CORONARY HEART DISEASE

The scope for prevention

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Office of Health Economics

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Introduction

One person in every four in England and Wales dies from coronary heart disease and at a minimum estimate the costs borne by the National Health Service in its treatment amount to £255 million. But of greater significance is the fact that it is a major cause of premature morbidity and mortality. Surveys indicate that at least one man in two will show evidence of diseased coronary arteries by the age of 65 years (Morris 1975) and that 38 per cent of the 73,000 male deaths between 30 years and retirement age are attributable to this cause. Among men in the age range 45 to 54 this proportion rises to 41 per cent.

Coronary heart disease is the collective term given to various symptomatic manifestations which are the result of injurious processes occurring in the coronary arteries. The latter become narrowed with consequent impairment of blood flow and hence supply of oxygen to the heart's muscle. These developments may give rise to a spectrum of events from angina through myocardial infarction to sudden death.

The disease processes involved have yet to be established. Epidemiological investigation has nevertheless uncovered a number of behavioural and other factors which appear to predispose to a greater likelihood of the development of symptomatic illness. Of these, cigarette smoking, elevated serum cholesterol levels and raised blood pressure have emerged as the most significant – together they can increase by eight-fold the chances of a 'coronary event'. Estimates suggest that about 20 per cent of men and women aged 30–49 have two or more concurrent major risk factors predictive for the disease (RCGP 1981b).

In spite of the aetiological uncertainties surrounding coronary heart disease the last decade has witnessed unprecedented advance in the potential for therapeutic intervention. Beta blocking drugs in conjunction with other medicines, now provide highly effective control of anginal pain in about three-quarters of patients. For more severe cases the development and refinement of coronary artery bypass surgery has facilitated relief for medically uncontrollable symptoms and in some instances substantially improved survival prospects. Before the 1970s there was little evidence to suggest that any specific therapeutic measure might be of value in reducing morbidity and mortality after myocardial infarction and many patients were simply subjected to prolonged periods of bed rest. Benefits in this area have since been shown to accompany the employment of aspirin, sulphinpyrazone, beta blocking drugs, thrombolytic agents such as streptokinase and a selective use of bypass surgery.

Continued thorough evaluation of these new therapeutic options should make it increasingly feasible to devise appropriate treatment strategies for most heart attack patients coming to care,

with significant savings in terms of both lives and subsequent coronary episodes. It requires emphasis, however, that in coronary heart disease all measures currently available or under investigation are only effected once the disease process has become manifest and as such they are not 'cures' but means of symptomatic relief and, hopefully, secondary prevention.

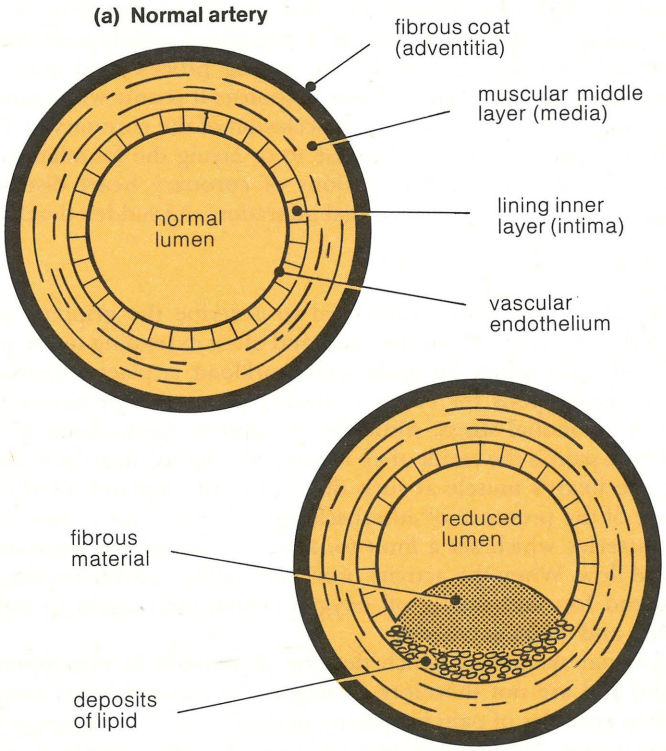
In spite of such promising therapeutic developments, primary prevention therefore constitutes the optimal approach to the management of the disease. This observation is also founded on the substantial treatment and social costs of coronary heart disease, the fact that the benefits of potentially valuable new treatments have so far only been demonstrated in highly selected patient samples, the side effects and risks associated with all medical and surgical interventions and the finding that in some 20 per cent of cases of coronary heart disease there is no contact with physicians at all, the first recognised occurrence being sudden (and often premature) death (Rose 1981). Yet recent mortality and morbidity trends suggest that, in sharp contrast to other countries such as the United States, relatively little has been achieved in this field in spite of the initiatives of many agencies including the UK Departments of Health. Following a detailed review of the current understanding of the nature of coronary heart disease and its epidemiology, this paper examines the issues surrounding the problems of primary prevention and explores the possibilities for more successful interventions in the future.

The nature of coronary heart disease and its occurrence

The heart is essentially a pump which circulates blood throughout the body by means of electrically-stimulated contractions of its muscle, the myocardium. The latter is the principal constituent of the wall of the heart and, like all other cells and muscles, is dependent on a continuous flow of blood if it is to function efficiently and survive. The heart muscle receives its blood supply before any other part of the body via arteries situated at the base of the aorta. Blood is initially channelled through three major arteries and is then distributed throughout the myocardium by a complex network of progressively smaller vessels. Any interruption of the normal circulation of blood in the heart will deprive the muscle of its supply of oxygen and essential nutrients and may give rise to a spectrum of consequences from minor transient discomfort to death depending on the extent and duration of the restriction of the myocardial blood flow.

In coronary heart disease such interruptions result from a number of processes including those which lead to a thickening of

Box 1 *The development of atheroma*



The initial stage in the evolution of atheroma involves damage to the endothelial lining of the vessel. The normal response to any such damage – which occurs most readily at points of stress or turbulence – is for platelets quickly to adhere to the area, covering and protecting it whilst it is repaired. In atheroma, it seems that this process fails to self limit. Aided by the high hydrostatic pressure, both platelets and lipids infiltrate the inner layer, beneath the endothelium, and release chemicals which induce smooth muscle cells to migrate from the middle to the inner layer of the vessel. This process can halt if new endothelium overgrows the plaque, but the narrowing of the arteries is irreversible and there is some loss of elasticity. More often, however, the process continues and may be complicated by becoming the focus of an intravascular thrombosis, which further narrows the lumen. In the end calcification and fibrosis (scarring) occur. Thus the mature atherosclerotic lesion, as it is now called, is not only occlusive but inelastic and thus incapable of dilating.

Source Burt *et al* 1982a.

the intima layer of the artery walls thereby narrowing the bore (lumen) of the vessels at the affected sites.[1] These lesions are patches of atheroma, consisting of deposits of lipids (fatty materials, including cholesterol) and scar tissue (see Box 1). The accumulation of some atheroma in the blood vessels is an almost inevitable accompaniment of the ageing process and does not necessarily invoke a symptomatic response. It is only when atherosclerosis is advanced that severe occlusion of the coronary arteries is more likely to occur, giving rise to or laying the foundation for the three principal manifestations of coronary heart disease – angina pectoris, acute myocardial infarction and sudden death.

Angina

Angina pectoris is the term used to describe the gripping pain experienced primarily in the chest and often extending to the neck and left arm when an additional workload is placed upon the heart, as happens for example during physical exertion or profound emotional stress. Although the precise mechanisms are ill-defined, pain is the result of an inadequate supply of oxygen reaching the heart's muscle at such times of extra demand usually because of the presence of atherosclerotic obstructions in the coronary arteries which set a limit to possible increases in myocardial blood flow. When the activity precipitating the episode ceases, the demand for, and supply of, oxygen return once again to equilibrium and the pain recedes.

Anginal symptoms which develop in persons at rest (often at night) and are not therefore prompted by a raised heart rate, as well as episodes of pain increasing in their frequency or severity of presentation, are together referred to as 'unstable' angina in order to differentiate them from their stable counterpart described above. Research in the 1950s by Prinzmetal and his colleagues (1959) suggested that a proportion of these events might result from the temporary occlusion of a diseased coronary artery due to a 'normal increase in tonus of the vessel wall'. Further investigations, notably by Maseri and his colleagues (1975, 1977), suggest that coronary artery spasm occurs more frequently than has hitherto

1 Impairment of the blood flow in the coronary arteries can be visually displayed by coronary arteriography. The technique, pioneered in the United States 20 years ago, involves the insertion of a catheter into either the brachial (Sones and Shirey 1962) or femoral artery (Judkins 1967) and its subsequent advancement to the aorta just above the heart. Radiographic contrast solution is then selectively injected into the coronary arteries which are filmed in several different projections to reveal the extent of any arterial occlusion. The hazards associated with the technique are now very low in experienced centres – an American collaborative study has recently reported death and non-fatal infarction rates among investigated patients of 2 and 2.5 per 1,000 respectively (Davis *et al* 1979) – and are largely confined to patients already at high risk of sudden death or myocardial infarction.

been recognised and that it may develop in vessels devoid of atherosclerotic disease. In the context of the last point, available data indicate that about 10 per cent of patients with angina have normal coronary arteries or no critical lesions (Maseri 1980). Coronary vasoconstriction may be induced by a variety of stimuli including exposure to cold temperatures, drugs such as ergonovine, withdrawal from prolonged industrial exposure to nitroglycerine and possibly emotional stress (*Lancet* 1980a) and work is now being directed at understanding their mode of action: proposed explanations include alpha adrenergic stimulation, thromboxane release and local prostacyclin deficit but none has been convincingly demonstrated (*Lancet* 1981a).

Myocardial infarction

The second major manifestation of coronary heart disease is acute myocardial infarction. Sustained loss of blood supply to any part of the myocardium rapidly leads to a cessation of normal contraction and is followed by death of the muscle in the affected area. The extent of this myocardial destruction has been shown to be an important determinant of the prospects for survival and further morbidity (Sobel *et al* 1972). The pathogenesis of acute myocardial infarction has, however, remained a source of debate for many years. The principal area of contention concerns the role of thrombosis: it has been argued that the formation of thrombi over atheromatous plaques is the principal cause of occlusion in the coronary artery lumen leading to myocardial infarction whilst others demote thrombosis to the status of a secondary consequence of the real events in the myocardium. (The prevalence of thrombotic coronary occlusion in myocardial infarction has been shown by Davies and co-workers (1976) to range from 30 to 97 per cent.) Evidence is available to support both points of view although it is also possible that the dispute to some extent reflects inappropriate comparisons of findings derived from investigations of dissimilar pathological entities.

Alongside this continuing debate consideration is increasingly being given to the role of thrombosis in the formation of atheroma. This represents a potentially important shift in atherosclerosis research which, during the past 30 years, has become 'almost synonymous with research on lipid and lipoprotein metabolism' and has failed to include investigation of haemostatic factors in epidemiological and clinical trials (*Lancet* 1981). Thus Meade and his colleagues (1980), for example, have described a 'hypercoagulable state' – reflecting elevated blood-clotting factors and fibrinogen levels – which appears to be associated with an increased risk of cardiovascular death. The authors postulated that these 'abnormalities' may be influential in terms of both the for-

mation of occlusive thrombi[2] and the development of atheroma. Focusing on the latter, immunohistochemical demonstration of fibrin layering in atherosclerotic plaques (Woolf 1978) appears to substantiate Duguid's (1946) contention that repeated mural thrombosis contributes to the growth of such lesions.

Contemporaneously, support has been gathering once again for the concept (which may be traced back to the work of Rokitansky in the previous century) that platelet deposition is important in the initiation of atheroma (*Lancet* 1981b). This 'revival' stems from the discovery of a substance in platelet granules capable of stimulating smooth-muscle proliferation which in turn constitutes an early lesion in the atheromatous blood vessel wall. Research suggests that platelet deposition is influenced by the interaction of thromboxane produced by platelets and prostacyclin generated in the vessel wall. Although both originate from the same system of synthesis, the former is a powerful aggregatory agent whereas the latter is a potent antiaggregatory vasodilator substance and it is postulated that disturbance of the natural state of equilibrium between the two might induce thrombogenesis (Moncada and Vane 1979). Much of this field of investigation is highly speculative at the present time. In addition Mitchell (1981a) has emphasised that not all platelet behaviour is dependent on prostaglandin pathways and that a system's existence does not necessarily mean that it is concerned in physiological or pathologic events. Nevertheless, continued research both here and more generally into thrombosis might be expected to generate findings which, synthesised with those derived from other investigations of atherosclerosis, should promote a better understanding of the aetiology of myocardial infarction as well as therapeutic advance.

Sudden death

The last of the three principal manifestations of coronary heart disease is designated 'sudden death' although use of the term frequently confuses two pathologically distinct entities. Post mortem examinations indicate that the majority of patients placed in this category show no evidence of occlusive thrombosis but have instead severe coronary atheroma, generally with over 85 per cent stenosis of the major vessels (Davies 1982). Death is usually the result of spontaneous ventricular fibrillation (although vasospasm may be a factor in some cases) and may be defined as 'sudden and unheralded' (Mitchell 1978) in order to differentiate such occurrences from fatalities occuring suddenly after infarction due, for example, to extensive myocardial necrosis leading to pump failure. The incidence of occlusive thrombi in sudden death

2 Fibrin is a significant constituent of most occlusive thrombi and fibrinogen concentration is a major factor in determining blood viscosity, increases in which may lead to impaired blood-flow including nutritive flow in tissue capillaries (*Lancet* 1981).

demonstrates considerable variation but is estimated to be on average around 30 per cent (Davies 1982).

Broadly defined sudden death has been shown to account for a significant proportion of overall coronary heart disease mortality. A study of all recorded heart attacks (comprising infarction, sudden death and acute coronary insufficiency) in persons aged 65 years or less residing in the London Borough of Tower Hamlets (Tunstall Pedoe *et al* 1975) found that 45 per cent of male cases had died within one year of the attack. Thirty-eight per cent of cases had died within 28 days[3] and 26 per cent had either died and were certified outside hospital or were dead on arrival at casualty. Further analysis revealed that of the deaths within 28 days, 70 per cent had probably occurred within 4 hours of the onset of the heart attack, 60 per cent within one hour and 50 per cent within 15 minutes.

Prognosis of coronary heart disease

Investigations of samples of patients undergoing repeated arteriography suggest that the extent of atherosclerosis in the coronary arteries frequently increases over time. For example, a study of 262 patients with at least 50 per cent obstruction in one or more coronary arteries at initial examination found that almost half of the sample satisfied the criteria for progression at recatheterisation 2 to 18 months later (Kramer *et al* 1981). Regression of atheroma, on the other hand, occurs relatively rarely; in a series of 256 non-operated patients receiving coronary arteriography twice, it was demonstrated in only 4.7 per cent of cases (Bruschke *et al* 1981). These data have to be interpreted with care: they generally refer to a highly selected sample of the total population; study time horizons will inevitably be an important influence on findings; arterial obstruction and subsequent changes can be subject to measurement inaccuracies; and indices of progression and regression do not necessarily reflect alterations in symptoms experienced by patients. Relatively few individuals have undergone arteriography; thus information concerning the progress of coronary heart disease has largely to be drawn from follow-up studies of patients presenting with the different manifestations of the disease.

Focusing on myocardial infarction the Tower Hamlets study suggested that 62 per cent of male and 54 per cent of female cases were alive one month after experiencing a coronary heart attack. Following this critical high risk period it may be estimated that of 100 patients who survive to leave hospital between 10 and 20 per cent will die within one year (*Lancet* 1981c). Subsequent mortality

3 A similar study undertaken on Teesside which included both men and women and covered all age groups found a moderately higher 28 day fatality rate of 50.5 per cent (Colling *et al* 1976).

among survivors falls to about five per cent per annum.[4] Expressed in a different way, the survivor of an acute infarction is about 30 times more likely to die in the first year than is a healthy man of comparable age (BMJ 1979); this excess risk declines with the passage of time and after 10 years the ex-patient and his healthy peer have equal survival prospects. The non-fatal sequelae of acute myocardial infarction include angina in approximately half the survivors (60 per cent of these cases developing it for the first time) and an increased risk compared with the general population for other cardiovascular disease (Kannel and Sorlie 1977).

In the case of stable angina Sorlie (1977) for example has shown that the cumulative probability of death for the five year period after diagnosis for men of all ages is 17.4 per cent and for women 11.4 per cent, each more than double that for those of the cohort previously free of the condition. Furthermore, data from the Framingham Study indicate that about 50 per cent of men over 45 years of age sustain a myocardial infarction within eight years of the onset of angina, twice as many as expected from the general population (Kannel and Feinleib 1972). It is also recognised, however, that angina may disappear temporarily or even permanently in some cases but there are no data to indicate the frequency of such improvements.

Investigations of unstable angina have generated a spectrum of often incomparable findings. Apart from the problems of reconciling the variety of concepts examined and those presented by differences in the stage of disease at which trial inclusion takes place, the description of the pain and the availability of supporting evidence from ECG and coronary arteriography vary greatly between series. Nevertheless, Duncan and her colleagues (1975) reviewed the 6 month prognosis of new and worsening angina in 251 males under 70 years referred by general practitioners to a special hospital clinic and observed the development of serious cardiac complications in 15.5 per cent of cases. Further analysis indicated that such complications arose in only a marginally greater proportion (17.2 per cent) of cases with recurrences or exacerbations of angina (which constituted almost half the sample). Over the longer term, prognosis has been shown to deteriorate: several studies have reported incidence rates of approximately 30 per cent for myocardial infarction or death and between 30 and 40 per cent for persistent angina within two to three years after an episode of

4 Of course, these estimates, while providing a broad picture of the outcome of myocardial infarction, disguise important patient subgroup disparities. Thus for uncomplicated, initially hospitalised events, Jelinek and his colleagues (1982) found one and three year mortality rates of 4.5 and 7.3 per cent respectively and recurrent heart attack rates of 8.2 and 18.5 per cent. Theroux *et al* (1979) found that infarct patients showing no change in ST segment during exercise testing prior to discharge from hospital had a one year mortality of 2.7 per cent compared to 27 per cent among patients who developed ST segment depression on the treadmill.

angina at rest associated with electro-cardiographic changes (Bulkley *et al* 1982).

Incidence

By the age of 40 years nearly all persons have developed patches of atheroma in the coronary arteries but generally they are too small to interfere seriously with the blood supply to the heart muscle and may only be detected at post mortem in persons dying from other causes. However, Morris (1981) has calculated that perhaps 50 per cent of men in their forties, fifties and sixties develop coronary heart disease and that in half of these cases it may be regarded as either very or potentially serious. A similar order of magnitude has been established by other observers: Silman (1981), for example, has calculated, that by the age of 65 years, 45 per cent of males will have acquired some form of coronary heart disease.

Reliable incidence data are in fact in short supply because few studies reflecting first manifestations of all coronary events which are also representative of the population as a whole have been undertaken. An important exception and hence much valued source of information is provided by the Framingham (Massachusetts) Study which was commenced in 1948 and has subsequently followed for 20 years, via biennial examinations, a sample of residents who were initially free of cardiovascular disease. The principal findings are contained in Table 1. In broad

Table 1 *Average annual incidence of coronary heart disease in the Framingham population previously free of the disease, rates per 1,000 population*

Age	*Sudden death*	*Myocardial infarction*	*Angina pectoris 'uncomplicated'*	*Coronary insufficiency*	*Total coronary heart disease*
MALES					
35–44	0.3	1.9	0.8	0.9	3.9
45–54	1.0	4.3	2.7	1.1	9.1
55–64	2.7	9.3	7.5	1.1	20.6
65–74	1.3	11.6	5.6	1.9	20.4
FEMALES					
35–44	0.0	0.2	0.4	0.1	0.7
45–54	0.2	0.8	1.5	0.3	2.8
55–64	0.4	1.8	5.8	1.3	9.3
65–74	1.4	3.4	6.5	1.1	12.4

Note 'Coronary insufficiency includes cases of coronary heart disease where the symptoms appear to be more severe than those of angina pectoris but less so than those of myocardial infarction. It often manifests itself as variable or progressively worsening forms of angina and therefore is frequently alluded to in the medical literature as unstable angina pectoris.'

Source Hartunian *et al* 1981.

Table 2 *Incidence of coronary heart disease, males and females by age, England and Wales 1971/72, rates per 1,000 population*

	Males			*Females*		
Age	*Acute myocardial infarction*	*Angina of effort*	*Other coronary heart disease*	*Acute myocardial infarction*	*Angina of effort*	*Other coronary heart disease*
15–24	0.1	0.1	—	0.1	0.1	0.1
25–44	1.2	0.8	0.5	0.4	0.5	0.0
45–64	9.1	7.7	5.7	2.6	4.9	2.5
65–74	17.3	14.7	6.5	6.0	12.3	7.2
75+	13.4	11.4	12.4	8.9	10.8	10.3
All ages	4.1	3.4	2.3	1.8	3.0	1.9

Source Royal College of General Practitioners, 1979.

terms they indicate that the incidence of coronary heart disease is considerably greater in males, that the frequent mode of presentation is myocardial infarction among males and angina among females, and that incidence increases with age for both sexes.

Incidence patterns of a similar nature have emerged from the Second National Survey of Morbidity in General Practice undertaken in England and Wales in 1971–72 (RCGP 1979). Applied to population data for 1980, the rates shown in Table 2 imply approximately 400,000 new cases per annum – an all ages incidence rate of 8.2 per 1,000 population. Within this total, 30 per cent of cases are attributable to males aged 45–64 years.

