Economic evaluation of high-dose (80 mg/day) atorvastatin treatment compared with standard-dose (20 mg/day to 40 mg/day) simvastatin treatment in Canada based on the Incremental Decrease in End-Points Through Aggressive Lipid-Lowering (IDEAL) trial

Wagner M, Lindgren P, Merikle E, Goetghebeur M, Jonsson B

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.

CRD summary
The objective was to assess the cost-effectiveness of high-dose atorvastatin versus standard-dose simvastatin for patients with a history of myocardial infarction. The authors concluded that, from a Canadian societal perspective, high-dose atorvastatin was cost-effective for these patients. The methods seem to have been appropriate and were clearly and transparently reported. The conclusions reached by the authors appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of high-dose atorvastatin versus standard-dose simvastatin for patients with a history of myocardial infarction (MI).

Interventions
High-dose atorvastatin, at 80mg per day, was compared with standard-dose simvastatin, at 20 to 40mg per day.

Location/setting
Canada/primary care.

Methods
Analytical approach:
A within-trial analysis was conducted, with the efficacy, resource use, and productivity losses all estimated from one clinical trial. The time horizon was the follow-up period, which was a median of 4.8 years. A Markov model was also constructed to simulate the ongoing risks of MI, revascularisation, and death, over a lifetime horizon. The data were from a variety of sources, based on a model used in Denmark, Norway, and Sweden (Lindgren, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details). The cycle length was one year and all patients were switched to simvastatin after five years. The age of the cohort at the start of the model was 62 years, the proportion of women was 30%, the proportion of participants with diabetes was 25%, and the baseline low-density lipoprotein cholesterol (LDL-C) level was 2.75 mmol/L (106 mg/dL). The authors stated that a Canadian societal perspective was taken for both analyses.

Effectiveness data:
The effectiveness data were from a prospective, randomised, open-label, blinded-end-point trial, called the Incremental Decrease in End-Points Through Aggressive Lipid-Lowering (IDEAL) trial. This followed-up 8,888 patients with a previous MI, who were from Northern Europe, over a median of 4.8 years. For the within-trial analysis, the end point-related events, such as stroke, heart failure, and cardiac transplant, from the clinical trial, were aggregated to produce the mean number of events per patient, for each arm. For the Markov model, the baseline risks of MI, revascularisation, and death with simvastatin were estimated by applying a Weibull regression calculation to the data from patients who had experienced the relevant event with simvastatin. The relative risk ratio of MI and revascularisation, with atorvastatin compared with simvastatin, were based on the trial and a published paper. It was assumed that the risk of death was the same for patients in the health state after revascularisation as in the health state at risk and it was assumed to be the same in both treatment arms. The main effectiveness outcome was the LDL-C level.
Monetary benefit and utility valuations:
The utility values for the Markov model were based on a published Swedish population survey that used the European Quality of life (EQ-5D) questionnaire. They were adjusted using a utility decrement from a cross-sectional survey, using the EQ-5D, of patients hospitalised at coronary care units in Sweden. An additional decrement was applied after an MI or a revascularisation. The values were assumed to return to at-risk levels in the second year after an event.

Measure of benefit:
In the within-trial analysis, the primary measure of benefit was the number of events avoided (including stroke, transient ischaemic attack, nonfatal MI, heart failure, angina pectoris, cardiac arrest, percutaneous coronary intervention, coronary artery bypass graft, cardiac transplant, other cardiothoracic procedures, and other vascular procedures) and these were not discounted. In the Markov model, the primary measure of benefit was quality-adjusted life-years (QALYs) and the secondary measure of benefit was life-years gained (LYG); both of these were discounted at a rate of 5% per annum.

Cost data:
The cost categories included hospitalisation, medications, and productivity lost, and these were collected from the IDEAL trial. In the within-trial analysis, the resource use and employment status were based on patient-level data collected during the trial. The unit costs were from standard sources. The cost of cardiothoracic procedures was assumed to be 1.39 times the cost of a bypass graft, while the cost of other vascular procedures was assumed to be the same as a percutaneous coronary intervention. These costs were not discounted.

In the Markov model, the costs for the at-risk health state included all the costs of a MI or revascularisation, while productivity losses were assumed to be zero. The resource use and productivity losses (compared with baseline) for the post-MI and post-revascularisation health states were based on data from the trial. The annual costs were assumed to return to those for the at-risk health state in the fourth year following an MI and the fifth year following a revascularisation; the cost of the event itself was included in the first-year after the event. These costs were discounted at a rate of 5% per annum.

The costs were reported in Canadian dollars (CAD) and the price year was 2006. Any cost adjustments were based on the Health and Personal Care component of the Consumer Price Index.

Analysis of uncertainty:
The uncertainty was explored using one-way, threshold, and probabilistic sensitivity analyses. In the within-trial analysis, the parameter uncertainty was explored, using threshold analysis of the acquisition costs of simvastatin, when the incremental costs of the two treatment arms were equal. Bootstrapping of the patient-level data, using angular transformation, was also conducted, with 1,000 samples, to produce confidence intervals. In the Markov model, the parameter uncertainty was explored using one-way sensitivity analysis and non-parametric bootstrapping of the patient-level data, with 1,000 simulations. The results were presented on a cost-effectiveness plane and a cost-effectiveness acceptability curve.

