CARDIOVASCULAR MEDICINE

American, British and European recommendations for statins in the primary prevention of cardiovascular disease applied to British men studied prospectively

P Mcelduff, M Jaefarnezhad, P N Durrington

Heart 2006;92:1213–1218. doi: 10.1136/hrt.2005.085183

Objective: To compare national and international recommendations for statin treatment in the primary prevention of cardiovascular disease (CVD) in middle-aged men.

Design: Application of the current American, British and European recommendations to results of a prospective study.

Participants: Men aged 49–65 years ($n = 1653$) who participated in the Caerphilly Prospective Study.

Main outcome measures: Proportion of patients who would receive statin treatment, the number needed to treat (NNT) to prevent one first CVD event (myocardial infarction or stroke) over 10 years and the potential number of events prevented over 10 years in the whole population (population impact) by the use of statins in accordance with each set of guidelines, assuming a reduction of risk in the range 10–50% from the observed events and baseline risk factors.

Results: 212 events were noted. For an anticipated reduction in first CVD events of 30% with statin treatment, the NNT was 26.0, if the whole population was treated. The lowest NNT was 12.1 for the National Service Framework, achieved when only 14% of the men received a statin. This prevented the lowest number of events (19.2/212), however, and had the smallest population impact on CVD incidence (–9.1%). The American and earlier Joint British Societies guidelines, although giving NNTs of around 21, prevented more events and had a greater population impact of –21.6% to –23.3%. They did, however, target about 60% of the male population. The British Hypertension Society guidelines and new Joint British Societies recommendations achieved the greatest population impact of –27% while maintaining the NNT at 22.2. They did, however, target three quarters of this population.

Conclusion: Even effective preventive treatment will have little impact in preventing disease if patients at typical risk are not treated. Whether cholesterol lowering on such a scale should be attempted with drugs raises philosophical, psychological and economic considerations, particularly in view of the high likelihood of individual benefit from statin treatment. More effective nutritional policies to reduce serum cholesterol on a population level and reduce the requirement for statins in primary prevention should also be considered.

See end of article for authors' affiliations

Correspondence to:
Professor Paul N Durrington,
Department of Medicine,
Manchester Royal
Infirmary, Oxford Road,
Manchester M13 9WL,
UK; pdurrington@
manchester.ac.uk

Accepted 3 March 2006
Published Online First
18 May 2006

The advent of statin treatment has raised fundamental issues both for medical practitioners and for society. In randomised clinical trials statin treatment is effective in decreasing coronary heart disease (CHD) and stroke risk, both in primary and in secondary prevention.^{1–3} The benefit of treatment with a statin is observed among people with annual levels of risk as low as 1%.⁴ Recent studies suggest that even at this level of risk statin treatment is cost effective within the terms of reference applied to other medical treatment.⁵ However, the typical annual CHD risk in countries with high incidence rates may not be far short of 1%.⁶ This would apply, for example, to Northern Europe, North America, Australia and New Zealand.⁷ Most men from middle age onwards and older women could logically therefore be considered for statin treatment on the basis of scientific evidence. The difficulty posed for purchasers of health care is thus not so much one of cost effectiveness as of the total cost of treating all those for whom there is evidence of benefit.⁸ It also raises questions about whether it is desirable or even practical for drug treatment to be provided to make patients of people, who might previously have been considered well. This is particularly so when the causes of the disease it is aimed at preventing, namely smoking, unhealthy

nutrition and lack of physical exercise,^{7 9 10} are overtly promoted on an industrial scale with public policy in confusion, either contributing to the problem through misdirected agricultural subsidies or providing only weak direction and legislation.

As the statin evidence has unfolded, national and international recommendations for statin use have evolved. The interpretation of statin trial evidence has been remarkably consistent in these recommendations. In every case it has been recognised that, for statins to be most effectively deployed, they should be prescribed in such a way that people at the highest risk receive priority.^{11–17} How this prioritisation is achieved has, however, given rise to the creation of methods to assist the clinician in estimating individual cardiovascular disease (CVD) risk unique to each of these guidelines. These methods differ enormously not only in their design but also in the threshold of risk at which

Abbreviations: ATP, Adult Treatment Panel; BHS, British Hypertension Society; CHD, coronary heart disease; CVD, cardiovascular disease; HDL, high density lipoprotein; JBS, Joint British Societies; LDL, low density lipoprotein; NNT, number needed to treat; NSF, National Service Framework

statins are recommended, what is defined as CVD risk, and the importance attached to lipoprotein concentrations. We have previously drawn attention to the substantial difference this can make to which patients referred to a lipid clinic receive treatment.¹⁸ We now examine the likely effect of the latest recommendations on the observed CVD event rate when applied to middle-aged men followed up prospectively.

