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Cost-effectiveness of atorvastatin for the prevention of coronary and stroke events: an economic analysis of the Anglo-Scandinavian Cardiac Outcomes Trial—lipid-lowering arm (ASCOT-LLA)

Peter Lindgren[a,b], Martin Buxton[c], Thomas Kahan[d], Neil R. Poulter[e], Björn Dahlöf[f], Peter S. Sever[e], Hans Wedel[g] and Bengt Jönsson[h] on behalf of the ASCOT investigators

[a]Karolinska Institutet, Institute of Environmental Medicine, Stockholm, [b]Stockholm Health Economics, Stockholm, Sweden, [c]Brunel University, Uxbridge, UK, [d]Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden, [e]Imperial College, London, UK, [f]Sahlgrenska University Hospital/Östra, Gothenburg, [g]Nordic School of Public Health, Gothenburg and [h]Stockholm School of Economics, Stockholm, Sweden.

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Background **The aim of this study is to assess the cost-effectiveness of the lipid-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT-LLA) where patients from seven countries with hypertension and no history of coronary heart disease (CHD) were randomized to receive 10 mg atorvastatin or placebo.**

Design **Economic analysis of a randomized controlled trial.**

Methods **Data on resource use were aggregated for all patients during the entire trial period (median 3.3 years) and multiplied with unit costs for Sweden and the UK. The total number of cardiovascular events and procedures avoided was used as the measure of effectiveness.**

Results **Patients treated with atorvastatin had an additional net costs of 449 € (4114 SEK) in Sweden and 414 € (£260) in the UK, but fewer events per patient (0.097 compared to 0.132). The incremental cost-effectiveness ratios were 12673 € (116119 SEK) and 11693 € (£7349) per event avoided.**

Conclusion **Based on comparisons with the WOSCOPS and 4S studies, atorvastatin at 10 mg to treat patients as in the ASCOT study, appears to be a cost-effective strategy. *Eur J Cardiovasc Prev Rehabil* 12:29–36 © 2005 The European Society of Cardiology**

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Introduction

The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) is a multicentre randomized trial in which the effect of two antihypertensive treatment strategies on the reduction of fatal coronary heart disease (CHD) or non-fatal myocardial infarction (MI) are being compared in patients with no prior history of CHD [1]. In addition, in a factorial design, the trial included a double-blind comparison of atorvastatin to placebo among those patients with a total cholesterol of 6.5 mmol/l or less (the ASCOT lipid-lowering arm—ASCOT-LLA). This part of the trial was closed early at the recommendation

Correspondence and requests for reprints to Bengt Jönsson, Centre for Health Economics, Stockholm School of Economics, Box 6501, 113 83 Stockholm, Sweden.
E-mail: Bengt.Jonsson@hhs.se

of the Data Safety Monitoring Board after a median follow-up of 3.3 years on the grounds that atorvastatin had resulted in a highly significant reduction in the primary endpoint as well as a reduction in the number of strokes.

Patients included in the ASCOT-LLA were men and women aged between 40 and 79 years, with either untreated hypertension (systolic blood pressure > 160 mmHg or diastolic blood pressure > 100 mmHg) or treated hypertension with systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg and who, while not being treated with a statin or fibrate, had a total cholesterol concentration of 6.5 mmol/l or less. Patients were also required to have at least three of the following risk factors: left ventricular hypertrophy, other specified abnormalities on electrocardiogram, type II diabetes, peripheral arterial disease, previous stroke or transient ischaemic attack, male sex, age 55 years or older, microalbuminuria or proteinuria, current smoker, a ratio of plasma total cholesterol to HDL-cholesterol of six or higher, or a family history of early CHD.

The previously reported results from ASCOT-LLA showed that primary prevention with 10 mg atorvastatin reduced the risk of non-fatal MI and fatal CHD by 36%, stroke by 27% and the risk of suffering any cardiovascular event or procedure by 21%. There was no difference in the number of adverse events between the groups [2]. It has become increasingly important to show that treatments are not only safe and effective, but also provide good value for money.

