Statins and the prevention of coronary heart disease: striking a balance that is desirable, affordable, and achievable

CORONARY heart disease (CHD) mortality rates in the United Kingdom (UK) have fallen in recent years but remain high in relation to the rest of the world.[1] These high rates of CHD death are associated with poor cardiovascular risk profiles and unhealthy lifestyles in men and women of all ages.[2,3] Early mortality following acute myocardial infarction (MI) is very high, approaching 50% at 28 days, including pre-hospital mortality,[1] and is approximately 4.5% per year over the following five years.[4] For these reasons alone, prevention of CHD must include a strategy for risk reduction in selected high-risk patients to prevent myocardial infarction, which carries such considerable risks of death and recurrent ischaemic events.

Coronary heart disease has a multifactorial aetiology and there are a number of potentially modifiable risk factors, including lipids.[5] Five outcome studies (two primary[6,7] and three secondary prevention[4,8,9]) using statins (HMG CoA reductase inhibitors) for lipid lowering have shown reductions in the incidence of fatal and non-fatal MI. Three of the five[4,6,9] were also able to demonstrate reductions in all-cause mortality. Other benefits include fewer coronary revascularisation procedures and strokes[10] and may include reductions in the incidence of anginal symptoms, congestive heart failure, disability, and improved quality of life.[11]

There are a number of major and controversial challenges arising from the compelling cardiovascular benefits of statins: (a) accurate definition of risks, benefits, and costs of treatment; (b) placing this analysis in the context of other CHD preventive measures; (c) establishing a policy for statins that is not only desirable on the basis of best evidence but also affordable and achievable; (d) improved methods of targeting individual patients and assessing risk; and (e) developing and evaluating new models of implementation in primary care.

A number of guidelines have been produced to address some of these challenges. In 1997, the Standing Medical Advisory Committee produced guidance which was circulated widely to general practitioners (GPs) in England and Wales.[12] This guidance attracted criticism on the one hand as being financially irresponsible,[13] and on the other as being overconservative, treating too few eligible individuals.[14] Other recent guidance includes: the Second European Joint Task Force,[15] the National Health Service (NHS) Centre for Reviews and Dissemination,[16] the Joint British Recommendations,[17] the Royal College of Physicians of Edinburgh Lipid Consensus Conference,[18] and the Scottish Intercollegiate Guidelines Network (SIGN) guidelines on primary[19] (see Box 1) and secondary[20] prevention of coronary heart disease. A plethora of guidelines does not always clarify but may serve to confuse — particularly in such a controversial area. Happily, the latest British guidelines have not been developed in isolation from each other and there is now a remarkable degree of consistency between them.[17-20] Statins should be considered for:

- secondary prevention of patients aged under 75 years with CHD or other major atherosclerotic disease with total cholesterol ≥5.0 mmol/l (LDL cholesterol ≥3.0 mmol/l).
- primary prevention in patients aged under 70 years with a 10-year absolute CHD risk exceeding 30% with total cholesterol ≥5.0 mmol/l as a first priority, progressively extending this to those with 10-year risk exceeding 15% when costs and resources permit.

Assessment of the clinical effectiveness of statins is necessary but is only a first step. Guidance must also take into account issues of cost-effectiveness, workload, and resource implications. The cost-effectiveness of statins in secondary prevention appears to be better than some preventive interventions (e.g. cervical cytology screening)[21] but poorer than others (e.g. smoking cessation activities; β-blockers or aspirin for secondary prevention).[16] In secondary prevention, the number needed to treat (NNT) would be 13 people for five years to prevent one CHD event.[4] The cost-effectiveness of statins in primary prevention is more problematic[16,19,21-23] and is less than in secondary prevention because of the lower absolute risk of CHD, except in high-risk patients. At a 10-year CHD risk threshold exceeding 30% for primary prevention, the comparable NNT has been estimated as 21.[19] This threshold is set at a high enough level to overlap with the lower end of the risk range for secondary prevention[14] where the average 10-year risk of a further event is ≥30%.[8,9] On this basis, those at high primary risk are not discriminated against compared with those at lower secondary risk.

