1 The epidemiology of cardiovascular disease

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Introduction

Cardiovascular disease has become the world's major cause of death, responsible for one-third of total global deaths in 2001 and the expectation that by 2020 its continuing increase in incidence will result in it far exceeding all other causes of death and disability (Figure 1.1).[1]

Traditionally thought of as a disease of developed economies, cardiovascular mortality is now rapidly rising in developing countries, largely due to uptake of a Western lifestyle, including smoking and dietary habits. In 2001, some 80% of all cardiovascular deaths worldwide took place in developing, low- and middle-income countries, while these countries also accounted for 86% of the total global burden of cardiovascular disease.

Precise estimates of the prevalence and incidence of the major cardiovascular diseases, and of their time trends, are variably available. Existing registries, such as national mortality statistics or disease-specific hospital admission rates, do provide useful information, albeit with inherent limitations, of misclassification, changes in coding systems and lack of information on non-hospitalised patients. The initiation of long-term follow-up measurement of established population cohorts has provided insights into the occurrence of cardiovascular disease and development of cardiovascular risk factors over time. The most widely cited of these cohorts (Table 1.1)[2–11] is the Framingham Heart Study (FHS).[2]

The number of people at risk of cardiovascular disease is rising as average life expectancy increases and the economic, social and cultural changes that have led to increases in vascular risk factors continue. Of particular concern are the recent rapid rises in obesity in children and adolescents (Figure 1.2),[12] largely the result of increased caloric intake coupled with an increasingly sedentary lifestyle. This trend is predicted to increase rates of insulin resistance, which is central to a cluster of cardiovascular risk factors, and therefore add to the global burden of cardiovascular disease. Perversely, increased survival and better secondary prevention in patients suffering from cardiovascular events are further increasing prevalence of cardiovascular disease.

Although in developed countries cardiovascular disease will remain the main cause of disability and mortality, several favourable trends in the epidemic of cardiovascular disease

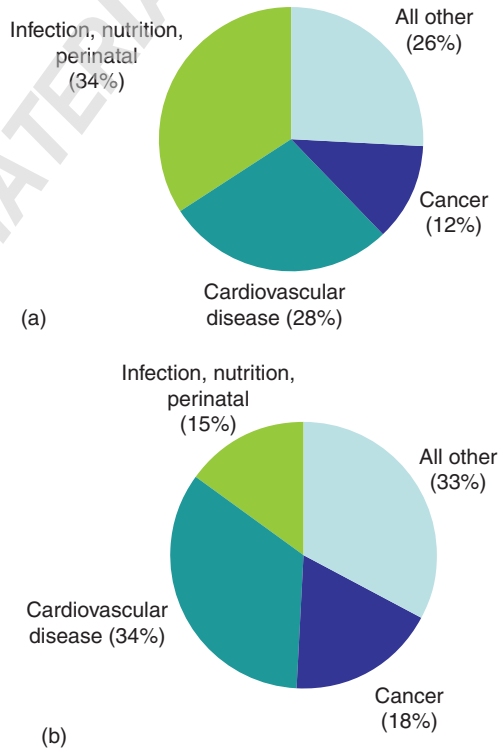

Figure 1.1 Distribution of major causes of mortality worldwide: (a) 1990 and (b) projected to 2020.[1]

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Table 1.1 Examples of population-based studies that increased the knowledge in the occurrence of and determinants of cardiovascular disease

Study	Countries	Numbers	Gender	Age	Period
Framingham Heart Study[2]	USA	5,209	M/F	30–62	1948–Present
Seven Countries Study[3]	Italy, Finland, Greece, Japan, Netherlands, USA, Yugoslavia	11,579	M	40–59	1957–Present
Study of men born in 1913[4]	Sweden	792	M	54	1963–Present
Whitehall Study[5]	England	17,530	M	20–64	1967–1977
PROCAM[6]	Germany	10,856	M	36–65	1978–Present
MONICA[7]	Worldwide	10 million	M/F	25–64	1980–1995
Cardiovascular Health Study[8]	USA	5,888	M/F	65+	1989–1999
Rotterdam Study[9]	Netherlands	7,983	M/F	55+	1990–Present
INTERHEART[10,11]	Worldwide	15,152 Case 14,820 Control	M/F	No age restriction, age range not available	1999–2002

