Estimating the Long-Term Costs Of Ischemic and Hemorrhagic Stroke for Australia: New Evidence Derived From the North East Melbourne Stroke Incidence Study (NEMESIS)
Dominique A. Cadilhac, Rob Carter, Amanda G. Thrift and Helen M. Dewey

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Estimating the Long-Term Costs Of Ischemic and Hemorrhagic Stroke for Australia
New Evidence Derived From the North East Melbourne Stroke Incidence Study (NEMESIS)

Dominique A. Cadilhac, PhD; Rob Carter, PhD; Amanda G. Thrift, PhD; Helen M. Dewey, PhD

Background and Purpose—Stroke is associated with considerable societal costs. Cost-of-illness studies have been undertaken to estimate lifetime costs; most incorporating data up to 12 months after stroke. Costs of stroke, incorporating data collected up to 12 months, have previously been reported from the North East Melbourne Stroke Incidence Study (NEMESIS). NEMESIS now has patient-level resource use data for 5 years. We aimed to recalculate the long-term resource utilization of first-ever stroke patients and compare these to previous estimates obtained using data collected to 12 months.

Methods—Population structure, life expectancy, and unit prices within the original cost-of-illness models were updated from 1997 to 2004. New Australian stroke survival and recurrence data up to 10 years were incorporated, as well as cross-sectional resource utilization data at 3, 4, and 5 years from NEMESIS. To enable comparisons, 1997 costs were inflated to 2004 prices and discounting was standardized.

Results—In 2004, 27,291 ischemic stroke (IS) and 4,291 intracerebral hemorrhagic stroke (ICH) first-ever events were estimated. Average annual resource use after 12 months was AU$6,022 for IS and AU$3,977 for ICH. This is greater than the 1997 estimates for IS (AU$4,848) and less than those for ICH (previously AU$10,692). The recalculated average lifetime costs per first-ever case differed for IS (AU$57,106 versus AU$52,855 [1997]), but differed more for ICH (AU$49,995 versus AU$92,308 [1997]).

Conclusion—Basing lifetime cost estimates on short-term data overestimated the costs for ICH and underestimated those for IS. Patterns of resource use varied by stroke subtype and, overall, the societal cost impact was large. (Stroke. 2009; 40:915-921.)

Key Words: cerebral infarct | intracerebral hemorrhage | costs | economics | outcomes

Similar to other countries, stroke is a leading cause of disease burden in Australia. Stroke has been estimated to affect more than 50,000 Australians each year. Mortality from stroke remains significant with about 20% dying within 28 days of a first-ever event. At 10 years after a first-ever stroke, the cumulative risk of a recurrent event is about 43%, and of being disabled or deceased is approximately 86%. Unsurprisingly, the costs of stroke to society are high. In Australia, approximately 2% (922 million Australian dollars [AUS]) of recurrent health expenditure is attributed to stroke. However, health expenditure data underestimate the overall costs because they only include the direct costs to government.

Dewey and colleagues reported the first comprehensive Australian cost-of-illness (COI) study for stroke, based primarily on data from the North East Melbourne Stroke Incidence Study (NEMESIS). The NEMESIS data used were derived from the pilot cohort recruited from May 1996 to April 1997 in 8 postcode areas. In total, 381 events were registered in a population of 133,816 residents, 72% being first-ever strokes. To estimate costs, an economic model named the Model of Resource Utilization, Costs, and Outcomes for Stroke [MORUCOS], was developed. The methods used in this model have been previously reported. Briefly, the model was constructed using an incidence-based patient-level costing approach from a societal perspective. Linked spreadsheets enabled the reporting of lifetime costs for various stroke subtypes (excluding transient ischemic attacks and subarachnoid hemorrhage). Costs included the direct costs of treatment, production losses from inability to work or...
perform household duties, as well as out-of-pocket expenses incurred by stroke patients, and informal care costs. In an independent comparison of published COI studies, the estimated expenditures reported from this Australian COI study were found to be comparable to those of other developed countries.

