Effect of pravastatin-to-simvastatin conversion on low-density-lipoprotein cholesterol

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 simvastatin to reduce low-density lipoprotein (LDL) cholesterol levels.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients receiving pravastatin at a Veterans Affairs medical centre.

Setting
The setting was the community.

Dates to which data relate
The effectiveness evidence and resource use data were gathered from 1997. The price year was 1997.

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

Link between effectiveness and cost data
The costing was carried out prospectively using the same patient sample as that used in the effectiveness study.

Study sample
Power calculations were not used to estimate the number of patients in the study. There was only one group of patients as this was a before-and-after study evaluating the same patient cohort. Patients were selected if they were undergoing treatment with pravastatin in order to lower their cholesterol levels. A total of 1,361 patients were considered eligible for the switching programme. Of these, 1,032 completed the programme and were evaluated in terms of the clinical outcome.

There were approximately 300 patients who did not complete the switching programme. The reasons for this were:

17 patients were enrolled in lipid protocols,
15 had moved from the area,
16 had no baseline data available in the hospital computer system, 15 were deceased, 37 had discontinued lipid-lowering treatment, 79 had not filled out repeat pravastatin prescriptions for 4 months, 35 had been switched to simvastatin before the programme, 15 were taking other lipid-lowering agents, 3 were in nursing home, 2 had adverse drug reactions, 36 never switched drugs, and 47 were lost to follow-up.

The study sample seems to have been relevant for the study question, as all eligible patients were included. In addition, both demographic and clinical baseline characteristics were presented.

**Study design**
This was a non-randomised, before-and-after study carried out in a single centre. The clinical outcome was measured at baseline and 6 weeks after conversion. There were 47 patients who switched drugs and were lost to follow-up. The outcome was assessed in an open fashion.

**Analysis of effectiveness**
The analysis of the clinical study was conducted for treatment completers only. A fasting lipoprotein profile was obtained at baseline and approximately 6 weeks after switching to the simvastatin therapy. The measures of clinical effectiveness were the change in cholesterol level, the proportion of patients reaching their LDL cholesterol goal, and the probability of coronary heart disease (CHD) over 10 years. The patients' goal for the LDL cholesterol level was specified by the National Cholesterol Education Programme. It was determined after identifying the risk factors for CHD and the presence of atherosclerotic disease. The study was conducted using only one patient cohort. A multivariate analysis to adjust for behaviour, time or non-patient-related confounding factors was not conducted.

**Effectiveness results**
The blood cholesterol values were analysed using the Wilcoxon signed rank test to compare median values, since the lipid indices and laboratory tests were generally skewed.

The median total cholesterol concentration was 197 mg/dL at baseline (i.e. for treatment with pravastatin) and 179 mg/dL after conversion to simvastatin therapy, (p<0.001).

The median LDL cholesterol concentration was 116 mg/dL with pravastatin therapy and 99 mg/dL after conversion to simvastatin, (p<0.001).

The proportion of patients reaching their LDL cholesterol goal was 44% with pravastatin therapy and 69% after conversion to simvastatin, (p<0.001).

The 10-year risk of CHD changed from 16.2% with pravastatin therapy, to 13.7% after conversion to simvastatin, (p<0.001).
Clinical conclusions
Changing the treatment from pravastatin to simvastatin resulted in a statistically significant improvement in the LDL cholesterol levels.

Measure of benefits used in the economic analysis
The study should be categorised as a cost-consequences analysis since no summary measure of benefit was reported.

Direct costs
The direct costs were not discounted since they were only incurred over one year. The resource use costs used in the analysis were those for drug acquisition and the introduction of the programme. The costs of the programme were the physician, nurse practitioner, pharmacist, pharmacy technician, laboratory technician, laboratory supply and laboratory evaluation. The source of the programme costs was not stated. The quantities were estimated from the actual data. However, the resource quantities and unit costs were not reported separately. The cost of medication was derived from the contract cost with the company supplying simvastatin.

