

CARDIOVASCULAR OUTCOMES

The importance of both primary and secondary prevention of cardiovascular disease is indisputable.



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The following five observations underline the rationale for an active approach to the prevention of cardiovascular disease (CVD):

- CVD is the major cause of premature death in the Western world. It is also an important cause of disability and contributes in no small part to the escalating costs of health care.
- The underlying pathology is usually atherosclerosis, which develops insidiously over many years, and is usually advanced by the time symptoms occur.
- Death, myocardial infarction and stroke nevertheless frequently occur suddenly and before medical care is available. Many therapeutic interventions are therefore inapplicable or at best only palliative.
- The mass occurrence of CVD relates to lifestyle and modifiable physiological factors.
- Risk factor modifications have been unequivocally shown to reduce mortality and morbidity, both in people with unrecognised or recognised CVD.

PREVENTION

The prevention, therefore, even of a small proportion of cases will save thousands of lives, avoid inestimable suffering and save enormous health care expense.

The multifactorial nature of atherogenesis makes the process of prevention complex. A combination of several risk factors, which include non-modifiable factors such as age, sex and race, behavioural characteristics, such as smoking, physical inactivity and obesity, and biochemical variables, such as serum cholesterol, all play a role. It is important to recognise that the aetiology of myocardial infarction, ischaemic stroke and peripheral artery disease is similar and hence decisions about whether to initiate specific preventive action in patients can be guided by estimation of risk of suffering any such vascular events, not just coronary events.

The cost-efficacy of any intervention varies according to the global risk in a given individual or population. It follows that a fundamental step in establishing a preventive strategy involves assessing an individual's risk of development of clinically relevant outcomes. Therefore, the higher the risk, the more urgently intervention is required and the more cost-effective this intervention will be.

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Table I. Evidence for association of risk factors with CVD and response to intervention

Risk factor	Evidence for association with CVD		Response to therapy	
	Epidemiological	Clinical trials	Non-pharmacological	Pharmacological
Category I (risk factors for which interventions have been proved to lower CVD risk)				
Cigarette smoking	+++	++	+++	++
LDL cholesterol	+++	+++	+++	+++
High-fat/high-cholesterol diet	+++	++	++	-
Hypertension	+++	+++ (stroke)	+	+++
Left ventricular hypertrophy	+++	+	-	++
Category II (risk factors for which interventions are likely to lower CVD risk)				
Diabetes mellitus	+++	+	++	+++
Physical inactivity	+++	++	++	-
HDL cholesterol	+++	+	++	+
Triglycerides; small, dense LDL	++	++	++	+++
Obesity	+++	-	++	+
Postmenopausal status (women)	+++	-	-	+++
Category III (factors associated with increased CVD risk which, if modified, might lower risk)				
Physiological factors	++	+	+	-
Lipoprotein (a)	+	-	-	+
Homocysteine	++	-	++	++
Oxidative stress	+	-	+	++
No alcohol consumption	+++	-	++	-
Category IV (factors associated with increased CVD risk but which cannot be modified)				
Age	+++	-	-	-
Male gender	+++	-	-	-
Low socioeconomic status	+++	-	-	-
Family history of early-onset CVD	+++	-	-	-

1+ = weak, inconsistent evidence; 2+ = moderately strong, consistent evidence; 3+ = very strong, consistent evidence; - = poor or non-consistent evidence.

RISK FACTORS

The recently published Interheart Study¹ emphasises the predictive value of multiple risk factor assessment. Over 90% of cardiovascular events can be predicted by the assessment of 9 factors, namely, cigarette smoking, hypertension, hyperlipidaemia, diabetes mellitus, psychosocial stress, abdominal obesity, with beneficial factors being regular alcohol intake, exercise and appropriate diet.

Table I outlines the evidence supporting the association of risk factors with

CVD and their responsiveness to interventions.