Data from both the Framingham Study and the sample of general practices in England and Wales suggest that myocardial infarction accounts for between 40 and 50 per cent of new manifestations of coronary heart disease among males in the 45–64 age range. This specific presentation has in fact been the subject of several epidemiological investigations in Britain. Thus Armstrong and co-workers (1972) found a coronary attack rate among Edinburgh men aged 40–69 years of 15.5 per 1,000. In contrast a rate of between 6 and 7 per 1,000 has been reported for a corresponding cohort in Oxford (Kinlen 1973). Between these extremes the Tower Hamlets Study (Tunstall Pedoe *et al* 1975) found a coronary heart attack (definite/possible episodes of cardiac infarction and acute coronary insufficiency as well as sudden death) rate of 10 per 1,000 for males aged 45–64 (2.7 per 1,000 for females in the same age group). Confining attention to definite acute myocardial infarction reduces the former rate to 7 per 1,000. The latter implies a total of 38,000 acute myocardial infarctions in England and Wales in 1980, a figure which appears broadly compatible with the Hospital Inpatient Enquiry (HIPE) estimate of 31,000 hospital admitted cases in 1978.[5]

Prevalence

It is not possible to calculate precisely the size of the population suffering from coronary heart disease. The fact that some individuals remain asymptomatic, sometimes in spite of the presence of relatively advanced atheromatous lesions, indicates that traditional measures of health service usage are likely to understate the true numbers involved. In the United States estimates suggest that investigation such as exercise testing, would uncover evidence of disease in about 10 per cent of asymptomatic males over 40 years with perhaps one-third of these having at least 50 per cent stenosis of one or more coronary arteries (Bridgers 1980). In this country a screening survey for cardiorespiratory disease and diabetes among 18,403 male civil servants aged 40–64 years (Reid *et al* 1974) found that only 23 per cent of those whose questionnaire replies suggested the presence of angina were under medical care.

The latter study does in fact provide one of the most detailed analyses of the prevalence of coronary heart disease. The authors found a combined prevalence of about 22 per cent for symptoms of chest pain and ischaemic changes based on electrocardiographic evidence among males aged 60–64 years. For the 40–49 and 50–59 age groups the prevalence rates were 11 and 17 per cent respectively. Extrapolating these findings to males in all occupations suggests that in England and Wales approximately 16 per cent of males aged 40–64 years are affected by coronary heart disease as defined above. This proportion is equivalent to approaching 1.1 million individuals, a figure which points up the limitations of health service usage data: the Second Survey of Morbidity in General Practice suggests that perhaps 190,000 males aged 45–64 years visit their GP at least once during a given 12 month period for coronary heart disease and the Hospital Inpatient Enquiry shows that admissions resulting from this cause among the same population totalled 50,000 in 1978. Thus together, ignoring questions of overlap, these two populations only account for between one-fifth and one-quarter of the estimated prevalence among males aged 45–64 years.

5 These data will lead to some degree of understatement for a number of reasons, notably the exclusion of unrecognised infarctions. An Israeli 5 year follow up study of male government employees aged 40 years or more reported that these events – diagnosed from positive electrocardiogram findings in the absence of historical or other evidence – accounted for 40 per cent of infarcts during the investigation period (Medalie and Goldbourt 1976). In half of these cases patients had no recollection of symptoms or illness whilst in the remainder there were atypical symptoms which were not associated with a heart attack. The study therefore suggests that for every clinical infarct detected there is probably one unrecognised episode in the same population.

Mortality from coronary heart disease

The Office of Population Censuses and Surveys' analysis of mortality in England and Wales indicates that diseases of the circulatory system accounted for 290,395 deaths in 1980, equivalent to half of all mortality in that year. Within this classification 154,371 deaths (53 per cent) stemmed from coronary heart disease. (Sixty-nine per cent of these fatalities involved acute myocardial infarction and a further 12 per cent were attributed to coronary atherosclerosis.) For every three female fatalities from this cause there are approximately four male deaths at all ages but more than eleven below the age of 65 years.

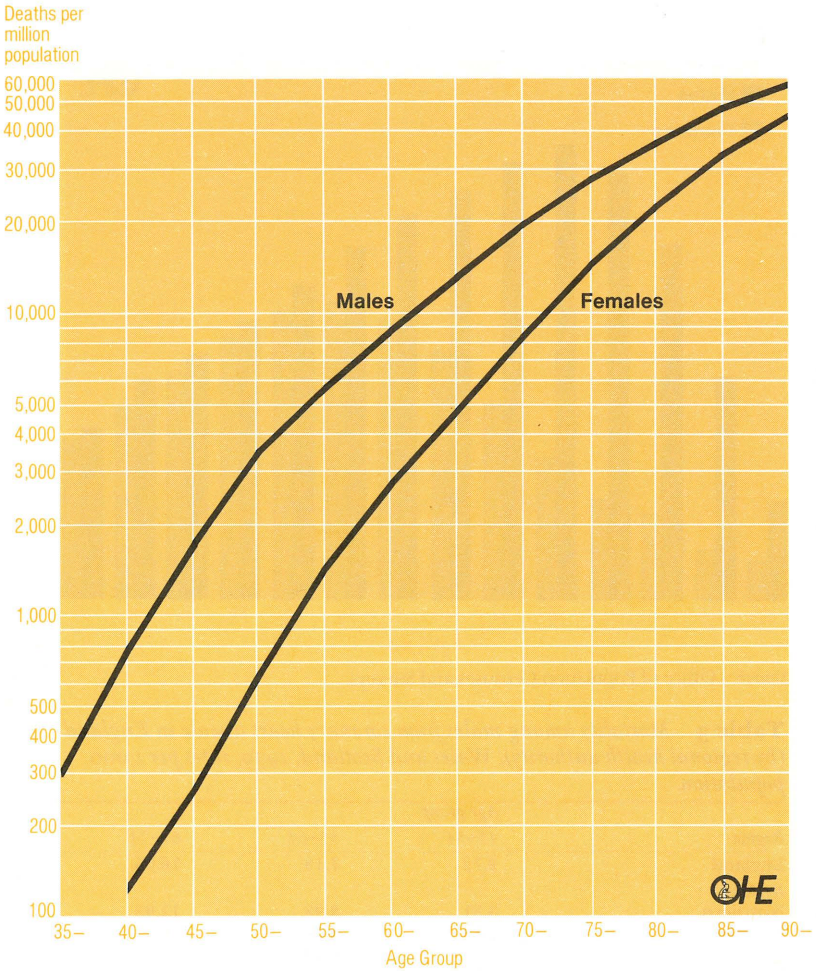
Coronary heart disease fatality rates for both sexes increase progressively with age (Figure 1): the rate for males aged 75–84 years, for example, is approximately double that prevailing for the preceding 10 year age grouping, four times that for males aged 55–64 and 11 times the 45–54 rate. Nevertheless almost one-quarter of coronary heart disease deaths involve persons yet to reach 65 years of age. Consequently, the disease makes a substantial contribution to premature mortality: it accounts for one-third of male deaths before the age of 70 years and slightly in excess of one fifth of female mortality before 75 years. Figure 2 shows that these proportions do in fact vary substantially with age. Thus for males between the ages of 45 and 54 years more than two out of every five deaths are the consequence of coronary heart disease.

Officially collected data also indicate that regional differences exist in mortality from coronary heart disease. In England and Wales, the standardised mortality ratio for females in 1979 was 50 per cent greater in the Northern Regional Health Authority than in North West Thames. For males, the excess of the worst region (North Western) over the best (South West Thames) was 34 per cent. Table 3 shows that for males the regional disparities are particularly pronounced at ages 45–54 years and that for all three age groups mortality tends to be higher in the northern regions and reaches a peak in Scotland.

There are in addition marked discrepancies in coronary heart disease mortality by social class. Figure 3 shows that among males aged 15–64 years in 1970–72, the latest year for which information is available, the standard mortality ratio for unskilled classes was 26 per cent greater than that for the professional groups.[6] Thus,

6 A recent occupation based analysis of the data contained in the Whitehall study of civil servants confirms this broad pattern (Rose and Marmot 1981). Age adjusted coronary mortality rates at seven and a half year follow up ranged from 1.07 per cent in the administrative grade, through 2.29 and 3.36 per cent for the professional/executive and clerical groups respectively, to 3.89 in the lowest grade of employment.

Figure 1 *Age specific death rates per million population for ischaemic heart disease (ICD 410–414), 1980, England and Wales.*



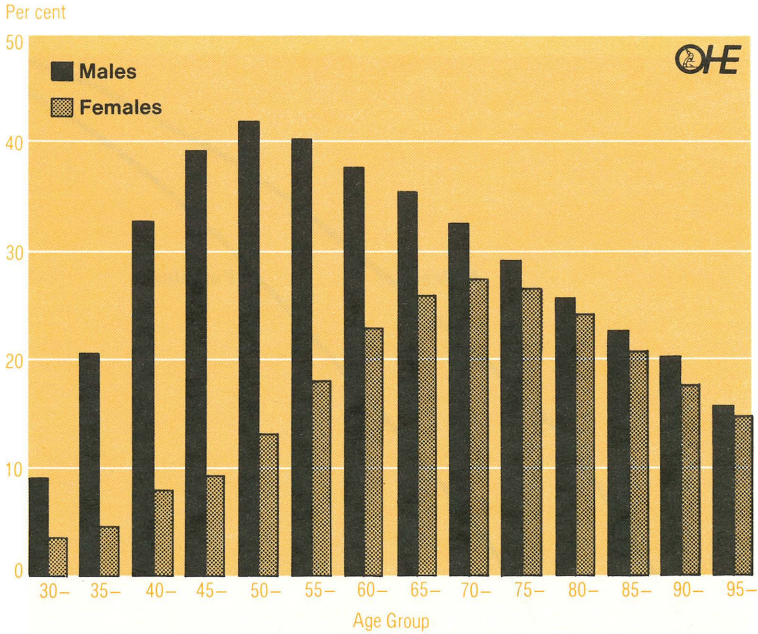
Source Office of Population Censuses and Surveys.

contrary to popular opinion, the disease does not have a relatively higher prevalence among the more affluent sections of society. This has not, however, always been true: until the 1950s heart disease was more common in social classes I and II (Marmot *et al* 1981).

Trends

Analyses of trends in heart disease mortality are complicated by a number of factors. Potential variations in the accuracy of the cause of death entered on the death certificate, for example, are a source

Figure 2 *Mortality from ischaemic heart disease (ICD 410–414) as a percentage of all deaths in selected age groups, males and females, England and Wales, 1980.*



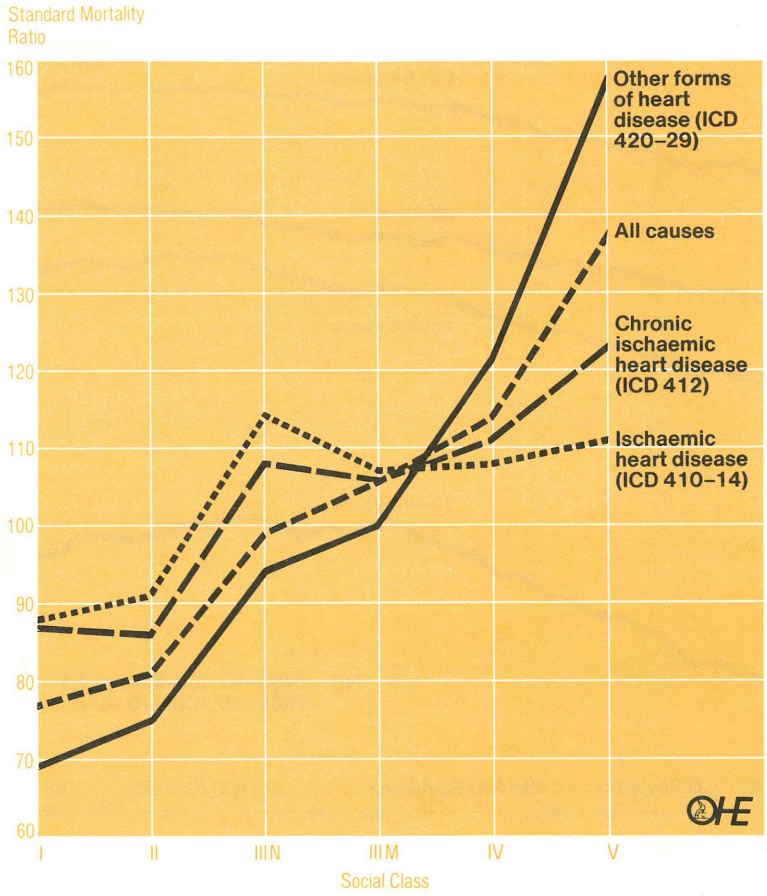
Source Office of Population Censuses and Surveys.

Table 3 *Mortality among males from coronary heart disease in England (by regional health authority), Wales and Scotland, 1979, rates per 1,000 population.*

	Age group		
Region	*45–54*	*55–64*	*65–74*
England	2.72	7.18	16.05
Regions:			
Northern	3.31	8.98	17.93
Yorkshire	3.12	8.04	18.42
Trent	2.87	7.44	16.55
East Anglian	2.07	5.75	14.47
NW Thames	2.44	6.42	14.22
NE Thames	2.52	6.96	15.00
SE Thames	2.35	6.63	14.93
SW Thames	2.26	5.90	14.08
Wessex	2.52	6.68	16.09
Oxford	2.17	5.65	14.14
South Western	2.45	6.96	16.14
West Midlands	2.76	7.05	15.68
Mersey	3.27	8.25	16.94
North Western	3.37	8.49	18.70
Wales	3.05	8.12	18.43
Scotland	3.65	9.12	19.82
Excess of highest rate over lowest	76 per cent	61 per cent	41 per cent

Source Office of Population Censuses and Surveys.

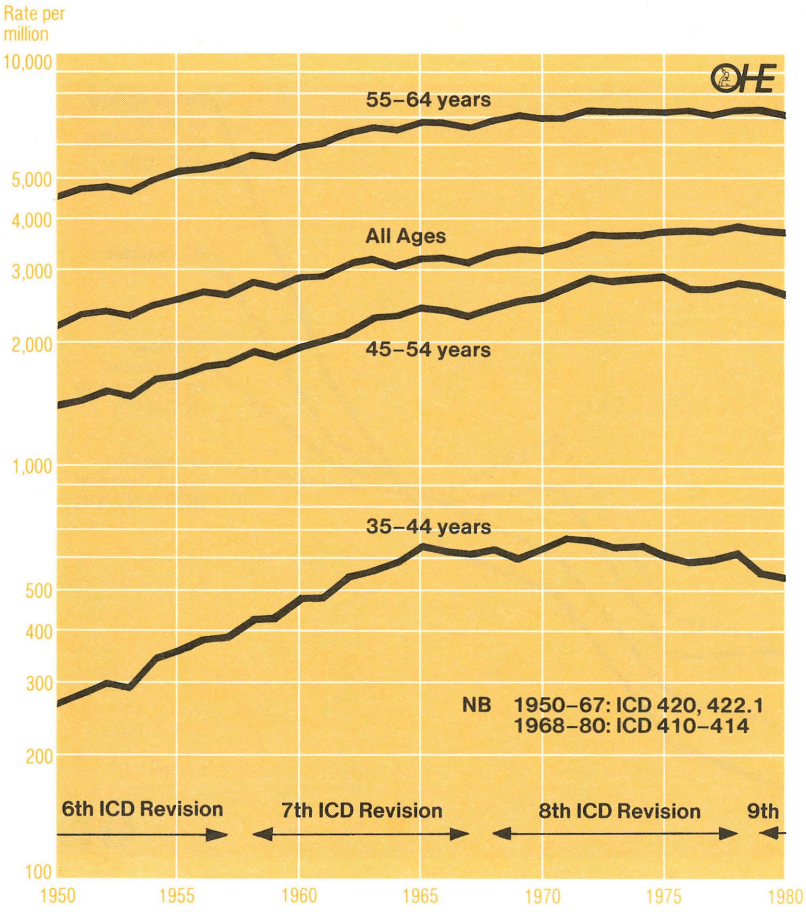
Figure 3 *Mortality from heart disease and all causes by socio-economic group, males aged 15–64 years, England and Wales 1970–72, standard mortality ratios.*



Source Office of Population Censuses and Surveys.

of concern. The principal difficulty, however, lies in the construction of a consistent time series and this arises because of modifications which have taken place periodically to the International Classification of Diseases. Since 1950 revisions have been implemented in 1958, 1968 and 1979. The first of these amendments involved no important alteration in the method of coding heart disease. The last, although resulting in changes which will require to be taken into account in future time series analyses, has occurred so recently that it need not enter the present examination of trends. The remaining 1968 (eighth) revision involved a substantially different nomenclature and coding of causes in the cardiovascular group.

Figure 4a *Deaths from arteriosclerotic/ischaemic heart disease, males, 1950–80, England and Wales, rates per million population.*

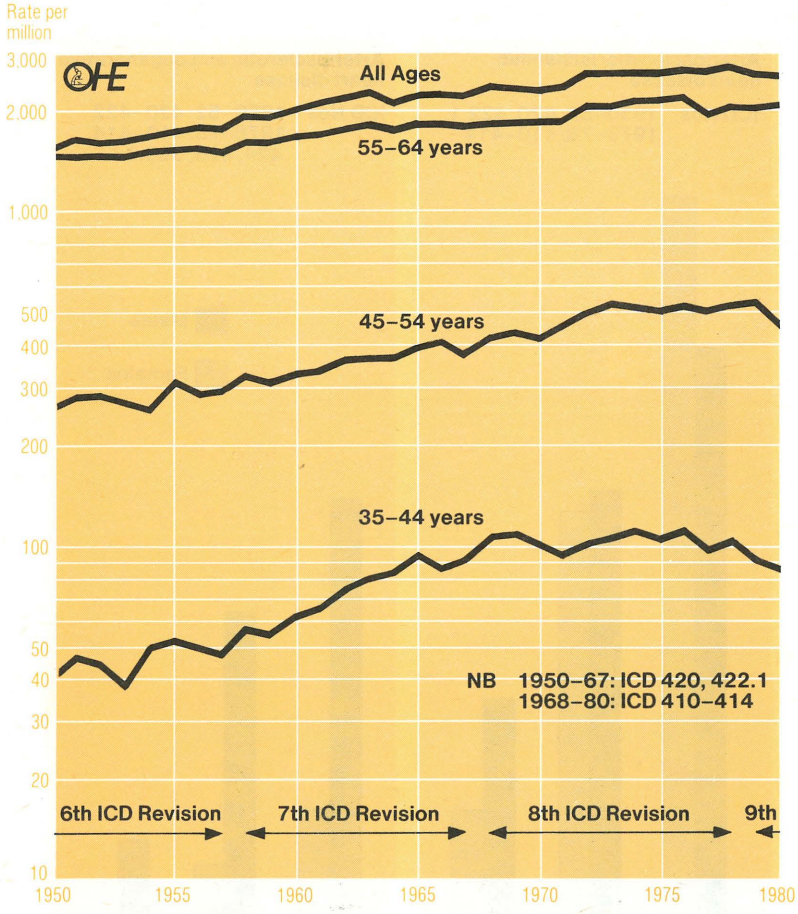


Source Office of Population Censuses and Surveys.

Various methods of reconciling the appropriate classifications before and after 1968 have been employed by different workers. Perhaps the most straightforward approach is to compare 'arteriosclerotic and degenerative heart disease' (ICD 420–422) before 1968 with the subsequent category entitled 'ischaemic heart disease' (ICD 410–414). However, this methodology embodies some degree of inconsistency in that 'other myocardial degeneration' is included in the data for 1950–67 (as indeed is chronic endocarditis not specified as rheumatic) whilst 'other myocardial insufficiency' is excluded in the following period (Clayton *et al* 1977).

An alternative approach, and the one adopted in this paper, is to

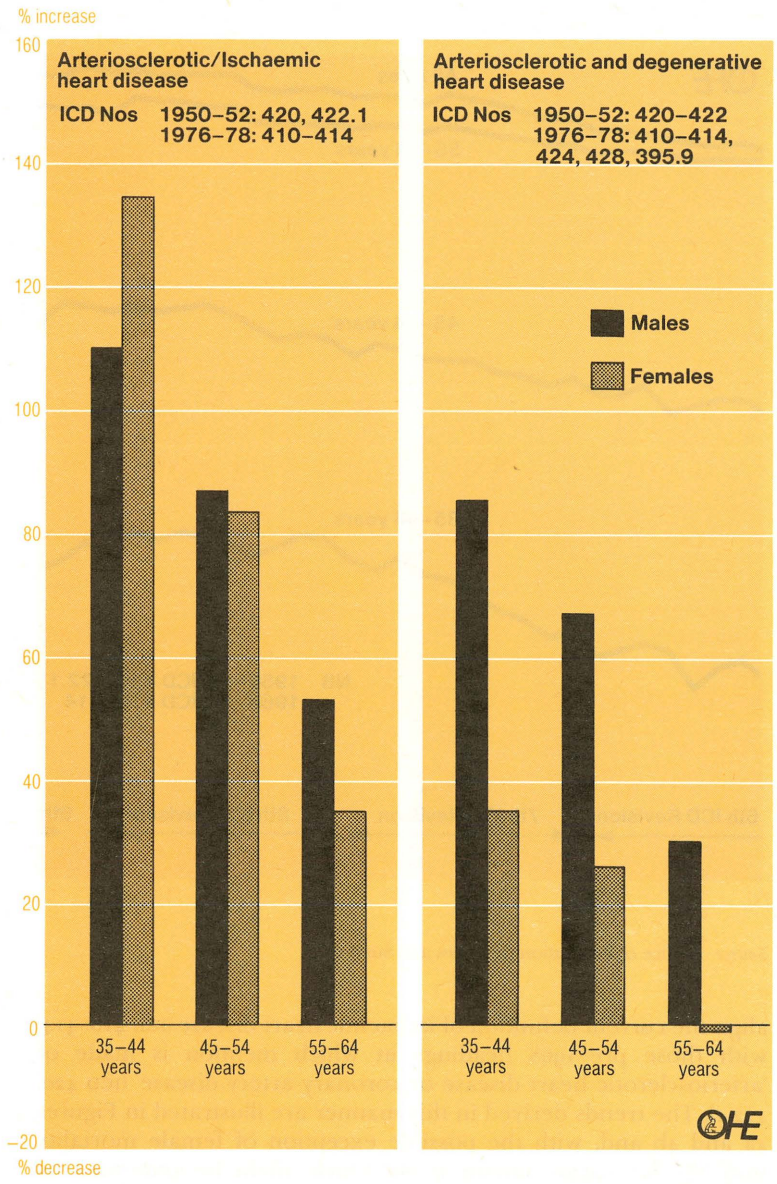
Figure 4b *Deaths from arteriosclerotic/ischaemic heart disease, females, 1950–80, England and Wales, rates per million population.*



Source Office of Population Censuses and Surveys.

align the current definition of ischaemic heart disease (ICD 410–414) with those pre–1968 headings in which mention is made of 'arteriosclerotic heart disease or coronary artery disease' (ICD 420, 422.1). The trends derived in this manner are illustrated in Figures 4a and 4b and, with the possible exception of female mortality until the late 1950s, mirror those which might be generated by exercises based on broader definitions (OPCS 1978). Nevertheless, as Figure 5 makes clear, choice of ICD classification may influence dramatically the magnitude of change between study period end-points and it is important therefore to specify which methodology is being employed.