It has been established that statin treatment is cost-effective in secondary prevention [3–5]. Few economic analyses have been performed focusing on primary prevention, and none in this group of hypertensive patients not previously considered as candidates for lipid-lowering therapy [6–8]. The purpose of this study was to investigate the cost-effectiveness of primary prevention with atorvastatin in patients at moderate cardiovascular risk by virtue of having hypertension and three additional risk factors, with total cholesterol concentrations below or equal to 6.5 mmol/l based on the ASCOT-LLA. The background and rationale for this health economics study has been outlined more fully in a prior publication [9].

Methods

The ASCOT-LLA included 10 305 patients, of which 5168 were randomized to receive treatment with atorvastatin 10 mg and the remaining 5137 patients to have a placebo. The median follow-up time was 3.3 years. Data from the entire trial period was used in this analysis, which was done on an intention-to-treat basis.

In order to have sufficient power in the analysis, the cost-effectiveness analysis was performed on resources and effectiveness aggregated from patients in all study countries but with two separate sets of prices (unit costs) from Sweden and the UK. The analysis was performed from a healthcare payer perspective, thus incorporating only direct healthcare costs. Since the analysis spans a limited time frame, and the costs and events are evenly distributed over the period, no discounting of the results was performed. All costs were adjusted to 2002 levels using the consumer price index. Costs were converted to Euros (€) using the average conversion rate during 2002 (1 € = 9.1627 SEK, 0.6285 GBP).

Resources were identified based on the information collected in the case report forms and costs were calculated by defining the number of times each type of resource was used by a patient and then multiplying this by the corresponding unit cost. Resources were divided into study drug, concomitant medications, out-patient visits and hospitalizations.

The number of days on the study drug was recorded, and this figure was multiplied by the cost of 10 mg atorvastatin in Sweden and the UK, respectively. A total of 66 000 prescriptions for concomitant medications were recorded in the database. We included only medications from the following pre-specified ATC (the Anatomical, Therapeutic and Chemical classification used by WHO) [10] classes: alimentary tract and metabolism, blood and blood-forming organs, cardiovascular system, musculoskeletal system and nervous system, as these were the body systems we judged could be affected by treatment. A statistical analysis of the number of prescriptions for all other classes of drugs showed no statistical difference in the number of drugs per patient in the two groups, with the exception of dermatological agents and 'various', in which there was a slight, but statistically significant higher number of prescriptions in the placebo group.

The ATC system uses five levels (groups): (1) the anatomical group; (2) the therapeutic main group; (3) the therapeutic/pharmacological subgroup; (4) the chemical/therapeutic/pharmacological subgroup; and (5) the chemical substance. The prescriptions were classified according to ATC groups, and drugs belonging to a fourth level group with less than five prescriptions were excluded. By these criteria, 43 000 prescriptions were included in the analysis. Each level 4 group was assigned a typical daily cost based on the daily-defined dose (which is the assumed average maintenance dose per day for a drug used for its main indication in adults specified by WHO) and cost of the most frequent low-level term in each group. In cases where the most frequent drug was unavailable in the country, the cost for the most

commonly used available drug in the same group was used instead.

All drug costs were obtained from the official Swedish price list and the Monthly Index of Medical Specialities [11,12]. For many medications, a start or stop date was not recorded in the database. To account for this, medications were classified as either long-term or short-term. Drugs for long-term use were assumed to be taken from randomization if the start date was missing and until the final date of the study (or death) if the stop date was missing. For short-term medications without a start or stop date, the median duration observed for the group was imputed.

The number of physician visits, both protocol driven and other visits, related to the treatment of hypertension and hyperlipidaemia (but excluding screening and randomization visits), was multiplied by a cost per visit gathered from the County Council of Stockholm in Sweden (data on file) and from published sources in the UK [13]. Table 1 gives a summary of the costs used.

