A cost-utility analysis of clopidogrel in patients with non-ST-segment-elevation acute coronary syndromes in the UK


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 study examined 1-year of treatment with 75 mg/day clopidogrel (with a 300-mg loading dose), an adenosine diphosphate receptor antagonist, in the treatment of non-ST-segment-elevation acute coronary syndrome (ACS).

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The hypothetical study population comprised patients within 24 hours of the onset of non-ST-segment-elevation ACS.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data related to 2000 to 2001, while the resource use data related to 2000. The price year was reported to be 2002.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was not undertaken on the same patient sample as that used in the effectiveness study. The authors stated that the baseline event rates and revascularisations obtained in the international study used to derive the relative risks (RRs) of clopidogrel compared with ASA were not representative of a UK patient population.

Study sample
Readers interested in further detail about the effectiveness study are referred to the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) Study (CURE Study Investigators 2001, see 'Other Publications of Related Interest' below for bibliographic details). The trial involved 12,562 patients.

Study design
The study was an international, multi-centre, randomised controlled trial.

**Analysis of effectiveness**
The primary health outcome was the composite end point of vascular death, nonfatal MI or stroke. For the purposes of the economic evaluation, the separate RRs of each end point were used.

**Effectiveness results**
The RR of nonfatal MI for clopidogrel compared with ASA was 0.71 (95% confidence interval, CI: 0.6 to 0.84).
The RR of nonfatal stroke for clopidogrel compared with ASA was 0.73 (95% CI: 0.5 to 1.09).
The RR of vascular death for clopidogrel compared with ASA was 0.93 (95% CI: 0.8 to 1.08).

**Clinical conclusions**
Clopidogrel was found to be associated with a significant reduction in the primary composite end point compared with ASA, (p<0.001).

**Modelling**
A decision tree and Markov model were used to estimate the cost-effectiveness of clopidogrel compared with ASA over a lifetime horizon. The decision tree covered the 1-year treatment period, during which time patients could experience acute percutaneous coronary intervention (PCI), acute coronary artery bypass graft (CABG), subsequent repeat revascularisations, myocardial infarction (MI), stroke, death or no event. At the end of the 1-year treatment period, all patients were assumed to receive ASA and a long-term Markov model was used to describe the annual probability of MI, stroke and death. The Markov model was run for 34 years using a hypothetical patient cohort aged 66 years. The baseline event rates in the model were informed by an alternative study to the one from which the effectiveness data were derived.

**Measure of benefits used in the economic analysis**
The measure of health benefits used was the quality-adjusted life-years (QALYs) gained. The utility values used for health states in the model were derived from published studies.

**Direct costs**
The study included direct costs to the UK health service. These covered the costs of medication, revascularisation, treatment for major bleeding events, ongoing hospital resource use costs by patients with ACS who were event-free and who experience MI, and acute care, ambulatory and non-acute care costs in the first year after stroke. The unit costs were reported separately. Their estimation was based on national pricing lists and databases. Where published estimates of cost were not available, expert opinion was used. A discount rate of 6% per annum was applied to the costs. The study reported the average costs.

**Statistical analysis of costs**
Individual sampled data for the costs were not available.

**Indirect Costs**
The indirect costs were not included in the analysis, which was appropriate given the perspective adopted.

**Currency**
Sensitivity analysis
The uncertainty around the mean cost of revascularisation was characterised using a triangular distribution based on the reported interquartile ranges. The uncertainty around the mean cost of treating bleeding events was characterised using a triangular distribution based on a range of 75 to 150% of the mean cost. The uncertainty around the annual costs of ACS patients who were event-free, and those who experience an MI, was characterised using a log-normal distribution based on the reported standard errors. A full probabilistic sensitivity analysis was conducted to characterise the uncertainty in the model results. One-way sensitivity analyses were used to test the robustness of the model results to modelling assumptions and variability in the data.

Estimated benefits used in the economic analysis
Twelve months' treatment with clopidogrel in addition to standard therapy for 1,000 patients with non-ST-segment-elevation ACS was estimated to result in 7,960.4 QALYs over a lifetime horizon, compared with a gain of 7,902.8 QALYs for treatment with ASA alone.

A discount rate of 1.5% was applied to the health outcomes. Treatment side effects were accounted for in the number of major bleeding events.

Cost results
Twelve months' treatment with clopidogrel in addition to standard therapy for 1,000 patients with non-ST-segment-elevation ACS was estimated to cost 11.756 million over a lifetime horizon, compared with 11.353 million for treatment with ASA alone. A discount rate of 6% per annum was applied to the costs.

Synthesis of costs and benefits
The costs and benefits were combined to calculate the cost per QALY gained.

The addition of 12 months' clopidogrel to standard care was estimated to cost 7,365 per QALY gained, compared with ASA, in a cohort of 1,000 patients with non-ST-segment-elevation ACS.

The results were most sensitive to a one-way sensitivity analysis that varied the RR of vascular death to the upper 95% CI, in which case clopidogrel was dominated by standard therapy.

The probabilistic sensitivity analysis indicated that clopidogrel had an 80% probability of being cost-effective for a decision threshold of 30,000 per QALY.

Authors' conclusions
The adoption of clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome (ACS) in the UK is likely to be cost-effective.

CRD COMMENTARY - Selection of comparators
The comparator was selected to represent current practice in the study setting. However, the dose of ASA provided in the effectiveness study was higher than that typically prescribed in the UK. You must decide whether the treatment patterns described in this study are representative of treatment in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a single study. The study was a randomised controlled trial, which was an appropriate study design for the study question. The analysis of effectiveness appears to have been handled credibly.
However, the dose of ASA used and the rates of revascularisation were not typical of the UK setting. The authors stated that their assumption that the RRs estimated in the effectiveness study were independent of the baseline risk was supported by published work in the field of glycoproteins. They stated that the effectiveness study was the only study available for the comparators of interest.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a decision tree and Markov model to extrapolate the study results to a lifetime horizon and to estimate cost-effectiveness in a UK setting. The model used was appropriate, although it was not reported whether the parameter estimates were derived systematically from the available literature.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted appear to have been included in the analysis. The authors chose to exclude a cost associated with vascular death, which they stated would be difficult to quantify. They stated that these costs were expected to impact equally in each arm. The unit costs were reported separately, which improves the generalisability of the study results. A sensitivity analysis of the costs was conducted. The use of triangular distributions for costs is less appropriate than the use of lognormal distributions, as data would typically not be distributed according to a triangular distribution. The date to which the prices related was reported. The authors might have updated prices to the reported year, but the method used was not reported.

Other issues
The authors compared their results with findings from other studies based on the same effectiveness trial, and with other studies that examined the prevention of vascular events. The issue of generalisability to other settings was addressed, and the authors stated that the analysis was tailored to the local UK perspective. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors acknowledged that the extrapolation of survival and characterisation of events such as stroke were relatively simplistic. They stated that contemporary data describing long-term outcomes are unavailable, hence the need to extrapolate the trial results.

Implications of the study
The authors stated that, if treatment with clopidogrel is to be introduced, it may be necessary to review which treatments to discontinue in order that health care budgets are not exceeded.

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Other publications of related interest

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