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Economic evaluation of phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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Title Page

Title

Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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Objectives While Very Early Mobilisation (VEM) intervention for stroke patients was shown not to be effective at 3 months, 12 -month clinical and economic outcomes remain unknown. It was aimed to assess cost-effectiveness of a VEM intervention within a Phase III randomised controlled trial (RCT).

Design An economic evaluation alongside a RCT

Setting Multi-country RCT involved 58 stroke centres.

Participants 2104 patients with acute stroke who were admitted to a stroke unit.

Intervention A very early rehabilitation within 24 hours of stroke onset

Methods Cost-utility analyses were undertaken according to pre-specified protocol measuring VEM against usual care (UC) based on 12 -month outcomes. The analysis was conducted using both health sector and societal perspectives. Unit costs were sourced from participating countries. Dichotomised Modified Rankin Scale (mRS) scores (0-2 vs 3-6) and Quality Adjusted Life Years (QALYs) were used to compare the treatment effect of VEM and UC. The base case analysis was performed on an Intention-To-Treat (ITT) basis and 95% confidence intervals (CI) for cost and QALYs were estimated by bootstrapping. Sensitivity analysis were conducted to examine the robustness of base case results.

Results VEM and UC groups were comparable in the quantity of resource use and cost of each component. There were no significant differences in the probability of achieving a favourable mRS outcome (0.030, 95%CI: -0.022 to 0.082), QALYs (0.013, 95%CI: -0.041 to 0.016) and cost (AUD1082, 95%CI: -\$2520 to \$4685) from a health sector perspective; or AUD\$102, 95%CI: -\$6907 to \$7111, from a societal perspective including productivity cost).

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The probability of VEM being cost-effective was between 19% and 44%. Sensitivity analysis achieved results with mostly overlapped CIs.

Conclusions VEM and UC were associated with comparable costs, mRS outcome and QALY gains at 12 months. Compared with to UC, VEM is unlikely to be cost-effective.

registration Australian Trial New Zealand ClinicalTrials Registry, number ACTRN12606000185561.

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- This is the first economic evaluation assessing the cost-effectiveness of a very early rehabilitation intervention within the largest Phase III randomised controlled trial in patients with stroke;
- The study assessed the long-term cost-effectiveness of this very early rehabilitation intervention at 12-month;
- The difficulty posed by the multi-country design of the trial and the percentage of missing data may undermine the confidence in the results.

Introduction

Stroke is one of the biggest killers and a leading cause of disability worldwide.^{1 2} 65% of stroke survivors live with some degree of disability that impedes their ability to carry out daily living activities unassisted.³ Therefore, ways of improving the outcomes of patients after stroke is an important focus of research.^{4 5} Early mobilisation after stroke is believed to contribute to better patient outcomes and clinical trials have been conducted globally.^{6 7}

The short-term efficacy and safety of a very early rehabilitation trial after stroke (AVERT) has been evaluated in a phase III randomised controlled trial (RCT) with 2,104 patients enrolled from Australia, New Zealand, United Kingdom, Singapore and Malaysia. The evidence from this trial indicated that at three months after stroke, early mobilisation of patients was associated with a reduction in the probability of a favourable outcome as defined by a modified Rankin Scale (mRS) score of 0-2 compared to that in the UC group. However, it is uncertain whether this intervention effect extended after the acute phase of stroke. Given the implications of stroke burden sustained beyond the acute phase (i.e., 3 months), it is also important to ascertain clinical outcomes at a longer time point. For example, it has been reported that the recurrence rate of stroke between 3 months and 1 year was approximately 3.1%. Moreover, "steady state" after an acute episode of stroke typically occurs within 3-6 months for patients with lower baseline mRS score (i.e. lower disability after stroke) and longer for those with higher initial mRS (i.e. higher level of disability after stroke).

From a decision-maker's perspective, the long-term outcomes of patients after stroke bear substantial economic and policy implications. With increasingly scarce health resources, it is imperative to examine the longer-term cost-effectiveness credentials of VEM in an early rehabilitation setting for patients after stroke even if this intervention was inferior to usual

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care at 3-month follow up.⁸ The clinical findings from Phase III AVERT trial were inconsistent with that of our Phase II study;¹¹ however, the short term follow-up (only 3 months), single country study design, and small sample size (N=71) of the Phase II study may account for this discrepancy, and rendered the conclusion of associated economic evaluation not generalizable to a broader context.

This economic evaluation was conducted alongside the Phase III RCT.⁸ The aim of this paper is to assess the cost-effectiveness of very early mobilisation within 24 hours after stroke in terms of improving patient outcomes at 12-months, in comparison to usual care (UC).

Methods

The economic analysis was undertaken following the previously published plan.¹² It also conforms to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.¹³ Ethics approval was granted by relevant institutions.

Intervention and comparator

The trial design has been reported in detail elsewhere.⁸ In brief, patients with confirmed stroke who were admitted to a stroke unit within 24 hours of stroke onset were randomised to receive usual stroke-unit care (UC) alone or VEM in addition to UC in a multinational Phase III trial.

Outcomes

The mRS at 12-months, a secondary outcome of the trial, and Quality-Adjusted life years (QALYs) derived from the Assessment of Quality of Life-4D (AQoL-4D)¹⁴ were used as the effectiveness measures in the economic evaluation. The AQoL-4D instrument is a multi-

attribute utility scale used to assess the health-related quality of life (HRQoL)¹⁵; it was administered at 3 and 12 months.

Outcome of mRS was dichotomised into "favourable" (mRS 0-2) and "poor" (mRS 3-6) based on patients outcomes at 12-month follow up.⁸ The difference in the probability of patients achieving a favourable mRS outcome (mRS 0-2) was used to estimate the incremental benefits between treatment groups for the primary efficacy outcome.

Due to the inherent difficulties of administering the AQoL instrument to acute stroke patients, the mRS score at baseline⁸ was used as a surrogate measure of patient utility during the acute phase. The detailed methods of this work are reported elsewhere¹⁶ and a brief description is supplied in the online supplementary document 1.

Costs

A societal perspective with a key focus on the health sector was adopted.

Intervention delivery

Intervention delivery costs consisted of the time costs of physiotherapists and nurses delivering VEM (or UC) to patients. The mean of the total physiotherapist time (across whole hospital stay) per patient was calculated. Given insufficient data, physiotherapist's mean time per session was used as a proxy for nurse time spent on delivering either VEM or UC.

Resource use

Unit costing

Costs were computed by applying country-specific unit costs to each resource item utilised. Therefore, five sets of unit costs (one for each of the participating countries) were compiled from the most up-to-date and reliable source (Supplementary document 3). Unit costs from a country with a similar economic status and healthcare system were used where local country-specific unit costs were unavailable.

All costs are expressed in Australian dollars (AUD) for the 2015 reference year value and can be converted to United States dollar (USD) using the Purchasing Power Parity rate 1 USD=1.463 AUD¹⁷. The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

The details of resource use and unit cost for acute stroke hospitalisation, rehospitalisation, rehabilitation, non-health sector costs and productivity cost are provided in Supplementary document 3.

Statistical analysis

All the costs that were attributable to stroke including healthcare costs, non-healthcare costs and productivity costs were accounted for in the economic analysis. Since a 12 month economic evaluation was undertaken, no discounting was applied to either costs or benefits.

Quantity of resource use and costs were summarised using medians and interquartile ranges (IQRs) due the skewness of the raw data. Means and standard deviations (SDs) were also reported. Base case analysis of the economic evaluation was performed based on the Intention-to-Treat (ITT) population¹⁸ with an assumption for the main analysis that data were Missing At Random (MAR). The difference in costs was analysed using Generalised Linear regression Model (GLM) with gamma family and a log link, with treatment groups as an independent variable, including baseline NIHSS, baseline mRS¹² and age as treatment covariates.

For the primary outcome, the mRS score at 12 months was compared following the method detailed in the Statistical Analysis Plan. ¹⁹ While for the secondary effectiveness outcome (i.e. the QALY gains at 12 months), a linear regression model with treatment group as the factor variable and 12 months AQoL-4D utility value as the dependent variable, adjusted for age, baseline mRS was utilised to estimate the difference in QALY gains over 12 months. Non-parametric bootstrap simulations with 2000 replications were used to calculate 95% confidence intervals (CIs) around mean difference in costs and effects for cost-effectiveness analysis. To examine the cost-effectiveness of VEM measured against UC, Incremental Cost-Effectiveness Ratios (ICERs) were calculated where applicable. For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost). The differences between groups in terms of costs and benefits (i.e. QALYs) were compared regardless of the statistical significance of the difference. ²⁰ Cost-effectiveness acceptability

curves were plotted to show the probability of VEM being the optimal choice. The ICERs were compared with a common benchmark in Australia of ≤AUD50,000 per QALY.²¹ All the analyses were performed using the STATA 14.0 statistical package (StataCorp. 2015. Release 14. StataCorp LP.)

Sensitivity analyses

To investigate the impact of using country-specific costs, a country dummy variable was added to the GLM analysis to adjust for country effect.²² Subgroup analysis on the basis of individual countries were also conducted to explore the difference in costs and benefits across countries.

Multiple imputation was performed to test the sensitivity of results to the missing data assumption. The missing patterns were explored with the use of logit regression to investigate if any of the other variables predicted whether a given variable was missing²³ (Supplementary document 4).

Secondary analyses were undertaken to assess the robustness of the base case results. Subgroup analyses were performed at the country-specific level to test for differences in efficacy and costs.

Results

Between July 2006 and October 2014, 2,104 patients (VEM 1,054; UC 1,050) were recruited across 58 sites from Australia (1,054), New Zealand (189), United Kingdom (610), Singapore (128) and Malaysia (123). At recruitment, over 80% of patients had no prior history of stroke; NIHSS was greater than 7 points (indicating a moderate to severe stroke) for around 45% of

patients; 26% aged over 80 years and 24% had received recombinant tissue plasminogen activator prior to randomisation⁸. Baseline characteristics were similar between the two treatment groups⁸. **Outcomes**

In terms of the mRS score, a comparable percentage of patients from both treatment groups achieved a favourable outcome at 12 months after stroke, resulting in a non-significant difference (0.030, 95%CI:-0.022 to 0.082, p=0.252) between groups in the analyses adjusted for baseline age and NIHSS (Supplementary document 5: Table III). Since there was no significant intervention effect together with no accepted willingness-to-pay (WTP) per unit increase in probability of achieving a better mRS outcome, further estimation of the ICER was considered not meaningful (i.e. no cost-effectiveness plane or cost-effectiveness acceptability curve could be generated). For the outcome of QALY gains across 12 months, a non-significant treatment effect was also observed (0.013, 95%CI:-0.041 to 0.016, p=0.389) (Supplementary document 5: Table III).

Given the excessive variability in observed AQoL (i.e. 3 and 12 months) within the same mRS category, it was considered inappropriate to apply the mapped utility to measure the incremental QALY gains between two treatment groups. Instead, the differences in AQoL-4D utility value measured at 12 months follow-up between treatment groups were used to approximate the incremental QALY gains across 12 months provided that patients were well balanced between two groups and there were no significant discrepancies in patients characteristics across all baseline variables, including baseline AQoL-4D utility value.

Costs

Generally, the differences between VEM and VC groups was \$1082 (95%CI: -\$2399, \$44563) for the total medical cost (Supplementary document 6: Table III) and \$3 (95%CI: -\$5, \$12) for the productivity cost per person at 12 months. Similarly, the between-group difference in the total non-health care cost was -\$1300 (95%CI: -\$3361, \$760) over the same period of time. The detailed costs of each resource item and summary costs are presented in Supplementary document 6: Table III.

The details relating to the resource use item collected, quantities of resource utilisation and intervention costs are summarized in Supplementary documents 6 and 7.

Cost-effectiveness analysis

The between group difference in both efficacy and cost outcomes generated from the GLM model are presented in Supplementary document 5: Table III.

In the base case health sector perspective analysis, the VEM yielded comparable total medical costs (\$1082, 95%CI: -\$2520 to \$4685, p=0.544) and QALY gains (-0.013, 95%CI: -

0.041 to 0.016) at 12 months, with a 19% probability being a cost-effective intervention compared to UC. When a societal perspective was adopted, the VEM entailed, again, similar costs with the UC group (\$102, 95%CI: -\$6907 to \$7111, p=0.982, including productivity costs) or (-\$6, 95%CI: -\$5476 to \$5463, p=0.933, excluding productivity costs), with a higher probability (42-44%) of being cost-effective (Table 1).

The cost-effectiveness planes and cost-effectiveness acceptability curves from the two perspectives are shown in Figures 1 and 2, and Supplementary document 8: Figures I to IV.

Sensitivity analyses

Inclusion of a country dummy variable in the analysis produced similar results to the base case (Supplementary document 5: Table I).

The analysis from imputed data including all randomised participants produced consistent results with regard to the incremental cost and effectiveness between treatment groups. From a health sector perspective, VEM was associated with similar costs (\$940, 95%CI: \$-4622 to \$4682) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) over 12 months. Likewise, if a societal perspective was taken, VEM was associated with comparable costs (\$1413, 95%CI:-\$4044 to \$6871, including productivity cost; \$1704, 95%CI:-\$3817 to \$7226, excluding productivity cost) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) (Supplementary document 6: Table IV). Even though the point estimate of difference in total costs between groups from a societal perspective varied considerably, the 95% confidence interval derived from base case and multiple imputation analyses were nearly identical (Supplementary document 5: Table IV). The cost-effectiveness plane derived from the multiple imputation

From a health sector perspective, the between-group difference for each participating country yielded consistent conclusions with the base case analysis. VEM was associated with both non-significantly different costs and benefits (i.e. QALY gains at 12 months) compared to the UC, although the point estimate of the cost difference between groups varied from country to country, ranging from -\$2836 (New Zealand) to \$2937 (UK) (Supplementary document 5: Table II).