The trial database included information on hospitalizations related to both endpoints and other causes. The former were assigned a diagnosis related group (DRG) based on the information given on the endpoint report forms. Potential endpoints within 7 days of each other were considered to belong to the same hospitalization. Endpoint-related hospitalizations were costed based on the typical cost for each DRG [14,15]. For patients undergoing revascularizations, it was not possible to discriminate if this was a coronary artery bypass grafting (CABG) or a percutaneous coronary intervention (PCI). These hospitalizations were given a weighted cost based on the observed frequency of these procedures in the general population [14,15]. The impact that the distribution between PCI and CABG could have on the results was explored in a sensitivity analysis.

For non-endpoint-related hospitalizations, not enough information was provided in the case report forms to allow a DRG classification. For these hospitalizations a daily cost based on the average daily cost across different wards (all wards excluding obstetrics and paediatrics) was multiplied by the length of stay [13,16]. For cases for which a start or stop date had not been recorded, the median length of stay was imputed. Hospitalizations within 7 days of a potential endpoint were considered to be associated with the original event to and thus excluded to avoid double counting.

Effectiveness was defined as the total number of cardiovascular events and procedures avoided. All cardiovascular events and procedures were included, namely fatal CHD, MI (silent and non-silent), fatal and non-fatal stroke, fatal and non-fatal heart failure, stable and unstable angina, peripheral artery disease and life-threatening arrhythmias. Procedures included revascularisation procedures such as CABG and PCI. First and subsequent events were included since, where non-fatal, intervention was continued after the first event. Analyses were also conducted based solely on the primary end-point of the trial, namely non-fatal MI plus fatal CHD, and with and without silent MI. A full definition of the events included in the trial has been reported previously [1].

Table 1 Unit costs (year 2002) used in the analysis

	Sweden		UK	
	SEK	€	GBP	€
Study drug (per day)	8.88	0.97	0.65	1.03
Visit to physician	728	79	86	137
Inpatient bed day	4613	503	460	732
DRG				
14 (Specific cerebrovascular disease except TIA)	42 295	4616	2005	3190
106 (coronary bypass with cardiac catheterization)	202 884	22 142	7378	11 739
107 (coronary bypass without cardiac catheterization)	126 534	13 810	6275	9984
112 (percutaneous cardiovascular procedures)	63 371	6916	2455	3906
106/107/112 (weighted average)	89 275	9743	4641	7384
121 (Other circulatory disorders with acute myocardial infarction and cardiovascular complication alive at fourth day of care)	44 577	4865	1634	2600
122 (Other circulatory disorders with acute myocardial infarction without cardiovascular complication alive at fourth day of care)	35 383	3862	1127	1793
121/122 (weighted average)	38 618	4215	1274	2027
123 (Other circulatory disorders with acute myocardial infarction, death within first 3 days of care)	37 403	4082	903	1437
127 (heart failure an shock)	28 346	3094	1847	2939
129 (cardiac arrest, unexplained)	84 456	9217	1134	1804
130 (peripheral vascular disorders with complication)	38 587	4211	1668	2654
131 (peripheral vascular disorders without complication)	26 368	2878	1207	1920
130/131 (weighted average)	30 845	3366	1484	2361
138 (cardiac arrhythmia and conduction disorders)	22 460	2451	1009	1605
140 (angina pectoris)	17 112	1868	1248	1986

SEK, Swedish Kronor; GBP, British Pounds; DRG, diagnosis related group; TIA, transient ischaemic attack.

The cost-effectiveness ratios were calculated by dividing the net cost of intervention by the number of events avoided. Confidence intervals (CI) around the cost-effectiveness ratios were estimated using the angular transformation based on 1000 bootstrap samples [17]. As an alternative way of representing the uncertainty around the estimates, cost-effectiveness acceptability curves based on the net-benefit statistic were constructed [18].

Role of the funding source

The Anglo-Scandinavian Cardiac Outcomes Trial was conceived, designed and co-ordinated by an investigator-led independent steering committee. The health economic evaluation was led by the health economic working group, in which the funding source had three non-voting members. Analysis and reporting was done independently of the funding source.

