An economic evaluation of rosuvastatin treatment in systolic heart failure: evidence from the CORONA trial

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Aims	To estimate the cost-effectiveness of 10 mg rosuvastatin daily for older patients with systolic heart failure in the Controlled Rosuvastatin Multinational Study in Heart Failure (CORONA) trial.
Methods and results	This within trial analysis of CORONA used major cardiovascular (CV) events as the outcome measure. Resource use was valued and the costs of hospitalizations, procedures, and statin use compared. Cost-effectiveness was estimated as cost per major CV event avoided. There were significantly fewer major CV events in the rosuvastatin group compared with the placebo group (1.04 vs. 1.20 per patient; difference 0.164; 95% CI: 0.075−0.254, $P < 0.001$). The average cost of CV hospitalizations and procedures was significantly lower for those receiving rosuvastatin (£1531 vs. £1769; difference £238; 95% CI: £73−403, $P = 0.005$); the additional cost of the statin resulted in significantly higher total costs for the rosuvastatin group (£1769 vs. £2072; difference £303; 95% CI: £138−468, $P < 0.001$). Overall, rosuvastatin was found to cost £1840 (95% CI: £562−6028) per major CV event avoided.
Conclusion	This economic analysis showed that a significant reduction in major CV events with rosuvastatin led to significantly reduced costs of CV hospitalizations and procedures. The reduction in associated costs for major CV events was found to offset partially (by 44%) the cost of rosuvastatin treatment in patients with systolic heart failure.
Keywords	Cost-effectiveness • Heart failure • Statins • Multinational trial

Introduction

Heart failure is a major public health problem. Incidence, prevalence, and risk have been found to be high in both Europe and the United States.[1,2] The Rotterdam study[1] found that a male (female) aged 55 years old has 33.0% (28.5%) chance of developing heart failure during their remaining lifetime; while the Framingham Heart Study[2] reported a lifetime risk at age 50 of 20.9% for men and 20.5% for women. The Rotterdam study further showed that the prevalence of heart failure increased with time and age; in 1998, 0.9% of subjects aged 55−64 had heart failure, compared with 17.4% of those aged 85 years or over. The combination of an

ageing population in most western countries, a population which has the greatest incidence of heart disease, and improved survival after acute myocardial infarction (MI) is, therefore, likely to further increase the prevalence of heart failure.[3]

This increasing clinical burden is expected to be matched with an increasing financial burden. Using a prevalence-based approach the economic burden of heart failure in the UK was estimated to be £905.3 million in 2000, a 26% increase on 1995 estimates, and equivalent to 1.91% of total NHS expenditure.[4] The major contributor to this financial burden is hospitalization, as such there is potential to reduce the burden if admissions to hospital and durations of hospital stay can be reduced. Indeed, it has been estimated that reducing length of stay by 1 day or reducing re-admissions by 50% could generate annual cost savings of between £50 and £120 million.[4]

HMG-CoA reductase inhibitors or 'statins' have been found to be beneficial in people with or at risk of cardiovascular (CV) disease, and importantly they have also been shown to be cost effective.[5] However, existing statin trials generally excluded patients with heart failure leading to uncertainty about their potential role in that condition.[6]

The Controlled Rosuvastatin Multinational Study in Heart Failure (CORONA) trial was the first large-scale, prospective, randomized, placebo-controlled study to determine the effect of statins on clinical outcomes in patients with heart failure.[7,8] This paper estimates the cost-effectiveness of a daily dose of 10 mg of rosuvastatin during the study treatment period.

Methods

Clinical trial

The CORONA trial assessed the effects of rosuvastatin on mortality and morbidity in patients with chronic systolic heart failure. Patients were allocated in a ratio of 1:1 to 10 mg rosuvastatin or matching placebo. Patients were recruited at 378 centres in 21 countries. The trial was approved by the Ethics Committee at each of the participating hospitals, and patients provided written informed consent. An economic analysis plan was drafted in advance of the data being released. The plan was developed using a slice of treatment-blinded trial data.

Details of the trial have been reported elsewhere,[7] but in short patients aged 60 years or older with chronic symptomatic (NYHA functional class II–IV) heart failure of ischaemic aetiology and with an ejection fraction of ≤0.40 (≤0.35 if NYHA class II) were included. Patients already on a statin (or other lipid lowering drug) or considered by their own doctor to need (or have a contraindication to) a statin were not randomized. Lipid lowering treatment could not be stopped to make a patient eligible for inclusion. Furthermore, patients who had been treated with a statin previously were not eligible for randomization until 6 months after withdrawal of the statin.