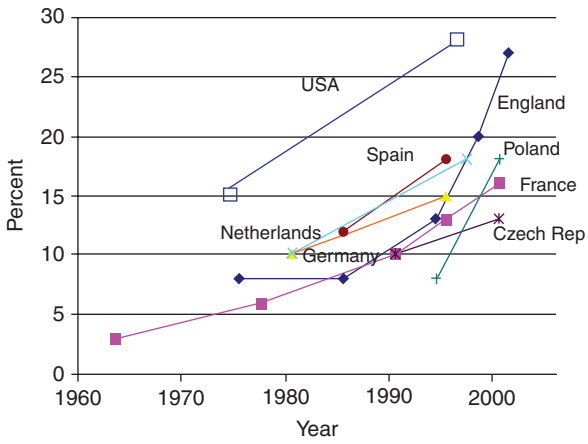

Figure 1.2 Rising prevalence of overweight children (5–11) in Europe in percentage. *Source*: Reproduced with permission from International Association for the Study of Obesity/International Obesity TaskForce.[12]

have been observed. These include a continuing decrease in the age-specific mortality rates from acute myocardial infarction (MI) since the 1970s[13] (Figure 1.3), and more recently and in fewer countries, a decrease in the number of hospitalisations for heart failure.[14,15] The former is primarily attributable to favourable changes in modifiable risk factors (both in individuals with or without manifest vascular disease) and increased availability of mortality-reducing interventions, such as thrombolysis and interventional procedures (percutaneous transluminal coronary angioplasty), and medications for treating hypertension, hyperlipidaemia and atherothrombosis.

Improved prognosis in patients with MI, together with the ageing population and improved therapy in patients with known heart failure, is a main contributor to the sharp increase in the number of hospitalisations for heart failure observed in Western societies in the 1980s and early 1990s. More recent analyses, however, show that this growth of heart failure may have reached its peak; a decline in hospitalisation rates were documented in several countries, including Scotland[14] and the Netherlands[15] (Figure 1.4). Improved care, including pharmacotherapy, is considered the cause of this positive trend.

Risk factors for cardiovascular disease may be present in childhood or early adulthood, but it may be decades before clinical disease manifests. Therefore, early identification of patients at risk coupled with provision of optimal risk management

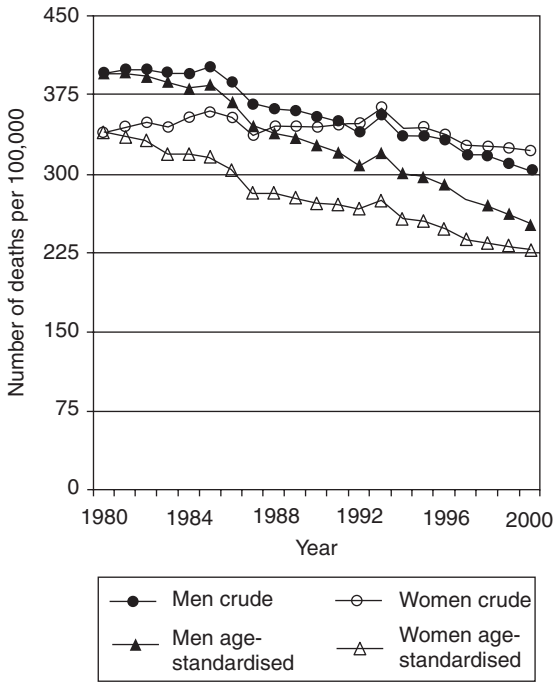

Figure 1.3 Decline in age-adjusted mortality from acute myocardial infarction in the Netherlands, 1979–2000. Mortality in 1979 was set at 100. *Source*: Reproduced with permission from statistics Netherlands. Ref. 13.