Results

Baseline characteristics were similar in the active and placebo groups of ASCOT-LLA, as has been reported previously [2]. Table 2 summarizes the resource consumption in these groups during the entire trial period (median 3.3 years). In most categories, patients allocated atorvastatin used fewer resources than patients receiving placebo. It can be noted that the use of other lipid-lowering agents (such as open label statins) was three-times higher in the placebo group.

Table 3 shows the mean cost per patient for the different resource categories. As a consequence of using fewer resources, patients allocated atorvastatin show cost savings in all categories with the obvious exception of the study drug. There was no difference in the number of recorded visits between the groups, and thus no difference in costs. More than 50% of the cost of the study drug is offset by reductions in costs of concomitant medication and hospitalizations. The net total cost over the trial period was 449 € for Sweden and 414 € for the UK.

Table 4 shows a summary of effectiveness and cost-effectiveness. In the atorvastatin arm there were an average of 0.097 (95% CI: 0.087–0.108) events, per patient (97 events per 1000 patients) during the trial period compared with 0.132 (95% CI: 0.119–0.145) events per patient (132 per 1000 patients) in the placebo arm, a difference of 0.035 events. This gives a cost-effectiveness of 12 673 € per event avoided (95% CI: 3679–36 228) for Sweden and 11 693 € per event avoided (95% CI: 190–35 486) for the UK. Excluding silent MIs from the analysis has only a small effect on the results (12 891 € or 11 895 € per event avoided for Sweden and the UK respectively).

Table 3 Mean per patient cost in 2002 € (95% confidence interval), per resource category

	Atorvastatin (n=5168)	Placebo (n=5137)
Sweden		
Study drug	1034 (1023–1045)	–
Outpatient visits	902 (894–910)	908 (899–916)
Concomitant medications	452 (432–471)	529 (508–549)
Open-label statins	21 (17–25)	64 (58–70)
DRG hospitalizations	450 (398–501)	660 (591–730)
Other hospitalizations	1332 (1196–1468)	1624 (1422–1826)
Total cost	4170 (4015–4324)	3721 (3499–3942)
UK		
Study drug	1086 (1075–1098)	–
Outpatient visits	1554 (1540–1568)	1563 (1548–1578)
Concomitant medications	591 (568–614)	682 (658–706)
Open-label statins	22 (18–26)	68 (61–74)
DRG hospitalizations	316 (279–353)	464 (413–515)
Other hospitalizations	1937 (1739–2134)	2361 (2067–2654)
Total cost	5484 (5274–5694)	5070 (4764–5375)

1 €=9.1627 Swedish Kronor, £0.6285. DRG, diagnosis related group.

Table 2 Mean per patient quantities (standard deviation) of resources used during the trial

	Atorvastatin n=5168	Placebo n=5137
Mean (SD) number of days on study drug	1067.2 (412.3)	
Mean (SD) number of outpatient visits	11.4 (3.8)	11.4 (4.0)
Mean (SD) number of days of prescriptions		
Alimentary tract and metabolism	394.8 (785.7)	408.5 (789.9)
Blood and blood forming organs	45.5 (206.9)	46.4 (208.6)
Cardiovascular system	394.0 (732.7)	476.9 (781.2)
Other lipid-lowering agents	21.6 (141.1)	66.3 (218.9)
Musculoskeletal system	86.9 (271.2)	89.6 (281.3)
Nervous system	423.0 (631.7)	451.1 (667.3)
Mean number of DRGs		
14 (specific cerebrovascular disease except TIA)	0.026 (0.171)	0.033 (0.191)
106/107/112 (CABG or PCI)	0.015 (0.128)	0.027 (0.192)
121/122 (MI, discharged alive)	0.009 (0.101)	0.019 (0.144)
123 (MI, discharged dead)	0.007 (0.082)	0.008 (0.088)
127 (heart failure and shock)	0.013 (0.137)	0.012 (0.124)
129 (cardiac arrest)	0.002 (0.042)	0.002 (0.044)
130/131 (peripheral vascular procedure)	0.006 (0.078)	0.009 (0.100)
138 (cardiac arrhythmias)	0.003 (0.056)	0.002 (0.044)
140 (angina pectoris)	0.015 (0.126)	0.022 (0.156)
Mean number of days in hospital (per patient, non-endpoint related)	2.7 (9.9)	3.2 (14.7)

