Lipid-lowering efficacy, safety, and costs of a large-scale therapeutic statin formulary conversion program


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 implementation of a therapeutic-interchange clinic for hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) was examined. The role of this clinic was to switch more than 1000 patients taking five statins at 17 dosages to two statins (cerivastatin and simvastatin), after the Department of Defence’s Pharmacoeconomic Centre mandated that all military treatment facilities limit the statins on the formulary to simvastatin and cerivastatin. Of these two statins, cerivastatin was listed as the preferred agent. The goal was to use this agent in 60 to 65% of all patients receiving a statin. Patients receiving cerivastatin sodium 0.2 or 0.3 mg/day, pravastatin sodium (10 to 80 mg/day), simvastatin (10 or 20 mg/day), fluvastatin sodium (20 or 40 mg/day), or atorvastatin calcium (10 mg/day) were switched to cerivastatin sodium 0.4 mg/day. Patients taking atorvastatin calcium (20 mg/day) or simvastatin (40 mg/day) were switched to cerivastatin sodium 0.8 mg/day. The clinic had several goals. For example, facilitating the rapid switching of the patient to these two statins, maximising the use of the preferred agent, maintaining or improving lipid control, monitoring safety and educating the patients about their treatment.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients of the Walter Reed Army Medical Center (WRAMC; Washington DC, USA) who were affected by the formulary change.

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

Dates to which data relate
The study was carried out between January and April 2000. The price year was not reported.

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 study.
Study sample
No power calculations to determine the sample size were reported and no specific sample size was planned. The patients were identified from a computerised search of all active prescriptions for statins filled at the WRAMC over 120 days. Letters were mailed to each patient on three staggered dates (according to the date of the last refill). The letter briefly explained the rationale for, and the process of, the conversion and asked patients to report to the clinic area instead of the outpatient pharmacy. Between January and April 2000 the therapeutic interchange clinic saw 1,356 patients. Of these, 942 agreed to have the efficacy and safety of their therapy monitored by the clinic, while the remainder chose to be monitored by their primary care provider. Of the 942 patients agreeing to be monitored in the clinic, 558 (59.2%) were males and 384 (40.8%) were females. The mean age for these patients was 68 (+/- 10) years.

Study design
The study was a within-group comparison study in one group of patients that was carried out in a single centre. The duration of follow-up was 6 weeks after the conversion date. Patient satisfaction was recorded once the patients met their goal low-density lipoprotein (LDL) cholesterol level. The authors reported no loss to follow-up.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The primary health outcomes used in the analysis were:

- the number of patients treated with cerivastatin and simvastatin;
- LDL and high-density lipoprotein (HDL) cholesterol levels;
- adverse events resulting in drug discontinuation;
- patient satisfaction with the clinic (from 755 randomly surveyed patients); and
- physician satisfaction with the clinic.

Statin conversion was based on an algorithm. There was a 72-hour washout period for all patients who had been treated with atorvastatin because of concerns about the longer half-life of this agent. LDL cholesterol was measured in non-fasting patients using a direct assay. Efficacy was assessed on the basis of the patients' serum LDL cholesterol concentrations. Compliance was determined with a computerised tracking system that included the patients' information, date of enrolment, medications, LDL cholesterol goal, and anticipated date of follow-up laboratory tests.

Effectiveness results
Before the formulary change, the most commonly prescribed statins were atorvastatin (44.0%) and pravastatin (42.0%). After the conversion policy, most of the patients were treated with cerivastatin sodium 0.4 mg (82.4%) or 0.8 mg (13.3%). The remaining patients (4.3%) received simvastatin 80 mg. Thus, 95.7% of the patients were treated with cerivastatin, far exceeding the goal of 65%.

Before the conversion policy, the patient's mean cholesterol concentration was 115 (+/- 29) mg/dL; 64.8% of the patients were at or below their target LDL cholesterol level. Six weeks after the conversion, the mean LDL concentration was reduced to 106 (+/- 25) mg/dL, a reduction of 9 mg/dL, (p<0.001), with a commensurate increase in the percentage of patients reaching their goal (74.5%, p<0.001).

