The economic consequences of non-adherence to lipid-lowering therapy: results from the Anglo-Scandinavian-Cardiac Outcomes Trial

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
This study assessed the costs and health outcomes of different levels of adherence to lipid-lowering therapy for the treatment of patients with hypertension. The authors concluded that high adherence to atorvastatin therapy was likely to significantly reduce cardiac events, compared with low adherence, and measures to improve adherence should be investigated. There were limitations in the transparency of the modelled estimates, costing methods, and results, which make it difficult to assess the conclusions.

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

Study objective
The aim was to assess the costs and health outcomes of varying adherence to lipid-lowering therapy for the treatment of patients with hypertension. The population was a hypothetical cohort of men and women, aged between 40 and 79 years, with hypertension and at least three more cardiovascular risk factors.

Interventions
Low adherence to statin therapy, defined as less than 50% of days covered, was compared with high adherence, defined as more than 80% of days covered. Patients received amlodipine-based therapy plus atorvastatin antihypertensive therapy.

Location/setting
Sweden/out-patient.

Methods
Analytical approach:
A Markov model was used to synthesise the published data from various sources, including a key randomised controlled trial. The time horizon was the patient’s lifetime and the authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The effectiveness data were primarily from the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT, Sever, et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details). This was a multicentre randomised trial. The health outcomes, for reduced adherence with amlodipine-based therapy plus atorvastatin, included a large range of cardiovascular events and procedures, such as myocardial infarction, stroke, heart failure, and stable or unstable angina. The main clinical effectiveness estimate was the adherence level. The impact of this on the population was estimated using two statistical models, Cox proportional hazards and Poisson regression, to produce the transition probabilities for the model.

Monetary benefit and utility valuations:
The health state values were from a published study on ASCOT patients, which used the European Quality of life (EQ-5D) questionnaire and UK tariffs (Dolan, et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details).

Measure of benefit:
The measures of benefit were life-years saved and quality-adjusted life-years (QALYs). Discounting was applied at an annual rate of 3.5%.

Cost data:
The direct medical costs included the resources used after cardiac events and the medications. The costs were based on those incurred during the ASCOT. They were discounted at 3.5% and reported in 2007 UK pounds sterling (£).

Analysis of uncertainty:
One-way sensitivity analyses were undertaken on the key parameters and a probabilistic sensitivity analysis was performed. Bootstrapping of the patient-level data was used for the transition probabilities, costs, and utility weights. The results were presented in a cost-effectiveness scatter plot of 1,000 replications and a tornado diagram.

Results
The results showed that, with high adherence, a first event was avoided in 100 treated patients and 10% of the treatment costs were offset by the cardiac events avoided. The total discounted costs were £1,689 with high adherence and £1,323 with low adherence. High adherence was associated with mean QALYs of 8.13 compared with 8.11 QALYs for low adherence.

In the base case, the incremental cost per QALY gained with high adherence was £19,000, compared with low adherence.

The results were most sensitive to the relative risk of cardiac events associated with high adherence and the drug costs with low adherence. The cost-effectiveness scatter plot showed that the incremental QALYs for high over low adherence were virtually all positive, and were within the range from -0.01 to 0.09 and the incremental costs were within the range from zero to £500.

Authors’ conclusions
The authors concluded that high adherence to atorvastatin lipid-lowering therapy was likely to significantly reduce cardiac events. They recommended that measures to improve adherence should be evaluated for their cost-effectiveness.

CRD commentary
Interventions:
The interventions appear to have been appropriate comparators and the population was well described. The authors provided a brief description of the statin therapy, but the dose and frequency were not reported. These details should be available in the original trial publications.

Effectiveness/benefits:
The key effectiveness parameters were from a large multicentre randomised controlled trial, which should have provided robust clinical estimates. A systematic review was not reported making it difficult to assess if all the best available evidence was used. The effectiveness and health state transition estimates and the ranges tested were not reported. The benefit measures were appropriate and the utility values were measured from the patients with hypertension who supplied the clinical event data. The values were derived using a well known and valid utility tool (EQ-5D) and the benefits were appropriately discounted.

Costs:
The details of the resource types, their values, and the unit costs were not provided, but should be available in another publication (Lindgren, et al. 2009, see ‘Other Publications of Related Interest’ below for bibliographic details). The costs appear to have been appropriately discounted and adjusted for inflation.

Analysis and results:
The model and its health state transitions were briefly presented, but its structure and any validation processes were not. These should be available in the other publication (Lindgren, et al. 2009), which should be consulted to assess the model's validity. Similarly, the values for the costs, resource use, utilities, and probabilities, were not provided. The
incremental costs and effects were reported separately, but the exact incremental cost per QALY ratio was not given and the ranges were only reported in a scatter plot.

Concluding remarks:
The study was not well reported. There were limitations to the transparency of the modelled estimates, costing methods, and results, but the analytic methods appear to have been appropriate. This limited reporting makes it difficult to assess the conclusions reached by the authors.

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