The primary trial outcome was the composite of CV mortality, non-fatal MI, or non-fatal stroke, analysed as time to the first event. The secondary outcomes were all-cause mortality, any coronary event, CV mortality, and number of hospitalizations (for CV causes, unstable angina, and worsening heart failure).

Endpoint classification

All serious adverse events were classified by an independent Endpoint Committee (Appendix 1), such that no pre-selection exclusion of potential clinical events was undertaken by the investigators at a site level. In contrast to most previous trials, the adjudication comprised all possible non-CV and CV events. The Endpoint Committee used all available information such as relevant case report forms, reports of serious adverse events, copies of hospital discharge summaries, ECGs, and enzymes (if an acute MI was suspected or reported), physicians' records, discharge letters, police reports, death certificates, and autopsy reports, blinded to subject identifiers. For each hospitalization one main reason was given for admission according to a pre-specified *Endpoint Classification Manual*. If a pre-specified complication (a new MI, new stroke, or unstable angina) occurred during the hospitalization, and was not the reason for admission, these were also adjudicated and recorded, as were pre-specified procedures (percutaneous transluminal coronary intervention (PCI), coronary artery bypass graft (CABG), and cardiac transplant). In addition if a non-fatal stroke occurred outside hospital this was also adjudicated and recorded.

Hospitalization was defined as care at an acute care hospital lasting ≥24 h. Cardiovascular causes were classified as cardiac causes (aggravated heart failure, acute MI, unstable angina, or other cardiac with diagnosis in full text) or non-cardiac (ischaemic, haemorrhagic or unclassifiable stroke, or other non-cardiac with diagnosis in full text). Non-CV causes were given in full text by the Endpoint Committee. Hospitalization for heart failure required documentation that worsening heart failure was the principal reason for hospitalization and, if competing reasons were judged to be of equal importance, heart failure was given preference. Deaths were classified in a similar way.

Health outcomes

Since the total number of major CV *events* was of greater interest than the primary endpoint (*patient*-based time to first event) from an economic perspective, the outcome used in the cost-effectiveness analysis was the total number of combined major fatal and non-fatal CV events avoided (as opposed to patients having events). 'Major CV events' were defined as any of the endpoints described earlier, that is: CV hospitalizations, additional CV events occurring while in hospital, CV events not requiring hospitalisation, and CV deaths. These events were aggregated for each individual (taking care to avoid double counting) and the total and mean number of events per patient were compared between the treatment and placebo groups.

Resource use and cost

The cost of health care comprises resource use counts and the unit cost of these resources. A range of resource use components were routinely collected during the trial. These include hospitalizations (the nature of the hospitalization and the length of stay), procedures, and medications. Primary care costs, over-the-counter medications, and patient costs were not collected. The perspective employed in the economic evaluation was that of the health care sector, i.e. direct costs to the patient and potential productivity costs to society were not estimated.

The index country for the cost analysis was the UK; all costs used 2005/06 as the base year (no inflationary adjustment was required). NHS Reference Costs[9] were employed to value all hospitalizations and procedures, and while the costs of the more specific hospitalizations (MI, stroke, heart failure, and unstable angina) were easily identified, there were numerous (and many rare) CV and non-CV hospitalizations which required valuation. In order to cost accurately these events, two members of the Independent Endpoint Committee assigned ICD-10 codes to all CV and non-CV hospitalizations (OPCS-4 codes were used when hospitalizations explicitly involved procedures). These codes were then mapped to HRG (Healthcare Resource Group) codes using HRG4 Reference Cost Grouper software[10] which were subsequently assigned a cost from the National Schedule

of Reference Costs for NHS Trusts.[9] Appendix 2 presents an example of the main unit costs that were employed in the analysis, the National Schedule (non-elective inpatient stay) gives the full list.[9] The same unit costs were employed whether the patient was discharged alive, or died during the hospitalization, as the reference costs are estimated from finished consultant episodes (FCE), which includes those discharged alive as well as those who died during a hospitalization.

The total number of hospital admissions for each specific type of inpatient stay is presented and compared across the treatment groups, as is length of hospital stay. NHS Reference Costs use an average length of stay (set nationally), that is the unit costs are per event not *per diem*. As this is a multinational study that employs UK specific costs, event costs were employed rather than per diem costs.

