Trial Application of a Model of Resource Utilization, Costs, and Outcomes for Stroke (MORUCOS) to Assist Priority Setting in Stroke

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Background and Purpose—Cost-effectiveness data for stroke interventions are limited, and comparisons between studies are confounded by methodological inconsistencies. The aim of this study was to trial the use of the intervention module of the economic model, a Model of Resource Utilization, Costs, and Outcomes for Stroke (MORUCOS) to facilitate evaluation and ranking of the options.

Methods—The approach involves using an economic model together with added secondary considerations. A consistent approach was taken using standard economic evaluation methods. Data from the North East Melbourne Stroke Incidence Study (NEMESIS) were used to model "current practice" (base case), against which 2 interventions were compared. A 2-stage process was used to measure benefit: health gains (expressed in disability-adjusted life years [DALYs]) and filter analysis. Incremental cost-effectiveness ratios (ICERs) were calculated, and probabilistic uncertainty analysis was undertaken.

Results—Aspirin, a low-cost intervention applicable to a large number of stroke patients (9153 first-ever cases), resulted in modest health benefits (946 DALYs saved) and a mean ICER (based on incidence costs) of US $1421 per DALY saved. Although the health gains from recombinant tissue-type plasminogen activator (rtPA) were less (155 DALYs saved), these results were impressive given the small number of persons (256) eligible for treatment. rtPA dominates current practice because it is more effective and cost-saving.

Conclusions—If used to assess interventions across the stroke care continuum, MORUCOS offers enormous capacity to support decision-making in the prioritising of stroke services. **(*Stroke*. 2004;35:1041-1046.)**

Key Words: cerebrovascular disorders ■ cost-benefit analysis ■ aspirin ■ thrombolytic therapy

Stroke is a major cause of mortality and morbidity in Australia, accounting for 5.4% of the total disability-adjusted life-year (DALY) disease burden.[1] Costs associated with the disease are high; total first-year costs of first-ever strokes in Australia in 1997 were estimated at US $427 million and the present value of lifetime costs were US $1 billion.[2]

Although there is considerable research evidence about the efficacy of stroke interventions,[3–5] data about their cost-effectiveness are limited. Although economic evaluations of individual interventions have been undertaken,[6–9] work comparing different interventions is confounded by methodological inconsistencies between studies (in terms of the discount rates and outcome measures used, methods for estimating health state preferences, and the range of costs and consequences considered). Furthermore, evaluation of interventions has largely been limited to acute therapy and has not involved the whole continuum from prevention to long-term care. The absence of an accurate and comprehensive picture of current stroke practice, as the base case comparator, poses a further barrier to economic evaluation.

The fundamental task of economic evaluation is to inform decision-makers about what difference a chosen intervention will make to the current disease burden and health service costs. Similar to other areas of health care, priority setting in stroke is becoming increasingly important given constrained resources. Policy-makers and clinicians need to find ways to make meaningful comparisons between new interventions and current practice to inform their expenditure decisions. The aim of this study was to illustrate the intervention module of MORUCOS through its use in an economic evaluation protocol that could be applied to all interventions for stroke in a standardized consistent manner to facilitate comparisons and their ranking in order of economic merit.

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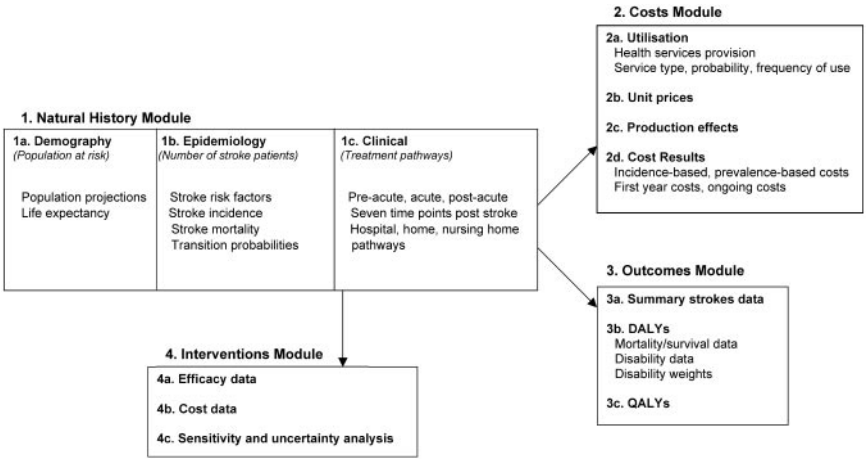