The country-specific analysis showed an inconsistent trend in the between-group differences for both costs and QALYs. It was found that VEM was likely to cost less and associated with a greater gain in QALYs in comparison to UC in New Zealand and Singapore. Meanwhile, except for total medical cost, VEM seemed to incur less cost while leading to less gain in QALYs at month 12 months for participants from Australia, whilst in the United Kingdom, VEM was associated with higher cost and lower QALY gains than UC. Lastly, for patients from Malaysia, VEM contributed to higher cost while greater QALY gains at 12 month follow-up. It is worth noting that none of the afore-mentioned between-group differences were statistically significant (Supplementary document 5: Table II).

When a societal perspective was assumed, again, the point estimate of difference in costs between groups across countries varied substantially, with the 95% confidence intervals mostly overlapping (Supplementary document 5: Table II).

Discussion

The 12 months within-trial cost-effectiveness analysis showed that VEM was associated with a low probability (19-49%) of being more cost-effective than UC in patients with stroke. Between-group differences in costs and benefits (probability of achieving a favourable outcome of mRS and differences in QALYs) over the one year study period were not significant, even though the point estimates indicated that VEM was dominated (less effective, more costly) by UC from a health sector perspective. The base case analysis showed that the probability of VEM being cost-effective was 21% from a health sector perspective and 45% from a societal perspective.

The cost-effectiveness acceptability curve showed that, with the increasing WTP per QALY threshold, the probability of the VEM intervention being cost-effective actually decreases. This is probably due to the fact that VEM was both less costly and less effective than UC, so the lower WTP/QALY threshold (<\$50,000) afforded a higher probability of being the cost-effective intervention, and vice versa.

Our earlier economic evaluation of the phase II AVERT trial which consisted of only 71 patients (38 VEM and 33 UC) from two Australian centres reported that VEM was likely to be a cost-effective intervention with both less cost and more benefit when compared to UC. 11 Since it was a national pilot study with a limited sample, the direct comparison between the results from this and our current economic evaluation is problematic. In addition, inconsistent with the pilot study, no service shifting was observed in the current study. Across all resource use components, the proportion of patients consuming specific types of resources were comparable between the two groups in this study. On the contrary, in the phase Phase II AVERT trial, patients from VEM group were more likely to be discharged earlier from hospital than their UC counterparts; those discharged early tended to use more care provided in the outpatient setting, which incurred lower costs; and informal care was not costed. In the current study, the LoS for acute hospitalisation and rehabilitation were similar between

treatment groups (median: VEM 16 vs UC 17 days). These differences between the two studies highlight the importance of large, adequately powered studies to inform health care policy.

In this study, resources used were valued on the basis of country-specific unit costs sourced for each participating country. To counteract any concern arising from the adoption of this approach, extensive sensitivity analyses were performed to test the robustness of the results. The conduct of incorporation of a country dummy variable into the model or country-specific analysis did not alter the outcomes substantially, with the resultant 95% confidence intervals overlapping to a great extent. Ramsey et al. 2015 suggest that a country-specific costing approach is likely to yield few qualitative differences in summary measures of cost-effectiveness among countries with similar levels of economic development.²² Therefore, it was believed that any differences in economic status of the participating countries (as reflected by the unit costs applied in our study) are unlikely to bear a major influence on the results of the cost-effective analysis.

This multinational trial also revealed that in managing patients post-stroke, practice of stroke care varied from country to country. Although 100% of patients with stroke were hospitalised for the initial acute care, the LoS differs significantly greatly, ranging from 4 days (Malaysia) to 25 days (New Zealand), which might be attributable to the different severity of stroke and/or differences in clinical practice care processes. Moreover, in Malaysia, patients tended to receive rehabilitation services in an outpatient rather than inpatient setting, compared to participants from other countries. Patients from western countries consumed more community services than their Asian counterparts, which reflects the difference in social welfare systems. The country-specific subgroup analysis also echoed these findings. It was

observed that, except for Malaysia, VEM was associated with less total non-medical cost than UC. The cost-effectiveness credentials varied from country to country: VEM was dominated by UC in United Kingdom and dominates UC in New Zealand and Singapore, while it was cost saving but had less QALY gains in Australia. This indicates that even though, compared with UC, VEM is unlikely to be cost-effective when compared to UC. However, in some countries (e.g. United Kingdom) where patients tend to have heavy use of non-medical health resources, VEM might be cost-saving in comparison to UC.

Economic evaluations have been conducted for other types of stroke rehabilitation interventions including early-supported discharge service, community- or home-based rehabilitation. 24-32 Generally, these interventions trended towards being cost-saving measured against usual practice. In regards to health-related quality of life (HRQoL) outcomes measured by a series of quality of life instruments (including SF-36, WHOQoL-Bref, Nottingham Health Profile, Sickness Impact Profile and EQ-5D), most studies did not detect an overall significant effect.^{24-28 30 31 33} Only one study reported a significant difference improvement in the overall HRQoL score.³² The conclusions drawn from these economic evaluations of stroke rehabilitation interventions were fairly consistent; the interventions were likely to cost less, ^{29 30 33-38} although the difference in costs was statistically significant in only one study.³⁷ None of these studies evaluated the costs and benefits, particularly benefits measured in terms of QALYs, in an aggregated manner, and all were limited by small sample sizes. Another study using a Markov model explored the increased intensity of physiotherapy for stroke patients from a health system perspective, concluding that increased physiotherapy could be cost-effective by improving health outcomes and reducing costs due to the resultant shorter stay in rehabilitation facilities.³⁹

Given that it is not practical to obtain a baseline utility value from patients with stroke, in this study, the baseline AQoL value was mapped from mRS score at baseline. 12 Whilst the

mapping exercise was carried out using the baseline mRS score and AQoL values at 3 and 12 months, the significant variation in the mapped baseline utility values for patients falling within the same category of mRS hampered its application to the current economic evaluation. Instead, only the 12-month utility values were compared to approximate the difference in QALY gains over one year between the two treatment groups. Comprehensive sensitivity analyses were undertaken surrounding this assumption. It was observed that there was no noticeable difference among approaches examining the annual QALY gain difference between VEM and UC, and the difference was unanimously statistically insignificant.

Whilst the results from the clinical study showed that there were no significant differences in either costs or effects between treatment groups, the cost-effectiveness analysis was still performed to investigate the possible ICER of the VEM intervention. It is possible to have greater confidence in the joint outcome of costs and QALYs than looking at them individually.⁴⁰

To the best of our knowledge, this study evaluated the cost-effectiveness of the largest international acute stroke rehabilitation trial ever conducted. The cost-effectiveness analysis was performed alongside the randomised controlled trial, where the costs and benefits data were collected prospectively. Moreover, the Cost CRF was completed by trained and blinded assessors via interviews with individual patients/carers and accessing medical records, which provides for greater accuracy than resource use questionnaires or diaries completed by participants themselves. Since the trial was designed in a pragmatic manner, with close resemblance to real clinical practice, it is believed that the assessment of its cost-effectiveness under this setting reflects the actual value for money of this intervention.

This study provides some insights for future economic evaluation alongside multi-country, multi-centre clinical trials. It is important to note that given the large number of centres

involved (56 stroke units across five geographical jurisdictions), it was not practical or reasonable to collect centre-specific unit costs which probably leads to huge variations even within a single country. Country-level unit costs were therefore applied to the valuation of resource uses across the trial sites. However, the heterogeneity in the resource utilisation and unit cost among the included countries undermines confidence in the conclusion. A countryspecific economic evaluation might be more appropriate in this regard but the lacking of statistical power poses another concern. The current study made a trade-off between them both approaches by presenting both the aggregated (i.e. base case of pooling all countries) and disaggregated (i.e. sensitivity analysis of individual countries) form of results. The resource utilisation, costs and benefits were also tabulated across all sites and individually to allow close scrutiny from various perspectives. ²⁴ It is believed that this practice can be recommended to other multi-country studies.

A couple of limitations of the study are acknowledged. Firstly, the missing data on total costs from a societal perspective was around 24%, and related mainly to the missing information on community services (10.9%) and productivity loss (10.7%). The base case analysis was based on the ITT population with an assumption of missing pattern being MAR. To account for this, the sensitivity analysis using multiple imputation was undertaken and yielded the identical conclusion (i.e. no significant difference in costs and benefits between treatment groups). Secondly, unit costs originating from individual countries were assigned to value resource use. The differences in health care systems and cost structures among the five participating countries may potentially confound the cost comparisons between groups. However, analysis by country produced results consistent with the base case, which overcomes any concern that the latter were heavily weighted towards Australia, the largest sample country.

This economic evaluation alongside a phase III RCT evidenced that based on the ITT population, the VEM intervention for patients with stroke was associated with higher costs from health sector and societal perspectives, lower QALYs at 12 months, and was unlikely to be cost-effective compared to UC, although the between-group difference in cost and QALYs gains were not statistically significant. The sensitivity analyses based on the multiple imputation and subgroup analyses by each country separately yielded fairly consistent results. Overall, the VEM intervention was demonstrated to be comparable with UC in terms of both benefits and costs at one-year, however given its poorer outcomes at 3 months, VEM cannot be recommended to clinicians, patients or policymakers.

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Figure Legends

Figure 1 cost-effectiveness plane_health sector perspective

Figure 2 cost-effectiveness plane societal perspective (including productivity cost)



Table 1. Baseline cost-utility analysis ITT

	QALYs	Per capita mean cost (AUD)	Probability of being cost-effective
Health care perspective			
Total medical costs	-0.013	\$1082 19%	
	(-0.041, 0.016)	(-\$2520, \$4685)	
Societal perspective			
Total medical and non-medical	cal -0.013 -\$6		42%
costs (excl. productivity cost)	(-0.041, 0.016)	(-\$5476, \$5463)	
Total medical and non-medical	-0.013	\$102	44%
costs (incl. productivity cost)	(-0.041, 0.016)	(-\$6907, \$7111)	

ITT: Intention-to-treat; QALYs: Quality-adjusted Life Years; AUD: Australian dollar; excl: excluding; incl: including

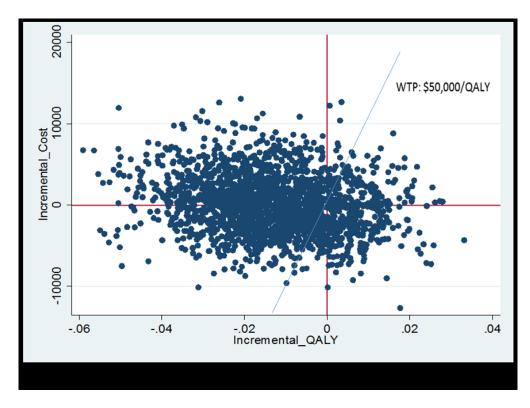


Figure 2 cost-effectiveness plane_ societal perspective (including productivity cost) $146 \times 109 mm \; (150 \times 150 \; DPI)$

Supplementary document 1: Mapping baseline mRS score to utility of AQoL-4D

Methods

Generalized additive model (GAM) with spline smother was used to map AQoL from premorbid mRS, stroke severity, and/ or age group. The performance of the models was evaluated using mean absolute, mean squared errors (MAE and MSE) and R2. 10-fold cross-validation was implemented for model validation. The mapped baseline utility of AQoL-4D was used in the following models.

The analyses are structured as follows:

Model 1:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and pre- morbid mRS + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 2:

- a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input;
- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity as a covariate;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity and age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 3:

a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value as a covariate;

- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 4:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Results

Table I. Difference in utility values between treatment groups by different models

	a	b	c	d	
				1	2
Model 1	-0.011	-0.015	-0.016	-0.026	0.006
	(-0.042, 0.020)	(-0.042, 0.011)	(-0.042,0.010)	(-0.062, 0.009)	(-0.030, 0.041)
Model 2*	-0.001	-0.007	-0.008	-0.007	0.005
	(-0.046, 0.044)	(-0.047, 0.034)	(-0.048, 0.031)	(-0.062, 0.048)	(-0.050, 0.060)
Model 3*	-0.008	-0.014	-0.015	-0.014	0.002
	(-0.043, 0.026)	(-0.043, 0.016)	(-0.043, 0.014)	(-0.052, 0.033)	(-0.050, 0.045)
Model 4	-0.008	-0.014	-0.015	-0.026	0.006
	(-0.043, 0.026)	(-0.043, 0.016)	(-0.043, 0.014)	(-0.062, 0.010)	(-0.030, 0.042)

^{*}models 2 and 3 used the mapped baseline AQol utility to estimate the QALY gains over 12 month for each patient.

utility value to calculate the difference in QALYs between treatment groups (results from models 2 and 3) yielded similar results to the primary analysis (-0.013, 95%CI [-0.043, 0.018]), and the 95% confidence

Supplementary document 2: Cost Case Report Form (CRF)

The Cost CRF was originally developed via pathway analysis during Phase II of AVERT to identify resource items associated with the trial 11. Since the Phase II of AVERT trial was a national project and resource utilisation tools were tailored to the Australian setting, the form was further modified to accommodate international differences in the acute service delivery, rehabilitation and post-acute care. An extensive review of country-specific literature and consultation with international AVERT project team members based in each country were undertaken to tailor the Cost CRF tool to each participating country.

Case Report Form - Cost

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PATIENT INITIALS

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Note: this one form is to be completed AND faxed following BOTH the 3 and 12 months at 12 months fax all pages 25.36 to the Date Page. When CRF Cost complete at 3 months AND at 12 months, fax all pages 25-36 to the Data Fax.

Instructions to the person responding: These questions are about health care provided as a consequence of the stroke which occurred on (give date of stroke) or as a result of any further stroke. I will be asking about health care such as visits to hospital, rehabilitation, the about home, equipment and work. To help us work out the cost of stroke to the community, and to you and your family, I will be asking about how often services were provided and their cost.