What are the implications for workload in primary care? In a recent analysis of the *Scottish Health Survey 1995*, for the SIGN primary prevention guideline,[19] 7.8% of the Scottish population aged 35 to 64 years were found to be potentially eligible for statins for secondary prevention[24] and 1.5% for primary prevention[25] using a 10-year CHD risk threshold of 30% (secondary:primary ratio — 5.2:1). Translated to an illustrative practice of 10 000 patients, 293 would require secondary prevention and 56 would be eligible for primary prevention.[21] A similar, earlier analysis has been done using the *Health Survey for England 1993*.[3,22,26] This type of analysis is indicative only and does not reflect the unique socioeconomic and morbidity profiles of individual practices. In areas of socioeconomic deprivation the prevalence of CHD is high[27] and the need for lipid lowering is greater. Implications for additional workload and increased prescribing bills are huge, although projected drug cost ceilings[21,22,26] are likely to be mitigated by several factors: (a) targeting patients will be a gradual process; (b) lower doses of statins are being used than those in trials; (c) newer, more cost-effective drugs are being prescribed; (d) there are likely to be significant price reductions when generic statins become available; and (e) actual 'real-world' patient compliance is likely to be lower than controlled trials — which were down to about 70% by the end of these studies.

Although identification of patients for secondary prevention appears initially straightforward, our record of achievement is not impressive.[28,29] Some structured approaches appear to have been successful[30,31] but others less so,[32,33] prompting calls for a more systematic approach[29] as specified recently by the ambitious National Service Framework on CHD.[34] Effective targeting of patients for primary prevention pivots on the availability of reliable risk assessment tools that must also be practical in the clinical setting. A choice of competing risk scores is available,

- Lifestyle measures remain the first priority in the primary prevention of coronary heart disease.
- Absolute rather than relative risk reduction gives a better estimate of the benefits of lipid-lowering drug treatment.
- The first priority for lipid-lowering drug therapy are patients with pre-existing cardiovascular disease.
- A patient should be considered for lipid-lowering drug therapy for primary prevention, usually following a trial of lifestyle measures and other appropriate interventions for at least three months, when the serum total cholesterol is ≥5 mmol/l and the 10-year risk of a major coronary event exceeds 30% using the Joint British Chart.
- Women should be considered for lipid-lowering drug therapy for primary prevention at the same risk threshold as men.
- Type 2 diabetics without evidence of nephropathy should be considered for lipid-lowering drug therapy for primary prevention at the same risk threshold as non-diabetics.
- Type 1 diabetics and Type 2 diabetics with nephropathy may have their risk underestimated using current scoring methods and intervention should be considered at a lower threshold.
- Patients with heterozygous familial hypercholesterolaemia (FH) should be treated aggressively with dietary advice and lipid-lowering therapy. Close monitoring and follow-up is essential.
- Targeted assessment should be undertaken in the age range 35 to 69 years, or at a younger age in patients with a family history of FH.
- Secondary causes of dyslipidaemia should be excluded before commencing lipid-lowering drug therapy.
- For primary prevention of CHD, statins are now drugs of first choice for lowering lipids.

Box 1. SIGN Guideline on lipids and the primary prevention of CHD — Key recommendations.[19]

presenting further dilemmas for the busy clinician. These include the Sheffield Table[35] which has been revised to include the total cholesterol/HDL cholesterol ratio[36,37] (currently the best lipid profile predictor of coronary risk),[38] the New Zealand Guidelines,[39] and the Joint British Chart.[17] All three are based on the Framingham risk function[40] which is valid for northern European populations[41] and assess absolute risk of developing an ischaemic event. Again, each of these scoring methods has attracted champions and detractors[19] with most of the arguments marshalled around accuracy.[36,41-43] The practical utility of the Sheffield, New Zealand, and Joint British scoring methods has been tested recently in the general practice setting by GPs and practice nurses.[44] The results of this study demonstrated that nurses interpreted the New Zealand Guidelines and Joint British Chart more accurately than the Sheffield Table and that more doctors and nurses preferred the New Zealand Guidelines and the Joint British Chart to the Sheffield Table.

Coronary risk score assessment continues to evolve: existing methods are deficient in a number of areas, including appropriate weighting of family history of premature CHD[45,46] and type 1 diabetes.[17,19,47] Those with heterozygous familial hypercholesterolaemia[48] and other inherited dyslipidaemias are also disadvantaged by current scoring methods and should be treated aggressively.[19] Advocates of computerised risk scores that have access to the full Framingham risk function suggest that they may also demonstrate risk reduction effects to patients and can facilitate audit.[17,49] However, it is likely that stand-alone computerised risk scores, which are not entirely novel,[50,51] will only maximise their impact when incorporated into the electronic patient record of the future.[43,44]