One of the major strengths of the Australian COI study for stroke has been the ability to describe the costs of first-ever stroke in detail, particularly for the first year. However, as longitudinal data beyond 12 months were unavailable, rest-of-life annual resource use was based on total average 6 to 12 month utilization, and adjusted by experts to exclude resources considered unlikely to continue beyond 12 months. This average annual estimate, together with the first-year costs, were then used to predict lifetime costs. For the 1997 reference year, total first-year costs of all first-ever strokes were estimated to be AU$555 million, and the present value of total lifetime costs $AU1.3 billion. Over a lifetime, the average cost per case was greatest for intracerebral hemorrhage (ICH; AU$73 542), followed by ischemic stroke (IS; AU$42 110), and undetermined stroke (those cases not undergoing brain imaging or autopsy; AU$12 031).

Because NEMESIS is a 10-year longitudinal study, there was an opportunity to validate assumptions made about resource use beyond 12 months. This procedure has been identified as an important validation step that is rarely undertaken. Moreover, establishing up-to-date cost estimates were perceived as important to ensure continued relevance. Therefore, we aimed to update MORUCOS and recalculate the long-term resource utilization of first-ever stroke patients and compare these estimates to those previously modeled. It was hypothesized that average subtype lifetime costs per first-ever stroke would be similar to previous estimates regardless of the cost method used.

Methods

After a critical review of MORUCOS, the IS and ICH models were updated and refined to represent a 2004 reference year. For example, epidemiological data on survival and recurrent events beyond 12 months previously obtained from the United Kingdom (UK) were replaced with new Australian data available up to 10 years; updated resident population estimates were incorporated; and a 3% discount rate used instead of a 5% rate to conform with current recommendations. The undisputed subtype model was not updated as few cases in NEMESIS contributed to this model and total costs were minor (≈2%) in contrast to the main subtypes of IS and ICH.

Literature reviews and internet searches were undertaken to find the best sources of Australian data to update the IS and ICH models. For the natural history of stroke, NEMESIS data were used, where possible, to maintain internal consistency. Five-year follow-up data from NEMESIS were complete at the time this research was undertaken. This included patient-level long-term resource use, recurrent stroke events, and survival data up to 5 years. In addition, incidence and survival data from the larger 22 postcode areas used in NEMESIS in years 2 and 3 of the case ascertainment period were used for the ICH model to improve the precision of estimates given the larger sample size. For age bands that had more than 5 years of life expectancy, general stroke survival between 5 and 10 years after stroke were estimated from the Perth Community Stroke Study (PCSS). In addition, we assumed that no cases would be carried forward in the model beyond average normal life expectancy for each respective age band and gender category. This was to avoid overestimating costs.

Unit prices were updated using standard references, such as the Medicare Benefits Schedule, Pharmaceutical Benefits Schedule, and the “Manual of resource items and their associated costs” (supplemental Table I, available online at http://stroke.ahajournals.org). Hospital costs and the probability of being discharged to home, rehabilitation and aged care settings were also verified (data not shown). This was because patterns of clinical care and associated resource use may have changed over time. Where unit costs for 2004 were unavailable, the total health price index (THPI) was used to adjust the costs to the appropriate reference year.

Long-Term Resource Utilization and Costs

At follow-up NEMESIS participants were questioned about resources used and were asked to report only stroke-related resources used. The majority of interviews were conducted face-to-face. Informal caregivers, such as family members and spouses, also reported time spent providing care to stroke survivors and out-of-pocket expenses.

For each year, the proportion of participants using a particular resource item was calculated and used to determine the probability of resource use. To be conservative, only half of reported general practitioner (GP) visits were assumed to be attributed to the stroke. A weighted average cost per case for each item was then calculated (average cost per case × probability of use). The results were then summed to derive a weighted average annual cost per case estimated for years 3, 4, and 5 after stroke. An average of the 3 years was then used, as this was considered a better estimate of the ongoing annual lifetime costs.

