in order to create an environment favourable to the perception of positive associations between various foods and healthy habits[11].

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The low fat/low cholesterol diet is ineffective

Ask almost any member of the general public about a diet which would reduce their chance of heart disease and the reply is the same: 'a low fat diet'. On closer questioning, this means a diet with a reduction in cholesterol and saturated 'animal' fats, i.e. less meat, butter, milk and cheese. Most national and international recommendations for the prevention of heart disease, whether for primary prevention or for patients who have developed the clinical manifestations of coronary heart disease, have made dietary restriction of total and saturated fats and of cholesterol the primary advice and often the sine qua non in relation to all other forms of management. To this extent they are to be congratulated that the message appears to be so universally accepted. Unfortunately, the available trials provide little support for such recommendations and it may be that far more valuable messages for the dietary and non-dietary prevention of coronary heart disease are getting lost in the immoderate support of the low fat diet.

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The origin of the 'low fat' diet

The international bodies which developed the current recommendations based them on the best available evidence[1–3]. Numerous epidemiological surveys confirmed beyond doubt the seminal observation of Keys in the Seven Countries Study of a positive correlation between the intake of dietary fat and the prevalence of coronary heart disease[4] although recently a cohort study of more than 43 000 men followed for 6 years has shown that this is not independent of fibre intake[5] or risk factors. The prevalence of coronary heart disease has been shown to be correlated with the level of serum total and low density lipoprotein cholesterol (LDL) as well as inversely with high density lipoprotein. As a consequence of these

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studies, it was assumed that the reverse would hold true: reduction in dietary total and especially saturated fat would lead to a fall in serum cholesterol and a reduction in the incidence of coronary heart disease. The evidence from clinical trials does not support this hypothesis.

The evidence from the dietary trials

It can be argued that it is virtually impossible to design and conduct an adequate dietary trial. The alteration of any one component of a diet will lead to alterations in others and often to further changes in lifestyle so it is extremely difficult to determine which, if any, of these produces an effect. Dietary trials cannot generally be blinded and changes in the diet of the 'control' population are frequently seen; they may be so marked as to render the study irrevocably flawed. It is also recognised that adherence to dietary advice over many years by large population samples, as for most individuals in real life, is poor and that the stricter the diet, the worse the compliance. Nonetheless, the evidence for a reduction in saturated fat from dietary trials for both primary and secondary prevention merits closer scrutiny.

Trials of low fat diets in primary prevention

There have been six randomized, controlled trials with long-term follow-up designed to modify the development of coronary heart disease in healthy subjects[6–11]. Remarkably, no primary prevention trial of sufficient size or sensitivity to examine the effect of a low total and saturated fat diet *alone* has ever been conducted. All these six primary prevention trials involved a reduction in total and saturated fats but they also involved alteration of one or more other risk factors such as cigarette smoking, blood pressure and exercise.

Of the three smallest trials (approximately 300–600 subjects per group), two suggested a significant reduction in coronary events. In the Oslo study[7], men at high risk were given dietary advice aimed at reducing saturated fat intake and modestly increasing polyunsaturated fat intake, and counselled to stop smoking. General advice was given to increase fish, whalemeat, vegetable and fruit intake. Over 5 years the mean difference in serum cholesterol between the two groups was relatively large for a dietary trial — 13% — and tobacco consumption was lower in the intervention group. There were fewer coronary events in the control group ($P<0{\cdot}028$) but the study was not powered to show any difference in coronary or total mortality. The second small trial to show a benefit, the Finnish Mental Hospital study[6], allocated test and control diets to the inmates of two separate institutions in a cross-over design lasting 12 years. Unfortunately the design was flawed since one third of the inmates changed over the period of the study and again, although there was a reduction in coronary events, the study was not powered to show any difference in mortality.

Curiously, the third and most recent of these small studies actually showed a significant adverse effect on coronary and total mortality[8]. In this trial, 1222 businessmen with one or more risk factors were randomly allocated to intensive dietetic measures to reduce saturated fat and cholesterol intake. They also were given advice on physical activity and smoking and had drug treatment for hypertension and hyperlipidaemia. After 5 years, the predicted risk of coronary heart disease had fallen by almost a half in the intervention group (with a 6% fall in total cholesterol) but there were actually more non-fatal myocardial infarctions ($P<0{\cdot}01$) and a trend towards more cardiac deaths. All the subjects were followed for a further 10 years after the end of the intervention period and all-cause mortality, cardiac deaths and deaths associated with violence were all significantly increased. No one has yet managed to rationalize these findings but at least it should not be assumed that such interventions are automatically without risk when assessing possible cost-benefits.

