Cost-effectiveness of sevelamer versus calcium carbonate plus atorvastatin to reduce LDL in patients with chronic renal insufficiency with dyslipidemia and hyperphosphatemia

Brophy D F, Wallace J F, Kennedy D T, Gehr T W, Holdford D A

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
Sevelamer (403mg, two capsules three times per day with meals) was compared with calcium carbonate (1g (400mg elemental calcium) three times per day with meals) plus atorvastatin calcium (10mg once daily) in the reduction of lipoprotein (LDL) in the treatment of dyslipidemia and hyperphosphatemia for patients with chronic renal insufficiency (CRI).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with CRI, but no cardiovascular disease, with moderate hyperphosphatemia (plasma phosphorus 6.0-7.5 mg/dl) and a borderline high-risk low-density LDL concentration (131-160 mg/dl) before dialysis.

Setting
The setting was the community and primary care; the economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were taken from studies published between 1997 and 1999. Cost data were taken from two sources published in 2000. The price year was 2000.

Source of effectiveness data
Effectiveness estimates were taken from a review/synthesis of previously completed studies.

Modelling
A one-year decision analytic model was used to determine the cost-effectiveness of sevelamer versus calcium carbonate plus atorvastatin for treatment of dyslipidemia. The model was based on clinical practice and guidelines of the National Cholesterol Education Program Adult Treatment Panel.

Outcomes assessed in the review
The review assessed the probability of achieving a 35% LDL reduction for the intervention and comparator.
Study designs and other criteria for inclusion in the review
The review included four non-randomised, uncontrolled trials and three randomised controlled trials on sevelamer and four trials on atorvastatin.

Sources searched to identify primary studies
MEDLINE was searched from January 1960 to February 2000.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Eleven primary studies were included.

Methods of combining primary studies
The method used to combine the results of primary studies was not reported.

Investigation of differences between primary studies
Not stated.

Results of the review
The probability of achieving a 35% LDL reduction was 0.502 with sevelamer and 0.742 with calcium plus atorvastatin.

Methods used to derive estimates of effectiveness
Authors’ assumptions about effectiveness were also used.

Estimates of effectiveness and key assumptions
The authors assumed that:
patients achieved a 35% LDL reduction from baseline after 12 weeks of treatment;
patients would receive one week of free drug samples to determine tolerability;
compliance rates were identical between groups;
outpatient monitoring of plasma calcium and phosphorus concentrations was performed at least four times a year;
liver function tests were performed at baseline, four weeks, three months and six months after starting atorvastatin therapy.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was the number of patients achieving a 35% LDL reduction.
Direct costs
Direct costs were not discounted due to the short time horizon of the study (one year). Quantities and costs were reported separately. Direct costs related to drug and monitoring costs. The quantity/cost boundary adopted was that of a third-party payer. Drug costs were derived from the 2000 Drug Topics Red Book of average wholesale prices. The costs of visits to the physician and laboratory monitoring costs were taken from the 2000 Medicare Fee Schedule. The price year was 2000. The costs for adverse events were not considered. Two physician office visits were carried out for monitoring, 4 and 12 weeks after drug therapy.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analysis was performed on the cost of sevelamer. Two-way sensitivity analysis was performed to test the sensitivity of the model to changes in the probability of a patient achieving the 35% LDL reduction.

Estimated benefits used in the economic analysis
The probability of achieving a 35% LDL reduction was 0.742 with calcium plus atorvastatin and 0.502 with sevelamer.

Cost results
Total costs were $1,029.60 for calcium plus atorvastatin and $1,579.70 for sevelamer.

Synthesis of costs and benefits
Calcium carbonate plus atorvastatin was more effective and less costly than sevelamer. A 50% reduction in the price of sevelamer made sevelamer less expensive but still less cost-effective than combination therapy. A two-way sensitivity analysis on the probability of achieving a 35% LDL reduction resulted in combination therapy remaining more cost-effective.

Authors' conclusions
The authors concluded that calcium carbonate plus atorvastatin calcium was more cost-effective than sevelamer for the treatment of dyslipidemia in predialysis patients with CRI.

CRD COMMENTARY - Selection of comparators
The justification for the comparator was that it represented traditional first-line therapy. You, as a user of this database, should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of effectiveness
The validity of the effectiveness results was based on a review of the literature plus authors' assumptions. The authors did search MEDLINE to retrieve studies but more details about the criteria for selecting studies and the methods of combining estimates from primary studies could also have been provided. To increase the validity of the results,
however, the authors carried out two-way sensitivity analysis to test the sensitivity of the model to changes in the probability of a patient achieving the 35% LDL reduction. Pooled data for sevelamer and atorvastatin were from different patient populations and were evaluated at different time points, which may reduce the consistency of the results. It is also worth noting that atorvastatin data were obtained from studies that evaluated hypercholesterolemic patients without concomitant renal dysfunction or diabetes. The authors noted that such data might confound a true comparison between sevelamer and atorvastatin.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis through the modelling that was undertaken. The morbidity and quality of life of patients who experienced rhabdomyolysis and myositis associated with atorvastatin were not considered, although they were relevant to the patient domain studied. The model did not address the issue of hypercalcemia in patients with CRI, which may clearly be an issue in the comparator technology.

**Validity of estimate of costs**
Good features of the cost analysis were that all relevant direct cost categories were included, quantities and costs were reported separately, sensitivity analyses were performed on the cost of sevelamer, and the price year was reported. This makes it possible to replicate the results in other settings. However, indirect costs were not considered although this would have been appropriate for the perspective analysed (third party payer). Also, the costs of adverse drug reactions were not included although they would be relevant for a wider perspective.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies, but did not address the issue of the generalisability of the results to other settings. The authors do not seem to have presented their results selectively. The study considered patients with CRI and hyperphosphatemia and this was reflected in the authors’ conclusions. The authors did not evaluate the cost-effectiveness of other agents such as calcium acetate, simvastatin, or lovastatin. Patients were switched from sevelamer to combination therapy and vice versa if they did not tolerate the first therapy. It was unclear how patients who switched therapy were dealt with in the economic analysis (intention to treat or treatment completers only). The authors noted that sevelamer is more likely to be used to treat hyperphosphatemia in patients with ESRD receiving haemodialysis.

**Implications of the study**
Within the caveats described above regarding the chosen methodology, calcium carbonate plus atorvastatin calcium is more cost-effective than sevelamer for the treatment of dyslipidemia in predialysis patients with CRI. However, long-term studies that assess LDL-lowering effects of sevelamer are needed.

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None stated.

**Bibliographic details**

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Costs; Heptanoic Acids /economics /therapeutic use; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /economics /therapeutic use; Hyperlipidemias /blood /etiology /drug therapy /economics; Kidney Failure, Chronic /complications /blood /economics; Lipoproteins, LDL /blood; Phosphates /blood; Polyethylenes /economics /therapeutic use; Pyrroles /economics /therapeutic use

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