A fundamental question for primary prevention remains: which patients should have their absolute coronary risk calculated? Priorities can be informed by examining the likely yield from screening patients for those with a 10-year CHD risk exceeding 30%. As indicated above, analysis of the *Scottish Health Survey 1995* confirms that 1.5% of the population aged 35 to 64 years have this risk level. A calculation of the number needed to screen (NNS) to find one individual with a 10-year risk exceeding 30% gives NNS = 100/1.5 or 67 (Range: NNS >1000, age 35 to 39; decreasing to NNS 20, age 60 to 64).[19] If the same calculation is repeated for diabetics aged 35 to 64 years the NNS drops to 8 and for hypertensives (systolic blood pressure =160 mmHg) the NNS is 9.[19] This amounts to a powerful disincentive for indiscriminate lipid screening in primary care while confirming the importance of assessing absolute risk of CHD as part of the routine care of diabetics and hypertensives: those already known to be in peril.

LEWIS D RITCHIE

Mackenzie Professor, Department of General Practice and Primary Care, University of Aberdeen, Foresterhill Health Centre

References

1. Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, *et al*. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations. *Lancet* 1999; **353:** 1547-1557.
2. Scottish Office Department of Health. *Scotland's health: Scottish health survey 1995*. Edinburgh: The Stationery Office, 1997.
3. Office of Population Censuses and Surveys for the Department of Health. *Health survey for England 1993*. London: HMSO, 1995.
4. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival study (4S). *Lancet* 1994; **344:** 1383-1389.
5. Tunstall-Pedoe H, Woodward M, Tavendale R, *et al*. Comparison of the prediction by 27 different factors of coronary heart disease and death in men and women of the Scottish Heart Health study: cohort study. *BMJ* 1997; **315:** 722-729.
6. Shepherd J, Cobbe SM, Ford I, *et al*. Prevention of coronary heart disease with pravastatin in men with hypercholesterolaemia. West of Scotland Coronary Prevention study group. *N Engl J Med* 1995; **333:** 1301-1307.
7. Downs JR, Clearfield M, Weis S, *et al*. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCaps. Airforce/Texas Coronary Atherosclerosis Prevention study. *JAMA* 1998; **279:** 1615-1622.
8. Sacks FM, Pfeffer MA, Love LA, *et al*. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and recurrent events trial investigators. *N Engl J Med* 1996; **335:** 1001-1009.
9. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol. The long-term intervention with pravastatin in ischaemic heart disease (LIPID) study group. *N Engl J Med* 1998; **339:** 1349-1357.
10. Bucher HC, Griffith LE, Guyatt GH. Effect of HMG CoA reductase inhibitors on stroke: a meta-analysis of randomised, controlled trials. *Ann Intern Med* 1998; **128:** 89-95.
11. Muldoon MF, Criqui MH. The emerging role of statins in the prevention of coronary heart disease. *BMJ* 1997; **315:** 1554-1555.
12. Standing Medical Advisory Committee. *The use of statins*. London: Department of Health, 1997. http://www.doh.gov.uk/cmo.statins2.htm.
13. Freemantle N, Barbour R, Johnson R, *et al*. The use of statins: a case of misleading priorities? *BMJ* 1997; **315:** 826-828.
14. Use of statins [Correspondence.] *BMJ* 1997; **315:** 1615-1620.
15. Wood D, de Backer G, Faergeman O, *et al*. Prevention of coronary heart disease in clinical practice. Recommendations of the second joint task force of European and other societies on coronary prevention. *Eur Heart J* 1998; **19:** 1349-1357.
16. University of York. NHS Centre for Reviews and Dissemination. Cholesterol and coronary heart disease: screening and treatment. *Effect Health Care Bull* 1998; **4(1):** 1-16. http://www.york.ac.u/inst/crd/ ehc41.htm.
17. Wood D, Durrington P, Poulter N, *et al*. On behalf of the British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society and British Diabetic Association. Joint British recommendations on prevention of coronary heart disease in clinical practice. *Heart* 1998; **80(suppl 2):** S1-S29.

