Analisis coste-efectividad de atorvastatina frente a simvastatina como tratamiento hipolipemiantes en pacientes hipercolesterolemicos en atencion primaria [Cost-effectiveness analysis of atorvastatin versus simvastatin as lipid lowering treatment for primary care patients with hypercholesterolaemia]

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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 of two lipid-lowering therapies, simvastatin (20 mg/day) and atorvastatin (10 mg/day), in patients with hypercholesterolaemia.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients older than 18 years of age, who had levels of total cholesterol (TC) and low-density lipoprotein cholesterol (cLDL) of greater than 240 mg/dl and greater than 160 mg/dL, respectively. The patients also presented some risk factors, but were without any prior episode of cardiovascular disease.

Setting
The setting was primary care. The economic study was conducted in five centres in the areas of Albacete and Cuenca, in Spain.

Dates to which data relate
The effectiveness and resource use data were gathered from January to June 1999. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not performed to determine the sample size. Patients presenting at the five study centres during the study period were selected and included in the analysis. The final group of patients administered atorvastatin comprised 48 patients. Their mean age was 66.8 (+/- 8.2) years and 42.5% were male. The group of patients administered simvastatin comprised 44 patients. Their mean age was 63.5 (+/- 10.2) years and 46.8% were male.
patient was excluded from the initial sample.

**Study design**
The study was an open, randomised clinical trial carried out in five centres in the areas of Albacete and Cuenca. The method of randomisation was not reported. The patients were followed-up for 6 months. Four patients in the simvastatin group and 1 in the atorvastatin group did not complete the follow-up. The reasons for the loss to follow-up were not specified. The patients were assessed at baseline and at 3 and 6 months.

**Analysis of effectiveness**
The clinical study was analysed on an intention to treat basis. The primary health outcomes were:

the rate of success at 3 and 6 months, in terms of the therapeutic reduction of cLDL control;

the percentage reductions in TC, cLDL, high-density lipoprotein cholesterol (cHDL), and triglyceride levels;

the percentage of patients reaching the therapeutic objectives set by the Spanish Society of Arteriosclerosis (Sociedad Espanola de Arteriosclerosis, SEA), such as cLDL levels of less than 155 mg/dL for patients with no more than one risk factor, and less than 135 mg/dL for those with at least two risk factors; and

the occurrence of adverse events.

The groups were shown to be comparable in terms of the demographics and lipid profile. However, patients in the simvastatin group had a statistically significantly lower level of TC.

**Effectiveness results**
The success rates in the atorvastatin group were 56% at 3 months and 51.2% at 6 months. The success rates in the simvastatin group were 54.3% at 3 months and 52% at 6 months.

At 3 months, the average percentage reductions in TC, cLDL, cHDL, and triglycerides were:

in the atorvastatin group, -21.5% (standard deviation, SD=13.2) for TC, -25.7% (SD=18.1) for cLDL, 1.3% (SD=24.9) for cHDL, and -14.6% (SD=38.1) for triglycerides;

in the simvastatin group, -16.4% (SD=14.2) for TC, -19.8% (SD=25.5) for cLDL, 4.1% (SD=30.1) for cHDL, and -0.5% (SD=35.6) for triglycerides.

At 6 months, the percentage reductions in TC, cLDL, cHDL, and triglycerides were:

in the atorvastatin group, -23.8% (SD=13.9) for TC, -29.6% (SD=18.6) for cLDL, 2.4% (SD=28.8) for cHDL, and -13.0% (SD=36.9) for triglycerides;

in the simvastatin group, -22.8% (SD=10.8) for TC, -26.1% (SD=18.3) for cLDL, -0.6% (SD=30.0) for cHDL, and -15.4% (SD=27.8) for triglycerides.

In terms of the SEA therapeutic objectives, 54.2% of the patients in the atorvastatin group and 50.0% of patients in the simvastatin group reached the set critical values of cLDL.

No occurrence of adverse events was reported in the study groups.

The statistical analyses indicated that at 3 months, the reductions in CT, cLDL, and triglycerides were significantly higher in the simvastatin group than in the atorvastatin group. However, at 6 months, no statistically significant difference was reported between the groups.
Clinical conclusions
Although patients in the simvastatin groups obtained significant reductions in their cholesterol levels in the short-term, no statistically significant difference between the study groups was found at 6 months. As a result, the two therapies were considered to be equivalent.

Measure of benefits used in the economic analysis
The benefit measures used in the economic analysis were the percentages of patients reaching the SEA therapeutic objectives and the percentage reduction in cLDL. Both benefit values were derived directly from the effectiveness analysis.

