Should cardiovascular disease prevention be undertaken by doctors or policymakers and politicians?

David A. Wood, MSc, FRCPE, FFPHM, FESC; Kornelia Kotseva, MD, PhD, FESC

Cardiovascular Medicine - National Heart and Lung Institute (NHLI) - Imperial College London - London - UK

The World Health Organization (WHO) report on Prevention of Cardiovascular Disease (CVD) describes three strategies for prevention: a population strategy, a high-risk strategy, and a secondary prevention strategy. The population strategy is paramount because it addresses the whole population the economic, social, and cultural determinants of CVD, whereas the high-risk and secondary prevention strategies only address a minority of the population, namely, high-risk and sick individuals. The 61st World Health Assembly of the WHO on May 24th, 2008, stated its implementation strategy for prevention and control of noncommunicable diseases, of which CVD is the most common. The foundation for this action plan is the global strategy for the prevention and control of noncommunicable diseases reaffirmed by the Health Assembly in 2000, the WHO Framework Convention on Tobacco Control in 2003, and the Global Strategy on Diet, Physical Activity, and Health in 2004. The plan is intended to support coordinated, comprehensive, and integrated implementation of strategies and evidence-based interventions across individual diseases and risk factors, especially at the national level. A societal approach—health in all policies—by policymakers and politicians is paramount to preventing CVD.

Keywords: cardiovascular disease; prevention; strategy; risk estimation; clinical practice

Address for correspondence: Prof David A. Wood, Cardiovascular Medicine, National Heart and Lung Institute (NHLI), Imperial College London, Charing Cross Campus, Fulham Palace Road, London W6 8RF, UK (e-mail: d.wood@imperial.ac.uk)

Dialogues Cardiovasc Med. 2009;14:83-98

The World Health Organization report on Prevention of Cardiovascular Disease (CVD) describes three strategies for prevention: a population strategy, a high-risk strategy, and a secondary prevention strategy.[1,2] The three strategies complement each other. However, the population strategy is paramount. The fundamental difference between these three strategies is that the population strategy addresses the whole population, whereas the high-risk and secondary prevention strategies only address a minority of the population, namely, high-risk and sick individuals. So the population strategy for prevention of CVD—not just coronary artery disease, but stroke and other atherosclerotic diseases—addresses all the causes in the whole population. The more successful this all-encompassing strategy is, the more it will favorably impact on the need for the other two clinical strategies by reducing the proportion of high-risk individuals in the population, and the number of new cases of symptomatic atherosclerotic disease. The high-risk strategy

SELECTED ABBREVIATIONS AND ACRONYMS

BMI	body mass index
CHD	coronary heart disease
CVD	cardiovascular disease
EUROASPIRE	EUROpean Action on Secondary and Primary prevention by Intervention to Reduce Events
PREVESE	PREVEnción Secundaria del infarto de miocardio en España
SCORE	Systematic Coronary Risk Estimation
TASPIC-CRO	Treatment And Secondary Prevention of Ischemic Coronary Events in Croatia

identifies those asymptomatic individuals who are apparently well, but at high multifactorial risk of developing CVD, with the object of reducing their total CVD risk through lifestyle, risk factor, and therapeutic management. However, its overall impact on the burden of disease is limited because it only targets high-risk individuals, who are a minority of the population. The secondary prevention strategy addresses those who've survived the development of symptomatic atherosclerotic disease—acute coronary syndromes, angina, stroke, transient cerebral ischemia, peripheral arterial disease—with the object of reducing the risk of recurrent cardiovascular events and improving quality of life and life expectancy. However, it also targets only a minority of sick individuals and is necessarily limited to survivors. For some, the first manifestation of CVD is sudden collapse and death from acute myocardial ischemia inducing fatal ventricular arrhythmias or massive cerebral infarction or ruptured aortic aneurysm. In addition, among those who survive the initial ischemic insult, consequent tissue damage may be so great that secondary prevention offers little gain. Prognosis is largely determined by the scale of myocardial or cerebral damage.

So a population strategy tackling the major social, economic, and cultural determinants of CVD at a societal level is paramount, and without such a strategy these diseases will remain a major cause of ill health and premature death, regardless of the evidence that high-risk and secondary prevention strategies directed at individuals do reduce cardiovascular morbidity and mortality.

POPULATION STRATEGY

The 61st World Health Assembly of the WHO announced on May 24th, 2008, its implementation strategy for prevention and control of noncommunicable diseases—CVD, cancer, chronic obstructive pulmonary disease, and diabetes—of which CVD is the most common. The report noted the rapid rise of noncommunicable diseases, which represents one of the major health challenges to global development, threatening economic and social development and the lives and health of millions of people. Using current trends, it estimates that by 2020 these diseases will account for 73% of deaths, and 60% of the disease burden worldwide. Low- and middle-income countries will suffer the greatest impact of noncommunicable diseases, and the rapid increase is seen disproportionately in poor and disadvantaged populations and is contributing to widening health gaps within and between countries. However, the major causes of these diseases are tobacco use, unhealthy diet, and physical inactivity, which in turn impact adversely on body weight and its distribution, blood pressure, lipids, and diabetes. The major causes of CVD are preventable.

The foundation for this action plan is the global strategy for the prevention and control of noncommunicable diseases reaffirmed by the Health Assembly in 2000.[3] It also builds on the WHO Framework Convention on Tobacco Control adopted by the Health Assembly in 2003,[4] and the Global Strategy on Diet, Physical Activity, and Health, endorsed by the Health Assembly in 2004[5] and the strategies to reduce public health problems caused by harmful use of alcohol. The plan is intended to support coordinated, comprehensive, and integrated implementation of strategies and evidence-based interventions across individual diseases and risk factors, especially at the national level. The plan has six objectives:

1. To raise the priority accorded to noncommunicable disease, and to integrate prevention and control of such diseases into policies across all government departments. Raising the priority is justified by the fact that noncommunicable diseases are closely linked to global social and economic development, and national policies in sectors other than health—treasury, environment, agriculture, education, etc—have a major bearing on the risk factors for noncommunicable diseases. So health in all policies is an important principle. In addition, inequalities in access to protection, exposure to risk, and access of care are the cause of major inequalities in the occurrence and outcomes of noncommunicable diseases.

2. To establish and strengthen national policies and plans for the prevention and control of noncommunicable diseases. Countries need to establish or strengthen existing policies and plans for prevention and control of noncommunicable diseases as an integral part of their national health policy. The three components are: (i) development of a national multisectoral framework for prevention and control; (ii) integration of prevention and control of noncommunicable diseases into a national health development plan; and (iii) reorientating and strengthening health systems to enable them to respond more effectively and equitably to the health care needs of people with chronic diseases.

3. To promote interventions to reduce the main shared modifiable risk factors for noncommunicable diseases: tobacco use, unhealthy diets, physical inactivity, and

harmful use of alcohol. As the underlying determinants of noncommunicable diseases often lie outside the health sector, strategies need the involvement of public and private actors in multiple sectors: agriculture, finance, trade, transport, urban planning, education, and sport.

4. To promote research for prevention and control of noncommunicable diseases. Priority areas include analytical, health system, operational, economic, and behavioral research required for program implementation and evaluation

5. To promote partnerships for the prevention and control of noncommunicable diseases. Strong international and national partnerships are required to provide effective public health responses to the threat posed by noncommunicable diseases. Collaborative work should be fostered among United Nations agencies, other international institutions, academia, research centers, nongovernmental organizations, consumer groups, and the business community.

6. To monitor noncommunicable diseases and their determinants and evaluate progress at the national, regional, and global levels. Monitoring noncommunicable diseases and their determinants provides the foundation for advocacy, policy development, and global action. Monitoring should include time trends in prevalence of risk factors and mortality rates in populations, and also evaluating the effectiveness and impact of interventions and progress made.

This international WHO strategy for prevention of noncommunicable diseases is complemented by the European Society of Cardiology (ESC) initiative, working in partnership with the European Heart Network and WHO Regional Office for Europe, to engage the European Union (EU) in a coordinated approach to prevention of CVD across Europe. A conference of these three partners was facilitated by the Irish Ministry of Health in February 2004 in Cork.[6] This informed the conclusions of the EU Council on Employment, Social Policy, Health, and Consumer Affairs in June 2004,[7] and an EU Heart Health Conference in 2005, which resulted in the Luxembourg Declaration.[8] This declaration defined the characteristics that are associated with cardiovascular health as:

- Avoidance of tobacco.
- Adequate physical activity (at least 30 minutes per day).
- Healthy food choices.
- Avoiding overweight.
- Blood pressure below 140/90 mm Hg in patients without diabetes or target-organ damage or multiple risk factors.
- Total blood cholesterol below 5 mmol/L (approx 200 mg/dL).