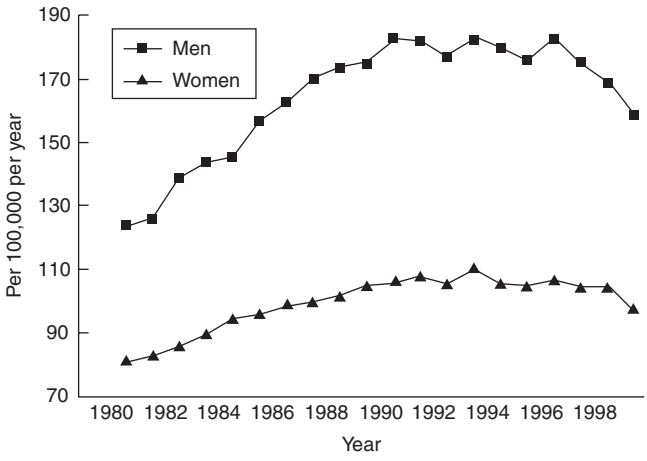

Figure 1.4 Age-adjusted discharge rates for heart failure, the Netherlands, 1980–1999. *Source*: Reproduced with permission from BMJ Publishing Group Ltd. Ref. 15.

is of vital importance in lowering the risk of cardiovascular morbidity and mortality and slowing disease progression. The reader is referred to the reference list for further background and statistics.[16–18]

Box 1.1 Classification of risk indicators

Major modifiable
- Blood pressure
- Blood lipids
- Glucose intolerance
- Cigarette smoking
- Physical activity
- Obesity
- Diet.

Non-modifiable
- Age
- Heredity or family history
- Gender
- Ethnicity
- Prior CVD.

Other modifiable
- Socioeconomic status
- Mental ill health (depression)
- Use of certain medication.

Proposed 'novel markers'
- Homocysteine levels
- Inflammatory markers (e.g. C-reactive protein)
- Blood coagulation (e.g. fibrinogen levels)
- Non-invasive measurements of atherosclerosis (e.g. carotid intima-media thickness, coronary calcifications on computerised tomography [CT] scan).

Box 1.2 Highlights of the main findings of the Framingham Heart Study[2]

- Cigarette smoking increases the risk of heart disease
- Switching to filtered cigarettes does not measurably reduce heart disease risk
- Some heart attacks are 'silent', or cause no pain
- The ratio of total cholesterol to high-density lipoprotein cholesterol (HDL-C) is a good predictor of risk
- High LDL-C leads to heart disease
- Low HDL-C leads to heart disease
- Obesity and inactivity increase the risk of heart disease
- Higher systolic or diastolic blood pressure increases the risk of heart disease

Risk factors for cardiovascular disease

Factors that indicate risk for coronary heart disease are well established (Box 1.1) with serum cholesterol, blood pressure and smoking identified as the three major modifiable risk factors as early as the mid-1950s.

The pivotal data came from the FHS,[2] which was initiated in 1948 to identify and evaluate factors influencing the development of cardiovascular disease in men and women free of these conditions at the outset (Box 1.2). In 1971 the Framingham Offspring study was initiated in children and spouses of the original cohort to study family patterns of cardiovascular

Box 1.3 Nine modifiable risk factors assessed in the INTERHEART study[10,11]

- Smoking
- Hypertension
- Diabetes/glucose intolerance
- Dyslipidaemia
- Obesity
- Physical activity
- Diet
- Alcohol consumption
- Psychosocial score

Box 1.4 Benefits associated with reducing blood cholesterol, blood pressure and smoking cessation

Serum cholesterol

- 10% decrease corresponds to a 30% decrease in risk of coronary heart disease.

Blood pressure

- 6 mmHg decrease in diastolic pressure > 90 mmHg (in patients with mild-to-moderate hypertension) results in a 16% decrease in coronary heart disease.

Smoking

- Cessation if cigarette smoking results in about a 50% decrease in risk of coronary heart disease.

Source: Based on data from Ref. 18.

disease and risk factors. In 2002 the Third-Generation Study began enroling grandchildren of the original enrolees.

Another important cohort of healthy men aged 40–59 years, the Seven Countries Study[3] (see Table 1.1), showed that cardiovascular risk is strongly related to both serum cholesterol and the proportion of saturated fatty acids in the diet.

Recently the INTERHEART study[10,11] confirmed that nine potentially modifiable risk factors (Box 1.3) were strongly associated with the development of a first MI by comparing patients with a first MI with asymptomatic individuals from 52 countries. The risk factors, including smoking, hypertension, diabetes, dyslipidaemia and obesity, accounted for 90% of the population risk of MI in all ethnic groups and across all geographical regions.

