

HEART DISEASE

(6) PRIMARY PREVENTION OF HEART DISEASE

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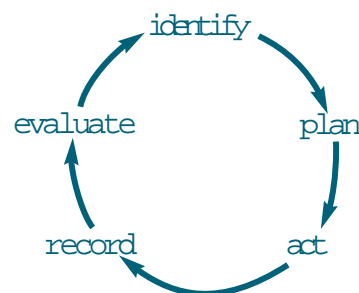
Many people are at risk of developing coronary heart disease but do not exhibit any signs or symptoms. This article looks at some interventions that may reduce the risks



identify gaps in your knowledge

1. How can you identify suitable subjects for primary prevention?
2. Name three primary prevention strategies.
3. Is there sufficient evidence for hormone replacement therapy to be used to reduce cardiovascular risk?

This article relates to the Royal Pharmaceutical Society's core competency of "common disease states and their drug therapies" (see "Medicines, ethics and practice — a guide for pharmacists", number 26, July 2002, pp105–6). You should consider how it will be of value to your practice.



Coronary heart disease (CHD) is a progressive disease. Symptoms develop in the latter stages, so the disease can be present for many years before a diagnosis is made. Primary prevention can be defined as using strategies to reduce the risk of cardiovascular (CV) events in people without CHD but who are at a high risk of developing it. In contrast, secondary prevention focuses on slowing the progression of established disease (P7, 30 November 2002, pp784–6). Primary prevention is challenging because it is difficult to convince people of the benefits of changing habits when they have no disease symptoms. Generally, compliance with any health maintenance plan requires individuals to perceive a disease as a threat, and the time and energy invested in preventive actions worthwhile.

According to the National Service Framework for CHD, general practitioners and primary health care teams should identify all people at significant risk of cardiovascular disease but who have not yet developed symptoms and offer them appropriate advice and treatment to reduce their risk, ie, active intervention. The definition of "significant risk" is an arbitrary value, currently defined as a 30 per cent or greater risk of having a CV event over the next 10 years.

RISK FACTORS

Many factors directly and indirectly affect the development of the atherosclerotic plaque that underlies CHD. The disease is multifactorial and the hazard posed by any one risk factor is significantly influenced by the presence of others. For example, the CV

risk associated with hypertension is usually lower in people with low cholesterol levels. Cardiovascular risk factors can be classed as non-modifiable or modifiable (see Table 1). Non-modifiable risk factors cannot be altered. For example, CV risk increases with age but we cannot reverse the ageing process. Similarly, men are at a greater risk of developing early CHD than women, and certain ethnic groups (eg, south Asians) and those with a family history of CHD (particularly early cardiac events) have a significantly increased risk. Primary prevention strategies focus on addressing modifiable risk factors through lifestyle changes and drug therapies.

CARDIOVASCULAR RISK ASSESSMENT

The decision to advise on lifestyle changes or offer drug treatment should be made following an assessment of absolute risk, which takes into account the complex interactions between risk factors. In order to calculate the absolute risk of CHD, it is essential to take the individual's full history and to undertake tests to identify the presence of risk factors such as hypercholesterolaemia and diabetes. A validated tool can then be used to allow the clinician to calculate "CHD risk". Such tools are devised primarily using data from epidemiological studies such as the Framingham Heart Study, a population based study providing information on cardiac risk factors over the past five decades.

Using a Joint British Societies coronary risk prediction chart is the preferred method for estimating CHD risk in the United Kingdom; charts can be found at

the back of the British National Form-ulary. Each chart focuses on gender, age, smoking status, blood pressure, cholesterol levels and the presence or absence of diabetes. Other acceptable tools include the Sheffield-risk table, the University College London Cardiorisk manager, the European coronary risk chart and the New Zealand cardiovascular risk prediction charts. These charts integrate the various risk factors present in an individual in order to quantify CHD risk over the following 10 years.

TABLE 1: RISK FACTORS FOR CHD

Non-modifiable	Modifiable
Age	Smoking
Gender	High cholesterol
Ethnicity	Hypertension
Family history	Diabetes
Previous cardiovascular event	Obesity
	Physical inactivity

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PRIMARY PREVENTION STRATEGIES TO REDUCE CHD RISK

Smoking cessation Cigarette smoking is associated with decreased levels of high-density lipoproteins (HDL), increased platelet aggregation and fibrinogen levels, inappropriate stimulation of the sympathetic nervous system, endothelial dysfunction and altered oestrogen metabolism, all of which contribute to atherosclerotic plaque formation. Cigarettes have a strong dose-response effect on the risk of myocardial infarction (MI); the risk is two to four times greater in heavy smokers (those who smoke at least 20 cigarettes per day) than in those who do not smoke, but no level of smoking has been determined to be safe. Of great concern is that although the incidence of smoking appears to be decreasing in middle-aged men, it is increasing in women.

