The cost-effectiveness of lipid lowering in patients with ischaemic heart disease: an intervention and evaluation in primary care

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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
Patients with evidence of ischaemic heart disease were identified from the computerised records held by general practitioners (GPs). The patient’s GP was then asked to confirm the diagnosis and to exclude any patients unsuitable for the lipid-lowering programme. These patients were then invited by letter to undergo a fasting lipid test. If, as a result of the test, the patient was considered to have hyperlipidaemia, a practice nurse gave them dietary advice and a diet sheet. Three months later the patients were invited to see their GP and were recommended to take a statin if they had pure hypercholesterolaemia. Patients with other categories of hyperlipidaemia were recommended for a fibrate.

The authors used a comparator group (no medication) of people suffering from osteoarthritis to control for non-drug effects on quality of life (QOL) and patient well being. There was no comparator group to assess the effects of the medication on heart disease, as the authors stated that any other treatment for hyperlipidaemia could not be defended ethically. The authors used a before-and-after approach to assess the effects on lipids, and the results of an earlier study (see Other Publications of Related Interest) to assess the effects on coronary events and deaths.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with evidence of ischaemic heart disease recorded on GPs’ records, who also satisfied the criteria for hyperlipidaemia, namely a fasting low-density lipoprotein (LDL) cholesterol of greater than 3.5 mmol/L or triglyceride level of greater than 3 mmol/L. Patients were excluded if they were currently being treated with lipid-lowering drugs, were aged older than 90 years, or if they had either terminal illness or dementia.

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

Dates to which data relate
The effectiveness data were derived from 1996. The authors also used the conclusions of the earlier effectiveness study (see Other Publications of Related Interest). The study used cost data collected in 1996, which were then extrapolated for 1996 to 2000. The price year was 1996.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was carried out on the same group of patients who provided the effectiveness data. It was unclear whether the costing was carried out prospectively or retrospectively.

Study sample
The sample size was constrained by the number of eligible patients who were willing to participate in the trial. The authors described a 'post-hoc' power calculation using GPOWER. This showed that 48 paired responses gave the study a 95% power at the 0.05 significance level to detect a change of three units in depression score, based on a standard deviation (SD) of the change in depression score of 4.1 units. The screening process initially identified 196 patients with raised lipids, of which 138 received dietary advice. Three months after this advice 116 of the patients still had raised lipid and were referred to their own GP for a consultation about lipid-lowering medication. Ninety-five of these 116 patients were willing to start lipid-lowering medication, but only 83 patients continued to take the drugs.

Study design
This was a single centre study that used a within-group comparison to assess heart disease symptoms. The authors also used the results from a published paper of a randomised controlled trial (see Other Publications of Related Interest) to assess the benefits. The authors used an indirect control group of arthritis sufferers to assess depression and QOL. Arthritis sufferers were chosen since they also suffered from a chronic condition that causes pain on exercise. The patients were assessed for heart disease symptoms at 12 months and for mood and QOL at 6 months.

Analysis of effectiveness
The primary health outcomes assessed were the LDL cholesterol and triglyceride levels, QOL (Short-Form Health Survey, SF-36) and depression scores (Hospital Anxiety and Depression Scale, HAD). The section of the study concerned with QOL and depression showed that in many respects the two groups were comparable apart from a 'borderline difference' in physical functioning and general health perception. The patients with ischaemic heart disease had higher depression scores than the control group.

Effectiveness results
After following the dietary advice, 22 patients had normal serum lipid concentrations. The mean LDL cholesterol level decreased from 5.69 to 5.12 mmol/L, (p=0.03), and the mean triglyceride concentration increased from 1.09 to 1.89 mmol/L, (p=0.39).

Among the patients (n=71) who took the lipid-lowering medication and for whom complete data were available, the mean LDL cholesterol level decreased from 5.91 to 4.66 mmol/L, (p<0.0001) and the mean triglyceride concentration decreased from 2.03 to 1.63, (p=0.001).

Out of 62 patients (65%) taking drugs whom filled in the adverse events questionnaire, 22 (34%) reported adverse effects and 12 discontinued treatment.

The QOL (SF-36) and anxiety and depression (HAD scale) showed no statistically significant difference with the control group suffering from osteoarthritis in terms of QOL. Complete data were available for 60 patients in the heart disease group and 48 in the control group. There was no statistically significant change in the median scores recorded by the SF-36 and HAD 6 months after starting medication in the lipid-lowering group.

Clinical conclusions
Dietary advice succeeded in lowering lipid levels to a satisfactory level in 22 (16%) of the patients. Among the remaining 73 patients who took the lipid-lowering medication and for whom data were available, the normal lipid level was reached in 18 (25%) of the patients. No harmful effects on QOL or depression were detected. Twenty-two (34%) of the patients who filled in the adverse events form reported adverse side effects.
Measure of benefits used in the economic analysis
The measures of benefit used were the coronary events and coronary deaths avoided. These were predicted using the results of the published paper (see Other Publications of Related Interest).