The unit costs for each procedure (PTCA, CABG, or cardiac transplant) were used in preference to the unit cost of an associated hospitalization as the reference cost for a procedure includes both these elements (the intervention and inpatient stay). Multiple procedures (e.g. two PTCAs) were conservatively costed as a single procedure.

Concomitant medications were recorded at each study visit during the trial. Doses were only recorded for heart failure specific medications (e.g. loop-diuretics, thiazide diuretics, beta-blockers, ACE-inhibitors, AT1-receptor blockers, aldosterone antagonists, and digitalis) at baseline.

The discontinuation of study medication (and compliance more generally) was checked at each follow-up visit and this information was used to estimate the number of days on rosuvastatin. The daily cost of 10 mg of rosuvastatin (in 2006) was £0.64.[11]

Combining unit costs and resource use counts provides an estimate of the cost of each component (CV hospitalization, procedures, medication), as well as the total cost per patient in each arm of the trial. The difference in costs (and significance) between the two groups was estimated for all categories of cost (CV and non-CV hospitalizations and procedures) and total cost.

Statistical and cost-effectiveness analysis

All analyses were carried out using all patients randomized using the principle of intention-to-treat (ITT). The ITT population was defined as all patients who received a bottle of a study drug. All analyses were performed using STATA10 (StataCorp, TX, USA).

The cost-effectiveness of statins within the trial period was estimated by combining the estimates of cost and effect as described earlier in an incremental cost-effectiveness ratio (ICER). The 95% confidence interval for this ratio was estimated using Fieller's Theorem, a technique that includes any correlation between cost and outcome.[12] Cost-effectiveness acceptability curves (CEACs), which allow decision-makers to assess the overall probability of a particular threshold, were also estimated.[13] A CEAC shows combinations of ceiling values for the ICER and the probabilities that the ICER falls below any given ceiling ratio based on the observed size and variance of differences in cost and events in the trial. All ICERs are appropriately discounted using the current discount rate for the United Kingdom (3.5%) to adjust for differential timing of costs and effects.[14] Where costs and effects are reported separately these are undiscounted (unless otherwise stated).

The cost of statin monitoring, to assess patient stability, was undertaken as sensitivity analysis. Statin monitoring was assumed to include a liver test[15] at the initial prescribing visits, and a further liver test and accompanying primary care visit, valued as a GP visit,[16] 6 weeks later.

Results

A total of 5011 patients were randomized in 21 countries; 2514 were assigned to receive rosuvastatin and 2497 to receive placebo. Both groups had similar characteristics at baseline (*Table 1*). The mean follow-up time was 907 days in the placebo group and 910 days in the treatment group. The average number of days on the study medication was 822 in the placebo group and 839 in the rosuvastatin group (difference 17 days; 95% CI: −3.7−38; *P* = 0.11).

Cardiovascular hospitalizations, procedures and deaths, the primary economic outcome measure of major CV events, and non-CV hospitalizations are presented in *Table 2*. Overall, there were significantly fewer CV hospitalizations in the treatment group (2191 vs. 2562; *P* < 0.001), and significantly fewer hospitalizations for any cause (CV and non-CV) (3685 vs. 4068; *P* = 0.006). There was no difference in the number of non-CV hospitalizations (1494 vs. 1506). The number of other CV events including: additional CV events occurring while in hospital; CV events not requiring hospitalization; CV deaths; and CV procedures were similar in the two treatment groups. When all CV events were combined, there were significantly fewer major CV events in the rosuvastatin group compared with the placebo group (2613 vs. 3006; *P* < 0.001). The average number of major CV events per patient was 1.20 in the placebo group, compared with 1.04 in the intervention group (*P* < 0.001), such that there were 13.7% (95% CI: 6.5−20.3%, *P* < 0.001) fewer major CV events in the rosuvastatin group. When considering fatal and non-fatal major CV events separately, there was a 2.7% (95% CI: −7.3−12.4%, *P* = 0.59) reduction in deaths, and 16.4% (95% CI: 8.0−23.9%, *P* < 0.001) fewer non-fatal major CV events in the rosuvastatin group.

Table 3 presents descriptive statistics for the mean length of stay for each category of hospitalization. There was no significant difference between the two groups.