18. Royal College of Physicians of Edinburgh consensus conference on lipid lowering to prevent vascular events. *Proc R Coll Phys Edinb* 1999; **29(suppl 5):** 2-4.
19. Scottish Intercollegiate Guidelines Network (SIGN). *Lipids and the primary prevention of coronary heart disease. A national clinical guideline — No 40*. Edinburgh: SIGN, 1999. http://www.sign.ac.uk.
20. Scottish Intercollegiate Guidelines Network (SIGN). *Secondary prevention of coronary heart disease after myocardial infarction. A national clinical guideline — Number 41*. Edinburgh: SIGN, 2000. http://www.sign.ac.uk.
21. Pickin M, McCabe CJ. Lipid lowering in the United Kingdom National Health Service: Effectiveness and cost — the economic view. *Proc R Coll Phys Edinb* 1999; **29(suppl 5):** 31-40.
22. Haq IU, Ramsay LE, Pickin DM, *et al.* Lipid lowering for prevention of coronary heart disease. *Clin Sci (Colch)* 1996; **91:** 399-413.
23. Van der Weijden T, Knottnerus JA, Ament AJHA, *et al.* Economic evaluation of cholesterol-related interventions in general practice. *J Epidemiol Community Health* 1998; ***52:*** 586-594.
24. Haq IU, Wallis EJ, Yeo WW, *et al.* Population implications of lipid lowering for secondary prevention of coronary heart disease: data from the 1995 Scottish Health Survey. *Heart* 1999; **81(suppl 1):** P29(93).
25. Haq IU, Wallis EJ, Yeo WW, *et al.* Population implications of lipid lowering for primary prevention of coronary heart disease: data from the 1995 Scottish Health Survey. *Heart* 1999; **81(Suppl 1):** P28(92).
26. Pickin DM, Payne JN, Haq IU, *et al*. For the Working Group on Acute Purchasing. *Statin therapy/HMG CoA reductase inhibitor treatment in the prevention of coronary heart disease.* Sheffield: Trent Institute for Health Services Research, 1996.
27. McLaren G, Bain M. *Deprivation and health in Scotland: insights from NHS data.* Edinburgh: Information & Statistics Division, NHS in Scotland, 1998.
28. Campbell NC, Thain J, Deans HG, *et al*. Secondary prevention in coronary heart disease: baseline survey of provision in general practice. *BMJ* 1998; **316:** 1430-1434.
29. Bradley F, Cupples ME. Reducing the risk of recurrent coronary disease. *BMJ* 1999; **318:** 1499-1500.
30. Cupples ME, McKnight A. Randomised controlled trial of health promotion in general practice for patients at high cardiovascular risk. *BMJ* 1994; **304:** 993-996.
31. Campbell NC, Ritchie LD, Thain J, *et al*. Secondary prevention in coronary heart disease: a randomised trial of nurse led clinics in primary care. *Heart* 1998; **80:** 447-452.
32. Jolly K, Bradley F, Sharp S, *et al.* Randomised controlled trial of follow up care in general practice of patients with myocardial infarction and angina: final results of the Southampton heart integrated care project (SHIP). *BMJ* 1999; **318:** 706-711.
33. Feder G, Griffiths C, Eldridge S, *et al.* Effect of postal prompts to patients and general practitioners on the quality of primary care after a coronary event (POST): randomised controlled trial. *BMJ* 1999; **318:** 1522-1526.
34. Department of Health. *Coronary heart disease National Service Framework*. London: Department of Health, 2000. http://www.doh.gov.uk/nsf/coronary.htm.
35. Haq IU, Jackson PR, Yeo WW, *et al*. Sheffield risk and treatment table for cholesterol lowering for primary prevention of coronary heart disease. *Lancet* 1995; **346:** 1467-1471.
36. Wallis EJ, Ramsay LE, Haq IU, *et al.* Coronary and cardiovascular risk estimation for primary prevention: validation of a new Sheffield Table in the 1995 Scottish Health Survey population. *BMJ* 2000; **320:** 671-676.
37. Isles CG, Ramsay LE, Wallis EJ, *et al*. Whom to treat in primary prevention? *Proc R Coll Phys Edinb* 1999; **9(suppl 5):** 16-25.
38. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risk by levels and ratios. *Ann Intern Med* 1994; **121:** 641-647.
39. 1996 National Heart Foundation clinical guidelines for the assessment and management of dyslipidaemia. Dyslipidaemia advisory group on behalf of the Scientific Committee of the National Heart Foundation of New Zealand. *NZ Med J* 1996; **109:** 224-231. http://cebm.jr2.ox.ac.uk/ docs/prognosis.html.
40. Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. *Am Heart J* 1991; **121:** 293-298.
41. Haq IU, Ramsay LE, Yeo WW, *et al*. Is the Framingham risk function valid for northern populations? A comparison of methods for estimating absolute coronary risk in high risk men. *Heart* 1999; **81:** 40-46.
42. Durrington P, Prais H, Bhatnagar D, *et al*. Indications for cholesterol-lowering medication: comparison of risk-assessment methods. *Lancet* 1999; **353:** 278-281.
43. Ritchie LD, Isles CG. Targeting lipid lowering drugs for the primary prevention of coronary heart disease: comparison of Sheffield Table and New Zealand Guidelines. *Br J Cardiol* 1999; **6:** 220-222.
44. Isles CG, Ritchie LD, Murchie P, *et al.* Risk assessment in primary prevention of coronary heart disease: a comparison of three scoring methods. *BMJ* 2000; **320:** 690-691.
45. Grover S. Gambling with cardiovascular risk: picking the winners and losers. *Lancet* 1999; **353:** 254-255.
46. Silberberg J. Better coronary risk assessment in women. *Lancet* 1999; **353:** 1637-1638.
47. Yudkin JS, Chaturvedi N. Developing risk stratification charts for diabetic and non-diabetic subjects. *Diabet Med* 1999; **16:** 219-227.
48. Scientific Steering Committee on behalf of the Simon Broome Register Group. Mortality in treated heterozygous familial hypercholesterolaemia: implications for clinical management. *Atherosclerosis* 1999; **142:** 105-112.
49. Hingorani AD, Vallance P. A simple computer program for guiding management of cardiovascular risk factors and prescribing. *BMJ* 1999; **318:** 101-105. Also available as: Deanfield J, Martin J, Vallance P. *CardioRisk Manager*. London: BMJ Books, 1999.
50. Änggard EE, Land JM, Lenihan CJ, *et al*. Prevention of cardiovascular disease in general practice: a proposed model. *BMJ* 1986; **293:** 177-180.
51. Ritchie LD. In: Poulter N, Sever P, Thom S (eds). *Cardiovascular disease: risk factors and intervention. Coronary heart disease screening: logistics and risk scores.* Oxford: Radcliffe Medical Press, 1993.