Figure 5 *Percentage change in 'coronary heart disease' mortality rates between 1950–52 and 1976–78, England and Wales.*



Source Office of Population Censuses and Surveys.

Figures 4a and 4b indicate that coronary mortality rates have increased throughout the age spectrum over the period 1950–52 to 1976–78. Focusing on the 35–64 grouping age standardised calculations suggest that in the second half of the 1970s there were 11,200 more male deaths per annum from coronary heart disease than at the start of the 1950s. For females, similar analysis yields an extra 2,400 deaths each year. The most striking aspect of the diagrams, however, is the substantial escalation in mortality among the younger age groups. Thus the rate for males aged 35–44 – which is six times that for females in the corresponding age group – more than doubled between 1950–52 and 1976–78. In sharp contrast, the mortality rate in this age group for all other causes combined fell by 44 per cent over the same period. For males aged 45–54, who were experiencing 3,700 extra coronary fatalities per annum in the second half of the 1970s compared with the early 1950s, the average death rate for coronary heart disease increased 87 per cent whilst that for all other causes fell by 39 per cent.

International comparisons

Difficulties akin to those highlighted in the discussion of mortality trends in England and Wales tend inevitably to be magnified in international comparisons. Nevertheless a broad appraisal of national trends in coronary heart disease can be derived by confining attention to the ICD category 'ischaemic heart disease' (ICD 410–414) over the period of its use, between 1968 and 1978.

Focusing on males of pre-retirement age (because this is the major source of premature heart disease mortality) Figures 6a, 6b and 6c show selected national death rates per 100,000 population for the age groups 35–44, 45–54 and 55–64 years. Three main points of significance emerge from the diagrams. First, it is clear that there is a broad spectrum of rates and that a substantial discrepancy persisted throughout the period between the highest and lowest mortality rates. Thus in 1978 the 35–44, 45–54 and 55–64 rates for Scotland were respectively 9, 12 and 10 times those found in Japan. (The rates for Finland are not illustrated but exceeded even those for Scotland – in 1977 by 18, 16 and 15 per cent at ages 35–44, 45–54 and 55–64 respectively.) Even if attention is focused exclusively on 'Western Society' the discrepancies are still substantial.

Second, the graphs show, in spite of occasional fluctuations, a general pattern of little overall change in rates over the period. This tendency is shared by European nations not included in the diagrams such as Denmark, West Germany, Norway and Austria, although it is possible that falling rates were experienced in Italy, France and Switzerland (*Lancet* 1980b). One perhaps surprising exception to both trends is provided by Sweden. Although frequently ranked as one of the most accomplished nations in many

Figure 6a *Deaths from ischaemic heart disease among males aged 35–44*

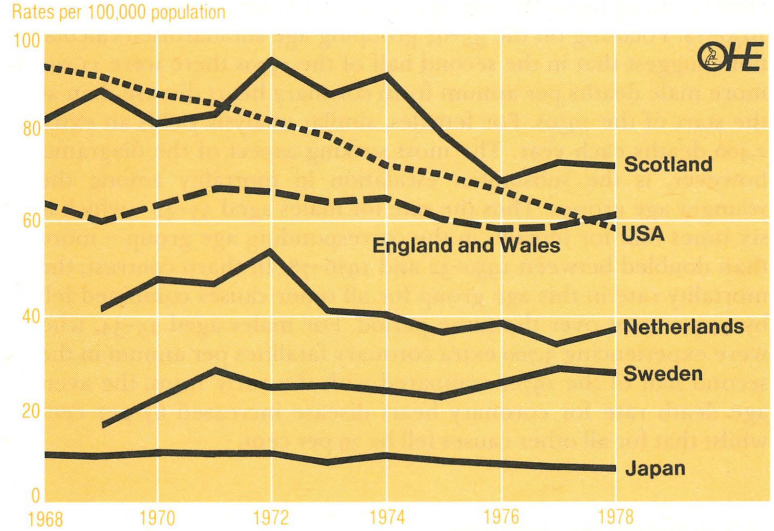


Figure 6b *Deaths from ischaemic heart disease among males aged 45–54*

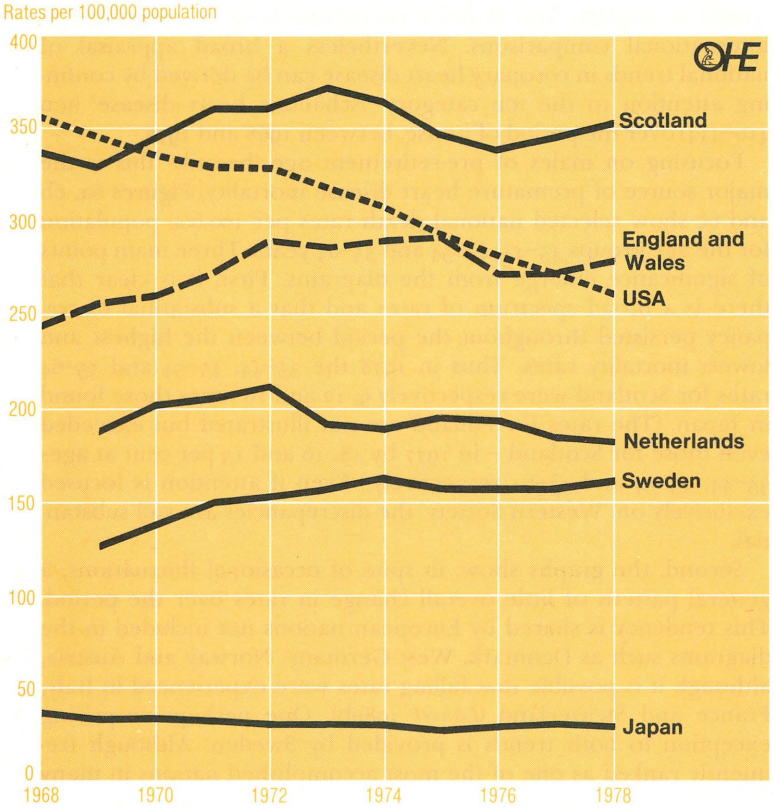
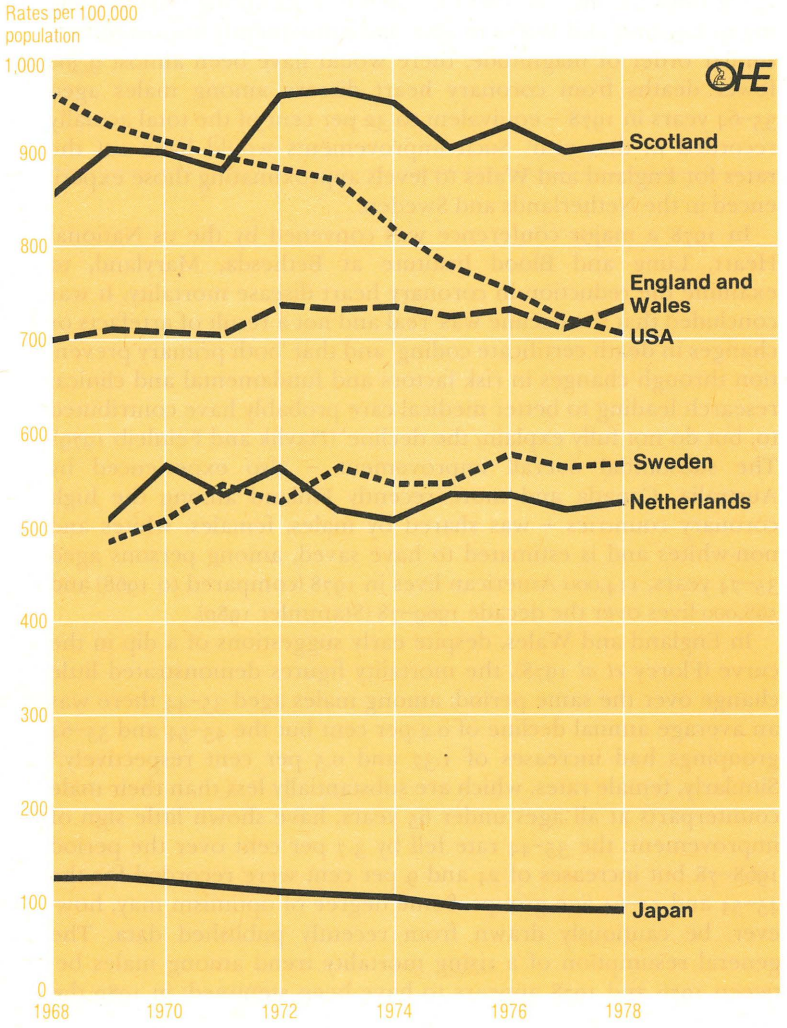


Figure 6c *Deaths from ischaemic heart disease among males aged 55–64 years in selected countries, 1968–78, rates per 100,000 population.*



Source World Health Organisation.

indices of health care, Figures 6a to 6c indicate that Swedish coronary heart disease mortality rates have increased quite significantly throughout the 1970s.

Finally, the most striking feature of these trends is the achievement of the United States. Sustained improvements have been experienced throughout the period and this culminated in 1978 with the US rates for all three age groups falling below the corresponding rates in England and Wales for the first time. Among

males aged 35–44 years there was a reduction in the US coronary heart disease death rate of 36 per cent; for both 45–54 and 55–64 age groups the improvement was 27 per cent.[7] If the rates prevailing in England and Wales in 1968 had subsequently improved by a similar order of magnitude, there would have been almost 9,300 fewer deaths from coronary heart disease among males aged 35–64 years in 1978 – equivalent to 32 per cent of the total actually recorded in that year. Such improvements would have cut the rates for England and Wales to levels approximating those experienced in the Netherlands and Sweden.

In 1978 a major conference was convened by the US National Heart, Lung and Blood Institute at Bethesda, Maryland, to examine the reduction in coronary heart disease mortality. It was concluded that the decline was 'real and not a result of artefacts or changes in death certificate coding' and that 'both primary prevention through changes in risk factors and fundamental and clinical research leading to better medical care probably have contributed to, but do not fully explain, the decline' (Havlik and Feinleib 1979). The substantial overall improvement – also experienced by Australia, Canada and more recently Finland among the high coronary countries – was shared by males, females, whites and non-whites and is estimated to have saved, among persons aged 35–74 years, 114,000 American lives in 1978 (compared to 1968) and 568,000 lives over the decade 1969–78 (Stammler 1980).

In England and Wales, despite early suggestions of a dip in the curve (Florey *et al* 1978), the mortality figures demonstrated little change over the same period: among males aged 35–44 there was an average annual decline of 0.2 per cent but the 45–54 and 55–64 groupings had increases of 1.37 and 0.5 per cent respectively.[8] Similarly, female rates, which are substantially less than their male counterparts at all ages under 65 years, have shown little sign of improvement: the 35–44 rate fell by 3.7 per cent over the period 1968–78 but increases of 24 and 9 per cent were recorded for the 45–54 and 55–64 age groups. Some degree of optimism may, however, be cautiously drawn from recently published data. The general resumption of a rising mortality trend among males between 1976 and 1978 appears to have been stemmed; in 1980 the

7 It may be noted that Japanese rates also showed quite substantial reductions over the period in question – falling by 27, 22 and 24 per cent respectively. Of course, because of the already low Japanese mortality rates these improvements are not depicted so dramatically in diagrams 6a, 6b and 6c.

8 These may be compared with corresponding reductions in the United States of 4.32, 3.04 and 3.05 per cent. Focusing on the 35–44 age group, a continuation of trends in the US will mean that the coronary heart disease death rate experienced in 1978 will be halved by 1994. In the same year the England and Wales figure will represent only a marginal improvement on the 1978 rate. In other words, in a period of 25 years the American death rate for coronary heart disease among men aged 35–44 could have shifted from being one and a half times the static England and Wales rate in the late 1960s to less than half the latter's value in the mid-1990s.

rates for the age groups 35–44, 45–54 and 55–64 were 12, 6 and 3 per cent respectively below those recorded in 1978. (For females the corresponding figures were 17, 12 and zero per cent.) To some extent these improvements are a function of changes incorporated in the 1978 (9th) revision of the International Classification of Diseases. For example, some of the chronic ischaemic heart disease fatalities have now been transferred out of the extant coronary heart disease rubric (410–414). Nevertheless, falling rates were recorded between 1979 and 1980 when the new classification system was operating and this may herald a more consistent improvement in trends than has hitherto been observed for coronary heart disease mortality in England and Wales.

Risk factors in coronary heart disease

Investigations of the disparities between populations in both the incidence of and mortality from coronary heart disease have played a significant role in promoting aetiological understanding of the disorder. Studies have taken place on differing scales between nations – for example, the Seven Countries Study of over 11,000 men aged 40–59 years (Keys 1970) and the Edinburgh–Stockholm study involving 189 40-year-old males (Logan *et al* 1978) – as well as within national boundaries, such as the British Regional Heart Study (Shaper *et al* 1981) and the Framingham Study in the United States, and have identified a number of key behavioural, medical and other factors which are associated with the presence of coronary heart disease. However, no single agent has been shown to be a necessary prerequisite for the occurrence of the disorder and the surveys suggest that both major and secondary factors may assume varying degrees of significance in different communities. It should also be emphasised that although these risk factors are frequently at the centre of discussions about the aetiology of coronary heart disease, their presence predisposes to a raised probability of clinical manifestation but does not necessarily imply the existence of primary causal relationships.

Cigarette smoking

Cigarette smoking is considered by many authorities to be potentially the major risk factor for coronary heart disease. The pooled results of several American studies (PPRG 1978) suggest that one out of every three 40-year-old men who smoke 20 cigarettes or more per day will suffer a major heart attack before they reach 65 years. Six out of seven non-smokers, however, will celebrate their 65th birthday without having experienced these events. The Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society (1976) on the prevention of coronary

Table 4 *Mortality from coronary heart disease in non-smokers and cigarette smokers by age and level of consumption*

Age group	Annual death rate per 100,000 men*			
	Non-smokers	Current smokers, cigarettes only: no. per day		
		1–14	15–24	⩾35
<45	7	46	61	104
45–54	118	220	368	393
55–64	531	742	819	1,025
<65	166	278	358	427
65–74	1,190	1,866	1,511	1,731
⩾75	2,432	2,719	2,466	3,247

*Indirectly standardised for age to make the four entries in any one line comparable.

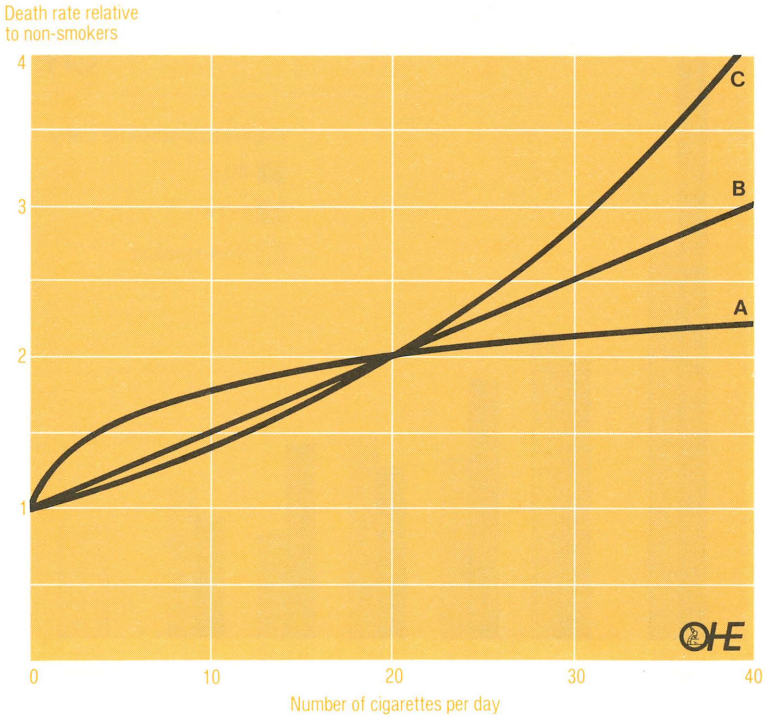
Source Doll and Peto 1976.

heart disease estimated that about one-quarter of coronary fatalities in men and women aged under 65 years are closely associated with the habit. This proportion implies approximately 9,000 deaths per annum in England and Wales.

The findings of a large number of epidemiological surveys suggest that overall the risk for smokers of dying from coronary heart disease is about twice that for non-smokers. This level of risk increases with consumption – a study by Bain and his colleagues (1978), for example, indicated that persons smoking 40 or more cigarettes daily are subject to a fourfold risk of death compared with non-smokers – although differences exist in magnitude and shape of the observed dose-response curves (Figure 7). Risk is also a function of age: Doll and Peto (1976) reported from the study of smoking habits among British male doctors that the relative risk of death in heavy cigarette smokers compared with non-smokers was 15 to 1 at ages under 45 years, 3 to 1 at 45–54 years and 2 to 1 at 55–64 years (Table 4). The apparent weakening of the effect of cigarette smoking with age may reflect a reduction in its relative significance due to other risk factors exercising an increasing impact as people get older. It is also possible that persons particularly at risk from the adverse effects of smoking are eliminated from the population at an earlier stage in their lives, leaving those who are less susceptible to advance to older age (Kannel 1981).

Evidence drawn from samples of individuals who have relinquished cigarette smoking is also indicative of a causal relationship. Doll and Peto (1976), for example, found that coronary deaths among male doctors aged 35–54 years who had been non-cigarette smokers for less than five years amounted to approximately half the number that would have been expected had this group contin-

Figure 7 *Examples of dose-response models for cigarette consumption and risk of coronary death.*

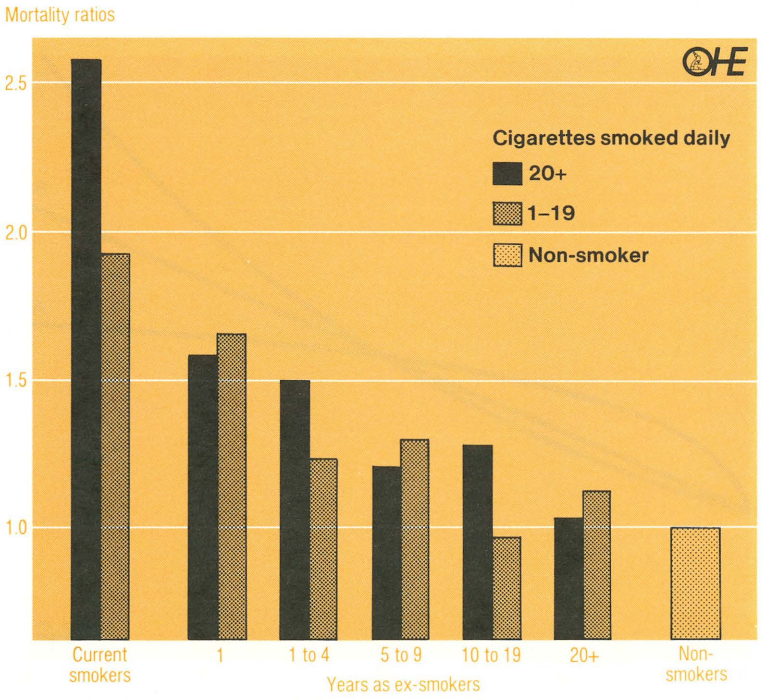


Source Kleinman *et al* 1979.