Because the mean number of concomitant oral medications prescribed during the trial was similar in the two treatment groups [14.0 (range: 0−119) in the placebo group and 13.5 (range: 0−103) in the rosuvastatin group; difference 0.4; 95% CI: − 0.13−1.01; *P* = 0.14] these were neither valued nor included in the estimation of total cost.

Table 4 presents the results of the cost analysis. The average cost of CV hospitalizations for those receiving rosuvastatin was found to be significantly less than those receiving the placebo (£1288 vs. £1517; difference £229; 95% CI: £96−362; *P* = 0.001). The summation of CV hospitalization and procedure costs gave a similar estimate; the average cost in the rosuvastatin group was again significantly lower (£1531 vs. £1769; difference £238; 95% CI: £73−403; *P* = 0.005). This equates to a 13.4% (95% CI: 4.4−21.7%, *P* = 0.004) reduction in CV hospitalization and procedure costs. The cost of rosuvastatin was estimated to be £540 per patient for the duration of the trial, therefore, the cost savings from fewer CV hospitalizations and procedures (£238) was outweighed by the cost of treatment. *Table 4* shows that combining the cost of CV hospitalizations with the cost of procedures and adding the cost of the statin resulted in a significantly higher average cost for those in the rosuvastatin group (£2072 vs. £1769; difference £303; 95% CI: £138−468; *P* < 0.001).

A comparison of this cost with the improvement in effect (that is an increase in the number of major CV events avoided) gave an ICER of £1840 (95% CI: £562−6028), i.e. rosuvastatin cost £1840

Table 1 Baseline characteristics (means and proportions)

	Placebo, *n* = 2497	Rosuvastatin, *n* = 2514	*P*-value
Age	72.7	72.7	0.99
Females	24	2	0.95
NYHA class			0.61
II	37	37	
III	62	61	
IV	1.6	1.4	
Ejection fraction	0.31	0.31	0.94
BMI[a]	27	27	0.53
Blood pressure			
Systolic[b]	129	129	0.52
Diastolic[b]	76	76	0.12
Heart rate	72	72	0.61
Current smoker[c]	8.3	8.9	0.41
Medical history			
MI	60	60	0.87
Past or current angina	72	73	0.71
CABG	17	17	0.62
PTCA/PCI	11	12	0.66
Hypertension	63	63	0.95
Diabetes	29	30	0.90
Current atrial fibrillation	23	24	0.51
Stroke	12	13	0.87
Aortic aneurysm	3.3	2.7	0.20
Intermittent claudication	13	13	0.96
Pacemaker	12	10	0.08
Implantable cardioverter-defibrillator	2.6	2.9	0.51

NYHA, New York Heart Association; BMI, body mass index; MI, myocardial infarction; CABG, coronary-artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty; PCI, percutaneous coronary intervention.
Sample size variations: [a]2492, 2505; [b]2497, 2513; [c]2494, 2513.

for each major CV event avoided (*Table 5*). When the costs of non-CV hospitalizations were included, the cost per major CV event was slightly lower (£1759) but the confidence interval was wider (95% CI: £398−6092). When the cost of statin monitoring was included, the cost difference increased and the ICER became £2090 (95% CI: £729−6576) per major CV event avoided. Given cardiac transplants are rare and expensive events and it is likely to be chance that the placebo group had three times as many as the rosuvastatin group (*Table 3*), further sensitivity analysis was conducted that excluded these from the estimation. *Table 5* shows that the exclusion of these also resulted in a slightly higher ICER of £1987 (95% CI: £705−6230).

The extent of the uncertainty in these cost-effectiveness estimates is presented in *Figure 1*. It is evident in each CEAC that as the threshold increases, the curves asymptote to 1 suggesting that there is very little uncertainty in these estimates.

Discussion

This within trial analysis of CORONA showed that the use of rosuvastatin in older patients with ischaemic systolic heart failure resulted in a 14% reduction in major CV events which corresponds

to a similar reduction in associated hospitalization and procedure costs compared to placebo. The additional cost of statin treatment, however, resulted in significantly higher total costs for those in the rosuvastatin group. As such the cost savings associated with hospitalizations and procedures for major CV events only offset partially the cost of rosuvastatin, so that treatment with rosuvastatin led to an ICER of £1840 per major CV event avoided.

Although this was a multinational study, we employed UK specific costs. A similar approach can be employed to estimate cost-effectiveness for other countries in the trial, using country-specific costs. However, we would expect to find few substantial differences because costs are merely weights for resource use.[17,18] To control for differences in resource use between the trial population and practice in the index country, we employed unit costs for specific types of hospitalization and procedures, rather than per diem costs. This meant that our analysis is less sensitive to variations in length of hospital stay between countries and that our results should be more generalizable. There was no significant difference between lengths of stay in the two treatment groups.