The three remaining dietary trials for primary prevention were much larger (4000–25 000 subjects in each group) and had sufficient power to examine overall mortality[9–11]. All of them were ineffective in reducing either coronary events or total mortality over the period of the trial. This is despite the fact that the Minnesota Coronary Survey trial[9] in seven mental hospitals managed to achieve similar reductions in serum cholesterol to the smaller trials above. A recently published follow-up of the MRFIT study[12] showed that deaths from acute myocardial infarction did become significantly lower in the original intervention group after 16 years although no data are available to indicate the compliance to the dietary advice over these years. Despite the size and long follow-up, there was still no significant reduction in overall mortality.

The message from these trials is that dietary advice to reduce saturated fat and cholesterol intake, even combined with intervention to reduce other risk factors, appears to be relatively ineffective for the primary prevention of coronary heart disease and has not been shown to reduce mortality.

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Trials of low fat diets in secondary prevention

There have been two trials of the effect of a low saturated fat diet alone in patients with coronary heart disease. The MRC study[13] followed 252 men randomized to a very low fat diet or no change in diet over 3 years; the low fat diet was poorly tolerated but achieved a 10% reduction in cholesterol. There was no difference in the rate of reinfarction or death and the researchers concluded that a low fat diet has no place in the treatment of myocardial infarction. An Australian trial of 458 men substituted polyunsaturated margarine for butter and found a slightly *lower* 5 year survival in the intervention group (3·3% deaths per year) than in the control group (2·4% deaths per year) although multivariate analysis showed that none of the dietary factors was significantly related to survival[14]. Following the negative results of these trials, no further studies of a low saturated fat diet alone have been conducted.

Should we be recommending diet at all?

The overwhelming importance of coronary heart disease in terms of morbidity, mortality and economic cost in the Western world made dietary advice, which was perceived to be cheap and safe, very attractive to Governments and their Health Departments. Vast sums of money have been invested in nutritional programs, dietary advice and nurse counselling to promote low saturated fat, low cholesterol diets — yet the trials to date for both primary and secondary prevention suggest that these diets do not work. However, this does not mean that all dietary interventions are futile. Other trials of secondary prevention have to a greater or lesser extent tried to alter the quality of the dietary fat intake and other components in patients with coronary heart disease, rather than restrict the quantity of saturated and total fat, and the results are more encouraging.

Trials of diets not dependent on fat reduction

Vegetable oil supplements were used in four of these trials[15–18]. In the LA Veterans Administration study, increased ingestion of corn, safflower, soyabean and cottonseed oils significantly reduced total cardiovascular events after 8 years[15]. The study by Rose *et al.* found no evidence of clinical benefit in patients given a low fat diet and supplements of olive or corn oil[16]. Similarly, the MRC group added soyabean oil as a supplement to the diet and found no difference in the incidence of death or myocardial infarction compared to men taking their normal diet[17] but a similar study from Oslo did show a significant reduction in pooled coronary heart disease relapses after 5 years and fewer fatal myocardial reinfarctions by 11 years[18]. However, none of these produced a significant difference in total mortality.

Saturated fat reduction, vegetable oil supplements and lifestyle changes in keeping with the current recommendations of the American Heart Association were advised for *both* the intervention and control groups in a study of Indian patients randomised within 48 h of a suspected myocardial infarction, but in addition the intervention group received a diet high in dietary fibre, omega-3 fatty acids (from fish and nuts), antioxidant vitamins and minerals[19]. The intervention group achieved remarkable wide-ranging and sustained changes in their nutrient intake associated with a modest reduction in serum cholesterol and weight loss. Cardiovascular events were reduced in the intervention group after only 6 weeks and after 1 year there was a significant reduction in myocardial infarction, a 42% reduction in cardiac deaths and a 45% reduction in total mortality compared to the control group on the standard 'low fat' diet. The study does not seem to have been continued beyond one year.

The first successful dietary study to show reduction in overall mortality in patients with coronary heart disease was the DART study reported in 1989[20]. The three-way design of this 'open' trial compared a low saturated fat diet plus increased polyunsaturated fats, similar to the trials above, with a diet including at least two portions of fatty fish or fish oil supplements per week, and a high cereal fibre diet. No benefit in death or reinfarctions was seen in the low fat or the high fibre groups. In the group given fish advice there was a significant reduction in coronary heart disease deaths and overall mortality was reduced by about 29% after 2 years, although there was a non-significant increase in myocardial infarction rates. The reduction in saturated fats in the fish advice group was less than in the low fat diet group and there was no significant change in their serum cholesterol.

Finally, the more recent Lyon trial[21] used a Mediterranean-type of diet with a modest reduction in total and saturated fat, a decrease in polyunsaturated fat and an increase in omega-3 fatty acids from vegetables and fish. As in the DART study there was little change in cholesterol or body weight, but the trial was stopped early following a 70% reduction in myocardial infarction, coronary mortality and total mortality after 2 years.