To achieve these healthy characteristics for the population as a whole requires a **population strategy** because it addresses the societal determinants of CVD in populations through national policies aimed at eliminating tobacco consumption, providing and promoting healthy food choices, and the opportunities to be physically active. A combination of a healthy diet and regular physical activity will keep a healthy weight and shape. It will also favorably impact on the prevalence of physiological and biochemical risk factors, eg, lipids, in the population. This all-encompassing strategy shifts the whole distribution of risk factors in the population toward more favorable levels without the need to medically examine individuals.

CLINICAL STRATEGIES: PRIMARY AND SECONDARY PREVENTION

In contrast, the high-risk primary prevention strategy identifies those individuals among the apparently healthy population with a high multifactorial risk of developing CVD, and the secondary prevention strategy addresses individuals who have developed symptomatic CVD. The primary prevention strategy requires some form of screening of the adult population to identify those at high CVD risk. The secondary prevention strategy does not require screening because patients present with symptomatic disease and are medically diagnosed. However, these two strategies share a common aim that is to reduce total cardiovascular risk through lifestyle interventions, management of other risk factors, and use of cardioprotective drug therapies. The distinction between primary and secondary prevention is to some extent artificial since risk is a continuum in the population, and many asymptomatic high-risk people have evidence of asymptomatic atherosclerosis.

Primary prevention

Primary prevention of CVD in individuals has traditionally focused on single risk factors such as "hypertension" rather than multiple risk factors—or the total risk approach—and as a consequence the much larger benefits of total CVD risk reduction have not been achieved. Although there is a continuous relationship between blood pressure and the risk of developing

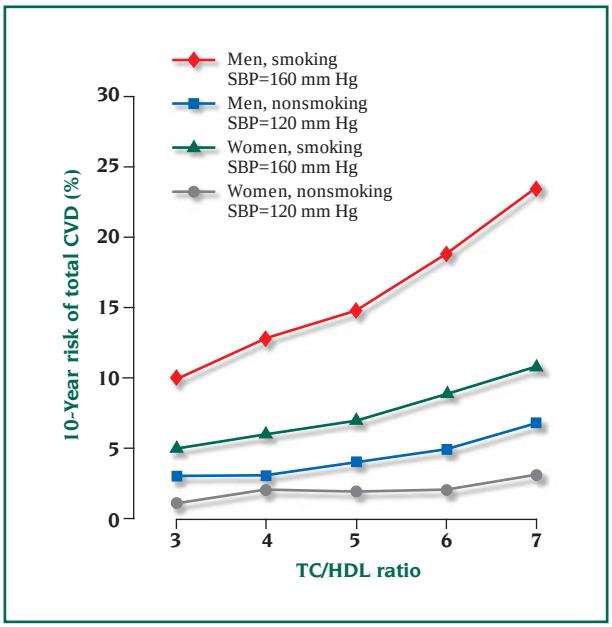

Figure 1. The relationship of total cholesterol/HDL cholesterol ratio to 10-year fatal CVD events.
Men and women aged 60 years with and without risk factors, based on a risk function derived from the SCORE project.

Abbreviations: CVD, cardiovascular disease; HDL, high-density lipoprotein; SBP, systolic blood pressure; SCORE, Systematic Coronary Risk Estimation; TC, total cholesterol.

Sex	Age (Years)	Chol (mmol/L)	BP (mm Hg)	Smoker	Risk (%)
F	60	8	120	No	2
F	60	7	140	Yes	5
M	60	6	160	No	8
M	60	5	180	Yes	21

Table I. Impact of combinations of risk factors on risk.

CVD, the higher the blood pressure the higher the risk, the term "hypertension" dichotomizes this distribution into those with a blood pressure consistently greater than a specified level, eg, 140/90 mm Hg, and those with a blood pressure less than this level, which is deemed "normal." The level of blood pressure defining "hypertension" is not based on the epidemiology of blood pressure and cardiovascular risk, but is rather deduced from randomized controlled trials which have shown evidence of benefit through reducing blood pressure in those with levels above say 140/90 mm Hg. The consequence of this approach is that someone with a blood pressure of 142/92 mm Hg is considered to be "hypertensive" and therefore receives blood pressure–lowering therapy, but another person of the same age and sex with a blood pressure of 138/88 mm Hg is considered to be "normotensive," and therefore requiring no treatment. Yet the risk of developing CVD is very similar for these two levels of blood pressure. More importantly, the total risk of developing CVD is not just a function of a single risk factor such as blood pressure, but of all the cardiovascular risk factors taken together. This is called total cardiovascular risk. This term is used to describe the probability of a person developing an atherosclerotic cardiovascular event, based on an assessment of all their risk factors, over a defined period of time.

The importance of estimating total CVD risk before a decision to intervene medically is made is illustrated in *Figure 1* and *Table I.* The figure illustrates that in a middle-aged man who is a nonsmoker with a blood pressure 120 mm Hg the absolute risk of developing fatal CVD progressively increases as the total cholesterol to high-density lipoprotein (HDL) cholesterol ratio rises. However, at every level of this lipid ratio, the absolute risk for a man of the same age who smokes cigarettes and has raised blood pressure is substantially higher. In fact, the absolute CVD risk of a ratio of 3.0 is actually higher in such a man than a ratio of 7.0 in a nonsmoking man with lower blood pressure. Although women are usually, age for age, at lower absolute risk of CVD than men, this advantage is lost at any level of the lipid ratio if the woman is a smoker with raised blood pressure. Another way of illustrating the same principle is *Table I.* Which person should receive lipid-lowering therapy? In the single risk factor paradigm the person with the highest cholesterol is the one most likely to be treated. But in the total risk paradigm it is the person at highest CVD risk, namely, the patient with the lowest cholesterol of 5.0 mmol/L, but with a total risk of 21%, who should receive lipid-lowering therapy.

The concept of total CVD risk assessment and management was first advanced by Jackson in 1993 in the context of treating "hypertension."[9] This was followed by the Joint European Societies recommendations in 1994,[10] which applied this principle to the management of all risk factors, including diabetes. The European coronary heart disease (CHD) risk chart developed by Graham was based on an original concept pioneered by Anderson[11] and used age, sex, smoking status, blood cholesterol, and systolic blood pressure to estimate the 10-year risk of a first fatal or nonfatal CHD event. There were separate charts for those with and without diabetes. A CHD risk of 20% was defined as sufficiently high to justify a more intensive lifestyle intervention and the use of drug therapies to lower blood pressure and cholesterol, and treatment targets for these risk

factors were set in the 1998 Joint European Societies guidelines.[12] However, these charts had several limitations. First, they were derived from American data from the Framingham community study and the applicability of this prospective cohort study of white middle-aged men and women to all European populations was uncertain. Second, the size of the cohort, just over 5000 individuals, was fairly small for an epidemiological study. Third, the definitions of nonfatal CHD events differed from those used in many other epidemiological studies making it difficult to validate the chart. Finally, estimating the risk of other manifestations of atherosclerosis such as stroke or aneurysm of the abdominal aorta was not possible.

The third edition of the Joint European Societies Guidelines published in 2003[13] used a new system for cardiovascular risk estimation called SCORE (Systematic Coronary Risk Estimation), based on data from 12 European prospective cohort studies: 205 178 subjects with 2.7 million years of follow-up and 7934 cardiovascular deaths.[14] Two charts were produced: one for high-risk regions, and the other for low-risk regions *(Figure 2, and Figure 3 page 88).*[13] SCORE estimates the 10-year risk of a first fatal atherosclerotic event, whether heart attack, stroke, aneurysm of the aorta, or other fatal manifestation of atherosclerotic disease. All ICD (International Classification of Diseases) codes that could reasonably be assumed to be atherosclerotic are included.