To estimate the lifetime costs, the discounted rest-of-life costs occurring in each year were then summed together with the first year costs. The future costs were estimated using current prices after standard economic evaluation practice. No adjustment was made for future inflation. A 3% discount rate was used as this rate reflects current time preferences and also the borrowing rate on marketable securities over periods up to 30 years.

Analysis

Intercooled STATA version 8 (Stata Corporation, 2003) and Microsoft Excel 2003 (Microsoft Corporation, 2003) were used to analyze data for this project. Standard statistical tests were applied. The level of significance was set at P<0.05 (2-sided).

Sensitivity and Uncertainty Analyses

One-way sensitivity analyses were performed by altering the discount rate between 0% and 5%. In addition, the probability of being discharged to home, inpatient rehabilitation, or aged care facilities after acute care was also varied using new 2004 estimates obtained from several Australian multicenter hospital studies and the Austin Health stroke register (where the 1997 acute hospitals costs were originally obtained).

Multivariable probabilistic uncertainty analyses were undertaken using @Risk software version 4.5 (Palisade Corporation 2005). The sampling variations incorporated for point estimates related to incidence, survival and costs are provided in supplemental Table II. Three thousand “Monte Carlo” simulations were undertaken to ensure convergence. Convergence was defined as less than 1.5% variation in primary outcome statistics, such as numbers of strokes. The 3000 individually simulated point estimates were used to estimate a “grand” mean, median, and 95% uncertainty interval for the cost results. These estimates together with their sample distributions were used to assess statistical differences between cost results.

Results

In 2004, 35 095 first-ever strokes were estimated to have occurred; 79% were IS, 12% ICH, and 9% had no imaging or autopsy. The majority were aged over 55 years (89%). The impact of using updated resident population data in MORUCOS resulted in an additional 3368 (8.4%) strokes for 2004.
Differences in Annual Cost Methods After the First Year

The NEMESIS response rates for completion of the “long-term costs” questionnaire at year 3 were 66% (n=11005), at 4 years 53% (n=216), and at 5 years 56% (n=188), potentially indicating unrepresentative data. However, few differences in participant characteristics such as age, socioeconomic status, and handicap scores were found. Therefore, these cross-sectional data were deemed to be representative of NEMESIS cases for those respective time periods.

Table 1 summarizes estimates obtained using the “new” updated long-term annual cost model, and the original method where long-term annual costs were based on adjusted 6- to 12-month resource use. Applying the original method, using 6- to 12-month adjusted estimate for annual resource use to the updated model, underestimated the annual costs per

Table 1. Comparison of Different Methods for Estimating Annual Long-Term Resource Use (After 12 Months) in MORUCOS

<table>
<thead>
<tr>
<th>Type of Stroke</th>
<th>Caregiver Costs Included</th>
<th>Average Cost per Stroke Case per Annum (Australian $)</th>
<th>Caregiver Costs Included</th>
<th>Average Cost per Stroke Case per Annum (Australian $)</th>
<th>Caregiver Costs Included</th>
<th>Average Cost per Stroke Case per Annum (Australian $)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Original Method (Using 6–12 Month Adjusted Estimate*)</td>
<td></td>
<td>UPDATE MODEL Applying ORIGINAL METHOD</td>
<td></td>
<td>UPDATE MODEL With NEW Long-Term (Average 3–5 Year) Annual Costs†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ischemic stroke No</td>
<td>$3495</td>
<td>Ischemic stroke No</td>
<td>$2874</td>
<td>Ischemic stroke No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$4847</td>
<td>683 730 427</td>
<td>$4407</td>
<td>683 730 427</td>
<td>$6022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>intracerebral hemorrhage $92 711</td>
<td>292 094 001</td>
<td>intracerebral hemorrhage $10 692</td>
<td>292 094 001</td>
<td>intracerebral hemorrhage $12 129</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inpatient</td>
<td>905 636 426</td>
<td>Inpatient</td>
<td>905 636 426</td>
<td>Inpatient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outpatient</td>
<td>683 730 427</td>
<td>Outpatient</td>
<td>683 730 427</td>
<td>Outpatient</td>
</tr>
</tbody>
</table>

*Based on patient data that were adjusted by experts to assess whether particular resource use would continue beyond 12 months. †New annual cost estimates based on data from NEMESIS survivors at 3, 4, and 5 years after stroke. All costs presented are the annual costs after the first year.