Acknowledgements

The author thanks all members of the SIGN Primary Prevention Guidelines Development Team.

Address for correspondence

Professor Lewis D Ritchie, Department of General Practice and Primary Care, University of Aberdeen, Foresterhill Health Centre, Westburn Road, Aberdeen AB25 2AY. E-mail: l.d.ritchie@abdn.ac.uk

The primary prevention of coronary heart disease with statins: practice headache or public health?

THERE can be no question that the prevention of coronary heart disease (CHD) in the United Kingdom (UK) remains one of the most important clinical and public health issues facing primary care. Increasing evidence of clinical benefit has encouraged the use of HMG CoA reductase inhibitors (statins) since the publication in 1994 of the 4S study.[1] Since then, numerous other studies have confirmed the findings that in patients with established CHD significant benefits arise from the use of statins, which is regarded as secondary prevention. An increasingly important issue facing health professionals in this country is the primary prevention of CHD and the implications for those who work in primary care. Clear, concise, and well-referenced guidelines are needed to inform clinical practice.

Most general practitioners (GPs) will therefore welcome the recent publication from the Scottish Intercollegiate Guidelines Network (SIGN), *Lipids and the Primary Prevention of*

Coronary Heart Disease,[2] which has everything expected from a quality guideline. It is evidence-based and the recommendations made are graded according to the strength of the studies supporting them. Unlike the majority of CHD guidelines, it appears to have been designed by and for those working in primary care and has a good primary care 'feel' to it.

Most GPs will welcome the structured approach that this SIGN guideline suggests. It includes several excellent flow charts and strategies that practices could adopt at a local level and customise for their use. Most of us will agree with the major recommendations encouraging lifestyle measures as the first priority in the primary prevention of CHD, stressing the importance of the patient's absolute risk as the prime indicator for drug treatment, and confirming that the first priority for lipid-lowering drug therapy is secondary prevention.

As far as primary prevention is concerned, again, few will quibble with the desire to encourage physical activity, reduce alcohol intake to moderate levels, promote the aggressive treatment of hypertension, and actively discourage smoking. It is also implicit in the SIGN document that primary care is the only arena within which primary prevention can take place. The increasing data input of risk factors and the increasing sophistication of GP computer systems, coupled with increasing team work within the practice, can only auger well — yet along with this opportunity comes a significant responsibility for primary care to deliver.