CVD mortality was used rather than total CVD (fatal + nonfatal) events because the definition and ascertainment of nonfatal events was not the same in the different cohort studies that make up SCORE. However, the use of mortality has the advantage that recalibration of the charts is possible in relation to changing time trends in CVD mortality. Any risk model will overpredict in countries in which mortality has fallen and underpredict in those in which it has risen. Recalibration of SCORE to allow for these secular changes in the population of a given country can be undertaken if good quality up-to-date mortality and risk factor prevalence data are available. The SCORE CVD mortality charts have been recalibrated for a number of European countries: Germany, Greece, Poland, Spain, Sweden, Cyprus, Bosnia and Herzegovina, and Russia. In the 2003 Joint European Societies guidelines, a 10-year risk of CVD of 5% or more for fatal events was defined as high risk, and people at this level of risk should receive a professional lifestyle intervention and, if appropriate, drug therapies to reduce total CVD risk. The choice of a 5% level was arbitrary as risk is a continuum in the population and there are no randomized controlled trial data that define the level of risk at which it is appropriate to intervene. However, there is evidence of benefit from trials of single risk factor reduction, which show benefit for individuals at levels of total risk below 5%. So a 5% CVD risk threshold for intervention is conservative. However, there are other more important factors to take into account when de-

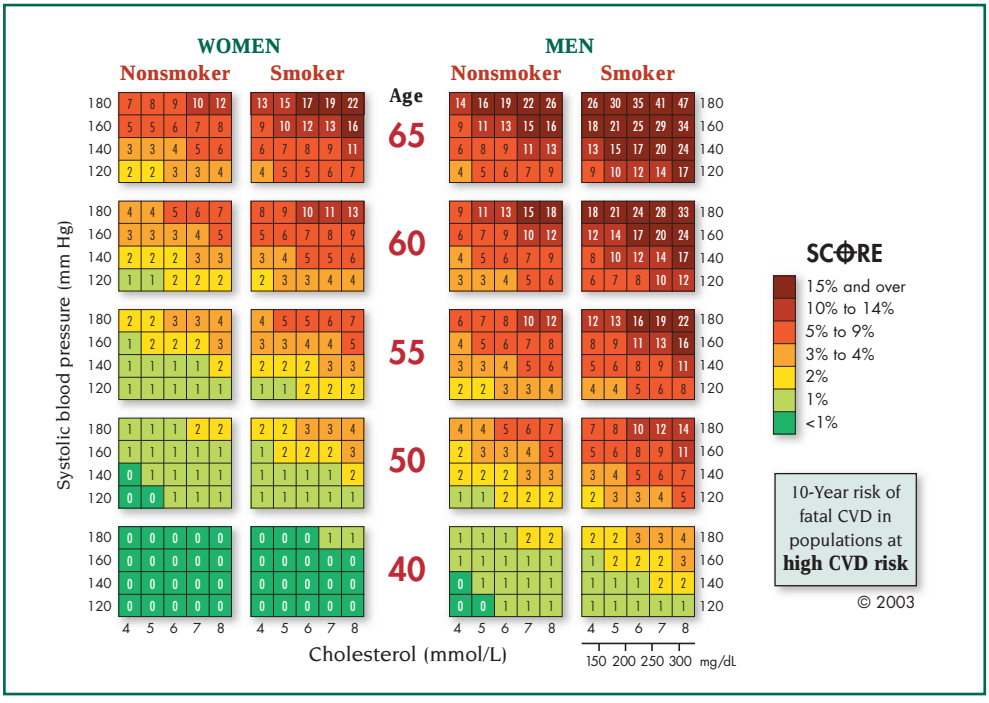

Figure 2. 2003 SCORE Chart for high-risk regions. *10-Year risk of fatal cardiovascular disease (CVD) in populations at high CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, total cholesterol.*

Reproduced from reference 13: De Backer G et al. Eur J Cardiovasc Prev Rehabil. *2003;10(suppl 1):S1-S78. © 2003, Lippincott Williams & Wilkins.*

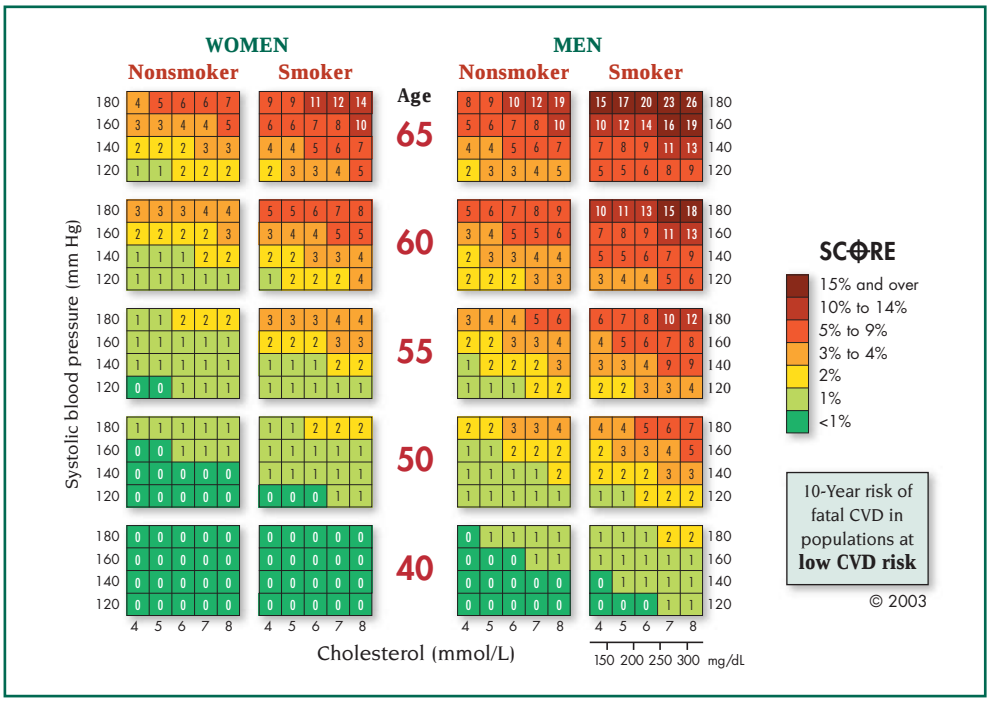

Figure 3. 2003 SCORE Chart for low-risk regions. *10-Year risk of fatal cardiovascular disease (CVD) in populations at low CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, total cholesterol.*

Reproduced from reference 13: De Backer G et al. Eur J Cardiovasc Prev Rehabil. *2003;10(suppl 1):S1-S78. © 2003, Lippincott Williams & Wilkins.*

ciding on a risk threshold for treatment at a national level, including the prevalence of high-risk individuals to be targeted and the practicalities and costs to the health care system of providing appropriate management. In the 2007 Joint European Societies guideline, the threshold of a 5% risk of cardiovascular death over 10 years was reaffirmed, but these patients were described as being at *"increased risk,"* in order to emphasize the continuum of risk in the population, rather than an arbitrary threshold for automatic intervention with drugs.[15] The treatment of an individual should be guided by their level of total CVD risk, but the physician also needs to take account of many other factors before committing a patient to life-long therapies.

Younger people, say below the age of 40 years, pose a different challenge in the context of total CVD risk. The charts show that at younger ages it is almost impossible to achieve the 5% CVD risk threshold, however high their risk factors are. But they will be at very high risk *relative* to people of the same age and sex, despite their low absolute risk. In the 2003 Guidelines, the recommendation was to extrapolate risk to age 60 years to illustrate the high-risk track of an individual if preventive action was not taken. It was not intended that young people should necessarily be treated as if they were 60 years old, as this could lead to excessive drug treatment in these age groups. The purpose of the extrapolation was to alert both the patient and their physician to the need for lifestyle change, and to signal the need for a lower threshold for intervention as they get older. In the most recent Joint European Societies guidelines published in 2007, a relative risk chart *(Figure 4)*[15] has been created so that younger persons at low absolute risk can be shown their risk relative to their peers.

At the other end of the spectrum, the vast majority of older people, especially men, will have an estimated risk of CV death over 10 years that exceeds the 5% threshold for intervention, based on age (and gender) alone, even when other CV risk factor levels are relatively low. So as for younger people, clinical judgment is required in deciding who is most likely to benefit from lifestyle and therapeutic interventions by taking account of lifestyle, comorbidity, the levels of individual risk factors, and target-organ damage. A CVD risk

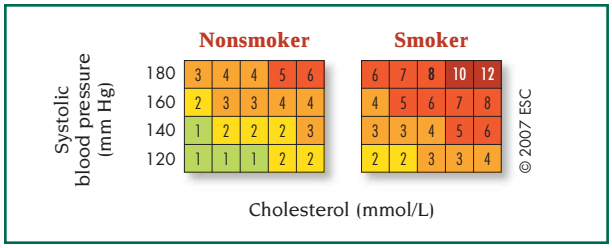

Figure 4. Relative risk chart (total cholesterol). *Reproduced from reference 15: Graham I et al.* Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2):S1-S113. Executive summary:* Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2): E1-E40;* Eur Heart J. *2007;28:2375-2414. © 2007, Oxford University Press.*