Notably, this economic evaluation did not employ the trial primary outcome, which was a time to first event analysis, for

Table 2 Cardiovascular and non-cardiovascular events

	Placebo *n* = 2497	Rosuvastatin *n* = 2514	*P*-value[a]
Hospitalizations (number of admissions)[b]			
Stroke	103	86	
Worsening heart failure	1298	1108	0.012
MI	142	109	
Unstable angina	90	73	0.28
Non-cardiac CV	336	296	
Other CV	593	519	
All CV hospitalizations[i]	2562	2191	<0.001
Hospitalizations (number of patients)			
Stroke	94	81	
Worsening heart failure	669	622	
MI	131	96	
Unstable angina	71	64	
Non-cardiac CV	231	226	
Other CV	406	394	
All CV hospitalizations	1164	1104	
Additional events while in hospital (not reason for hospitalization)[ii]			
Stroke	10	9	
Acute MI	19	28	
Unstable angina	3	3	
Additional events not requiring hospitalization[iii]			
Stroke	5	3	
CV deaths			
Worsening heart failure deaths	191	193	0.97
MI deaths	9	15	0.23
Sudden deaths	327	316	0.58
Other CV deaths	6	8	
Non-cardiac CV deaths	60	49	
Total CV deaths	593	581	0.43
CV deaths while hospitalized	186	202	
CV deaths not while hospitalized[iv]	407	379	
Procedures			
CABG	28	32	
PCI	93	93	
Cardiac transplant	3	1	
Major CV events[c]			
Total number[i+ii+iii+iv]	3006	2613	<0.001
Average number (per patient)	1.204	1.039	<0.001
Non-CV hospitalizations (number of admissions)	1506	1494	
Non-CV hospitalizations (number of patients)	840	839	
All hospitalizations (number of CV and non-CV admissions)	4068	3685	0.006
All hospitalizations (number of patients)[d]	1523	1489	

CV, cardiovascular; MI, myocardial infarction; CABG, coronary-artery bypass grafting; PCI, percutaneous coronary intervention.
[a]*P*-values are only presented for the pre-specified trial endpoints.
[b]Detailed analysis of hospitalizations revealed a number of duplicate and simultaneous hospitalizations, these were investigated and corrected and as such the number of hospitalizations reported in this table differ slightly from those reported in the clinical trial paper.[8]
[c]Major CV events are the summation of (i) CV hospitalizations, (ii) additional CV events while in hospital, (iii) events not requiring hospitalization, and (iv) CV deaths not while in hospital for a CV cause.
[d]The number of patients hospitalized for CV causes and non-CV causes sums to more than the number of patients hospitalized for all causes, as patients could be hospitalized for both CV and non-CV causes during the course of the trial.

a composite of death from CV causes, non-fatal MI, or non-fatal stroke. This outcome was used at the request of a regulatory authority to be in keeping with prior statin trials. It did not, however, include the most common and expensive non-fatal outcome in patients with heart failure, i.e. hospitalization for worsening heart failure. For the economic evaluation of CORONA, we felt it was

Table 3 Length of stay (days) by type of hospitalization, mean (standard error), median (interquartile range)

	Placebo	Rosuvastatin	P-value
Stroke	15.0 (1.4), 11 (7,18)	13.5 (1.4), 10 (5, 16)	0.47
Worsening heart failure	12.6 (0.3), 9.5 (6, 15)	11.9 (0.3), 9 (6, 15)	0.09
MI	14.8 (1.2), 11 (7, 19)	12.9 (1.0), 11 (6, 17)	0.24
Unstable angina	12.2 (1.6), 9.5 (6, 14)	13.3 (1.0), 12 (7, 18)	0.58
Non-cardiac CV	12.8 (1.0), 8 (5, 12)	13.2 (0.9), 8 (4, 15)	0.77
Other CV	8.7 (0.4), 5 (3, 10)	9.2 (0.4), 6 (3, 11)	0.37
Non CV	11.2 (0.3), 8 (4, 14)	11.2 (0.3), 8 (4, 14)	0.88

CV, cardiovascular; MI, myocardial infarction.

