

Cost-effectiveness of simvastatin in people at different levels of vascular disease risk: economic analysis of a randomised trial in 20 536 individuals

Heart Protection Study Collaborative Group*

Summary

Background Statin therapy reduces the rates of heart attack, stroke, and revascularisation among a wide range of individuals. Reliable assessment of its cost-effectiveness in different circumstances is needed.

Methods 20 536 adults (aged 40–80 years) with vascular disease or diabetes were randomly allocated 40 mg simvastatin daily (10 269) or placebo (10 267) for an average of 5 years. Comparisons were made of hospitalisation and statin costs (2001 UK prices) during the scheduled treatment period between all simvastatin-allocated versus all placebo-allocated participants. Cost-effectiveness was estimated among different categories of participant.

Findings Allocation to simvastatin was associated with a highly significant 22% (95% CI 16–27; $p < 0.0001$) proportional reduction in hospitalisation costs for all vascular events, with similar proportional reductions in every subcategory of participant studied. During an average of 5 years, estimated absolute reductions in vascular event costs per person allocated 40 mg simvastatin daily ranged from UK£847 (SE 137) in the highest risk quintile studied to £264 (48) in the lowest. Mean excess cost of statin therapy among participants allocated simvastatin was £1497 (8), with similar absolute increases in every subcategory. Costs of preventing a major vascular event with 40 mg simvastatin daily ranged from £4500 (95% CI 2300–7400) among participants with a 42% 5-year major vascular event rate to £31 100 (22 900–42 500) among those with a 12% rate (corresponding to 5-year major coronary event rates of 22% and 4%, respectively).

Interpretation Statin therapy is cost effective for a wider range of individuals with vascular disease or diabetes than previously recognised (particularly with lower-priced generics). It would be appropriate to consider reducing the estimated level of vascular event risk at which statin therapy is recommended.

Introduction

The MRC/BHF Heart Protection Study (HPS) has shown that lowering LDL cholesterol concentrations with 40 mg simvastatin daily produces substantial reductions in the rates of major vascular events (ie, heart attacks, strokes, and revascularisation procedures) among a wide range of high-risk individuals, irrespective of their pretreatment blood cholesterol concentrations.^{1–4} Such treatment may, therefore, be cost effective for many types of high-risk patient who would not be prescribed statin therapy according to current guidelines.

The aim of this report is to estimate the cost-effectiveness of 40 mg simvastatin daily during the scheduled study treatment period among people at different underlying levels of risk for vascular events. This information should help determine appropriate risk thresholds for initiating statin therapy.

Methods

The perspective of these economic analyses is that of the UK National Health Service, and all costs are reported in UK£ for the year 2001 (ie, the year in which HPS ended).

Recruitment and follow-up

Details of HPS have already been reported.^{1–4} Men and women aged about 40–80 years with non-fasting blood total cholesterol concentrations of at least 3.5 mmol/L

(135 mg/dL) were eligible provided they had a medical history of: coronary disease; cerebrovascular disease; other occlusive arterial disease; diabetes mellitus; or treated hypertension (if also male and aged at least 65 years). People were ineligible if their doctor considered statin therapy to be clearly indicated or contraindicated, or if they had: recent stroke, myocardial infarction, or angina hospitalisation; chronic liver disease or abnormal liver function; severe renal disease or substantially impaired renal function; inflammatory muscle disease or other muscle problems; concurrent treatment with contraindicated drugs; child-bearing potential; severe heart failure; life-threatening condition other than vascular disease or diabetes; or conditions that might limit compliance.

At the initial screening visit, potentially eligible people who agreed to participate entered an 8–10 week prerandomisation run-in treatment phase. Compliant individuals not considered by their doctors to have a clear indication for, or contraindication to, statin therapy were then randomly allocated to receive 40 mg simvastatin daily or matching placebo for about 5 years. Randomised participants were to be followed at 4, 8, and 12 months, and then 6-monthly. Compliance with study treatment was assessed at every follow-up by reviewing the calendar-packed tablets remaining and recording the use of any non-trial statin. Information was recorded at



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See <http://www.hpsinfo.org>

every follow-up about any suspected serious adverse events,¹ and the duration of any hospital admission. Further details were sought from general practitioners and, if necessary, hospital records about all reports that might relate to heart attacks, strokes, other major vascular events, cancers, or deaths, and from UK national registries about any cancers and the certified causes of any deaths. All such information (including hospitalisation duration) was reviewed by coordinating centre clinical staff blind to study treatment allocation and coded according to prespecified criteria. For all deaths, the duration of any hospitalisation immediately prior to death was sought from hospital records.

