Coronary heart disease

multiple risk factors and risk assessment

Identification and modification of known behavioural and environmental risk factors have the potential to reduce the large toll exacted by coronary heart disease.

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The burden of cardiovascular disease in Australia

Cardiovascular disease (CVD), which comprises heart attack, stroke and peripheral blood vessel disease, is the major cause of death and the leading cause of disability in Australia.[1] CVD is the cause of approximately 37% of all deaths, with one death occurring every 10 minutes. The direct costs of CVD constitute the largest economic health burden for Australia – an estimated $7.6 billion in 2004, which is 11% of all direct health spending.[2] Much of the burden associated with CVD relates to hospitalisation and residential care, particularly in the 12% of the population who are aged 65 years and over. Because of progressive ageing of the population and other factors, such as the increased use of pharmaceutical agents, the direct costs have been predicted to increase to approximately $11.5 billion by 2011.[2]

Coronary heart disease (CHD) is the most important single disease state in CVD. It is also an important paradigm for considering approaches to prevention and treatment of other chronic non-communicable diseases, such as diabetes and stroke.

Risk factors

The landmark INTERHEART study, a very large case–control study of myocardial infarction undertaken in 52 countries (including Australia), provides important information about risk factors and the potential for prevention of CHD.[3] This study showed that the population attributable risk (the percentage decrease in events if risk factors were at 'ideal' levels) for myocardial infarction was about 90% in both younger and older individuals. Findings did not differ between regions of the world or between men and women. Individual risk factors are discussed below in the context of the significant independent risk factors identified in the INTERHEART study.

IN SUMMARY

- **In the landmark INTERHEART study of myocardial infarction, the ApoB/ApoA1 ratio was the most powerful predictor of risk of myocardial infarction.**
- **In both men and women, potentially modifiable risk factors account for over 90% of the risk of an initial acute myocardial infarction.**
- **Stopping smoking by the age of 30 years eliminates the negative effect on an individual's life expectancy. Stopping at a later age is still beneficial.**
- **Smoking, elevated blood pressure and dyslipidaemia account for about 75% of the variations in risk for future CHD events in people without diabetes.**
- **Recent changes to PBS criteria for eligibility for subsidy of statins in people with diabetes acknowledge the high risk of CHD events in such patients.**
- **GPs have a key role in reinforcing education about the need for early presentation to hospital if patients with known CHD experience 10 to 15 minutes of chest pain that might herald the onset of myocardial infarction. Provision of an action plan can be of assistance.**
- **There is good evidence to support the use of aspirin (and clopidogrel in selected patients), statins, beta blockers and ACE inhibitors in patients with known CHD.**

Dyslipidaemia

The lipid measure used in the INTERHEART study was the apolipoprotein (Apo) ratio ApoB/ApoA1, which was the most powerful predictor of risk of myocardial infarction in the study. This is arguably a better measure of risk associated with dyslipidaemia than LDL cholesterol, HDL cholesterol, triglycerides, total cholesterol, and the total:HDL cholesterol ratio. This is because ApoB reflects the total atherogenic particle number, accounting for the increased atherogenicity of small dense LDL particles and risk associated with triglycerides. Both aspects are particularly important in the context of diabetes and the metabolic syndrome. ApoA1 reflects the antiatherogenic properties of HDL cholesterol. Importantly, the ApoB/ApoA1 ratio can be estimated from nonfasting blood samples.