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The most effective diet for secondary prevention is therefore not reduction of saturated fats and cholesterol but appears to be an increase in polyunsaturates of both omega-6 and omega-3 fatty acids. Unfortunately, the design and conduct of these trials are insufficient to permit conclusions about which polyunsaturates and other elements of these diets are the most beneficial. The long-term effects of these trials[20,21] and compliance with the dietary regimes remain to be seen. But the mechanism of any benefit of the omega diets would appear not to be associated with reduction in the total or LDL cholesterol levels and may be more related to reduction of a thrombotic tendency.

The case for recommending similar changes in diet in primary prevention is less clear cut. Although the benefit of olive oil receives strong epidemiological support from several Mediterranean countries, particularly Crete, and short-term studies of diets rich in oleic acid (the principal monounsaturate in our diet) have demonstrated a reduced LDL susceptibility to oxidation, no formal randomized long-term trial of monounsaturates has yet been attempted. There is no consensus from population or cohort follow-up surveys about the protective effects of increased fish consumption on coronary mortality. The recently published report from the Physicians Health study[22] found no evidence of an inverse association between the intake of fish or fish oils and the risk of myocardial infarction and, while the highest coronary mortality was found among men who ate no fish, the risk did not decrease with increasing fish intake. At present, there does not appear to be any dietary advice which is effective in primary prevention.

Is drug treatment better?

An important aspect of the lipid-lowering dietary trials is that on average they were only able to achieve about a 10% reduction in total cholesterol. The results of recent drug trials have demonstrated that there is a linear relation between the extent of the cholesterol, or LDL, reduction and the decrease in coronary heart disease mortality and morbidity, and a significant effect is seen only when these lipids are lowered by more than about 25%[23].

Until 1994, the trials with lipid lowering therapy for primary and secondary prevention had been as disappointing and confusing as the trials with diet. They tended to show a reduction in coronary events, including deaths from myocardial infarction, but no reduction in overall mortality. Even though an excess of deaths from cancers and suicide was not shown to have any causal relationship with the treatment, there was no widespread acceptance of lipid lowering therapy.

This changed in 1994 with the publication of the seminal 4S study on secondary prevention of coronary heart disease in 4444 patients with cholesterol levels greater than 5·5 mmol . l^{-1} who were randomized to treatment with simvastatin or placebo in addition to 'usual care' including dietary advice[24]. The 4S study showed highly significant (30%) reduction in cardiac events and deaths from myocardial infarction and, for the first time, in overall mortality. The benefits were apparent after 18 months and the difference between the treated and the control groups continued to increase over the 5 years of follow-up. The more recent CARE study showed a very similar outcome with a 28% reduction in reinfarction using pravastatin in 4159 patients following myocardial infarction despite the fact that their cholesterol levels before treatment were *not* high (mean 5·4 mmol . l^{-1})[25]. As part of their usual care, patients in this study also received high levels of antiplatelet agents and beta-blockers and 55% had undergone revascularization with angioplasty or bypass surgery. There was no change in coronary heart disease deaths or in all-cause mortality. Over the 5 years of follow-up in both these statin trials the treatment was extremely well tolerated with around 90% compliance and no serious adverse effects — indeed there was almost no difference in the side-effect profiles between the statins and placebo.

With primary prevention the results of treatment with the statins appears equally encouraging. The West of Scotland Coronary Prevention study treated over 6000 healthy men (aged 44–65 years) who had total cholesterol levels greater than 6·5 mmol . l^{-1} with either pravastatin or placebo[26]. Again the trial was continued for 5 years, and normal advice was given to both the intervention and the controls groups. The risks of death from coronary heart disease and non-fatal myocardial infarction were reduced significantly in the pravastatin group by 31%, and there was a non-significant but favourable trend for all-cause mortality (− 22%) with no adverse effect on non-cardiovascular mortality.

The cost-effectiveness of treatment with the statins has been assessed at current prices for both primary and secondary care. It varies greatly according to the risk, being obviously more efficient for those at the highest risk, but has been shown to be greater than drug treatment for mild-to-moderate hypertension which is widely endorsed and used in general practice. For those at lower risk, diet should be able to provide a cheaper regimen but at present none has proved sufficiently beneficial.

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Conclusions

The commonly-held belief that the best diet for prevention of coronary heart disease is a low saturated fat, low cholesterol diet is not supported by the available evidence from clinical trials. In primary prevention, such diets do not reduce the risk of myocardial infarction or coronary or all-cause mortality. Cost-benefit analyses of the extensive primary prevention programmes, which are at present vigorously supported by Governments, Health Departments and health educationalists, are urgently required.

Similarly, diets focused exclusively on reduction of saturated fats and cholesterol are relatively ineffective for secondary prevention and should be abandoned. There may be other effective diets for secondary prevention of coronary heart disease but these are not yet sufficiently well defined or adequately tested. The circumstantial evidence of benefit from oils, particularly olive oil, vegetables, fruit and fish is strong.

For those at high risk, drug therapy with the statins provides effective primary and secondary prevention and should be considered, with or without a diet, in the same way as drug treatment for mild or moderate hypertension.

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