However, the devil, as always, is in the detail and the real impact of guidelines such as these is not the strength of the evidence but the size of the workload. This workload can be divided into screening and treatment. As with most UK guidelines, the SIGN authors stress the importance of screening specific subgroups for primary prevention and estimating the patient's absolute risk, rather than blanket population screening. This must be sensible in primary care. They estimate that the overall number needed to screen (NNS) for all men aged 35 to 64 years is 35 (i.e. 35 men need to be screened to detect one man with an absolute risk above the required threshold [3%]). The NNS is much higher in women (200). This level of screening is plainly impractical, hence the concentration on high-risk groups with a more 'manageable' NNS; for example, every eleventh patient with hypertension and every eighth patient with diabetes will have an absolute risk greater than 3%.

The SIGN document therefore recommends targeted assessment of patients aged 35 to 69 years who smoke or who have hypertension, diabetes, a strong family history or signs of hyperlipidaemia. They also suggest screening at a younger age in those patients who have a family history of heterozygous familial hypercholesterolaemia — which would approximate to one family per GP. Superficially, even this high risk approach seems manageable, yet the inclusion of all smokers, in whom the NNS is relatively high at 25, will rapidly escalate the workload with only minimal benefit in terms of pick-up. Each practice will need to review these figures very carefully and decide how they wish to proceed.

The drive for more sensitive absolute risk measurements in general practice has led to a recent crop of absolute risk assessment tools, including the Sheffield Table,[3] the New Zealand guidelines,[4] and the Joint British guidelines.[5] A feature common to all three guidelines is the use of the total cholesterol:HDL ratio as the most sensitive predictor of CHD risk. This measurement, however, is not universally available in the UK and unless a national policy is adopted it may depend on the vagaries of each local laboratory.

Fortunately, the SIGN guidelines do not reinvent the wheel but use the recommendations of the Joint British guidelines.[5] These are essentially that patients should be considered for lipid-lowering drug therapy using statins as primary prevention if, following a trial of lifestyle measures and other appropriate interventions of at least three months, their total serum cholesterol remains greater than or equal to 5.0 mmol/l *and* their 10-year risk of a major coronary event exceeds 30%. This approximates to a one-year risk greater than or equal to 3% as assessed by the Joint British chart.

Numerous questions arise from screening alone. Who within the primary care team will undertake such a large targeted screening programme? What resources will be made available to general practice to enable this to be performed? Which absolute risk assessment tool is best suited, both to the busy practice and to the computers therein? These are important questions that will need to be addressed as soon as possible.

Treatment recommendations in this guideline are of course supported by the evidence from WOSCOPS[6] and AFCAPS/TexCAPS,[7] both studies having demonstrated the effectiveness of two different statins in primary prevention. As this guideline points out, however, the numbers needed to treat (NNT) are higher in the AFCAPS/TexCAPS study (50) and WOSCOPS (42) than in the secondary prevention studies. Nevertheless, these relatively low NNTs coupled with the high prevalence of coronary risk factors in the population means that, even in a single practice, lives will be saved through the implementation of a primary prevention strategy.

General practitioners watch with increasing concern the debate about the respective merits of treating patients with a 3% risk, as recommended by the Department of Health (DoH), in contrast to the 2% or 1.5% risk suggested by many leading lipidologists.[8] Until there is consensus on the absolute risk threshold at which treatment should be commenced patients may not receive the best available treatment.

Even taking a conservative level of risk of 3%, the SIGN guidelines estimate from their Scottish Health Survey database that 7.8% of the Scottish population aged 35 to 64 years would be eligible for secondary prevention and 1.5% for primary prevention — meaning that in total, 9.3% of this age group could be placed on statins. There is an urgent need for dialogue about lowering the absolute risk threshold to 2%, or even to 1.5%. This will in turn lead not only to a corresponding increase in costs[9] but also to a dramatic increase in workload. Initially it seems that a structured approach to statin implementation along the lines of diabetes or hypertension would be the best way forward, yet the most effective way of combining the GP, nurse, and patient has yet to be determined.

There is broad agreement that implementation of evidence-based medicine in this context will be expensive for the National Health Service (NHS), yet most estimates will be conservative unless the whole economic context is considered. First, there are the costs of such an extensive risk assessment programme; secondly, the costs of the statins themselves; and thirdly, the often forgotten primary care costs. These include the cost of increased doctor and nurse consultations (face-to-face and on the phone), the staff and administrative costs of setting up and running a recall system, and the laboratory costs of monitoring at least one-tenth of the population on a single group of drugs.