Within a few months of stopping smoking, CHD risk begins to decline. Within two to three years, the risk decreases to approximately the level found in people who have never smoked, regardless of the amount smoked, duration of the habit and age at cessation.¹

Interventions that improve smoking cessation rates include counselling and support from specialist clinics, nicotine replacement therapy (in those smoking more than 10 cigarettes per day), and bupropion. A meta-analysis of structured cessation programmes has indicated that NRT nearly doubles chances of successfully stopping but, despite these data, smoking cessation rates, even in the most successful programme, remain low.² The use of NRT and bupropion has been recommended in a recent National Institute for Clinical Excellence review. In view of the evidence that supports smoking cessation as a strategy to reduce CV risk, pharmacists can take a number of steps:

- Enquire about smoking status in people believed to be at risk of CHD
- Encourage smokers to consider quitting at every opportunity
- Refer patients expressing a desire to stop to an appropriately trained smoking cessation facilitator or offer your own smoking cessation support service
- Recommend the use of NRT or other smoking cessation aids available over the counter, where appropriate

Blood pressure reduction Elevated systolic (>140mmHg) or diastolic (>90mmHg) blood pressure is a risk factor for the development of CHD and stroke. Hypertension increases shear stress and may therefore lead to plaque rupture. In addition, high BP is believed to cause endothelial damage, and may enhance the migration of lipoproteins into the vessel wall. The thresholds for intervention to reduce BP depend on calculated CHD risk. In all patients, even those at low risk of CHD, lifestyle advice and, if necessary, drug therapy should be initiated at BP levels >160/100mmHg, but a lower threshold (>140/90mmHg) would be appropriate in those at higher risk (>15 per cent over 10 years).

In patients with high or borderline high BP, it is important to identify any contributing factors including obesity, excessive alcohol intake (>3 units per day), excessive salt intake and lack of exercise.³ Overweight patients should be advised to reduce their calorie intake — weight loss is associated with a modest reduction in BP. An intake of more than 21 units of alcohol per week is associated with increased BP, that can be reversed by reducing intake to within recommended limits. A reduction in salt intake from 10 to 5g daily can lower BP by up to 4/3mmHg.⁴ Physical inactivity is in itself associated with increased incidence of hypertension and regular aerobic activity has been shown to reduce BP.

Lifestyle changes may be sufficient to reduce CV risk below the currently recommended 30 per cent over 10 years threshold but, in many cases, drug therapy may be required (*PJ*, 11 January, pp52–54). In summary:

- All patients at any risk of CHD should have their blood pressure evaluated
- Dietary intervention, increasing exercise and weight loss should be initial recommendations
- Antihypertensive therapy should take other existing medical conditions into account and the benefits of compliance should be fully explained

action : practice points

1. Consider how you might advise a woman with a family history of heart disease, asking about HRT. Visit www.mca.org.uk and look at the safety update (reference 12).
2. Ensure you understand how cardiovascular risk is assessed and used by looking at *Merec* Bulletins 7 and 8; 2000, (www.npc.co.uk/merec_index.htm) and working through the four risk scenarios in bulletin number 8. Use a Joint British Societies prediction chart to estimate the absolute 10-year risk of developing CHD for one or more of your patients.
3. Visit www.nice.org.uk and read the guidance on the use of NRT and bupropion (technology appraisal no39). How does this fit in with your practice? Next time you advise someone on smoking cessation, reflect on how you have applied what you have learnt.

evaluate

How could your learning have been more effective?
What will you do now and how will this be achieved?

Cholesterol reduction Studies have clearly established that as circulating cholesterol levels increase, so does the risk of coronary events. Across the world, societies with low cholesterol levels have reduced CHD mortality (eg, Japan), while those with higher cholesterol levels have increased CHD mortality (eg, UK). As a result, cholesterol is sometimes referred to as the “permissive factor” in the development of CHD. Up until the menopause, women generally have higher levels of protective HDL cholesterol than men, which may account for the reduced early CHD event rate in women.

Reducing the consumption of saturated fat and increasing polyunsaturated fat, fruit, vegetable and fibre intake are standard healthy eating recommendations that may have a modest impact on cholesterol levels. Average cholesterol reductions achieved through diet are in the order of 5 per cent and even the most rigorous low-fat diet has been found to reduce cholesterol by an average of only 15 per cent.⁵ Some foods, such as margarines, now incorporate stanol esters and plant sterols to inhibit cholesterol absorption from the gastrointestinal tract but trials have had mixed results, depending on trial design, sterol intake and initial cholesterol levels. Current evidence suggests that these new foods may reduce cholesterol concentration in individuals consuming an average diet, but may lack similar efficacy in those already following a low-fat diet. For this reason, drug therapy is frequently required in patients at a high risk of CV events.

Statins are the treatment of choice. In combination with dietary modification, they have been found to reduce total cholesterol levels by 20–30 per cent and low-density lipoprotein (LDL) cholesterol levels by 30–40 per cent or more. The role of statins in primary prevention has been established by studies such as WOSCOPS,⁶ where significant reductions in death from all causes, death from CHD and non-fatal MI were reported over the course of the five-year follow-up in non-CHD trial populations.