Note Each curve is constructed so that those smoking 20 cigarettes per day have twice the death rate of non-smokers. Curve A is logarithmic and implies that risk increases rapidly with small doses then tapers off. Curve B is linear – each additional cigarette carries the same increase in relative risk. Curve C is exponential, implying that each additional cigarette is more harmful the more one smokes. Kannel (1981) suggests that the American Cancer Society (Hammond 1966) and British physicians (Doll and Peto 1976) studies provide examples of curve A; the Veterans Administration Study (Kahn 1966) illustrates the linear dose response model; and the Pooling Project data (McGee and Gordon 1976) are consistent with the exponential model.

ued to smoke. Figure 8 indicates that the benefit of giving up the habit is particularly marked for heavy smokers during the first year of abstention. Yet there is some dispute about such findings. In a trial of the effect on middle aged men of advice to stop smoking, Rose and Hamilton (1979) did not observe (at eight year follow up) any significant difference between the mortality rate for the intervention group (58 per cent of whom claimed to have stopped smoking at 3 years) and that for controls (14 per cent of whom had

Figure 8 *Effect of stopping smoking on deaths from coronary heart disease in light and heavy smokers.*



Source Ball and Turner 1974.

apparently relinquished the habit at the same stage). Furthermore, Seltzer (1980) in a paper challenging the whole smoking/coronary heart disease hypothesis, has argued that the favourable results reported from observational studies are invalid because ex-smokers are not representative of those who persist with the habit with regard *inter alia* to baseline coronary risk levels and various potentially relevant socio-personal characteristics.

The otherwise clear message to be drawn from the epidemiological data which has accumulated over the last 20 years or so contrasts sharply, however, with the uncertainty that continues to surround the pathological processes underlying the relationship between cigarette smoke and coronary heart disease. There is evidence to suggest that the clinical consequences of smoking might be mediated through deleterious effects on atheroma (*BMJ* 1977), on thrombosis (*BMJ* 1980) as well as directly on the heart itself (Lewis and Boudoulas 1974). None of these hypotheses has been established beyond equivocation as indeed is the case with the identity of the agents contained in cigarette smoke which might be

responsible for such disturbances. More than 4,000 chemical substances are produced by the burning of tobacco in cigarettes (Castelli *et al* 1981) but only nicotine and carbon monoxide[9] have been investigated in any depth, generating considerable debate as to the relative significance of each (see, for example, Wald *et al* 1981, Jarvis and Russell 1981).

Dietary considerations

Unanimity of opinion is less marked with regard to the role of dietary factors in coronary heart disease than is the case with cigarette smoking. Debate has ranged for example over the significance of alcohol, salt, sugar and cereal fibre intake. It is also uncertain whether the negative correlation between the hardness of domestic water supplies and local coronary heart disease mortality rates – Pocock and co-workers (1980) have estimated from a study of 253 towns in Britain that in areas with very soft water cardiovascular mortality is 10–15 per cent higher than in locations with medium to hard water supplies – is explained by the existence of a risk factor which is more soluble in soft water than in hard water or the presence of some protective substance in the latter.

The principal debate in the context of diet and coronary heart disease has centred, however, on the contention that diets rich in saturated fats are a cause of elevated levels of serum cholesterol and that the latter constitute a major risk factor for coronary heart disease. The hypothesis is underpinned by reports that relevant changes in dietary composition can raise or lower plasma cholesterol concentrations in a predictable way (Shaper and Marr 1977) and by the biochemical finding that cholesterol lipids are an important component of the atheromatous plaques found in diseased coronary arteries. It has been shown that lipids comprise between 50 and 60 per cent of raised plaques but because little cholesterol is synthesised by human arterial cells this accumulation appears to be the result of a transfer process from plasma to the arterial intima (Lewis 1980). Indeed, there is evidence that both the amount

9 Nicotine, which may be absorbed by heavy smokers in quantities of between 50 and 100 mg daily, elevates the heart rate, blood pressure and cardiac output, promotes myocardial irritability (with greater risk of dysrhythmias), increases free fatty acids which may contribute to the fatty cellular lesions of atherosclerosis and enhances platelet stickiness with important implications for thrombus formation (Ball and Turner 1974). The effects of carbon monoxide, too, are manifold. The affinity of haemoglobin in the red blood cells for carbon monoxide is considerably greater than for oxygen, which is therefore readily displaced. This may lead to carboxyhaemoglobin levels of up to 15 per cent in heavy smokers compared with 0.5 to 1 per cent usually found in non-smokers. The result is a depleted supply of oxygen to the myocardium – aggravated by an impaired diffusion of transported oxygen caused by the capacity of carbon monoxide to combine with myoglobin – at a time when the work of the heart has been stimulated by nicotine absorption. In addition, there is some evidence that the accumulation of carbon monoxide produces hypoxia of the arterial endothelium interfering with its function as a barrier to lipid infiltration of the intima (Kannel 1981).

and rate of cholesterol deposition correlate well with serum concentrations of the latter.

Further support for the hypothesis may be drawn from the results of epidemiological investigation. Intercountry comparisons have revealed positive associations between coronary heart disease mortality rates and both plasma cholesterol and certain dietary factors, particularly the proportion of energy derived from saturated fats. Positive associations have also been demonstrated between the latter and serum cholesterol concentrations.

Intranational studies have similarly established that for individuals the risk of subsequent coronary heart disease increases directly with plasma cholesterol levels: the risk for men in the top quintile of the cholesterol distribution is 2.4 times that in the lowest two quintiles (PPRG 1978). But surveys within communities have generally failed to relate disparities in plasma cholesterol concentrations between individuals to differences in dietary intake (Morris *et al* 1963, Kannel and Gordon 1970). This missing epidemiological link, which is regarded as important negative evidence by critics of the dietary fat hypothesis, is probably explained to some extent by difficulties in accurately measuring dietary intake, the large day-to-day variations in the lipid composition of individuals' diets, the influence of non-dietary factors on serum cholesterol levels and the possible existence of a critical threshold limit of fat consumption. Furthermore, new evidence has recently emerged from a 19 year follow-up study in the United States showing a positive association of coronary mortality with dietary cholesterol and with combined measures of saturated fat, polyunsaturated fat and cholesterol in the diet (Shekelle *et al* 1981).

Support for the hypothesis may also be drawn from the findings of primary prevention trials of cholesterol lowering dietary regimens. These have recently been reviewed by Oliver (1981) who concluded that, in spite of certain shortcomings in trial design and methodology, the studies suggest that dietary modification may reduce serum cholesterol concentrations and that this can promote a decline in the incidence of non-fatal myocardial infarction.[10] There has, however, been no convincing demonstration of a beneficial effect in terms of diminished cardiac mortality. More dramatic results than those so far reported might be expected from long-term trials involving younger persons; but given the requirement of an unmanageably large number of subjects to obtain meaningful results and the costs involved, there is little scope for such investigations (Glueck *et al* 1978, Mann 1979).

10 Positive results have also emerged from a large randomised double blind trial of clofibrate carried out under the auspices of the World Health Organisation (Committee of Principal Investigators 1978). The treated group achieved a 9 per cent reduction in serum cholesterol compared to controls receiving olive oil placebo and although there was no decline in cardiovascular mortality, a significant (25 per cent) decrease in non-fatal myocardial infarction was recorded.

Finally, evidence for the cholesterol/coronary heart disease link may be drawn from clinical and experimental observations. In the context of the former, familial hypercholesterolaemia (FH) – a genetic disorder resulting in two or threefold increases in plasma cholesterol concentrations and arterial lesions typical of atherosclerosis – raises the coronary risk in affected males by a factor of ten. It has been estimated that up to 60 per cent of males and over 30 per cent of females suffering FH develop angina or sustain infarction before the age of 50 years (Sugrue *et al* 1981). Experimentally, non-human primates fed high levels of cholesterol and saturated fat have been found to develop extensive arterial occlusion which subsequently recedes on discontinuation of the diet. The relevance of these experimental lesions to disease in man has however been questioned (Oliver 1981).

In spite of the wealth of epidemiological and experimental evidence now to hand, the aetiological significance of dietary/serum cholesterol in coronary heart disease continues to be debated. Opponents of the hypothesis such as Mann (1977) and McMichael (1979) have challenged the protagonists' interpretation of available data in certain areas of debate and have simultaneously cited countervailing evidence. But perhaps the major source of dispute concerns the issue of polyunsaturated fats. The results of a number of studies suggest that the latter may in some way be 'protective' against heart disease. Thus Morris and his colleagues (1977) found an inverse relationship between the ratio of polyunsaturates to saturates and coronary incidence and Shekelle and co-workers (1981) have reported a similar (statistically significant) association between coronary mortality and consumption of polyunsaturated fat. Findings such as these have underpinned the recommendation of many committees that some addition of fats from polyunsaturated sources to the diet would be desirable, apart from anything else, as a means of facilitating reductions in saturated fat intake.[11]

But advice along these lines has been criticised by a number of observers. Concern has been expressed (and, of course, challenged) at the possibility that reduced serum cholesterol concentrations linked with raised polyunsaturate levels in the diet lead to an increased incidence of gallstones, cancer of the colon in males and non-cardiovascular mortality. McMichael (1979) has argued against substitution on the basis of the experience of Israel, where the average diet is very high in polyunsaturates yet mortality from coronary heart disease in middle aged males surpasses that in many western nations. Additionally, polyunsaturated fatty acids

11 The critical argument in relation to polyunsaturated fat supplementation is that foods rich in the latter are precisely those which are high in saturated fatty acids so that recommended reductions in the latter necessarily entail a fall in intake of polyunsaturates. For this reason, and because they are essential and non-synthesizable by man, polyunsaturate supplementation is argued to be necessary (Shaper 1982).

are not a homogenous group and specific differences unrecognised in general recommendations may have important implications for, say, thrombus formation. Little is also known about the potentially different ways in which saturated and polyunsaturated fats might affect, *inter alia*, the immunoresponsiveness of lymphocytes and the permeability of cell membranes to drugs, viruses and bacteria (Ahrens 1979).

One of the 'benefits' of this continuing debate has been the stimulus it has provided to further research effort and in this context two areas of investigation are of particular significance. The first concerns the shift of interest away from the association between disease risk and total serum cholesterol to the relationships between the former and specific cholesterol-transporting lipoproteins in the blood – low and high density lipoproteins (LDL and HDL). Epidemiological surveys have reported that the occurrence of coronary heart disease is correlated negatively with plasma HDL concentration as well as positively with LDL cholesterol levels. Further, angiographic studies have shown that the severity of coronary artery disease escalates with decreasing HDL and increasing LDL concentrations (*Lancet* 1981d).

High density lipoprotein, which is now recognised to be a complex family of particles of differing size, density, lipid composition and apoprotein content (see for example Miller *et al* 1981), therefore appears to afford protection against the development of coronary heart disease although the mechanism underlying this effect has yet to be clarified: it may be that HDL is responsible for the removal of excess cholesterol from arterial walls and its transportation back to the liver or it may bind to LDL receptors, inhibiting LDL from cellular uptake. The determinants of HDL concentration also require further elucidation; so far it has been found to be correlated positively with regular exercise and moderate alcohol consumption[12] and negatively with cigarette smoking and obesity (Tyroler 1980). The discovery of the protective effect of HDL might have important implications for the conventional dietary fat hypothesis but at the moment Kannel and Castelli (1979) argue that 'there is no basis for discarding total or LDL cholesterol as predictors of coronary heart disease or for the substitution of HDL cholesterol for these proven atherogenic lipid fractions'.

The second line of research is concerned with the role of thrombosis in heart disease and in this context Shekelle and co-workers' (1981) observation of an association between dietary fat and coronary mortality that was independent of the level of serum cholesterol and of other risk factors may be of significance (*Lancet* 1981e).

12 This might go some way to explaining the finding of a multi-nation study of a strong and specific negative association between coronary heart disease and wine consumption (St Leger *et al* 1979). In addition, moderate alcohol consumption appears to be associated with increased fibrinolytic activity (Meade *et al* 1979).

As an alternative to the 'infiltration' hypothesis that high fat diets increase serum cholesterol levels giving rise to the atheromatous plaques found in coronary heart disease, it has been proposed that the aetiological relevance of dietary intake may derive more specifically from its content of certain essential polyunsaturated fatty acids (Vane 1979, Sinclair 1980). Eicosapentaenoic acid from marine animals is an example of the latter which appears to be a precursor for a type prostacyclin in the vessel wall and to have direct anti-aggregatory activity on platelets. It has therefore been suggested that a replacement of the normal precursor for prostacyclin/thromboxane (arachidonic acid obtained from linoleic acid in vegetables and arachidonic acid in farm animals) with a more polyunsaturated fatty acid, such as eicosapentaenoic acid, could swing the balance of the thrombotic/antithrombotic equation beneficially (Vane 1982). Certainly coronary artery disease is rarely found in Eskimos whose diet is substantially marine based and recent experimental work suggests that appropriate dietary supplementation in patients may diminish the risk of the disease (Hay *et al* 1982).

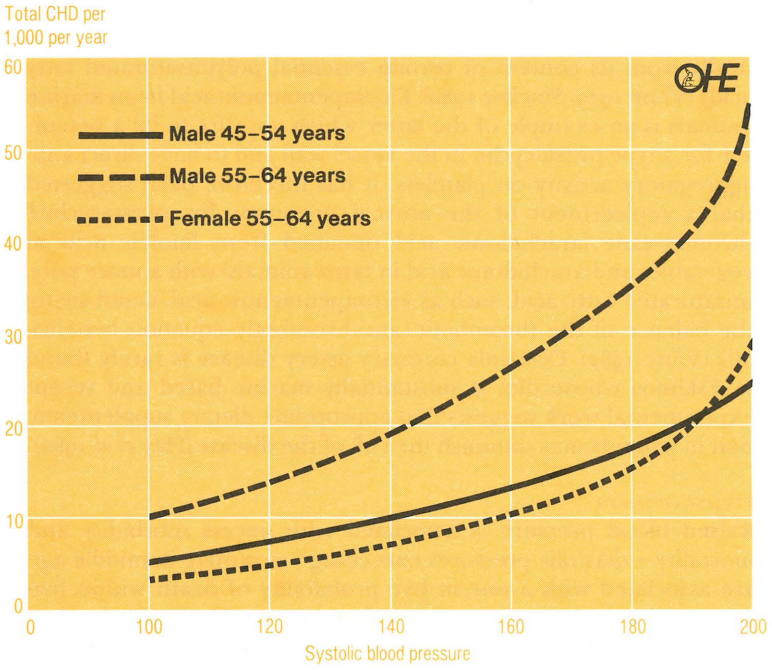
Hypertension

Raised blood pressure is associated with excess morbidity and mortality – diastolic pressures exceeding 110 mmHg in middle age are associated with a one in five probability of death within five years and measurements greater than 100 mmHg imply a reduction in life expectancy of 15 years for persons in their mid-thirties – and this mainly involves cardiovascular and/or renal diseases. Focusing specifically on heart disease, data from the Framingham Study indicate that coronary incidence rises by nearly 20 per cent for each 10 mm increase in systolic pressure, so that at 160 mm the risk is almost twice that at 110 mm (Figure 9). Given that 26 per cent of males aged 45–64 years may be classified as mildly or moderately hypertensive or worse[13] (Hawthorne *et al* 1974) raised blood pressure might therefore be expected to be an important contributory factor to the development of coronary heart disease and to premature mortality from this cause.

The precise mechanisms whereby raised blood pressure predisposes to coronary heart disease have yet to be elucidated. One possible explanation is that through a continuous process of attrition it results in damage to the linings of arteries, establishing a foundation for subsequent development of atheroma. But more fundamentally, with the exception of specific causes such as kidney disease, phaeochromocytoma (adrenalin secreting tumour) and Conn's disease (aldosterone hypersecretion), the aetiology of raised

13 That is, diastolic pressures above 95 mmHg. For the population as a whole, approximately 65 per cent of persons have 'normotensive' diastolic pressures of 90 mmHg or below; 30 per cent fall in the arbitrarily defined mild/moderate hypertensive range from 90 to 110 mmHg and the remaining 5 per cent exceed 110 mmHg (Burt *et al* 1982).

Figure 9 *Coronary heart disease incidence (averaged over a 16-year period) in relation to blood pressure at initial examination.*



Source Kannel and Gordon 1970.

blood pressure itself remains unclear in approximately 85 per cent of cases and as such is designated essential hypertension. There is evidence to suggest that it may be a genetically determined disease although its prevalence has been shown within national boundaries to vary between geographical regions, urban and rural communities and socio-economic groups, suggesting an input from 'environmental' factors. In this context consideration has been given to poisoning from metals such as lead and cadmium, alcohol consumption,[14] emotional stress, inadequate physical exercise and diet (Bulpitt 1981). Of these, the last has perhaps attracted most attention, with emphasis particularly on obesity (explaining, in part, its frequent inclusion as a 'secondary' risk factor for coronary heart disease) and salt consumption (*BMJ* 1981).

14 In a study of cardiovascular risk factors in men aged 40–59 years in 24 British towns, Shaper and his colleagues (1981) reported that the highest systolic and diastolic blood pressures were found in men having more than six drinks daily or on each day at weekends. This level of drinking was reported by 25 per cent of all men in the study, suggesting that in Britain the impact of alcohol on hypertension may be considerable.

Other risk factors

Smoking, raised cholesterol levels and hypertension are widely recognised as the three major independently acting risk factors for coronary heart disease. A number of other factors, generally reflecting lifestyle, also appear to be associated with clinical presentation. Whilst they do not by themselves appear to possess high degrees of 'causal' significance it may be that their presence serves as a final trigger in the development of a coronary event in persons already at risk. As such these characteristics are designated, appropriately or not, secondary risk factors.

It has long been recognised that personality and behavioural traits may influence the outcome of organic disease in particular patients (*Lancet* 1981f). The possibility that personality might be associated specifically with coronary heart disease was first propounded in the 1930s and 1940s (Davies 1981) and subsequently investigated by Friedman and Rosenman (1959). The latter authors reported that men with behaviour patterns (Type A) characterised by intense ambition, competitive drive, constant preoccupation with deadlines and sense of urgency experienced seven times more clinical coronary artery disease than individuals with converse lifestyles and that this disparity could not be accounted for by differences in cigarette smoking, working hours, exercise, alcohol consumption, dietary habits or heredity. Subsequently, the association has been further investigated but the difficulties of quantifying different behavioural patterns, the extent of myocardial damage and potential links between the two in the presence of many confounding factors imply that it is not possible to gauge the raised level of risk associated with Type A behaviour any more accurately than Rosenman and colleagues' (1976) estimate that it approaches the general levels for hypertension and smoking.

Stress is another secondary risk factor for coronary heart disease: in some instances, the onset of clinical symptoms appears to be related to stressful life events such as residential or occupational relocation, bereavement, unemployment and other forms of social disorientation. The causal pathways involved remain unclear although it has been postulated that prolonged stress may result in the liberation of free fatty acids into the bloodstream (to provide a source of energy) which, in the absence of physical exercise, are not fully utilised and may predispose to the development of atheroma. In addition, high levels of sympathetic arousal may render the coronary circulation and cardiac metabolism less efficient, precipitating angina or even infarction (Davies 1981).

The foregoing suggests that physical activity might function as an effective 'antidote' to the potential hazards of a stressful lifestyle. In a broader context, there is certainly evidence from occupation-based surveys to indicate that physical exertion is protective against coronary heart disease. Studies of London busmen, for

example, demonstrated that active bus conductors experienced substantially fewer coronary events than their driver colleagues (Morris 1975). Similarly, postmen have been found to suffer fewer heart attacks than clerks and other sedentary post office workers. More recently, a long-term follow-up investigation of coronary heart disease mortality among dock workers in the USA (Paffenbarger and Hale 1975) discovered that high activity workers had fatality rates almost half those found in workers in the medium and low categories.

Yet the benefits of physical activity are less and less likely to be derived from occupational sources since an ever declining proportion of the work force is employed in jobs which are physically demanding. Compensation has therefore increasingly to be sought in exercise taken during leisure time which too has been shown to reduce coronary risk. In a six to ten year follow-up study of 17,000 male alumni of Harvard University, Paffenbarger and co-workers (1978) observed that individuals not engaging in 'strenuous' sports activities were at a 38 per cent greater risk of a first heart attack than those who did. Focusing on 'vigorous' but not extreme exercise in leisure time (including swimming, tennis, jogging and keep fit exercises) Morris and his colleagues (1980) studied nearly 18,000 office bound middle aged male civil servants for a period of eight and a half years and found that individuals taking part in such activities had risks of fatal heart attack and non-fatal coronary event which were about 40 and 50 per cent respectively those of otherwise very similar non-participants.[15]

The mechanisms underlying the protective effect of regular physical exercise against heart disease have still to be firmly established. Recent experiments with monkeys suggest that it may prevent or retard coronary atherosclerosis associated with atherogenic diets (Kramsch *et al* 1981). The benefits of exercise may derive variously from a redistribution of cholesterol fractions in favour of high density lipoprotein, lower heart rate, enhanced fibrinolysis and a reduction in ECG abnormalities reflecting minor heart disease. Differences of opinion also persist with regard to the optimal nature, duration and frequency of activity as well as to the benefits or otherwise of commencing or resuming physical exercise in middle age. Further uncertainty concerns the influence of other factors that may predispose certain people to be more active and at the same time protect against coronary heart disease. Unfortunately clarification of these issues as well as definitive 'proof' of the value of exercise is inhibited by the difficulty of controlling the everyday behaviour of sufficiently large numbers of

15 Taking smoking habits into account as well, the authors found that individuals who did not smoke and undertook vigorous exercise had a fatal first coronary rate which was 20 per cent that of their colleagues who were not so active and smoked cigarettes.

people to carry out an appropriate trial over an adequate period of time (Morris 1979).

