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Lipids and secondary prevention of ischaemic heart disease

Lipid lowering treatment is now indicated for patients with "normal" cholesterol concentrations

Ischaemic heart disease remains the major cause of death for men and women in the developed world and, with stroke, is a key area for health promotion in *The Health of the Nation*.[1] The importance of primary prevention (reducing risk in people with no evidence of disease) is highlighted by the fact that about a quarter of new cases of ischaemic heart disease present as sudden death.[2] Secondary prevention (reducing risk in people with evidence of disease) should be approached with the same vigour as primary prevention because morbidity and mortality from ischaemic heart disease have considerable social and financial implications for individuals as well as communities.

Measures that improve survival after myocardial infarction include treatment with thrombolytic agents, aspirin, and β adrenergic blockers, and stopping smoking. Lowering serum lipid concentrations in patients with ischaemic heart disease and hypercholesterolaemia has been shown to reduce the risk of subsequent cardiovascular death. Concerns have been raised that the cardiovascular benefits of lowering cholesterol concentrations might be outweighed by the increased risk of other causes of death. However, the Scandinavian simvastatin survival study (4S), a large randomised, placebo controlled trial of simvastatin in patients with ischaemic heart disease and total cholesterol concentrations of 5.5-8.0 mmol/l, showed significant improvements in mortality from ischaemic heart disease with no evidence of increased mortality from non-cardiovascular causes in the simvastatin group compared with the placebo group.[3]

Further analysis of this study's data showed that reduction in risk of major coronary events was similar for subjects in each of the four groups of baseline total cholesterol concentration (5.50-6.24, 6.25-6.74, 6.75-7.24, 7.25-8.00 mmol/l).[4] Many patients with ischaemic heart disease have cholesterol concentrations below conventional thresholds for treatment.[5,6] Two randomised placebo controlled trials have addressed the question of whether people with ischaemic heart disease and "normal" cholesterol concentrations would benefit from treatment with pravastatin.[7,8] The results of the CARE (cholesterol and recurrent events) study have just been published after a median five year follow up.[7] Over 4000 men aged 21-75 and postmenopausal women in the United States and Canada with total plasma cholesterol concentrations below 6.2 mmol/l, low density lipoprotein cholesterol concentrations of 3.0-4.5 mmol/l, and triglyceride concentrations below 4.0 mmol/l, who had had a myocardial infarction 3-20 months previously were recruited for the study. Cholestyramine was prescribed in addition to pravastatin or placebo for subjects whose low density lipoprotein cholesterol concentrations remained above 4.5 mmol/l. There was a 24% reduction in relative risk (95% confidence interval 9% to 36%, P = 0.003) in the primary end points of fatal and non-fatal myocardial infarction in the pravastatin group, a similar result to that obtained in the 4S study.

Novel findings of the CARE study included significant reductions in relative risk in the pravastatin group for major coronary events in women (46%, P<0.001) and in patients with impaired left ventricular function (28%, P = 0.02) and for stroke (31%, P = 0.03). Treatment with pravastatin was equally effective in subjects aged over 60 years as in younger subjects. In contrast to the results of the 4S study, the size of the reduction in relative risk of coronary events showed a graded response depending on low density lipoprotein cholesterol concentrations at recruitment. There was a 35% (P = 0.008) reduction in relative risk of major coronary events in the subgroup of patients with the highest low density lipoprotein cholesterol concentrations (>3.9 mmol/l). For those with intermediate concentrations of low density lipoprotein cholesterol, representative of average concentrations for people with ischaemic heart disease (3.2-3.9 mmol/l), there was a 26% reduction in relative risk of major coronary events (P<0.001). However, in the patients with the lowest low density lipoprotein cholesterol concentrations (<3.2 mmol/l) there was no difference in incidence of major coronary events between the pravastatin and placebo groups. These data suggest the possibility that a threshold exists at very low concentrations of low density lipoprotein cholesterol, below which lipid lowering treatment is not effective in secondary prevention of ischaemic heart disease. This issue will be addressed by the LIPID (long-term intervention with pravastatin in ischaemic disease) study, which includes 9014 men and women in Australia and New Zealand aged 31-75 and is expected to continue until 1997.[8]

In summary, recently available evidence suggests that aggressive lipid lowering treatment is clinically indicated for both men and women who have proved ischaemic heart disease across a wide range of low density lipoprotein cholesterol concentrations. The results of the CARE study have shown that secondary prevention with pravastatin is effective in both women and men with low density lipoprotein cholesterol concentrations in the "normal" range. Advice and support for behavioural modification, including recommendations for a healthy diet and stopping smoking, should be made available to all patients with ischaemic heart disease. The theoretical benefits of dietary supplementation with antioxidant vitamins have not been confirmed in population studies, and results of further trials are awaited. The potentially beneficial effects of moderate alcohol consumption and hormone replacement therapy as aspects of secondary prevention should also be considered in the management of individual patients with ischaemic heart disease. The effectiveness of hormone replacement therapy in primary prevention of ischaemic heart disease

has recently been confirmed in the Nurses' Health Study,[9] and the results of a secondary prevention study (heart and oestrogen/progestin replacement study) are expected in 1999.