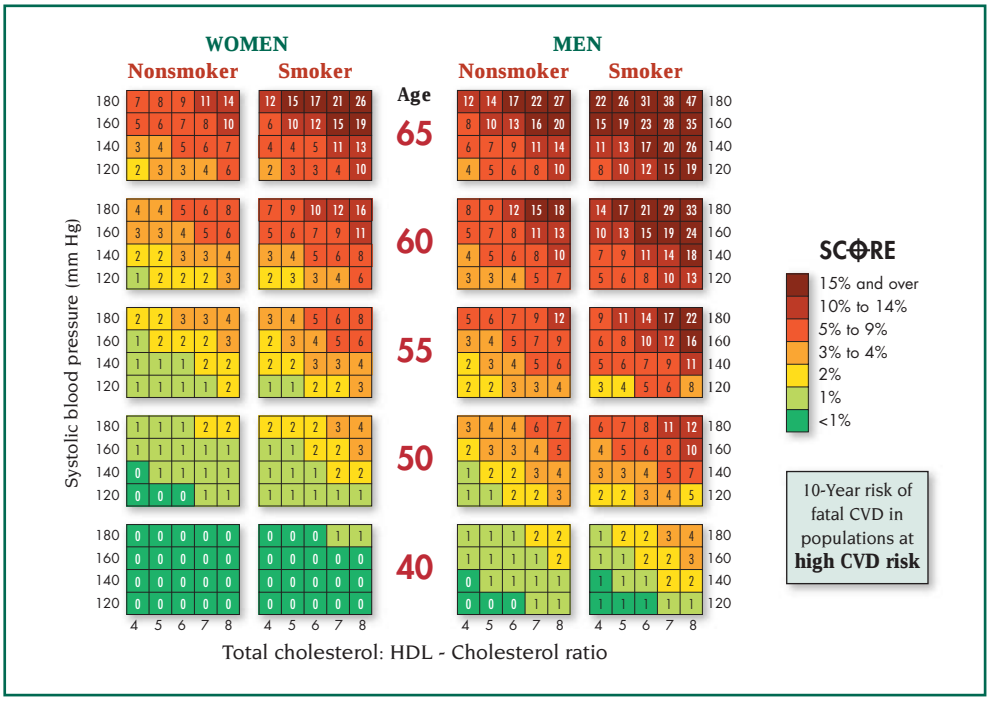

Figure 5. 2007 SCORE Chart for high-risk regions. *10-Year risk of fatal cardiovascular disease (CVD) in populations at high CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, total cholesterol (TC)/high-density lipoprotein (HDL) cholesterol ratio.*

Reproduced from reference 15: Graham I et al. Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2):S1-S113. Executive summary:* Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2):E1-E40;* Eur Heart J. *2007;28:2375-2414.*

of 5% or higher in the older population is not an automatic indication for drug therapies. Separate charts are available for both total cholesterol alone, and the total cholesterol:HDL cholesterol ratio *(Figures 2, 3, 5, and 6).*[13,15] Ideally, the risk chart based on the lipid ratio is preferred because HDL cholesterol makes an independent contribution to CVD risk, especially for women and those in the middle years of life. However, measurement of HDL cholesterol is not routine in many parts of Europe and so total cholesterol can be used instead. The electronic, interactive version of SCORE, called HeartScore, is available from the ESC (http://www.heartscore.org/Pages/welcome. aspx). By using the SCORE risk charts it is possible to identify

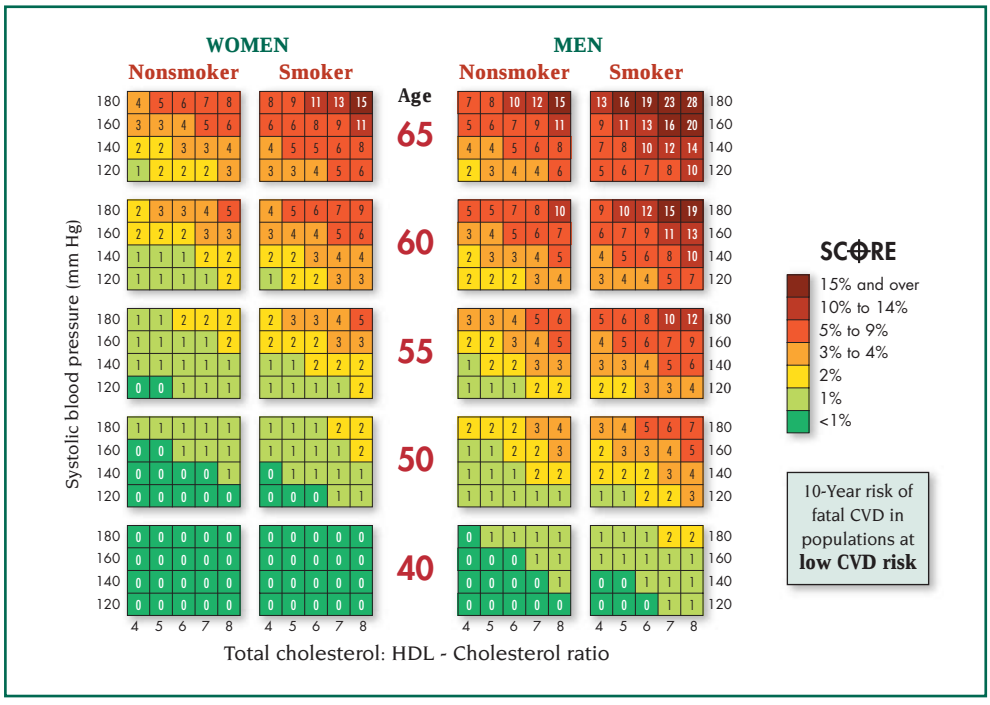

Figure 6. 2007 SCORE Chart for low-risk regions. *10-Year risk of fatal cardiovascular disease (CVD) in populations at low CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, total cholesterol (TC)/high-density lipoprotein (HDL)cholesterol ratio.*

Reproduced from reference 15: Graham I et al. Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2):S1-S113. Executive summary:* Eur J Cardiovasc Prev Rehabil. *2007;14(suppl 2):E1-E40;* Eur Heart J. *2007;28:2375-2414.*

from the apparently healthy population those individuals who are at high risk of dying from CVD, ie, a 5% or higher risk of fatal CVD over 10 years. The advantages of using the SCORE CVD risk charts are summarized in *Table II.*

There is no separate SCORE chart for people with diabetes because in the 2007 Joint European Societies guidelines they are now automatically classified as high CVD risk and treated accordingly. There are two reasons for classifying people with diabetes as high risk. Firstly, individuals diagnosed with diabetes tend to already have a clustering of other risk factors—obesity and central obesity, elevated blood pressure, low HDL cholesterol, raised triglycerides—which puts them at high multifactorial risk of developing CVD. Secondly, people with diabetes presenting with symptomatic CVD have a higher case fatality compared with people without diabetes. Overall, the impact of diabetes on CVD risk in SCORE appears to be greater than that for diabetes in the Framingham study, with relative risks of approximately 3 in men and 5 in women.

Although the principle of total CVD risk assessment is now widely accepted as the most appropriate way of identifying those asymptomatic individuals requiring lifestyle and therapeutic intervention, the evidence for multifactorial intervention is less compelling. In a systematic review of 10 trials with disease outcome data, there was no significant effect on total or coronary mortality, but a small and potentially important 10% reduction in CHD mortality may have been missed.[16] This apparent lack of effect on coronary mortality reflects a modest reduction in smoking and small changes in blood pressure and lipids, the latter due to limited drug treatment, in these trials. In contrast, numerous single risk factor trials using drug therapies to lower blood pressure and lipids have shown comparable reductions in CVD risk that would be predicted from the epidemiological relationships. Therefore, if multifactorial interventions achieve the same treatment effects as those in unifactorial trials, this will achieve a substantial cumulative reduction in total CVD risk. The challenge is to achieve such risk reductions through a combination of lifestyle and, where appropriate, drug therapies.

Secondary prevention

All patients with atherosclerotic CVD—coronary artery disease, cerebral artery disease, peripheral arterial disease—are eligible for secondary prevention. However, the focus of secondary prevention has been on patients with coronary disease, and particularly those who've had a myocardial infarction or been revascularized. Exercise-based cardiac rehabilitation of coronary patients reduces both cardiac and total mortality.[17] This meta-analysis showed no difference in mortality effect between exercise-only cardiac rehabilitation and comprehensive cardiac rehabilitation. Importantly, the effect of cardiac rehabilitation on total mortality was independent of CHD diagnosis, type of cardiac rehabilitation, dose of exercise intervention, or duration of follow-up. The contribution of secondary prevention programs with or without exercise was evaluated in a separate meta-analysis. The effects on mortality and myocardial infarction were similar for programs that included both exercise and risk factor education, or risk factor education without exercise, or for exercise alone.[18] In a systematic review of trials of secondary prevention, multidisciplinary disease management programs led to a reduction in admissions to hospital and recurrent myocardial infarction.[19] However, this distinction between cardiac rehabilitation and secondary prevention is artificial and these meta-analyses demonstrate, from different perspectives, the benefits of a comprehensive approach to reducing total cardiovascular risk. This comprehensive approach through smoking cessation, diet, and physical activity, and supplemented with control of blood pressure, lipids and glucose, and the use of cardioprotective drug therapies, should be available to all patients with atherosclerotic CVD, whatever arterial territory is affected.