Overall significance of risk factors

The DHSS prevention document *Avoiding Heart Attacks* (1981) discussed 10 factors which have been linked to the occurrence of coronary heart disease although, reflecting established epidemiology, just three were given prominence as being of major independent importance: cigarette smoking, hypertension and raised cholesterol levels (Table 5). Each of these exerts a powerful influence on the probability of the development of coronary heart disease irrespective of the presence or absence of other factors: the first two, for example, both lead to an overall doubling of the risk. In combination the effect is more substantial: raised cholesterol levels in conjunction with high blood pressure and cigarette smoking increase the risk of coronary heart disease to more than eight times that for individuals without these factors (Stamler and Epstein 1971). Inevitably estimates of this type are based upon arbitrary definitions – individuals are classified simply as hypertensive or not hypertensive, smokers or non-smokers – and may substantially underestimate the risks confronting specific population subsets. Khosla and his colleagues (1977), for example, have calculated theoretically from American data that males aged 55–59 who smoke heavily and have blood pressure and cholesterol levels at

Table 5 *Risk factors for coronary heart disease*

	Characteristic	*Effects on the risk of coronary heart disease*
Principal risk factors	Smoking (cigarettes)	The greater the amount smoked currently, the greater the risk.
	Blood pressure	The higher the pressure the greater the risk.
	Blood cholesterol	The greater the concentration the greater the risk.
	Diabetes	People with diabetes have a higher risk.
	Family history	The longer parents live, the less the risk to their children.
	Obesity	Being overweight may increase the risk (unproven).
	Stress	Stress may increase the risk (unproven).
	Personality	Some types may be more prone than others (unproven).
	Physical activity	The less exercise customarily taken, the greater may be the risk (unproven).
	Hardness of tap water	The softer the tap water the greater may be the risk (unproven).

Source DHSS 1981.

the 99th percentile have a risk for coronary heart disease which is 90 times that for men in the 40–44 age group who don't smoke and have normal blood pressure and cholesterol measurements.

In spite of the apparently substantial risks associated with the presence of these and other factors, they do not provide a complete explanation for the occurrence of coronary heart disease. Thus the Pooling Project Research Group's (1978) collation of results from five prospective studies undertaken in the United States showed that 'only' 40 per cent of men in the highest risk category according to smoking habits, blood pressure and cholesterol levels can be expected to develop coronary heart disease during the period when they are aged 40–64 years old – as will 6 per cent in the lowest risk category. To some extent the former finding may be explained by changes in behaviour by some individuals during the study period resulting in reduced levels of risk and hence a more favourable outcome at age 65 years than would have been predicted at trial entry. In addition, both observations may reflect the presence or absence of other deleterious or protective factors, some of which have yet to be identified. It is also probable that more refined risk factor measurement (to take account, for example, of specific smoking careers rather than broadly categorised consumption levels) and closer integration of haemostatic (Meade *et al* 1980) and metabolic (Logan *et al* 1978) characteristics into the conventional risk factor concept would facilitate greater accuracy in the prediction of subsequent coronary risk.

Nevertheless, it would still seem feasible to argue that for some individuals the apparent insignificance of the presence of coronary risk factors might derive from a low genetically determined vulnerability to the disease. Equally, its occurrence in individuals with seemingly low risk profiles might reflect a family history for the disease. There is no gene for coronary heart disease as such but there is some evidence that genetic factors may in part determine individual susceptibility to clinical manifestation.

The most obvious influence is a person's sex: men are more likely to develop coronary heart disease than women. The fact that this sex difference appears to diminish after the menopause has led to the suggestion that female sex hormones (oestrogens) may exert a protective effect, a possibility supported by evidence that premature menopause raises the risk of developing coronary disease (Oliver 1977).[16]

16 This contention appears to conflict with the observation that hormone administration in the form of oral contraceptives may increase the risk of coronary heart disease. The Royal College of General Practitioners' study of mortality associated with the pill (RCGP 1981) has estimated that current and former users together have a death rate from coronary heart disease of 8 per 100,000 woman-years compared to 2 per 100,000 among controls. Age and smoking habits magnify the risks involved. Thus, focusing on all circulatory disease, the rate for non-smoking users aged 25–34 years is 4.4, rising to 63.4 for users aged 35–44 who smoke. (The corresponding rates for non-users are 2.7 and 15.2 respectively.)

Genes may be involved in other ways. Abnormalities akin to but less severe than that believed to be responsible for familial hypercholesterolaemia might explain, in part at least, blood cholesterol variations among apparently normal persons. Studies of twins indicate that coronary heart disease is more likely to develop in both individuals if they are identical twins than if they are non-identical (DHSS 1981). Ethnic disparities in incidence (*BMJ* 1980a) and familial clustering (Rissanen and Nikkila 1977) also portend a genetic influence in the aetiology of the disease although in both a shared environment may be equally if not more important.

In spite of these considerations and certain apparent 'epidemiological inconsistencies' – for example, the fact that the recent decline in coronary mortality in the United States was most pronounced among women even though the proportion of females who smoke has been increasing (Stallones 1980) and the wide disparity between male mortality rates in Edinburgh and Stockholm in the presence of almost identical serum cholesterol levels (Oliver *et al* 1975) – the steady accumulation of evidence from reliable sources does nevertheless strongly suggest that lifestyle and habits are the principal determinants of the development of coronary heart disease.

Treatment of coronary heart disease

The scope for therapeutic intervention in coronary heart disease has increased substantially since the publication of the last Office of Health Economics' paper on the subject in 1966. The optimism expressed in the context of extending the availability of coronary intensive-care units has, however, been tempered by reports suggesting that in many instances of myocardial infarction hospital admission confers no significant advantage in terms of reduced mortality over care at home (Mather *et al* 1976; Colling *et al* 1976; Hill *et al* 1978). It is beyond dispute that such facilities are essential to the survival of certain patient sub-groups but hopes that they might reduce overall mortality by as much as 25 per cent (OHE 1966) appear excessive in comparison with more recent calculations from UK data indicating maximum potential improvements of between four and five per cent (Rose 1975). Advance has therefore derived from other sources. The research and development effort of the pharmaceutical industry, for example, has yielded medicines which not only offer effective control of anginal symptoms for many patients but also appear to be valuable in reducing post-infarction mortality. In addition, the development of coronary artery bypass grafting has provided a means of alleviating medically uncontrollable anginal pain and extending the survival pros-

pects for individuals with severe disease of the coronary arteries. It should be emphasised, however, that none of these measures constitutes a 'cure'; all are effected once the disease process has become manifest, either to provide relief during acute episodes or as secondary preventive measures.

Angina

Glyceryl trinitrate constitutes the cornerstone of acute pain relief in angina and appears to work via peripheral vasodilatation (resulting in reduced left ventricular workload and hence oxygen requirement) rather than through any increase in coronary artery blood flow (*Lancet* 1979). Administered sublingually, the drug is rapidly effective but has only a short duration of action so that doses have to be repeated – with an increasing possibility of side effects such as headache, flushing and postural hypotension – until the pain abates. Slow release formulations of other nitrates may be employed as a prophylactic measure but in view of the need for relatively high doses to attain appropriate blood levels as well as doubts regarding effectiveness (Burt *et al* 1982a) this therapeutic function is largely fulfilled by medicines which block the beta adrenergic receptors in the heart. The latter action diminishes cardiac activity and oxygen demand and facilitates an increase in the amount and duration of pain-free activity. Unfortunately, beta blockers are associated with a number of side effects and contra-indications although to an increasing extent such limitations have been overcome by continued pharmaceutical industry research in this area: a broad range of medicines is now available and choices are possible between preparations which are cardio- and non-cardio-selective, long and short acting and those with and without intrinsic sympathomimetic activity (that is partial agonist activity). Consequently, it has been estimated that beta blockade, alone or in combination with other medicines, constitutes a highly effective treatment for 70 or 80 per cent of patients with classic angina (Opie 1980).

Nitrates and beta blockers also play a major role in the treatment of 'unstable' angina. In recent years, however, they have been supplemented by a new class of drugs, the calcium antagonists. These agents inhibit the transport of calcium through the channels in cell membranes with the effect of modifying cardiac rhythms and producing vasodilatation (*BMJ* 1981a). Of the drugs currently available, attention has focused particularly on the use of verapamil and nifedipine in 'unstable' angina. The latter, for example, has been shown to provide relief in patients with symptoms which appear to be attributable to coronary artery spasm (Prinzmetal's 'variant' angina). Further, combined with beta blocker and nitrate therapy, the drug appears to facilitate more successful longer-term management of unstable manifestations than conventional regimens alone (Gerstenblith *et al* 1982).

Nifedipine and other calcium antagonists are also effective in classic angina of effort and may be particularly valuable in cases where beta blockade poses clinical problems (*BMJ* 1981) or does not provide full relief by itself (Bassan *et al* 1982).

Coronary artery bypass grafting (CABG)

It was not until the introduction of the cardio-pulmonary bypass machine in the 1950s and coronary arteriography in the early 1960s that a direct surgical approach to the coronary artery became feasible. The first successful operation, in which myocardial blood flow was restored by the grafting of a length of reversed saphenous vein between the aorta and the diseased coronary artery beyond its point of occlusion, took place in Texas in 1964 (Wheatley and Dark 1982). The Americans have pioneered and led the adoption of this technique and it is estimated that approximately 110,000 procedures were performed in the US in 1980 (Hopkins Tanne 1982). This compares with a figure of approximately 4,500 in England and Wales (English 1982).

Given the variations in both the identity of the arteries affected in coronary heart disease and the severity of occlusion there is no straightforward means of evaluating coronary artery by-pass grafting. Borrowing the language of economics, a 'cost-benefit' form of approach is initially required to weigh the risks of surgical intervention, both morbidity and mortality, against potential gains measured in terms of symptomatic relief and extended life expectancy. This has then to be followed by 'cost-effective' analysis to determine the place of surgery amongst available medical or surgical alternatives in achieving specified therapeutic goals. Although the procedure has its origins in the mid-1960s and was subsequently adopted with great enthusiasm, especially in the United States, dilatory evaluation of the technique has meant that the data required for the resolution of these issues have only recently become available.

Focusing on the cost side of the equation, CABG procedures can now be performed in major surgical centres with an operative mortality rate of between one and two per cent (NIH 1981). This low figure is, however, dependent upon experience and selection of low-risk patients (less than 70 years of age, with a normal sized heart, good ventricular function, no recent infarction and no co-existing adverse medical diseases) suffering chronic stable angina (WHO 1978); early intervention in unstable angina may be accompanied by a 6 per cent mortality risk and in patients with very severe myocardial dysfunction there is a hospital mortality rate of between 15 and 20 per cent. Non-fatal sequelae range from problems with wound healing, instability of the sternum and local discomfort to perioperative infarction. The incidence of the latter, diagnosed by strict electrocardiographic criteria, is reported to have fallen from between 10 and 15 per cent to approximately 5

per cent (Honey 1982) although this figure may be nearer 10 per cent in some cases of unstable angina (NIH 1981).[17]

The benefits of CABG vary according to the nature and severity of coronary artery disease. In stable angina, immediate relief of pain is observed in over 90 per cent of patients, although early recurrence of symptoms occurs in a number of cases, probably due to graft occlusion. Thus it is estimated that disabling angina which is inadequately controlled by optimal medical treatment may be relieved, with impressive results, in three-quarters of surgically treated patients (Honey 1981). Subsequently, angina will recur or progress in about five per cent of patients per annum (NIH 1981) and although long-term data are currently wanting, some studies indicate that within ten post-operative years up to 50 per cent of patients will have redeveloped anginal symptoms (Hilton 1981). This deterioration may reflect 'technical factors' such as graft failure (although 80 per cent are patent at two years with apparently little change in this proportion over the following 3 to 4 years) or the progression of the original disease. Re-operations have been performed but the success rate is reported to be half that of primary procedures.

It is only recently that the effects of CABG on survival have been clarified. The European Coronary Surgery Study Group (1980) in a prospective randomised study of CABG in stable angina pectoris found a survival rate at five years of 84.1 per cent for patients receiving medical therapy compared with 93.5 per cent for the surgical group. Retrospective stratification of the patients into subgroups by the number of coronary arteries involved revealed, however, that this general finding resulted from substantial improvements in survival for the surgical subgroups with left main artery disease and triple vessel disease: the survival rate at 5 years was 61.7 per cent for medical and 92.9 per cent for surgical patients with left main disease and the corresponding values for medical and surgical patients with triple vessel disease were 84.8 and 94.9 per cent.[18] No significant difference in survival was observed

17 Psychometric tests and biochemical observations suggest that some degree of brain injury may be another attendant risk of open heart surgery. The reported incidence has fallen from 44 per cent in 1970 to 15 per cent in 1975 although findings such as these reflect the sensitivity of the tests employed (*Lancet* 1982c). Cerebral damage appears to arise mainly from the formation of platelet thrombi in the extra corporeal circulation which are then transported into the brain.

18 There is some dispute about the efficacy of CABG in promoting survival in patients with triple vessel disease (which has been reported in 30–40 per cent of angiographic studies). In contrast to the European Study findings, the initial results of the Veterans Administration co-operative trial (Murphy *et al* 1977) did not demonstrate increased survival with surgery. Although a reworking of the data excluding the three (out of 13) hospitals with an average operative mortality of 23 per cent does indicate a substantial improvement in survival in triple vessel disease associated with surgical intervention further studies are warranted to resolve the present uncertainty.

among patients with two vessel disease – the cumulative survival rate at 5 years was 87.5 per cent for the medical and 91.6 for the surgical subgroups.

It has therefore been established that coronary artery bypass grafting is of proven value in providing symptomatic relief of angina in patients for whom medical approaches are inadequate and this constitutes the principal indication for the procedure. In addition, CABG might be indicated in patients with certain manifestations of 'unstable' angina or continuing pain after infarction, depending on the results of comprehensive investigation and the potential risks of operation. In these and other situations the value of CABG remains equivocal (*Lancet* 1980c) and further studies are required to clarify these specific issues and, perhaps more fundamentally given the European Study's findings on survival, the indications for arteriographic examination in the first instance.

Avoiding myocardial re-infarction

Once the acute stage of myocardial infarction has been successfully managed – involving, for example, diamorphine for analgesia, oxygen to compensate for poor cardiac performance, diuretics and vasodilators in heart failure and lignocaine or beta blockers for their anti-arrhythmic effects according to patient requirements – attention may be given to prognostic considerations. Before the 1970s, reflecting the belief that coronary blood coagulation was the cause of coronary thrombosis leading to myocardial infarction (Mitchell 1981), investigations had focused principally on anticoagulant therapy as a means of avoiding re-infarction and death following the index event. However, clinical evaluation, dating back to the late 1940s/early 1950s, generally lacked the conceptual and methodological qualities demanded of contemporary investigation and much confusion persisted. In an attempt to provide clearer guidelines an analysis was undertaken of the combined results of nine controlled trials of long-term anticoagulant therapy carried out between 1950 and 1965 (International Anticoagulant Review Group 1970). The principal finding was a 20 per cent reduction in mortality in males given anticoagulants but in view of a number of remaining questions the authors emphasised the need for further controlled investigations. Recently, some clarification has emerged from a study undertaken in the Netherlands (Sixty Plus Re-infarction Study Research Group 1980). The latter found a two year total mortality of 13.4 per cent in the placebo group compared with 7.6 per cent in those treated with anticoagulants and recurrent myocardial infarction incidence rates of 15.9 and 5.7 per cent respectively. These results have led to proposals that anticoagulant therapy should be re-evaluated (Meade and Thompson 1981) but such exercises will now have to compete for resources with those concerned with other chemical entities shown during the last decade to be of value following myocardial infarction.

The recognition during the 1960s of the presence of large numbers of blood platelets in arterial thrombi in addition to fibrin provided a potential explanation for the limited success of anticoagulants in reducing post infarction mortality[19] and stimulated a search for agents which might modify platelet behaviour. Within this group, dipyridamole has not by itself been shown to influence outcome after myocardial infarction (Mitchell 1980) although in combination with aspirin it appears to be of some benefit (PARIS 1980). Limited (that is, not statistically significant) success has also been reported from specific trials of aspirin which prevents the formation of proaggregatory thromboxane in blood platelets (Elwood *et al* 1974, Elwood and Sweetman 1979). More recently, a major United States trial (Aspirin Myocardial Infarction Research Study Group 1980) reported almost identical results for aspirin and placebo at three primary trial end-points. In spite of these individually disappointing results,[20] the pooling of observations from these and two other studies led the Society for Clinical Trials to the conclusion that aspirin does generate some reduction in the risk of cardiovascular mortality after myocardial infarction (*Lancet* 1980d).

Sulphinpyrazone, which was originally developed as an agent for lowering serum urate levels and hence application in gout, also inhibits platelet aggregation and has been shown to diminish post-infarction mortality (Anturan Re-infarction Trial Research Group 1980). In a multicentre study in the United States the drug had reduced the incidence of cardiac death by 32 per cent in post-infarction patients at 24 months. More significantly, it had a pronounced protective effect against sudden death in the high risk period following myocardial infarction: between the second and seventh months there was a sulphinpyrazone-induced reduction in mortality of 74 per cent. On the basis of these findings, which might reflect mechanisms other than platelet modification such as anti-arrhythmic effects, Braunwald (1980) commented that 'sulphinpyrazone should be approved for use after infarction and made available to the American public at the earliest possible time'. However, criticisms levelled at the design and methodology of the trial (Temple and Pledger 1980, Mitchell 1980) dissuaded the Food and Drug Administration from granting a licence recognising post

19 Mitchell (1981) has also argued that the disappointing reduction in post infarction mortality associated with the administration of anticoagulant therapy was due to the failure to differentiate, and hence the inclusion in trials of, sudden unheralded deaths and fatalities from infarction linked pump failure or dysrhythmia, neither of which could have been reduced by an antithrombotic regimen.

20 In addition to the enzyme which leads to the formation of the proaggregatory thromboxane in the blood, aspirin inhibits antiaggregatory prostacyclin in the vessel wall. This dual effect may therefore provide an explanation for the disappointing results with aspirin. McNicol (1980) and Mitchell (1980) have suggested that the solution might lie in an intermittent administration of smaller than conventional doses as such a regimen might constrain thromboxane but not prostacyclin formation.

myocardial infarction as an indication for the drug. Subsequently, a reassessment of the study data (Pitt *et al* 1982) has dispelled some of the reservations surrounding the original report, but, given the somewhat dissimilar nature of the benefits observed for sulphinpyrazone in a recent Italian investigation (Anturan Re-infarction Italian Study Group 1982) it may be argued that further clinical evaluation should precede considerations of more widespread employment of the drug (Hood 1982).

Secondary prevention with beta blockers

Another potentially major advance in the care of patients following myocardial infarction stems from the discovery that the administration of beta blocking agents commenced soon after the event can reduce subsequent mortality levels.[21] Following a number of inconclusive investigations highly encouraging results have been reported from a well designed and conducted trial of timolol (Norwegian Multicentre Study Group 1981): when deaths that occurred during treatment or within 28 days of trial withdrawal were taken into account the cumulated sudden-death rate over 33 months was found to be 13.9 per cent in the placebo group and 7.7 per cent in the timolol group. During 1982 statistically significant reductions in mortality have also been observed to accompany the use of propranolol in studies conducted in the United States (Beta blocker Heart Attack Trial Research Group 1982) and Norway (Hansteen *et al* 1982). At the time of writing, the most recently reported evidence comes from a British trial of sotalol which found that at one year follow up there were 18 per cent fewer deaths among treated patients compared with the placebo group, although this benefit did not reach statistical significance (Julian *et al* 1982).

In spite, and to some extent because, of these and other findings (trial size, method of analysis and choice of end-points all have a significant bearing on results) many issues remain equivocal (Mitchell 1981b). Perhaps one of the most important unresolved questions is whether the different results in the various trials reflect disparities in the drugs tested or in the patients studied (Hampton 1981). The beta blocking agents currently available differ in their selectivity, possession of intrinsic sympathomimetic activity and membrane stabilising activity and to some extent these properties in turn are dose-related. There may also be other less well defined actions of significance: there is evidence, for example, that some of these drugs may lower high density lipoprotein levels (Oliver 1982, Day *et al* 1982) whilst conflict exists regarding the

21 Beta blockade may also limit the size of myocardial infarction. In a randomised trial of patients entering a coronary care unit Yusuf *et al* (1980) found that the early administration of intravenous atenolol reduced infarct size, as estimated by ECG changes and enzyme measurements, by one-third in patients with definite infarct at entry.

effects on platelet aggregation (Winther Hansen *et al* 1982; Campbell *et al* 1981). The patients included in the trials have varied in terms of age, severity of illness and have frequently been highly selected – in the Norwegian propranolol investigation, for example, only 11.4 per cent of the 4,929 patients with definite acute myocardial infarction screened for possible inclusion were admitted to the trial. In addition to such questions relating to drug choice and patient selection criteria, uncertainties persist concerning optimal dosage levels, the timing of the commencement of therapy and the appropriate duration of the latter. Progress towards the resolution of these issues and a clearer understanding of the preventive mechanisms involved may result from further investigation. In the meantime, the cumulative evidence from 11 clinical trials involving more than 13,000 patients suggests that moderately prolonged beta blockade in the period after discharge from hospital reduces mortality by about 25 per cent (*Lancet* 1982b); so far, however, only timolol has been granted a licence by the UK Committee on Safety of Medicines for use in the prevention of myocardial reinfarction.

The costs of medical care for coronary heart disease

Table 6 shows that at the average level of prices prevailing throughout 1981 medical care for coronary heart disease in England and Wales is estimated to have cost the National Health Service £255 million. Sixty per cent of this total stemmed from expenditure on hospital inpatient care – the Hospital Inpatient Enquiry indicates that coronary heart disease accounts for just

Table 6 *Estimated costs of medical care for coronary heart disease in 1981, England and Wales*

	£ million
Hospital care:	
Approximately 2.5 million in-patient days	153.8
Out-patients	6.6
Pharmaceuticals: approximately 18.2 million prescriptions for preparations acting on the heart (1980 data)	84.5
General Medical Services: coronary heart disease accounts for 1.66 per cent of consultations	9.9
	254.8

Source OHE estimates.

over four per cent of the average number of hospital beds occupied daily. Medicines prescribed by general practitioners for the control of the various manifestations of the disease are responsible for one-third of the cost shown in Table 6. These estimates are based mainly on 1978/1979 service usage and costing data (the latter being inflated to 1981 values) and should only be seen as providing crude orders of magnitude. Nevertheless, they suggest that coronary heart disease currently absorbs one pound in every fifty spent by the NHS.