Subject's stroke date

vnload t Supe	vnload t Supe text a			om CRF - Screening Day 0	Obtain fr
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Please note: this is the 'normal' living arrangement of the respondent with respect to the subject, even if the Subject is currently in hospital					





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1) DISCHARGE					230 c		
Date of discharge from acute care	Acute discharge des		Date of admission	to inpatient reh	~ N	Discharge destination aft	ter inpatient rehab
/	Home Rehabilitation ward/ho Supported residential	ospital	Date of discharge	from inpatient r	May 20139 Enseigha eha	Rehabilitation hospital Supported residential servi	
	Hostel]/[Down	Hostel Nursing home	
	Nursing home Other Unknown		Date of discharge Leave dates BLAN Please note: inpat inclusive of geriatri transitional care.	NK if not applical ient rehabilitation c evaluation and	ગીoaded from h Superieur (AB ext and data m	Other Unknown	
2) LIVING ARRANGEMENT					m http://b (ABES) . ta mining	Leave BLANK if not app	plicable
Pre-stroke residential address		Residential address a	t 3 months*		R ≧ sid e ntia	al address at 12 months*	
Own house, flat – alone		Own house, flat – alone			Ogin higuse	e, flat – alone	
Own house, flat – with family/relative/frie	end 🗆	Own house, flat – with	family/relative/friend		Q∰m hoguse	e, flat – family/relative/friend	
Home of relative/friend		Home of relative/friend			H e me o f re	elative/friend	
Supported residential service (SRS)		Supported residential s	service (SRS)		S	residential service (SRS)	
Hostel		Hostel			Heste		
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Case Report Form - Cost

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3) CHANGE IN LIVING ARRANGE	MENTS		230 o		
As a consequence of your stroke, have you n	eeded to change your place	e of residence?	3 moRths 2	′es □ No □	Unknown □
If NO, proceed to question 4. * Please note: if subject has been a hospital	inpatient this is NOT a char	nge of residence	ະຫຼຸກ ສັກ 3-12 ຫຼືກູສຸກສາຣ \	′es □ No □	Unknown □
DATE OF MOVE	LOCATION		2019. D eignem related		
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2) /	Nursing home Other Own home or unit Home of relative/friend SRS Hostel Nursing home Other		from h ur (AB data m		
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4) / / /	Own home or unit Home of relative/friend SRS Hostel Nursing home Other		ttp://bmjopen.bmj.com/ on June 13, 2025 ES) . nining, Al training, and similar technologi		
4) AMBULANCE TRANSFERS: EI	MERGENCY AND NO	N-EMERGENCY	5 at A jies.		
As a consequence of your stroke, have you if NO, please proceed to question 5	equired ambulance transpo	ort after your acute admission to hospital?	?* 3 months	Yes ☐ No	Unknown 🗆
Count number of ambulance trips (recrui	ment to 3 months)	* Include post-acute transfers (eg - acu	3-12 Bontl io io gr te to rehab) ap	ns Yes □ No	☐ Unknown ☐
Count number of ambulance trips (fro	om 3 to 12 months)		hiq		







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5	HOSPITALISATIOI	N OR EMERGEN	NCY DEPARTMEN'	Γ ATTENDANCES

If NO, proceed to question 6

5) HOSPITALISATION OR EMERGENCY DEP	ARTMENT ATTENDA	ANCES	0 on			
a) Have you been readmitted to hospital or attended the emr	ergency department as a	consequence of another stroke	ਰ 3 months	Yes 🗆	No 🗆	Unknown [
To any shore related problems.			us ∰2 month	s Yes □	No 🗌	Unknown
ONLY include information for admissions and attendances troke-related problems and CRF completion manual for fur		s (see below for summary list of	2019. eigner relate			
NO, proceed to question 6						
b) If YES, Start with the earliest admission or attendance. If parates BLANK (complete dates at 12 month assessment)	tient NOT discharged at 3 m	onth assessment, leave discharge	Downloaded nent Superied d to text and			If patient n discharged 12 month
Admission or Attendance 1 - Hospital name	Hospital code	Date admitted	from Date	discharged		assessmer
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Admission or Attendance 2 - Hospital name	Hospital code	Date admitted	≥ 3.	discharged		
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Admission or Attendance 3 - Hospital name	Hospital code	Date admitted	Date / Date	discharged		
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Admission or Attendance 4 - Hospital name	Hospital code	Date admitted	chr 13	discharged		
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Admission or Attendance 5 - Hospital name	code	Date admitted	-	discharged		
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Stroke related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary catheter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11. Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional pre-lem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting 19. Surgery or procedural management of of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21. Inabies to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26. Pressum sores.

Unknown □

Unknown □

Unknown

If patient not

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of DAYS

attended

6) INPATIENT	T REHABILITATION	ADMISSION
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After your stroke on (give date of stroke), were you admitted to a Rehabilitation Hospital or other hospital where you received rehabilitation treatment? Please include admissions with the care type 'rehabilitation', 'geriatric evaluation' and 'transitional care'

If NO, proceed to question 7.

If YES, complete inpatient rehabilitation admission details, starting from your first inpatient rehabilitation admission. If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

Admission 1- Rehabilitation hospital name	
	O _A
Admission 2- Rehabilitation hospital name	
Admission 3- Rehabilitation hospital name	

ssions with the ca	re type 'rehabilitation', 'geriatric	3-12 months	Yes 🗆	No 🗆	Unknown □
ates BLANK (com Rehab hospital code	ent rehabilitation admission. plete dates at 12 month assessment) Date admitted / /	lay 2019. Downloaded Enseignement Superionses related to text and	Date dischare	ged	If patient not discharged at 12 month assessment, cross box.
Rehab hospital code	Date admitted	l fro eur (i dat	Date discharg	ged	
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Rehab hospital	Date admitted	s) ing,	Date discharg	ged	
		Mjoper Al trai	/ / _		

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Yes □

7) OUTPATIENT REHABILITATION PROGRAM

Did you attend or are you attending an outpatient rehabilitation program as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech therapy, etc

An outpatient rehabilitation program is any rehabilitation program where the patient attends a facility. The program can be located at a hospital or community facility.

If NO, proceed to question 8.

If YES, complete outpatient rehabilitation details, starting from your first outpatient rehabilitation visit,

atient NOT discharged at 3 month assessment, leave dis			plete dates a 12 Month assessment)
Admission 1 - Outpatient rehabilitation name	Rehab facility code	Date admitted	୍ରିଟ୍ର Late discharged
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Admission 2 - Outpatient rehabilitation name	Rehab facility code	Date admitted	ਨ੍ਹੇ Date <mark>d</mark> ischarged	
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Admission 3 - Outpatient rehabilitation name	Rehab facility code	Date admitted	Date discharged	
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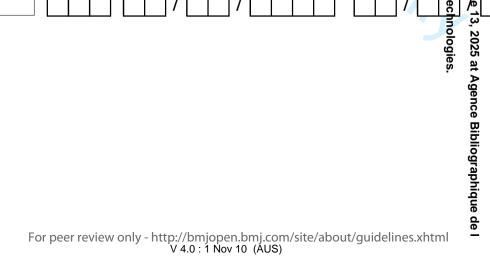
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8) REHABILITATION SERVICES PR	ROVIDED AT HOME OR IN A NURSING HOME	026230 includir	·	
Have you had a rehabilitation program provide as a consequence of your stroke? e.g. with p		3 months of Nes □	No ☐ Unknown ☐]
If NO, proceed to question 9. If YES, complete rehabilitation details, starting frosessions.	om the first visit since your stroke. Count number of t, leave discharge dates and number of sessions BLANK	Say 2019. Downlo	Total	If patient not discharged at 12 month
ime 1 - Rehabilitation service name	Rehab service code Start date	Cease of trom	SEGGIONIS	assessment, cross box.
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9a) D	id you receive any community services	in the yea	ar PRIOF	R to you	r stroke	?			g fo	on i	Yes 🗆	No ☐ Unknown ☐
	ommunity services are individual care s	services p	rovided	at home	and do	NOT inc	clude rel	nabilitation the	erapy.	22 Ma)		
	YES, which service/s did you receive in	the year	PRIOR t	o your s	troke?				How many tinge the past year Ri			
Г		Which	service	did you	receive	? (One s	ervice c	ode per line)	receive the segv	ce?		
	Community service codes 1 = Nursing Service 2 = Delivered Meals	□1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	d to to	Down!		
	3 = Personal Care (Bath/Shower) 4 = Housework help		□ 2	3	□ 4	□ 5	□ 6	□ 7	xt and	oaded		
	5 = Gardening/home maintenance6 = Home respite	□1	□ 2	□ 3	□ 4	□ 5	□ 6	7	d data	l from		
	7 = Other service, specify	□ 1	□ 2	□3	□ 4	□ 5	□ 6	□ 7	min min	P http		
		If "oth	er" (cod	le 7), ple	ase spe	cify			ing) 		
					<u> </u>	_ _			A	//bmjo		
ah) Ha	eve you received community services S	INCE the	stroko?						train	ě	o 🗖 Ni	o □ Unknown □
Co	ommunity services are individual care s			at home	and do	NOT inc	lude reh	abilitation the	3 mona 3	3		o □ Unknown □ o □ Unknown □
	NO, proceed to question 10. YES, which service/s did you receive Al	TER you	r stroke'	?					o 12 land		3 🗀	O LI CHIKHOWII L
Fo	or each service, complete a seperate line onths, and then add service data for 3-1	e. If a serv	vice is o	ngoing a		th interv	view, ent	er data for 3	How many $\frac{\omega}{\Xi}$	n/ on	How many	Note: hours per service
				-		? (One s	service o	ode per line)	times did you	vi s e?	hours per service?	NOT applicable to delivered meals
Г		□ 1	. 55. Med	3	□4	5	□ 6	□ 7	echno	e 13,		
	Community service codes 1 = Nursing Service					_		_	oo oo	s, 2025	\vdash	
	2 = Delivered Meals 3 = Personal Care (Bath/Shower)	□ 1	∐ 2	□ 3	∐ 4	□ 5	□ 6	□ 7	ologies.	at		
	4 = Housework help 5 = Gardening/home maintenance	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7		Agen		
	6 = Home respite 7 = Other service, specify	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7		ence Bibliographique		
L		□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	7		bliog		
36		□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7		rap		
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10) HOME MODIFICATIONS			230 udii		
Has your home been modified as a conseq		adifications at	હું <u>o</u> કુmonths	Yes ☐ No ☐	Unknown 🗌
e.g. installation of rails, bathroom modificationIf NO, proceed to question 11If YES, please indicate the type of modification			7 Ses r	Yes ☐ No ☐	Unknown 🗌
Type of modification	SUPPLIERS 1 = Hospital/rehabilitation centre 2 = Patient/family	3 = Veteran's Affairs 4 = Local Council	6 = Charago	sion 7 = Ot	her (specify)
(check box for each type supplied)	Who supplied the modificat	ion? If supplier is "	other", plose		
☐ Rail(s) for steps/stairs	1 2 3 4 5	1 1 1 1	perice	Cost to you/family* - \$	
☐ Ramp(s)	12345	5	from data n	Cost to you/family* - \$	
☐ Platform step(s)	□1 □2 □3 □4 □5	5 6 7	E s) . nining	Cost to you/family* - \$	
☐ Shower, bath and toilet rail(s)	□1 □2 □3 □4 □5	;	Al tra	Cost to you/family* - \$	
☐ Shower(s) modification	<pre>□1 □2 □3 □4 □5</pre>	; 🗆 6 🗆 7 📗 📗	lining	Cost to you/family* - \$	
☐ Toilet(s) modification	<pre>□1 □2 □3 □4 □5</pre>	;	and siii	Cost to you/family* - \$	
☐ Remove/modify door(s) from shower/toilet/bath	<pre>□ 1 □ 2 □ 3 □ 4 □ 5</pre>	;	on June imilar te	Cost to you/family* - \$	
☐ Kitchen modifications	<pre>□1 □2 □3 □4 □5</pre>	6 🗆 7 📗 📗		Cost to you/family* - \$	
☐ Other modification (specify below) Other home modification - 1			2025 <i>a</i>		
		5 6 7	s at Age	Cost to you/family* - \$	
Other home modification - 2	1 2 3 4 5	5	nce Bi	Cost to you/family* - \$	
If total costs includes any aids, describ	e in brief below (see also list of aids on p	page 33):	ıı, t∭geofmo	rall cost is provided, plea difications above, and p	rovide the



itemised costs listed above: For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml V 4.0 : 1 Nov 10 (AUS)



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11) SPECIAL EQUIPMENT AND A	פחוא		30 or ding		
Have you been given, hired or purchased an	y special equipment, aids or special	food as a consequence of stroke?	ding on 3 mooths	Yes □	No ☐ Unknown ☐
			3-12 km gn 3 s	Yes 🗆	No ☐ Unknown ☐
Prompt: These may have been provided by an If NO, proceed to question 12	Occupational Therapist or Physiothera	apist. What about a?	y 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 as related to text and data mining, Al training, and similar technologies.		
Walking aids	Mobility aids	Eating aids	Dov ed to		Kitchen aids
☐ Single point stick	☐ Manual wheelchair	☐ Built-up cutlery	vnlo t Su tex		☐ Tap handles
☐ Three or four point stick	☐ Electric wheelchair/scooter	☐ Plate guard	ade Iperi t an		☐ Chopping board
☐ Walking frame - pick up	☐ Car steering wheel knob	☐ Non-slip mat	d fro leur d da		☐ Modified knife
☐ Walking frame - wheelie		☐ Special food e.g. NG/PEG	(AB		☐ Vitamiser/blender
☐ Walking frame - gutter (forearm suppt)		If yes, number of days used:	ninir		☐ Non-slip mat
☐ Crutch(es)		3 months	· ig, A		·
		3-12 months	jope VI tra		
			inin b		
Laures and hadroom aguinment	Detha and aminorate	Continence aids	nj.c g, a		General aids
Lounge and bedroom equipment	Bathroom equipment	☐ Urine bottle	nd s		☐ Long handled aid
☐ Chair platform/blocks raise	Over-toilet seat		<u>ä</u> 9		☐ Blood pressure machine
☐ Cushion to relieve pressure	☐ Toilet surround	Bedpan	Jun lar t		☐ Treadmill
☐ Special chair (NOT wheelchair)	☐ Bathroom and grooming aids	☐ Commode	e 13 echr		☐ Stationary bike
☐ Table - bedside/wheelie	☐ Shower chair/stool	☐ Incontinence sheet (bed protect	tor) 6 20		☐ Intercom (portable)
☐ Bed platform/block raise	Over bath seat	☐ Incontinence sheet (kylie/bluey	25 at gies		☐ Modified tap handles
Bedstick	☐ Hand held shower	If yes, number of days used - 3 mo	nths C		If yes, number supplied
☐ Hospital bed (eg - height/tilt adjust)	☐ Non-slip mat	☐ Incontinence pads 3-12 mo	nths 8]	
☐ Mobile hoist/lifter		If yes, number of days used - 3 mo	nths 🖁		☐ Personal alarm If yes, number of days supplied:
Any other aids/equipment, specify		☐ Catheter 3-12 mo	nths g]	3 months
		If yes, number of days used - 3 mo	nths \$\frac{\frac{a}{b}}{\frac{b}{b}}\$.]	3-12 months
		3-12 mo	nths 5]	