Table 4 Average cost per patient (£sterling, 2005/06 prices)

	Placebo (std. error)	Rosuvastatin (std. error)	Difference (95% CI)	P-value
Cost components				
Cost of CV hospitalization [a]	1517 (51)	1288 (44)	−229 (−362, −96)	0.001
Cost of procedures [b]	252 (33)	243 (27)	−9 (−92, 75)	0.84
Cost of non-CV hospitalizations [c]	739 (31)	726 (29)	−13 (−97, 70)	0.76
Cost of statin [d]	-	540 (5)	540 (531, 550)	<0.001
Total costs				
Total cost excluding statin costs and non-CV hospitalization [a+b]	1769 (64)	1531 (54)	−238 (−403, −73)	0.005
Total cost excluding statin costs [a+b+c]	2508 (75)	2257 (65)	−251 (−446, −57)	0.011
Total cost excluding non-CV hospitalization [a+b+d]	1769 (64)	2072 (54)	303 (138, 468)	<0.001
Total cost [a+b+c+d]	2508 (75)	2798 (65)	289 (95, 484)	0.004

CV, cardiovascular.

Table 5 Cost, effect, and cost-effectiveness (cost per major CV event avoided) (£sterling, 2005/06 prices)

Rosuvastatin vs. placebo	Point estimate (95% CI)	ICER (95% CI)[a]
Incremental effect[b]	0.164 (0.075, 0.254)	
Incremental total cost (CV hospitalization, procedure and Tx costs)	£303 (138, 467)	£1840 (562, 6028)
Incremental total cost, including non-CV hospitalization	£289 (95, 484)	£1759 (398, 6092)
Incremental total cost, including monitoring visits	£343 (179, 509)	£2090 (729, 6576)
Incremental total cost, excluding cardiac transplantations	£328 (176, 481)	£1987 (705, 6230)

CV, cardiovascular; Tx, treatment; ICER incremental cost-effectiveness ratio.
[a]95% confidence interval for the ICER estimated using Fieller's Theorem.
[b]This is the difference between an average of 1.204 major CV events per patient in the placebo group and 1.039 in the rosuvastatin group, see *Table 2*.

important to examine the total burden of CV events in these patients, including hospitalization for worsening heart failure and other associated CV causes, as well as CV procedures. Our analyses showed the merit of undertaking an economic evaluation of what was a 'non-conclusive' clinical trial result, 8% observed relative risk reduction compared with 16% assumed relative risk reduction.

The estimated ICER is consistent with that reported in similar studies of statin treatment. For example, in the Heart Protection Study (HPS), 40 mg of simvastatin once daily in a group of patients which mainly excluded those with heart failure, the cost per major vascular event avoided was £11600; while in a subgroup of high-risk patients (individuals with a 42% 5 year risk of a major vascular event) an ICER of £4500 per major vascular event avoided was
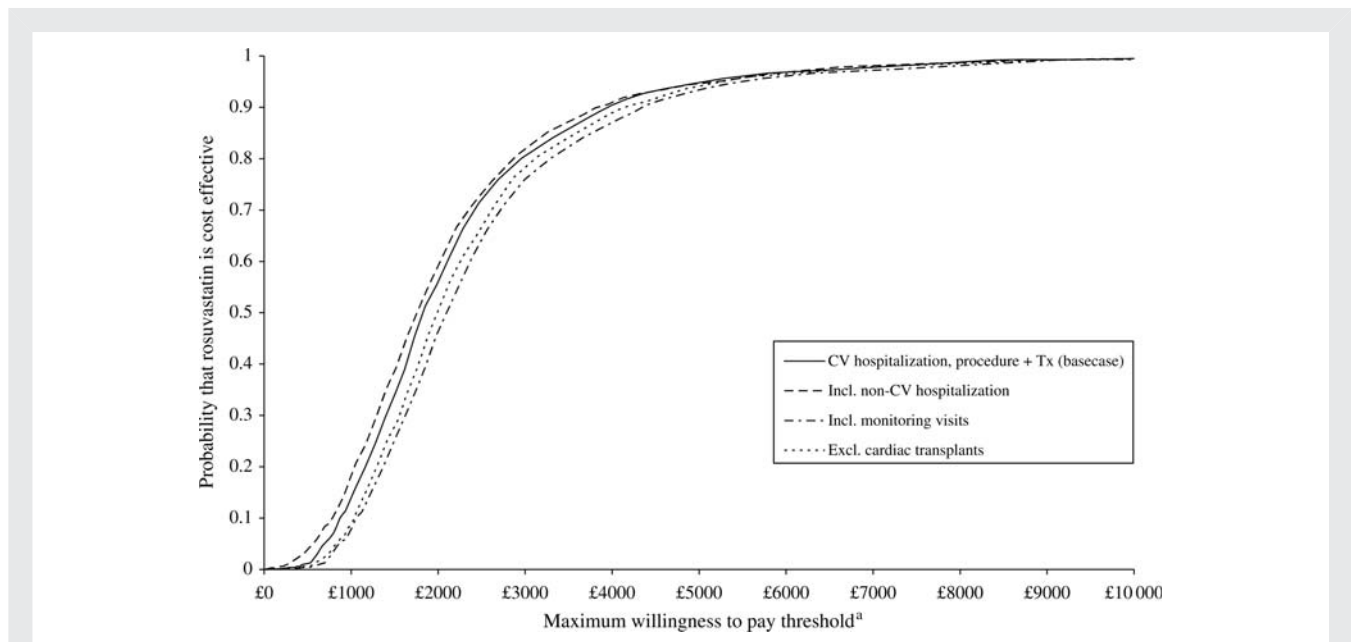
Figure 1 Cost-effectiveness acceptability curves.
[a]Maximum willingness to pay to avoid one major CV event.