Health outcome events and associated costs

All serious adverse events recorded during the scheduled treatment period, not just the first event of any particular type, were included in the present economic analyses. Every such event was classified as major vascular (ie, non-fatal myocardial infarction or coronary death, non-fatal or fatal stroke, or arterial revascularisation), other vascular (ie, admission for angina, heart failure, or other vascular problems) or non-vascular (ie, all other serious medical or surgical events). Deaths were also classified as either vascular (9th International Classification of Diseases [ICD] codes 390–459) or non-vascular (ICD 0–389 and 460–E999). Further updating of the database for the present analyses resulted in slight differences in the numbers of subsequent (but not first) major vascular events compared with previous reports.^{2–4} To estimate the costs of hospitalisations, every serious adverse event was mapped to one of 40 hospital specialties. Missing information about length of hospital stay was imputed for 8% of vascular and non-vascular events using the average value for corresponding types of event with known duration (which did not differ significantly between the treatment groups). The cost per inpatient day from UK Trust Financial Returns for these specialties in 1999–2001^{5,6} was then applied to the observed or imputed length of stay to generate the cost per hospitalisation episode. Where a single hospitalisation involved serious adverse events in more than one specialty, a hierarchy of specialties (based on clinical review blind to treatment allocation) was used to estimate the likely duration in every specialty. No cost was attributed to the small proportion (8.6%) of vascular events that did not involve a hospital admission.

Statin treatment costs

Participants recorded at a scheduled follow-up as having stopped their allocated study simvastatin at the previous follow-up or as having taken less than 10% of it since that follow-up were attributed no cost for study statin during that follow-up period (since it was considered that, in such circumstances in ordinary clinical practice, prescriptions would not typically be repeated). Otherwise, participants allocated 40 mg simvastatin

incurred a daily cost of £1.06 (2001 UK prices⁷) throughout all of their scheduled study treatment period. Use of non-study statin was recorded at every follow-up, but the type and dose was recorded only at the final follow-up visit. In these analyses, participants who started any non-study statin were attributed daily costs (based on the 2001 UK price of the type and dose recorded at the final visit) from the midpoint between the follow-up at which its use was first recorded and the previous follow-up until the scheduled end of the trial.

Statistical and cost-effectiveness analysis

Intention-to-treat comparisons were made of hospitalisations and statin costs during the scheduled treatment period after randomisation among all simvastatin-allocated versus all placebo-allocated participants (with no difference observed between the treatment groups in the small numbers lost to follow-up²). Previous analyses of HPS had indicated that proportional reductions in the risk of first vascular events with allocation to 40 mg simvastatin daily were similar in different categories of participant.^{2–4} Consequently, it was hypothesised that the proportional reductions in hospitalisation costs associated with vascular events would also be similar across different subgroups. By contrast, the absolute differences in the cost of statin treatment between the study treatment groups were expected to be similar in different categories of participant. Hence, to minimise random error in the cost-effectiveness estimates, the absolute reduction in the costs of vascular event hospitalisations in any particular subgroup was to be derived by applying the overall proportional reduction in vascular event costs observed among all participants to the vascular event costs observed in the placebo group for that particular subgroup (and absolute reductions in vascular events and deaths within subgroups were to be estimated similarly). These estimated cost savings were then to be subtracted from the overall excess cost of statin treatment to estimate the net absolute cost of treatment for the subgroup of interest. Finally, these net absolute costs were to be divided by the estimated number of vascular events or deaths avoided to provide a subgroup-specific cost-effectiveness estimate. Costs of hospitalisations for non-vascular events or of concomitant medication were not anticipated to be included in the cost-effectiveness analyses since simvastatin allocation had not been found to produce any significant effect on these outcomes,^{2–4} and their inclusion would unduly increase the random error of these estimates.