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AVERT Very Eurly Exhabilization Trial					-	<u>.</u> . ∞		PATIENT INI	TIALS
12) PR	IVATE PHYSIOTHERAPY					026230 oı İncluding			
Have you	paid for private physiotherapy sessions after your st	roke? (NOT while	a hospital inpatie	ent)		for 22 V	Yes 🗆	No □	Unknown 🗌
If no, pro	ceed to question 13					is Elä Panomiths		No □	Unknown 🗆
If yes, nur	mber of sessions - 3 months					2019 eigne relat			
	3-12 months). Down ement S			
13) RES	SPITE CARE					load Supe			
As a cons	equence of your stroke, have you been admitted to a	respite bed in a r	nursing home or h	ospital?	3 moi		Yes 🗌	No 🗆	Unknown 🔲
If NO, pro	ceed to question 14				3-12 ו	at Of the s	Yes 🗆	No □	Unknown 🗌
f yes, how	many days of respite have you received since your	stroke? 3 month	s			ninir NES)			
		3-12 month	s			ig. A			
						n <mark>jopen.l</mark> Al traini			
14) EM	PLOYMENT STATUS/ PAID WORK				(ng, s			
Were you	working up to the time of your stroke? Yes ☐	No □ L	Jnknown □ of this work? F	ull time 🗆	Part time □	om/ on Ju and similar			
	How many	hours did you worl	k each week?			ne 13, 2025 at technologies			
Since the	stroke, have you returned to this work?	3 months	Yes □ No	□ Unk	known 🗆	2025 ologic			
		3-12 months	Yes □ No	o □ Unk	known 🗆	at Ag			
Have you	returned to normal hours or decreased hours?	3 months	Normal	☐ Decre	eased	ence			
		3-12 months	Normal	☐ Decre	eased	Bibli			
How ma	my hours per week of work have you performed since	e the last assessr	nent?			liogr			
02020	Record average amount per week over the 3	month period	If more than	0 but less	than 1hr, reco	Ω			
	Record average amount per week over the period 3					ue de			
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15) INFORMAL CARE - 3 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hospital in patients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at home. Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services.

15a) OVER THE LAST WEEK, have you received any assistance with your daily activities from a carer as a result of the stronger.

This might include assistance with community tasks (such as help with your banking, paying your

bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning) or assistance with personal care tasks (such as bathing, toileting and feeding)

If the answer is NO, no further questions are required in this section

15b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to question 15c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening; handyman tasks; grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to guestion 15d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

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Yes

Hours

Yes

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16) INFORMAL CARE - 12 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hospital inpatients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at come. Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon # activities of daily living, the carer is the person who provides most of this help beyon Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the base, feeding). Supervision of daily activities to ensure safety should also be included as care.

16a) OVER THE LAST WEEK, have you received any assistance with your daily activities from a carer as a result of the str点腺管

This might include assistance with community tasks (such as help with your banking, paying your bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning) or assistance with personal care tasks (such as bathing, toileting and feeding)

If the answer is NO, no further questions are required in this section

16b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to guestion 16c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening: handyman tasks: grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to question 16d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

Hours

Yes □

Hours

Yes 🗆

Hours

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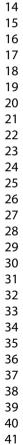
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Supplementary document 3: Resource uses, Unit costs and valuation of costs

Resource use items recorded in the cost CRF

Healthcare resource use

 The quantity of resources used for the following health care resource items was recorded: number of ambulance transfers (emergency and non-emergency), acute hospitalisation (including length of stay [LoS]), rehospitalisation (number of occasions and LoS for each occasion), rehabilitation hospital admission (number of occasions and LoS for each occasion), outpatient rehabilitation program (number of occasions and number of days for each occasion), rehabilitation provided at home/nursing facility (number of occasions and number of sessions for each occasion), private physiotherapy (number of sessions), respite care (number of sessions) and individual outpatient (including physiotherapy, occupational therapy, and speech and language therapy) visits (service type and number of sessions) for patients from United Kingdom, Singapore and Malaysia only.

Non-healthcare resource use

The quantity of resources used was recorded for the following non-heath care resource items: accommodation move due to stroke (location moved to and date of move), community service (type of service use and number of service used both for prior to and post-stroke), home modification (type of modification, supplier and cost), special equipment and aids (type of equipment/aids and quantity consumed), informal care (purpose of the care and hours used), live-in maids (number of maids prior to and post stroke) (for Singapore and Malaysia only), changes to employment (employment status and weekly hours of working both prior to and post-stroke).

Resource use reported at 3 (i.e. resources used between 0 and 3 months) and 12 (i.e. resources used between 4 and 12 months) months was used to calculate the total annual resource use for each participant. Generally, where patients were still using a particular resource at the time of 12-month data collection, the last day of 12 months' follow-up (calculated from the day of index stroke) was used to estimate the duration of that resource utilisation. In the event of a

 patient dying, resource use data for the period prior to death was ascertained from their carer and medical records, wherever possible.

Unit costs for hospitalisation, rehabilitation, non-health sector costs and productivity costs

Acute stroke hospitalisation costing: Unit costs for acute stroke hospitalisation for all countries at baseline were categorised by stroke severity, using the National Institute of Health Stroke Scale (NIHSS) to group patients into three severity levels: mild (0-7), moderate (8-16) and severe (>16). (1)·(2) It was assumed that severity as classified by the NIHSS was consistent with the stroke severity that corresponded to three levels of unit cost for acute hospitalisation. Length of Stay (LoS) together with stroke severity were used to estimate the cost of acute hospitalisation for Australia and New Zealand patients (i.e. the cost of acute hospitalisation was weighted by the LoS). LoS was taken as the difference between the date of hospital discharge and date of hospital admission (plus one day or not) in accordance with country-specific practice. For the other countries, only stroke severity was considered in the assignment of a unit cost to acute stroke hospitalisation due to insufficient health sector data.

Re-hospitalisation and rehabilitation costing: Due to the diversity of causes for patients being readmitted to hospital after the index stroke, the average daily cost of hospitalisation for all disease conditions from individual countries in combination with LoS was used to gauge the cost of readmission for stroke-related causes, while the average cost for an emergency department visit was assigned whenever a patient was hospitalised for one day only. Similarly, the unit cost of rehabilitation hospital admission was taken from the national average cost for all disease conditions. The median cost was used where there was more than one unit cost identified for the same resource item.

Non-health sector costs: Unit costs of non-health sector resource items (e.g. community service, accommodation changes, special aids and equipment) were sourced on a country-specific basis from official websites or published literature where applicable. No unit cost was retrieved for home modification items since the cost of home modifications was generally reported in the Cost CRF.

Productivity cost: Lost productivity was valued based on a human capital approach using average earnings across all occupations up to normal retirement age. The average wage of a

The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

All the unit costs from participating countries are summarised in Table I.

Table I. Unit cost (in Australian dollars) across five countries, 2015 reference year

Resource items	Unit cost (AUD)							
	AU	NZ	UK	SG	MA			
Healthcare								
Acute hospitalisation*								
Severe (per episode)	\$19157	\$10867	\$15327	\$4371	\$2066			
Moderate (per episode)	\$9553	\$6104	\$8115	\$2126	\$1572			
Mild (per episode)	\$6279	\$4370	\$4272	\$1493	\$1363			
Stroke-related rehospitalisation (per	\$1925	\$320	\$701	\$789	\$230			
day)								
Emergency department attendance	\$610	\$325	\$227	\$111	\$68			
(per attendance)								
Rehabilitation hospital admission [†]								
Severe (per episode)	\$1010 [‡]	\$8032	\$19136 [§]	\$157 [‡]	\$1293			
Moderate (per episode)		\$5727	\$29788 [§]					
Mild (per episode)		\$5727	\$13920 [§]					
Same day (per episode)		\$758	N/A					
Outpatient rehab visit (per/session)	\$239	\$164	\$213	\$36	\$17			
Rehab services at home/nursing	\$239	\$212	\$922	\$36	\$51			
facility (per/session)								
Private physiotherapy (per session)	\$64	\$153	\$162	\$116	\$8			
Respite care (per hour)	\$45	\$14	\$26	\$15	\$2			
Individual allied health visit								
Physiotherapy	N/A	N/A	\$243	\$239	\$8			
Occupational therapy	N/A	N/A	\$243	\$36	\$7			
Speech and language therapy	N/A	N/A	\$69	\$36	\$4			
Ambulance transfer	\$508	\$646	\$575	\$265	\$52			
Non-healthcare								
Community services	Not listed	here due to	the number of	fitems				
Home modifications			individual pa					
Special aids and equipment				ıl number of it	ems			
Accommodation changes			the number of					
Professional carer (per hour)	\$24	\$14	\$14	\$10	\$2			
Living-in maid (per month)	N/A	N/A	N/A	\$571	\$103			
Average weekly earnings				,				
Male	\$1137	\$621	\$1152	\$973	\$137			
Female	1		\$957 ¹		,			

Unit cost for intervention [#]						
Hospital physiotherapist (per	\$33	\$32	\$30	\$21	\$5	
hour)						
Hospital nurse (per hour)	\$30	\$25	\$29	\$21	\$5	

AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia;

Sources of CPI:

Australian Bureau of Statistics. Consumer price index inflation calculator. Accessed

 $from \underline{:} \underline{Http://www.Abs.Gov.Au/websitedbs/d3310114.Nsf/home/consumer+price+index+inflation+calculator}.\ 2017 \underline{:} \underline{Http://www.Abs.Gov.Au/websitedbs/d3310114.Nsf/home/consumer+price+index+inflation+calculator}.$

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Https://www.Dosm.Gov.My/v1/index.Php?R=column/cthemebycat&cat=106&bul_id=zi9pmutpvzixb042mlptt1buellazz09&menu_id=bthzthqxn1zqmvf6a2i4rkzondfkqt09. 2017

*severity was determined by baseline NIHSS score; †severity was classified by baseline mRS score; †it is the per day cost; \$cost was assigned according to the baseline mRS score (mild 0-2; moderate 3-5; severe 6); † the National Survey of Household Income was provided on gender basis, so the weekly earnings for UK patients were assigned corresponding to this; #hourly wage of hospital physiotherapist and nurse were assigned; N/A: not applicable. Main sources of unit cost: AU: Independent Hospital Pricing Authority (IHPA), Australia, National Efficient Price Data (2015-16); National Hospital Cost Data collection (hospitals-cost-report-2013-2014-round-18); Department of Health, Revised residential care subsidies (https://agedcare.health.gov.au/aged-care-funding/aged-care-subsidies-and-supplements); Australian Bureau of Statistics

(http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/E9FF9F13B417A488CA257F630014DF30 ?opendocument

NZ: Ministry of Health (http://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations); World Health Organisation (http://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations); Cost Resource Manual Version 2.2 (https://www.pharmac.govt.nz/assets/pfpa-v2-2-cost-resource-manual.pdf); study by Te Ao et al 2011 (Te Ao BJ et al. Are stroke units cost effective? Evidence from a New Zealand stroke incidence and population-based study. Int. J. Stroke. 2012;7:623-630); Statistics New Zealand

(<u>http://www.stats.govt.nz/browse_for_stats/income-and-</u>

work/employment and unemployment/LabourMarketStatistics HOTPJun15qtr.aspx); District Health Board, Multi Employer Agreement, New Zealand Nurses Organisation(http://www.bopdhb.govt.nz/media/58613/psa-ronz-allied-meca-2015-2017.pdf);

UK: National Health Service (NHS) reference costs 2014 to 2015, United Kingdom

(https://www.gov.uk/government/publications/nhs-reference-costs-2014-to-2015); NICE Technology Appraisal (Davis,S., Holmes,M., Simpson,E., Sutton,A. Alteplase for the treatment of acute ischaemic stroke [review of technology appraisal 122]: A Single Technology Appraisal. ScHARR, The University of Sheffield 2012, https://www.nice.org.uk/guidance/ta264/documents/stroke-acute-ischaemic-alteplase-review-of-ta122-evidence-review-group-report2); Personal Social Services Research Unit (PSSRU)(http://www.pssru.ac.uk/); Information Services Division, Scotland (http://www.isdscotland.org/); Annual Survey of Hours and Earnings 2015, Office for National Statistics

(https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2015provisionalresults); Payscale UK

(http://www.payscale.com/research/UK/Job=Care_Worker/Hourly_Rate); NHS pay and benefits

(https://www.healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates);

SG: Ministry of Health, Hospital Bill Sizes, Singapore

(https://www.sg/content/moh_web/home/costs_and_financing/HospitalBillSize/stroke.html.); Outpatient Charges, Singapore General Hospital (https://www.sgh.com.sg/patient-services/charges-payment/pages/outpatient-charges.aspx); Charges, Ren Ci Hospital (https://www.byh.org.sg/patients-guide/charges-2/); Hospital rates and charges, Bright Vision Hospital (https://www.byh.org.sg/hospital-rate-charge.html); Ministry of Manpower (https://stats.mom.gov.sg/Pages/Occupational-Wages-Tables2014.aspx);

MA: study by Mohd Nordin et al 2012 (Mohd Nordin et al.: Estimating cost of in-patientmedical care for stroke using Casemix data. BMC Health Services Research 2012 12(Suppl 1):P10.); Ministry of Health Malaysia (http://www.moh.gov.my/english.php/pages/view/160); Study by Akhavan Hejazi et al 2015(Akhavan Hejazi SM, et al. Cost of post-stroke outpatient care in malaysia. Singapore Med. J. 2015;56:116-119); Department of Statistics Malaysia

(https://www.dosm.gov.my/v1/index.php?r=column/pdfPrev&id=czRyNkJIbDFyYXJFbU5YTVJ1V1BHZz09).

