Using triple antiplatelet therapy in patients with non-ST elevation acute coronary syndrome managed invasively: a cost-effectiveness analysis
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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 glycoprotein IIb/IIIa inhibitors in high-risk patients with non ST-segment elevation acute coronary syndrome, who were pre-treated with a combination of aspirin and clopidogrel and who received early invasive treatment, compared with aspirin and clopidogrel alone. The authors concluded that the early addition of a glycoprotein IIb/IIIa inhibitor was cost-effective, particularly in younger patients. Overall, the methodology and reporting of the study were satisfactory and the results appear to be reliable.

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

Study objective
The objective was to assess the cost-effectiveness of glycoprotein IIb/IIIa inhibitors, under the current clinical conditions, in patients with non ST-segment elevation acute coronary syndrome, who were pre-treated with a combination of aspirin and clopidogrel and who received an early invasive treatment strategy compared with aspirin and clopidogrel alone.

Interventions
Triple anti-platelet therapy using glycoprotein IIb/IIIa inhibitors in addition to aspirin and clopidogrel was compared with standard antiplatelet therapy using aspirin and clopidogrel only. The three strategies were: tirofiban or eptifibatide for all patients before coronary angiography; after coronary angiography, abciximab only for those patients who required immediate percutaneous revascularisation; and no additional therapy.

Location/setting
Spain/secondary care.

Methods
Analytical approach:
The study was based on a Markov model, which captured the utility and costs of the ongoing risk of bleeding and adverse cardiac events over time, using published evidence. The authors stated that the perspective was that of the Spanish public health system, and the time horizon was the lifetime of a 65-year-old patient.

Effectiveness data:
The clinical data were obtained from the published literature. This included a systematic review and meta-analysis, of nine clinical trials, for the efficacy of double compared with triple antiplatelet therapies and one randomised controlled trial for the effectiveness of before angiography versus selective after angiography use of glycoprotein IIb/IIIa inhibitors. The key clinical parameters were the risks of death and of acute myocardial infarction.

Monetary benefit and utility valuations:
The utility estimates for each health state and event described by the model were obtained from a non-systematic review of the literature.

Measure of benefit:
The primary measure of benefit was the number of quality-adjusted life-years (QALYs), which were discounted at a
rate of 3% per annum. The authors also calculated the number of adverse events avoided and life-years gained.

Cost data:
The health care costs were obtained from a number of Spanish studies, and included the costs of treatment, hospitalisation, surgical intervention, and adverse events, and the typical annual costs of patients with an old myocardial infarction. These costs were reported in Euros (EUR) and were adjusted for inflation using the Spanish consumer price index. They were based on a price year of 2006 and they were discounted at 3% per annum.

Analysis of uncertainty:
A univariate sensitivity analysis was performed by varying the model inputs across wide ranges and the joint effects of the main determinants were assessed in a multivariate sensitivity analysis. A probabilistic sensitivity analysis was also performed to evaluate the simultaneous effects of variations in the parameters on the results.

Results
The costs were EUR 20,993 for standard antiplatelet therapy, EUR 21,440 for selective triple therapy after angiography, and EUR 21,599 for triple therapy for all before angiography. The QALYs were 10.29 for standard therapy, 10.31 for after angiography, and 10.33 for before angiography, which was an incremental gain of 0.02 QALYs for after angiography and 0.04 for before angiography compared with standard therapy.

Compared with standard therapy, the incremental cost was EUR 15,150 per QALY gained for before angiography and EUR 22,350 for after angiography. The strategy of selective triple therapy after angiography was subject to extended dominance compared with before angiography, as it had a higher incremental cost per QALY.

The key determinants of the incremental cost-effectiveness ratio were found to be the risk of events, the incremental effectiveness of the glycoprotein IIb/IIIa inhibitor, and the age of the patient. The probabilistic sensitivity analysis showed that triple therapy for all patients before angiography was cost-effective in 91% of cases at a cost-effectiveness threshold of EUR 50,000 per QALY gained.

Authors' conclusions
The authors concluded that the early addition of a glycoprotein IIb/IIIa inhibitor, before coronary angiography, to therapy for high-risk ST-segment elevation acute coronary syndrome patients, who were pre-treated with aspirin and clopidogrel, was cost-effective, particularly for younger patients.

CRD commentary
Interventions:
The interventions were described in detail. The analysis included standard antiplatelet therapy, which appeared to be the current practice.

Effectiveness/benefits:
The effectiveness data were obtained from evidence of differing strengths ranging from a meta-analysis of nine randomised controlled trials, to data from a single randomised controlled trial. The methods used to identify the evidence were not described, which makes it difficult to evaluate whether the best of sources of evidence were used. The utility estimates were identified through a non-systematic review process and it is possible that the best estimates were not identified. The approach used to calculate the utility estimates was not described, nor was the population from which the estimates were obtained. Important aspects of the calculation of the QALYs are therefore unclear. The QALY was an appropriate measure of benefit to assess the impact of treatment on survival and quality of life.

Costs:
The perspective was stated and it appears that the relevant costs were considered; these were presented clearly in a table with all sources referenced. The price year, method of inflation, and discount rate were provided. Adjustment to a price year was appropriate, but the inflation of the health care costs using the health care component of the consumer price index would have been more appropriate than the overall consumer price index, as health care inflation tends to be higher than that of the overall economy.
Analysis and results:
The analytical approach was generally well reported and the model structure was described and supplemented with diagrams. An incremental analysis was appropriate for determining the cost-effectiveness of the strategies. The issue of the parameter uncertainty was appropriately addressed using one-way, multivariate and probabilistic sensitivity analysis. The results of the base-case and sensitivity analyses were adequately described. The authors discussed the strengths and limitations of their analysis.

Concluding remarks:
Overall, the methodology and reporting of the study were satisfactory and the results appear to be reliable.

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