The benefits of the statin investment will be seen in reduced admissions, revascularisation procedures, and the like, yet the cost initially will be borne by each practice within a cash-limited prescribing budget, already damaged by the recent generic price increase, and a cash-limited staff budget. The costs of statins alone have recently been estimated at £50 000 per year for primary prevention and £200 000 for secondary prevention in a practice of 10 000 patients.[10] This quantum leap in drug costs may also set individual practices that are implementing these

guidelines on a collision course with their primary care group. How can GPs prescribe in line with the evidence yet manage to remain within budget? This issue will need to be addressed urgently. If not, patients will be denied the beneficial treatment they need purely on financial grounds and practices will be penalised by lost incentive payments.

The recently published and long-awaited National Service Framework for Coronary Heart Disease does not include extra funding for drugs in primary care.[11] The advance of evidence-based medicine in this area has for the first time outstripped the ability of the NHS to cope financially. Doctors have an ethical and professional obligation to advise their patients what they believe is best for them. When that belief is based on incontrovertible evidence from gold-standard trials, and indeed is confirmed by the DoH, it seems perverse to deny patients that treatment. If family doctors cannot match their advice with an appropriate prescription then the health service is sadly heading for meltdown. The political will appears to be to reduce CHD, yet no one has as yet fully addressed the escalating anxieties of the practitioners on the frontline.

PHILIP H EVANS

GP and Lecturer in General Practice, Institute of General Practice, School of Postgraduate Medicine and Health Sciences, University of Exeter

References

1. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol in 4444 participants with coronary heart disease: the Scandanavian Simvastatin Survival Study. *Lancet* 1994; **344:** 1383-1389.
2. Scottish Intercollegiate Guidelines Network. *Lipids and the Primary Prevention of Coronary Heart Disease. A National Clinical Guideline*. Edinburgh: SIGN, 2000.
3. Ramsay LE, Haq IU, Jackson PR, *et al*. Targeting lipid-lowering drug therapy for primary prevention of coronary heart disease: an updated Sheffield Table. *Lancet* 1996; **348:** 387-388.
4. Jackson R, Barham P, Bills J, *et al*. Management of raised blood pressure in New Zealand: a discussion document. *BMJ* 1993; **307:** 107-110.
5. British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, and British Diabetic Association. Joint British Recommendations on Prevention of Coronary Heart Disease in Clinical Practice. *Heart* 1998; **80(2):** S1-S26.
6. Shepherd J, Cobbe SM, Ford I, *et al*. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995; **333:** 1301-1307.
7. Downs JR, Clearfield M, Weis S, *et al*. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. *JAMA* 1998; **279:** 1615-1622.
8. Enoch P, Akehurst RL, Sheridan P, *et al*. Adequacy of SMAC's statement should be judged by clinicians, not health economists. [Letter.] *BMJ* 1997; **315:** 1615.
9. Trent Institute for Health Services Research. *Statin Therapy/HMG Co-A Reductase Inhibitor Treatment in the Prevention of Coronary Heart Disease. Guidance Note for Purchasers 96/04.* Sheffield: TIHSR, 1996.
10. Campbell N. Edinburgh: consensus conference on lipid lowering. *Trends Cardiol Vas Dis* 1999; **July/August:** 31-34.
11. Department of Health. *National Service Framework: Coronary Heart Disease.* London: DoH, 2000.

Address for correspondence

Dr Philip Evans, Institute of General Practice, Postgraduate Medical Centre, Barrack Road, Exeter EX2 5DW.

Management of UTI in general practice: a cost effective analysis. A commentary to facilitate an understanding of economic evaluation

This paper should be read in conjunction with Fenwick et al, which appeared in last month's Journal (50: 635-639).

Introduction

Against a background of increasing demands on limited resources, an economic evaluation facilitates decisions in health by relating the outputs of alternative interventions to the resources that they consume. Practitioners will be presented with an increasing number of economic studies relevant to all levels of health care delivery and this commentary aims to illuminate some key health economic concepts. To undertake an economic analysis, relevant outputs must be defined, costs should be measured, and studies undertaken that can relate these outputs to their costs.[1]

Relating costs to benefits

Ideally, economic analysis should be undertaken alongside a control trial where all options, including doing nothing, are tested. Often, this is not possible and economists undertake modelling exercises, analysing the probability of events and their outcomes ('decision tree analysis'), using data where it is available and expert opinion where it is not.[2]

In the case of Fenwick et al,[3] the costs and benefits of seven possible options are considered and the most cost-effective strategy defined (treating everyone with antibiotics to provide two symptom-free days at a cost of £14). Above this baseline an incremental cost-effectiveness ratio is calculated - the extra increment we would have to pay to receive an extra increment of benefit, e.g. adding laboratory culture at an additional cost of £215 per symptom day averted.