METHODS

Study population

The Medical Research Council Caerphilly Prospective Study Steering Group (www.epi.bris.ac.uk/caerphilly/caerphillyprospectivestudy.htm) kindly gave us permission to use its dataset. The general design and methods of this epidemiological study have been described.¹⁹ Men aged 49–65 years living in Caerphilly (South Wales), randomly selected from the electoral register, were invited to participate between 1984 and 1988. A detailed medical, lifestyle and family history was obtained, the London School of Hygiene and Tropical Medicine chest pain questionnaire²⁰ was administered, a 12-lead ECG was recorded, and full anthropometric details and fasting blood samples were obtained. The occurrence of a coronary or stroke event was monitored over an average of 15 years. In the present study the coronary and stroke event rate were combined as CVD risk because statins decrease the incidence of both to a similar extent.^{1–3} A CHD event was defined as fatal (*International classification of diseases*, ninth revision) or non-fatal myocardial infarction (confirmed from the hospital notes as typical symptoms and cardiac enzyme rise to at least twice the upper limit of normal). Strokes were adjudicated against the hospital records and general practitioners' notes, defined as focal or global neurological impairment of sudden onset lasting more than 24 h (or leading to death) of presumed vascular aetiology. Patients with non-fatal subarachnoid haemorrhage were not included. Of the full cohort of men, 536 already at entry had a history or ECG suggestive of coronary or cerebrovascular disease and they were excluded from this analysis. So also were 52 men with diabetes mellitus, because only the older guidelines under comparison recommend estimating risk for patients with diabetes to decide who should receive statin treatment.¹¹ For 157 of the remaining patients cholesterol or blood pressure values were unavailable. The study population thus consisted of 1653 men without evidence of CHD at recruitment, all of whom had complete data for risk evaluation by all of the methods being compared. Low density lipoprotein (LDL) cholesterol was calculated from serum cholesterol, high density lipoprotein (HDL) cholesterol and fasting triglycerides by the Friedewald formula.²¹ We wrote a computer programme for each of the recommendations as follows.

National Cholesterol Education Program Adult Treatment Panel III

The Adult Treatment Panel (ATP) III estimates risk on the basis of 10-year risk of fatal and non-fatal myocardial infarction calculated from tables published by the National Cholesterol Education Program.¹⁴ A statin is recommended if the person has ≥ 2 risk factors and (a) a risk $\geq 20\%$ and LDL cholesterol ≥ 100 mg/dl (2.6 mmol/l) or (b) a risk $\geq 10\%$ to 20% and LDL cholesterol ≥ 130 mg/dl (3.4 mmol/l) or (c) a risk $< 10\%$ and LDL cholesterol ≥ 160 mg/dl (4.1 mmol/l), or if the person has < 2 risk factors and LDL ≥ 190 mg/dl (4.9 mmol/l) (option of > 160 mg/dl).

First Joint British Societies

The first Joint British Societies (JBS 1) recommend use of a statin is based on 10-year risk of fatal and non-fatal myocardial infarction and new angina calculated from

equations published by Anderson *et al.*²² (The JBS Cardiac Risk Assessor Programme is available, for example, on the British National Formulary website, <http://bnf.org>, under BNF Extra and the British Hypertension Society (BHS) website, www.bhsoc.org, under Guidelines section.) Statin treatment is recommended if the person's risk is $\geq 15\%$ and total cholesterol ≥ 5 mmol/l or LDL cholesterol ≥ 3 mmol/l.^{11–12}

National Service Framework

The recommendations of the National Service Framework (NSF) are as those of the JBS, but risk must be $\geq 30\%$ over 10 years to receive a statin.¹³

Fourth British Hypertension Society (BHS IV) and second JBS (JBS 2)

According to the BHS IV and JBS 2 recommendations, risk based on 10-year $> 30\%$ risk of fatal or non-fatal myocardial infarction, new angina and stroke estimated from equations from Anderson *et al.*²² with the age projected forward to 49 years if the current age is < 50 , to 59 if the current age is 50–59, and to 69 if the current age is ≥ 60 years as shown in the charts in Williams *et al.*¹⁶ and Wood *et al.*¹⁷ Statin treatment is recommended if the patient's risk is $\geq 20\%$ and total cholesterol ≥ 4 mmol/l or LDL cholesterol ≥ 2 mmol/l.

Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice

The European recommendation is based on 10-year risk of a fatal CVD event estimated from charts published by De Backer *et al.*¹⁵ A statin is recommended if risk is $\geq 5\%$ and total cholesterol ≥ 5 mmol/l or LDL cholesterol ≥ 3 mmol/l, or regardless of calculated risk if serum cholesterol is ≥ 8 mmol/l or LDL cholesterol ≥ 6 mmol/l.

The reduction in CVD risk with statin treatment was modelled for each 10% interval in the range from 10–50%. This is the range encountered in randomised clinical trials.^{1–3}

Data were statistically analysed with Stata V.8 (StataCorp, College Station, Texas, USA). The observed CVD risk was adjusted to the first 10 years of observations to be compatible with the risk estimation methods used in the various recommendations.

RESULTS

Table 1 shows the characteristics of the men investigated.

The observed CVD risk for the cohort was 12.8% over 10 years. The distribution of risk estimated by the methods recommended in the different guidelines varied considerably. This was largely explicable by the different CVD end points each uses. What was critical for the proportion of the men who would receive statin treatment was how each risk assessment method performed with its recommended risk

Table 1 Cardiovascular risk factors in 1653 men aged 49–65 years at initial examination

Age (years)	56.8 (4.5)
Systolic BP (mm Hg)	146.6 (22.8)
Diastolic BP (mm Hg)	84.8 (12.1)
Serum cholesterol (mmol/l)	5.61 (0.98)
LDL cholesterol (mmol/l)	3.72 (0.9)
HDL cholesterol (mmol/l)	1.03 (0.25)
Triglycerides (mmol/l)	1.59 (1.15–2.25)
Smokers	45.9%

Data are mean (SD), median (interquartile range), if non-gaussian or percentage.
BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein.

Figure 1 Frequency distribution of coronary heart disease (CHD) or cardiovascular disease (CVD) risk in the men studied according to the risk estimation method accompanying the Joint British Societies (JBS), Adult Treatment Panel (ATP III), British Hypertension Society (BHS) IV (the same as the new JBS) and European recommendations. In each case the hatched areas show men exceeding the critical risk thresholds above which statins are recommended. For JBS the heavier hatching shows the threshold of 30% 10-year CHD risk recommended in the National Health Service Framework and in the case of BHS IV the unshaded area shows the frequency distribution curve without age projected forward to 49, 59 or 69 years. ATP III recommends statins when risk exceeds 20% when low density lipoprotein (LDL) cholesterol is >100 mg/dl (2.6 mmol/l; heavier hatching) and between 10% and 20% when LDL is >130 mg/dl (3.4 mmol/l; lighter hatching). Lower levels of risk may also be treated according to ATP III when LDL concentration is higher than these.

threshold (fig 1). The highest proportion of the population identified for statin treatment was 77% by the BHS IV and JBS 2 recommendations and the lowest was 14% by the NSF (table 2).

The NSF, however, included only 64 of the 212 men destined to have a CVD event. The JBS and ATP III recommendations identified a remarkably similar proportion of the men (around 60%) and this was not greatly influenced by whether the option of treating men with LDL cholesterol concentrations down to 160 mg/dl (4.1 mmol/l) was exercised. The European guidelines targeted statins at only 46% of the men and achieved a population impact that was only marginally less than that of JBS and ATP III. When all the methods were considered, any increase in the proportion of events correctly predicted (sensitivity) was closely related to increasing numbers of events incorrectly predicted.

The number needed to treat (NNT) for statin treatment was best for the methods that identified the smallest number

of men for statin treatment. Thus, NNTs ranged from 7.3 for a 50% statin effect on CVD incidence according to the NSF guidelines to 78.0 for a statin benefit of only 10% and providing statins for all men (table 3).