It is, however, most probable that the overall estimate significantly under-represents the true level of costs. Focusing on the hospital sector, apart from omitting such expenditures as those arising from the use of emergency ambulance services, understatement is implicit in the unavoidable use of average cost figures. Heart disease patients admitted to medical wards may require a greater number of particularly costly diagnostic tests, closer and prolonged surveillance and more expensive pharmaceutical therapy than patients in other specialities. Similarly, coronary artery bypass grafting requiring preliminary investigative arteriography and subsequent intensive care probably generates *per capita* hospital case costs which are markedly under-represented by the averages shown in the published hospital costing returns.

The cost of pharmaceuticals shown in Table 6 is also likely to be an underestimate. First, it excludes the various costs of dispensing and pharmacist fees. Second, it refers only to 'preparations acting on the heart' which accounted for almost 10 per cent of the estimated net ingredient cost drug bill totalling £776 million in England and Wales in 1980. To this sum may be added part of the cost of the vasoconstrictors and vasodilators prescribed in that year. Furthermore, given that raised blood pressure is an important risk factor for coronary heart disease it might be deemed appropriate to attribute a certain proportion of the annual cost of prescriptions for antihypertensives and diuretics to the cost of therapy for the disease. Finally, some of the expenditure on tranquilisers might also be included as these medicines constitute an aspect of therapy for some heart patients. Taken together the above groups of drugs accounted for 25 per cent of the net ingredient cost drug bill in 1980. It may not therefore be too misleading to suggest that between 15 and 20 per cent of the nation's drug bill is attributable to coronary heart disease.

Future Trends

Future trends in the real costs of treating disease are a function, *inter alia*, of alterations in incidence (and severity) and in the potential for therapeutic intervention. In recent years the former, reflected in mortality trends at least, has shown little if any sign of change, so that shifts in the economic burden of coronary heart disease in the immediate future will probably stem in the main

from the uptake of the therapeutic advances described in the preceding section. The extent of the latter and, of course, the nature of the therapies entering into established clinical practice, will determine the degree of expenditure growth.

At the lower end of the cost spectrum, the general introduction of beta blocking agents into post-infarction prophylactic therapy would (in spite of the fact that the average net ingredient cost per prescription for preparations acting on the heart is almost double the average for all preparations together – 1980 figures) add relatively little to existing NHS expenditures. If, for example, the recommended prophylactic dose of timolol was administered to all (nearly 90,000 in 1978) patients admitted to hospitals in England and Wales for acute myocardial infarction, basic NHS costs would rise by £5.8 million per annum (at June 1982 prices). This figure, however, represents an absolute maximum: some survivors of infarction – perhaps 20 to 30 per cent (Hampton 1981) – have in any event a conventional indication for beta blockers to control anginal pain implying that 'extra' costs would not be involved and, more significantly, clinical investigations to date have been based on highly selected patient samples suggesting, in conjunction with actual trial findings, that such therapy is contraindicated or inappropriate in some patient groups. Although these cost implications might be counterbalanced to some extent by additional patient monitoring requirements and extra demand from cases unrecorded in the hospital data, the potential reductions in fatalities and re-infarctions necessitating expensive intensive care facilities strongly suggest that prophylactic beta blockade offers a high benefit to cost ratio.

Coronary artery bypass grafting might in some respects be expected to present a contrasting picture. Unpublished data compiled by the Society of Thoracic and Cardiovascular Surgeons suggests that approximately 4,500 CABG procedures (that is 91 per million population) were undertaken in 1980 in England and Wales (English 1982). Yet epidemiologically based measures of potential demand in conjunction with currently accepted clinical indications for CABG suggest that this figure represents an inappropriately 'conservative' level of supply. The World Health Organisation (1978) for example, has estimated that the number of new patients aged 65 or less meriting surgery for relief of severe angina is about 150 per annum per million population. On this basis, it may be calculated that almost 7,400 new cases requiring surgery arise each year in England and Wales. Application of the United States' operation rate in 1980 (495 per million) to the population of England and Wales would imply a trebling of this figure.

The economic consequences of aligning supply to the level of potential demand indicated by the WHO paper may be demonstrated by employing the case expenditure data reported by Monro and co-workers (1978). Updating their calculation of the

costs of cardiac surgery (including catheterisation, operation, intensive care and ward stay) to December 1981 prices generates a cost per CABG procedure of almost £3,400, which is broadly consistent with estimates from other centres (Mollow 1982, Wheatley and Dark 1982). It might therefore be calculated that redressing the apparent 1980 shortfall between supply and new annual demand would currently cost an extra £9.8 million.

This figure is almost certainly an underestimate given *inter alia*, the absence of any allowance for the use of capital resources and the exclusion of the additional capital and revenue costs that would accompany necessary service expansion. Furthermore, account is taken neither of the backlog of demand existing in the community – estimated by WHO at 400 per million – nor of other surgery-justifying cases which would probably be revealed by any extension of the indications for arteriographic investigation considered appropriate in view of the proven efficacy of, and saving of life associated with, CABG. Yet even a raising of the 1980 England and Wales operation rate to, say, half that prevailing in the United States to take account of these factors would only generate a relatively modest new basic requirement of £26 million. However, this sum derives from high *per capita* case costs and the economic significance of these can only be judged in the context of counterbalancing benefits.

The problems involved in attributing values to enhanced physical capability, reduced pain, improved self-care and general social functioning as well as to survival itself, have so far discouraged evaluation in the form of 'orthodox' cost-benefit analysis. Instead, against a background of increasing concern with the resource implications of 'high technology medicine' (Golding and Tosey 1980), justification for the costs of CABG has frequently been sought in terms of the reduction in social security payments and increased tax contributions resulting from patients' post-operative return to work. Wasfie and Brown (1981), for example, have calculated on the basis of the questionnaire replies from 68 patients who had received a coronary artery bypass graft that, on average, NHS costs per case are recovered within 6 years 10 months as a result of reduced social security payments and the restoration of taxation contributions. If estimated post-operative savings in drug expenditure and various other items are also taken into account this repayment period may be reduced to 2 years 10 months.

Such exercises are valuable in generating broad estimates of the costs of different surgical procedures and in promoting a raised general awareness of the resource implications of clinical practice. In the specific example relating to CABG it is clear, however, that the results are strongly dependent on the variables included in the analysis and that substantial variations in individual circumstances limit the general relevance of the findings. More fundamentally, the use of post-operative return to work as a measure of the value

of therapeutic intervention and as an argument for increasing the number of procedures undertaken is dubious: for some individuals subsequent occupation opportunities simply do not exist (especially perhaps in times of economic recession) whilst in other cases return to work may be determined by factors other than health status, such as duration of pre-operative sickness absence (Oberman (1979) has estimated that periods of invalidity exceeding 6 months increase the probability of permanent inactivity by 50 per cent), attitudes on the part of both patients and doctors and the availability of alternative income.[22]

In cases where CABG constitutes the only feasible course of therapeutic action, economic considerations operate principally at a macro level where they contribute along with political and other factors to decisions concerning the availability and broad allocation of health care resources. At the micro level economic appraisal has a more specific and potentially valuable contribution to make in terms of helping to guide choices in situations identified by clinical investigation where surgical and medical approaches offer broadly comparable therapeutic success rates for patients with angina. Such cost-effectiveness studies are confronted by many difficulties, notably in measuring the service and non-service (that is, patient) costs involved, in equating the different treatment risks and in defining an appropriate time horizon for study. Nevertheless, the incorporation, where relevant, of analyses along these lines into major clinical investigations such as the European CABG study (with subsequent re-evaluation when changes occur in the status of variables or new treatments emerge) might be expected to contribute more to achieving an appropriate use of scarce health care resources than some of the broad generalisations concerning medical and surgical costs appearing in the literature to date.

Primary prevention of coronary heart disease

In the past decade a renaissance has taken place in the status accorded to preventive medicine and its potential contribution to the alleviation of many contemporary health care problems. In

22 Wide disparities have emerged from investigations of post-operative return to work patterns. Barnes (1975) reported only a 16 per cent return to work after operation in patients in full-time employment beforehand whereas Westaby *et al* (1979) found in a sample of 117 men that the proportion in work after CABG was 73 per cent compared to 40 per cent before operation. Interstudy discrepancies severely inhibit comparisons of results but in the United States at least, the consensus view is that expectations that improvements in symptoms and functional capacity associated with CABG should enable more patients to resume employment have not been realised (NIH 1981).

large part this reflects the onset of diminishing returns in curative or acute care, that is, a stage has been reached where improvements in morbidity and mortality can frequently only be achieved with disproportionately large increases in expenditure. Concurrently, this shift of emphasis has been fostered by the accumulation of evidence confirming the role of behavioural factors in the aetiology of many major diseases. In both these and other respects, premature coronary heart disease may be regarded as one of the most appropriate targets for preventive strategies.

The direct treatment costs outlined in the previous section indicate that potentially substantial savings could flow from effective primary prevention, particularly in the hospital sector where, for example, coronary heart disease accounts for approaching 10 per cent of beds occupied daily by males aged 45–64 years. To these costs must be added those stemming from sickness absence: in 1979/80, 26 million lost working days were attributable to coronary heart disease,[23] resulting in payments from the National Insurance Fund totalling £115 million. In addition, account should be taken of the social burdens generated by the disease. Generally these sequelae – such as the occurrence of psychiatric morbidity among males following myocardial infarction (Lloyd and Cawley 1978) and the psychological and social consequences of such events for supporting wives (Mayou *et al* 1978) – are rarely susceptible to quantification as indeed are the numbers currently experiencing differing degrees of activity restriction and other handicaps as a result of the various disease manifestations.[24] It is at least clear that coronary heart disease is responsible for a substantial amount of premature bereavement: for males between the ages of 15 and 64 years deaths each year from the disease generate an estimated 250,000 years of lost potential life. This is equivalent to 20 per cent of the total years of working life lost from all causes. (Cancers, the second most important group, account for 18 per cent and accidents 15 per cent.) For females, the loss attributable to coronary heart disease is estimated at 63,000 years (8 per cent of the total).

Perhaps the principal 'indication' for preventive action stems from the nature of the disease itself combined with current thera-

23 Of this total 24.6 million days were attributable to males, so that coronary heart disease accounts for nearly one day in every ten of male sickness absence. In many instances the spell of inactivity is protracted: one in eight of the 506,000 male claimants of invalidity benefit (which replaces sickness benefit if incapacity continues beyond 168 days in any period of interruption of employment) were off work as a consequence of coronary heart disease.

24 The survey of the 'Handicapped and Impaired in Great Britain' undertaken in the late 1960s estimated that 129,000 persons over 16 years of age were impaired by coronary disease and that approaching 30,000 were handicapped appreciably or worse (Harris *et al* 1971). Given the exclusion of persons in hospitals and other institutions as well as the problems related diagnostic accuracy these data cannot be expected to represent the true size of the 'social burden' of the disease.

peutic limitations. In 1980, an estimated total of 81,000 medically notified coronary heart attacks (58,000 'definite' acute myocardial infarctions) among persons aged less than 65 years in England and Wales resulted in 26,245 deaths (ICD 410 – acute myocardial infarction). Of the latter, probably half occurred rapidly, within one hour of the onset of the symptoms (Tunstall Pedoe *et al* 1975). The latter group's study also suggested that approximately one-quarter of all attacks lead to death before hospital care can be obtained. In other manifestations, for example angina pectoris, all available medical and surgical interventions are employed once the presence of disease has been diagnosed either to control acute symptomatic episodes or as prophylaxis against subsequent clinical presentations of varying degrees of severity. None of these measures directly influences the underlying disease processes and each one is associated with side effects and risks of differing significance. Intervention success rates also vary: one year after cardiac surgery, for example, one patient in five remains unable to resume employment and nearly one in two reports some continuing restriction of activity (Ross *et al* 1981). Further, anginal pain has been found to recur or progress after bypass surgery in about 5 per cent of patients per year and graft failures develop in 15–20 per cent of cases by two post-operative years (NIH 1981). Against this background, the case for effective primary prevention is beyond dispute.

The feasibility of primary prevention

The concept of primary prevention in coronary heart disease predicates the existence of 'causally' significant risk factors and their susceptibility to modification. The evidence concerning the former has been discussed at length in this paper and in spite of many remaining areas of contention there is a broad consensus that the occurrence of disease is linked strongly to the presence of certain risk factors. The feasibility of amending the latter is to some extent implicit in the finding of risk reversibility by many of the investigations into specific risk factors but perhaps more appropriate evidence of the scope for preventive strategies may be drawn from the success of several community based multifactorial intervention trials reported in recent years.

The Stanford University Heart Disease Prevention Programme in the United States, for example, has demonstrated the potential for widespread reductions in the risk of cardiovascular disease (Farquhar *et al* 1977). The project was conducted in three Californian towns, one of which served as a control to the other two where extensive mass media campaigns were provided over a two year period, with personal counselling in one of the towns for a small subset of persons at high risk. In the control community the composite risk factor score increased over the study period, but in the two 'intervention' towns it fell by between 25 and 30 per cent.

The experiment therefore suggested that behavioural habits set in culture and custom and associated with a raised risk of heart disease can be modified by, in this instance, health education messages channelled through the mass media and research is now under way to see if the results can be replicated on a larger scale (Taylor 1982).

Similar improvements have been reported from a randomised controlled trial in British industry (Rose *et al* 1980). Twenty-four factories or other occupational groups, employing in total more than 18,000 men aged between 40 and 59 years, were formed into matching pairs. One of each pair was allocated randomly to receive a five to six year programme of medical examinations and intervention to reduce the levels of the main coronary risk factors,[25] delivered mainly through existing occupational medical services. Assuming that a reduction in risk factors is accompanied by a commensurate decline in overall coronary risk, it was estimated that the latter fell by an average of 4 per cent for the intervention group as a whole and by 11 per cent for those at particularly high risk. The authors commented, however, that these small but nevertheless significant benefits were not sustained when the preventive effort was relaxed.

In North Karelia, Finland, a comprehensive programme integrating health information facilities and linked environmental services into the existing health and social services has further confirmed that the successful revision of risk factor levels observed in individual subjects can be replicated on a community-wide basis (Puska *et al* 1979). It did not prove possible, however, to discern these improvements in terms of diminished cardiovascular morbidity and mortality: reductions in the latter were compared with those in a matched control area and the difference was not found to be significant (Salonen *et al* 1979).

More optimistic findings have nevertheless been reported from a project conducted in Oslo involving middle aged males (Hjermann 1981). From an initial screening survey of more than 16,000 men aged 40–49 years 1,232 healthy normotensive individuals at high risk of coronary heart disease were selected for a 5 year randomised trial to investigate whether lowering of serum lipids and cessation of smoking could reduce disease incidence. Members of the intervention group were acquainted with the risk factor concept and given dietary and anti-smoking advice. During the trial, mean serum cholesterol concentrations in this group were found to be approximately 13 per cent below those prevailing in the control sample and 25 per cent of smokers in the intervention group relinquished cigarette smoking compared with 17

25 Men at factories in the intervention group were given advice on dietary reduction of plasma cholesterol concentrations, stopping or reducing cigarette smoking, regular exercise for the sedentary and reduced energy intake for the overweight; hypertension was also treated.

per cent of controls. At the end of the observation period the incidence of myocardial infarction (fatal and non-fatal) and sudden death among those receiving advice was 47 per cent lower than that in the control group.

It is of course possible that the significant differences found between the experimental and control groups might reflect factors in addition to changes in dietary and smoking habits. Referring to the 'Hawthorne effect', Kringlen (1982) has suggested that the closer attention received by members of the intervention group in conjunction perhaps with greater social support and encouragement from their families might have made some contribution to the observed improvements. Intervention trials are inevitably beset by a gamut of sampling difficulties which, together with specific variable and intra-community selection, inhibit extrapolation to other populations. Nevertheless, the results of the Oslo study are encouraging because, unlike many previous trials, they substantiate the belief that primary prevention constitutes a feasible strategy in the control of coronary heart disease. Further, they suggest that the appearance of benefit may swiftly follow intervention (Rose 1982).

Initiatives in prevention

Increasing concern at the 'epidemic' of coronary heart disease prompted, in the mid-1970s, the establishment of joint working-parties of the Royal College of Physicians of London and the British Cardiac Society to consider cardiac rehabilitation, patient care and prevention. The aim of the report on the last of these subjects, which was published in 1976, was 'to formulate the best possible advice which can at present be given to medical practitioners towards the prevention of coronary heart disease'. Emphasis was placed on the multifactorial concept of risk and the authors commented that in individual cases 'the overall degree of coronary risk must be considered rather than deciding whether any particular factor has reached a "critical" level requiring treatment'. The document reviewed and concurred with the findings relating to the conventional risk factors but in the context of diet it proposed that appropriate reductions in saturated fat intake might in part be achieved by substitution with polyunsaturated fats. This recommendation represented a significant departure from the view adopted in the 1974 *Diet and Coronary Heart Disease* report by the Committee on Medical Aspects of Food Policy (DHSS 1974) and added fuel to a controversy that continues unabated.

Following the publication of the Joint Working Party report in 1976 two members of the committee became founders, with others, of the Coronary Prevention Group. The organisation was formed 'to continue discussions with economists and agriculturalists, the food manufacturing industry and specialist and medical opinion in order to examine ways of reducing and preventing coronary heart disease'. The principal thrust of this body appears

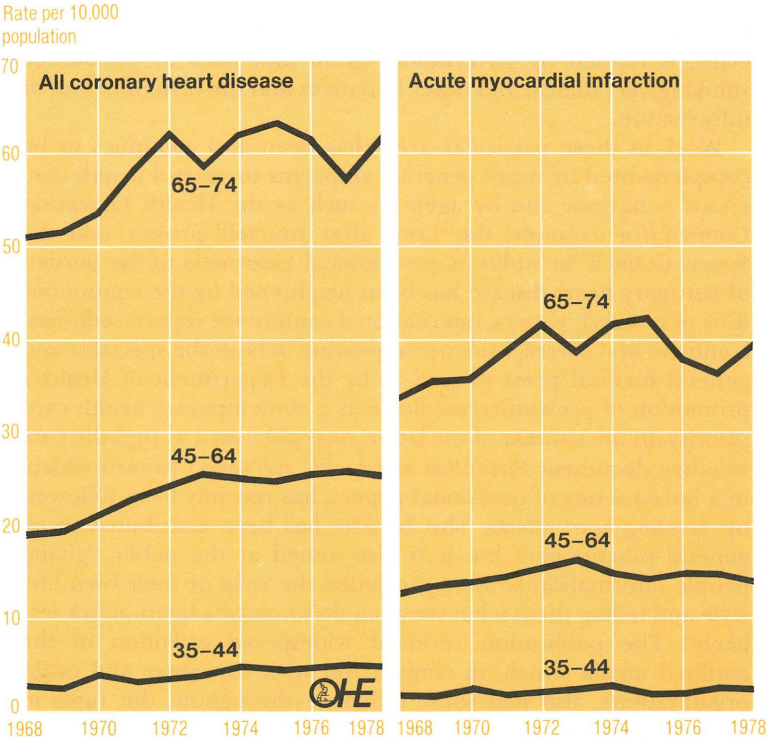
so far to have been concerned with dietary issues, leaving the health implications of cigarette smoking largely in the province of Action on Smoking and Health (ASH). This pressure group, which was set up in 1971 under the auspices of the Royal College of Physicians, is funded by government grant and aims to discourage smoking via political and other initiatives and the dissemination of information.

Work in these particular areas has been and continues to be complemented by more general campaigns to extend health conscious behaviour run by agencies such as the Health Education Council (for example, the 'Look after yourself' project) and the Sports Council. In addition, professional awareness of the burden of coronary heart disease has been heightened by the continuous flow of research papers, international conference reports, editorial comment and correspondence appearing in both the specialist and general medical press as well as by the Department of Health's promotion of preventive medicine as a contemporary health care priority. In the context of the latter, DHSS published in 1976 the consultative document *Prevention and health: everybody's business* which, in a linked series of occasional papers, has recently been followed by *Avoiding heart attacks.* This booklet has been distributed to all general practitioners but it is also aimed at the public, 'giving people information so they can judge the risks of their own lifestyle and telling them what they can do to make a heart attack less likely'. The publication received widespread attention in the national media which, in conjunction with consumer and other organisations, also had some influence throughout the 1970s in drawing public attention to the causes of the disease and the possibilities for prevention.

Impact of initiatives

In spite of these activities, however, little impact may be discerned in terms of either reduced morbidity and mortality from coronary heart disease or 'favourable' behavioural change. This paper has already shown that death rates in England and Wales remained unaltered throughout the 1970s whilst substantial improvements were being experienced in other countries and Figures 10 and 11 reveal that hospital admissions for the disease actually increased over the period. The Hospital Inpatient Enquiry indicates, for example, that total coronary discharges and deaths for males aged 45–64 years rose by 29 per cent between 1968/9 and 1977/8 and those for acute myocardial infarction by 8 per cent. These data have, however, to be interpreted with caution because they reflect changes in admission policies and therapeutic potential as well as disease prevalence and severity. Perhaps the wisest conclusion to be drawn from the diagrams, therefore, is that there is no evidence of any improvement during the 1970s in hospital measured morbidity for persons aged less than 65 years.