Direct costs
The costs were broken down into the quantities and costs. The costs incurred by the primary care centre were included in the analysis. These were for all medical and administrative staff time, all drug costs, and all other costs. The staff included the GP, practice manager, receptionist, secretary and nurse. The drugs used were fluvastatin, fenofibrate and simvastatin. The other costs were for postage, telephone, syringes, needles, test tubes, laboratory costs, thyroid function test, urea, electrolytes, liver function test and creatinine kinase. The costs were measured for 1996 and then extrapolated for a further 4 years. A discount rate of 6% was applied.

Statistical analysis of costs
The costs were not treated in a stochastic way.

Indirect Costs
No indirect costs were included.

Currency
UK pounds sterling (?).

Sensitivity analysis
A sensitivity analysis was not carried out.

Estimated benefits used in the economic analysis
After 5 years of treatment, the estimated benefit was the prevention of 5.5 coronary events (95% CI: 3.6 - 7.5) and 2.9 (95% CI: 1.7 - 4) coronary deaths. It was assumed that 15 patients needed to be treated for 5 years to prevent one coronary event, and that 29 patients needed to be treated for 5 years to prevent one death.

Cost results
The total cost of running the programme for one year was 27,019. After extrapolation to calculate the costs for 5 years, and then discounting by 6%, the total cost of the programme was 94,257.

Synthesis of costs and benefits
The cost per coronary event prevented was 17,138 (95% CI: 12,568 - 26,183) and the cost per coronary death prevented was 32,502 (95% CI: 23,564 - 55,445).

Authors' conclusions
The study showed that a programme of prescribing lipid-lowering drugs was feasible in a primary care setting in the UK and that there were no associated adverse effects on mood and quality of life (QOL). The authors used the results of an earlier study (see Other Publications of Related Interest) to calculate the cost per coronary event and cost per coronary death avoided. However, they pointed out that their results, as far as lipid lowering was concerned, did not show such a large effect as the Swedish study.

CRD COMMENTARY - Selection of comparators

NHS Economic Evaluation Database (NHS EED)
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The main drawback with the study design was that there was no comparator group of patients who underwent no screening programme, no lipid testing, no dietary advice and no recommendation on lipid-lowering medication. The authors explained that they did not consider it ethical to recruit participants into a trial for lipid lowering and not offer them lipid-lowering medication. The choice of the comparator (patients with osteoarthritis) used to assess depression and QOL, was justified by arguing that both groups of patients suffered similar limitations on their lives and had similar psychological profiles. However, the baseline data suggested higher depression scores among the heart patients.

**Validity of estimate of measure of effectiveness**
The drawback in the study design meant that the results on the effectiveness of lipid-lowering medication might be biased, as the authors did not develop a model that could account for all determinants of lipid levels. The authors used their own data to assess the outcomes measuring QOL, depression and the effects of lipid-lowering medication.

**Validity of estimate of measure of benefit**
After deriving the effectiveness results, the authors derived a measure of benefit making two series of assumptions. They extrapolated the 12-month results on lipid lowering to 5 years without any justification. They then used the results from the Swedish study to estimate the coronary events and deaths avoided for 5 years. However, since they pointed out differences between the patients in their study and those in the Swedish study, the validity of using the Swedish results is questionable. The UK study had less effect than the Swedish study on lowering lipids. The authors listed some factors in the UK patients that would imply either a higher or lower coronary risk. In conclusion, the measure of benefit was of doubtful validity.

**Validity of estimate of costs**
All the categories of direct cost relevant to the first year of running the programme were included, but the indirect costs were not. The costs that were included were clearly broken down into prices and quantities. The authors obtained the price information from a combination of published sources and local sources. The price year was 1996. The quantity information was derived from the study. The authors used a discount rate of 6%, which they did not justify. This approach reduced the estimated costs of the programme in comparison with using a more conventional rate of 3%.

The authors did not carry out a sensitivity or statistical analysis of the prices or quantities. This means that the generalisability of the results to other settings is uncertain.

**Other issues**
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability was not addressed, but the clear breakdown of the costs would help decision-makers in other settings.

The authors did not present their results selectively, but their conclusions did not completely reflect the scope of the analysis. The side effects and withdrawal rate and their possible effects on the reliability of the results were not discussed in detail. The data were incomplete, which may have affected the reliability of the conclusions. The authors realised that the use of Swedish data may have been inappropriate.

**Implications of the study**
The results suggested that the programme of prescribing lipid-lowering medication was feasible and acceptable within primary care. However, the ongoing cost implications should be considered in view of the costs and benefits of alternative interventions.

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Other publications of related interest

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