Measuring costs

Direct costs are those arising directly from the intervention, such as drug and medical costs. Indirect costs include economic costs arising from loss of work. 'Intangibles' are non-marketable items that may require a monetary value, such as loss of leisure time or loss of life. The perspective of an exercise defines which costs to count and different answers may be obtained from the viewpoint of the individual patient, practice, health authority, National Health Service (NHS) or society.

Studies undertaken at different times or places may not be comparable unless standard costing procedures are used. Evaluating costs is not a straightforward exercise and costs can vary in the way they are valued and combined. For example, distributing the undergraduate and postgraduate training costs across the expected lifetime of a general practitioner (GP) will increase the cost of a consultation by almost 25%. The context of the economic exercise will determine which cost elements are relevant.[4]

This study adopts a limited NHS perspective counting only GP consultations, laboratory tests, and drug costs but, in general, health economists will favour a societal perspective.

Measuring outcomes

The majority of economic evaluations are cost-effectiveness studies[5] where outputs are defined in natural units - in this case, symptom-free days per episode. Two problems arise. First, the multiple benefits and disbenefits that can occur with each intervention option cannot be captured. Secondly, dissimilar interventions cannot be compared if their outcomes are different.

A cost utility analysis[6] attempts to overcome these limitations and allocates a value of between one (perfect health) and zero (death) to any health state and combines it with the time spent in this state to derive the quality-adjusted life year (QALY). This method has the advantage that disparate interventions can be compared across a broad range of resource allocation choices. However, there remain a number of methodological problems with this approach. In the discussion of this study, a symptom day is associated with a disutility value of 0.2894 and the next best strategy over baseline yields a cost of £270 000 per QALY - not good value when compared with other ways of spending limited health care resources.

Dealing with uncertainty

For practical purposes, statistical approaches in economic evaluation remain limited and health economists adopt a pragmatic approach. When uncertainty exists over the accuracy of data, a sensitivity analysis tests the conclusion of a study to the range of values that are likely to occur. Table 23 shows the range of values over which the model is tested and the conclusions remain valid over all model parameters.

Conclusion

Ideally economic evaluation should be undertaken alongside pragmatic trials that reflect the context of the environment where the intervention is delivered. Decision analysis can offer decision-makers valuable insights but can never adequately model the contingencies of primary care where outcomes are often complex, occur over long time horizons, and where there may be difficulties with attribution.

Further resources

Jefferson T, Demicheli V, Mugford M. Elementary economic evaluation in health care. London: BMJ Publishing, 1996.
Drummond M, Maynard A. Purchasing and providing cost effective health care. London: Churchill Livingstone, 1993.
Drummond M, Stoddart GL, Torrance GW. Methods for the economic evaluations of Health Care Programmes. Oxford: Oxford University Press, 1997.
Office of Health Economics, 12 Whitehall, London SW1A 2DY. www.ohe.org.uk
The NHS Economic Evaluation Database, NHS Centre for Reviews and Dissemination, York. Free access to database on http://www.york.ac.uk/inst/crd/info.htm

DAVID KERNICK
General Practitioner, St Thomas's Medical Group, Exeter

References

1. Drummond M. Economic analysis alongside control trials. London: Department of Health, 1994.
2. Rittenhouse B. The use of models in economic evaluations of medicines and other health technologies. London: Office of Health Economics, 1996.
3. Fenwick EAL, Briggs AH, Hawke CI. Management of urinary tract infection in general practice: a cost-effectiveness analysis. Br J Gen Pract 2000; 50: 635-639.
4. Kernick D. Costing principles in primary care. Fam Pract 2000; 17: 66-70.
5. Robinson R. Cost effectiveness analysis. BMJ 1993; 307: 793-795.
6. Robinson R. Cost effectiveness analysis. BMJ 1993; 307: 859-862.

Acknowledgements

St Thomas's Medical Group is a research practice funded by the South & West NHS Research & Development Directorate.

Address for correspondence

Dr David Kernick, St Thomas's Medical Group, Cowick Street, Exeter EX4 1HJ. E-mail: su1838@eclipse.co.uk