CLINICAL PRIORITIES, TOTAL CVD RISK ESTIMATION, AND OBJECTIVES

Priorities

The following priorities are recommended for CVD prevention in clinical practice in the 2007 Joint European Societies guidelines[15] based on the principle that individuals at the highest levels of CVD risk gain most from risk factor management.

- Patients with established atherosclerotic CVD, whether of the coronary, peripheral, cerebral vessels or of the aorta, even if asymptomatic.
- Asymptomatic individuals who are at high total risk of developing symptomatic CVD because of:
  - Multiple risk factors resulting in a markedly raised total CVD risk.
  - Markedly raised levels of single risk factors: cholesterol ≥8 mmol/L (309 mg/dL), low-density lipoprotein (LDL) cholesterol ≥6 mmol/L (232 mg/dL), blood pressure ≥180/110 mm Hg.
  - Type 2 diabetes and type 1 diabetes with microalbuminuria.

Advantages of SCORE risk chart
• Intuitive, easy to use tool
• Takes account of the multifactorial nature of CVD
• Allows flexibility in management—if an ideal risk factor level cannot be achieved, total risk can still be reduced by reducing other risk factors
• Allows a more objective assessment of risk over time
• Establishes a common language of risk for clinicians
• Shows how risk increases with age
• The new relative risk chart helps to illustrate how a young person with a low absolute risk may be at a substantially high and reducible relative risk

Table II. Advantages of using the Systematic Coronary Risk Estimation (SCORE) risk chart.

• Close relatives of persons with early-onset atherosclerotic CVD (typically before age 60), or at particularly high CVD risk.

As a general guide, a middle-aged person with a 10-year risk of CVD death of 5% or more, is regarded as being at sufficiently high risk to justify professional lifestyle intervention and, where appropriate, drug therapies to reduce that risk. As the total risk increases, so does the likelihood of requiring medication to lower blood pressure, modify blood lipids, and control glucose levels. In addition, aspirin or other antiplatelet therapies may be required.

Total CVD risk estimation

Patients who have a clinical event such as an acute coronary syndrome or stroke have already declared themselves to be at high risk of a further cardiovascular event and automatically qualify for intensive lifestyle and risk factor management. They do not require CVD risk estimation using the SCORE charts. In addition, patients who are diagnosed with diabetes are now classified as high CVD risk and therefore total CVD risk estimation is also not required. The SCORE charts are intended for estimating CVD risk in the asymptomatic population with no history of CVD or diabetes.

How to use the SCORE risk estimation charts

• The low-risk charts are recommended for use in Belgium, France, Greece, Italy, Luxembourg, Spain, Switzerland, and Portugal, and also in countries that have recently experienced a substantial decline in CVD mortality rates. The high-risk charts are recommended in all other countries of Europe. Several countries have recalibrated the SCORE chart to allow for time trends in mortality and risk factor distributions and these country-specific charts will be more accurate for their respective populations.

• To estimate a person's 10-year risk of CVD death, find the table for their gender, smoking status, and age. Within the table, find the cell nearest to the person's blood pressure and total cholesterol, or total cholesterol:HDL cholesterol ratio. Risk estimates will need to be adjusted upwards as the person approaches the next age category.

• Low-risk persons should be offered advice to maintain their low-risk status. While no threshold is universally applicable, the intensity of advice should increase with increasing risk. In general, those with a risk of CVD death of 5% or more qualify for intensive advice, and may benefit from drug treatment. At risk levels over 10%, drug treatment is more frequently required. In persons older than 60, these thresholds should be interpreted more leniently, because their age-specific risk is normally around these levels, even when other CV risk factor levels are "normal." Therefore, uncritical initiation of drug treatments in the elderly should be discouraged.

• Relative risks may be unexpectedly high in young persons, even if absolute risk levels are low. The relative risk chart may be helpful in identifying and counseling such persons.

• The charts may be used to give some indication of the effects of reducing risk factors, although with the caveat that there will be a time lag before risk is reduced to these lower levels. For example, those who stop smoking in general halve their risk, but this occurs over several years

Qualifiers

• The charts can assist in CVD risk assessment and management, but must be interpreted in the light of the clinician's knowledge and experience, especially with regard to local conditions.

• Risk will be overestimated in countries with a falling CVD mortality, and underestimated in countries in which mortality is increasing.

• At any given age, risk estimates are lower for women than men. This may be misleading, since, eventually, at least as many women as men die of CVD. The charts illustrate that risk is merely deferred in women, with a 60-year-old woman resembling a 50-year-old man in terms of total CVD risk.

Risk will also be higher than indicated in the charts in:

• Sedentary subjects and those with central obesity; these characteristics determine many of the other aspects of risk listed below.

- Socially deprived subjects.
- Subjects with a strong family history of premature CVD.
- Subjects with diabetes.
- Subjects with low HDL cholesterol, increased triglycerides, fibrinogen, apolipoprotein B and lipoprotein(a) levels, and perhaps increased high-sensitivity C-reactive protein (CRP) and homocysteine levels.
- Asymptomatic subjects with preclinical evidence of atherosclerosis, for example, on ultrasonography.

A relative risk chart *(Figure 4)* has been developed to inform younger patients of their risk relative to some one of the same age and sex with no risk factors for CVD. So a younger person whose total risk is low can be up to 12 times more likely to develop CVD than a person of a similar age and sex who does not smoke and has low blood pressure and lipid levels. Clinical judgment is then required to decide, beyond lifestyle, if there is a need to start drug therapies.

Objectives of CVD prevention

In the most recent Joint European Societies guidelines, a new emphasis is given to assist those at low risk of CVD to maintain this state lifelong.

The desirable characteristics of low total risk include:
- No smoking.
- Healthy food choices.
- Physical activity; 30 minutes of moderate exercise a day.
- Body mass index of <25 kg/m^2 to avoid central obesity.
- Blood pressure of <140/90 mm Hg.
- Total cholesterol <5 mmol/L (190 mg/dL).
- LDL-cholesterol <3 mmol/L (115 mg/dL).
- Glucose < 6.0 mmol/L (110 mg/dL).

In those with established atherosclerotic CVD or diabetes or at high multifactorial risk of developing CVD, the objective is to lower their total risk in order to reduce cardiovascular mortality and morbidity. In addition to a healthy lifestyle, more rigorous control of other risk factors is recommended:
- Rigorous blood pressure and lipid control is desirable in the highest-risk subjects and particularly those with established atherosclerotic CVD or diabetes:
  – Blood pressure <130/80 mm Hg if feasible.
  – Total cholesterol <4.5 mmol/L (175 mg/dL), with an option of <4 mmol/L (155 mg/dL) if feasible.
  – LDL-cholesterol of <2.5 mmol/L (100 mg/dL), with an option of <2.0 mmol/L (77 mg/dL) if feasible.
  – Glucose < 6.0 mmol/L (110 mg/dL).
- Prescribing cardioprotective drug therapies—antiplatelet therapies, β-blockers, angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs), statins, anticoagulants—in particular groups, especially those with established atherosclerotic CVD.

IMPLEMENTATION OF CVD PREVENTION IN CLINICAL PRACTICE

Although the Joint European Societies guidelines on prevention of CVD in clinical practice published in 1994, 1998, 2003, and 2007 have made recommendations for a healthier lifestyle and set goals for blood pressure, lipid and glucose management, and the use of cardioprotective drugs, there is a gap between these standards of care for all priority groups of patients and the reality of clinical practice.

Surveys of clinical practice such as EUROASPIRE I, II, and III (EUROpean Action on Secondary and Primary prevention by Intervention to Reduce Events), which have monitored the trends of preventive cardiology practice in Europe over the last decade, have shown that integration of CVD prevention into daily clinical practice is inadequate.[20-22] The first EUROASPIRE survey was carried out in 1995/96 in nine European countries: Czech Republic, Finland, France, Germany, Hungary, Italy, the Netherlands, Slovenia, and Spain.[20] The second EUROASPIRE survey was undertaken in 1999/2000 in 15 European countries including those countries which participated in the first survey, and Belgium, Greece, Ireland, Poland, Sweden, and the UK.[21]

One of the objectives of the second survey was to see if the practice of preventive cardiology in coronary patients had improved in those countries and centers that took part in EUROASPIRE II.[22] This comparison of results from the two surveys should be a cause for considerable concern to all cardiologists, physicians, and others responsible for the care of coronary patients in hospital and the community. The adverse lifestyle trends, particularly the increase in smoking in younger female patients, and the substantial increase in obesity and central obesity in every country, makes a compelling case for more effective lifestyle programs.