Table 2. Summary of Updated Cost Results for First-Ever Stroke Cases

<table>
<thead>
<tr>
<th>Subtype Costs</th>
<th>Sensitivity Analysis Varying Discount Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Point Estimate (3% Discounting) 0% 5%</td>
</tr>
<tr>
<td>Ischemic stroke (n=27 660)</td>
<td>AUS</td>
</tr>
<tr>
<td>Total first year costs*</td>
<td></td>
</tr>
<tr>
<td>Direct costs‡</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td></td>
</tr>
<tr>
<td>Total lifetime costs by category</td>
<td></td>
</tr>
<tr>
<td>Direct costs‡</td>
<td></td>
</tr>
<tr>
<td>Indirect costs</td>
<td></td>
</tr>
<tr>
<td>Total lifetime costs</td>
<td></td>
</tr>
<tr>
<td>Lifetime cost/case</td>
<td></td>
</tr>
<tr>
<td>Intracerebral hemorrhage (n=4291)</td>
<td></td>
</tr>
<tr>
<td>Total first year costs*</td>
<td></td>
</tr>
<tr>
<td>Direct costs‡</td>
<td></td>
</tr>
<tr>
<td>Indirect costs</td>
<td></td>
</tr>
<tr>
<td>Total lifetime costs</td>
<td></td>
</tr>
<tr>
<td>Lifetime cost/case</td>
<td></td>
</tr>
</tbody>
</table>

*Costs occurring in the first year are not subjected to discounting; †provides a comparison of estimates between long-term cost methods used in the previous model compared with the updated model using the 5% discount rate; ‡direct costs include patient out-of-pocket expenses and informal caregiver costs.
case beyond 12 months for IS by about one third (AUS$4407 original method versus AUS$6022 updated long-term estimates). In contrast, when the same method is applied to the updated ICH model, annual long-term resource use is overestimated by more than 3-fold (AUS$12 129 original method versus AUS$3977 updated long-term estimates).

Using the original subtype model, with costs updated to the 2004 reference year, the total average lifetime costs per case was estimated to be AUS$52 855 for IS and AUS$92 308 for ICH. As the original subtype model uses a 5% discount rate this rate is used for comparisons. The net present value of lifetime average costs per case in the “new” updated subtype model with 5% discounting was AUS$57 106 for IS and AUS$49 995 for ICH (Table 2). Although the estimates for IS are similar (an 8% difference), the original subtype model gave a lifetime cost estimate for ICH that was about 85% greater (Figure 1).

New Cost-of-Illness Estimates

The updated costs of IS and ICH are outlined in Table 2. A total average lifetime cost per case was estimated to be AUS$64 733 for IS and AUS$54 721 for ICH (3% discount rate). The total lifetime costs for all first-ever IS and ICH events in 2004 was approximately AUS$2 billion. Total outpatient and community costs were greater than costs of inpatient hospital care for both IS and ICH.

The total costs in the first year accounted for 38% of IS and 53% of ICH lifetime costs, indicating that ICH cases are more expensive to treat in the first year. Inpatient hospital costs accounted for about 43% of total costs in the first year for both IS and ICH. The breakdown of the first year costs are provided in Table 3. In the first year, ICH cases were more expensive to treat than IS in terms of hospitalization, rehabilitation, aged care, and use of community services. ICH cases also incurred more out-of-pocket expenses. In contrast, IS cases experienced greater costs for hospitalizations attributable to recurrent events or complications from stroke, caregiver costs, medications, GP care, investigations, and respite care. Long-term annual costs per case according to stroke subtype are provided in Figure 2. The largest cost differences in long-term resource use were for aged care and community services, which where considerably greater for IS.