The population impact (decrease in the overall incidence of CVD) was clearly greatest if all men were to receive statin treatment (table 2). All of the recommendations achieved two thirds or more of the greatest impact with the exception of the NSF, which decreased CVD rates by only 9.1%. The BHS IV/JBS 2 guidelines achieved almost the maximum possible population impact.

DISCUSSION

Our study shows both major differences in the outcome of different national and international recommendations and perhaps some surprising similarities. The most critical factor determining the proportion of men who could receive statin treatment was not the method of risk prediction, but the

Table 2 Comparison of likely effects of various guidelines on statin treatment in 1653 men aged 49–65 in a prospective follow up

Treatment recommendation (reference)	Number treated	First events*	Prevented events†	NNT for 10 years to prevent 1 event	Population impact‡
Whole study population	1653 (100%)	212	63.6	26.0	–30%
BHS IV ¹⁶ and New JBS 2 ¹⁷	1272 (77%)	191	57.3	22.2	–27%
JBS 1 ^{11 12}	1030 (62%)	165	49.5	20.8	–23.3%
ATP III ¹⁴					
Optional thresholds	992 (60%)	154	46.2	21.5	–21.8%
Threshold*	960 (58%)	153	45.9	20.9	–21.6%
European ¹⁵	757 (46%)	138	41.4	18.3	–19.6%
NSF ¹³	232 (14%)	64	19.2	12.1	–9.1%

*First cardiovascular events (coronary heart disease + stroke) in 10 years in men identified by the guidelines to require statin for primary prevention of cardiovascular disease; †assuming a 30% reduction with statin treatment; ‡percentage decrease in first cardiovascular events in the population anticipated from treatment in the study and according to the guidelines; §low density lipoprotein (LDL) ≥ 160 mg/dl (4.1 mmol/l); *LDL ≥ 190 mg/dl (4.9 mmol/l). ATP, Adult Treatment Panel; BHS, British Hypertension Society; CPS, Caerphilly Prospective Study; JBS, Joint British Societies; NNT, number needed to treat; NSF, National Service Framework.

Table 3 NNT according to the various recommendations for CVD prevention for estimated statin-induced risk reductions of 10% to 50%

Treatment recommendation	Risk reduction				
	10%	20%	30%	40%	50%
Whole study population	78.0	39.0	26.0	19.5	15.6
BHS IV and JBS 2	66.6	33.3	22.2	16.6	13.3
JBS 1	62.4	31.2	20.8	15.6	12.5
ATP III					
Optional threshold*	64.4	32.2	21.5	16.1	12.9
Threshold†	62.7	31.4	20.9	15.7	12.5
European	54.9	27.4	18.3	13.7	11.0
NSF	36.3	18.1	12.1	9.1	7.3

*Low density lipoprotein (LDL) ≥ 160 mg/dl (4.1 mmol/l); †LDL ≥ 190 mg/dl (4.9 mmol/l).

ATP, Adult Treatment Panel; BHS, British Hypertension Society; CPS, Caerphilly Prospective Study; CVD, cardiovascular disease; JBS, Joint British Societies; NNT, number of men who would need to receive statin treatment to prevent one cardiovascular disease event; NSF, National Service Framework.

threshold of risk for the initiation of statin treatment. Thus, the NSF with the highest threshold ($\geq 30\%$ CHD risk over 10 years) stands out as the cheapest, but least effective, and in terms of making the best use of evidence for the benefit of the members of a healthcare scheme, the worst. This undoubtedly reflects the difficulty for a socialised healthcare system of responding to the overall cost implications of major medical advances when the additional expense must be met by lowering costs of other aspects of medical care or by increasing taxes, rather than being paid by those who stand to benefit. On the other hand the concept of reintroducing individual choice, at least in the case of statins purchased without a physician's prescription, has been equally contentious in both Britain²³ and the USA.^{24–25} The National Institute for Health and Clinical Excellence, which calculates the average annual cost of statin treatment to be £152.52, has recently recommended a 10-year CVD risk of $\geq 20\%$ for the introduction of statin treatment⁸ in line with the BHS and both the old and new JBS recommendations.^{11 16 17}