Cigarette smoking

Cigarette smoking is the single most important modifiable risk factor for CVD.² Despite this well-recognised fact, the rate of tobacco use is increasing worldwide, especially among adolescents and young adults, and there are nearly 1 billion active smokers worldwide. The impact on health is enormous, with nearly half a million people dying annually in the USA from smoking-related complications.

Numerous prospective studies clearly document the increasing risk of cigarette smoking in a dose-dependent manner, which is linear.

Smoking cessation constitutes the single most important intervention in preventive cardiology. For instance, smoking cessation alone after a first myocardial infarction reduces the risk by nearly 65%. Importantly, so-called 'low-yield' cigarettes do not appear to reduce the risks of myocardial infarction. Unfortunately, although elevated cardiovascular risks decrease after smoking cessation, the risk of cancer

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of the lungs, pancreas and stomach persists for more than a decade, as does the risk of developing chronic obstructive pulmonary disease.

Primary prevention of smoking and smoking cessation are therefore critical lifestyle modifications in improving cardiovascular outcomes.

Hypercholesterolaemia

Elevated serum cholesterol is causally associated with an increased risk of CVD. In many observational studies and clinical trials a 10% increase in serum cholesterol is associated with a 15 - 20% increase in the risk of CVD. Conversely, clear benefits have been demonstrated for dietary and pharmacological treatments that lower serum cholesterol. The longer treatment is maintained, the greater the reduction in CVD events that can be achieved. Thus long-term compliance with lifestyle modification is important for successful intervention.

In general, total plasma cholesterol should be below 5 mmol/l and low-density lipoprotein (LDL) below 3 mmol/l. For patients with clinically established CVD and for those with diabetes, these goals should be lowered to a total cholesterol of less than 4.5 mmol/l and an LDL of less than 2.5 mmol/l, or even less than 2 mmol/l.

In asymptomatic individuals the first step is to assess total cardiovascular risk and to identify those components of risk that are to be modified. If the 10-year risk of death is less than 5%, advice regarding balanced diet, physical activity and smoking cessation should be given to keep the risk low. Risk assessment should be repeated every 5 years. If the 10-year risk of cardiovascular death is greater than 5%, intensive lifestyle advice should be given. If the risk remains above 5%, then lipid-lowering therapy should be instituted in order to lower LDL cholesterol levels to less than 2.5 mmol/l.

In patients with existing disease, drug intervention should be used early (note the Heart Protection Study) with the aim of lowering LDL to less than 2 mmol/l.³

Note. There are two risk assessment methods in use. The European Guidelines on CVD Prevention use a cardiovascular *death prediction* of 5% as a critical level, whereas other guidelines use a Framingham risk of 20% for the development of *cardiovascular events*. These two more or less equate with each other at these levels.

There are now many randomised intervention studies which define the benefits of lipid-lowering therapy on cardiovascular outcomes, both with lifestyle modification and drug therapy.^{2,4}

Hypertension

The risk of CVD increases continuously as blood pressure rises from levels considered to be in the normal range. Especially in the developed world, hypertension rates are rising rapidly with urbanisation and changes in lifestyle habits. Hypertension is becoming an increasingly important risk factor.⁵

In hypertensives, the decision to start treatment depends not only on the level of blood pressure, but also on the assessment of total cardiovascular risk and the presence or absence of target organ damage. Numerous tri-

als have shown that lowering blood pressure reduces the risk of CVD.

Individuals with a systolic blood pressure lower than 140 mmHg and a diastolic pressure lower than 90 mmHg usually do not require drug therapy (only patients with a very high cardiovascular risk profile and those with diabetes may benefit from lowering the pressure below these levels pharmacologically).

In patients with higher pressures, lifestyle modification (reduction of salt intake, weight loss, regular exercise) is an important intervention. In many clinical trials, however, adequate blood pressure control has only been achieved by the combination of two or even three drugs in addition to these lifestyle changes.