When the discount rate was varied in sensitivity analyses, the net present value of lifetime costs per case for first-ever IS ranged from approximately AUS$57 000 to AUS$75 000 per case, and AUS$50 000 to AUS$61 000 per case for ICH (Table 2). The effects on total lifetime costs were more marked for...
IS than for ICH (Table 2). When the probability of discharge destinations for home, inpatient rehabilitation, and aged care facilities were varied the estimates differed marginally (data not shown). For example, the lifetime estimates per case varied least for ICH (between AU$1565 and AU$110). For IS the variation in lifetime costs per case was AU$1556 to AU$1504.

Uncertainty Analysis
The uncertainty analyses indicated that the total costs of stroke may range between AU$1.58 billion to AU$1.94 billion for IS, whereas for ICH the range was AU$216 million to AU$249 million (Table 4). The median lifetime cost per incident IS was AU$64 208 and for ICH was AU$54 745. When these costs were compared, there were statistically significant differences in the average costs generated from the multivariate probabilistic uncertainty analysis, whereby first-year costs were more expensive for ICH (ICH mean costs AU$29 244 [SD AU$1063] than IS AU$24 737 [SD AU$884] P<0.001). However, the average lifetime costs per case were greater for IS than ICH (IS mean cost per case AU$64 297 [SD AU$3330] versus ICH mean cost per case AU$54 763 [SD AU$1868], P<0.001).

Discussion
The total costs of stroke have significantly increased since they were estimated in 1997. Previously, the total cost burden of IS and ICH was estimated at approximately AU$1.3 billion.9 The new estimates for 2004 indicate that the cost burden is now about AU$2 billion. This estimate is much larger than that stated in government reports (about AU$1 billion), where only the direct costs of stroke to the health sector in any one year are considered.19 In contrast, the COI estimates in this present study were based on a community-based incidence cohort meeting “gold” standards for case ascertainment. The included cases were those treated in the community, as well as in hospital.

Estimated lifetime resource use was different for ICH than previously reported. Prior methods overestimated the lifetime costs for ICH.9 Incorporation of better information about long-term resource use patterns in survivors following ICH into the COI model has provided evidence that average total lifetime costs are AU$9534 less for ICH than IS. However, costs in the first year were AU$4507 greater for ICH than IS. Detailed sensitivity and uncertainty analyses provided evidence that the point estimates generated were robust.

We found that lifetime cost estimates differed between our study and those reported by Dewey and colleagues (2003).
The main reason for these differences relates to the assumptions about long-term resource use after the first 12 months after stroke. The preexisting lifetime estimates, using an annual cost method based on short-term (6 to 12 months) data, overestimated annual costs for ICH. However, the original annual cost method for IS was more robust. There are a number of explanations for these findings. The most important are: (1) the small sample size for ICH in the original study (n = 40 compared with n = 174 in the updated ICH model); and (2) the differences in resource use patterns between the first year and subsequent years of survival. Noticeably, IS patients used more aged care, inpatient rehabilitation, and community services than the ICH cases. These are each important contributors of cost, and largely reflect the different mean (median) ages between these subtypes. Moreover, compared with IS cases, ICH cases tend to have greater case fatality within the first year, but because these cases are usually younger they have better life expectancies.

Few investigators have examined the differences in costs between IS and ICH subtypes. Most have reported the cost differentials within the first year or during the inpatient hospital period. As suggested by these authors and supported by the results presented, the costs of the acute phase (within 12 months) are greater for ICH. Other studies, also designed to describe the long-term costs of stroke in unselected stroke populations, have recently been published. In each of these studies only direct health sector costs are reported. Moreover, lifetime resource use has only been modeled in one of these studies, and was limited to an analysis of IS. Costs for both IS and ICH were reported by the other two groups. However, one of these studies was limited to people aged 65 years or older. Direct comparison between these studies and the present one is therefore difficult. Nonetheless, results about the differences in total costs per case according to stroke subtype appear consistent.

That is, IS costs over time tend to be greater than those for ICH. For example, McGuire et al (2007) have reported mean total costs over 11 years as £18 629 for ICH and £21 505 for IS for the UK.