The risk threshold is so critical because, regardless of the method of risk determination, if it does not include or come close to including the average level of risk in a population, it will have only limited impact on reducing overall CVD incidence. This is the tension that exists between this high risk strategy and the population approach to disease prevention. Targeting treatment at patients at highest risk provides the best NNT but, unfortunately, far greater numbers of people will have coronary events or strokes with levels of risk closer to the average, simply because they are more numerous.²⁶ This means that to be effective in CVD prevention, statin treatment must be provided for most men from middle age onwards and for most older women. This concept may be horrifying to some, but the reality is that already a quarter of some age groups are regularly prescribed drugs, such as proton pump inhibitors.²⁷ Furthermore, in the UK more than a quarter of all adults²⁸ and three quarters of elderly people also self-medicate with over-the-counter drugs,²⁹ spending the equivalent of more than one third of the total cost of the drugs supplied by the NHS in the process. To this must be added people taking drugs from sources other than pharmacists. Presumably such treatment, unlike statins, has never been shown to extend life. Also, the wider use of effective, but less expensive, aspirin in lower risk populations is limited by the risk of serious adverse events such as gastrointestinal and cerebral haemorrhage.³⁰ Evidence suggests that the balance of side effects and benefit from

statins extends to much lower levels of CVD risk than is the case for aspirin.³¹

The risk estimation method was next in importance to the risk threshold chosen for statin intervention in determining the effectiveness of guidelines. Overprediction of CVD risk in the British Regional Heart Study by the risk equations derived from the Framingham Study has previously been reported.³² Our investigation does show that these equations are perhaps less effective than the new European risk charts. Used in conjunction with the European recommendations, these charts identified 138 of the men destined to have a CVD event out of 757 estimated to be at high enough risk for statin treatment. Although the Framingham risk equation of Anderson and colleagues²² used with the JBS guidelines identified correctly 165 men destined to have a CVD event, this was out of 1030 who would be advised to receive statins. The population impact at around -20% was slightly worse, however, with the European method than with the JBS method, which was -23% . The difference between the methods was probably related to their different end points, which are non-fatal myocardial infarction, stroke and new angina in the Framingham risk equation, whereas the European charts predict only fatal myocardial infarction and stroke. Caution is required in the interpretation of our results, because the European risk prediction method may perform to its best advantage in middle-aged men. It does not include HDL, which is often less critical in men than in women. Attention has previously been drawn to the importance of HDL in risk prediction in women.¹⁸ Furthermore, we have not estimated CVD risk projecting the age of men forward to 60 years, which the European recommendations propose as an option.¹⁵ Had we done so, results would have been similar to those of the ATP III, JBS and BHS IV guidelines as fig 1 shows. The BHS IV and JBS 2 risk prediction chart based on both CHD and stroke risk^{16 17} would have identified a substantially smaller proportion of men for statin treatment than the 77% shown in table 2, had age not been projected forward to the 49th, 59th or 69th year by the design of its accompanying charts. The modified version of the Framingham risk equation, excluding new angina and cerebrovascular disease as an end point and which was used as an algorithm in the ATP III guidelines,^{14 33} appeared to offer no advantage over the older equation, which is used in conjunction with the JBS recommendations.

The scale of benefit in statin trials ranges from around a 10% decrease in CVD events to about 50%, with most studies clustering around the 30% used in table 2.^{1–3} A 30% decrease in CVD risk would be expected from a decrease in LDL cholesterol of 1.4 mmol/l even in the first year of treatment.³ This degree of LDL reduction is what most of the recommendations aim at achieving with statin treatment, to judge from their targets and the likely pretreatment LDL cholesterol values in Europe and the USA. Our conclusions would be similar, however, if we had assumed a smaller treatment effect. Interestingly, even providing statins untargeted at the whole male population and achieving only a 10% decrease in CVD risk, the NNT is still 78, which would be better than most other treatments including for hypertension.³⁴ That is because statins are more effective than antihypertensive agents in decreasing CHD risk, and CHD accounts for three quarters or more of CVD events even in hypertension.³⁵