Smoking

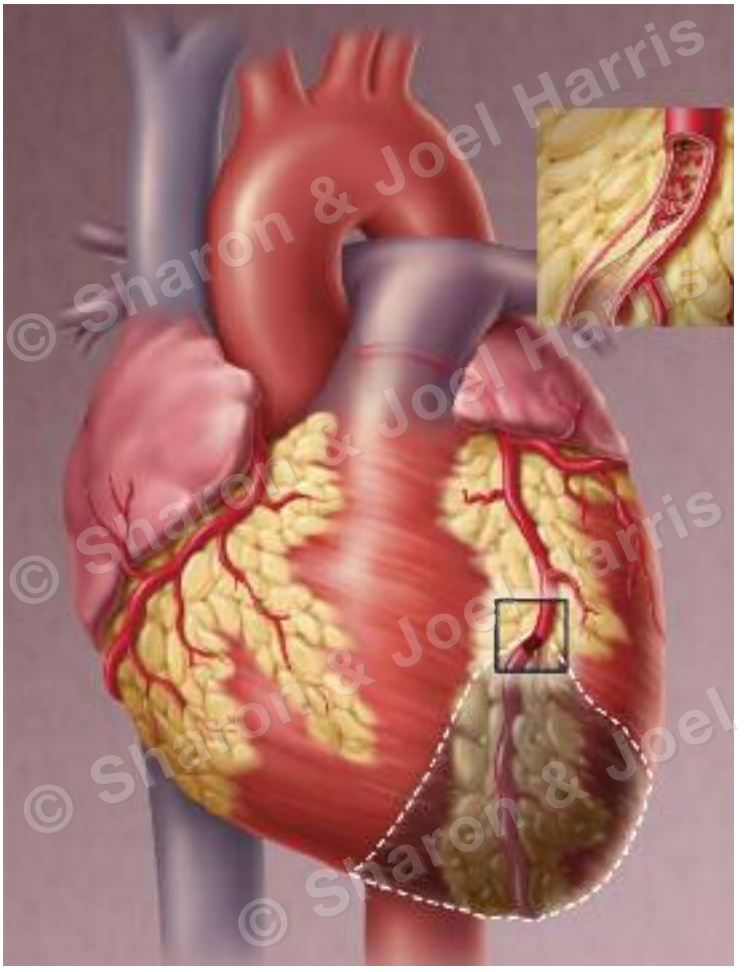
A subsequent analysis of the INTERHEART study has provided more detailed information relating to the risk of myocardial infarction associated with smoking.[4] The increase in risk was significant when as few as two to four cigarettes were smoked daily and increased in a linear manner as the number of cigarettes increased. The analysis also showed the risk to be very similar for different methods of tobacco use.

Important results were also obtained from a recent study of the long term risk associated with smoking and the effect of stopping at different ages.[5] Over a follow up period of 50 years, British doctors who smoked had a decrease in average life expectancy of about 10 years if they did not stop. However, this shortening in life expectancy was eliminated when smoking was stopped by the age of 30 years. The associated 'reward' decreased with increasing age for stopping smoking, but benefits accrued even for stopping up to the age of at least 60 years.

Hypertension

The risk associated with blood pressure above the ideal level (systolic blood pressure of 115 mmHg) is greater for stroke than for CHD,[6] but it is still important for the latter and other cardiac manifestations (e.g. heart failure). The risk relationships are continuous, and use of the terms 'hypertension' and 'normotension' is arbitrary and therefore somewhat misleading. The concept of a continuous risk relationship is also applicable to other risk factors (e.g. dyslipidaemia).

Coronary heart disease



CHD is the principal health problem for Western countries such as Australia. Population-wide measures and aggressive treatment of high risk individuals are complementary approaches to prevention and management.

Diabetes

The AusDiab survey has shown that about 7.4% of the Australian population have diabetes and another 16.4% have impaired glucose tolerance and/or impaired fasting glucose.[7] Again, the risk associated with abnormal glucose state represents a continuous relationship.[8]

The increased risk of CHD associated with diabetes is higher for women than for men.[9] This relates partly to greater abnormalities in women in other risk factors such as blood pressure associated with diabetes. Higher risk with diabetes could also reflect less aggressive approaches to treatment being used in women.

Abdominal adiposity

The INTERHEART study showed that the risk of myocardial infarction is associated particularly with the measure of waist circumference, rather than with body mass index (BMI), a finding that has emerged in a number of other studies. It is therefore recommended that abdominal circumference be measured as well as, or in preference to, BMI.[10] Abdominal adipose tissue is associated particularly with inflammatory cytokine release and abnormalities in hormonal levels that predispose to atherosclerosis.

Psychosocial factors

In the INTERHEART study, the risk of myocardial infarction associated with depression and other psychosocial factors such as social isolation was of the same order of magnitude as that associated with more conventional risk factors, such as dyslipidaemia, elevated blood pressure and smoking. This association was independent of other risk factors. An Australian systematic review came to a similar conclusion.[11]

Fruit and vegetable intake

Although the INTERHEART study found higher intake of fruit and vegetables to be protective against myocardial infarction, trials of such intervention are difficult to fund and to perform. However, the association with other risk factors, such as blood pressure, is well established.

Exercise

Physical activity is protective against CHD and results in decreased blood pressure, a more favourable lipid profile and less overweight. The current recommended level is at least 30 minutes of moderate activity, such as brisk walking, on most days.

Alcohol consumption

Results from the INTERHEART study showed alcohol consumption to be protective against myocardial infarction in older individuals. However, recent studies have been less conclusive than older epidemiological reports in establishing the level of this protection. This may relate to more effective control for confounding factors and higher overall quality of more recent studies. It is not recommended that individuals drink alcohol only to gain any protective effect against CHD. High alcohol consumption is also associated with elevated blood pressure.

