Cost-effectiveness analysis of antiplatelet therapy in the prevention of recurrent stroke in the UK: aspirin, dipyridamole and aspirin-dipyridamole

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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.

Health technology

The use of antiplatelet therapies, specifically aspirin, dipyridamole and a combination of the two, in the prevention of recurrent stroke, myocardial infarction and other vascular events in patients who have already experienced an initial ischaemic stroke.

Type of intervention

Secondary prevention.

Economic study type

Cost-effectiveness analysis and cost-utility analysis.

Study population

A hypothetical typical cohort of 30 day survivors of a primary ischaemic stroke in the UK with mean age of 70 years.

Setting

Hospital, primary and community care. The economic analysis was conducted in London, UK.

Dates to which data relate

Resource and effectiveness data were taken from primary studies published in 1991 and 1997 and from 1991 statistical data. Further resource data were derived from published data from 1995 and 1996, and information supplied by an expert panel of clinicians. 1996 price years were used.

Source of effectiveness data

Effectiveness data were taken from a review of data previously published in a large randomised trial, the Second European Stroke Prevention Study, the Oxfordshire Community Stroke Project study and also from UK national statistical publications.

Modelling

A semi-Markov decision analytic model was used to estimate the number of future events, costs, disability-free life years, disabled life years and stroke-free life years for each treatment strategy. Model cycles lasted for three months

Outcomes assessed in the review

The effectiveness of interventions in reducing risk of further strokes, transient ischaemic attacks, other non fatal vascular events were identified. In addition the probabilities of adverse events, probabilities of events recurring without interventions, 25 year mortality rates and probability of disablement following further vascular events were extracted.

Additional mortality data were taken from published statistical data.

Study designs and other criteria for inclusion in the review
One 2 year multi-centre multi-country randomised placebo controlled clinical trial comparing low dose aspirin, modified release dipyridamole and a co-formulation of the two for patients who had experienced a first stroke and also one five year population cohort study of stroke patients.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
2 primary studies, one randomised controlled trial and one population cohort study were included in the review.

Methods of combining primary studies
Studies were not combined, effectiveness data for the first two years were taken from the randomised controlled trial and data from the population cohort study was used to determine long term mortality and morbidity outcomes.

Investigation of differences between primary studies
Not applicable.

Results of the review
The percentage risk reduction of all strokes when using dipyridamole, aspirin and the co-formulation compared with a placebo were 16.29%, 18.08% and 39.96% respectively. Similarly the percentage risk reductions for transient ischaemic attack were 20.06%, 24.42% and 35.90% respectively and the risk reductions for other non-fatal vascular events were 12.69%, 31.78% and 56.50% respectively. 30 day mortality rates for each treatment group were 14.8% for placebo, 20.4% for dipyridamole, 17.5% for aspirin and 19.8% for the co-formulation. Withdrawal rates in the first three months were 9% for both the placebo and aspirin groups and 17% for dipyridamole and the co-formulation. Between months 4 and 12 (per 3 month cycles) these rates were between 3.0% and 1.5% for all groups and after 1 year per three month cycle withdrawal rates were estimated to be 1.5% for all four groups. The percentage of withdrawals due to adverse events was estimated to be 30% for all four groups.

Probability rates of recurrent strokes without therapy in years 1 and 2 were estimated to range between 4.88% and 1.53% per three month cycle and between 1.25% and 2.52% for three month cycles in years 3 to 24. The probability of transient ischaemic attacks without therapy in years 1-2 was estimated to range between 2.68 and 1.42% and to be 1.42% thereafter. Similarly probabilities of other non- fatal vascular events were 1.18% and 0.47% in the first two years and then at 0.47% per three month cycle in subsequent years. Non-stroke mortality rates prior to recurrent stroke per 3 month cycle were 5.4%-2.0% for the first year, 1.5% in years 2 to 5, 3.6% in years 6 to 15 and 4.5% in years 16 to 25.

All cause mortality rates after recurrent stroke per three month cycle were estimated as follows:

first year, age 70-74, 2.1%;

first year, age 75-84, 5.8%;

first year, age 85+, 12.9%;

subsequent years, age 70-74, 2.7%;

subsequent years, age 75-84, 4.6%;

subsequent years, aged 85+, 5.8%.

30.9% of initial stroke survivors were estimated to be disabled (3-5 on the modified Rankin scale) and 35.6% of previously non-disabled survivors would subsequently become disabled.