found.[19] We estimate that the baseline risk for patients in our placebo arm was ~17% per annum, nearly twice as high as the annual risk for high-risk patients in HPS (~9%), this coupled with higher cost reduction in HPS (22% reduction in hospital costs compared with 13%) means that the HPS ICER of £4500 is approximately consistent with our ICER of £1840. Notably, in the HPS lifetime analysis, statin treatment for high-risk patients was found to be cost saving.[5]

However, it is important to emphasize that the patients in HPS were very different to those in CORONA, in that they had a much better prognosis than the CORONA patients (as indicated by the baseline risk) and there was also a significant difference in the number of fatal events in the HPS study, such that the two outcome measures, while similar, are not directly comparable. It is a limitation of the analysis that the composite endpoint used is a clinical outcome measure, rather than a quality adjusted life year (QALY) as favoured by economists. To appropriately estimate cost per QALY would require generic health-related quality of life data (like the EQ5D[20]) which were not collected in the trial, and also would necessitate extrapolation beyond the 3 year trial follow-up. As survival data were collected, it would be possible to estimate the cost per additional life year gained. However, it would not be informative to estimate the cost per additional life year gained since, as detailed in the trial paper,[8] there is no significant difference in survival, such that any comparison of costs and outcomes would revert to a mere cost analysis, which would be uninformative as it would ignore the quality of life benefits of avoiding events.

As shown in HPS, it is important to consider the role of baseline risk and the sensitivity of cost-effectiveness estimates. Work is ongoing in this area; however, the methodology of heterogeneity issues is not trivial and it requires further understanding and development. Furthermore, the model that has been developed is based on a subsample of patients[21] (due to missing data) while our economic analysis is applicable to the sample as a whole, such that further research is required.

In conclusion, although the primary outcome of the CORONA study was not met, this economic analysis shows that a significant reduction in major CV events with rosuvastatin led to significantly reduced costs of CV hospitalizations and procedures. The reduction in associated costs for major CV events was found to offset partially (by 44%) the cost of rosuvastatin treatment in patients with systolic heart failure.

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Appendix 1: The members of the CORONA study group

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Appendix 2

Unit costs for major cardiovascular hospitalizations and procedures (£sterling, 2005/06 values)

Resource	Unit cost
Hospitalizations	
Heart failure	1694
Unstable angina (ischaemic heart disease)	1005
Acute MI	1695
Ischaemic stroke	2433
Haemorrhagic stroke	2237
Unclassifiable (non-transient) stroke	2433
Arrhythmia	1072
Peripheral vascular disease	1313
Syncope or collapse	951
Other cardiac procedures	1256
Procedures	
PCI	3401
CABG	8333
Cardiac transplant	32 113
Monitoring costs	
Liver test	5
General practice clinic visit	31
Investigational product	
Rosuvastatin (10 mg—28 day tab)	18

Sources: Department of Health[9]; Healthcare Commission[15]; Netten and Curtis[16]; British Medical Association and Royal Pharmaceutical Society of Great Britain[11]. CV, cardiovascular; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary-artery bypass grafting.

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