Comparing hyperlipidemia control with daily versus twice-weekly simvastatin

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 statins to control hyperlipidaemia was examined. Patients needing treatment to manage hyperlipidaemia were given either 40 or 80 mg simvastatin twice a week. The comparator treatment was 10 or 20 mg simvastatin daily.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised veterans of the US military attending a primary care clinic at the Southern Arizona Veterans Affairs Healthcare system who were taking simvastatin, 10 or 20 mg/day. The patients had to be at least 18 years old and to have been on the daily simvastatin dosage for at least 3 months at enrolment. Patients were excluded if they had had a myocardial infarction or unstable angina in the last 6 months, or if they had taken less than 90% of their simvastatin dose in the last month. Also excluded were those with serum triglyceride levels higher than 400 mg/dL, or a low-density lipoprotein cholesterol level greater than 160 mg/dL at the initial visit. Patients who could not return for follow-up assessments for any reason were also excluded.

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

Dates to which data relate
The effectiveness and resource evidence was from 2002 to 2003. No price year was given.

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

Link between effectiveness and cost data
The same patients provided the effectiveness data and the cost data. However, the cost data were not the actual costs incurred but hypothetical costs based on the cost of the medication. The costing was carried out retrospectively.

Study sample
No power calculations were reported. There was no control group; all patients in the study received the intervention treatment and their health outcomes were compared before and after the intervention. Of the 31 patients in the study, 30 completed the follow-up questionnaire at week 12. Initially, 41 patients consented to participate but 10 patients
either withdrew voluntarily or had to be excluded due to a protocol violation.

**Study design**
This was a single-centred, before and after study in which the patients were studied before and after their medication was changed. The patients were followed up for 12 weeks.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcomes were levels of low-density and high-density lipoprotein cholesterol (LDL-C and HDL-C, respectively), total cholesterol and triglycerides. The proportion of patients reaching the LDL-C goal level was also measured. There was only one group of patients. Patient satisfaction was assessed by asking which dose regimen was the easiest to follow.

**Effectiveness results**
The LDL-C level went from 97 (standard deviation, SD=17) to 111 (SD=17) mg/dL at week 12, (p=0.001).

Total cholesterol went from 171 (SD=21) to 186 (SD=21) mg/dL at week 12, (p=0.001).

HDL-C was unchanged, initially 47 (SD=12) mg/dL and then 47 (SD=11) mg/dL at week 12.

Triglycerides went from 136 (SD=66) to 141 (SD=78) mg/dL at week 12, (p=0.262).

Three patients reported muscle soreness and two of these withdrew from the study.

One patient had a myocardial infarction at week 5 and withdrew from the study.

The proportion of patients at the LDL-C goal level was 87% at enrolment and 68% at week 12.

Forty-two per cent of the patients were indifferent about the two drug regimens, while 13% preferred the twice-weekly regimen and 45% preferred the once-daily regimen.

**Clinical conclusions**
The authors concluded that switching to a twice-weekly regimen for simvastatin did not adversely affect two thirds of the patients. Among the remaining patients, some of them had not reached their target because of the change in regimen. The increase in mean levels of LDL-C showed that the change in regimen could sometimes have an adverse affect on patient health.

**Measure of benefits used in the economic analysis**
No summary measure of benefits was produced as the authors, in effect, carried out a cost-consequences analysis.

**Direct costs**
No discounting was carried out since the costs were incurred during less than one year. Only one cost was analysed, the cost of simvastatin. This cost was obtained from the Veterans Administration. The estimated cost per patient was based on the prescribed drug regimen and not the actual cost incurred. No price year was given.

**Statistical analysis of costs**
No statistical analysis of the costs was carried out.

**Indirect Costs**
No indirect costs were calculated.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was carried out.

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

**Cost results**
The cost of the twice-weekly regimen was $2.69 to $2.94 dollars per month per patient lower than the once-daily regimen.

The costs of adverse effects were not taken into consideration.

**Synthesis of costs and benefits**
The costs and benefits were not combined as the study was, in effect, a cost-consequences analysis.

**Authors' conclusions**
The twice-weekly regimen cost less than the once-daily regimen. The authors hypothesised that the health of many patients would not suffer with the twice-weekly regimen and, therefore, if they could be targeted then it could be recommended.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator (the once-daily regimen) was justified by it being the standard treatment in many settings. You should decide if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness data were derived from a single study. The study design was appropriate for the hypothesis; as there was no comparator group of patients taking the daily regimen, it was a before and after study. The authors acknowledged that the validity of the study would have been enhanced by a prospective, appropriately powered randomised study with a comparator group of patients taking the daily regimen. Patients who withdrew from the study were not included in the results.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit, thus the health benefits are those associated with the effectiveness outcomes. The comments in the 'Validity of estimate of measure of effectiveness' field (above) therefore apply.

**Validity of estimate of costs**
>From the cost perspective adopted (i.e. the health care organisation), many cost elements were missing as the authors considered only the costs of simvastatin and not the costs of adverse events. Since adverse effects included myocardial infarction this could be a significant omission. The costs and the quantities of simvastatin were reported separately. The
resource use quantities were taken from the single study, while the prices were taken from the authors' setting. No statistical or other analyses of the quantities or prices were carried out. The price year was not reported, which will hinder cost reflation exercises. Bearing in mind these issues, the cost results should be treated with a degree of caution.

Other issues
The authors did not compare their results with those from other studies. The issue of generalisability to other settings was not addressed. The authors presented their results selectively in one aspect of the study. More specifically, they reported the percentage of patients who were satisfied with the twice-weekly regimen but not the percentage who were dissatisfied. Patients who had dropped were not included in the effectiveness results. The authors acknowledged that their conclusions need to be treated with caution given the limitations of the study. The limitations reported included the small sample size and short follow-up period.

Implications of the study
A large randomised controlled trial with a long follow-up period, which accounts for all patients recruited into the study and calculates all health care costs, is needed to evaluate the twice-weekly simvastatin regimen.

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