By the 1960s, the relationship between risk factor elevation and risk of coronary heart disease was so well established that intervention trials to determine whether reducing modifiable risk factors would reduce risk were initiated. Many studies have now established there are significant benefits to lifestyle changes and pharmacotherapy to reduce blood cholesterol, blood pressure and stop smoking (Box 1.4) both as primary prevention in at-risk individuals with no symptoms and as secondary prevention of recurrent events in patients with established cardiovascular disease.[19]

Calculating cardiovascular risk

The wider availability of interventions that can reduce cardiovascular risk offers the potential for preventing, modifying or delaying cardiovascular disease. However, in order to treat modifiable risk factors it is necessary to identify at-risk individuals. This is simple in patients who have suffered a cardiovascular event, such as the onset of angina, since they are symptomatic. Randomised trials have shown unequivocally that risk factor intervention in these patients is cost-effective.[20] However, risk assessment in individual patients without manifest cardiovascular disease is more complex because of the need to assess the impact of multiple risk factors.

Although the population at large would certainly derive benefit from interventions aimed at primary prevention of cardiovascular disease in all individuals, such 'population strategies' are outside the scope of medicine, though there are debates over the potential of 'polypill' strategies in all middle-aged people.[21] Health systems therefore need to identify those at greatest absolute risk of cardiovascular disease to prioritise management of those with most to gain – the 'high-risk strategy'. Using such risk estimation enables health systems to nominate a risk threshold above which people are eligible for intervention, based on the ability of that society to afford treatment, by limiting the population which is at most risk to above the cut-off.

Most countries now advocate the threshold to consider initiation of pharmacological intervention to be above a 10-year risk of major cardiovascular events of 20% (or coronary heart disease of 15%). Current European guidelines advocate a 5% cardiovascular disease *mortality* threshold based on fatal, as opposed to all, cardiovascular events.[22]

Several risk calculators have been developed to better predict an individual's absolute risk of experiencing a cardiovascular event over a given period of time (e.g. 10-year risk of cardiovascular disease or coronary heart disease).[23] Currently, the most widely used risk charts and tables are based on the Framingham risk equation, using data from the FHS. Other risk algorithms have been developed, such as the Prospective Cardiovascular Munster Heart Study (PROCAM),[6,24] based on a German population. However, due to these studies being based on small populations, the risk charts have limitations (Box 1.5).

More recently, the European Systematic Coronary Risk Evaluation (SCORE) charts were created to address some of the limitations of existing risk prediction systems.[25,26] SCORE is based on asymptomatic individuals from 12 European cohort studies with no evidence of pre-existing cardiovascular disease. Studies across multiple countries enabled charts to be drawn up for high- and low-risk countries, and because atherosclerotic

Box 1.5 The limitations of the Framingham study as a basis for risk calculators

- Participants were mainly North American, Caucasian participants of certain socio-economic class.
- Therefore, applicability to different ethnic and socio-economic groups is uncertain, for example, risk calculators overestimate risk in European populations.
- Does not incorporate all risk factors.
- Some endpoint definitions differ from those used in other studies and the choice of endpoints has changed over time.

cardiovascular disease mortality was the endpoint, these charts are expected to provide more accurate estimates of overall cardiovascular risk than algorithms predicting all cardiovascular events.

Risk calculators should be used as part of an overall strategy to identify and assess which patient is at risk and the level of treatment they require.

Guidelines for cardiovascular risk management

To effectively forestall the rising incidence of cardiovascular disease, national efforts must be made to modify lifestyle trends. To do this, strategies to reduce risk factors should be taken into account in public policy and education. In addition, identification of high-risk patients and intervention, often including drug treatment, is crucial.

In the past decade, a large number of guidelines for cardiovascular disease prevention have been developed by professional organisations and national societies to guide health professionals. These guidelines have incorporated evidence from landmark clinical trials to produce 'evidence-based' recommendations as well as using other lines of evidence – epidemiological studies, clinical experimentation and expert judgement.

Most guidelines recommend thresholds (when to start treatment) and target levels for certain modifiable risk factors (Box 1.6) and using therapies for achieving these goals for individuals at different levels of risk. Reducing low-density lipoprotein cholesterol (LDL-C) and blood pressure are the most frequently recommended treatment goals.