Doctors and managers are understandably concerned about the cost implications of widespread use of lipid lowering treatment. However, a cost minimisation analysis of the 4S study's data concluded that the reduced use of hospital services that would result from use of simvastatin in a similar group of patients in the United States would offset most of the cost of treatment.[10] Cost effectiveness of expensive drug treatments such as the statins depends on risk of ischaemic heart disease. A cost effectiveness study based on the findings of the 4S study estimated that simvastatin treatment of men aged 55-64 who have suffered a myocardial infarction would cost £6000 per life year saved, whereas it would cost £361 000 per life year saved for women aged 45-54 with angina.[11] Consideration of the direct costs to health services of morbidity from ischaemic heart disease or the indirect costs of mortality or morbidity to patients, families, and society would reduce these estimates, and further economic analyses are required. In conclusion, data are now available to show that treatment with lipid lowering drugs is effective in reducing major coronary events in people with ischaemic heart disease and "normal" cholesterol concentrations. In an era of evidence based medicine this finding is likely to have major financial implications for the providers of health care.

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Allocating budgets for fundholding and prescribing

Practice based needs assessment may be the only real answer

The way in which health authorities come to their decisions about budgets for fundholding and prescribing must seem like an arcane art to many general practitioners. The principle underlying the setting of these budgets is that general practices should receive a fair share of NHS resources and one that reflects the healthcare needs of their patients.[1 2] However, there are great practical problems in setting budgets fairly. The main problem is that attempts to explain variations in the use of fundholding procedures and in prescribing costs have not been very successful.[3-5] The variations between practices are just too large to be explained by currently available information. The most important reason for this is that general practices serve small populations that differ greatly from each other in their demographic, social, and clinical characteristics. There are also large differences in the way in which general practitioners provide care. Hence, resource allocation formulae, such as those used by the NHS Executive to allocate budgets to health authorities, will not work well at practice level.

Despite these problems, there have been some recent developments in setting general practice budgets. For example, many health authorities are using capitation based formulae to allocate budgets to practices that are total fundholders (responsible for buying all the health services received by their patients). The budgets of these practices are large (around £4m for a practice with 10 000 patients), and health authorities, quite rightly, want to fund them fairly so that neither their patients nor the patients of other practices are disadvantaged. To help achieve this aim, some health authorities have used the new NHS Executive resource allocation formula to allocate budgets to total fundholders.[6 7] The NHS Executive will use this formula to allocate budgets for hospital and community health services to health authorities, and the use of this formula by health authorities to allocate budgets to total fundholders seems reasonable.

However, there are a number of problems with this approach. Firstly, the NHS Executive applied the weighting for need in the formula to only 76% of funding and not 100%. The effect of this is to reduce the resources allocated to health authorities with a high need for care.[8] If health authorities follow the executive's example, this will result in smaller budgets for practices located in deprived areas. Secondly, the census variables used by health authorities in their calculation of practice budgets are estimates, and we do not know if these estimated values are accurate enough to be used in resource allocation formulae. Finally, routine sources of data such as the census contain only limited information on many groups with a high need for care, such as the homeless or refugees.

There have also been some developments in setting prescribing budgets. Prescribing allocations to health authorities have traditionally been based on historical spending. The NHS Executive hopes to move away from this approach and is considering the introduction of a weighted capitation formula to allocate prescribing budgets to health authorities. The NHS Executive has identified age, sex, cross boundary flows, and chronic illness as the best predictors of prescribing costs. Health authorities that were 2% below the predicted spending per person on drugs were given a slightly larger increase in their 1996-7 budget than other health authorities.[2] The NHS Executive has commissioned further work, and it is likely that prescribing budgets to health authorities will eventually be allocated using weighted capitation.

Although the NHS Executive is encouraging health authorities to think about using weighted capitation when they in turn allocate budgets to practices, they will find this difficult to do. Attempts to explain variations in prescribing costs between