Since the univariate subgroups considered previously did not provide a wide range of vascular risk levels (table 1), a multivariate risk score was derived. First, the 5-year risk of a major vascular event was estimated using a standard Cox proportional hazards model, with baseline prior vascular disease or diabetes, sex, age, plasma LDL and HDL cholesterol, midpoint of systolic

and diastolic blood pressure,⁸ smoking status, plasma creatinine, and statin allocation entering the model as significant predictive factors. Participants were then rank-ordered by their predicted risk and quintiles used to determine five multivariate risk subgroups. χ^2 tests for heterogeneity were used to test the hypothesis that simvastatin allocation was associated with similar proportional reductions in vascular event hospitalisation costs, and similar absolute increases in statin treatment costs, across the subgroups studied. CIs were estimated for the treatment:placebo ratios of events and costs using Fieller's method,⁹ and for cost-effectiveness ratios by non-parametric bootstrapping.¹⁰ All cost-effectiveness ratios are reported using the UK Treasury approved discount rate of 3.5% to adjust for differential timing of costs and effects. Where costs and events are reported separately these are undiscounted (unless otherwise stated).

Role of the funding source

The investigators were responsible for the study design, data collection, data analysis, data interpretation, and writing of the report, independently of all funding sources.

Results

Vascular and non-vascular events

Table 1 shows the risk of first major vascular event among HPS participants in univariate subgroups and multi-

	Number of patients	5-year rate of first event		
		MVE	MCE	Vascular death
Prior disease*				
Any CHD	13386	26%	13%	9%
No CHD				
CVD	1820	23%	8%	9%
PVD	2701	31%	10%	10%
Diabetes	3982	18%	8%	6%
Sex				
Male	15454	27%	13%	9%
Female	5082	18%	7%	6%
Age (years)				
<65	9839	21%	8%	5%
≥65 to <70	4891	26%	13%	10%
≥70	5806	30%	16%	14%
LDL cholesterol (mmol/L)				
<3.0	6793	22%	10%	8%
≥3.0 to <3.5	5063	24%	11%	8%
≥3.5	8680	27%	12%	9%
Risk group				
1	4107	12%	4%	3%
2	4107	18%	7%	5%
3	4107	22%	10%	7%
4	4107	28%	13%	10%
5	4108	42%	22%	18%
Overall	20536	25%	11%	9%

*There is some overlap (and, hence, non-additivity) within the "no CHD" category. CHD=coronary heart disease; CVD=cerebrovascular disease; PVD=peripheral vascular disease.

Table 1: Estimated 5-year rate of a first major vascular event (MVE), major coronary event (MCE), or vascular death in univariate and multivariate risk subgroups

	Simvastatin (n=10 269)	Placebo (n=10 267)	Ratio (95% CI)	Events avoided per 1000 (SE)	p
Events (non-fatal and fatal)					
Major vascular	2773	3689	0.75 (0.71–0.80)	89 (10)	<0.0001
Other vascular	4355	4905	0.89 (0.83–0.94)	54 (14)	0.0002
Non-vascular	12 432	12 718	0.98 (0.94–1.02)	28 (25)	0.3
Deaths					
Vascular	781	937	0.83 (0.76–0.91)	15 (4)	<0.0001
Non-vascular	547	570	0.96 (0.86–1.08)	2 (3)	0.5

Table 2: Total (first and subsequent) vascular and non-vascular outcomes during 5-year mean follow-up

variate risk quintiles, with the 5-year risk ranging widely from 42% in the highest risk quintile to 12% in the lowest. It also shows the 5-year risk of first major coronary event (ie, non-fatal myocardial infarction or coronary death), which is the outcome most commonly used as a basis for treatment guidelines, and the risk of vascular death. In previous HPS analyses,^{2,4} allocation to simvastatin produced a highly significant 24% (95% CI 19–28; $p<0.0001$) proportional reduction in the rate of first major vascular event, with this reduction of about a quarter observed in a variety of different univariate subgroups. When the larger numbers of first and subsequent major vascular events were considered, a highly significant 25% (20–29; $p<0.0001$) proportional reduction was also found (table 2),³ and reductions of about a quarter were again observed in univariate and multivariate risk groups (webfigure 1). Overall, this reduction of a quarter in the rate of first or subsequent major vascular events translated into 89 (95% CI 70–108) fewer events per 1000 patients (table 2). In addition, simvastatin allocation prevented an average of 54 (26–82; $p=0.0002$) other vascular events and 15 (8–23; $p<0.0001$) vascular deaths per 1000 patients. Although there were somewhat fewer non-vascular events and deaths among simvastatin-allocated patients, these differences were not significant and were small by comparison with the reductions in vascular events and deaths.

