
Cost-effectiveness of clopidogrel in acute coronary syndromes in Canada: a long-term analysis based on the CURE trial

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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 determine the long-term cost-effectiveness of clopidogrel plus acetylsalicylic acid (ASA) compared with ASA alone. The authors concluded that clopidogrel plus ASA therapy was cost-effective compared with ASA alone. Overall the methodology was good and both the results and the methods were reported clearly and in detail. Given the scope of the analysis, the authors' conclusions are appropriate.

Type of economic evaluation

Cost-effectiveness analysis

Study objective

The objective was to determine the long-term cost-effectiveness, in the Canadian health care system, of clopidogrel plus acetylsalicylic acid (ASA) compared with ASA alone for patients who presented with acute coronary syndromes with no segment elevation.

Interventions

The intervention was clopidogrel plus ASA. Patients received a 300mg loading dose of clopidogrel plus 75mg of ASA, followed by 75mg of clopidogrel and 75mg to 325mg of ASA daily. This intervention was compared with ASA alone.

Location/setting

Canada/outpatient secondary care.

Methods

Analytical approach:

The effectiveness and resource use data were derived from the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial and the Percutaneous Coronary Intervention subset of the CURE trial (PCI-CURE). The results of this trial were extrapolated over the remaining lifetime of the patient. The authors reported that the perspective was that of the Canadian health care system.

Effectiveness data:

The effectiveness data were derived from the CURE and PCI-CURE trial. The CURE trial was a randomised, double-blind, placebo controlled trial comparing clopidogrel plus ASA with placebo plus ASA. It was conducted in 28 countries, including Canada, and comprised 6,259 patients randomised to clopidogrel plus ASA and 6,303 patients randomised to placebo plus ASA. The PCI-CURE subset was a planned analysis of the efficacy of clopidogrel in patients undergoing PCI during the course of the CURE trial. All patients were followed up for a period ranging from three to 12 months. The primary outcome of the trial was the composite of death due to cardiovascular cause, stroke or non-fatal myocardial infarction. The mean survival beyond the trial period was estimated by integrating survival curves and adjusting for various patient characteristics.

Monetary benefit and utility valuations:

Not relevant.

Measure of benefit:

The measure of benefit was life-years gained.

Cost data:

The costs were the direct medical costs for hospitalisations and drug costs. Health care resource use was derived from the CURE and PCI-CURE trial and was recorded prospectively, including diagnostic tests, therapeutic procedures, hospitalisations, and medications. The costs of ambulatory care and outpatient diagnostic procedures and testing were not included. The unit costs for hospitalisation were based on a Canadian case mix group for the province of Alberta, because this had the most detailed level of data. Retail prices were used for clopidogrel and ASA. All costs were updated to 2004 prices using the inflation index for health care. As the costs could be incurred over a lifetime, the future costs were discounted at an annual rate of 3%. The currency was Canadian dollars (CAD).

Analysis of uncertainty:

A one-way sensitivity analysis was performed by reducing life expectancy gains by 50% and 80%, using estimated life expectancy from the Framingham Heart study, and increasing the costs of ASA. In order to derive 95% confidence intervals, the results from the analysis were bootstrapped 5,000 times. A cost-effectiveness acceptability curve was also plotted for a range of cost-effectiveness thresholds from CAD 0 to CAD 100,000.

Results

In the CURE trial, the life-years lost for patients receiving clopidogrel plus ASA were 0.3910 and for placebo plus ASA were 0.4592. The average cost for patients receiving clopidogrel plus ASA was CAD 12,423 and for placebo plus ASA was CAD 12,160.

In the PCI-CURE trial, the life-years lost for patients receiving clopidogrel plus ASA were 0.3337 and for placebo plus ASA were 0.4222. The average cost for patients receiving clopidogrel plus ASA was CAD 15,210 and for placebo plus ASA was CAD 14,877.

The costs and benefits were compared using an incremental cost-effectiveness ratio (i.e. the additional cost per life-year gained). When clopidogrel plus ASA was compared with placebo plus ASA, the incremental cost-effectiveness ratio was CAD 3,856 for CURE trial patients and CAD 3,763 for PCI-CURE patients.

The results from the cost-effectiveness acceptability curve showed that, when the threshold was below CAD 20,000 per life-year gained, the probability that clopidogrel plus ASA was cost-effective was 97.5% for CURE trial patients and 90.4% for PCI-CURE trial patients. The results of the one-way sensitivity analysis showed that, if the gains in life-expectancy were only 20% of those projected, the cost-effectiveness ratio would be CAD 19,338 for CURE trial patients and CAD 18,814 for PCI-CURE trial patients.

Authors' conclusions

The authors concluded that clopidogrel plus ASA therapy was cost-effective compared with ASA alone.

CRD commentary

Interventions:

The interventions were appropriately reported with their full details. Although no explicit justification was given for using ASA alone as the comparator, it would appear to have represented current practice in the authors' settings.

Effectiveness/benefits:

The effectiveness data were derived from two studies, both of which were based on a large randomised controlled trial. The authors gave appropriate details of the CURE and PCI-CURE trial including the study sample, a summary of the methods used, the outcome measures, and the follow-up. Due to the large sample size, randomisation, and blinding of the trial, its results should have high internal validity. In addition, well conducted randomised controlled trials, such as this one, are the gold standard design when comparing health care interventions. In order to predict beyond the trial period, the authors adequately extrapolated life-expectancy using published survival estimates. In addition, the estimates of the survival benefit were varied in the one-way sensitivity analysis.

Costs:

The perspective was adequately reported. For this perspective, although the authors reported that some resource use categories were not included in the analysis, all the major relevant costs appear to have been included. Both the sources

of resource use data, which were derived directly from the CURE and PCI-CURE trial, and the unit costs were adequately reported. The price year, time horizon, and discount rate used were adequately reported. However, as the authors acknowledged, CURE was a multinational trial, and therefore costing all resource use in Canadian unit costs will not have accounted for possible differences in treatment practices and resource use consumption between countries or health care systems.

Analysis and results:

Both the methods employed and the results of the analysis were reported in detail. A series of one-way sensitivity analyses was conducted in order to vary the survival benefit used to extrapolate the results of the CURE and PCI-CURE trial. In addition, the effects of patient variation were explored using bootstrap techniques and the results were clearly presented on a cost-effectiveness acceptability curve. In their discussion, the authors highlighted the limitations of their analysis.

Concluding remarks:

Overall, the methodology was good. Both the results and the methods were reported clearly and in detail. Given the scope of the analysis, the authors' conclusions are appropriate.

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Bibliographic details

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Other publications of related interest

Weintraub WS, Mahoney EM, Lamy A, et al. Long-term cost-effectiveness of clopidogrel given for up to one year in patients with acute coronary syndromes without ST-segment elevation. *J Am Coll Cardiol* 2005;45:838-45.

Lamy A, Jonsson B, Weintraub WS, et al. The cost-effectiveness of the use of clopidogrel in acute coronary syndromes in five countries based upon the CURE study. *Eur J Cardiovasc Prev Rehabil* 2004;11:460-5.

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MeSH

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