The issues surrounding medicating huge sections of a high risk population, such as that of Britain, with statins would not arise if the serum cholesterol were not so high. In China, for example, where the average cholesterol in the adult population was until recently less than 4 mmol/l, CHD was uncommon.⁷ With the increase in dietary fat intake and obesity in urban areas this situation is changing even more rapidly than it did in Britain when diet changed similarly

over a more prolonged period from the latter half of the 19th century.¹⁰ The lack of resolve in tackling Britain's unhealthy diet as a consequence of anachronistic farming subsidies and a lack of government consistency in directing the food industry and encouraging physical education has resulted in one in three of Europe's obese children being British.³⁶ Despite the decline in the premature death from CHD in Britain since the early 1980s,³⁷ the prevalence of the disease and its morbidity are set to rise for many years more. Whereas the decline in mortality among people known to have CHD can be attributed to improved treatment, including statins, the mortality decline among people without a previous CVD event may be substantially due to decreased smoking and improved cholesterol and blood pressure.³⁸ In the USA this decline in serum cholesterol and CHD ceased from around 1990.³⁹ Recent statistics from Britain show that the decline in cholesterol here too halted between 1998 and 2003 as obesity increased.⁴⁰ Renewed effort in this direction is therefore needed if the use of statins is not to extend to perhaps most of the population.

The men in the Caerphilly study may be viewed as a relatively high risk group. At the time they entered the study the proportion who smoked was high. On the other hand, while smoking rates have since declined, obesity has become more prevalent in Britain, which will adversely affect cholesterol and blood pressure so that, in terms of overall risk, general conclusions about CVD prevention drawn from the Caerphilly men may be as relevant today. We cannot even speculate about the outcome of different CVD prevention guidelines for women. There is clearly a need to make CVD recommendations objective in terms not just of clinical trial evidence but also of their practical application. More investigations of the type reported here are therefore cogently needed. These should include both men and women, and should span a wider age range.

ACKNOWLEDGEMENTS

We are grateful to the original Caerphilly and Speedwell Study investigators for permission to use their data and to Ms C Price for expert preparation of the manuscript. MJ received a Travelling Fellowship from the Birjand University of Medical Sciences, Iran. PM and MJ have no interests to declare. PND has received research funding and fees for lectures and consultation from pharmaceutical companies producing statins.

Authors' affiliations

P McElduff, Hunter New England Population Health, Hunter New England Area Health Service, Wallsend New South Wales, Australia

M Jaefarnezhad, Department of Cardiology, Birjand University of Medical Sciences, Birjand, Iran

P N Durrington, University of Manchester Division of Cardiovascular and Endocrine Science, Department of Medicine, Manchester Royal Infirmary, Manchester, UK

PND is the guarantor. He conceived the study and obtained permission to use the data. All three authors developed the protocol. MJ did a preliminary data analysis and PM did the computer programming and complete statistical analysis. All three authors contributed to writing the manuscript.