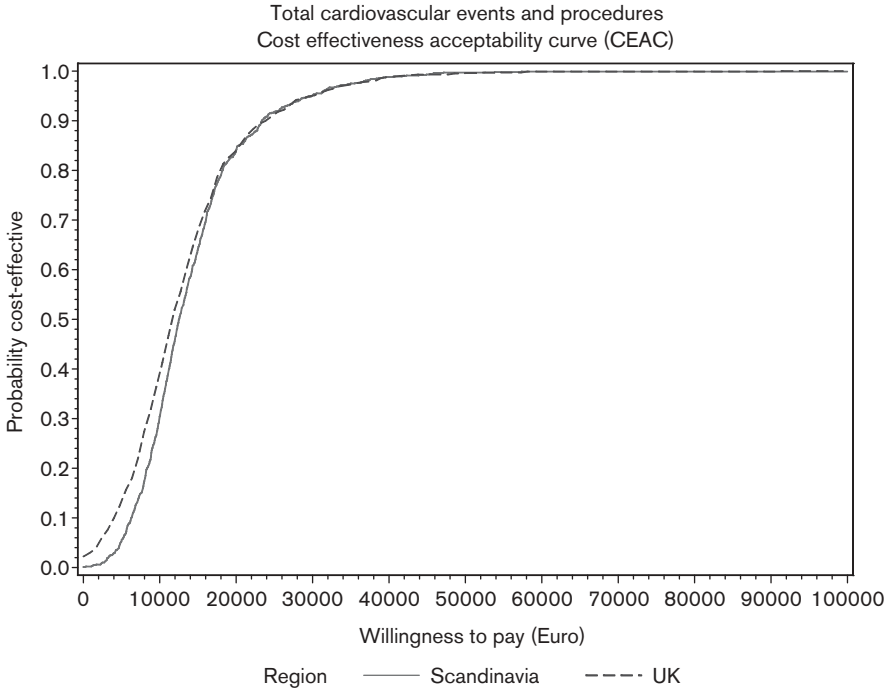
SD, standard deviation; DRG, diagnosis related group; TIA, transient ischemic attack; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; MI, myocardial infarction.

Table 4 Mean number of events per patient, mean number of events avoided and cost-effectiveness (€ per event avoided) for different definitions of events

Events included	Placebo	Atorvastatin	Events avoided	ICER Sweden	ICER UK
All events and procedure (95% CI)	0.132 (0.119–0.145)	0.097 (0.087–0.108)	0.035 (0.018–0.053)	12 673 (3679–36 228)	11693 (190–35 486)
Fatal CHD and non-fatal MI (95% CI)	0.032 (0.027–0.037)	0.020 (0.016–0.024)	0.012 (0.005–0.018)	38 682 (11 994–109 218)	35 689 (981–107 918)
Fatal CHD and non-fatal MI, excluding silent MI (95% CI)	0.029 (0.024–0.033)	0.018 (0.014–0.021)	0.011 (0.005–0.017)	40 792 (12 443–113 680)	37 637 (822–72 961)

ICER, incremental cost-effectiveness ratio; CHD, coronary heart disease; MI, myocardial infarction; CI, confidence interval. 1 € = 9.1627 Swedish Kronor, £0.6285, costs in 2002 values.

Fig. 1



Cost-effectiveness acceptability curve on the cost per total event and procedures avoided.