For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost).



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Supplementary document 4. Missing cost data analyses

Table I. Number of missing data for each cost item

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Supplementary doo Table I. Number of missing			cost data	analyses			ight, including for	bmjopen-2018-026230 on 22			
Cost variable	Missing						n Se				
	Total	AU		NZ		UK	S	SG		MA	
10	N=2104	VEM	UC	VEM	UC	VEM	UC at a	©VEM	UC	VEM	UC
1	1(0.050()	N=522	N=532	N=94	N=95	N=311	N=299 ₺∃	N=64	N=64	N=62	N=61
Acute hospitalisation	1(0.05%)	1(0.2%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%) 5		0(0%)	0(0%)	0(0%)
3 Stroke-related rehospitalisation	51(2.4%)	8(1.5%)	7(1.3%)	0(0%)	0(0%)	17(5.5%)	8(2.7%)		3(4.7%)	7(11.3%)	1(1.6%)
Ambulance transfer	53(2.5%)	8(1.5%)	10(1.9%)	0(0%)	0(0%)	16(5.1%)	7(2.3%)	<u> </u>	3(4.7%)	7(11.3%)	1(1.6%)
Rehabilitation hospital admission	55(2.6%)	9(1.7%)	9(1.7%)	0(0%)	0(0%)	18(5.8%)	8(2.7%)	IO	3(4.7%)	7(11.3%)	1(1.6%)
Outpatient rehabilitation program	47(2.2%)	0(0%)	0(0%)	0(0%)	0(0%)	23(7.4%)	10(3.3%	3 0(0%)	3(4.7%)	9(14.5%)	2(3.3%)
8 Rehabilitation provided at home/nursing facility	67(3.2%)	11(2.1%)	10(1.9%)	0(0%)	0(0%)	23(7.4%)	1(3.7%)	0(0%)	3(4.7%)	7(11.3%)	1(1.6%)
10 Individual allied health visit§	0(0%)	-	-	-	-	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Private physiotherapy	76(3.6%)	12(2.3%)	11(2.1%)	0(0%)	1(1.1%)	27(8.7%)	13(4.4%	2 1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Respite care	77(3.7%)	12(2.3%)	11(2.1%)	1(1.1%)	1(1.1%)	27(8.7%)	13(4.4% ≩ .	1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Subtotal (medical cost)	94(10.7%)	14(2.7%)	13(2.4%)	1(1%)	1(1.1%)	36(11.6%)	14(4.7%)	1(1.6%)	3(4.7%)	9(14.5%)	2(3.3%)
Accommodation moves	60(2.9%)	15(2.9%)	11(2.1%)	1(1.1%)	1(1.1%)	15(4.8%)	10(3.3%	0(0%)	2(3.1%)	5(8.1%)	0(0%)
26 Community services	230(10.9%)	63(12.1%)	87(16.4%)	4(4.3%)	5(5.3%)	32(10.3%)	27(9.0% \$	1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Home modifications	13(0.6%)	3(2.6%)	6(1.1%)	0(0%)	1(1.1%)	0(0%)	2(0.7%)	(%0)گ	1(1.6%)	0(0%)	0(0%)
Special aids and equipment	48(2.3%)	7(1.3%)	8(1.5%)	1(1.1%)	1(1.1%)	16(5.1%)	14(4.7%	1 (1.6%)	0(0%)	0(0%)	0(0%)
nformal care	72(3.4%)	11(2.1%)	12(2.3%)	0(0%)	1(1.1%)	26(8.4%)	10(3.3%	<u>မ</u> ျှ(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Living-in maids [‡]	=	-	-	-	=	-	- 0	8 1(1.6%)	3(4.7%)	7(11.3%)	2(3.3%)
Subtotal (non-medical cost)	304(14.5%)	77(14.8)%	97(18.2%)	6(6.4%)	7(7.4%)	54(17.4%)	46(15.4%)	<u>a</u> 2(3.1%)	5(7.8%)	8(12.9%)	2(3.3%)
Productivity cost	225(10.7%)	50(9.6%)	46(8.7%)	14(14.9%)	10(10.5%)	27(8.7%)	23(7.7%)	2 17(25.6%)	13(20.3%)	14(22.6%)	11(18.0%)
Total cost (exc. productivity cost)	319(15.2%)	80(15.3%)	97(18.2%)	6(6.4%)	7(7.4%)	61(19.6%)	48(16.1%)	5 2(3.1%)	5(7.8%)	10(16.1%)	3(4.9%)
Total cost	512(24.3%)	124(23.8%)	136(25.6%)	20(21.3%)	16(16.8%)	80(25.7%)	68(22.7%)	T17(26.6%)	16(25.0%)	22(35.5%)	13(21.3%)

[§]only applicable to UK, Singapore and Malaysia patients; †only applicable to Singapore and Malaysia patients

Table II. Missing pattern analysis based on logit regression

Resource use items with missing data	Predictor of missingness
Stroke-related rehospitalisation	Age (p=0.001)
Rehabilitation hospital admission	Age (p=0.009), NIHSCORE (p=0.037)
Outpatient rehabilitation program	Age (p=-0.003)
Rehabilitation service provided at home/nursing facility	Age (p=0.014),
Community services used prior to stroke	NIHSCORE (p=0.001)
Community services used at 3 months	Age (p=0.003)
Community services used at 12 months	NIHSCORE (p=0.008)
Aids or special equipment uses at 3 months	Age (p=0.012)
Aids or special equipment uses at 12 months	Age (p=0.035), NIHSCORE (p=0.013)
Private physiotherapy uses at 3 months	Age (p<0.0001)
Private physiotherapy uses at 12 months	Age (p=0.006), NIHSCORE (p=0.034)
Respite care use at 3 months	Age (p<0.0001)
Respite care use at 12 months	Age (p=0.017), NIHSCORE (P=0.018)
Informal care use at 3 months	Age (p=0.003)
Informal care use at 12 months	Age (p<0.0001)

If any of the other variables were able to predict the missingness of a given variable representing resource use, the MAR assumption was deemed to be held true. More specifically, multiple imputations were used to replace the missing values (missing mRS, AQoL-4D data or cost categories) with plausible estimates, and generated 30 datasets. Results were provided as pooled estimates of these sets. Identical analyses were carried out to estimate the incremental costs and benefits between groups on the basis of imputed data following the methods outlined in the statistical analysis section above. As the probability of all the resource use items being missing could be predicted by one or more of the other variables, it is likely that the Missing-at-Random (MAR) assumption could be held true. (https://www.ssc.wisc.edu/sscc/pubs/stata_mi_decide.htm).

Supplementary document 5. Sensitivity analyses

Generally, the difference in QALY gains between VEM and UC groups were fairly consistent across different methods.

Table I. Between-group differences based on the Generalised Linear Model

	Adding country dummies									
	mRS	QALYs	Cost							
Total medical costs	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	\$704 (-\$1968, \$3376)							
Total cost (excl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$335 (-\$4953, \$4283)							
Total cost (incl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$238 (-\$6012, \$5537)							

mRS: modified Rankin Scale; QALYs: Quality-adjusted Life Years

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

(-0.126, 0.132)

NZ AU **UK** SG MA (N=1054)(N=189)(N=610)(N=128)(N=123)-\$2836 Total medical \$2937 \$948 -\$81 \$137 (-\$3635, \$9509)(-\$324, \$599)costs (-\$4352, \$6248) (-\$8403, \$2730) (-\$2789, \$2627)-\$3959 Total -\$1318 -\$1387 -\$3164 \$200 nonmedical costs (-\$3038, \$403) (-\$7769, -\$150)(-\$7331, \$4557)(-\$6834,\$505)(-\$232, \$631) Total -\$1735 \$479 -\$8981 \$1870 -\$2636 cost (incl. (-\$8482, 5013)(-\$13955, \$17694) (-\$9233, \$3961)(-\$487, \$1446)(-\$18380, \$418) productivity) -\$1185 -\$7610 -\$1534 \$2552 \$416 Total cost (-\$7184, \$4815) (-\$15302, \$82) (-\$11377, \$16481) (-\$6464, \$3395) (-\$364, \$1196)(excl. productivity) -0.036 0.086 -0.010 0.008 0.003 **QALY** gains

(-0.064, 0.044)

(-0.106, 0.123)

Table II. Results of country-specific analysis of costs and benefits

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AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia; QALY: Quality-adjusted Life Year.

(-0.003, 0.176)

(-0.076, 0.003)

From a health sector perspective, VEM was associated with similar costs (\$940, 95%CI: \$-4622 to \$4682) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) over 12 months. Likewise, if a societal perspective was taken, VEM was associated with comparable costs (\$1413, 95%CI:-\$4044 to \$6871, including productivity cost; \$1704, 95%CI:-\$3817 to \$7226, excluding productivity cost) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) (Supplementary document 6: Table IV). Even though the point estimate of difference in total costs between groups from a societal perspective varied considerably, the 95% confidence interval derived from base case and multiple imputation analyses were nearly identical (Supplementary document 6: Table IV).

From a health sector perspective, the between-group difference for each participating country yielded consistent conclusions with the base case analysis. VEM was associated with both non-significantly different costs and benefits (i.e. QALY gains at 12 months) compared to the UC, although the point estimate of the cost difference between groups varied from country to country, ranging from -\$2836 (New Zealand) to \$2937 (UK) (Supplementary document 6: Table II).

It was found that VEM was likely to cost less and associated with a greater gain in QALYs in comparison to UC in New Zealand and Singapore., Meanwhile, except for total medical cost, VEM seemed to incur less cost while leading to less gain in QALYs at month 12 months for participants from Australia, whilst in the United Kingdom, VEM was associated with higher

^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

cost and lower QALY gains than UC. Lastly, for patients from Malaysia, VEM contributed to higher cost while greater QALY gains at 12 month follow-up. However, none of the aforementioned between-group differences were statistically significant.

When a societal perspective was assumed, again, the point estimate of difference in costs between groups across countries varied substantially, with the 95% confidence intervals mostly overlapping



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Table III. Between-group differences based on the Generalised Linear Model_ base case analysis vs. multiple imputation analysis

	ITT (not imputed)			ITT (imputed)		Way Ens
	mRS score	QALYs	Cost (AUD)	mRS	QALYs	Cost PAUD)
Health Sector Perspec	ctive					. Dow
Total medical costs	0.030	-0.013	\$1082	0.042	-0.019	\$\$\text{\$\ext{\$\text{\$\exitin}\$\$\text{\$\exitit{\$\text{\$\text{\$\text{\$\text{\$\text{\$\text{\$\text{\$\text{\$\text{\$\text{\$\}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}
	(-0.022, 0.082)	(-0.041, 0.016)	(-\$2399, \$4563)	(-0.008, 0.092)	(-0.046, 0.007)	(3) 2 5 6 4, \$4465)
Societal Perspective						from ur (A data
Total cost (excl.	0.030	-0.013	-\$6	0.042	-0.019	望,押
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$5703, \$5690)	(-0.008, 0.092)	(-0.046, 0.007)	(a) 5423, \$8832)
Total cost (incl.	0.030	-0.013	\$102	0.042	-0.019	\$ <u>\$</u> 41 <u>\$</u>
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$6945, \$7149)	(-0.008, 0.092)	(-0.046, 0.007)	(2 \$59 2 0, \$8766)

ITT: intention to treatment; mRS: modified Rankin Scale; AUD: Australian dollars

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

Table IV. Cost-utility analysis based on multiple imputation analysis

	Efficacy (QALYs)	Cost (AUD)	Probability of being cost-effective
Health Sector Perspectiv	ve		
Total medical costs	-0.019	\$940	25%
	(-0.044, 0.005)	(-\$4622, \$4682)	
Societal Perspective			
Total cost (excl.	-0.019	\$1704	20%
productivity cost)	(-0.044, 0.005)	(-\$3817, \$7226)	
Total cost (incl.	-0.019	\$1413	23%
productivity cost)	(-0.044, 0.005)	(-\$4044, \$6871)	

QALYs: Quality-adjusted Life Years; AUD: Australian dollar.

^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

Supplementary document 6. Outcomes

Table I. Results of mRS score at 3 and 12 months follow-up

Modified Rankin Scale Score	UC group n=1050		VEM group n=1054			
	3M	12M	3M	12M		
0	96	132	90	137		
1	204	231	200	219		
2	225	175	190	166		
3	218	199	238	186		
4	127	95	140	113		
5	103	83	92	59		
6	72	118	88	139		
Total	1045	1033	1038	1019		
Missing data	5	17	16	35		

Number of patients falling into each category

Since there was no significant intervention effect together with no accepted willingness-to-pay (WTP) per unit increase in probability of achieving a better mRS outcome, further estimation of the ICER was considered not meaningful (i.e. no cost-effectiveness plane or cost-effectiveness acceptability curve could be generated).

Table II. Time and cost associated with delivering VEM and UC (mean, 95%CI)

	VEM		UC		Between group difference		
	Total time Cost (AUD)		Total time	Cost (AUD)	Total time	Cost (AUD)	
	(min)		(min)		(min)		
Physiotherapist	243	\$117	95	\$48	147	\$69	
	(232, 254)	(\$111, \$123)	(90, 101)	(\$45, \$51)	$(135, 159)^*$	(\$63, \$75)*	
Nurse [†]	494	\$225	439	\$202	55	\$23	
	(456, 532)	(\$207, \$244)	(404, 474)	(\$185, \$219)	(4, 106)*	(-\$2, \$48)	
Total cost	-	\$342	-	\$250	-	\$92	
		(\$320, \$364)		(\$231, \$269)		(\$63, \$121)*	

VEM: very early mobilisation; UC: usual care; CI: confidence interval

Because VEM and UC were supplied by the same group of physiotherapists and nurses, the key difference was that a patient randomised to VEM received early rehabilitation within 24 hours of stroke onset and more out-of-bed mobilisation sessions of early mobilisation.

