the pretreatment absolute risk. However, applying this to the general population may not be cost effective. It will lead to a large proportion of the adult population receiving statins. Even in some high-resource settings, current practice is to recommend drugs for this group only if serum cholesterol is above 8mmol/l (320 mg/dl).

g There are no clinical trials that have evaluated the absolute and relative benefits of cholesterol lowering to different cholesterol targets in relation to clinical events.


THANK YOU
FOR YOUR
ATTENTION