Conceptual Overview of MORUCOS. Source: Mihalopoulos et al.[13]

Methods

Study Parameters

The study group was the 1997 Australian population, and the interventions were targeted at first-ever in a lifetime stroke cases. Evidence for the effectiveness of each intervention was reviewed in a consistent manner using the approach of Carter,[10] which considers the strength of the evidence and the size and relevance of the effect.

The perspective was of the health sector, with a focus on the cost impact of stroke on government and the private sector as well as on patients and their carers. Key unit costs and their sources are listed. Services were valued in 1997 Australian prices. All costs were converted to US dollars using the appropriate Organisation for Economic Cooperation and Development (OECD) purchasing parity power.[11] A discount rate of 5% was used for costs and consequences.[12]

Interventions were assumed to be operating in a "steady state" (ie, fully implemented and operating in accordance with efficacy potential), and they were applied to all eligible patients who presented during a 1-year period. Interventions were applied for a duration that realistically reflected their real-world use. The time horizon for tracking associated costs and consequences extended over the lifetime of the target population (or as long as costs and benefits continued to accrue).

Use of an Economic Model

MORUCOS was developed by the Program Evaluation Unit at The University of Melbourne in collaboration with the North East Melbourne Stroke Incidence Study (NEMESIS) investigators at the National Stroke Research Institute. It is a detailed model consisting of 4 modules: natural history, costs, outcomes, and interventions, and was developed through a series of linked spreadsheets[13] (Figure).

In this study, MORUCOS was used to fulfill 2 roles. Firstly, the model includes stroke incidence, mortality, and service utilization data from NEMESIS, a community-based stroke incidence study that provides the most realistic picture of current practice stroke care, including postacute care in Australia.[2,14–16] It was used as the base case against which each of the interventions was compared. Secondly, the model provided a framework to simulate each of the interventions.

TABLE 1. Aspirin Therapy: Summary of the Intervention

Medication	Aspirin 150 mg/d
Commencement	Within 48 h of stroke
Patient inclusion	Patients with ischemic stroke
Patient exclusion	Patients with hemorrhagic stroke, cardiac disease more suited to warfarin, contraindications to aspirin, assessed as suitable for thrombolysis
Duration	2 to 4 wk
Compliance	100%
Effectiveness	↓ 9 deaths from first-ever strokes per 1000 treated[17,18]
	↓ 7 recurrent strokes per 1000 treated[3,18,19]
	↑ 2 hemorrhages per 1000 treated[19]
Setting	Any pathway
Resources used & unit costs	Aspirin US $0.22 per daily dose (over-the-counter) (PBS)*[21]
	Hospitalization of hemorrhages US $6480 (NEMESIS)†
Patients already receiving treatment	36% of first-ever stroke patients
Additional patients treated	9153
Parameters varied in uncertainty analysis	Unit cost of aspirin
	↓ Recurrent stroke incidence
	↓ First-ever stroke mortality

*Pharmaceutical Benefits Schedule. † North East Melbourne Stroke Incidence Study.