Direct costs
No discounting was carried out since the time horizon of the study was 6 months. The unit costs and the quantities of resources were reported separately. The cost/quantity boundary adopted was unclear. The costs included in the analysis were for the drugs, outpatient visits, laboratory tests, and the direct costs of hours of work lost by patients attending physician visits. It was assumed that each physician visit would last for 4 hours. It was also assumed that the patients lost at the final follow-up were included in the final computation of the total costs. The quantities were estimated using data derived from the clinical trial. The costs were estimated using actual data derived from different sources. These sources included the catalogue of pharmaceuticals for drug acquisition costs, a published database for visits and laboratory tests, and the Ministry of Labour for the minimum wage in 1999. The quantities of resources were collected from January to June 1999. The price year was 1999.

Statistical analysis of costs
No statistical analysis of the costs was conducted.

Indirect Costs
The indirect costs were not included.

Currency
Spanish pesetas (Pta).

Sensitivity analysis
Two sensitivity analyses were conducted to take into account the uncertainty around the estimated variables. These used the lower and upper limits of the 95% confidence intervals (CIs) of the following:

the success rate of the therapy, according to the SEA therapeutic objectives (95% CI: 39.30% - 68.40% in the atorvastatin group; 95% CI: 34.80% - 65.20% in the simvastatin group); and

the percentage reduction in cLDL (95% CI: 24.2% - 35.0% in the atorvastatin group; 95% CI: 20.4% - 31.8% in the simvastatin group).

It appears that one-way analyses were conducted.

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

Cost results
The total cost of the therapy was Pta 2,482,092 in the atorvastatin group and Pta 2,229,359 in the simvastatin group.
The drug acquisition costs, as a percentage of the total cost, were 63% in the atorvastatin group and 64% in the simvastatin group.

The cost per patient was Pta 51,710 in the atorvastatin group and Pta 50,667 in the simvastatin group.

Synthesis of costs and benefits
The costs and the benefits in the two study groups were combined using average and incremental cost-effectiveness analyses.

The average cost-effectiveness per patient who conforms with the SEA objectives was Pta 95,406 in the atorvastatin group and Pta 101,335 in the simvastatin group.

The average cost per estimated reduction in cLDL was Pta 1,747 in the atorvastatin group and Pta 1,941 in the simvastatin group.

The incremental cost of simvastatin over atorvastatin was Pta 24,833 per SEA objective reached, and Pta 297 per estimated reduction in cLDL.

The sensitivity analyses showed that the average and incremental cost-effectiveness ratios were not sensitive to variations in the success rates (according to the SEA therapeutic objectives) and reductions in cLDL.

Authors' conclusions
The analysis indicated that both statins were equally effective in reducing cholesterol levels at 6 months. However, atorvastatin showed a better cost-effectiveness ratio, due to the low costs per patient.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparator was clear. Atorvastatin represented the more recent therapy, while simvastatin was a drug of proven efficacy. You should assess whether these represent widely used drug therapies in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis was likely to be of high validity due to the randomised design. However, the study groups were shown to be statistically different at baseline in terms of their TC levels, which appears to have been a crucial factor in the analysis. In addition, power calculations were not performed to determine sample size. This could explain why the outcome measures were not statistically different between the groups, especially since, as the authors acknowledged, the sample size was quite small. Finally, the time horizon of the study was too short to detect the long-term effects of the therapies.

Validity of estimate of measure of benefit
The benefit measures used in the economic analysis were directly derived from the effectiveness study. Although no statistically significant difference was found between the drug treatments, an incremental cost-effectiveness analysis was conducted to assess the costs of an additional benefit of simvastatin over atorvastatin.

Validity of estimate of costs
The perspective adopted in the study was unclear. The productivity losses were included in the cost analysis, although the authors stated that only the direct costs were accounted for. It would have been more appropriate to have included these cost items in the relevant field. The costs and the quantities were treated deterministically. The estimation of the costs appears to have been somewhat specific to the study setting.
Other issues
The study results confirmed the findings of most published studies with similar design. Sensitivity analyses were conducted on the benefit measures, which represented crucial variables. However, the estimated cost-effectiveness ratios were quite robust. The issue of generalisability to other settings and countries was implicitly addressed through the sensitivity analyses. The authors stated that the study had some limitations in relation to the study design.

Implications of the study
Atorvastatin appears to be the most cost-effective statin treatment for patients with hypercholesterolaemia. However, the incremental cost-effectiveness of simvastatin was relatively low.

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