Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: a systematic review and economic evaluation


CRD summary
This review, conducted by CRD, found evidence to suggest that some treatment strategies using clopidogrel and/or modified-release dipyridamole in the secondary prevention of occlusive vascular events were potentially cost-effective. However, further direct comparisons of clopidogrel and modified-release dipyridamole in combination with aspirin were required.

Objectives
To examine the clinical and cost-effectiveness of clopidogrel and modified-release dipyridamole (anti-platlet agents) relative to prophylactic doses of aspirin for the secondary prevention of occlusive vascular events.

Review methods
A wide range of electronic bibliographic databases were searched for relevant literature on effectiveness, cost-effectiveness, side effects of aspirin treatment and costs related to heart disease.

Randomised controlled trials (RCTs) and economic evaluations that compared clopidogrel or dipyridamole alone or in combination with aspirin versus aspirin were included.

Data extraction and study quality assessment were undertaken by one reviewer and checked for accuracy by a second. Disagreements were resolved by discussion. These data were tabulated and summarised in the report. Economic evaluations based on patient-level data and those based on decision models were critiqued using different but appropriate tools.

Results of the review
For the clinical effectiveness, two RCTs (CAPRIE and ESPS-2) were identified. Both RCTs were considered high quality. For the assessment of cost-effectiveness, eight reviews were identified.

Clinical effectiveness
In one trial (CAPRIE), the point estimate for the primary outcomes (ischaemic stroke, myocardial infarction or vascular death) favoured clopidogrel over aspirin, but the boundaries of the confidence intervals raised the possibility that clopidogrel was not more beneficial than aspirin. Other statistically significant results included the incidences of rash and diarrhoea which were higher in the clopidogrel group than the aspirin group.

In the other trial (ESPS-2), treatment with modified-release dipyridamole alone did not significantly reduce the risk of any of the primary outcomes compared with aspirin. Aspirin plus modified-release dipyridamole was significantly more effective than aspirin alone in patients with stroke or transient ischaemic attacks in reducing the outcome of stroke and marginally more effective in reducing stroke and/or death. The number of strokes was statistically significantly reduced in the aspirin plus modified-release-dipyridamole group compared with the modified-release-dipyridamole group.

No conclusions could be made on the relative effectiveness of modified-release-dipyridamole, alone or in combination with aspirin, and clopidogrel.

Cost effectiveness
The probabilistic state transition model assessed the cost-effectiveness of differing combinations of treatment strategies in four patient subgroups, under a number of different scenarios over a 40 year period. The results of the model were sensitive to the assumptions made in the alternative scenarios, in particular the impact of therapy on non-vascular deaths.
For a willingness-to-pay range of £20,000 to £40,000 per additional quality-adjusted life-year, assuming no disablement after the initial (qualifying) stroke: in the stroke and transient ischaemic attack subgroups, aspirin plus modified-release dipyridamole would be the most cost-effective therapy given a two-year treatment duration; for a lifetime treatment duration, aspirin plus modified-release dipyridamole would be considered more cost-effective than aspirin. In patients left disabled by their initial stroke, aspirin was the most cost-effective therapy.

In the myocardial infarction and peripheral arterial disease subgroups over a lifetime treatment duration, clopidogrel would be considered more cost-effective than aspirin, as long as treatment effects on non-vascular deaths were not considered and patients were not left disabled after the initial (qualifying) stroke.

Conclusions
There was some evidence to suggest that some treatment strategies were potentially cost-effective. However, further direct comparisons of clopidogrel and modified-release dipyridamole in combination with aspirin were required.

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This is a high quality systematic review involving CRD that meets the criteria for inclusion on DARE. As CRD reviews are of high quality this structured abstract presents a brief summary of the review methods, the results and conclusions.