TABLE 2. Thrombolytic Therapy: Summary of the Intervention

Medication	Recombinant tissue-type plasminogen activator (rtPA)
Dosage	0.9 mg/kg, maximum 90 mg
Method of administration	Intravenous, 10% dose as a bolus followed by 1 h of infusion
Commencement	Within 3 h of stroke onset
Patient inclusion	Patients with ischemic stroke with a clearly defined time of onset
Patient exclusion	Patients with: hemorrhagic stroke, another stroke in previous 3 mo, recent myocardial infarction or major surgery, other contraindications to thrombolysis
Effectiveness	5.8% ↑ Risk of hemorrhage in first few days[22,23]
	20% ↓ In mortality at 3 months[4]
	12% ↑ In proportion discharged home[4]
Setting:	Acute stroke unit
Prerequisite	Brain imaging (CT or MRI)
Resources & unit costs	RtPA US $1647; extra nursing US $162; physician call-back US $412; reduction in bed-days −US $392; hemorrhage US $2127 (expert opinion)
Patients treated	5% Time-eligible patients=256 patients
Parameters varied in uncertainty analysis	Unit cost of treatment % Time-eligible patients treated
	↑ Intracerebral hemorrhage rate
	↑ Proportion discharged home
	↓ Proportions discharged to residential care/rehabilitation

Specification of the Interventions

Two interventions were chosen for this pilot study. The interventions were clearly defined to facilitate pathway analysis. This required specification of details such as the treatment, dosage, commencement, duration, patient eligibility criteria, resources used and unit costs from the research literature, clinical guidelines, and expert opinion.

Aspirin is the only antiplatelet agent that has been comprehensively evaluated as an acute stroke treatment.[3,17–19] The intervention entailed daily administration of aspirin to ischemic stroke patients, commencing within 48 hours of stroke onset and continuing for 2 to 4 weeks (Table 1). Patient eligibility criteria were in accordance with the Australian National Health and Medical Research Council guidelines,[20] and a standard dosage of 150 mg/d was used, in line with local practice.

The thrombolysis intervention entailed intravenous administration of recombinant tissue-type plasminogen activator (rtPA) to patients with ischemic stroke within 3 hours of symptom onset (Table 2).[4,22,23] Patient eligibility criteria conformed to the American Heart Association guidelines.[24] Because rtPA use requires specialized, coordinated acute stroke care systems, its use was confined to patients managed in a dedicated stroke unit. For thrombolysis to be initiated within the 3-hour time window, symptom recognition, transport to hospital, neurologic evaluation, and informed consent needed to occur within ≈2 hours of stroke onset.

Simulating the Interventions

Key parameters in the model were changed to simulate the interventions in terms of their incremental health impacts and associated resource use. The number of persons to whom the interventions could be reasonably applied was calculated, taking into account the eligibility criteria and number of persons already receiving the intervention under current practice. For aspirin, it was estimated that an additional 9153 first-ever stroke patients could be targeted (bringing the total treated to 67.6% of total first-ever strokes). This excluded the 5% of ischemic stroke patients likely to have contraindications to aspirin and the small number suitable for thrombolysis.[6] Thrombolysis was directed at a conservative 5% of time-eligible patients, meaning that only 256 patients were treated[6] (none was treated in the base case).

Concept of Benefit

Benefits were calculated by a 2-stage process. Firstly, the health gain attributable to each intervention was estimated using DALYs. The Dutch disability weights for generic stroke,[25] as used in the Australian Burden of Disease study,[1] were used, and outcomes were measured at 3 and 12 months after stroke.

The second stage involved assessment of broader issues important for resource allocation decision-making such as equity, feasibility, and acceptability to stakeholders.[10] The second-stage filters were treated as dichotomous constraints (ie, pass or fail).

Incremental Cost-Effectiveness Analysis

Incremental costs and benefits of interventions were analyzed against the comparator (current practice). Incremental cost-effectiveness ratios (ICERs), the additional lifetime costs imposed by an intervention over current practice compared with its additional health benefits, were calculated.

In addition to univariate uncertainty analysis, probabilistic uncertainty analysis was conducted using the @RISK software to perform a Latin Hypercube simulation[26] with 2000 iterations.

Results

Under current practice, a total of 198 164 DALYs were lost from all strokes experienced by the cohort of 30 895 first-ever stroke patients (Table 3). Aspirin saved 964 DALYs, reflecting reductions in stroke mortality and recurrence. Thrombolysis yielded a more modest saving of 155 DALYs but was more effective in terms of the number needed to treat (Table 3).

Thrombolysis was dominant (ie, more effective and cost-saving) over current practice. In this situation, it is not common practice to report an ICER[27] (Table 4). Aspirin was not cost-saving, resulting in modest additional lifetime costs of US $1421 per DALY saved (Table 4).