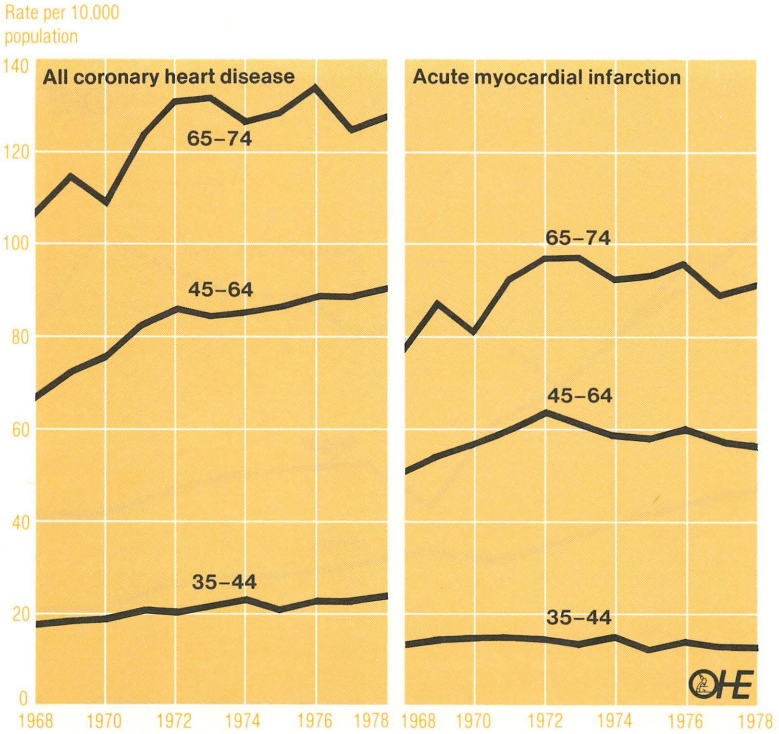
Figure 10 *Hospital discharges and deaths for coronary heart disease, females, England and Wales, 1968–78, rates per 10,000 population.*



Source Hospital Inpatient Enquiry.

Similar patterns emerge from a crude analysis of available data relating to risk factors. Focusing on dietary considerations, information obtained by the National Food Survey (Figure 12) shows that weekly *per capita* consumption of red carcase meat, an important source of saturated fat, grew by 22 per cent between 1973 and 1980 whereas intake of fish and poultry and chicken products only increased by 2 and 9 per cent respectively. Thus the level of meat consumption was 46 per cent greater than that for fish and poultry combined in 1980 compared with an excess of 27 per cent in 1973. The steady decline in sugar intake (a fall of one-third between 1970 and 1980) represents a more healthy trend although the extent to which this is counterbalanced by increases derived indirectly from other sources is unknown. For the protagonists of the dietary fat hypothesis perhaps the greatest source of encouragement to be drawn from the data lies in the progressive switch from butter to margarine. However, margarines constitute a heterogenous group of products – not only are there differences in the extent to which hydrogenation of polyunsaturated fats during the manufacturing

Figure 11 *Hospital discharges and deaths for coronary heart disease, males, England and Wales, 1968–78, rates per 10,000 population.*

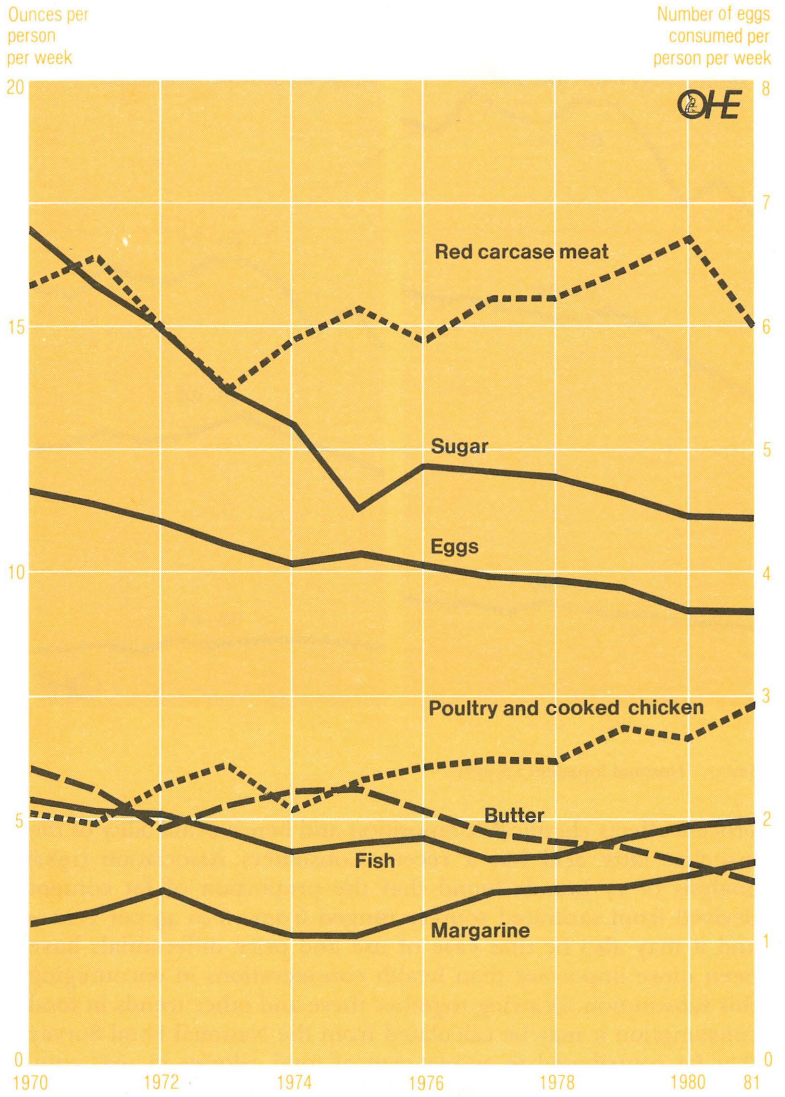


Source Hospital Inpatient Enquiry.

process affects chemical composition and hence availability of the essential fatty acid but a recent Consumers Association (1982) analysis of 17 brands found that the proportion of fat content derived from saturated sources ranged from 18 to 49 per cent – and it may also be that ease of use and price differentials have been more important than health considerations in encouraging this substitution. Drawing together these and other trends in food consumption it may be calculated from the National Food Survey that fat contributed to 39 per cent of total calories in 1979 compared with the recommended target of 30 per cent. In the same year, the ratio of fats from polyunsaturated sources to those from saturated sources (0.22) was less than half that found in southern European countries where low rates of coronary heart disease prevail (Marr and Morris 1982).

Analagously, the accumulation of evidence suggesting that regular vigorous exercise protects against coronary disease failed to stimulate widespread sporting involvement among the public. Information derived from the General Household Survey (Figure

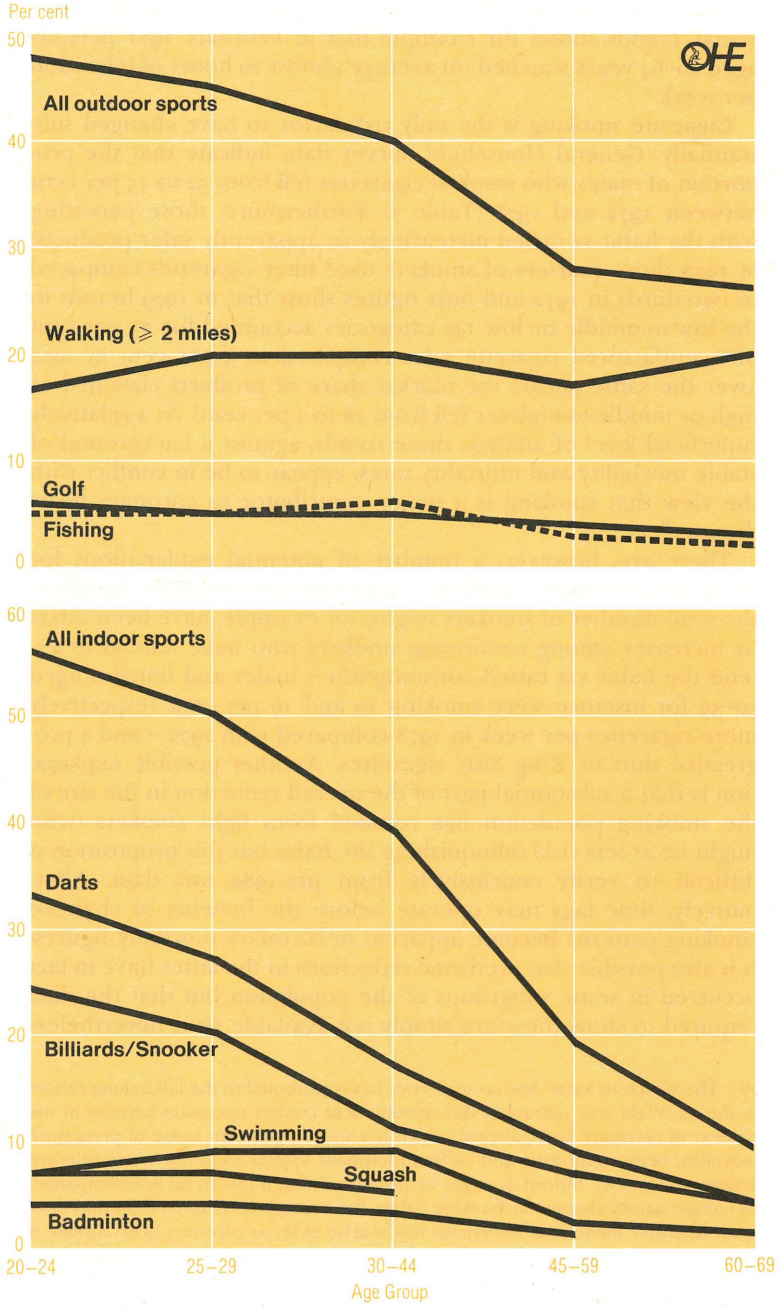
Figure 12 *Estimated average weekly consumption of selected foods, Britain, 1970–81, ounces per person per week.*



Source Ministry of Agriculture, Fisheries and Food.

13) reveals that participation rates decline rapidly with age and that there is a pronounced predilection for the more 'sedentary' activities. Focusing, for example, on males aged 30–44 years the survey for 1977 found that only two out of every five had been engaged in indoor sports or activities – generally darts, snooker or billiards – during the four weeks preceding interview. Swimming

Figure 13 *Percentage of males aged 20–69 years participating in indoor and outdoor sports activities, Britain, 1977.*



Source General Household Survey.

was the most popular active sport but this still only attracted less than one man in ten. Increasingly, leisure time is being absorbed by activities which involve little or no physical exercise: the latest Social Trends shows for example that in February 1981 persons aged 20–64 years watched on average almost 20 hours of television per week.

Cigarette smoking is the only risk factor to have changed substantially. General Household Survey data indicate that the proportion of males who smoked cigarettes fell from 52 to 45 per cent between 1972 and 1978 (Table 7). Furthermore, those persisting with the habit switched increasingly to apparently safer products: in 1978 three-quarters of smokers used filter cigarettes compared to two-thirds in 1972 and DHSS figures show that in 1979 brands in the low-to-middle or low tar categories accounted for 23 per cent of manufactured cigarette sales compared to 5 per cent in 1972 (over the same period the market share of products classified as high or middle-to-high tar fell from 18 to 1 per cent). At a relatively superficial level of analysis these trends, against a background of stable morbidity and mortality rates, appear to be in conflict with the view that smoking is a major contributor to coronary heart disease.[26]

There are, however, a number of potential explanations for these inconsistencies. Mortality reductions generated by the fall in the total number of smokers might, for example, have been offset by increases among continuing smokers who have tended to extend the habit via raised consumption – males and females aged 50–59 for instance were smoking 10 and 16 per cent respectively more cigarettes per week in 1978 compared with 1972 – and a progressive shift to 'King Size' cigarettes. Another possible explanation is that a substantial part of the overall reduction in the size of the smoking population has resulted from light smokers (who might be at less risk) relinquishing the habit but this proposition is difficult to verify conclusively from pre-1980 GHS data. Alternatively, time lags may operate before the benefits of changed smoking patterns become apparent in coronary mortality figures. It is also possible that predicted reductions in the latter have in fact occurred in some subgroups of the population but that the data required to show these are simply not available. (It is nevertheless

26 The switch to 'safer' low tar cigarettes has contributed to the fall in lung cancer in the UK (Wald *et al* 1981a) but this development confers uncertain benefits in the context of coronary heart disease (which is a more significant cause of premature mortality) because nicotine and carbon monoxide appear to be the more relevant aetiological factors. Indeed, it might be postulated that if this trend is accompanied by compensatory changes in smoking habits, for example increased consumption or more intensive inhalation, disbenefits might arise as far as coronary heart disease is concerned. In addition evidence from the Framingham Study does not suggest that filter cigarettes (of the type in use in the 1960s and early 1970s at least) are associated with a lower incidence of coronary heart disease than non-filtered products (Castelli *et al* 1981).

Table 7 *Cigarette smoking habits in Britain by age and sex, 1972, 1978 and 1980, percentages*

	Men			*Women*		
	Current non-smokers			*Current non-smokers*		
Age Group	*Never smoked*	*Ex-regular*	*Current smokers*	*Never smoked*	*Ex-regular*	*Current smokers*
16–19						
1972	53	4	43	57	4	39
1978	61	4	35	62	5	33
1980	62	5	32	63	4	32
20–24						
1972	36	9	55	44	8	48
1978	46	9	45	49	8	43
1980	48	8	44	51	9	40
25–34						
1972	27	17	56	41	10	49
1978	33	18	48	44	14	42
1980	34	18	47	43	13	44
35–49						
1972	22	24	55	41	11	48
1978	26	26	48	44	13	43
1980	27	27	45	44	13	43
50–59						
1972	16	30	54	41	12	47
1978	17	35	48	39	18	42
1980	18	35	47	39	17	44
60 +						
1972	18	35	47	66	9	25
1978	18	43	38	60	16	24
1980	19	45	36	57	19	24
All aged 16 and over						
1972	25	23	52	49	10	41
1978	29	27	45	49	14	37
1980	30	28	42	49	14	37

Source General Household Survey.

known that the decline in cigarette consumption among British doctors has been accompanied by a fall in their mortality from coronary heart disease.)

In the context of the last point, the General Household Survey has highlighted substantial differences by social class in the extent to which cigarette smoking has been abandoned: in 1978, 25 per cent of the professional group compared with 60 per cent in the unskilled category continued to smoke following reductions of 24

and 6 per cent respectively since 1972. This data source also points up class differences in participation in exercise activities: 8 per cent in the combined professional/employer grouping had been swimming in the 4 weeks before interview compared with 3 per cent in the pooled semi-skilled and unskilled category; for squash and walking (a distance of 2 miles or more) the appropriate figures were 8 and 1 per cent and 26 and 15 per cent respectively. These behavioural disparities may be reflected in the social class mortality rates which will eventually be calculated on the basis of findings of the 1981 population census. Nevertheless, the overall absence of improvement at a time when other nations have been experiencing falling coronary mortality rates remains an unassailable fact which requires explanation if future preventive initiatives are to achieve more success than has hitherto been apparent.

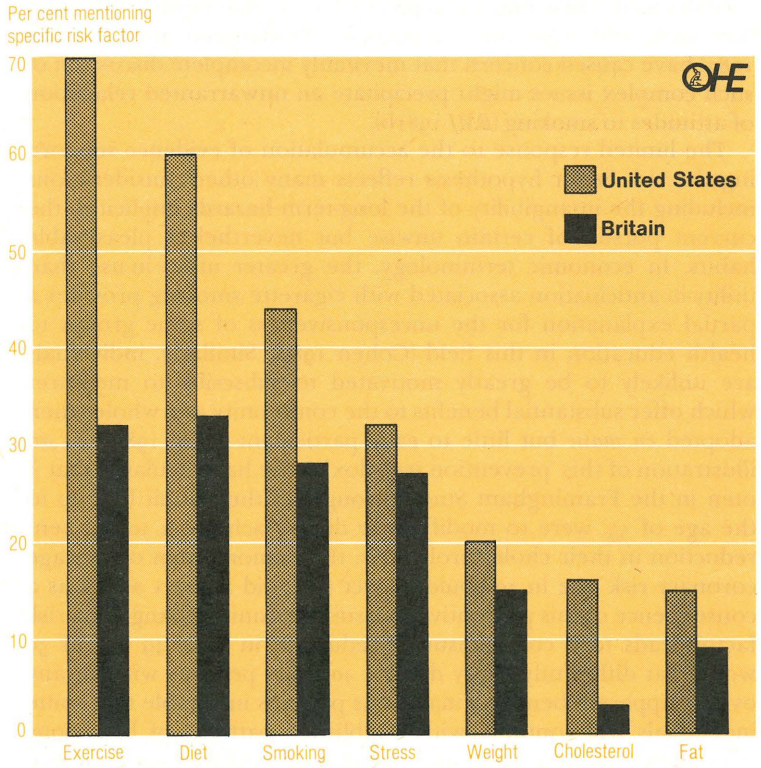
Explaining the 1970s trends

In a recent review paper, Kannel (1982) has reiterated the concluding comment of a *Lancet* leading article published in 1980 suggesting that the stability of heart disease rates in England and Wales might reflect 'respectable scientific doubt' concerning preventive efforts or perhaps simple apathy.[27] Whilst there is no clear way of evaluating either of these two contentions, surveys have suggested that at least part of the problem derives from an inadequate understanding of the 'causes' of heart disease on the part of the public. A recent Health Education Council survey among persons aged 16 years and over found that 53 per cent of those questioned considered stress to be the major cause of heart attacks. Obesity and cigarette smoking were cited by 36 per cent and lack of exercise by 20 per cent. High cholesterol levels and hypertension were selected by only six and five per cent respectively (*Health Education News* 1981).

In reply to a survey question about the means of avoiding heart disease, stopping or cutting down cigarette smoking was suggested by 28 per cent of the sample but only two per cent considered that checking and treating raised blood pressure would be valuable. The level of knowledge implicit in these answers is significantly below that observed in the United States (Figure 14) and may reflect a number of factors including, for example, resources available for and the targetting of health education. The finding of the British survey that more than half of all respondents and 89 per cent of males aged 35–44 were not concerned about heart attacks

27 In this context it is perhaps relevant that the genesis of preventive strategies in the United States significantly predates its British counterpart. The initial call for an effort to prevent coronary disease was the 'Statement on Arteriosclerosis, Main Cause of "Heart Attacks" and "Strokes" ' in 1959 by White and his colleagues. It was followed by American Heart Association statements on links between coronary disease and smoking in 1960 and diet in 1961 (Stamler 1980).

Figure 14 *Knowledge of risk factors in US and Britain: Percentage of samples mentioning specific factors in response to the question 'is there anything you can do to prevent heart attacks?'*



Source Taylor 1982a.

might also suggest a degree of 'fatalism' not found among United States citizens.[28]

Scientific dispute regarding the significance of specific risk factors in coronary heart disease has frequently been brought to the public's attention giving rise to confusion which in turn has probably contributed to the insubstantial overall change in certain behavioural patterns. The controversy within the medical profession surrounding the links between fats, cholesterol and heart disease, for example, generated an apparent questioning of traditional belief in the value of foods such as meat, eggs and milk which like the current margarine versus butter debate has helped

28 A nationally representative sample of residents in the state of Massachusetts has recently indicated prevalence figures for smoking of 31 and 34 per cent among males and females respectively and a claim to undertaking exercise at least two times per week by 56 per cent of those questioned (Lambert *et al* 1982).

to create public uncertainty about the nature of appropriate dietary strategies. More recently, in the context of cigarette smoking, it has been suggested that non-coronary disbenefits such as enhanced stress may be associated with abandoning the habit (Lee 1979) and subsequent reports in the national press (Loshak 1981) have caused concern that inevitably incomplete discussion of such complex issues might precipitate an unwarranted relaxation of attitudes to smoking (*BMJ* 1981b).

The limited response to the accumulation of evidence supporting the risk factor hypothesis reflects many other considerations including the intangibility of the long-term hazards implicit in the current pursuit of certain unwise but nevertheless pleasurable habits. In economic terminology, the greater utility-in-use than utility-in-anticipation associated with cigarette smoking provides a partial explanation for the unresponsiveness of some groups to health education in this field (Cohen 1982). Similarly, individuals are unlikely to be greatly motivated to subscribe to measures which offer substantial benefits to the community as a whole when adopted *en masse* but little to each participant (Rose 1981). As an illustration of this 'prevention paradox', Rose has calculated that if men in the Framingham Study throughout their adult life, up to the age of 55, were to modify their diet to achieve a 10 per cent reduction in their cholesterol levels, then among men of average coronary risk one in 50 could expect to avoid a heart attack as a consequence of this preventive measure (assuming change in a risk factor leads to a commensurate reduction in risk); 49 out of 50 would eat differently every day for 40 years perhaps without any overtly apparent benefit. Finally, it is perhaps inevitable that some individuals will continue with established patterns of behaviour irrespective of the quality and strength of available scientific evidence: in a sample of patients suffering myocardial infarction, Lloyd and Cawley (1980) found that 44 per cent of pre-event cigarette smokers were persisting with the habit at four month follow-up. And the European CABG Study Group found that 31 per cent of patients who had undergone surgery either resumed or commenced cigarette smoking during the three years following the operation.