The total health practitioner (physiotherapist and nurses) time devoted to the delivery of the VEM and UC differed significantly, with the VEM group receiving substantially longer mean service time from both the physiotherapist (VEM: 243 mins, 95%CI: 232 to 254 vs UC: 95 mins, 95%CI: 90 to 101, p<0.0001) and nurse (VEM: 494 mins, 95%CI: 456 to 532 vs UC: 439 mins, 95%CI: 404 to 474, p<0.0001). The resultant difference in costs between groups was significant (\$92, 95%CI: \$63 to \$121, p<0.0001).

^{*}p<0.0001 (adjusted for age, baseline NIHSS and mRS); † nurse's time devoted to delivery of VEM/UC was not recorded in the process of data collection, so the physiotherapist time was used as a proxy

	AU (N=1054)		NZ (N=189)		UK (N=610)		SG (N=128)	ncludin)2623 MA (N=	123)	All Countries	
	VEM	UC	VEM	UC	VEM	UC	VEM	UC G	₹EM	UC	VEM	UC
						alth care cost (AU	D)	ď	22	1	II.	
Acute hospi	talisation					,		sn	mŞ			
Median,	\$6294	\$6294	\$6104	\$6104	\$2763	\$3109	\$1493		ᠯ \$1363	\$1363	\$6294	\$6294
QR	(6294, 9553)	(6294, 9553)	(4370, 6104)	(4370, 6104)	(1382, 6563)	(1727, 6563)	(1493, 1809)	(1493, 1493) ਨ			(2279, 9535)	(2418, 9553)
Mean, SD	\$9883 (9484)	\$10010(10508)	\$6635 (3244)	\$6549 (3555)	\$5714(7876)	\$5885 (7101)	\$1721 (547)	\$1676 (432)	3 6 482 (2	12) \$1472 (200)	\$7369 (8469)	\$7521 (8916)
Stroke-relate	ed rehospitalisation							ed	30			
Median,	\$0	\$0	\$0	\$0	\$227	\$227	\$111	\$111 6	9 68	\$68	\$111	\$111
QR	(0, 3850)	(0, 3850)	(0, 325)	(0, 2243)	(227, 1401)	(227, 227)	(111, 111)	(111, 111) 5	ch ₹8, 68)	(68, 68)	(0, 1401)	(0, 610)
Mean, SD	\$6030 (17114)	\$6473 (21590)	\$651 (1371)	\$1507 (2828)	\$4524 (13968)	\$3494(11349)	\$2756 (7565)	\$1679 (3465)	र्म 8 714 (10	08) \$603 (1479)	\$4610 (14518)	\$4551 (16707
dmission t	o rehab hospital							an a	de d eri			
Median,	\$13134	\$13134	\$11262	\$11262	\$0	\$0	\$0	\$1298	<u>2</u> <u>₹</u> 0	\$0	\$0	\$1136
QR	(0, 36371)	(0, 38391)	(0, 30983)	(0, 26486)	(0, 29788)	(0, 29788)	(0, 2921)	(0, 3570)	ed (*) (*) (*) (*)	(0, 0)	(0, 29788)	(0, 29788)
Mean, SD	\$25667 (38892)	\$26648(38315)	\$16871(18536)	\$15573(16848)	\$12539(19682)	\$11758 (18390)	\$1815 (2759)	\$2798 (5082	4 5 0 (0)	\$43 (234)	\$18197 (31241)	\$18458 (3081
3									<u></u>			
9					Outpati	ent rehab program	(AUD)	j	<u>ي</u>			
Median,	\$0 (0, 2451)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	3 33 5 0, 265)	\$0	\$0	\$0
QR		(0, 1913)	(0, 0)	(0,0)	(0, 0)	(0,0)	(0, 0)	(0, 36)	5 0, 265)	(0, 249)	(0,478)	(0, 239)
Mean, SD	\$2081 (4183)	\$1934 (5316)	\$821 (2236)	\$721 (1991)	\$266 (1026)	\$155 (676)	\$364 (1090)	\$562 (1478)	8 174 (23	6) \$126 (206)	\$1246 (3244)	\$1142 (3976)
Rehab provi	ded at home/nursing	g facility						\$0 9	- -			
Median,	\$0	\$0	\$1168	\$212	\$922	\$0	\$0	<u>ق</u> 0\$	5 0	\$0	\$0	\$0
QR	(0,717)	(0,956)	(0, 4299)	(0, 3821)	(0, 11064)	(0, 11064)	(0,0)	(0, 0) a \$5 (42)	(0, 0)	(0, 0)	(0, 1913)	(0, 1913)
Mean, SD	\$1382 (4069)	\$1551 (4252)	\$3171 (4960)	\$3111 (5754)	\$12085 (28516)	\$11051 (26723)	\$93 (570)	\$5 (42)	97 (719	\$7 (53)	\$4447 (16294)	\$4180 (15203
	llied health visit							\$0 Sin	0 /			
Median,	N/A	N/A	N/A	N/A	\$0	\$0	\$0	\$0	5 0 £0 ,0)	\$0	N/A	N/A
QR					(0,0)	(0,0)	(0,0)			(0,0)		
Mean, SD	N/A	N/A	N/A	N/A	\$375 (1144)	\$329 (1291)	\$432 (1521)	\$1126 (3150 g		\$0.2(2)	N/A	N/A
mbulance	transfers							i i	13			
Median,	\$508	\$508	\$0	\$0	\$0	\$0	\$0	\$0 (0, 265) Q \$113 (208) Q	SO , (1)	\$0	\$0	\$0
QR .	(0, 1015)	(0, 1015)	(0, 646)	(0, 646)	(0, 1150)	(0, 575)	(0, 265)	(0, 265)	X2 , 0)	(0, 0)	(0, 611)	(0, 610)
Mean, SD	\$671 (1057)	\$623 (946)	\$543 (1082)	\$605 (928)	\$790 (3209)	\$701 (3150)	\$164 (348)	\$113 (208)	§ 6 (26)	\$14 (64)	\$627 (1920)	\$578 (1838)
rivate phys	iotherapy								<u> </u>			
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	% 0	\$0	\$0	\$0
QR	(0, 0)	(0,0)	(0,0)	(0,0)	(0, 0)	(0, 0)	(0,0)	(0, 0)	ह), 0)	(0, 0)	(0, 0)	(0,0)
Mean, SD	\$70 (375)	\$124 (797)	\$245 (1308)	\$4 (36)	\$128 (780)	\$174 (2102)	\$238 (1096)	\$333 (1938)	§ 4 (19)	\$1 (9)	\$109 (693)	\$132 (1336)
Respite care									<u>≅</u>			
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$ 0	\$0	\$0	\$0
QR	(0,0)	(0,0)	(0,0)	(0,0)	(0, 0)	(0,0)	(0,0)	(0, 0)	(A) , (1)	(0, 0)	(0,0)	(0,0)
Mean, SD	\$48 (355)	\$20 (182)	\$7 (46)	\$2 (15)	\$9 (95)	\$58 (686)	\$0(0)	\$0 (0)	5 0 (0)	\$1 (8)	\$27 (259)	\$27 (386)
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Page 61 of 7	76					BMJ Open		d by copyright	bmjopen:			
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В	AU (N=1054)		NZ (N=189)		UK (N=610)		SG (N=128)	<u>n</u>	MA (N=123)	<u> </u>	All Countries	
4	VEM	UC	VEM	UC	VEM	UC	VEM	UC <u>G</u>	E EM	UC	VEM	UC
5 Sub-total	V LIVI	00	V LIVI	00	V LIVI	00	V LIVI	ling	OLIVI	00	V LIVI	00
6 Median	\$29278	\$29441	\$20621	\$23722	\$18896	\$20843	\$4525	\$4687 o	% 1713	\$1746	\$19271	\$20411
7 (IQR)	(8218, 63622)	(9811, 62489)	(6068, 46909)	(7316, 40162)	(4030, 48999)	(3682, 47908)	(1604, 8668)	(2724, 10926)	431, 2532)		(6294, 52637)	(7238, 63835)
Maan	\$45620 (51458)	\$47453(53715)	\$28898 (25011)	\$27986(22676)	\$34863 (42509)	\$32842 (39517)		\$8358 (8787 % •	2385(1587)	\$2269(1574)	\$36351 (45620)	\$36604 (46309)
8 (SD)		, , , , , , , , , , , , , , , , , , , ,	, , , , ,	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	()	, (/	(S	y 2019.	, , ,	()	, , , , , , , , , , , , , , , , , , , ,
9					N	on-health care cos	st	e	01			
10 Accommoda	ation moves							ıte				
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	8 0	\$0	\$0	\$0
1 2 QR	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(5), 0)	(0,0)	(0,0)	(0,0)
1 3 Mean, SD	\$2089 (8518)	\$2482 (9323)	\$5975 (19614)	\$9135 (26918)	\$2901 (12958)	\$2532 (11125)	\$72 (578)	\$108 (507)	2 5 425 (1893)	\$104 (501)	\$2460 (11036)	\$2821 (12212)
14 ommunity								<u>a</u> <u>a</u>	ad ad			
1 Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0 a	2. 20 0	\$0	\$0	\$0
1 Mean, SD	(0, 0)	(0, 0)	(0,0)	(0,0)	(0, 430)	(0, 174)	(0,0)	(0, 0)	(9), (1)	(0, 0)	(0, 0)	(0,0)
	\$570 (2681)	\$1091 (8556)	\$238 (950)	\$1022 (4113)	\$22275 (294988)	\$10738 (57306)	\$0(0)	\$244 (1902) \$	\$ 21 (110)	\$0 (0)	\$6870 (160318)	\$3786 (31893)
Home modi		1	+-					3,	<u> </u>	1 + - 1		+ -
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0		2 00	\$0	\$0	\$0
19 _{QR}	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)		(2.50)	(0, 0)	(0, 0)	(0, 0)
2Mean, SD	\$805 (6338)	\$751 (7715)	\$833 (4862)	\$565 (3204)	\$352 (2133)	\$834 (7091)	\$234 (1079)	\$62 (299)	3 49 (369)	\$64 (237)	594 (4840)	\$676 (6734)
2 Special aids	and equipment \$0	Φ0	ф 7 0	φ102	Ф27	фО	Φ0	T #0 \$	0 1.5	Φ2.6	фо	фО
2 Median,	\$0	\$0	\$70	\$103	\$27	\$0	\$0	\$0 a i	\$ 15	\$36	\$0	\$0
2kQR Maan SD	(0, 332) \$1986 (7668)	(0, 318) \$2787 (10396)	(0, 549) \$2198 (7993)	(0, 357) \$1798 (7229)	(0, 786) \$1354(3649)	(0, 846) \$1720 (5083)	(0, 240)	\$1079 (5483 9	50 , 218)	(0, 186) \$193 (658)	(0, 414) \$1660 (6426)	(0, 414) \$2141 (8328)
Mean, SD	31980 (7008)	\$2787 (10390)	\$2198 (1993)	\$1798 (7229)	\$1334(3049)	\$1720 (3083)	\$1117 (5843)	\$1079 (3483 9	(232)	\$193 (038)	\$1000 (0420)	\$2141 (8328)
Madian	\$24	\$48	\$14	\$0	\$29	\$29	\$0	\$0	2 24	\$9	\$24	\$24
260R	(0, 503)	(0, 455)	(0, 283)	(0, 149)	(0, 471)	(0, 375)	(0, 114)	(0, 238) S	Q 0, 60)	(0, 50)	(0, 407)	(0, 407)
2 Informal car 2 Median, 2 IQR 2 Mean, SD	\$414 (747)	\$405 (758)	\$236 (536)	\$152 (311)	\$324 (516)	\$324 (645)	\$144 (285)	\$159 (300)	§ 43 (57)	\$27 (34)	\$335 (633)	\$322 (660)
28 iving-in m	aids	ψ+03 (730)	Ψ230 (330)	ψ132 (311)	ψ32+ (310)	Ψ324 (043)	Ψ1++ (203)		<u> </u>	Ψ27 (34)	Ψ333 (033)	Ψ322 (000)
2 Median,	N/A	N/A	N/A	N/A	N/A	N/A	\$0	\$0 8	\$ 0	\$0	N/A	N/A
3 0 QR	11/11	1,712	1,111	1,712	1,712	1 1/1 1	(0,0)	(0,0)	£9 ,0)	(0,0)	1,712	11/11
3 Mean, SD	N/A	N/A	N/A	N/A	N/A	N/A	\$3154 (8146)	\$4268(11338	3 79 (930)	\$83 (504)	N/A	N/A
32 Sub-total								gi	25	,		
33 Median	\$459	\$673	\$381	\$638	\$758	\$471	\$25	\$194	2 74	\$57	\$358	\$438
DO (ICD)	(0, 3334)	(0, 5209)	(0, 3674)	(103, 14551)	(0, 5097)	(0, 4725)	(0, 1293)	(0, 6999)	20 , 285)	(0, 318)	(0, 3334)	(0, 4561)
Mean	\$6104 (15582)	\$6985 (17554)	\$7752 (17751)				\$4802 (10366)	\$6177 (13942)	9 861 (2272)	\$484 (1113)	\$12043 (164026)	\$9360 (36504)
34 (IGR) Mean 35 (SD) 36									10(
36						Productivity cost			Ü			
3Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	5 ()	\$0	\$0	\$0
3 8 QR	(0,0)	(0,0)	(0, 0)	(0,0)	(0, 0)	(0, 0)	(0,0)	(0, 0)	8 0, 0)	(0,0)	(0, 0)	(0,0)
3 Mean, SD	\$75 (317)	\$84 (391)	\$29 (130)	\$14 (54)	\$17 (152)	\$44 (245)	\$6 (29)	\$8 (35)	3 1 (4)	\$0.4 (3)	\$46 (246)	\$58 (312)
4 T otal cost									p <u>h</u>			
41									<u>a</u>			
42						21			Ō			
43				F	1 1		. / /	July and the state of	ĕ			
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,	AU (N=1054)		NZ (N=189)		UK (N=610)		SG (N=128)	<u></u>	MA (N=123)		All Countries	
1	VEM	UC	VEM	UC	VEM	UC	VEM	UC 01 88810 00	S EM	UC	VEM	UC
Median	\$33203	\$35143	\$29934	\$32216	\$25374	\$30537	\$6960	\$8810	\$ 2016	\$1816	\$25675	\$27042
5(IGR)	(9687, 71902)	(12696, 74070)	(8528, 65781)	(15710, 68292)	(4712, 64285)	(4629, 67012)	(1674, 26187)	(3426, 19493	1 561, 3994)	(1537, 3301)		(7257, 63824)
		\$56408(62536)	\$40381(37242)	\$43901(43170)	\$65530(332044)	\$49627(78644)	\$15036(16921)	\$16340(196 5 0)	\$3609(3985)	\$2938(2350)		\$47627(64249
Mean (SD)		\$56408(62536) ortion (i.e. less that a patient's immedia.	\$40381(37242) an 50%) of patient diate admission to		\$65530(332044)	22		ÿ	13, 2025 at Agence Bibliographique de l	\$2938(2350) n of stay for acute stroke hosp	\$50448(184931)	

interval overlapped to a great extent. Given the concern raised by the large variability in mapped utility for patients within the same mRS category (≤ 2 or ≥ 3) and the fairly consistent results across different models, only the 12 month AQol utility values were employed to estimate the difference in QALYs gains between two treatment groups.