The conversion policy led to significantly higher HDL cholesterol concentrations, increasing from 50 (+/- 14) mg/dL to 51 (+/ 14) mg/dL, (p<0.001).

Adverse events resulting in drug discontinuation occurred in 28 (3%) patients. Fifteen patients reported myalgia, while 5 patients who had been treated with atorvastatin calcium had definite myositis.

In terms of patient satisfaction, 81.7% were "extremely satisfied" and 11.9% were "very satisfied". The patients
overwhelmingly responded that they had been educated about the therapeutic interchange process (94.8%) and that they had received their medication (99.9%) and their laboratory test results (95.9%). However, only 68.2% knew the name of their medication and only 27.9% knew their LDL cholesterol goal.

Of 221 physician respondents to a separate pharmacy survey, 36% were satisfied with the clinic, 52% had a neutral opinion and 12% were dissatisfied.

**Clinical conclusions**

The therapeutic interchange clinic was an effective way of switching a large number of patients to an alternative statin therapy.

**Modelling**

A decision model was developed for the cost analysis only. The probabilities of adverse events, complaints and drug toleration were derived from the clinical study.

**Measure of benefits used in the economic analysis**

No summary measure of benefit was derived. In effect, the study was a cost-consequences analysis.

**Direct costs**

The unit costs were reported separately. The direct costs included were those of the health service. These were for setting up the clinic, personnel, mailing, drugs, administration, laboratory monitoring and adverse events. Direct cost data came from the clinical effectiveness study. Discounting was irrelevant since all the costs were incurred during 4 months. Hence, all the costs were left undiscounted. The study reported the average costs. The price year was not reported.

**Statistical analysis of costs**

The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**

The indirect costs were not included in the study.

**Currency**

US dollars ($).

**Sensitivity analysis**

No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**

See the "Effectiveness Results" section.

**Cost results**

The clinic cost a total of $199,760, including $189,000 for personnel costs and $10,760 for mailing costs. When considering all major cost components (including drugs, administration, laboratory monitoring and adverse events), the conversion policy saved an average of $115 per patient in the first year.
Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
The therapeutic interchange clinic at a large military medical centre provided an efficient means of switching a large number of patients to alternative statin therapy, of monitoring the outcomes, and of individualising patient care.

CRD COMMENTARY - Selection of comparators
The authors chose no conversion policy as the comparator. You should decide if the availability of five different types of statin represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The basis of the analysis was a within-group comparison study in one group of patients. This was appropriate for the study question, as the authors intended to assess the impact of the conversion policy and the interchange clinic by comparing the before and after outcomes. Since outcomes of the conversion policy were measured 4 weeks after, factors such as improved medical trends, better health technologies and other such trends taking place over time, which have the potential of biasing results derived from before-and-after studies, may not have affected the authors' results. The study sample was representative of the study population. Further, appropriate statistical techniques were undertaken. These tested for any significant outcomes before and after the conversion policy. No information on the loss to follow-up was provided, so it was unclear whether all 942 patients completed the study.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. In effect, the analysis was a cost-consequences analysis.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. In addition, it would appear that for each cost category all the relevant costs have been included. The unit costs were reported but the quantities, which were derived from the decision model, were not. The source of the unit costs was also reported. The authors did not report the results of any statistical tests or sensitivity analyses that may have been performed in this study. Discounting was unnecessary since all the costs were incurred during 4 months. Due to the lack of information on the sources used to derive the costs, it was not possible to determine whether charges were used to proxy prices. The dates to which the prices related were not reported, which will hamper any future reflation exercises.

Other issues
The authors made no appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not addressed, and was hampered by the lack of detail in the costs. The authors do not appear to have presented their results selectively. The authors' conclusions reflected the scope of the analysis. The authors reported no limitations of their study. However, they noted that cerivastatin was withdrawn both from the American and European markets one year after the interchange policy, because of multiple reports of rhabdomyolysis.

Implications of the study
The authors reported that, even though a therapeutic interchange clinic costs money to implement, it could prove very cost-effective when a pronounced cost-differential exists between formulary agents. However, the cost perspective (i.e. that of the health care system, patient or others) should be carefully considered. A priori cost and saving thresholds need to be set to determine the fiscal merits of the programme.
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Other publications of related interest


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