REFERENCES

- Hebert PR, Gaziano JM, Chan KS, *et al.* Cholesterol lowering with statin drugs, risk of stroke, and total mortality: an overview of randomised trials. *JAMA* 1997;**278**:313–21.
- Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. *BMJ* 2003;**326**:1423–7.
- Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90056 participants in 14 randomised trials of statins. *Lancet* 2005;**366**:1267–78.
- Downs GR, Clearfield M, Weiss S. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of the AFCAPS/TEXCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study), *et al.* *JAMA* 1998;**279**:1615–22.
- Heart Protection Study Collaborative Group. Cost-effectiveness of simvastatin in people at different levels of vascular disease risk: economic analysis of a randomised trial in 20536 individuals. *Lancet* 2005;**365**:1779–85.
- Jackson PR, Ramsay LE. Debate: at what level of coronary heart disease risk should a statin be prescribed? *Curr Opin Lipidol* 2000;**11**:357–61.
- Mackay J, Mensah GA. *The atlas of heart disease and stroke*. Geneva: WHO, 2004.
- National Institute for Health and Clinical Excellence. *Statins for the prevention of cardiovascular events in patients at increased risk of developing cardiovascular disease or those with established cardiovascular disease*, Technology appraisal 94. London: NICE, 2006, <http://www.nice.org.uk/page.aspx?o=TA094> (accessed 13 Apr 2006).
- Keys A. Coronary heart disease: the global picture. *Atherosclerosis* 1975;**22**:149–92.
- Charlton J, Quaife K. Trends in diet 1841–1994. In: Charlton J, Murphy M, eds. *The health of adult Britain: 1841–1994*. London: The Stationery Office, 1997:93–113.
- Wood D, Durrington PN, Poulter N, *et al.* Joint British recommendations on prevention of coronary heart disease in clinical practice. *Heart* 1998;**80**(suppl 2):S1–29.
- British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, British Diabetic Association. Joint British guidelines on prevention of coronary heart disease in clinical practice: summary. *BMJ* 2000;**320**:705–8.
- Department of Health. *National Service Framework for coronary heart disease*. London: Department of Health, 2000, <http://www.dh.gov.uk/assetRoot/04/05/75/26/04057526.pdf> (accessed 13 Apr 2006).
- National Cholesterol Education Program. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* 2001;**285**:2486–97.
- De Backer G, Ambrosioni E, Borch-Johnsen K, *et al.* European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of eight societies and by invited experts). *Atherosclerosis* 2003;**170**:145–55.
- Williams B, Poulter NR, Brown MJ, *et al.* British Hypertension Society Guidelines. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV, *J Hum Hypertens* 2004;**18**:139–85.
- Wood D, Wray R, Poulter N, *et al.* JBS2: Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. *Heart* 2005;**91**(suppl V):v1–52.
- Durrington PN, Prais H, Bhatnagar D, *et al.* Indications for cholesterol-lowering medication: comparison of risk-assessment methods. *Lancet* 1999;**353**:278–81.
- Bainton D, Miller NE, Bolton CH, *et al.* Plasma triglyceride and high density lipoprotein cholesterol as predictors of ischaemic heart disease in British men: the Caerphilly and Speedwell Collaborative Heart Disease Studies. *Br Heart J* 1992;**68**:60–6.
- Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ* 1962;**27**:645–58.
- Friedewald WT, Levy RI, Frederickson DS. Estimation of the concentration of LDL-cholesterol in plasma, without the use of preparative ultracentrifuge. *Clin Chem* 1972;**18**:499–502.
- Anderson KM, Odell PM, Wilson PWF, *et al.* Cardiovascular disease risk profiles. *Am Heart J* 1990;**121**:293–8.
- Anon. Simvastatin over the counter. *Drug Ther Bull* 2005;**43**:25–8.
- Brass EP. Consumer behaviour in the setting of over-the-counter statin availability: lessons from the consumer use study of OTC Mevacor. *Am J Cardiol* 2004;**94**(suppl):22F–9F.
- McKenney JM, Brown WV, Cohen JD, *et al.* The National Lipid Association Surveys of consumers, physicians and pharmacists regarding over-the-counter statin in the United States: is this a good idea. *Am J Cardiol* 2004;**94**(Suppl):16F–21F.
- Rose G. Strategy of prevention: lessons from cardiovascular disease. *BMJ* 1981;**282**:1847–51.
- Drummond A, Kwok S, Morgan J, *et al.* Costs of aspirin and statins in general practice. *QJM* 2002;**95**:23–6.
- Thomas DHV, Noyce PR. The interface between self-medication and the NHS. *BMJ* 1996;**312**:688–90.
- Barnett NI, Denham MJ, Francis SA. Over-the-counter medicines and the elderly. *J R Coll Physicians Lond* 200, **34**:445–6.
- Loke YK, Bell A, Derry S. Aspirin for the prevention of cardiovascular disease: calculating benefit and harm in the individual patient. *Br J Clin Pharmacol* 2003;**55**:282–7.
- Sniderman AD. Is there value in liver function test and creatine phosphokinase monitoring with statin use? *Am J Cardiol* 2004;**94**(Suppl):30F–4F.
- Brindle P, Emberson J, Larue F, *et al.* Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. *BMJ* 2003;**327**:1267–70.
- Grundey SM, Pasternak R, Greenland P, *et al.* Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations. A statement for healthcare professionals from the American Heart Association and American College of Cardiology. *Circulation* 1999;**100**:1481–92.
- Collins R, MacMahon S. Blood pressure, antihypertensive drug treatment and the risks of stroke and of coronary heart disease. *Br Med Bull* 1994;**50**:272–98.