			NZ (N=189)						bmjopen-20				
Supplementar	ry docum	ent 7. Qua	antity of	resource	use ove	er 12 moi	nths (IT	ਸ਼ (m ਵੁੱ ਧ ਵਿੱਚ	dan, IQR)			
	AU (N=1054)		NZ (N=189)		UK (N=610)		SG (N=128)		MA (N=123)		All Countries		
	VEM	UC	VEM	UC	VEM	UC	VEM	UC G	NSVEM	UC	VEM	UC	
Acute hospitalisation) Ses	nseinsein				
% of patients using	100	100	100	100	100	100	100	100	0 0 0 100	100	100	100	
LoS (days)	21(6-42)	22(7-46)	23(6-57)	25(8-48)	12(4-45)	13(5-4)	16(4-25)	100 at ed 25 at 25	5(3-8)	4(2-8)	16(4-41)	17(5-41)	
Stroke-related rehospita	alisation							± ext	Miloaded 18				
% of patients using	30	29	28	33	28	23	20	20		23	28	27	
No. readmission/s	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	2(1-2) a	5 6 1(1-2)	1(1-2)	1(1-2)	1(1-2)	
Admission to rehabilita	tion hospital [†]			Co				⊥ ta う m.c	B http://www.min.com				
% of patients using	62	56	60	65	35	34	45	56 50 .		2	50	47	
No. of admission/s	1(0-1)	1(0-1)	1(0-1)	1(0-1)	0(0-1)	0(0-1)	0(0-1)	1(0-1) >	0(0-0)	0(0-0)	0(0-1)	1(1-1)	
Outpatient rehabilitation	on program							train	y en				
% of patients using	40	39	23	19	12	10	19	25	52	48	30	28	
No. of services	15(6-29)	12(6-28)	16(7-28)	17(12-34)	12(6-21)	7(4-14)	32(20-77)	29(3-115)	15(7-24)	16(4-22)	15(6-28)	12(6-27)	
Rehabilitation provided	l at home/nursing	facility						similar 2	or				
% of patients using	30	33	57	52	50	46	3		E ²	2	35	34	
No. of services	9(4-22)	10(4-25)	18(8-29)	16(9-30)	12(6-28)	12(6-30)	81(63-99)	9(9-9)	104(104-104)	8(8-8)	12(5-27)	12(5-28)	
Ambulance transfer	I				l		l	molc	<u>3,</u> 20				
% of pts using	51	53	34	48	41	38	36	28 es	20 25 ₅ a	8	43	44	
No. of trips	2(1-3)	2(1-3)	2(1-3)	1(1-3)	2(1-3)	2(1-3)	1(1-2)	1(1-2)	2(2-3)	2(1-3)	2(1-3)	2(1-3)	
Individual allied health	therapy	<u> </u>		_1	l	1	l	I	ence		l		
% of pts using	N/A	N/A	N/A	N/A	19	15	-	2	B 20	25	-	-	

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	AU (N=1054)		NZ (N=189)		UK (N=610)		SG (N=128) Cu		6MA (N=123))	All Countrie	s
	VEM	UC	VEM	UC	VEM	UC	VEM	UC j	S EVEM	UC	VEM	UC
No. of services	N/A	N/A	N/A	N/A	8(2-12)	8(4-15)	-	2(2-2)	8(3-10)	16(8-31)	-	-
Private physiotherapy								uses	<u></u>			
% of pts using	9	8	11	1	5	5	8	8 7		2	8	6
No. of services	5(3-19)	6(4-19)	13(6-18)	3(3-3)	12(6-33)	7(1-14)	18(16-24)			8(8-8)	15(4-20)	24(3-19)
Respite care								14(7-24)	D K			
% of pts using	3	2	3	2	2	3	-	- X 2	ownloaded from	2	2	2
No. of services	21(10-43)	15(11-35)	12(10-20)	7(5-8)	24(9-40)	21(12-80)	-	- and c	d-	30(N/A)	18(9-39)	18(9-41)
Accommodation moves					1	1	1	- da la	5 5 S	I		
% of pts using	18	17	19	28	13	14	11	20	1 = 23 0 = 23	10	16	17
No. of moves	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	- 	2(1-2)	1(1-1)	1(1-1)
Community Services used p	prior to having	a stroke over the	past year	4	101			<u> </u>	-Bjop	l .		
% of pts using	13	17	6	7	5	5	-	ining,	B -	-	9	11
No. of services	26(26-52)	26(26-52)	52(39-88)	46(14-52)	52(25-104)	40(15-131)	-	_ <u>.</u> a		-	27(26-52)	26(26-52
Community services used of	over 12 months	after stroke	-1		1			and s	•m/	l .		
% of pts using	30	35	32	28	31	28	-	3 3	§ 6	-	27	28
No. of services	28(18-72)	32(12-78)	130(47-233)	48(17-256)	42(12-185)	90(12-310)	-	3(3-3)	6(3-73)	-	39(14-119)	39(12-12
Home modifications under	taken over 12 m	onths	<u>'</u>	1	•	1	•	chno	ည်	-1	•	
% of pts using	27	30	20	17	36	33	16	19 0	202 3	10	27	28
No. of mods	2(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	1(1-2)	<u>u</u> 1(1-1)	1(1-1)	1(1-2)	2(1-2)
Aids and appliances used o	ver 12 months	·	•	•		•			Gen 58	-	•	
% of pts using	46	47	55	63	58	51	44	45	ho	59	51	50
No. of aids/appliance used	2(1-5)	2(1-4)	3(2-6)	2(1-4)	4(2-6)	4(2-6)	2(2-3)	2(1-3)	2(1-3)	2(1-3)	3(1-5)	3(1-5)
Working prior to stroke									gra			
		For	peer review o	nly - http://bm	27 njopen.bmj.c	com/site/abo	out/quidelin	es.xhtml	ographique de l			

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	AU (N=1054	AU (N=1054)		NZ (N=189)		UK (N=610)		inclu	SMA (N=123	SMA (N=123)		es
	VEM	UC	VEM	UC	VEM	UC	VEM	UC j	PVEM	UC	VEM	UC
% of patients	24	23	38	34	19	21	52	52 Q	N ⁴⁵	33	27	26
Hrs worked/week	40(27-50)	40(30-50)	40(37-40)	40(37-40)	40(25-48)	37(25-40)	48(40-56)	45(36-50)	42(40-56)	45(32-50)	40(30-50)	40(30-50)
Proportion working at	t 12 months							s rela	N N			
% of patients	15	12	20	16	7	9	25	22 66	24	15	14	12
Hrs worked/week	38(18-40)	25(12-40)	40(20-40)	40(38-40)	35(26-40)	30(24-37)	39(16-46)	35(23-40)	2 40(32-47)	45(30-50)	38(20-41)	30(16-40)
Patients from Malaysi	a and Singapore wh	o had a maid prio	or to stroke					text a	loac		_	
% of patients	-	-		-	-	-	19	16 ठ ह	6 .5	10	-	-
No. of maids	-	-	- /		-	-	1(1-1)	1(1-1) # 2	B 1(1-1)	1(1-1)	-	-
Patients from Singapo	re and Malaysia wh	o had a maid at 12	2 months follow	ving stroke							_	
% of patients	-	-	-	-	<i>i</i>	-	23	22 6	5	7	-	-
No. of maids	-	-	-	-	4-01	-	1(1-1)	1(1-1)	1(1-1)	1(1-1)	-	-
Receipt of informal ca	re at 12 months						1	⊥ ai ni ni n			1	
% of patients	35	39	37	33	41	40	30	36 6	.42	44	37	39
No. of hrs/week	15(6-34)	12(4-31)	8(3-21)	14(6-30)	21(9-34)	17(7-35)	35(13-46)	16(4-30	22(10-38)	16(5-26)	18(7-35)	14(5-32)

ITT: Intention-to-treat; AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia; LoS: length of stay; pts: patients; No.: number; hrshours; mod: modification; -: no such resource use; all numbers were expressed as median and interquartile range (IQR); *includes any admissions to rehabilitation hospital following the indexed stroke; June 13, 2025 at Agence Bibliographique de l

Supplementary document 8: Figures

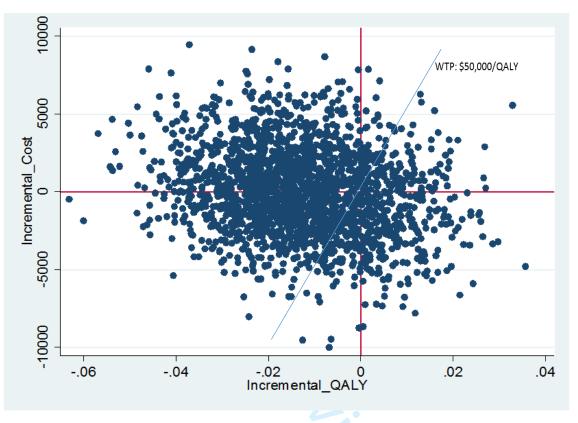


Figure I cost-effectiveness plane_societal perspective (excl. productivity cost)

^{*}Probability of VEM being cost-effective is 42%; WTP: willingness-to-pay; QALY: quality-adjusted life year

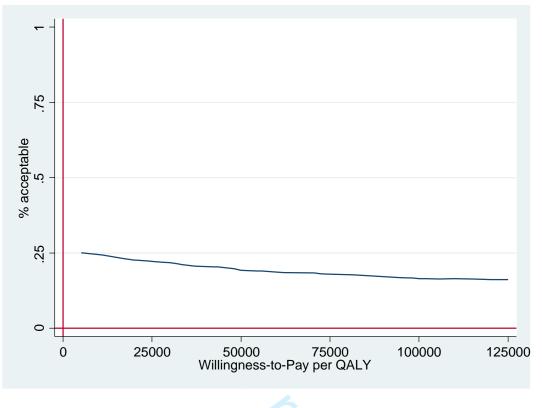


Figure II Cost-effectiveness acceptability curve for medical cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

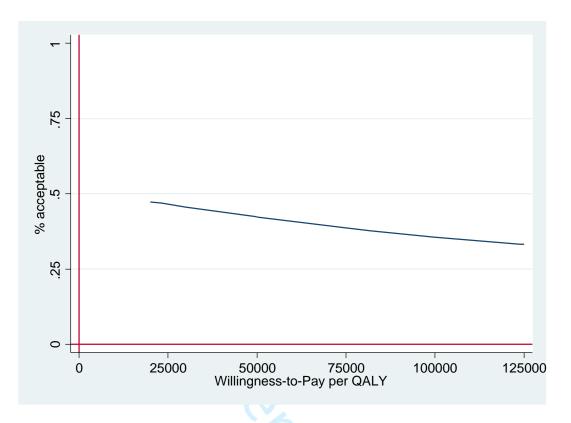


Figure III Cost-effectiveness acceptability curve for total cost excluding productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

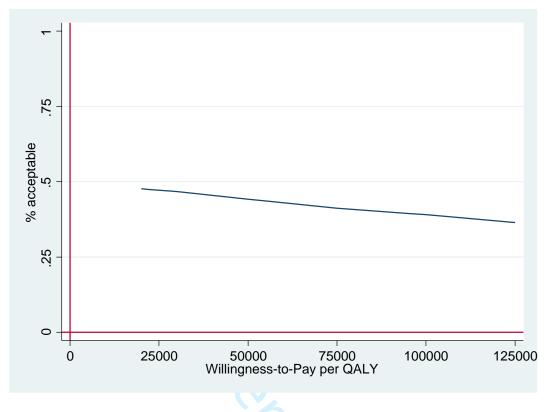


Figure IV Cost-effectiveness acceptability curve for total cost including productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

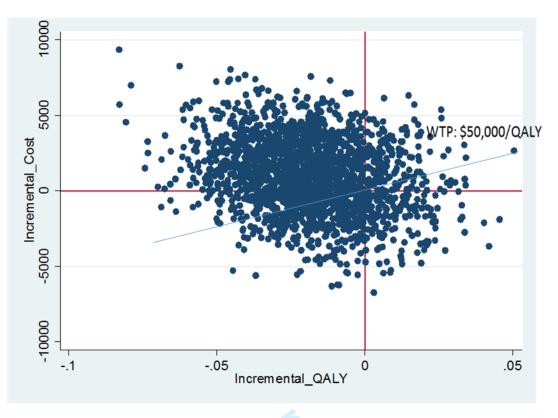


Figure V Cost-effectiveness plane_health sector perspective (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

