Cost-Effectiveness Analysis of Antiplatelet Therapy in the Prevention of Recurrent Stroke in the UK
Aspirin, Dipyridamole and Aspirin-Dipyridamole

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Abstract

Objectives: To evaluate the cost effectiveness from a UK health and social services perspective of antiplatelet therapies tested in the Second European Stroke Prevention Study (ESPS-2) in preventing recurrent stroke. To demonstrate the value of modelling studies in this area.

Design and setting: A decision-analytic model was developed to evaluate health outcomes and associated costs. Sources of data for efficacy, adverse events, background event risks, disability and mortality were ESPS-2, the Oxfordshire Community Stroke Project and UK national statistics. Published national unit costs were applied to clinician panel estimates of resource use for acute stroke, rehabilitation and long term care. Outcome measures were strokes or disabled life-years averted, and disability-free, stroke-free or quality-adjusted life-years gained.

Patients and interventions: 30-day survivors of ischaemic stroke treated with low dose aspirin, modified-release dipyridamole; the coformulation of low dose aspirin plus modified-release dipyridamole, or no antiplatelet therapy.

Main outcome measures and results: The model predicted that over 5 years the coformulation prevented 29 more strokes than aspirin alone per 1000 patients, at an additional cost of £1900 per stroke averted (1996 values). Over 5 years, each antiplatelet therapy was cost saving compared with no therapy. Results were sensitive to the cost of acute care, the cost of long term care of disabled stroke survivors, the effectiveness of therapy and the background risk of recurrent stroke. In sensitivity analyses, the cost effectiveness did not exceed £7000 per stroke averted or £11 000 per quality-adjusted life-year (QALY) gained, except when varying the effectiveness parameter.

Conclusions: Application of a decision-analytic model to the results of ESPS-2 indicated that first-line therapy with the coformulation of modified-release dipyridamole and low dose aspirin to patients with a previous ischaemic stroke is likely to generate significant health benefits at modest extra costs to health and social services. The extra costs of treatment are balanced by the savings in future costs.
of acute care and long term care of the disabled. Future economic evaluations in this area should pay particular attention to the cost perspective, the duration of analysis, the selection of trials from which effectiveness data are derived, and the impact of the pooling of outcome events with potentially different economic consequences.

Stroke is a leading cause of death and disability. It is unique in that not only is it a leading cause of death in developed countries but it is also a major cause of long term disability.[1] Population ageing and improved organisation of acute hospital services for stroke patients are resulting in an increasing prevalence of stroke survivors in the community, many of whom are dependent on formal or informal care. It has been estimated that stroke accounts for over 4% of UK national health service expenditure and 6% of hospital costs.[2,3] The lifetime direct cost of a stroke has not been estimated for the UK, but estimates (converted to pounds sterling; 1996 values) reported for other countries have been £33 000 (Netherlands),[4] £57 000 (Sweden)[5] and £38 000 (US).[6] The cost categories included and the methods used in these studies vary.[7]

Approximately one quarter of strokes are recurrent and many of these are preventable by surgery for those with severe carotid stenosis, anticoagulation for those with atrial fibrillation, and antiplatelet therapy for those with prior ischaemic stroke or transient ischaemic attack (TIA). The Antiplatelet Trialists’ Collaboration (ATC) reported an overall odds reduction for antiplatelet therapy in preventing myocardial infarction (MI), stroke or vascular death in a wide variety of high risk patients of 27% [95% confidence interval (CI) 23 to 31%] and 22% (14 to 30%) in patients with prior stroke or TIA, respectively.[8] The agent of choice is aspirin, for which an odds reduction for preventing serious vascular events in all high risk patients is 25% (21 to 29%),[8] but the preferred dosage is not established. Ticlopidine has been demonstrated to have greater effectiveness in preventing recurrent vascular events compared with aspirin – 12% relative risk reduction (RRR) [–2 to 26%][9] – or with placebo – 23% RRR [1 to 41%].[10] However, ticlopidine is expensive and remains unlicensed for this indication in the UK. Dipyridamole alone compared with placebo has been demonstrated to prevent vascular events in high-risk patients.[8] In the first European Stroke Prevention Study the combination of aspirin and dipyridamole reduced the risk of stroke and/or death by 33%, and stroke by 38% (95% CI not given),[11] compared with placebo.

Two major trials of alternative antiplatelet agents have recently been reported. The second European Stroke Prevention Study (ESPS-2) compared low dose aspirin (25mg twice daily), modified-release dipyridamole (200mg twice daily), the coformulation of these 2 agents (same dosages) and placebo in 6602 patients with qualifying TIA or stroke.[12,13] The trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE) compared aspirin (325mg once daily) with clopidogrel (75mg once daily) in 19 185 patients with ischaemic stroke (6431 patients), myocardial infarction or peripheral arterial disease.[14]

Both of these studies reported significant reductions in risks of recurrent events for the new agents compared with aspirin. ESPS-2 reported RRRs for the coformulation compared with aspirin of 13% (95% CI 1 to 25%; outcome stroke and death) and 23% (9 to 37%; outcome stroke only).[12] CAPRIE reported RRRs for clopidogrel compared with aspirin of 9% (0 to 17%; primary outcome event cluster – ischaemic stroke, MI or vascular death combined) and 6% (95% CI not given; outcome event–recurrent stroke only) in the entire trial cohort. RRRs in the cohort of patients with a qualifying stroke were 7% (–6 to 19%; primary outcome event cluster) and 8% (95% CI not given; recurrent stroke only).[14]

At a recent consensus conference on the medical management of stroke it was acknowledged that