Active intervention to lower cholesterol is currently recommended in any individual with a significant CHD risk plus a cholesterol level >5.0mmol/L in which a three month dietary intervention has been unsuccessful.⁷ In the absence of significant CV risk, raised cholesterol may not need routine treatment, although dietary advice may be appropriate and other issues should be considered such as secondary hyperlipidaemia and familial hypercholesterolaemia.

Obesity Obese people are at an increased risk of many illnesses, including type 2 diabetes, hypertension, dyslipidaemia, cardiovascular disease, stroke, sleep apnoea, gall bladder disease, gout and osteoarthritis. The Nurses' Health Study (120,000 women) demonstrated that the risk of CHD is two to three times greater in overweight women than in lean women.⁸ Abdominal obesity is more significant than generalised or peripheral obesity in middle-aged and older women predisposed to CHD. All obese patients should be

advised to reduce body weight through diet and increased physical activity. Frequent fluctuations in weight are also associated with increased risk of CHD so weight-loss programmes must not only encourage weight loss but maintain it.

Blood glucose control The presence of diabetes increases CHD mortality by two to three times in men and four to six times in women. In patients with non-insulin dependent diabetes mellitus (NIDDM), metabolic disturbances that may interact to promote atherogenesis include hyperinsulinaemia, hypertension, central obesity and dyslipidaemia (elevated LDL and triglycerides, with low HDL). Insulin resistance is a central defect in NIDDM and primary prevention of CHD includes improving insulin sensitivity, reducing body fat and increasing physical activity. The association between high blood glucose levels and risk of cardiac events is well-established, although trials investigating the role of blood glucose control have not been entirely convincing. In one trial, a significant reduction in all-cause mortality and MI was only seen in the sub-group of obese patients treated with metformin, although favourable trends were seen across the whole diabetic population.⁹

Aspirin Using aspirin to prevent ischaemic events in patients without a history of CHD has been controversial. A 28 per cent reduction in the risk of cardiac events has been demonstrated with regular aspirin use in a number of groups including men over the age of 40 years, post-menopausal women and younger patients with multiple CV risk factors.¹⁰ Targeting use of aspirin to patients at high CV risk is necessary to maximise the risk-benefit ratio. For example, treating 1,000 people with a 5 per cent risk of cardiac events over the next five years with aspirin could prevent six to 20 MIs, with a risk of two haemorrhagic strokes and two to four major gastrointestinal bleeds. If the five-year risk was only 1 per cent, only one to four MIs would be prevented, but just as many bleeding events would occur.¹⁰

Current recommendations for preventing CHD in clinical practice advocate the use of low-dose aspirin for primary prevention in patients over the age of 50 years with CHD risk >15 per cent over 10 years.¹¹ Co-existing hypertension should be well-controlled before aspirin is initiated to minimise the risk of stroke. For patients at an increased risk of gastrointestinal bleeding episodes, co-prescription of a gastroprotective agent should be considered.

OTHER ISSUES

Hormone replacement therapy The delay in development of CHD in women is largely attributable to the presence of endogenous protective oestrogen before menopause. Currently, most women live approximately one third of their lives post-menopause, during which they have a CV risk similar to that of men. Although observational studies have previously indicated that HRT may reduce the frequency of CV events in patients at increased cardiac risk, current evidence indicates that HRT should not be used for the prevention of CHD post-menopause¹² and the recent Women's Health Initiative study indicates that CHD risk may even be increased by HRT.¹³

Antioxidant therapy The process of lipid oxidation is evident at all stages of atherosclerosis especially in macrophage-rich and early atherosclerotic lesions. It has been hypothesised that dietary antioxidants such as vitamins E and C, beta carotene and flavonoids might prevent CHD. Epidemiological studies have shown an association between high dietary intake or high serum concentrations of vitamin E and lower rates of ischaemic heart disease. Despite the theoretical advantages of antioxidant therapy, the results in recent clinical trials have not demonstrated that antioxidant therapy has any benefit in reducing CHD in clinical practice. The HOPE trial investigated the use of vitamin E in a population at a high risk of CV events and found no significant differences in the incidence of secondary CV outcomes or in death from any cause when compared with placebo.¹⁴ Similar results were reported in a recently published study, which was not able to demonstrate a difference between antioxidants and placebo in over 20,000 patients in the UK.¹⁵

CONCLUSION

In summary, it is important to identify patients at high risk of developing CHD. This can be achieved through assessing the presence or absence of specific risk factors in an individual and calculating his or her cardiac risk over the next 10 years. Lifestyle modification is essential, but pharmacological options may be needed to control blood pressure, blood glucose and lipids and to reduce the risk of thrombotic events. Pharmacists frequently have contact with people before they experience CHD symptoms, therefore they can play an important part in primary prevention and in the primary care team.

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