At risk populations

Social, ethnic, cultural and geographic factors contribute to CHD risk. Aboriginal and Torres Strait Island peoples, for example, are at much higher risk than the general Australian population.[12]

CHD prevention

An approach to risk assessment

The absolute risk of future CHD and CVD events in the general population and subgroups is depicted in Figure 1. The concepts of absolute risk and relative risk are described in the box on page 17.

Estimation of absolute risk in order to distinguish high risk individuals in the general population is based on application of multivariate risk equations that weight for the importance of independent risk factors. Such equations are derived from longitudinal follow up of cohorts; those in current use in Australia are based on observations from the Framingham Heart Study, which was initiated in Massachusetts, USA, in 1948. The New Zealand cardiovascular risk calculator (www.nzgg.org.nz) and other online tools (e.g. www.absoluterisk.com) are also based on Framingham data.

There is a need to develop contemporary local risk equations that have been validated in different Australian subpopulations.[12] There is also a need to refine risk assessment by possible inclusion of additional important variables, such as psychosocial and socioeconomic factors, and to establish how best to deal with advancing age, which is the single most important driver of absolute risk. Present risk equations favour increased treatment of elderly patients (typically, after subclinical atherosclerosis has developed) and ignore the great number of quality life years that remain for younger individuals. This is particularly relevant as about one-third of

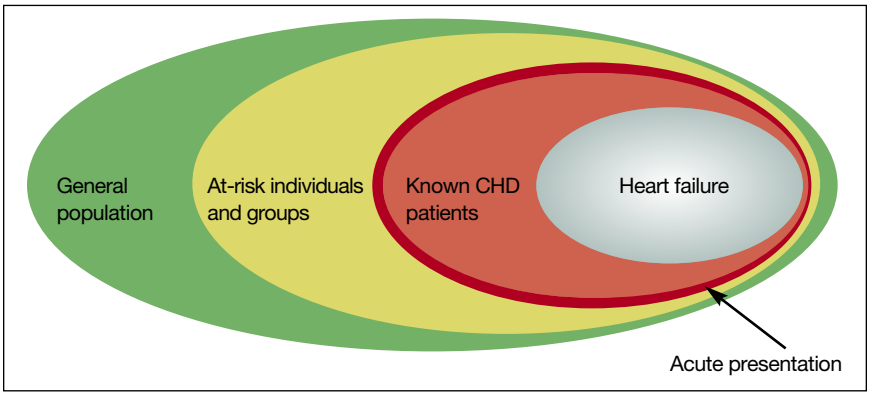


Figure 1. Absolute risk of future CHD or CVD events in the general population and subgroups. At-risk individuals are those with other diseases (e.g. diabetes, chronic kidney disease), extreme levels of risk factors, and Aboriginal and Torres Strait Islander peoples.

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first CHD presentations result in sudden death or fatal myocardial infarction.

Extreme levels of risk factors and age

Multivariate risk equations relate particularly to individuals who do not have extreme abnormalities of individual risk factors. In general, the Framingham equations should not be applied to people:

- under 20 or over 79 years of age
- with total cholesterol levels above 8 mmol/L, or
- who have blood pressure above 180/105 mmHg.

Diabetes

Risk of CHD events varies among people with diabetes. However, it has been established that important determinants of risk include:[14]

- length of time since diabetes was diagnosed
- dyslipidaemia (in particular)
- blood pressure
- adequacy of glycaemic control, as measured by HbA_{1c} level.

Recent changes to PBS criteria for eligibility for subsidy of statins in people with diabetes acknowledge the high risk in such patients. Furthermore, evidence supports the setting of aggressive targets for blood pressure[15] and LDL cholesterol and adequate glycaemic control[16] in such patients.

Chronic kidney disease

Patients with chronic kidney disease have a much higher risk of death due to CHD and associated conditions.[17] Potential novel risk factors for CHD in patients with chronic kidney diseases include homocysteine, markers of inflammation and oxidative stress, advanced glycation end-products and arterial stiffness and calcification. However, conventional risk factors are still important and guidelines recommend aggressive control of blood pressure, in particular. The value of statin therapy has been demonstrated for lesser degrees of renal impairment, but trials are ongoing to examine the place of these agents in chronic kidney disease. Future research must concentrate on the role of markers of kidney disease, such as microalbuminuria, in CVD risk assessment.

