Cost effectiveness of rosuvastatin in treating patients to low-density lipoprotein cholesterol goals compared with atorvastatin, pravastatin, and simvastatin (a US Analysis of the STELLAR Trial)

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use rosuvastatin (10, 20 or 40 mg) in the treatment of patients with hypercholesterolaemia.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised men and women who were at least 18 years of age and had hypercholesterolaemia. Hypercholesterolaemia was defined as low-density lipoprotein (LDL) cholesterol concentrations of at least 160 mg/dL but below 250 mg/dL; triglyceride concentration of less than 400 mg/dL.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from a study published in 2003. The price year was 2004.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The information on sample selection was limited since the clinical study had already been published. A sample of 2,431 patients was enrolled. Patient demographics were not reported.

Study design
This was a prospective, randomised, parallel-group, open-label, multi-centre clinical trial. The length of follow-up was 6 weeks. No further details on randomisation and follow-up were reported.
Analysis of effectiveness
The primary outcome measures used in the analysis were the change in plasma LDL cholesterol concentration from baseline to 6 weeks and the proportion of patients who reached the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guideline LDL cholesterol goals. The percentages of patients reporting side effects were also assessed. The baseline comparability of the study groups was not discussed. It was not stated whether the analysis of the efficacy data were conducted on an intention to treat basis.

Effectiveness results
The mean percentage decreases in LDL cholesterol were as follows:
- Rosuvastatin 10 mg, 45.87; rosuvastatin 20 mg, 52.34; and rosuvastatin 40 mg, 54.96;
- Atorvastatin 10 mg, 36.73; atorvastatin 20 mg, 42.57; atorvastatin 40 mg, 47.79; and atorvastatin 80 mg, 51.05;
- Pravastatin 10 mg, 20.13; pravastatin 20 mg, 24.29; and pravastatin 40 mg, 29.68; and
- Simvastatin 10 mg, 28.30; simvastatin 20 mg, 34.98; simvastatin 40 mg, 38.81; and simvastatin 80 mg.

The proportions of patients reaching their LDL cholesterol goal were as follows:
- Rosuvastatin 10 mg, 0.82; rosuvastatin 20 mg, 0.89; and rosuvastatin 40 mg, 0.89;
- Atorvastatin 10 mg, 0.69; atorvastatin 20 mg, 0.75; atorvastatin 40 mg, 0.85; and atorvastatin 80 mg, 0.82;
- Pravastatin 10 mg, 0.31; pravastatin 20 mg, 0.44; and pravastatin 40 mg, 0.55; and
- Simvastatin 10 mg, 0.51; simvastatin 20 mg, 0.63; simvastatin 40 mg, 0.66; and simvastatin 80 mg, 0.82.

The percentages of patients who reported adverse events were similar across treatment groups and ranged from 40 to 56% per group.

Clinical conclusions
The effectiveness analysis showed that, in terms of milligram-equivalent doses, rosuvastatin provided the greatest clinical effects on LDL cholesterol.

Measure of benefits used in the economic analysis
The summary benefit measures were the change in plasma LDL cholesterol concentration from baseline to 6 weeks and the proportion of patients who reached the NCEP ATP III guideline LDL cholesterol goals. Both were estimated directly from the effectiveness analysis.

Direct costs
The cost analysis was undertaken from the perspective of the health care payers and included only drug costs. The authors justified their exclusion of the costs of side effects (no statistically significant differences were observed between groups), costs associated with physician and nurse visits and laboratory tests (such costs were largely driven by the design of the clinical trial and were nearly identical in all treatment arms), and costs associated with dose titration (no titrations were carried out during the 6-week trial period). The unit costs of the drugs were presented separately from the quantities of doses used. Resource use was estimated using data collected prospectively alongside the clinical trial, assuming that patients had remained on their fixed statin dose for a period of one year. The costs came from wholesale acquisition costs (the net price that manufacturers charge wholesalers for a drug. Discounting was not relevant since the costs were incurred during one year. The price year was reported.
**Statistical analysis of costs**
No statistical analyses of the costs were performed.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Threshold sensitivity analyses were carried out on the price of each statin that was required to change the decision about the most cost-effective treatment strategy. This analysis was performed in order to take the effect of price discounting in the US statin market into consideration.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The estimated annual costs were:

- $813.95 with all rosuvastatin dosages;
- $755.55 with atorvastatin 10 mg, $1,095.00 with atorvastatin 20 mg, $1,095.00 with atorvastatin 40 mg, and $1,095.00 with atorvastatin 80 mg;
- $945.35 with pravastatin 10 mg, $963.60 with pravastatin 20 mg, and $1,412.55 with pravastatin 40 mg; and
- $803.00 with simvastatin 10 mg, $1,397.95 with simvastatin 20 mg, $1,397.95 with simvastatin 40 mg, and $1,397.95 with simvastatin 80 mg.

**Synthesis of costs and benefits**
Average cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative statins. Cost-effectiveness was also calculated in terms of the net monetary benefit (NMB), which allows probabilistic comparisons of multiple treatments. Cost-effectiveness was also presented using cost-effectiveness acceptability curves, which show the certainty of a statin being cost-effective for different values of willingness to pay for an improvement in the benefit measure.