The fact that ICH lifetime costs are less than previously estimated only had a minor effect on the total cost burden of stroke in Australia. This is because about two-thirds of strokes are ischemic. The effect of the new ICH costs was to shift the proportion of total costs attributable to ICH from 26% to about 12%. However, the overall increase in total costs was largely driven by new IS costs that had previously been underestimated. Therefore, even a small increase in an average cost per case for IS would have a large impact on total costs because ischemic stroke is more common. We also acknowledge that predicting future costs has limitations because prices, technology, and clinical practice may change. To address such limitations multivariate probabilistic uncertainty analysis was undertaken allowing for variations in stroke incidence, mortality and recurrent event rates, as well as prices.

### Conclusions
In this study, the present value of the total lifetime cost burden of first-ever IS and ICH was estimated to be more than AU$2 billion in 2004. To our knowledge, this is the only study to include a community-based incidence cohort with resource use estimates out to 5 years. The benefits of these comprehensive data highlight the large contribution of costs resulting from out-of-pocket expenses, informal care, and productivity losses associated with stroke. These costs are not captured in other studies. Patterns of resource use were shown to vary by stroke subtype within the first year and over a lifetime. These data may be useful for planning health service requirements to meet the growing needs of society. This is because there is strong evidence that the number of stroke

### Table 4. Results of Uncertainty Analyses on Cost Estimates (Australian $)

<table>
<thead>
<tr>
<th>Stroke Subtype</th>
<th>Modeled Point Estimates*</th>
<th>95% Uncertainty Interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of strokes</td>
<td>27 291</td>
<td>27 344</td>
</tr>
<tr>
<td>Total first-year direct cost ‡</td>
<td>675 078 632</td>
<td>674 735 296</td>
</tr>
<tr>
<td>Total lifetime direct costs ‡</td>
<td>1 708 784 593</td>
<td>1 706 509 568</td>
</tr>
<tr>
<td>Total lifetime indirect costs ‡</td>
<td>45 945 498</td>
<td>46 039 134</td>
</tr>
<tr>
<td>Total incidence costs ‡</td>
<td>1 754 730 091</td>
<td>1 752 269 184</td>
</tr>
<tr>
<td>Lifetime cost/ incident stroke †</td>
<td>64 297</td>
<td>64 208</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of strokes</td>
<td>4239</td>
<td>4247</td>
</tr>
<tr>
<td>Total first-year direct cost ‡</td>
<td>123 956 819</td>
<td>124 029 072</td>
</tr>
<tr>
<td>Total lifetime direct costs ‡</td>
<td>219 485 125</td>
<td>219 562 080</td>
</tr>
<tr>
<td>Total lifetime indirect costs ‡</td>
<td>12 645 181</td>
<td>12 671 905</td>
</tr>
<tr>
<td>Total incidence costs ‡</td>
<td>232 130 305</td>
<td>232 227 064</td>
</tr>
<tr>
<td>Lifetime cost/ incident stroke †</td>
<td>54 763</td>
<td>54 745</td>
</tr>
</tbody>
</table>

*3000 simulations; †3% discount rate used; ‡direct costs include patient out-of-pocket expenses and informal caregiver costs.
events will increase as the population ages. In considering the societal costs of stroke, a greater understanding of the cost impact of this disease to families and patients is achieved because a more comprehensive assessment of the costs attributable to stroke was used. These costs were shown to be substantial and may be used to better support the development of policies, such as for caregiver and disability payments.

Acknowledgments
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Disclosures
None.

References
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The version of the article, “Estimating the Long-Term Costs Of Ischemic and Hemorrhagic Stroke for Australia: New Evidence Derived From the North East Melbourne Stroke Incidence Study (NEMESIS)” by Cadilhac et al that published ahead-of-print on January 29, 2009 and appears in the March 2009 issue of the journal (Stroke. 2009;40:915–921) contained an error in Table 1. The Yes and No columns have been transposed. The results that include the Caregiver costs should be larger than when these costs are not included.

The table has been corrected in the online version of the article.