Clopidogrel versus aspirin in patients with atherothrombosis: CAPRIE-based calculation of cost-effectiveness for Germany

Berger K, Hessel F, Kreutzer J, Smala A, Diener H C

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 examined the cost-effectiveness of clopidogrel versus aspirin as secondary prevention for patients who had experienced myocardial infarction or ischaemic stroke or were diagnosed with peripheral arterial disease. The authors concluded that clopidogrel was a cost-effective alternative to aspirin as secondary prevention of cardiovascular or cerebrovascular events from the perspective of German third-party payers. The study was well conducted, although the economic analysis could have been presented more clearly. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study used key data from a clinical trial to examine the cost-effectiveness of clopidogrel versus aspirin as secondary prevention for patients who had experienced myocardial infarction (MI), or ischaemic stroke (IS), or were diagnosed with peripheral arterial disease (PAD).

Interventions
Clopidogrel monotherapy (75mg once daily) was compared with aspirin (325mg once daily) as secondary prevention for patients with atherothrombosis.

Location/setting
Germany/primary and secondary care.

Methods
Analytical approach:
This economic evaluation was based on a published Markov model. The time horizon was two years and the authors stated that the analysis was conducted from the perspective of the third-party payers.

Effectiveness data:
The clinical data for treatment effect were derived directly from the clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE) trial; a double-blind, randomised controlled trial (RCT) with 19,185 patients who received either clopidogrel or aspirin and who were followed up for a mean period of 1.91 years. The key clinical endpoint was survival, which was estimated using two databases, namely the Framingham and the Saskatchewan, for two separate scenarios.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
Life-years (LYs) were the summary benefit measure and were discounted at a 3% annual rate. The number of atherothrombotic events at two years was also reported.

Cost data:
The economic analysis included the costs associated with prophylaxis, treatment of cardiovascular or cerebrovascular
events (MI, IS, and PAD), concomitant medications, and management of adverse events. Both the direct and indirect costs were included and were presented as macro-categories. The resource use and costs were based on a previous study of cardiovascular or cerebrovascular events and on the CAPRIE trial. The costs of adverse events were determined by a panel of experts and drug costs were calculated using recommended dosages and prices from the Rote List. All costs were in Euros (EUR) and the price year was not explicitly reported. A 3% annual discount rate was applied.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was carried out to investigate the uncertainty underlying the key model inputs such as treatment costs, adverse event costs, costs of concomitant medications, discount rates for both costs and benefits, and manufacturer's discount for clopidogrel. The alternative ranges of values were determined by the authors.

Results
In a hypothetical cohort of 1,000 patients, the number of LYs saved, due to vascular deaths avoided, using clopidogrel compared with aspirin was 86.35 in scenario one (using Framingham database survival data) and 66.07 in scenario two (using Saskatchewan database survival data). The incremental two-year cost of clopidogrel over aspirin was EUR 1,241,440. Thus, the incremental cost per LY saved with clopidogrel over aspirin was EUR 14,380 in scenario one and EUR 18,790 in scenario two.

The sensitivity analysis identified the expected survival, discount rate, and daily cost of clopidogrel as the most influential model inputs. However, even in the worst scenario (5% discount rate for both costs and benefits), the incremental cost per LY saved was only EUR 24,700.

Authors' conclusions
The authors concluded that clopidogrel was a cost-effective alternative to aspirin as secondary prevention of cardiovascular or cerebrovascular events from the perspective of German third-party payers.

CRD commentary
Interventions:
The selection of the comparators was appropriate in that the new treatment was compared with the usual one, which was aspirin, for patients who had already experienced a cardiovascular or cerebrovascular event. The dosages were clearly reported. These comparators are also likely to be valid in other settings.

Effectiveness/benefits:
A RCT was the source for the clinical evidence. Generally, RCTs are considered to be a valid source of clinical data given the strengths of their design, which should provide unbiased and robust data. The authors pointed out that the CAPRIE trial was chosen, from among other available trials, due to its large number of patients. Some key features of the trial were reported, but the full details were in the primary publication. The authors considered two scenarios for life expectancy data because the widely used Framingham method is often criticised for the potential overestimation of survival. LYs are a valid benefit measure, which capture the impact of the interventions on the most relevant dimension of health, namely survival, and can be readily compared with the benefits of other health care interventions. However, the authors did not consider the issue of quality of life, which might have been relevant due to the treatment-related adverse events.

Costs:
The analysis of costs is likely to have reflected the perspective. The authors included some indirect costs that were not described and which may not have been related to productivity loss, but to non-medical direct costs. Except for drug costs, a breakdown of cost items was not presented. Disease costs were reported with respect to health conditions (MI, IS, and PAD), because they were derived from a published study. Adverse events costs were presented in a similar manner. In general, the unit costs and quantities of resources used were not reported separately. This approach might reduce the transparency of the economic evaluation. The price year was not reported, which may hinder reflation exercises.

Analysis and results:
The use of an incremental approach to synthesising the costs and benefits was appropriate. The issue of uncertainty was
investigated using a univariate approach which, according to the authors, offered transparent interpretation of the findings. The most influential model inputs were identified, but the use of a more comprehensive approach would have been useful and the clinical inputs were not varied. The findings (both for the base case and sensitivity analyses) were clearly presented. A relatively short time horizon was considered to reflect the CAPRIE trial follow-up period. The authors pointed out that a longer horizon would probably have improved the expected survival, but in a similar manner for both arms of the study. A potential limitation of the model was the fact that it did not allow for risk differentiation among patients, which means that subgroup analyses could not be performed. The authors acknowledged that the analysis focused on the German setting and caution would be required if generalising the findings to other health care systems. However, similar results were found for Italy, France and Belgium.

Concluding remarks:
On the whole, the study was well conducted, although the economic analysis could have been presented more clearly. The authors’ conclusions appear to be robust.

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