Measure of benefits used in the economic analysis

Stroke-free life years gained, strokes prevented, disability-free life years gained, and disabled life years avoided were the benefit measures. Quality-adjusted life years (QALYs) gained were also estimated using a published estimate of patients' own valuations for disability. A semi-Markov decision analysis model was used to determine long term outcomes. Health care benefits were not discounted.

Direct costs

Costs of antiplatelet medication and costs of treating adverse events were estimated. The costs of treating strokes included acute care, ambulatory rehabilitation and long term care. Resources used were estimated from consultation with an expert panel of clinicians and using cost estimates published by the Chartered Institute of Public Finance and Accountancy, the Personal Social Services Research Unit and the CHKS company. Antiplatelet medication costs were taken from the manufacturers and the monthly index of medical specialities (MIMS). Costs were determined from the perspective of the English National Health Service and local authority social services and were discounted at a rate of 6% per annum. 1996 price years were used, with estimates of costs adjusted to these values using PSSRU estimates of inflation for hospital and community health services.

Indirect Costs

Not included.

Currency

UK pounds sterling ().

Sensitivity analysis

A series of univariate sensitivity analyses was conducted, as well as a three way sensitivity analysis on key parameters. These parameters included effectiveness, cost and disability estimates as well as discounting health outcomes at 6% per annum.

Estimated benefits used in the economic analysis

In the 2 year analysis the incremental numbers of strokes averted per 1000 survivors (post 30 days) using co-formulation versus aspirin were 21. 27 stroke-free life years were gained, 8 disability-free life years would be gained and 5 disabled life years would be averted. For aspirin versus no therapy, 22 incremental strokes would be averted and 28 stroke-free life years would be gained. In addition, 7 disability-free life years would be gained and 7 disabled life years averted. Similarly the incremental benefits gained using dipyridamole compared with no therapy were 19 strokes averted, 24 stroke-free life years gained, 4 disability-free life years gained and 8 disabled free life years averted. Incremental benefits gained using the co-formulation compared with no therapy were 43 strokes averted, 55 stroke-free life years gained, 15 disability-free life years gained and 12 disabled free life years averted.

In the 5 year analysis the incremental number of strokes averted per 1000 survivors (post 30 days) using co-formulation versus aspirin were 29, with 92 stroke-free life years were gained, 31 disability- free life years gained and 17 disabled life years averted. For aspirin versus no therapy, 31 incremental strokes would be averted, 97 stroke-free life years would be gained, 27 disability-free life years would be gained and 20 disabled life years averted. Similarly the incremental benefits gained using dipyridamole compared with no therapy were 26 strokes averted, 82 stroke-free life years gained, 16 disability-free life years gained and 25 disabled free life years averted. Incremental benefits gained using the co-formulation compared with no therapy were 60 strokes averted, 189 stroke-free life years gained, 57 disability-free life years gained and 37 disabled free life years averted.

In the lifetime (25 year analysis) the incremental number of strokes averted per 1000 survivors (post 30 days) using co-formulation versus aspirin were 34, with 275 stroke-free life years gained, 115 disability-free life years gained and 41 disabled life years averted. For aspirin versus no therapy 34 incremental strokes would be averted and 279 stroke-free life years would be gained. Furthermore, 92 disability-free life years would be gained and 40 disabled life years averted. Similarly the incremental benefits gained using dipyridamole compared with no therapy were 28 strokes averted, 303 stroke-free life years gained, 57 disability-free life years gained and 57 disabled free life years averted. Incremental benefits gained using the co-formulation compared with no therapy were 68 strokes averted, 554 stroke-free life years gained, 206 disability-free life years gained and 81 disabled life years averted.

All benefits were undiscounted in the base case analysis and adverse events were taken into account. An incremental gain of 19 quality adjusted life years was estimated for the cohort in the 5 year model when comparing the co-formulation with aspirin only.

Cost results

The discounted costs per initial stroke survivor for no therapy, aspirin, dipyridamole and the co-formulation for 2 years were 7,245, 7,107, 7,253 and 7,140 respectively. These costs for 5 years were 15,093, 14,817, 15,056 and 14,873 and for 25 years costs per initial stroke survivor were 24,881, 24,491, 24,738 and 24,574 respectively. These costs include those for dealing with adverse events.

Synthesis of costs and benefits

In the 2 year analysis the incremental cost using co-formulation compared with aspirin per stroke averted was 1,600, the incremental cost per stroke-free life year gained was 1,200, costs per disability-free life year gained were 4,000 and costs per disabled life year averted were 6,100.