About one fifth of coronary patients still continued to smoke cigarettes, with a significant increase in smoking among women patients, despite increasing availability of new and effective treatments to help patients stop smoking. The physician's advice to stop smoking is the most important first step in the smoking cessation process, but this advice should be reiterated and rein-

forced by all health professionals. Body weight continued to increase dramatically: 4 out of 5 patients in the second survey had a body mass index (BMI) ≥25 kg/m^2 and one third were obese (BMI ≥30 kg/m^2)—an increase from one quarter in the first to one third of all patients in the second survey. Waistlines also increased, with more than half of all patients being centrally obese (waist circumference ≥102 cm men and ≥88 cm women) in the second survey. Weight reduction interventions include dietary modification, increased physical activity, and some drug treatments such as inhibitors of intestinal fat absorptions and drugs acting on the central nervous system to suppress appetite. These adverse trends in body weight and distribution reflect the same trends in the general population, and contribute to a worsening of other risk factors such as rising blood pressure, dyslipidemia, and diabetes.

Blood pressure management showed no improvement over the two surveys. More than half of all patients still had blood pressures above the recommended target (<140/90 mm Hg), which increases their risk of recurrent coronary disease, stroke, kidney disease, and heart failure. Therapeutic control in patients using blood pressure–lowering medication remains unchanged across the two surveys, which leaves more than half of all patients not reaching the blood pressure goal in the second survey. This failure to improve management of blood pressure more effectively was despite large increases in prescriptions for all classes of antihypertensive medications.

In contrast to blood pressure, the management of blood lipids improved dramatically across the two surveys, largely because of the increasing use of statins. The proportion achieving the total cholesterol target of <5.0 mmol/L increased from 14% to 41%, nearly threefold. Therapeutic control of total cholesterol in those using lipid-lowering medication improved more than twofold. However, this still leaves nearly half of patients who did not achieve the total cholesterol target. The new Joint European Societies Guidelines (2007) have set lower cholesterol targets of <4.0 mmol/L for total cholesterol and <2.0 mmol/L for LDL cholesterol where feasible, and these will be an even tougher challenge.

Comparison between the two EUROASPIRE surveys shows that the prevalence of diabetes continued to increase, from 18% in the first to 22% in the second survey, reflecting the rise in obesity and central obesity. It is of particular concern that the prevalence of undetected diabetes increased nearly fourfold, from 4% in the first to 15% in the second survey. Therapeutic control of self-reported diabetes remained poor, with only one fourth of patients with a history of diabetes having a fasting glucose <6.1 mmol/L in the second survey.

The use of cardioprotective drug therapies has been shown to reduce cardiovascular and total mortality and the risk of recurrent coronary events in patients with CHD: aspirin or other platelet-modifying drugs, β-blockers, in people with myocardial infarction; ACE inhibitors in people with left ventricular dysfunction; and anticoagulants in post–myocardial infarction patients with increased risk of thromboembolism. In EUROASPIRE, prescriptions for cardioprotective medications increased across the two surveys for antiplatelet therapies (81% to 84%), β-blockers (54% to 66%), ACE inhibitors (29% to 43%), and statins (18% to 58%). However, despite the impressive increase in prescriptions for all these drug classes, the majority of coronary patients in Europe had still not achieved the blood pressure and total cholesterol targets as defined in the 1998 Joint European Societies guidelines on prevention of CHD.

The comparison between these two EUROASPIRE surveys demonstrates a substantial gap between the standards set in the CVD prevention guidelines and clinical practice. These surveys, uniquely spanning 5 years of European clinical practice, show that lifestyle trends in patients with CHD are a growing cause for concern. Other surveys have also reported inadequate risk factor management and underuse of prophylactic drug therapies in patients with CHD in Spain (PREVEnción Secundaria del infarto de miocardio en España [PREVESE] I and II, in 1994 and 1998),[23,24] France (PREVENIR, 1998 and 1999; Usik 1998 and 2000),[25] and Croatia (TASPIC-CRO [Treatment And Secondary Prevention of Ischemic Coronary Events in Croatia], in 1998 and 2003).[26] The EUROASPIRE III survey in 22 countries was undertaken in 2006/2007 in 22 countries, including 14 of those countries that participated in EUROASPIRE II, and the principal results on coronary patients in hospital and high-risk patients in primary care have been presented on the ESC Web site (www.escardio.org/euroaspire).

What is abundantly clear from these European surveys is that drug therapies are simply not sufficient and they have to be combined with a professional lifestyle intervention. Patients need professional support to make lifestyle changes and also manage their risk factors more effectively. Simply giving a drug prescription is not enough. Patients need to understand the nature of their disease and how to manage it through achieving

a healthy lifestyle as well as adhering to cardioprotective drug therapies over the long term. Most importantly of all, the adverse lifestyle trends in coronary patients reflect the same unfortunate trends in the general populations of these countries, which makes a compelling case for a societal strategy for CVD prevention. They illustrate how difficult it is for individual patients to change their behavior, despite the development of life-threatening disease, given that their unhealthy lifestyles are shared by an ever-increasing proportion of the adult population. To help patients to quit smoking, adopt a healthy diet, and increase physical activity requires sustained professional support. Yet only a third of patients with coronary disease access cardiac rehabilitation programs in Europe.[27] All patients with coronary disease as well as those at high risk of developing CVD should be able to access preventive cardiology programs.

At present, the health care systems in Europe are predominantly focused on acute salvage of ischemic tissues through medical interventions, devices, and pharmacological treatments; and not on addressing the underlying causes of the disease to prevent further morbidity and mortality. However, patients require professional support to make lifestyle changes and to have their other risk factors monitored and managed according to the standards defined in the guidelines. The ESC EUROACTION demonstration project in preventive cardiology took up this challenge by providing a nurse-coordinated multidisciplinary preventive cardiology program for both patients in hospital with coronary disease and for asymptomatic high-risk individuals in primary care, together with their families.[28,29] The object of this project was to demonstrate whether such a professional program could help more patients and their families achieve the lifestyle, risk factor, and therapeutic goals set out in the prevention guidelines. This EUROACTION program was set up in 8 countries and 24 hospital and general practice centers and evaluated in a matched pair cluster randomized controlled trial.

In the hospitals, cardiologists and nurses recruited eligible patients and their families. After a multidisciplinary assessment of lifestyle, risk factors, and drug treatment by a nurse, dietitian, and physiotherapist, couples attended at least eight sessions—one every week—in which they were assessed by each member of the team (nurse, dietitian, and physiotherapist) and, as required, by their cardiologist. The patients and their partners then attended a group workshop and a supervised exercise class. The cardiologists initiated and uptitrated the cardioprotective drugs and the nurses monitored risk factors and adherence to drug treatments at each session. At 16 weeks, patients and their partners were reassessed by the whole team and a report was sent to their family doctors. In the general practice centers, family doctors and nurses recruited patients and their families. The program started with the same nurse assessment of lifestyle, risk factors, and drug treatment as for the hospital patients, but was open-ended. At each visit—one every week—couples were assessed by the nurse—who led the group workshops—and by the family doctors responsible for drug treatment. The patients and their partners did not have supervised exercise classes. Patients in the hospital and general-practice centers were assessed for family lifestyle, risk factors, medications, health beliefs, anxiety, and depression, illness perception, and mood. Patients were provided with a personal record card for lifestyle and risk factor targets, and their families with family support packs (see www.escardio.org/euroaction)

The EUROACTION program incorporated several important principles. It was intentionally set up in busy general hospitals and general practices, outside specialist cardiac rehabilitation centers, to provide a service for all coronary and high-risk patients in routine clinical practice. Integration of the diagnosis and management of patients with continued preventive care in the same medical facility is likely to result in increased and sustained participation. In the EUROASPIRE survey, only a third of coronary patients attended cardiac rehabilitation,[27] whereas two thirds joined the EUROACTION program. Recruitment was even better in primary care, with 9 out of 10 patients joining the program. EUROACTION was inclusive because it addressed all the high-priority patient groups as defined in the guidelines.[15] We made no distinction between symptomatic coronary disease (secondary prevention) and those at high risk (primary prevention). All these patients are at high risk of CVD and need professional support to achieve the same lifestyle and risk factor targets. EUROACTION was a family-centered program and actively involved patients' partners and other family members. A family intervention is appropriate because married couples show concordance for lifestyle, and concordance for change.[30,31]