Specific populations

Guidelines that account for different populations are key as various non-modifiable factors may strongly influence an individual's cardiovascular risk. Factors such as age and sex are well established as influencing an individual's risk. Ethnicity is also important: specific factors confer additional cardiovascular risk, for example, in migrant South Asians the combination of genetics and acquired insulin resistance promotes the metabolic syndrome and increases vascular risk.

Box 1.6 Risk factors for which guidelines provide recommended treatment goals

- Cigarette smoking
- Serum lipid levels
  - LDL-C
  - Total cholesterol
  - Total cholesterol: HDL-C ratio
- High blood pressure
- Obesity/overweight
  - Body Mass Index/waist circumference
- Atherogenic diet
- Physical inactivity/sedentary lifestyle.

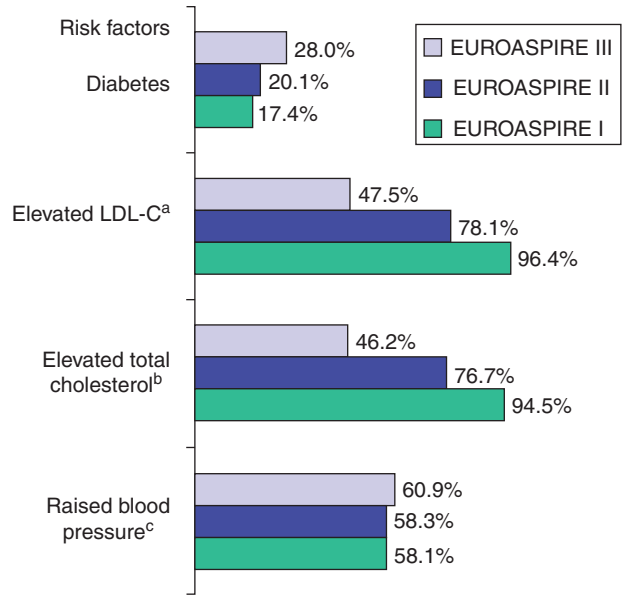

Figure 1.5 Results of the EUROASPIRE I, II and III surveys. *Source*: Prevalence of modifiable risk factors in coronary patients interviewed in EUROASPIRE surveys. Ref. 29.

Implementation of guidelines

Successful implementation of risk-reducing strategies remains patchy. The European Action on Secondary Prevention through Intervention to Reduce Events Surveys I and II (EUROASPIRE I and II)[27,28] showed that although 85% of physicians reported using risk assessment tools/guidelines, there was still a high prevalence of modifiable risk factors in coronary patients (Figure 1.5) and inadequate use of prophylactic therapies across

Europe. Results of the EUROASPIRE III survey reported at the European Society of Cardiology 2007 Congress[29] showed that despite impressive increases in the use of cardiovascular medications, smoking levels have remained the same or increased in some groups, body weight has dramatically increased and the prevalence of diabetes has risen since the first survey. Blood pressure management has shown no improvement since the EUROASPIRE surveys started.

EUROACTION is the first pan-European project which aimed to raise the standards of preventive cardiology in Europe by demonstrating that the Joint European Societies' Guidelines on lifestyle, risk factors and therapeutic goals for cardiovascular disease prevention can be realised in everyday clinical practice thus closing the gap between guidelines and practice. The results of EUROACTION showed that a nurse-led multidisciplinary team approach, coupled with the support and involvement of a patient's partner and family, can yield significant improvements in lifestyle and risk factors compared to usual care.[30]

Conclusion

Cardiovascular disease is a major and increasing health issue worldwide. It reduces quality of life and is the commonest cause of premature death in the middle-aged population but is substantially modifiable, with reduction of risk factors proven to reduce cardiovascular events. Guidelines for cardiovascular disease prevention have been developed by professional organisations and national societies to guide health professionals to this goal. However, successful implementation of prevention strategies remains poor.

One reason for the lack of full and effective implementation of official recommendations is reported to be the plethora of guidelines that physicians are confronted within clinical practice. This chapter is the first in a book that aims to provide a practical guide for primary care physicians on the key guidelines on cardiovascular risk management and to illustrate the use of these guidelines.

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