Using aspirin compared with no therapy the corresponding incremental costs were: -6,300, -5,000, -19,500 and -21,300. Using dipyridamole compared with no therapy the corresponding incremental costs were 400, 300, 1,800 and 1,000. Using the co-formulation compared with no therapy the corresponding incremental costs were: -2,500, -1,900, -6,900 and -8,800.

In the 5 year analysis the incremental cost using co-formulation compared with aspirin per stroke averted was 1,900, the incremental cost per stroke-free life year gained was 600, costs per disability-free life year gained were 1,800 and costs per disabled life year averted were 3,200.

Using aspirin compared with no therapy the corresponding incremental costs were: -9,000, -2,800, -10,300 and -13,600. Using dipyridamole compared with no therapy the corresponding incremental costs were: -1,400, -400, -2,300 and -1,500. Using the co-formulation compared with no therapy the corresponding incremental costs were: -3,700, -1,200, -3,800 and -5,900.

In the lifetime (25 year) analysis the incremental cost using co-formulation compared with aspirin per stroke averted was 2,500, the incremental cost per stroke-free life year gained was 300, the costs per disability-free life year gained were 700 and 2,000 per disabled life year averted.

Using aspirin compared with no therapy the corresponding incremental costs were: -11,400, -1,400, -4,300 and -9,700. Using the co-formulation compared with no therapy the corresponding incremental costs were: -4,500, -600, -1,500 and -3,800.

The incremental costs per QALY gained using the co-formulation compared with aspirin only were 6,800, 2,900 and 1,000 for the 2 year, 5 year and 25 year models respectively. The model was sensitive to changes in the risk of recurrent strokes (without intervention). A 25% variation in probability of recurrent strokes would double and halve the cost per stroke averted. The effectiveness of antiplatelet therapies also had a sensitive impact on the results. The model was also sensitive to changes in the costs of long term and acute care. In a three way sensitivity analysis the cost effectiveness of the co-formulation versus aspirin in the 5 year model ranged from -2,000 per stroke averted, with high background risk of strokes and high costs of acute and long term care to 6,900 with low probabilities of recurrent strokes and low acute and long term care costs with treatment of recurrent strokes.

Authors' conclusions

The use of a co-formulation of aspirin and dipyridamole is likely to lead to significant health benefits at modest extra costs to health and social services in the prevention of further strokes and other vascular events when compared with aspirin alone; and dipyridamole alone also appears to represent a cost-effective alternative to no treatment for patients for whom aspirin cannot be tolerated. This analysis is determined from the perspective of the UK health and social services, and illustrates the importance of taking these longer term treatment and rehabilitation costs into account. All interventions were found in the base case scenario to become more cost effective over time and became cost saving compared with placebo in the lifetime (25 year) analysis. This illustrates the importance of using models to extrapolate long term costs and benefits for which trial data may not be available. Pooling different types of outcome event (eg: stroke, TIA, MI, vascular death etc) may have an impact on the economic analysis.

CRD COMMENTARY - Selection of comparators

A justification was provided for the comparators used in the analysis. All the antiplatelet treatments options included in the analysis have previously been shown to be effective in preventing recurrent vascular events.

Validity of estimate of measure of benefit

The effectiveness data were taken largely from a single 2 year multi- country trial, with longer term estimates of effectiveness and risk of recurrent vascular events, mortality and disability derived from a population-based cohort study and UK statistical data. As the authors note, pooling effectiveness results from a number of trials may have some impact on effectiveness estimates compared with those used in this model. However, uncertainty over effectiveness was tested in sensitivity analysis. Benefits were not discounted in the base line analysis although this parameter was varied in sensitivity analysis and was not found to have an impact on the overall results. It would also have been helpful to present more details from the model of quality-adjusted life years gained for more treatment options.

Validity of estimate of costs

Sufficient details were provided on the sources of costs used in the analysis. Resource estimates were largely based on expert panel considerations and, as such, are subject to some uncertainty, although this was tested in sensitivity analysis. The analysis was conducted from the perspective of UK health and social care and anyone conducting future economic analyses may also wish to consider the costs to others in society, in particular the costs of informal care for this population group may be substantial.

Other issues

The model based cost results are not generalisable outside the UK health and social care sector, although the results of the model illustrate the importance of considering a wider economic perspective to that of the health care payer alone.

Implications of the study

Future long term economic evaluations are required, to assess the cost-effectiveness of various antiplatelet and alternative treatments (eg: surgery, anticoagulation and antiplatelet therapy) for the prevention of recurrent strokes and other vascular events in a variety of geographical and institutional settings.

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