see [Lancet Online](#) for webfigure 1

Hospitalisation and drug treatment costs

Table 3 shows the mean per person number of days in hospital for vascular and non-vascular events during the scheduled treatment period, along with the associated costs. The average length of stay per hospitalisation did not differ by treatment group (data not shown). As a

	Simvastatin (n=10 269)	Placebo (n=10 267)	Mean difference (SE)	p
Days in hospital				
Vascular related*	4.8	6.0	-1.3 (0.21)	<0.0001
Non-vascular related	6.7	7.1	-0.5 (0.24)	0.06
Hospitalisation cost				
Vascular related*	£1800	£2301	-£501 (78)	<0.0001
Non-vascular related	£1858	£1968	-£109 (65)	0.09

*Includes major and other vascular events.

Table 3: Mean days in hospital and costs of hospitalisation per person during 5-year mean follow-up

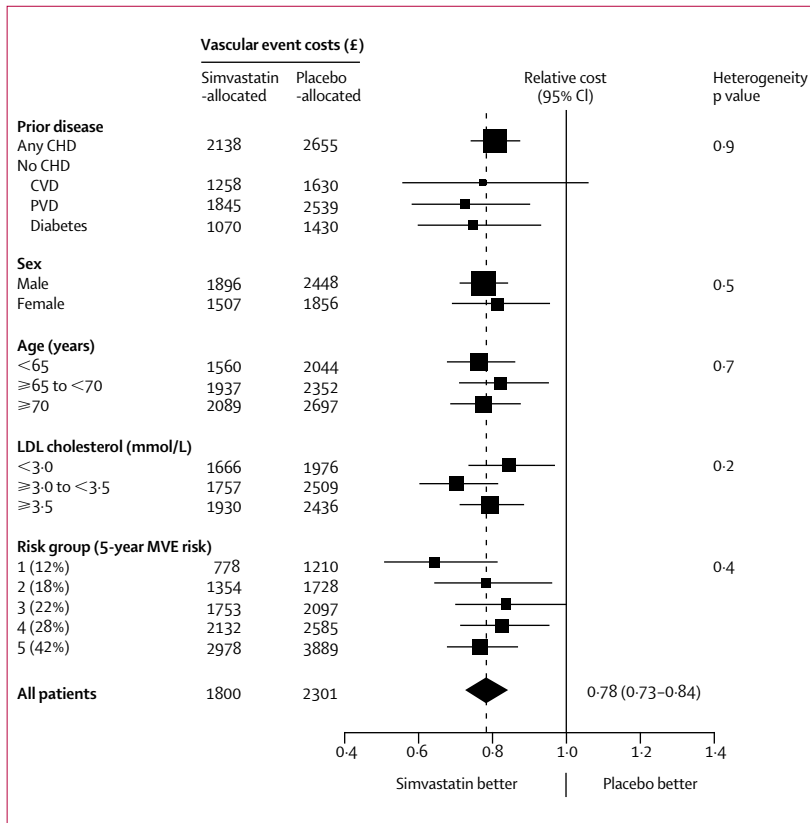


Figure 1: Proportional reductions in vascular event costs with simvastatin allocation by prior disease, sex, age, LDL cholesterol, and multivariate risk subgroups
 CHD=coronary heart disease; CVD=cerebrovascular disease; PVD=peripheral vascular disease; MVE=major vascular event.

see [Lancet Online](#) for webtable 1

consequence of the highly significant effect of statin allocation on vascular events, there was a highly significant 22% (95% CI 16–27) reduction in the costs of hospitalisations for vascular events (figure 1). As was the case for vascular events, the relative reduction in these vascular event costs did not differ significantly across any of the univariate or multivariate subgroups considered. In line with the lack of a significant effect of statin allocation on non-vascular events, no significant effect on the costs of hospitalisations for

non-vascular events was found (table 3). Consequently, the costs of non-vascular events were excluded from the cost-effectiveness analysis.