The risk factor assessment is critical, i.e. the higher the overall risk, the greater the benefit to be achieved. Rapid detection and management of hypertension are highly cost-effective interventions.

Physical inactivity

Physical inactivity is an exceptionally common and modifiable risk factor. While no large-scale randomised trials of physical activity are available, numerous moderate-sized trials have been conducted among healthy indi-

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viduals and among those at high risk of developing CVD. These trials demonstrate the benefit of physical activity with reduction in cardiovascular mortality of up to 25% in patients with existing disease. Physical activity will also clearly modify many of the other risk factors, such as hypertension, obesity and high-density lipoprotein (HDL) and LDL cholesterol levels.

Obesity and the metabolic syndrome

The prevalence of obesity is rising dramatically in both the developed and the developing world. In part, the increased risk associated with obesity is mediated by other risk factors such as hypertension, dyslipidaemia, and glucose intolerance. The metabolic syndrome, which is discussed on pp. 274 and 276 in this edition of *CME*, is now recognised as an important additional risk factor. Reduction of obesity and modification of the risk factors comprising the metabolic syndrome will significantly improve cardiovascular outcome.

Diabetes mellitus

Atherosclerotic CVD is a major complication of diabetes. The age-adjusted rates for CVD are 3 - 7 times higher in diabetics than in non-diabetics. The rapid increase in the incidence of diabetes in the developed world is therefore even more alarming. Great benefit can be obtained by primary prevention. Diet, exercise and avoidance of obesity are integral components of the treatment and prevention of the onset of diabetes, while diabetics should observe strict dietary control and maintain tight glycaemic control with medication. All other risk factors should be aggressively treated. Cardiovascular outcomes are dramatically improved by aggressive therapy.

CONCLUSION

In conclusion, CVD is the leading cause of death worldwide. Multiple risk factor intervention is often required in order to improve cardiac outcomes.⁶ Changes in many patterns of individual behaviour are necessary in a large majority of patients with established CVD or at high risk of CVD, but surveys suggest a serious gap between recommendations for behavioural change and advice actually provided by physicians in routine practice. Changes in risk behaviour (unhealthy diet, smoking, sedentary lifestyle) need a professional approach. These changes are difficult, especially in patients who are socially and economically disadvantaged, or who have significant psychosocial stress. Moreover, negative emotions, including depression, anger and hostility, constitute barriers to preventive efforts, also in high-risk patients.

The following strategic steps may be used to enhance the effectiveness of behavioural counselling:

- Develop a therapeutic alliance with the patient.
- Ensure that patients understand the relationship between behaviour, health and disease.
- Help patients to understand the barriers to behavioural change.
- Gain commitments to behavioural change from patients.
- Involve patients in identifying and selecting risk factors to change.
- Use a combination of strategies, including reinforcement of a patient's own capacity for change.
- Design a lifestyle modification plan.
- Monitor progress through follow-up contact.
- Involve other health care staff wherever possible.

There is overwhelming evidence that

lifestyle modification, coupled with judicious use of appropriate medication, will not only improve the quality of life and well-being of patients, but also have significant and long-term beneficial effects on cardiovascular outcomes.

References available on request.

IN A NUTSHELL

CVD is the major cause of premature death and disability in the Western world.

A number of important risk factors have now been identified which play a pivotal role in the development of CVD.

Lifestyle modification and therapy of many of these modifiable risk factors can have a significant impact on the growing incidence of CVD, improving the prognosis of many potential sufferers of this disease.

Risk stratification of patients identifies those at highest risk for the development of CVD.

Therefore, patients with established CVD need intensive therapy, which includes lifestyle changes (smoking, healthy food choices and physical activity) as well as treatment with statins, antihypertensives and aspirin, when indicated.

Patients at potentially high risk should also be counselled about lifestyle modification as mentioned above, and considered for pharmacological intervention.

Aggressive treatment of risk factors and lifestyle modification will have significant long-term beneficial effects on cardiovascular outcomes.