Using only the primary endpoint of the trial as the effectiveness measure gives a cost-effectiveness ratio of 38 682 € per event avoided (95% CI: 11 994–109 218) for Sweden and 35 689 € per event avoided (95% CI: 981–107 918) for the UK. The higher cost per event avoided compared to when using total events and procedures, despite a greater relative risk reduction, is explained by the lower absolute number of primary endpoint events. Again, excluding silent MIs has only a small impact on the results: 40 792 € per event avoided in Sweden and 37 637 € per event avoided in the UK.

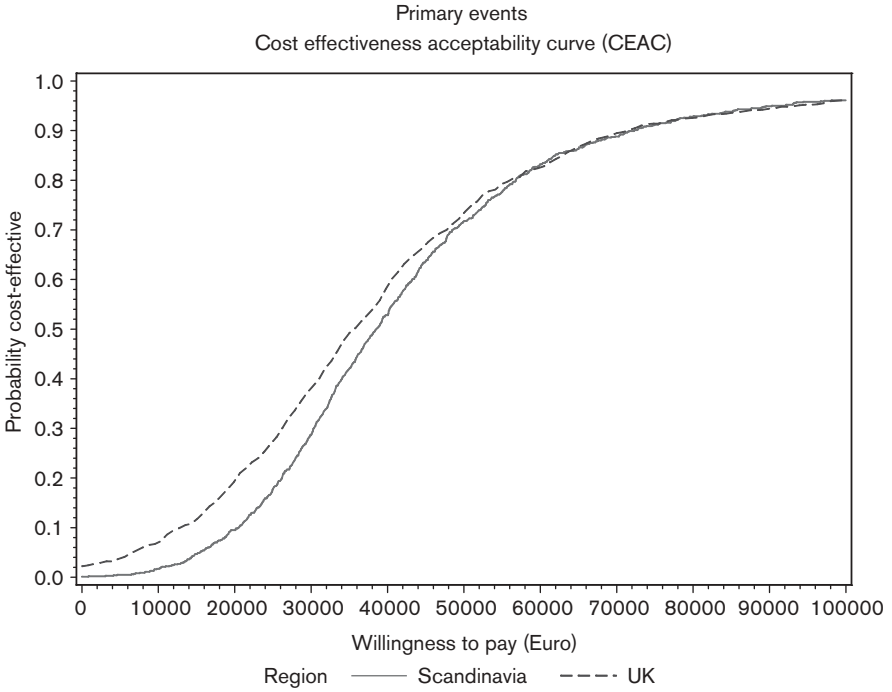
Figures 1 and 2 show the cost-effectiveness acceptability curves for Sweden and the UK for total cardiovascular events and procedure and fatal CHD and non-fatal MI. The curves can be interpreted as the probability that the treatment is cost-effective at various levels of willingness to pay for an avoided event, based on the ASCOT-LLA data.

Variation in assumptions about the fraction of patients undergoing PCI or CABG had only a small impact on the results. For example if 90% of patients were assumed to undergo a PCI (less expensive) or CABG (more expensive) respectively, the ratio varied between 13 396 and 11 299 € per event avoided in Sweden and between 12 754 and 10 678 € per event avoided in the UK.

Discussion

Our results show that in ASCOT-LLA, over half (56% in Sweden, 62% in the UK) of the cost of treatment was

Fig. 2



Cost-effectiveness acceptability curve on the cost per fatal coronary heart disease and non-fatal myocardial infarction avoided.

offset by savings due to less use of other resources. The main drivers of these savings were endpoint- and non-endpoint-related hospitalizations. The latter is somewhat surprising; one explanation may be that patients with manifest cardiovascular disease may be kept in hospital longer than non-cardiovascular patients when admitted for other causes. There was also an indication of lower cost from the use of concomitant medications in the atorvastatin arm, the key difference being a lower use of open-label statins, however this played only a smaller part in the cost-offset.

There was no difference in the recorded number of outpatient visits between the two arms. There is a possibility that patients may have made visits to physicians that were not recorded, for example if they made visits to physicians other than those participating in the study. Nevertheless the impact of this is likely to be small since they are likely to be few.