The overall numbers of days per person on study and non-study statin treatment are shown in table 4. Non-study statin use increased gradually during the scheduled 5-year treatment period, and averaged 5% in the simvastatin-allocated group versus 17% in the placebo-allocated group. Overall, the difference in the cost of statin use between the treatment groups was £1497 (SE 8) per person during an average of 5 years of follow-up. Table 5 indicates that the absolute difference in statin cost did not differ materially from this overall estimate in any of the univariate or multivariate risk subgroups considered (although they were statistically significantly different). Use of concomitant medication other than statins was recorded at baseline and at the final follow-up visit. But, although the proportions of patients using certain types of concomitant medication changed during follow-up, they did not differ significantly between those allocated simvastatin and those allocated placebo (data not shown). Consequently, the costs of these treatments were excluded from the cost-effectiveness analysis.

Cost-effectiveness

Simvastatin-allocation was associated with similar proportional reductions in vascular events and in hospitalisation costs for vascular events, and with similar absolute increases in statin cost, across the different subgroups studied. Absolute reductions in vascular events and related costs in any particular risk subgroup were, therefore, derived by applying the overall relative reduction in event rates or costs respectively to the absolute level of vascular event rates or costs observed in the placebo group for that subgroup (see methods). Webtable 1 shows the discounted incremental costs per patient derived by subtracting these subgroup-specific estimates of the absolute reductions in vascular event costs from the overall absolute excess cost of statin treatment. The discounted incremental cost of statin allocation ranged from £630 (SE 126) in the highest risk quintile to £1164 (45) in the lowest.

Overall, the cost of avoiding a major vascular event was estimated to be £11 600 (95% CI 8500–16 300), but this result masks substantial variation between the risk subgroups (webtable 1). For example, among individuals with a 42% 5-year risk of a major vascular event, the estimated cost-effectiveness was £4500 (2300–7400) per major vascular event avoided. By contrast, among those with a 12% 5-year risk, it was estimated to be £31 100 (22 900–42 500). Corresponding results for vascular deaths ranged from £21 400 (10 700–46 100) in the highest risk quintile to £296 300 (178 000–612 000) in the lowest. Due to the similar flow of costs and events over time, these results are

	Simvastatin (n=10 269)	Placebo (n=10 267)	Mean difference (SE)	p
Days on statin treatment				
Study statin	1553	..	1553 (6)	<0.0001
Non-study statin	77	261	-184 (5)	<0.0001
Any statin*	1599	261	1339 (7)	<0.0001
Statin treatment cost				
Study statin	£1647	£0	£1647 (7)	<0.0001
Non-study statin	£65	£215	-£150 (5)	<0.0001
Any statin	£1712	£215	£1497 (8)	<0.0001

*Total days on any statin is not the sum of the two preceding rows since about 40% of the participants in the simvastatin group who took non-study statin continued to take study simvastatin.

Table 4: Days on statin and costs of statin per person during 5-year mean follow-up

	Simvastatin	Placebo	Difference (SE)
Prior disease			
Any CHD	1756	262	1494 (10)
No CHD	1628	126	1503 (12)
CVD	1643	130	1513 (24)
PVD	1594	142	1452 (20)
Diabetes	1635	130	1504 (15)
Sex			
Male	1728	219	1509 (9)
Female	1663	203	1460 (16)
Age (years)			
<65	1756	262	1494 (11)
≥65 to <70	1729	215	1514 (16)
≥70	1622	134	1488 (14)
LDL cholesterol (mmol/L)			
<3.0	1665	88	1577 (12)
≥3.0 to <3.5	1730	194	1536 (15)
≥3.5	1737	326	1411 (13)
Risk group (5-year MVE risk)			
1 (12%)	1712	157	1555 (16)
2 (18%)	1752	215	1536 (17)
3 (22%)	1761	227	1534 (17)
4 (28%)	1718	233	1485 (18)
5 (42%)	1613	242	1371 (19)
All patients	1712	215	1497 (8)

CHD=coronary heart disease; CVD=cerebrovascular disease; PVD=peripheral vascular disease; MVE=major vascular event.

Table 5: Statin cost (£) per person by baseline characteristics during 5-year mean follow-up

insensitive to changes in the UK Treasury approved annual discount rate of 3.5% (webtable 2).