The EUROACTION preventive cardiology program reduced the risk of CVD compared with usual care mainly through lifestyle changes by families, who together made healthier food choices and became more physically active *(Figures 7 and 8).*[29] This change led to some weight loss and, for high-risk patients, a signifi-

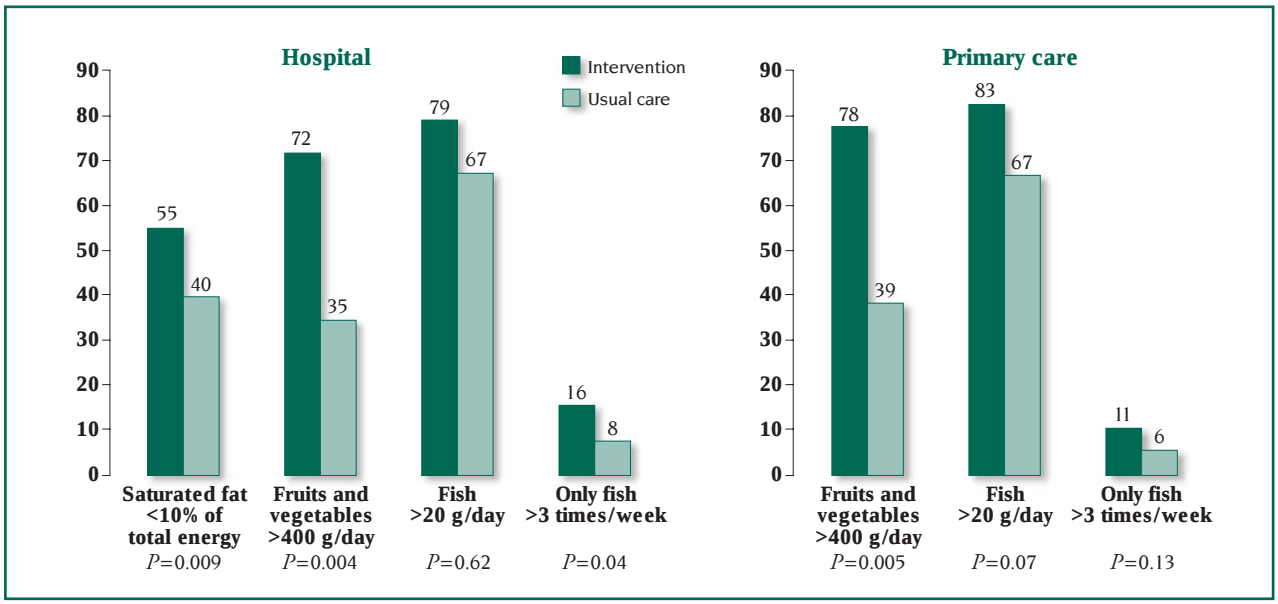

Figure 7. EUROACTION: Proportions of patients achieving the European targets for healthy diet at 1 year.

Modified from reference 29: Wood DA et al. Lancet. *2008;371:1999-2012. © Elsevier Ltd.*

cant reduction in central obesity. Blood pressure control was significantly improved in both coronary and high-risk patients, and for patients with coronary disease this was achieved without the use of additional antihypertensive drugs. Control of blood cholesterol concentrations in coronary patients was improved in both the intervention and usual-care groups; and for high-risk patients changes over 1 year showed a significant improvement in the proportion achieving the total and LDL-cholesterol targets because of increased use of statins. Cardioprotective drugs—aspirin, β-blockers, ACE inhibitors, and statins—were commonly prescribed for coronary patients in both the intervention and usual care groups. However, the use of all cardioprotective drugs was substantially lower in primary care, but in intervention there was a significantly increased use of ACE inhibitors and statins compared with usual care. Although these results are encouraging there is scope for further improvement. The smoking cessation intervention based on advice reduced relapse in patients with CHD, but had no effect on the prevalence of smoking in high-risk patients. Even though the protocol recommended the use of smoking cessation therapies, these were not used because of cost. Although the same protocol for risk-factor management was used in hospital and general practice, use of blood pressure and lipid-lowering drugs was much more conservative in general practice. As a consequence, most of the high-risk patients did not achieve lipid targets. Diabetes care could have been further improved if the intervention nurses had taken personal responsibility for diabetes management.

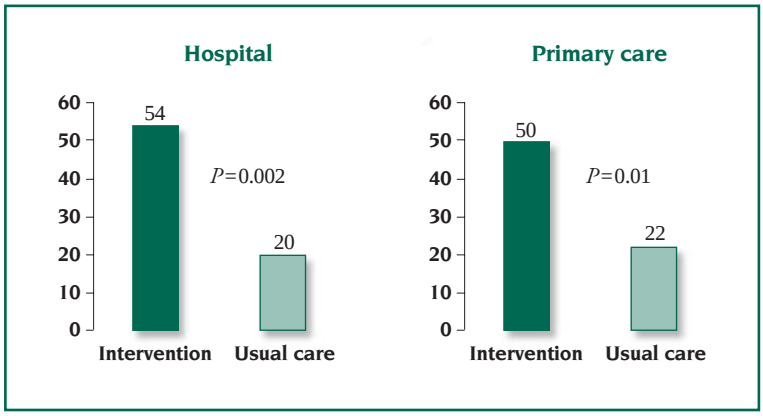

Figure 8. EUROACTION: Proportions of patients achieving the European targets for physical activity at 1 year.

Modified from reference 29: Wood DA et al. Lancet. *2008;371:1999-2012. © Elsevier Ltd.*

In summary, the EUROACTION demonstration project in preventive cardiology showed that standards of preventive care in general hospitals and general practices across Europe can be improved. This nurse-coordinated, multidisciplinary, family-based, ambulatory program achieved healthier lifestyle changes and improvements in other risk factors for patients with CHD and those at high risk of CVD, and also their partners, compared with usual care. EUROACTION

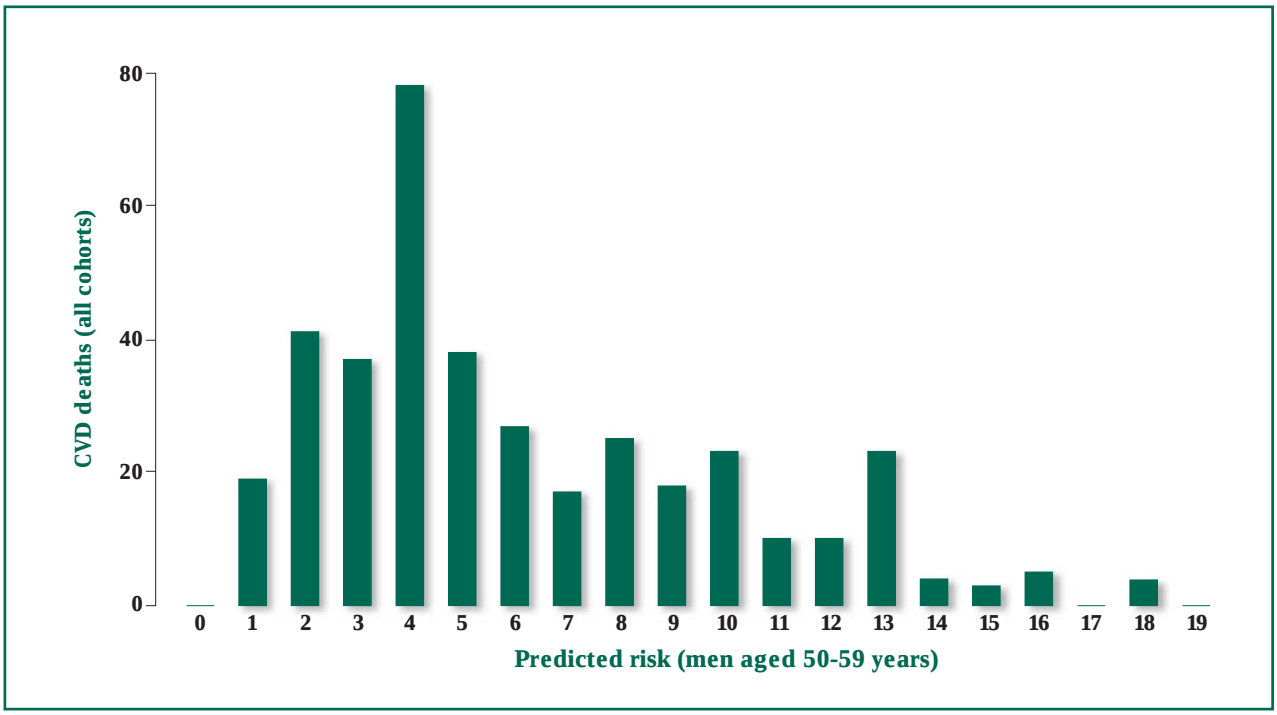

Figure 9. Illustration of the Rose Paradox.
The expected number of cardiovascular (CVD) deaths at increasing levels of predicted risk (expressed in % over 10 years). Illustration of the fact that most events occur in low-risk individuals simply because they are more numerous compared to high-risk individuals who, paradoxically, develop fewer events in absolute terms.