- 35 **Green R**, Kwok S, Durrington PN. Preventing cardiovascular disease in hypertension: effects of lowering blood pressure and cholesterol. *QJM* 2002;**95**:821–6.
- 36 **British Medical Association Board of Science**. Preventing childhood obesity. London: BMA 2005. [http://www.bma.org.uk/ap.nsf/AttachmentsByTitle/PDFchildhoodobesity/\\$FILE/PreventingObesityfinal.pdf](http://www.bma.org.uk/ap.nsf/AttachmentsByTitle/PDFchildhoodobesity/$FILE/PreventingObesityfinal.pdf) (accessed 13 Apr 2006).
- 37 **Charlton J**, Murphy M, Khaw K, et al. Cardiovascular diseases. In: Charlton C, Murphy M, eds. *The health of adult Britain 1841–1994*, vol 2. London: The Stationery Office, 1997:60–81.
- 38 **Unal B**, Critchley J, Capewell S. Modelling the decline in coronary heart disease deaths in England and Wales 1981–2000: comparing contributions from primary prevention and secondary prevention. *BMJ* 2005;**331**:614.
- 39 **Pearson TA**. The epidemiologic basis for population-wide cholesterol reduction in the primary prevention of coronary artery disease. *Am J Cardiol* 2004;**94**(suppl):4F–8F.
- 40 **Sprison K**, Primatesta P, eds. Risk factors for cardiovascular disease. *Health Survey for England 2003*, vol 2. London: The Stationery Office, 2004.

IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2005.080168

Subacute cardiac tamponade with very large pericardial effusion in a postpartum woman

A 30-year-old woman with a history of hypothyroidism presented to the hospital two weeks following an uncomplicated delivery complaining of progressive dyspnoea on exertion for four weeks. She had severe bilateral pitting oedema of lower extremities and her blood pressure was 150/90 mm Hg with no pulsus paradoxus. The chest x ray (panel A) showed huge cardiomegaly and the ECG showed low QRS voltage. The echocardiogram (panel B) showed very large pericardial effusion and 2 litres of fluid was drained in pericardiocentesis. The patient's dyspnoea then resolved.

Patients with subacute tamponade may be asymptomatic or complain of dyspnoea, chest discomfort, peripheral oedema, fatigability, or other symptoms caused by increased filling pressures and limited cardiac output. Hypotension with narrow pulse pressure is common but patients with pre-existing hypertension may remain hypertensive due to the increased sympathetic activity. Although the effusion could be idiopathic in our patient, hypothyroidism is an important aetiology particularly in patients with large and chronic effusion. Low QRS voltage and electrical alternans may be seen on ECG and they are more specific for tamponade than pericardial effusion alone. QRS voltage may remain low for a few days after treatment. Absence of pulmonary congestion despite the presence of cardiomegaly is a feature that can distinguish this condition from congestive heart failure and cardiomyopathies on chest x ray. Echocardiography is the diagnostic modality of choice. Pericardiocentesis is the treatment. Large chronic pericardial effusion has a high recurrence rate and it should be followed up by echocardiograms. About 20% of these patients may need pericardiectomy, which in most patients is well tolerated.

A A Sovari
K Moazemi
C K Bodine
alizadeh@uiuc.edu

doi: 10.1136/hrt.2005.079095

Left atrial calcification in rheumatic heart disease: a rare presentation

A 42-year-old man with chronic rheumatic heart disease, who underwent closed mitral valvuloplasty in 1984, presented with atrial fibrillation and gross congestive heart failure. His echocardiogram revealed severe calcific mitral stenosis (left panel) with mitral valve area of 0.5 cm² on two dimensional echocardiography, severe mitral regurgitation with jet area 21 cm²/left atrial area 39 cm², severe aortic regurgitation and moderate aortic stenosis with peak systolic gradient of 70 mm Hg, and severe tricuspid regurgitation. Cine radiography showed extensive calcification of the left atrial wall and mitral valve apparatus (right panel). Cardiac catheterisation revealed normal epicardial coronaries and the pulmonary artery pressure was 50/34 mm Hg. The patient was advised

to undergo aortic and mitral valve replacement with tricuspid valve repair.

Extensive left atrial calcification following chronic rheumatic heart disease is a rare entity, and in this case required a modified surgical approach during mitral valve surgery.

R Vijayvergiya
H Jeevan
A Grover
rajeshvijay999@hotmail.com