Aboriginal and Torres Strait Islander peoples

An alarming increase in age-specific mortality rates is occurring among Aboriginal and Torres Strait Islander peoples compared with the general population. CHD is the major reason for the difference in life expectancy, which is, on average, 15 to 20 years shorter for indigenous Australians. Care systems must address inequalities in access to, and delivery of, appropriate care and preventive measures to indigenous people.

Preventing CHD events: using absolute risk and relative risk

Absolute risk describes the actual risk of events occurring during a defined period of time in the future. It is usually expressed as a percent likelihood in the next five or 10 years. The concept of absolute risk is applied particularly to the assessment of risk in individuals who have not previously experienced clinical events, but it extends to all subgroups. The risk of future CHD events is highest in people who have already been hospitalised with diagnosed CVD.

Relative risk is an expression of risk relative to others of the same age and gender. For estimating CHD risk, relative risk is inferior to absolute risk because it excludes the two most important drivers of risk – age and gender. Therefore, absolute risk remains the method of choice for identifying patients who need aggressive treatment.

Clinical discord may occur between absolute and relative risk. Individuals with a high relative risk and moderate or low absolute risk are primarily protected by their relative youth, and they will eventually develop a high absolute risk if appropriate behavioural intervention such as the Smoking, Nutrition, Alcohol and Physical activity (SNAP) program is not commenced.[13] An approach to dealing with discord between relative risk and absolute risk is shown in Figure 2 below.

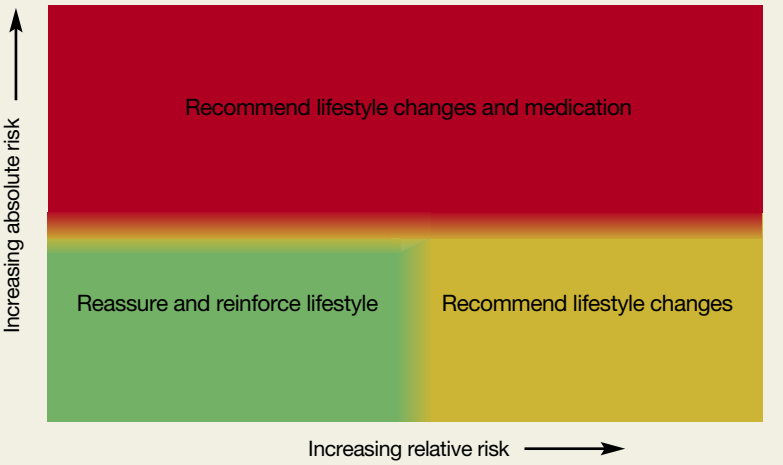

Figure 2. Discord between relative risk and absolute risk in an individual can occur. For example, a young woman with moderately elevated total cholesterol may be at low absolute risk but high relative risk of CHD (orange box). She is very unlikely to benefit from a statin or other drug and just as likely to have an adverse effect from medication; she should therefore simply receive behaviour modification advice.

Acute coronary syndromes

Unfortunately, surveys by the National Heart Foundation of Australia over the last 10 years have not shown any decrease in the median time to hospital presentation for people with possible myocardial infarction.[18] It is also disappointing that the delay in presentation is no different for those with a previous diagnosis of CHD compared with the general population. For patients with known CHD, GPs have a key role in assisting and reinforcing education about the need for early hospital presentation if they experience 10 to 15 minutes of chest pain that might herald the onset of myocardial infarction. Provision of an action plan for chest pain or discomfort, including advice about use of antianginal medication and emergency action, can assist such patients.

Patients with known CHD

An important analysis based on data linkage in Western Australia has shown that over a three-year period about half of all CHD deaths and nonfatal myocardial infarctions occurred in individuals who had been hospitalised during the previous 15 years with a diagnosis of CHD and remained alive (Michael Hobbs, personal communication). This observation mandates the need for systems such as CHD patient registries that might enable automatic recall and prescription of proven therapies to patients with CHD. Patient concordance remains a major challenge.

The evidence base supporting the use of aspirin (and clopidogrel ([Iscover, Plavix] in selected patients), statins (irrespective of cholesterol levels), beta blockers (particularly in patients with previous large myocardial infarction or associated heart failure) and ACE inhibitors in this context is one of the most robust in medicine.

Concluding comments

CHD is the principal health problem for Western countries such as Australia and is rapidly becoming so for other world regions. Genes may have a modulating role, but nearly all of the individual variations in risk for myocardial infarction relate to behavioural and environmental factors. Population-wide measures and aggressive treatment of high risk individuals are complementary approaches to tackling the very large toll exacted by CHD.[19] MT

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