Progress in prevention

The foregoing discussion suggests that improved strategies regarding the health education of the public might be expected to contribute to a more effective preventive effort. Clearly there is a need to enhance public understanding of the 'causes' of coronary heart disease without generating confusion which could undermine subsequent initiatives. In the specific context of dietary factors, for example, several contentious issues remain (some of which might be resolved, it is hoped, by the reconvened panel of the DHSS's Committee on Medical Aspects of Food Policy) but in areas where

a broad consensus exists, such as the need to avoid obesity and the advisability of limiting saturated fat intake, appropriate advice must be straightforward, acceptable and practical if it is to be productive (Marr and Morris 1982).

It has also become increasingly apparent that the nature of information and its presentation are important factors in the success of health education. 'Campaigning' approaches, exhorting behavioural change under threat of dire consequences, are therefore being superseded by those which emphasise the individual's ability to influence – indeed responsibility to promote – his own well-being (and indirectly that of his dependants) and highlight the benefits of adopting healthier lifestyles. The latter apply, of course, not just to the individual concerned but to family and friends: thus advice against cigarettes, for example, might draw greater attention to the links between parental smoking and subsequent uptake of the habit by children, the financial gains of abstention (a husband and wife both ceasing a daily consumption of 20 cigarettes would release an extra disposable income exceeding £700 per annum) and to the reported hazards for others of a smoke laden environment (*Lancet* 1982).

At the same time, campaigns such as those run by the Health Education Council, now generally include the offer of further information as a means of encouraging more sustained public interest than has tended to accompany the straightforward advertisements in the past. In addition, growing recognition of the possibility that individuals might be dissuaded from responding to health education by sensations of isolation and a lack of support has led to a greater frequency of projects which encourage active participation; the six-part BBC series *So you want to stop smoking*, aimed principally at the two-thirds of smokers who would respond positively to this question (ASH 1981), provides a recent example of this type of approach.

But perhaps the major potential for a more permanent extension of health conscious behaviour lies in the education of children and adolescents. A recent statement by those attending a workshop convened by the Coronary Prevention Group (1982) to discuss the prevention of coronary heart disease in the UK reported a consensus that special attention should be directed at children since dietary, smoking and exercise habits are often established in early life. The widespread interest and participation in the current *Superman* campaign against smoking indicates that in certain areas at least, approaches aimed directly at children may provide valuable support to initiatives channelled through the classroom. The latter itself offers a unique opportunity for health education on a broad front and for counteracting the inertia and harmful influences of the external environment; it may also provide a useful base from which favourable attitudes may filter back into the wider community. It is unfortunate, therefore, that in spite of the

projects, materials, training facilities and other leads provided by the Health Education Council, Schools Council and other agencies, health education of the young may be regarded as a 'chancy affair', determined largely by the strength of local interest (Morris 1981).[29]

The role of the general practitioner

Several of the studies reported in this paper in conjunction with other research suggest that the hitherto often ephemeral interest stimulated by health education campaigns may be converted into behavioural change of greater permanancy if the provision of such information is complemented by approaches at a more personalised level. In this context it has been argued that 'of all the many sources of health information available to the adult population it is the general practitioner who is the most trusted and whose advice has most impact' (McCran and Budd 1979). Furthermore, general practice provides an excellent framework for preventive medicine – virtually everyone is registered with a family practitioner and two-thirds of patients consult their doctor at least once each year (the average number of attendances exceeding 3 for males and 4 for females), a proportion rising to 90 per cent over a five year period (Fowler 1982). The recent initiatives in this area by the Royal College of General Practitioners (RCGP 1981a, 1981b) might therefore be seen as offering real prospects for future reductions in the burden of coronary heart and other avoidable diseases.

There is good controlled evidence that personal counselling by general practitioners against smoking can be effective in encouraging patients to relinquish the habit. A study reported in 1979 by Russell and his colleagues found a one year success rate of 5.1 per cent among individuals who had received advice, an information leaflet and warning of follow-up. The authors calculated that a GP adopting this approach could achieve 25 committed ex-smokers each year, a success rate yielding over half a million on a national basis. The Royal College of General Practitioners report on the prevention of arterial disease therefore suggested that the family doctor has a key role to play in motivating individuals, especially those in social classes 3 to 5 where 'conventional' health education has had least success, to relinquish the habit. The report recommended that the smoking behaviour of all individuals aged under 64 years should be ascertained and discussed and in a joint project to encourage such developments the Health Education Council, Action on Smoking and Health and the Scottish Health Education

29 Encouragingly, the Health Education Council's annual report for 1980/81 draws attention to research conducted during 1980 indicating that at least 600,000 children aged 5–13 annually attend lessons based on a health education project originally developed by the Schools Council and disseminated nationally since 1977. Yet this figure is equivalent to only one in ten of the relevant child population.

Group have issued anti-smoking kits to all family doctors for use with their patients.[30]

The Royal College's prevention document also drew attention to the evidence that mortality from coronary heart disease may be reduced by controlling hypertension. It recommended that at least one measurement of arterial pressure should be obtained every five years from each patient aged 20–64 consulting his or her doctor and that individuals with pressures at or exceeding 180/105 should be offered treatment and followed up at intervals not exceeding four months.

In addition, the report noted the accumulation of data concerning the treatment of hypertension in the diastolic range 90–104 mmHg. An Australian trial (Reader *et al* 1980) of chemotherapy in mild hypertension (95 to 110 mmHg) among persons aged 30 to 69 years, for example, found a small but not quite statistically significant reduction in coronary heart disease mortality in the treated group. The authors commented, however, that the evaluation of therapy in this specific context 'is bound to be difficult when overall benefits, particularly in relation to strokes, prohibit the prolongation of trials to allow the occurrence of a sufficient number of ischaemic events to demonstrate or refute benefit. Furthermore, prolonged treatment may be necessary to influence the natural history of disease'. Against a background of inconstant trial findings in respect of this specific indication (WHO/ISH 1982), concern at the possibilities of unexpected adverse reactions occurring after years of drug exposure (Oliver 1982)[31] and workload considerations, the Royal College report concluded that although 'evidence that treatment should be initiated at a diastolic threshold of 90 to 95 mmHg is persuasive . . . that of 105 mmHg should be mastered first . . .'

30 Russell, one of the co-authors of the study underpinning this initiative, has argued that another anti-smoking aid, nicotine-containing chewing gum, should also be made more generally available (Scrip 1982). The product, which is currently only available through GPs on private prescription and estimated to cost up to £50 for a four-month course, supplies nicotine at a rate and in a quantity sufficient to reduce the withdrawal symptoms of smoking abstinence and has been shown in a controlled trial to assist individuals to give up smoking (Fee and Stewart 1982).

31 It has been speculated, for example, that any reduction of coronary risk conferred by long-term antihypertensive therapy might be offset by the latter's apparent lowering of high density lipoproteins (*Lancet* 1980e). General concern in this area stems to some extent from the unexplained findings of the WHO trial on primary prevention of coronary heart disease using clofibrate to lower serum cholesterol. Over a mean observation period of 9.6 years (5.3 in the trial and 4.3 afterwards), 25 per cent more deaths were observed in the clofibrate treated patients compared to the high serum cholesterol controls (Committee of Principal Investigators 1980). Thus it has been argued that in the management of hypertension, control should wherever possible be sought initially via treatment of obesity and reductions in salt intake and alcohol consumption before proceeding to pharmacological therapy.

The control of smoking and of hypertension were regarded by the authors of the RCGP paper on the prevention of arterial disease as the principal targets for action by general practitioners although recognition was also given, *inter alia*, to the importance of avoiding obesity and encouraging physical exercise. It seems likely, however, that only a relatively small proportion of the 26,000 general practitioners in the UK have been undertaking preventive activities of this nature: just 10 per cent of smokers claim they have been advised to give up the habit (Fowler 1982a) and a random sample study of 697 persons aged 20 or over in one part of Central London showed that only 20 per cent had had blood pressure measurements taken by their GPs in the previous five years and that 39 per cent of hypertensives detected in this way had not been followed up (Heller and Rose 1977). Consequently, substantial changes in current practice will be required if, as the paper suggests, anticipatory care is to be the main direction of growth for the primary medical services in the foreseeable future. Aside from clearly important considerations of training, additional workload and incentives, the response to this proposal will reflect the extent to which family doctors themselves accept that there are opportunities unused, needs unmet, responsibilities not yet heeded and changes which can be achieved (*Lancet* 1981g). Motivation will therefore also be influenced by the public's disposition to recognise and undertake their role in promoting their own well-being and the co-operation of other agencies in helping to create a more health conscious society.

In the context of the last point, a number of observers have drawn attention to the contribution required from other professionals in the NHS. Thus Taylor (1982b) in a *British Medical Journal* editorial introducing a series of articles aimed at encouraging the extension of prevention in general practice emphasised the need for teamwork, commenting that 'one essential is to plan and develop co-operative links with community physicians, nurses, health visitors and health education units'. The potential of the first of these groups was highlighted in advance of their succession to the original Medical Officers of Health in the 1974 NHS Reorganisation (Morris 1969), yet the health promoting role of community physicians has been far from fully realised, in part perhaps because of the substantial amount of time absorbed by administrative functions (USHP 1981). Health education officers in addition to planning and executing local campaigns and supporting non-specialist health educators such as teachers, could also provide general practices with valuable advice, materials and the means for evaluating preventive efforts although shortfalls in personnel appear to limit the scope for significant developments in this area (Pike 1982). Currently there are around 420 health education officers in post – 1 per 131,000 members of the population – and as their employment is to remain under the new administrative arrangements at

the discretion of district health authorities it might be expected that disparities heretofore in local provision (Evans 1982) will persist.[32] Finally, there is also an important role for community pharmacists in health education.

Government, too, has an important 'enabling' function to discharge in the promotion of a healthier society and this extends beyond the provision of appropriate funds to organisations such as the Health Education Council and Action on Smoking and Health.[33] Thus Morris (1981), for example, has argued that there is a need for more vigorous central and local government action in facilitating exercise and Ball (1982) has expressed the view that greater efforts should be made to support the dietary recommendations of DHSS and other committees by promoting the availability of 'healthier' types of food (such as low fat milk) and reconsidering the subsidies on full fat milk to schools and on butter to hospitals and other institutions. Action has nevertheless already been taken to restrict some of the promotional activities of the cigarette manufacturers and evidence from Norway and Finland suggests that a ban on all tobacco advertising might be associated with a valuable reduction in cigarette smoking by children. Yet in March 1982, in spite of strong opposition registered by leaders of the medical profession (Robson *et al* 1982), a new agreement was signed by the Department of the Environment and the tobacco companies permitting the latter to spend an inflation-proofed £4.5 million per annum on sports sponsorship until the end of 1985. Extensive television coverage is given to many of the supported events, thereby yielding a form of atypically inexpensive advertising (Koshi 1981) which often has the especially unfortunate effect of linking smoking and healthy outdoor activity (*BMJ* 1982) and serves to undermine efforts both to erode the social acceptability of smoking and to dissuade young persons from taking up the habit which the DHSS itself calculates to cost the NHS £155 million (at November 1981 prices) as well as 50,000 premature deaths and 50 million days of sickness absence each year. To some extent, the apparent ambiguity of certain elements of government activity given the desired goal of a more health conscious society reflects an inconsistent recognition of the health dimension present in

32 Research currently under way is also examining the hypothesis that District Health Authorities could make a useful contribution to prevention in primary care by employing someone with educational, community nursing and management skills who would work as a facilitator as well as offering practical help to practices interested in developing prevention (Gray 1982).

33 The 1982/83 budget of the Health Education Council has recently been increased to £8.572 million (including £2 million for anti-smoking activities) and Action on Smoking and Health receives approximately £100,000. In sharp contrast, it is estimated that the annual expenditure on promotion by the tobacco industry totals £100 million (Lloyd 1982).

many of the policy decisions of different departments. It might be argued that such considerations merit more detailed exposition in policy formation and in this respect the concept developed by the Unit for the Study of Health Policy (1981) of 'health promotion teams' with a brief to monitor developments and stimulate debate when appropriate would appear to be an innovation worthy of further examination.

Conclusions

During the past decade or so research into and knowledge of the underlying pathology of coronary heart disease have advanced at an unprecedented pace; it appears to have been confirmed, for example, that spasm can be a cause of acute ischaemia in angina and interest in the aetiological significance of thrombotic processes has been rekindled by new understanding of platelet behaviour. Concurrently, the scope for successful therapeutic intervention has increased significantly: the development of the beta blocking agents and, more recently, the calcium antagonists has, in conjunction with the nitrates, extended the possibility of effective symptomatic control to large numbers of patients suffering from angina. In cases where pharmacological management is inadequate, coronary artery bypass grafting offers a solution of proven value which, in certain disease presentations, also facilitates significant improvements in life expectancy.

The period following heart attack has been another focus of clinical research. At the beginning of the 1970s there was only meagre evidence that means might exist of successfully reducing post-infarction morbidity and mortality. During the last 10 years, however, the potential for promoting survival in this period has expanded substantially and arguments can now be advanced for a selective use of CABG, anticoagulants, aspirin, sulphinpyrazone and beta blockers. The latter in particular have been the subject of a host of clinical trials with one drug – timolol – demonstrating such a degree of advantage that the UK licensing authorities have granted a licence for its use in post-infarction patients. Nevertheless, a number of questions concerning the administration of beta blockers and other drugs in this specific context remain; an overriding priority must now be to maximise the potential benefits of the last decade of research by further thorough evaluation both to confirm efficacy and to establish which of the 'new' therapies are best suited to specific subgroups of patients.

In the future, therapeutic promise is offered by a new generation of potential antithrombotics including thromboxane inhibitors and synthetic prostacyclin analogues (Lewis 1982); clinical assessment in these areas might be expected to yield confident

results with a minimum of delay given the lessons of trial design and administration learnt in the recent past. Surgically, continued progress in the understanding of and hence ability to control immune response linked with improved survival prospects should enhance the scope for an extended application of cardiac transplantation technology, perhaps eventually employing completely artificial replacements.

Of perhaps more immediate interest is the development of percutaneous transluminal coronary angioplasty (PTCA) as a potential non-surgical alternative to coronary artery bypass grafting for angina. This procedure, pioneered by Gruntzig and his colleagues in 1977, involves the insertion into an obstructed artery of a balloon-tipped catheter which is then inflated to compress the atherosclerotic area into the vessell wall. In the United States, the National Heart, Lung and Blood Institute has since 1979 been compiling a register of new PTCA procedures undertaken and has recently convened a workshop to re-evaluate the technique. Reports on 1,586 lesions in which PTCA had been attempted indicated a successful dilatation rate (defined as a 20 per cent or greater improvement in the stenosis) of 63 per cent although complications occurred in approximately 21 per cent of procedures undertaken (Levy *et al* 1981). Inevitably, long-term follow-up data are not yet available but Petch (1982) has argued that in the short term at least there are grounds for cautious optimism.

Contemporaneously, research has been directed at the potential for attacking thrombi occuring in myocardial infarction with streptokinase. The technique involves the fusion of the enzyme into the coronary arteries in order to activate the plasminogen that is bound to fibrin in a thrombus, leading to lysis. Such action might facilitate early reperfusion of a twilight zone of ischaemic but viable tissue, or might prevent extension of the initial thrombus and the formation of new thrombi, thereby limiting the area of myocardial necrosis and hence improving prognosis (*BMJ* 1979a). Following a series of generally inconclusive trials, the European Co-operative Study Group's (1979) investigation of streptokinase in acute myocardial infarction found a 6 month fatality rate of 15.6 per cent in the treated group compared with 30.6 per cent among controls. The technique thus appears to offer considerable promise but at this stage further controlled trials to confirm efficacy and to resolve a variety of uncertainties (for example, the time after onset of symptoms at which benefit may still be obtained and the optimum type, dose and mode of administration of the fibrinolytic agent (*Lancet* 1982a)) constitute the essential requirement rather than a premature dissemination of the approach which might threaten confusion akin to that created by the over enthusiastic initial response to CABG (Muller *et al* 1981).

Given the complexity of coronary heart disease it would, in the short term at least, be unrealistic to anticipate the discovery of a

single therapeutic 'magic bullet' (Braunwald 1980). Nevertheless, continued research in the areas described above and elsewhere should facilitate progress in the aetiological understanding of the disease as well as in control over its clinical presentations. It requires emphasis, however, that current and immediately foreseeable therapies offer only alleviative or prophylactic possibilities without modifying the underlying disease. In addition, the evolution of post-infarction treatments is of no relevance to persons dying rapidly following a heart attack: almost 60 per cent of coronary victims who die within one year of their heart attack do not in fact reach hospital alive. These observations, in conjunction with the extent of premature mortality caused by the disease and the economic and social sequelae for patients and their dependents, strongly posit the case for effective primary prevention.

Yet it may be argued that initiatives in this area appear so far to have been associated with limited success. Focusing on mortality rates for England and Wales, this paper has shown that little or no improvement took place over the period 1968–78 when substantial reductions were being achieved elsewhere. In the United States, for example, coronary heart disease fatality rates fell to such an extent that replication in England and Wales would have generated 9,300 fewer deaths among males aged 35–64 years in 1978 than the number actually recorded. This sum would have been equivalent to nearly one-third of the deaths officially coded to coronary heart disease for this age group. But even an improvement on this scale would still have left nearly 20,000 deaths attributable to this cause among males aged 35–64 years (equivalent to more than one-quarter of all fatalities at these ages).

The absence of a decline in mortality rates, at a time when increasing recognition has been given to the need for effective preventive medicine, has been equally apparent in morbidity data and would seem to be linked with an insufficient response to the evidence for a strong behavioural component in the aetiology of coronary heart disease. Thus within certain sections of the community cigarette smoking habits have altered relatively little and some smokers have even raised their level of consumption; only a minority of the population have incorporated regular physical exercise into their lifestyles; dietary intake of saturated fats has shown insignificant change; and the monitoring of blood pressure has been both irregular and limited in extent.[34]

34 The only coronary heart disease mortality rate to have shown any sign of improvement is that for males aged 35–44. Between 1971 and 1980 this rate declined by 19 per cent although the trend has been erratic and may also reflect changes in disease classification towards the end of the period. Consequently, perhaps the most significant cause for optimism to be derived from the data presented in this paper relates to the drop in the numbers of young people taking up smoking: in 1980 48 per cent of males aged 20–24 had never or only occasionally smoked compared with 36 per cent in 1972.

A number of factors underpin this behavioural obduracy. There is good evidence to show, for example, that even now public awareness of the risk factors for coronary heart disease is disappointingly inaccurate although enhanced knowledge is of course no guarantee of appropriate 'remedial action'. (Data from the General Household Survey, for example, indicate that 70 per cent of current heavy smokers believe that smoking is harmful to their health and a further 16 per cent accept that smoking 'excessively' can damage health.) The intangibility of the long-term hazards associated with certain patterns of behaviour or habits is another relevant factor as indeed is some degree of genuine scientific disquiet with the risk factor concept. Apart from controversy in specific areas, it appears that the major factors do not provide a complete explanation for coronary heart disease: it has been estimated that 'only' 40 per cent of men in the highest risk category according to smoking habits, blood pressure and cholesterol levels can expect to develop the disease over the period when they are aged 40 to 64 years.

This observation might reflect, *inter alia*, the protective influence of other recognised and possibly as yet unidentified risk factors as well as behavioural characteristics differing at the time of risk status evaluation from those preceding and following assessment. Related to the last point, it is perhaps unrealistic to expect a few static measurements to explain a risk which depends upon a long, dynamic and variable natural history and thus uncritically to equate statistical with biological explanations for disease (Shaper 1982). Yet other considerations such as genetic susceptibility may also be relevant and in the absence of definitive proof of aetiological relationships the lifestyle and other traits embodied in the risk factor concept are perhaps most appropriately seen as elements strongly predisposing to the development of disease. Nevertheless, it remains clear from the wealth of epidemiological evidence that has accumulated over the past twenty years or more that action on these risk factors, within the population as a whole rather than among high risk subgroups alone (Rose 1981), provides the key to significant reductions in the burden of coronary heart disease. Furthermore, maximum impact on the latter would appear to require the establishment of appropriate behavioural patterns early on in life, in spite of the benefits shown to follow suitable modifications at later ages and even after disease manifestation (ISFCS 1981).

In recent analyses of cardiovascular mortality trends in the United States, Kannel (1981, 1982) has concluded that the falls of the past decade reflect increased efforts towards healthier lifestyles and better management of high blood pressure. More specifically he has calculated that '50 per cent of the decline is a result of a decrease in smoking, 25 per cent is due to a reduction in serum cholesterol and 25 per cent is a consequence of improved control

of hypertension.[35] In this country, the Royal College of General Practitioners (1981b) has estimated that appropriate modification of these and other risk factors might be expected to prevent one-quarter of the deaths from coronary heart disease which occur among persons under 70 years each year (saving, that is, approaching 15,000 lives). Furthermore, the gains from behavioural change would not of course be confined to morbidity and mortality from this disease alone: reductions in the prevalence of smoking for example should generate falls in the incidence of lung cancer and chronic bronchitis whilst control of hypertension would substantially diminish the occurrence of strokes. It is to be hoped, therefore, that initiatives designed to encourage individuals to undertake greater responsibility for their own well-being than has hitherto been the case, including an extension of the family doctor's role in health promotion and perhaps most significantly health education of the young, are given maximum support, for it is here that the key lies to preventing a significant proportion of today's health care problems.

35 Conflicting with this degree of precision, it has also been argued that the changes in mortality were already apparent before any substantial alterations occurred in risk factors and that it is unclear to what extent the reduction in the former reflects falls in incidence or declining case fatality rates. Further, evidence from Rochester in the United States, recently reviewed by Hampton (1982), suggests that a fall in coronary heart disease incidence might have preceded the drop in mortality by 10 years, raising important questions about potential causes and the nature of the time lags involved.

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