Sensitivity analysis on price of 40 mg simvastatin

Figure 2 shows the estimated reductions (and 95% CI) in vascular event costs in the five risk subgroups. The excess statin cost was approximately £1500 per person over 5 years based on 2001 prices, and the estimated reductions in vascular event costs ranged from £847 (SE 137) per person in the highest risk quintile to about £264 (48) in the lowest. Similarly, the percentage of the excess statin cost that was offset by reductions in

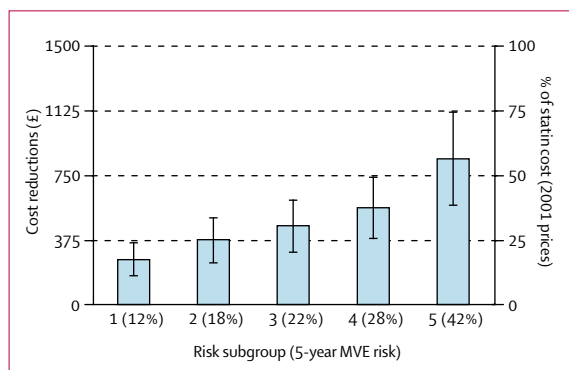


Figure 2: Reductions in 5-year vascular event costs (and 95% CI) with simvastatin allocation by baseline risk subgroups

Cost reductions attributed to simvastatin are plotted as UK£ on left axis and as percent of excess cost of statin treatment (2001 prices) on right axis. MVE=major vascular event.

vascular event costs ranged from 57% in the highest risk group to 18% in the lowest. But, since the UK patent on simvastatin expired in May, 2003, its price is falling as generic products enter the market. Consequently, the percentage of the excess statin cost that is offset by reductions in vascular event costs will increase as the simvastatin price falls. For example, if the price of simvastatin were to fall to 25% of the 2001 price then figure 2 indicates that 40 mg simvastatin daily would generate cost savings during the treatment period for individuals with a 5-year risk of major vascular events greater than 18% (or, equivalently, of major coronary events greater than 7%) and could be approximately cost-neutral for individuals with somewhat lower 5-year risks.

Discussion

The present analyses demonstrate clearly that the cost-effectiveness of statin therapy among a wide range of individuals with vascular disease or diabetes depends chiefly on their underlying risk of vascular events and the costs of statins. Previous analyses of HPS had involved intention-to-treat comparisons of all those allocated simvastatin versus all those allocated placebo. But, since an average of about a sixth of those allocated simvastatin stopped taking the study drug during the 5 year scheduled treatment period, and about a sixth of those allocated placebo started to take statin therapy, such analyses underestimate the effects of actually taking 40 mg simvastatin daily. Moreover, those analyses generally involved the effects of allocation to simvastatin on the incidence rate of just the first major vascular event during the scheduled treatment period. By contrast, the present cost-effectiveness analyses have taken account of the costs of statin use in both treatment groups, as well as the costs of hospitalisations for first and subsequent major or other vascular events. Consequently, this report provides more complete estimates of the cost-effectiveness of actually using 40 mg simvastatin daily during the scheduled 5-year treatment period.

Any costs related to non-vascular events or to concomitant medications were excluded from the analyses because there were no significant effects of simvastatin allocation on those costs. Exclusion of such costs does not materially alter the cost-effectiveness estimates, but it does improve their precision, which is particularly important for reliable subgroup analysis. Although the observed reduction in vascular events would also have been expected to have an impact on primary care and outpatient resource use, such data were not collected in HPS. The costs of those services are, however, likely to be small by comparison with the hospitalisation costs, which have been shown in similar studies to be the main cost driver.¹¹ Costs of laboratory monitoring and drug dispensing were also not included in these cost-effectiveness analyses. Regular safety monitoring in HPS found no important adverse effects

see [Lancet Online](#) for webtable 2

of 40 mg simvastatin daily on liver or muscle enzyme levels,² and routine laboratory monitoring is no longer considered necessary.^{12,13} Moreover, the effects of simvastatin among participants with vascular disease or diabetes were not much influenced by measurements of blood lipid concentrations either before or during statin treatment.² Most patients in the UK receive one or two packs of treatment per prescription, with an average of 38 daily doses reported per prescription.¹⁴ Based on an estimated dispensing cost of £1.45 per prescription,¹⁵ which equates to about £0.04 per day, inclusion of prescribing costs would have little impact on the cost-effectiveness estimates.