Under current practice, in the first year after first-ever stroke, resource costs totalled US $344 million in 1997 (Table 4). Aspirin resulted in increased first-year costs of US $0.8

TABLE 3. Incremental Cost-Effectiveness* and Filter Analysis

Variable	Aspirin Therapy	Thrombolytic Therapy
Point Estimate (result from model)		
DALYs recovered	964	155
Incremental incidence costs	US $1 695 390	−US $382 865
Incidence cost per DALY recovered	US $1758	Dominant
Mean Estimate from @RISK iterations (95% UI)†		
Incidence cost per DALY recovered	US $1421 (US $1413 to US $1429)	Dominant (dominant to US $2553)
Filters		
Level of evidence	"Sufficient" evidence	"Sufficient" evidence
Size of problem ‡	Appropriate to 30% stroke patients	Appropriate to <1% stroke patients
Equity §	No issue	Major equity issue given small N eligible
Feasibility¶	No issue	Restricted by licensing, time eligibility, stroke unit access
Acceptability to stakeholders‖	No issue	Safety, increased early risk of death
Affordability**	No issue	Treatment expensive

*Based on incidence costs converted to $US using a purchasing power parity of 1.3 in accordance with OECD rates for 1997.[11]
†Uncertainty interval.
‡Scale of the issue.
§Extent to which addresses burden equally across affected group.
¶Feasibility of implementation.
‖Acceptability to policy-makers, clinicians, consumers, etc.
**Includes implementation costs.

million, with the major components being additional nursing home costs (US $0.28 million) and inpatient rehabilitation (US $0.08 million), given the increased number of patients surviving stroke. In contrast, thrombolysis raised first-year resource costs by only US $0.13 million, because the increased inpatient costs associated with therapy (US $0.5 million) were nearly offset by cost-savings in inpatient rehabilitation (−US $0.3 million) and nursing home expenditure (−US $0.1 million).

Over the life of the cohort, thrombolysis translated into modest cost-savings (US $0.4 million), whereas aspirin increased total incidence costs by US $1.7 million. Under the aspirin intervention, more patients survived stroke and consequently consumed more stroke-related resources over the rest of their lifetime.

Second-Stage Filter Analysis

Both interventions were potential options for change, but there were some important issues, primarily in relation to thrombolysis, which should be considered by policy-makers when making resource allocation decisions (Table 5). This included the potential for thrombolysis to impact on only a few stroke patients, the inequitable use of resources, acceptability, and ethical issues arising from balancing the higher risk of early death against improved long-term outcomes,[28] and the high upfront costs borne by hospital budgets.

Discussion

Aspirin and thrombolysis were both cost-effective options for the treatment of acute ischemic stroke. Although not cost-saving, aspirin therapy was well within the range of ratios likely to be acceptable to policy-makers. Although dominant interventions are attractive to funding bodies, the small-scale health gain and cost-saving stemming from thrombolysis indicated that policy-makers should not dismiss aspirin therapy.

Furthermore, there were caveats on the thrombolysis findings. Although highly effective in terms of the number needed to treat, thrombolysis had limited potential to impact on the stroke population. With improved access to stroke units, the potential patient population would be expected to increase. However, the total number of candidates meeting the stringent clinical requirements would remain relatively low. In contrast, aspirin, although less effective, was appropriate for most ischemic stroke patients.

There was a large uncertainty interval (UI) around the mean ICER for thrombolytic therapy given the greater risks and wider range of costs involved. However, the intervention remained cost-effective throughout this range. In accordance with the evidence for thrombolysis,[7] a 12% increase in the proportion of patients discharged home was modeled, which impacted positively on both first-year and rest-of-life costs. If we assume no change in discharge destinations resulting from thrombolysis, the ICER would be similar to the aspirin therapy point estimate.

