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 study investigated two different stroke interventions. One was the daily administration of aspirin to ischaemic patients, commencing within 48 hours of stroke onset and continuing for 2 to 4 weeks, at a standard dosage of 150 mg/day, in line with local practice. The other was thrombolytic therapy (recombinant tissue type plasminogen activator). This was administered to patients with ischaemic stroke, managed within a coordinated acute stroke care centre, within 3 hours of symptom onset.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised the Australian population in 1997. The interventions were targeted at first-ever stroke in a lifetime stroke cases. Patients given aspirin therapy had to have suffered ischaemic stroke. Patients with haemorrhagic stroke, cardiac disease more suited to warfarin, contraindications to aspirin, and those assessed as suitable for thrombolysis, were excluded from this study sub-group. Patients receiving thrombolytic therapy should have suffered ischaemic stroke with a clearly defined time of onset. They were excluded if they had haemorrhagic stroke, another stroke in the last 3 months, recent myocardial infarction or major surgery, or other contraindications for thrombolysis.

Setting
The study setting was secondary care. The economic study was carried out in Australia.

Dates to which data relate
The effectiveness and resource use data appear to have been collected from studies published between 1995 and 2002. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from published studies, mainly the North East Melbourne Stroke Incidence Study (NEMESISS), (Dewey et al., see Other Publications of Related Interest). The authors also made several assumptions.

Modelling
A model was used to assess the cost-effectiveness of the interventions considered at analysis (i.e. the MORUCOS model), taking the natural history of the disease, costs, outcomes and interventions into consideration.
Outcomes assessed in the review
The outcomes assessed in the review that were reported in the paper were:

- the reduction in the number of deaths from first-ever strokes per 1,000 patients;
- the reduction in the number of recurrent strokes per 1,000 patients;
- the increase in haemorrhages per 1,000 patients treated with aspirin therapy;
- the increase in the risk of haemorrhage during the first days after stroke;
- the reduction in the mortality rate after 3 months; and
- the increase in the proportion of patients discharged home for those treated with thrombolytic therapy.

The number of persons to whom the interventions could be reasonably applied was also estimated and reported. This took the eligibility criteria and the number of persons already receiving the intervention under current practice into account.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Evidence for the effectiveness of each intervention was reviewed using the approach of Carter et al. (see Other Publications of Related Interest), which considers the strength of the evidence, and the size and relevance of the effect.

Methods used to judge relevance and validity, and for extracting data
The authors stated that the approach of Carter et al. also allowed an assessment of the size and relevance of the effect, although the results of the assessment were not reported in the present paper.

Number of primary studies included
At least 11 studies were included in the review, four of them reporting data from the NEMESIS study.

Methods of combining primary studies
It was unclear whether data from different studies were combined.

Investigation of differences between primary studies
Not reported.

Results of the review
Among patients treated with aspirin therapy:

- there was a reduction of 9 in the number of deaths from first-ever strokes per 1,000 patients;
there was a reduction of 7 in the number of recurrent strokes per 1,000 patients; and

there were two more haemorrhages per 1,000 patients.

For patients treated with thrombolytic therapy:

there was a 5.8% increase in the risk haemorrhage during the first days after stroke;

there was a 20% reduction in the mortality rate after 3 months; and

there was a 12% increase in the proportion of patients discharged home.

With aspirin, it was estimated that an additional 9,153 first-ever stroke patients could be targeted. This number excluded 5% of ischaemic stroke patients likely to have contraindications. Thrombolytic therapy was directed at a conservative 5% of time-eligible patients, meaning that only 256 patients were treated.

Methods used to derive estimates of effectiveness

The authors made assumptions to supplement the results of the review.

Estimates of effectiveness and key assumptions

The interventions were assumed to be operating in a "steady state" (i.e. fully implemented and operating in accordance with efficacy potential). It was also assumed that they were applied to all eligible patients who presented during a 1-year period.

The authors assumed 100% compliance for patients treated with aspirin.

Measure of benefits used in the economic analysis

The measure of benefits used was the number of disability-adjusted life-years (DALYs). The DALYs were estimated using the Dutch disability weights for generic stroke, as used in the Australian Burden of Disease study. The time horizons considered were one year and lifetime. The estimated health benefits were discounted at a rate of 5%. The authors reported some other health outcomes. More specifically, the number of patients needed to avoid one DALY, to avoid one stroke, to avoid one death, and to avoid one person permanently disabled; and the numbers of deaths from first-ever strokes and from recurrent strokes.

Direct costs

The direct costs included in the analysis were those to the health care system (both private and public), as well as those for patients and their carers. However, the authors did not report all the cost categories included in the analysis. The sources of the costs were actual data, obtained from published studies and expert opinion. Some but not all of the resources used were reported separately from the costs, while some unit costs were given in an aggregated manner. The estimated costs were the total and incremental costs one year after the first-ever stroke and for the lifetime of the patient. Considering this latter time horizon, the costs were appropriately discounted at an annual rate of 5%. The price year was 1997.

Statistical analysis of costs

The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs

The indirect costs were not included.
Currency
All the costs were converted from Australian dollars (Aus$) to US dollars ($) using the Organisation for Economic Cooperation and Development (OECD) purchasing power parity.