A potential problem in all economic evaluations based on clinical trials is the introduction of protocol-driven costs, that is, costs that occur as a direct consequence of the protocol of the trial and that would not have occurred in regular clinical practice. In ASCOT-LLA there is a possibility that patients made more visits to the physician than they would have under normal circumstances. However, as the number of outpatient visits was similar in both arms, this has no effect on the cost-effectiveness ratios, only on the total costs and it is therefore a minor problem.

The reported confidence intervals around the cost-effectiveness ratios are quite wide. This is common in economic evaluations based on clinical trials, since they are mainly powered and designed to detect differences in the primary endpoints, not in costs.

The trial enrolled patients in seven countries. We aggregated the resource use for patients from all countries when performing our analysis. This may have posed a problem if resource consumption (i.e., the quantities used in the analysis) differed markedly between countries. However, if we compare patients from the Nordic countries and that in the UK and Ireland applying one set of unit costs, the mean costs are similar, indicating that combining countries are not likely to have biased these analyses. A study by Gandjuor and colleagues [19] comparing treatment patterns for patients with a MI in five European countries reported that the proportion of patients receiving systemic thrombolysis was higher in the UK than in Sweden while angiography was more common in Sweden. However, the remaining resource categories reported (use of glycoprotein IIb/IIIa inhibitors, PCI with and without stents, days in the critical care and general medicine wards) was very similar. An

alternative approach would have been to study each country separately, however this could not be done since it would mean losing the power to detect a difference in endpoints.

It might be expected that treatment would be more cost-effective in patients with higher absolute risk of disease compared to those at lower risk. To investigate this, we performed a subgroup analysis (data not shown) dividing patients into age and sex categories and stratifying by cardiovascular risk within these categories. The results were inconclusive, however, probably because such analyses require considerably larger study populations in order to provide valid information.

No generally acceptable criteria of what should be considered a cost-effective ratio for the endpoints in the ASCOT-LLA are available. The reason for this is that only a limited number of studies with similar endpoints exist. An endpoint often used is life years gained (LYG) and it is possible to perform a rough estimation on the potential number of life years gained in our study by comparing the expected survival of patients with and without events. Patients in the trial were on average 63 years old. In Sweden the expected remaining lifespan for a 65-year-old is 20.3 years [20]. Annemans and colleagues [21] have presented data from Saskatchewan indicating that a patient 62.5 years old with a myocardial infarction has a life expectancy of 12.9 years. Peeters *et al.* [22] reported a life expectancy of 10.8 years in a 60-year-old man and 11.6 years in a woman with cardiovascular disease. By avoiding a MI, roughly 7.4 life years would be gained (using the more conservative figure). This assumes that event rates (and costs) are the same in both arms after the trial. We have shown that treatment with 10 mg atorvastatin leads to 0.012 fatal CHD events or non-fatal MIs being avoided which would correspond to 0.09 LYG. This is similar to an estimate by Szucs and colleagues [23] who studied the cost-effectiveness of atorvastatin in this indication in Germany, and calculated the gain in survival to 0.085 years. This would indicate an incremental cost-effectiveness ratio (ICER) of 5000 € per LYG in Sweden and 4600 € per LYG in the UK. The study by Szucs indicated an ICER of 7300 € in Germany. This would indicate a cost-effectiveness ratio well below the WHO-criteria of three times GDP per capita [24]. A reasonable comparison for the UK is the West of Scotland Coronary Prevention Study (WOSCOPS), which studied lipid lowering using 40 mg pravastatin in primary prevention in men at high risk of CHD [6]. This study showed a cost per life year gained of 20 000 GBP (31 821 €). This was considered cost-effective in relation to a benchmark value of 25 000 GBP per life year gained (the unofficial NICE bench-mark is generally considered to be 30 000 GBP per quality adjusted life-year, [QALY]) [25]. The WOSCOPS only included event-specific costs. If we take the same approach and exclude other hospitalizations, the cost-effectiveness ratio in the UK becomes 9300 €. The cost-effectiveness ratios in ASCOT-LLA are thus lower than those reported from WOSCOPS. The difference is explained by a lower absolute risk of events in the WOSCOPS population, and by lower costs in ASCOT-LLA. Part of the difference in costs is due to the longer treatment time in WOSCOPS (5 years compared to 3.3 years) and by the fact that for the WOSCOPS analysis the cost of physician visits was additional to the cost of the treatment *per se*. Since the ASCOT-LLA population consists of patients on treatment for hypertension, the number of outpatient visits was similar in both treatment arms. This means that no additional costs related to the administration of the lipid-lowering agent needed to be added, which is one strength of this treatment approach in terms of economic consequences.