The focus of the present report is on cost-effectiveness during the scheduled study treatment period, and the results have been reported both in terms of cost per major vascular event avoided and cost per vascular death avoided. The first of these estimates may be more readily interpreted by clinicians and their patients, whereas the second estimate facilitates comparisons with other life-saving interventions. Typically, cost-effectiveness is described in terms of cost per year or quality-adjusted year of life gained, but analyses of life-years gained during the trial period alone would seriously underestimate the gains during longer follow-up. Instead, estimates of life-years gained from 5 years of simvastatin treatment (or, perhaps more relevantly, from even longer treatment) require extrapolation beyond the scheduled treatment period. Such extrapolations depend on various strong assumptions, and this will be the subject of future work. It will be of particular importance to allow fully for the impact of age, since the rapid rise in vascular disease risk with increasing age is mitigated by the reduction in life expectancy.

Previous cost-effectiveness analyses^{16–18} of lipid-lowering trials have tended to focus on the overall cost-effectiveness for the trial population, although a few reports have also considered cost-effectiveness in specific categories of patient (such as those with diabetes¹⁹). A key finding from the current analysis is that estimates of cost-effectiveness in the trial as a whole can mask important variations in cost-effectiveness between patients at differing levels of vascular disease risk. Simvastatin allocation produced similar proportional reductions in the risks of vascular events and related hospitalisation costs in the different univariate and multivariate subgroups studied. Hence, estimates of the absolute costs of hospitalisations for vascular events in a particular subgroup were determined by applying this overall relative effect on vascular event hospitalisation costs to the absolute costs of such hospitalisations among placebo-allocated participants in that same subgroup. Similarly, as the absolute excess cost of statin treatment among simvastatin-allocated patients appeared to be about the same in these different subgroups, this overall

difference was applied to every subgroup. By using the overall results in this way, the present subgroup-specific estimates of cost-effectiveness should be much less prone to the play of chance than would be estimates based on the results observed separately within particular subgroups (which have typically been used in economic evaluations). Indeed, CIs for estimates derived from subgroups considered separately would have been about 50% wider than those provided in webtable 1 and webtable 2. For example, the discounted cost per major vascular event avoided for the lowest risk quintile was estimated from the overall results to be £31 100 with a 95% CI of £22 900–42 500, whereas an estimate derived from the results only within that subgroup has a 95% CI of £10 700–44 600. As a consequence, figure 2 (and webtable 1 and webtable 2) demonstrates clear trends in the cost-effectiveness estimates across different underlying levels of vascular risk, but analyses within subgroups considered on their own would not (despite the large size of HPS).

The absolute risks of coronary and other vascular events among participants in a trial may well differ markedly from those of apparently similar people in different circumstances. Consequently, the exact definition of the multivariate risk groups used in the present analyses is not particularly relevant to the extrapolation of the findings. However, these estimates of cost-effectiveness at different levels of risk are likely to be generalisable to a wide range of different settings using appropriate local data to estimate the risks for particular individuals. Current guidelines^{20,21} generally recommend the initiation of statin therapy when the estimated 10-year risk of a non-fatal heart attack or coronary death is at least 15–20%. Previous analyses of HPS^{2–4} have demonstrated that statin therapy produces substantial reductions not just in these major coronary events but also in strokes and revascularisation procedures, which suggests that such guidelines should be based on the risks of all such major vascular events (and not just major coronary events). Moreover, as simvastatin and other statins come to the end of their patent life, the fall in the drug cost should produce a corresponding improvement in the cost-effectiveness of treatment. In the UK, the patent expired in May, 2003, and the price of generic simvastatin has already fallen to about 15% of the 2001 proprietary price;²² as has also occurred elsewhere.²³ Figure 2 shows that, at this price, the cost savings from reduced hospitalisations during the treatment period would outweigh the cost of 40 mg simvastatin daily for people with a 5-year major vascular event risk down to at least 12%—or, approximately equivalently, major coronary event risk of at least 4%. Hence, it now seems appropriate to consider reducing the estimated level of risk for coronary and other vascular events at which initiation of statin therapy is recommended.

MRC/BHF Heart Protection Study collaborative group

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Conflict of interest statement

The Clinical Trial Service Unit (writing committee members: J Armitage, R Collins, S Parish) has a staff policy of not accepting honoraria or other payments from the pharmaceutical industry, except for the reimbursement of costs to participate in scientific meetings. Staff in the Health Economics Research Centre (writing committee members: B Mihaylova, A Briggs, A Gray) occasionally act as paid consultants to the pharmaceutical industry.

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