The estimated costs per 1% decrease in LDL cholesterol were:

- $17.74 with rosuvastatin 10 mg, $15.55 with rosuvastatin 20 mg, and $14.81 with rosuvastatin 40 mg;
- $20.57 with atorvastatin 10 mg, $25.72 with atorvastatin 20 mg, $22.91 with atorvastatin 40 mg, and $21.45 with atorvastatin 80 mg;
- $46.96 with pravastatin 10 mg, $39.67 with pravastatin 20 mg, and $47.59 with pravastatin 40 mg; and
- $28.37 with simvastatin 10 mg, $39.96 with simvastatin 20 mg, $36.02 with simvastatin 40 mg, and $30.54 with simvastatin 80 mg.

The estimated costs per patient reaching the LDL cholesterol goal were:
$992.62 with rosuvastatin 10 mg, $914.55 with rosuvastatin 20 mg, and $914.55 with rosuvastatin 40 mg;

$1,095.00 with atorvastatin 10 mg, $1,460.00 with atorvastatin 20 mg, $1,288.24 with atorvastatin 40 mg, and $1,335.37 with atorvastatin 80 mg;

$3,049.52 with pravastatin 10 mg, $2,190.00 with pravastatin 20 mg, and $2,568.27 with pravastatin 40 mg; and

$1,574.51 with simvastatin 10 mg, $2,218.97 with simvastatin 20 mg, $2,118.11 with simvastatin 40 mg, and $1,704.82 with simvastatin 80 mg.

The cost-effectiveness acceptability curve showed that rosuvastatin 10 mg was the most cost-effective statin when the value of a 1% decrease in LDL cholesterol was $6 to $54, or when the value of a patient who reached the LDL cholesterol goal was $449 to $8,368. The range of values for the willingness to pay for an improvement in the benefit measures over which rosuvastatin 10 mg was most frequently the more cost-effective option was large.

Atorvastatin 10 mg was the cheapest drug and the most cost-effective treatment option when the value of a 1% decrease in LDL cholesterol was less than $6, or when the value of a patient who reached the LDL cholesterol goal was less than $449. As the value of willingness to pay per 1% decrease in LDL cholesterol increased to more than $30, the probability of cost-effectiveness decreased for rosuvastatin 10 mg and increased for atorvastatin 80 mg.

As the value of the willingness to pay for a patient who reached the LDL cholesterol goal increased to more than $2,000, the probability of cost-effectiveness decreased for rosuvastatin 10 mg and increased for atorvastatin 40 mg and 80 mg.

The sensitivity analysis showed that, in general, rosuvastatin remained the most cost-effective strategy. For example, when each 1% decrease in LDL cholesterol was valued at $80, the price of atorvastatin 10 mg would have to decrease by 89% (from $2.07 to $0.23 per day) to have the equivalent cost-effectiveness as rosuvastatin 10 mg. When the value of the willingness to pay was $2,500 per patient who reached the LDL cholesterol goal, the price of atorvastatin 10 mg would have to decrease by 35% to have the same cost-effectiveness as rosuvastatin 10 mg, whereas the price of simvastatin 10 mg would have to decrease by 95%.

Authors' conclusions
The clinical superiority of rosuvastatin that had been demonstrated in the STELLAR trial translated into an economic advantage in comparison with other statins such as atorvastatin, pravastatin and simvastatin.

CRD COMMENTARY - Selection of comparators
The selection of the comparators appears to have been appropriate as all drugs examined in the study are widely used for the treatment of patients with hypercholesterolaemia. It was unclear whether other statins could have also been considered as potential comparators. Different dosages were considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from a clinical trial, which was appropriate for the study question and generally has a high internal validity. However, since the clinical trial had been published already, limited information on the methods of sample selection, randomisation, and outcome assessment was provided. Thus, it was not possible to assess the robustness of the clinical data.

Validity of estimate of measure of benefit
The summary benefit measures were specific to the disease considered in the study and are not comparable with the benefits of other health care interventions. Both measures represent intermediate clinical end points of the interventions rather than final measures of the impact of the treatments on patients’ health, such as survival. The impact of the therapies on quality of life was not investigated.
Validity of estimate of costs
The cost analysis included only the costs of the drugs. A justification for the exclusion of other categories of costs was provided. The inclusion of costs associated with further care, such as reduced cardiovascular events, would have been interesting. The unit costs and the quantities of resources used were presented separately, which enhances the possibility of replicating the analysis in other settings. The source of the data was reported. The costs were treated deterministically but the drug price was varied in the sensitivity analysis, thus increasing the generalisability of the results. The price year was reported, which aids reflation exercises in other time periods.

Other issues
The authors did not compare their findings with those from other studies. The issue of the generalisability of the study results to other settings was addressed in respect of drug costs only. The authors noted that their analysis assumed that efficacy achieved after 6 weeks of statin treatment was comparable to the efficacy achieved after 1 year of continued treatment, which might not reflect real-world situations. Further, the issue of treatment compliance was not specifically addressed. The study referred to patients with hypercholesterolaemia and this was reflected in the authors' conclusions.

Implications of the study
The study results supported the use of rosuvastatin for the treatment of hypercholesterolaemia in the USA. The authors suggested that future studies should evaluate the long-term clinical effect of statin therapy.

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None stated.

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Other publications of related interest


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