No good comparison exists for primary prevention in Sweden. In secondary prevention, the Scandinavian Simvastatin Survival Study (4S) showed that treatment with simvastatin led to an increased cost of 13 500 SEK (1500 €) during the trial period (5.4 years) which gave an ICER of 6800 € per LYG [3]. Our study indicates a lower cost-effectiveness ratio, which is surprising since patients requiring primary prevention have a lower absolute risk. However, the study by Annemans *et al.* [21] indicates that the survival benefits of avoiding a second MI is lower than avoiding the first, which may explain this difference. The 4S study also included only event-specific cost. Excluding the cost reduction from other hospitalizations in our study, the cost-effectiveness ratio in Sweden becomes 8200 € which is quite close to the ratio reported in 4S.

A previously reported modelling study investigated the risk levels at which primary prevention with cholesterol lowering should be initiated at different threshold values for a gained QALY [26]. The study used three threshold values: 40 000, 60 000 and 100 000 US dollars (USD) per QALY gained and tested how high the 5-year risk of cardiovascular disease (defined as MI, unstable or stable angina pectoris) needed to be in order for the cost-effectiveness ratios to fall below these threshold values. The 40 000 USD value represented a very conservative measure of cost-effectiveness. The value 60 000 USD was based on a survey among health economists. For the lowest cut-off value the risk had to exceed 11.59% for the treatment to be considered cost-effective in 60-year-old men. The corresponding figure for women was 10.08%. For the middle cut-off value, the corresponding risks were 7.19 and 6.11%. In the placebo arm of ASCOT-LLA (mean age 63 years, 18.9% women) the 5-year risk of events was 6.6%. This population does not therefore reach the lowest criteria for cost-effectiveness and is close to the cut-off values for the 60 000 USD per QALY gained cut-off. However, it should be taken into consideration that physician visits make up 25% of the treatment cost in the model, and this cost is

avoided by considering patients already on treatment for hypertension. The total intervention cost is also lower in ASCOT-LLA. This indicates that the mean risk can be lower among the ASCOT-LLA patients, and the threshold values still be met.

This study includes only direct medical costs. Widening the scope of our analysis to include indirect costs, namely costs related to loss of production, is likely to improve cost-effectiveness ratios since one-third of the ASCOT population is below the age of 60, and patients suffering from cardiovascular events in general and stroke in particular have long periods of sick-leave and a high rate of early retirement. In order to estimate these and other costs that stretch over a time span longer than that covered in the trial, as well as be able to estimate the potential QALY gains from this intervention, a modelling approach is necessary. The simple calculation performed in this discussion only takes the effect of avoiding MI into consideration, whereas the ASCOT-LLA trial also showed a reduction in strokes and revascularization procedures. The true ICER per LYG could thus be even lower. To estimate the full effect on survival in a more robust way taking the survival among patients identical to those in the trial rather than relying on rough estimates is also a rationale for future modelling studies.

Based on the comparisons with WOSCOPS (pravastatin 40 mg) and 4S (simvastatin 20–40 mg) we conclude that treatment of patients such as those included in the ASCOT study, who would not previously have been considered candidates for lipid-lowering therapy, with 10 mg atorvastatin appears to be a cost-effective treatment strategy.

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