The conclusion drawn from this trial application was that MORUCOS is useful for facilitating priority setting in stroke. It provided a realistic framework for the economic evaluation of interventions based on a consistent, robust methodology. A consistent comparator was provided based on the best approximation of current practice stroke care in Australia. It relied on a rigorous approach to the measurement of costs and benefits and readily facilitated sensitivity and uncertainty analysis. 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 outcomes. However, the disability weights used are based on a variant of the EuroQol classification, which includes dimensions for anxiety/depression and cognitive functioning. Alternatively, the

TABLE 4. Incremental Health Gains and Numbers Needed to Treat

Component of DALY	Base Case (Current Practice)	DALYs/Adverse Events Saved: Aspirin Therapy	DALYs/Adverse Events Saved: Thrombolysis
First-Ever Strokes			
Total years of life lost (YLL)	71 198	480	60
Total years of life lived with a disability (YLD)	52 128	238	95
DALYs	123 326	718	155
Recurrent Strokes			
YLL	55 299	182	0
YLD	19 539	64	0
DALYs	74 838	246	0
All Strokes (first-ever and recurrent)			
YLL	126 497	662	60
YLD	71 667	302	95
DALYs	198 164	964	155
Strokes			
First-ever strokes	30 895	0	0
Recurrent strokes	15 238	46	0
Deaths			
From first-ever strokes	10 665	80	8
From recurrent strokes	6926	21	0
N Needed to Treat to Avoid			
One DALY		10	2
One stroke		199	NA
One death		91	32
One person permanently disabled		155	12
One death or permanent disability		57	9

NA indicates not applicable.

model equally lends itself to the use of QALYs based on scores from a multi-attribute utility instrument.

The model is adaptable to decision contexts, settings, target groups, and geographical areas other than those used in this study. It is readily recalibrated with alternative data inputs for other geographical regions, providing detailed resource utilization data are available. It is, however, acknowledged that the description of current practice stroke care used as the comparator case is based on the patterns of resource use determined for NEMESIS, and these data may not necessarily be generalizable to stroke practice throughout Australia or overseas.

Given the sound resource use and epidemiological data built into the model, MORUCOS offered the potential to

TABLE 5. Incremental Prevalence and Incidence Costs

Category of Costs	Base Case US $*	Aspirin Therapy	Thrombolytic Therapy
		Incremental Costs in US $*	
Prevalence Costs†			
Resource costs of first-ever strokes in first year	$343 866 958	+$770 442	+$128 244
Ongoing costs of previous strokes‡	$414 847 377	$0	$0
Total prevalence based costs	$758 714 336	+$770 442	+$128 244
Incidence Costs§			
Resource costs of first-ever strokes in first year	$343 866 958	+$770 442	+$128 244
Rest-of-life costs	$470 147 762	+$924 948	−$511 108
Total incidence costs	$814 014 721	+$1 695 390	−$382 865

*Costs converted to US $ using OECD Purchasing Power Parity rate for 1997.[11]
†Annual costs of all strokes in any year (first-ever and recurrent).
‡Costs incurred in reference year for patients experiencing first-ever stroke in previous years.
§Costs that a cohort of first-ever stroke patients incur during their lifetime.

overcome the gap between evidence about the health gains of individual interventions and their resource implications. The model offers the capacity to consider a broad range of interventions from across the whole clinical care pathway for stroke from primary prevention (eg, blood pressure-lowering drugs, smoking cessation measures, anticoagulation for atrial fibrillation patients), acute treatment (stroke units), secondary prevention (antiplatelet therapy, carotid endarterectomy) and postacute management (early rehabilitation, home rehabilitation) together in a holistic manner. Given the potential to aid complex decision-making, the restriction of this pilot study to aspirin and thrombolysis may be questioned. Although both interventions are recommended as components of best-practice stroke care, they have not been previously compared using a rigorous methodology capable of application to any stroke intervention. This pilot study enabled an informed judgment to be made on the credibility of the intervention module of MORUCOS before its intended application to a wider selection of interventions for stroke.

Contrary to other approaches, MORUCOS allows consideration of the "big picture" for stroke and sets an example of both national and international relevance for stroke priority setting to be firmly grounded in the evidence and based on a rational approach. The provision of such comprehensive data to policy-makers offers the chance to influence policy and its transcription into practice and thereby to effect cost-savings and reductions in disease burden.

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