Results
From a societal perspective, the within-trial analysis showed that atorvastatin was more effective and less costly than simvastatin, dominant (95% CI dominant to CAD 24,562). When only the direct costs were considered, atorvastatin had an incremental cost per event avoided of CAD 4,844 (95% CI 359 to 14,743).

Threshold analysis indicated that the total incremental cost per event avoided was zero when the cost of simvastatin was reduced to CAD 1.0489 per pill (CAD 1.10 in the base case). When the cost of simvastatin was reduced to zero, the incremental cost of atorvastatin was CAD 16,843 per event avoided.

The Markov model showed that the incremental cost of atorvastatin over simvastatin was CAD 17,573 per LYG or CAD 26,795 per QALY. When only the direct costs were considered, it was CAD 25,469 per LYG or CAD 38,834 per QALY.

The results were most sensitive to the baseline age, ranging from CAD 8,931 per QALY for a patient aged 50 years to CAD 35,686 per QALY for a patient aged 64 years. They were also sensitive to the baseline LDL-C level, rising to CAD 30,337 per QALY with a level of 2.38 mmol/L, and the proportion of patients with diabetes, ranging from CAD 18,733 per QALY when all patients had diabetes to CAD 30,428 per QALY when none had diabetes. The probabilistic
sensitivity analysis showed that atorvastatin was the most cost-effective strategy in 78% of simulations at a willingness-to-pay of CAD 50,000 per QALY, 87% at CAD 70,000 per QALY, and 95% at CAD 120,000 per QALY.

**Authors’ conclusions**
The authors concluded that from a Canadian societal perspective, high-dose atorvastatin was cost-effective compared with standard-dose simvastatin in patients with a previous MI.

**CRD commentary**

Interventions:
The interventions were well described and relevant to the primary care setting, but it was not clear if all the options were considered and the authors did not state which statin was the usual care in Canada. These comparators might be relevant in other settings.

Effectiveness/benefits:
The estimates of treatment efficacy were well reported in tables and they were from a randomised controlled trial. There was no indication that a systematic review was conducted, so it is unclear whether all the relevant data were assessed. Adverse events were excluded and a justification was given, but a significant increase in discontinuation of atorvastatin, compared with simvastatin, due to adverse events, might have affected the results. The health state utilities were presented in a table and the methods used to measure them were described.

Costs:
The costs for each analysis (within trial and Markov model) were adequately reported and the cost categories were relevant to the perspective. All the adjustments made to the cost data were reported and were appropriate.

Analysis and results:
The two analyses were both appropriate for this disease and the methods were generally well reported. The results were reported as the cost per event, cost per LYG, and cost per QALY, which was appropriate and these should be generalisable to other settings. The results, including those of the uncertainty analyses, were well reported. A diagram of the Markov model was given. The authors discussed the limitations of their analyses, such as the exclusion of adverse events.

Concluding remarks:
The methods seem to have been appropriate and were clearly and transparently reported. The conclusions reached by the authors appear to be appropriate.

**Funding**
Funded by Pfizer Inc.

**Bibliographic details**
Wagner M, Lindgren P, Merikle E, Goetghebeur M, Jonsson B. Economic evaluation of high-dose (80 mg/day) atorvastatin treatment compared with standard-dose (20 mg/day to 40 mg/day) simvastatin treatment in Canada based on the Incremental Decrease in End-Points Through Aggressive Lipid-Lowering (IDEAL) trial. Canadian Journal of Cardiology 2009; 25(11): e362-e369

**PubMedID**
19898698

**Original Paper URL**
http://www.pulsus.com/journals/abstract.jsp?CurrPg=abstract&jnlKy=1&atlKy=9139&isuKy=883&isArt=t&fromfold=

**Other publications of related interest**
Lindgren P, Graff J, Olsson AG, Pedersen TJ, Jonsson B. Cost-effectiveness of high-dose atorvastatin compared with

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Oral; Aged; Aged, 80 and over; Atorvastatin Calcium; Canada; Cardiovascular Diseases /drug therapy /mortality /prevention & control; Confidence Intervals; Cost of Illness; Cost-Benefit Analysis; Dose-Response Relationship, Drug; Drug Administration Schedule; Female; Follow-Up Studies; Health Care Costs; Heptanoic Acids /administration & dosage /economics; Hospitalization /economics; Humans; Hyperlipidemias /drug therapy; Hypolipidemic Agents /administration & dosage /economics; Male; Markov Chains; Middle Aged; Myocardial Infarction /diagnosis /drug therapy /mortality; Probability; Pyrroles /administration & dosage /economics; Risk Assessment; Simvastatin /administration & dosage /economics; Survival Rate; Treatment Outcome

**AccessionNumber**
22010000319

**Date bibliographic record published**
04/08/2010

**Date abstract record published**
24/11/2010