Cost-effectiveness of clopidogrel treatment in percutaneous coronary intervention: a European model based on a meta-analysis of the PCI-CURE, CREDO and PCI-CLARITY trials

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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 conduct a cost-effectiveness analysis of pre-treatment and long-term treatment with clopidogrel in percutaneous coronary interventions in three European countries. The authors concluded that clopidogrel was cost-effective using commonly accepted thresholds in the three countries. The methodology was appropriate, apart from some concern about the potential omission of relevant trials, and the study was clearly and transparently reported. The conclusions reached by the authors appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to conduct a cost-effectiveness analysis of pre-treatment and long-term treatment with clopidogrel in percutaneous coronary interventions in three European countries.

Interventions
In three trials with different populations, clopidogrel plus aspirin was compared against aspirin alone. Clopidogrel was given at a loading dose of 300mg, followed by 75mg daily for various time periods from two days to 28 days.

Location/setting
Sweden, Germany, and France/hospital in-patient and out-patient.

Methods
Analytical approach:
A decision model that combined a decision tree with a Markov model was used to follow patients for three time horizons (one month, one year, and after the first year until death). The authors stated that they used a societal perspective for Sweden, and a payer perspective for Germany and France.

Effectiveness data:
The effectiveness data came from a meta-analysis of data from three randomised controlled trials; the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE), Clopidogrel for the Reduction of Events During Observation (CREDO), and Clopidogrel as Adjunctive Therapy (CLARITY) trials. Fixed-effect meta-analysis was used to derive the summary data. The main clinical outcomes were myocardial infarction, stroke, bleeding, and deaths.

Monetary benefit and utility valuations:
Not reported.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The direct costs included were those of the drugs, the events (myocardial infarction and stroke), and gastrointestinal bleeding. For the societal perspective, productivity costs were also included. The sources were adequately reported. The
currency was Euros (EUR) and the price year was 2006. Reflation of older costs was reported.

Analysis of uncertainty:
Several one-way and scenario analyses were performed. In one scenario analysis, the costs of additional life-years were included. Probabilistic sensitivity analysis was performed and cost-effectiveness acceptability curves were generated. The probability distributions were satisfactorily reported.

Results
For pre-treatment only, clopidogrel was a dominant strategy, which means it was less costly and more effective, compared with aspirin alone.

For pre-treatment and long-term treatment, in Sweden, placebo was associated with 9.997 QALYs and clopidogrel with 10.090 QALYs. In Germany, placebo was associated with 9.682 QALYs and clopidogrel with 9.772 QALYs. In France, placebo was associated with 10.152 QALYs and clopidogrel with 10.246 QALYs. In Sweden, placebo cost EUR 2,551 and clopidogrel EUR 2,944. In Germany, placebo cost EUR 2,420 and clopidogrel EUR 3,129. In France, placebo cost EUR 2,056 and clopidogrel EUR 2,550.

Thus, the incremental cost-effectiveness of clopidogrel was EUR 4,225 per QALY in Sweden, EUR 7,871 per QALY in Germany, and EUR 5,226 per QALY in France.

Sensitivity analysis confirmed that these results were robust and there was a high probability that the intervention was cost-effective with a EUR 50,000 willingness to pay per QALY. At a willingness to pay of EUR 10,000, 91% of the simulations showed that clopidogrel was cost-effective in Sweden, 87% in France and 59% in Germany.

Authors' conclusions
The authors concluded that pre-treatment and long-term treatment with clopidogrel in percutaneous coronary intervention for up to one year was cost-effective, using commonly accepted thresholds, in the three countries.

CRD commentary
Interventions:
The comparators seemed to be relevant to the objective and their selection was justified. Other important comparators may have been omitted.

Effectiveness/benefits:
The trials were sufficient, but no search strategy was reported and it is not clear if other relevant trials were missed. This could have changed the results.

Costs:
The costs included appeared to reflect the perspectives stated by the authors. The resource use data and the costs were well reported and the costs data appeared to be appropriate for the study population and setting. Other costing details, such as the sources of the cost data, price year and discount rate, were provided, which will facilitate the replication of the study in other settings and time periods.

Analysis and results:
The authors performed an acceptable synthesis using meta-analysis to derive the main effectiveness parameters. The results were reported, and the impact of uncertainty was thoroughly evaluated and addressed. Some limitations were reported by the authors and these mainly referred to the difficulty of combining trial data from different patient populations, with ST elevation and non-ST elevation myocardial infarction.

Concluding remarks:
The methodology seemed to be appropriate, apart from some concern about the potential omission of relevant trials, and the study was clearly and transparently reported. The conclusions reached by the authors appear to be appropriate.
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