Sensitivity analysis
The authors stated that, in addition to a univariate uncertainty analysis, a probabilistic uncertainty analysis was conducted to perform a Latin Hypercube simulation with 2,000 iterations.

Estimated benefits used in the economic analysis
Under the current practice, 198,164 DALYs were lost from all strokes experienced by the cohort of 30,895 first-ever stroke patients during their lifetime. Aspirin saved 964 DALYs, while thrombolytic therapy yielded a saving of 155 DALYs.

The number of DALYs lost during the first year (due to first-ever strokes) was 123,326 under current practice, 718 for patients under aspirin therapy, and 155 for patients under thrombolytic therapy.

The number of patients needed-to-treat to save one DALY was 10 for aspirin and 2 for thrombolytic therapy.

Cost results
Under current practice, in the first year after a first-ever stroke, the resource costs totalled $344 million. Aspirin resulted in increased first-year costs of $0.78 million. In contrast, thrombolytic therapy raised the first-year resource costs by $0.13 million.

Over the life of the cohort, the use of thrombolytic therapy translated into cost-savings of $0.38 million, whereas aspirin increased the total incidence costs by $1.7 million.

Synthesis of costs and benefits
The costs and benefits were combined by means of incremental cost-utility ratios. These were calculated as the additional lifetime costs imposed by an intervention over current practice, compared with its additional health benefits. Thrombolytic therapy was found to be dominant (i.e. more effective and cost-saving) over current practice. Aspirin resulted in additional lifetime costs of $1,421 per DALY saved.

The results from the probabilistic sensitivity analysis showed that the 95% confidence intervals of the cost-utility ratios ranged from $1,413 to $1,429 per DALY saved for aspirin therapy, and from dominant to a ratio of $2,553 per DALY saved for thrombolytic therapy.

Authors' conclusions
Both aspirin and thrombolytic therapy were cost-effective options for the treatment of acute ischaemic stroke.

CRD COMMENTARY - Selection of comparators
The authors used current practice as the comparator. However, they did not provide any details of this intervention, making it impossible for the reader to establish whether this intervention is valid in other settings. Afternote: the authors have informed us that details of current practice can be obtained from a previous paper (Moodie M 2003, see "Other Publications of Related Interest" below for bibliographic details).

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature was undertaken to identify the relevant research and to minimise biases. The authors used data mainly from the NEMESIS study to populate their model, although no details
of the other studies included in the review were provided. They noted that a specific approach was used to consider the strength of the evidence, and the size and relevance of the effect, although the results of these assessments were not provided. The lack of detail on the methodology and results of the review hampered the internal validity and generalisability of these results to other settings.

Validity of estimate of measure of benefit
DALYs were used as the summary measure of benefit. This seems to have been an appropriate measure as it allows comparisons of the study findings with those from other interventions. However, as the authors acknowledged, the study was limited by the coarseness of the generic disability weights for stroke and the consequent insensitivity of the DALY in capturing quality of life considerations. The estimation of benefits was modelled. The estimated health benefits were appropriately discounted given that a lifetime horizon was considered at analysis.

Validity of estimate of costs
As the authors did not report the cost categories included in the study, only reporting total costs, it was unclear whether all the relevant cost categories and individual costs were considered at analysis. This will hamper the generalisability of the authors’ results. The costs were converted into US dollars using appropriate exchange rates. Not all of the resource quantities were reported separately from the costs, which would hinder reflation exercises in other settings. Since the costs were incurred over the lifetime of the patient, future costs were appropriately discounted. The price year was reported, which will aid future inflation exercises. The authors performed probabilistic sensitivity analyses around their incremental cost-utility ratios, but even though they reported that univariate analyses were performed, no details or results of these were given.

Other issues
The authors reported that there is considerable research evidence about the effectiveness of stroke interventions, but cost-effectiveness evidence was limited and it has been confounded by methodological inconsistencies between studies and the range of costs and consequences considered. The authors also stated that the patterns of resource utilisation considered in the study may not be generalisable to other settings. The authors do not appear to have presented their results selectively. However, their conclusions need to be treated with caution, as insufficient details on the methodology used for the estimation of effectiveness and costs were reported.

Implications of the study
The authors reported that the MORUCOS model was useful in facilitating priority settings in stroke, and it provided a realistic framework for the economic evaluation of interventions based on a consistent and robust methodology. They recommended considering issues such as equity, acceptability, and ethical issues arising from the fact that thrombolytic therapy has limited potential to impact on stroke patients.

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Bibliographic details

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DOI
Other publications of related interest


Moodie M. Trial application of MORUCOS (Model of Resource Utilisation, Costs and outcomes of Stroke) to assist priority setting in stroke. Submitted as thesis for Doctorate of Public health, School of Public Health, The University Melbourne.

Indexing Status

Subject indexing assigned by NLM

MeSH
Acute Disease; Aspirin /economics /therapeutic use; Cost-Benefit Analysis; Fibrinolytic Agents /economics /therapeutic use; Health Care Costs; Health Priorities; Humans; Models, Economic; Outcome Assessment (Health Care); Platelet Aggregation Inhibitors /economics /therapeutic use; Quality-Adjusted Life Years; Recombinant Proteins /therapeutic use; Stroke /drug therapy /economics; Thrombolytic Therapy /methods; Tissue Plasminogen Activator /economics /therapeutic use; Utilization Review

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