The analysis was based on incremental costs for the new programme of simvastatin treatment. This was described in another publication (see Other Publications of Related Interest).

Statistical analysis of costs
A statistical analysis was conducted on the mean reduction in drug acquisition costs per patient. However, the authors did not state how the cost data were analysed.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not carried out.

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

Cost results
The difference in drug acquisition costs before and after the programme (i.e. the cost of simvastatin therapy minus the cost of pravastatin therapy) was $-0.23 (±/175) per patient. The authors stated that this was not statistically significantly different from zero. The cost of the pravastatin to simvastatin switching programme, including the drug acquisition costs, was $39.12 (±/174.81) per patient.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The use of a pravastatin to simvastatin switching programme increased the number of patients reaching their target low-
density lipoprotein (LDL) cholesterol level. This was achieved at a slight reduction in the medication acquisition costs when the cost of introducing the programme was excluded.

**CRD COMMENTARY - Selection of comparators**
The authors were evaluating a drug conversion programme, and so the therapies included in the study were relevant for the study question. The choice of comparators was justified on the grounds that the new therapy (simvastatin) would represent 'current practice' after the introduction of the programme.

**Validity of estimate of measure of effectiveness**
The measure of effectiveness was derived from a before-and-after study. This study design is more prone to bias and confounding than prospective randomised controlled trials. The authors acknowledged that one of the study's limitations was that the number of patients meeting their pre-programme target (i.e. on pravastatin) may have been underestimated. This was because the measure of previous drug use was estimated from pharmacy records, which may not accurately reflect patient adherence.

The study design was appropriate to the study hypothesis. However, a randomised comparison of drug swapping may have been more valid as an indicator of the clinical effectiveness. The clinical data were analysed using appropriate non-parametric statistical methods, although no allowance was made for possible confounding. For example, there could have been a time trend, whereby prior treatment with pravastatin had effects beyond its cessation. Also, there could have been other changes, for example in patient behaviour, which were responsible for some of the change.

The measure of effectiveness, the percentage reaching their LDL cholesterol target, seems to have been appropriate given that it reflected guidelines apparently directly related to the risk of CHD and other atherosclerotic diseases. Its precise value depends partly on the value of risk reduction in these diseases, relative to other quality of life factors. It also depends on it reflecting sufficiently the change in risk due to the drug; i.e. other physiological changes do not lead to confounding.

**Validity of estimate of measure of benefit**
There was no summary measure of benefit.

**Validity of estimate of costs**
It was difficult to assess the validity of the cost estimate since the resource use and unit costs were not reported separately. However, all relevant cost categories appear to have been included, considering that the study was undertaken from the perspective of the health care payer.

**Other issues**
The authors compared their results with those of other relevant studies. The proportion of patients with well-controlled LDL cholesterol levels was comparable to other studies in similar populations. The issue of generalisability was not explicitly addressed. The authors suggested that the results may be transferred to other Veterans Affairs Centres. This would only be valid if other centres achieved the same discount on the drug costs from the manufacturer.

The authors acknowledged two limitations of their study. First, the baseline LDL cholesterol levels may have been underestimated. Second, the follow-up measurements may have been influenced by the fact that patients knew they were being monitored (the 'Hawthorne effect').

The authors' conclusions generally reflected the scope of the analysis. However, the authors commented that the results of the study supported a multidisciplinary approach for improving the LDL cholesterol levels of patients in Veterans Centres, for which the current statin treatment tends to be inadequate. The value of a "multidisciplinary approach" was not being tested here; in fact it could have led to confounding.
Implications of the study
The authors commented that this was the first therapeutic interchange programme introduced in order to increase the number of patients reaching their LDL cholesterol goals. Previous programmes have tended to focus on reducing the medication costs. Further, they stated that the programme was efficient in switching patients from one treatment to another at low costs and with better clinical outcomes. In fact, the likely extent of the efficiency is unknown. It was, however, discussed in terms of the savings in hospital treatment due to the prevention of CHD and other atherosclerotic diseases.

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Other publications of related interest

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