Modified after reference 32: Rose G. BMJ (Clin Res Ed). *1981;282:1847-1851. © 1981, BMJ Publishing Group.*

is a model of preventive cardiology, which has been successfully implemented and assessed, and can be used in routine clinical practice. To achieve the effects of EURO-ACTION, we need to go beyond specialized cardiac rehabilitation services and provide local preventive cardiology programs, appropriately adapted to the medical, cultural, and economic setting of a country.

CONCLUSIONS

However good our clinical prevention programs are, ultimately it is very difficult for patients to quit smoking, eat healthily, and be physically active for the rest of their lives if the society in which they live is not conducive to a healthy lifestyle. A preventive clinical strategy will reduce disability and save the lives of some individuals, but its impact on the overall burden of disease is necessarily limited. This is because most deaths in a population come from those at lower levels of CVD risk, simply because they are more numerous compared with high-risk individuals who, paradoxically, have fewer events in absolute terms—the Rose Paradox *(Figure 9).*[32,33] So a societal approach—health in all policies—by policymakers and politicians is the paramount strategy for the prevention of CVD.

REFERENCES

1. World Health Organization.
Prevention of Recurrent Heart Attacks and Strokes in low and middle income populations. Evidence-based recommendations for policy makers and health professionals.
Geneva, Switzerland: World Health Organization; 2003.

2. World Health Organization.
Prevention of Cardiovascular Disease. Guidelines for assessment and management of cardiovascular risk.
Geneva, Switzerland: World Health Organization; 2006.

3. Report by the Director General.
Global strategy for the prevention and control of noncommunicable diseases.
Geneva, Switzerland: World Health Organization; 2000 (Document A53/14).

4. WHO Framework Convention on Tobacco Control.
Geneva, Switzerland: World Health Organization; 2003.

5. World Health Assembly Resolution WHA57.17.
Global strategy on diet, physical activity and health.
Geneva, Switzerland: World Health Organization; 2004.

6. Shelley E, Ryden L.

Promoting heart health — a European consensus.

Eur J Cardiovasc Prev Rehabil. 2004;11:85-86.

---

7. *Press Release from the 2586th Council Meeting on Employment, Social Policy, Health and Consumer Affairs, Luxembourg, 1-2 June 2004.*

Eur J Cardiovasc Prev Rehabil. 2004;11:456-459.

---

8. ***www.ptkardio.pl/files//file/luxembourgdeclarationfinal.pdf.***

---

9. Jackson R, Barham P, Bills J, et al.

Management of raised blood pressure in New Zealand: a discussion document.

BMJ. 1993;307:107-110.

---

10. Pyörälä K, De Backer G, Graham I, Poole-Wilson PA, Wood D.

Prevention of coronary heart disease in clinical practice. Recommendations of the Task Force of the European Society of Cardiology, European Atherosclerotic Society and European Society of Hypertension.

Eur Heart J. 1994;15:1300-1331.

---

11. Anderson K, Wilson PW, Odell PM, Kannel WB.

An updated coronary risk profile. A statement for health professionals.

Circulation. 1991;83:356-362.

---

12. Wood D, De Backer G, Faergeman D, Graham I, Mancia G, Pyörälä K.

Prevention of coronary heart disease in clinical practice. Recommendations of the Second Joint Task Force of European and other Societies on coronary prevention.

Eur Heart J. 1998;19:1434-1503.

---

13. De Backer G, Ambrosioni E, Bort-Johnsen K, et al.

European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice.

Eur J Cardiovasc Prev Rehabil. 2003;10(suppl 1):S1-S78.

---

14. Conroy RM, Pyörälä K, Fitzgerald AP, et al.

Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project.

Eur Heart J. 2003;24:987-1003.

---

15. Graham I, Atar D, Borch-Johnsen K, et al.

European Guidelines on Cardiovascular Disease Prevention in Clinical Practice: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Prevention in Clinical Practice (Constituted by representatives of nine societies and by invited experts).

Eur J Cardiovasc Prev Rehabil. 2007;14(suppl 2):S1-S113. Executive summary: ***Eur J Cardiovasc Prev Rehabil.*** 2007;14(suppl 2):E1-E40; Eur Heart J. 2007;28:2375-2414.

---

16. Ebrahim S, Beswick A, Burke M, Davey Smith G.

Multiple risk factor interventions for primary prevention of coronary heart disease.

Cochrane Database of Systematic Reviews. 2006 Issue 4. Art. No.: CD001561. DOI: 10.1002/14651858.CD001561.pub2.

---

17. Taylor R, Brown A, Ebrahim S, et al.

Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomised controlled trials.

Am J Med. 2004;116:682-692.

---

18. Clark A M, Hartling L, Vandermeer B, McAlister FA.

Meta-analysis: secondary prevention programs for patients with coronary artery disease.

Ann Intern Med. 2005;143:659-672.

---

19. McAlsiter F A, Lawson F M E, Teo K K, Armstrong PW.

Randomised trials of secondary prevention programmes in coronary heart disease: systematic review.

BMJ. 2001;323:957-962.

---

20. EUROASPIRE Study Group. EUROASPIRE.

A European Society of Cardiology survey of secondary prevention of coronary heart disease: principal results.

Eur Heart J. 1997;18:1569-1582.

---

21. EUROASPIRE Study Group.

Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries. Principal results from EUROASPIRE II. Euro Heart Survey Programme.

Eur Heart J. 2001; 22: 554-72.

---

22. EUROASPIRE Study Group.

Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries.

Lancet. 2001;357:995-1001.

---

23. De Velasco JA, Cosin J, Lopez-Sendon JL, et al.

La prevencion secundaria del infarto de miocardio en Espana. Estudio PREVESE [Secondary prevention of myocardial infarction in Spain. The PREVESE study].

Rev Esp Cardiol. 1997;50:406-415.

---

24. De Velasco JA, Cosin J, Lopez-Sendon JL, De Teresa E, De Oya M, Sellers G.

Nuevos datos sobre la prevencion secundaria del infarto de miocardio en Espana. Resultados del estudio PREVESE II [New data on secondary prevention of myocardial infarction in Spain. Results of the PREVESE II study].

Rev Esp Cardiol. 2002;55:801-809.

25. Danchin N, Hanania G, Grenier O, et al.

Évolution du traitement de sortie après hospitalisation pour syndrome coronaire aigu en France entre 1995 et 2000: données des études Usik 1995, PREVENIR 1 et 2 et Usic 2000 [Trends in discharge prescriptions for patients hospitalized for acute coronary syndromes in France from 1995 to 2000. Data from the Usik 1995, PREVENIR 1, 2 and Usic 2000 surveys].

Ann Cardiol Angeiol. 2003;52:1-6.

---

26. Reiner Z, Mihatov S, Milicic D, Bergovec M, Planinc D; TASPIC-CRO Study Group Investigators.

Treatment and secondary prevention of ischemic coronary events in Croatia (TASPIC-CRO study).

Eur J Cardiovasc Prev Rehabil. 2006;13:646-654.

---

27. Kotseva K, Wood D, De Bacquer D, et al; EUROASPIRE II Study Group.

Cardiac rehabilitation for coronary patients: lifestyle, risk factor and therapeutic management. Results from the EUROASPIRE II survey.

Eur Heart J. 2004;6(suppl J):J17-J26.

---

28. Wood DA, Kotseva K, Jennings C, et al; EuroAction Study Group.

EUROACTION: a European Society of Cardiology demonstration project in preventive cardiology.

Eur Heart J. 2004;6(suppl J):J3-J15.

---

29. Wood DA, Kotseva K, Connolly S, et al; EUROACTION Study Group.

Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired cluster randomised controlled trial.

Lancet. 2008;371:1999-2012.

---

30. Wood DA, Roberts TL, Campbell M.

Women married to men with myocardial infarction are at increased risk of coronary heart disease.

J Cardiovasc Risk. 1997;4:7-11.

---

31. Pyke SD, Wood DA, Kinmonth AL, Thomson SG.

Change in coronary risk and coronary risk factor levels in couples following lifestyle intervention. The British Family Heart Study.

Arch Fam Med. 1997;6:354-60.

---

32. Rose G.

The strategy of prevention: lessons from cardiovascular disease.

BMJ (Clin Res Ed). 1981;282:1847-1851.

---

33. Rose G.

Sick individuals and sick populations.

Int J Epidemiol. 1985;14:32-38.