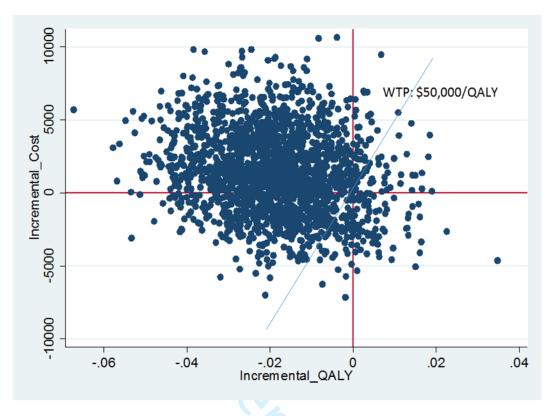


Figure VI Cost-effectiveness plane_societal perspective including productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

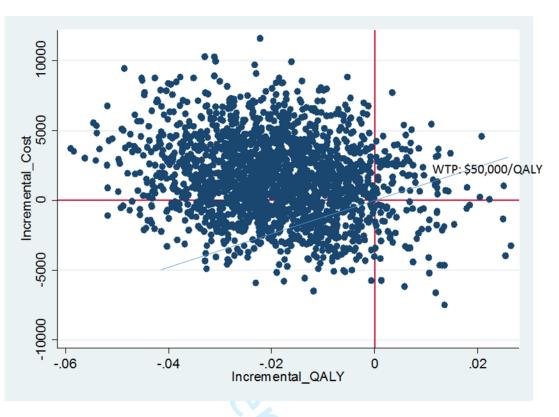


Figure VII Cost-effectiveness plane_societal perspective excluding productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

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- Claesson L, Gosman-Hedstrom G, Johannesson M, Fagerberg B, Blomstrand C. Resource utilization and costs of stroke unit care integrated in a care continuum: A 1-year controlled, prospective, randomized study in elderly patients: the Goteborg 70+ Stroke Study. Stroke 2000;31(11):2569-77.
- Bernhardt J, Dewey H, Thrift A, Collier J, Donnan G. A very early rehabilitation trial for stroke (AVERT) phase II safety and feasibility. Stroke 2008;39(2):390-6.



Section/item	Item No	Recommendation					
Title and abstract	item No	Recommendation	line No				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness					
Title		analysis", and describe the interventions compared.	1				
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	4-5				
ntroduction							
Background and objectives	3	Provide an explicit statement of the broader context for the study.					
Methods		Present the study question and its relevance for health policy or practice decisions.	0				
Farget population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	12				
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	9				
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9				
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	8				
ime horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	11				
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	11				
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	8-9				
Measurement of effectiveness	11a	Single study-based estimates: Describe fully the design features of the single effectiveness stude and why the single study was a sufficient source of clinical effectiveness data.	y 12				
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.					
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	9				
Estimating resources and costs	13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	9-10				
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.					
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	10				
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providinga figure to show model structure is strongly recommended.					
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.					
Analytical methods 17 Describe a with skewe approache		Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	11-1				
Results							
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	N/A				
ncremental costs and outcomes	19	For each intervention, report mean values is strongly recommended. For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.					
Characterising uncertainty	20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	14				
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.					
naracterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained byvariations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.					
Discussion							
udy findings, limitations,	22	Summarise key study findings and describe how they support the conclusions reached. Discuss					

Other							
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.					
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	22				

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

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Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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 Title Page

Title

Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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Economic evaluation of AVERT trial

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 Objectives While Very Early Mobilisation (VEM) intervention for stroke patients was shown not to be effective at 3 months, 12 -month clinical and economic outcomes remain unknown. It was aimed to assess cost-effectiveness of a VEM intervention within a Phase III randomised controlled trial (RCT).

Design An economic evaluation alongside a RCT

Setting Multi-country RCT involved 58 stroke centres.

Participants 2104 patients with acute stroke who were admitted to a stroke unit.

Intervention A very early rehabilitation within 24 hours of stroke onset

Methods Cost-utility analyses were undertaken according to pre-specified protocol measuring VEM against usual care (UC) based on 12 -month outcomes. The analysis was conducted using both health sector and societal perspectives. Unit costs were sourced from participating countries. Details on resource use (both health and non-health) were sourced from Cost Case Report Form. Dichotomised Modified Rankin Scale (mRS) scores (0-2 vs 3-6) and Quality Adjusted Life Years (QALYs) were used to compare the treatment effect of VEM and UC. The base case analysis was performed on an Intention-To-Treat (ITT) basis and 95% confidence intervals (CI) for cost and QALYs were estimated by bootstrapping. Sensitivity analysis were conducted to examine the robustness of base case results.

Results VEM and UC groups were comparable in the quantity of resource use and cost of each component. There were no differences in the probability of achieving a favourable mRS outcome (0.030, 95%CI: -0.022 to 0.082), QALYs (0.013, 95%CI: -0.041 to 0.016) and cost (AUD1082, 95%CI: -\$2520 to \$4685) from a health sector perspective; or AUD\$102, 95%CI:

-\$6907 to \$7111, from a societal perspective including productivity cost). Sensitivity analysis achieved results with mostly overlapped CIs.

Conclusions VEM and UC were associated with comparable costs, mRS outcome and QALY gains at 12 months. Compared with to UC, VEM is unlikely to be cost-effective.

Trial registration Australian New Zealand ClinicalTrials Registry, number ACTRN12606000185561.

Strength and limitations

- This is the first economic evaluation assessing the cost-effectiveness of a very early rehabilitation intervention within the largest Phase III randomised controlled trial in patients with stroke;
- The study assessed the long-term cost and cost-effectiveness of this very early rehabilitation intervention at 12-month;
- The difficulty posed by the multi-country design of the trial and the percentage of missing data may undermine the confidence in the results.

Introduction

Stroke is one of the biggest killers and a leading cause of disability worldwide.¹² 65% of stroke survivors live with some degree of disability that impedes their ability to carry out daily living activities unassisted.³ Therefore, ways of improving the outcomes of patients after stroke is an important focus of research.⁴⁵ Early mobilisation after stroke is believed to contribute to better patient outcomes and clinical trials have been conducted globally.⁶⁻⁹

The short-term efficacy and safety of a very early rehabilitation trial after stroke (AVERT) has been evaluated in a phase III randomised controlled trial (RCT) with 2,104 patients enrolled from Australia, New Zealand, United Kingdom, Singapore and Malaysia. 10 The evidence from this trial indicated that at three months after stroke, very early mobilisation (VEM) of patients was associated with a reduction in the probability of a favourable outcome as defined by a modified Rankin Scale (mRS) score of 0-2 compared to that in the usual care (UC) group. 10 In the research field of stroke, primary endpoint is usually assessed at month 3 after stroke¹¹⁻¹⁴, which means there is a paucity of data in terms of long-term resource use and cost of care for patients with stroke. Given AVERT provided a longer-term (i.e. 12 months) comprehensive measurement of costs relating to stroke care (i.e. direct medical, direct non-medical, and indirect costs), and the broader representativeness of patients across countries and regions (>2000 patients were recruited from both developing and developed world), together with the implications of stroke economic burden sustained beyond the acute phase (i.e., 3 months), holistically examining the cost of stroke care that falls within health and non-health sectors could potentially advance understanding of pattern of resource use post stroke and identify any gaps to improve care for stroke and chances to curb the increasing economic burden of disease.

This examination also benefits healthcare funders (i.e. governments, insurance companies) and the public with addition of substantial knowledge of long-term rehabilitation cost for stroke.

This economic evaluation, which was part of the registered trial protocol (Australian New Zealand Clinical Trials Registry, ACTRN12606000185561) and planned prior to knowledge of outcomes, was conducted alongside the Phase III RCT,¹⁰ The aim of this paper is to assess the cost-effectiveness of very early mobilisation within 24 hours after stroke in terms of improving patient outcomes at 12-months, in comparison to usual care (UC), with a particular focus on examining the resource use and cost of care after stroke.

Methods

The economic analysis was undertaken following the previously published plan.¹⁵ It also conforms to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.¹⁶ Ethics approval was granted by relevant institutions.

Intervention and comparator

The trial design has been reported in detail elsewhere.¹⁰ In brief, patients with confirmed stroke who were admitted to a stroke unit within 24 hours of stroke onset were randomised to receive usual stroke-unit care (UC) alone or VEM in addition to UC in a multinational Phase III trial.

Outcomes

The mRS at 12-months, a secondary outcome of the trial, and Quality-Adjusted life years (QALYs) derived from the Assessment of Quality of Life-4D (AQoL-4D)¹⁷ were used as the effectiveness measures in the economic evaluation. The AQoL-4D instrument is a multi-

attribute utility scale used to assess the health-related quality of life (HRQoL)¹⁸; it was administered at 3 and 12 months.

Outcome of mRS was dichotomised into "favourable" (mRS 0-2) and "poor" (mRS 3-6) based on patients outcomes at 12-month follow up.¹⁰ The difference in the probability of patients achieving a favourable mRS outcome (mRS 0-2) was used to estimate the incremental benefits between treatment groups for the primary efficacy outcome.

Due to the inherent difficulties of administering the AQoL instrument to acute stroke patients (i.e. most of patients were not able to respond to these questions at baseline), the mRS score at baseline¹⁰ was used as a surrogate measure of patient utility during the acute phase. The detailed methods of this work are reported elsewhere¹⁹ and a brief description is supplied in the online Supplementary document 1.

Costs

A societal perspective with a key focus on the health sector was adopted.

Intervention delivery

Intervention delivery costs consisted of the time costs of physiotherapists (PT) and nurses delivering VEM (or UC) to patients. The mean of the total physiotherapist time (recorded by a log documented by each participating PT across whole hospital stay) per patient was calculated. Given insufficient data, physiotherapist's mean time per session was used as a proxy for nurse time spent on delivering either VEM or UC.

Resource use

All resource use during the study period was electronically collated using a validated Cost Case Report Form (Cost CRF) administered and recorded by trained staff at 3- and 12-months using face to face assessments with patients and carers, and medical records. Cost CRF used in Australia is supplied as an example (Supplementary document 2). Cost CRF from other participating countries could be requested from corresponding author.

Healthcare resource use

The quantity of resources used for the following health care resource items was recorded: number of ambulance transfers (emergency and non-emergency), acute hospitalisation (including length of stay, LoS), rehospitalisation (number of occasions and LoS for each occasion), rehabilitation hospital admission (number of occasions and LoS for each occasion), outpatient rehabilitation program (number of occasions and number of days for each occasion), rehabilitation provided at home/nursing facility (number of occasions and number of sessions for each occasion), private physiotherapy (number of sessions), respite care (number of sessions) and individual outpatient (including physiotherapy, occupational therapy, and speech and language therapy) visits (service type and number of sessions) for patients from United Kingdom, Singapore and Malaysia only.

Non-healthcare resource use

The quantity of resources used was recorded for the following non-heath care resource items: accommodation move due to stroke (location moved to and date of move), community service (type of service use and number of service used both for prior to and post-stroke), home modification (type of modification, supplier and cost), special equipment and aids (type of equipment/aids and quantity consumed), informal care (purpose of the care and hours used), live-in maids (number of maids prior to and post stroke) (for Singapore and Malaysia only),

changes to employment (employment status and weekly hours of working both prior to and post-stroke).

Resource use reported at 3 (i.e. resources used between 0 and 3 months) and 12 (i.e. resources used between 4 and 12 months) months was used to calculate the total annual resource use for each participant. Generally, where patients were still using a particular resource at the time of 12-month data collection, the last day of 12 months' follow-up (calculated from the day of index stroke) was used to estimate the duration of that resource utilisation. In the event of a patient dying, resource use data for the period prior to death was ascertained from their carer and medical records, wherever possible.

Unit costing

Costs were computed by applying country-specific unit costs to each resource item utilised. Therefore, five sets of unit costs (one for each of the participating countries) were compiled from the most up-to-date and reliable source (Supplementary document 3). Unit costs from a country with a similar economic status and healthcare system were used where local country-specific unit costs were unavailable.

All costs are expressed in Australian dollars (AUD) for the 2015 reference year value and can be converted to United States dollar (USD) using the Purchasing Power Parity rate 1 USD=1.463 AUD²⁰ (December 2015). The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

The details of unit cost for acute stroke hospitalisation, rehospitalisation, rehabilitation (inpatient and outpatient), non-health sector costs (home modifications, community services, aids etc.) and productivity cost are provided in Supplementary document 3.

Statistical analysis

 All the costs that were attributable to stroke including healthcare costs, non-healthcare costs and productivity costs were accounted for in the economic analysis. Since a 12 month economic evaluation was undertaken, no discounting was applied to either costs or benefits.

Quantity of resource use and costs were summarised using medians and interquartile ranges (IQRs) due the skewness of the raw data. Means and standard deviations (SDs) were also reported. Base case analysis of the economic evaluation was performed based on the Intention-to-Treat (ITT) population²¹ with an assumption for the main analysis that data were Missing At Random (MAR). The difference in costs was analysed using Generalised Linear regression Model (GLM) with gamma family and a log link, with treatment groups as an independent variable, including baseline National Institutes of Health Stroke Scale (NIHSS), baseline mRS¹⁵ and age as treatment covariates.

For the primary outcome, the mRS score at 12 months was compared following the method detailed in the Statistical Analysis Plan.²² While for the secondary effectiveness outcome (i.e. the QALY gains at 12 months), a linear regression model with treatment group as the factor variable and 12 months AQoL-4D utility value as the dependent variable, adjusted for age, baseline mRS was utilised to estimate the difference in QALY gains over 12 months. Non-parametric bootstrap simulations with 2000 replications were used to calculate 95% confidence intervals (CIs) around mean difference in costs and effects for cost-effectiveness analysis. To

 examine the cost-effectiveness of VEM measured against UC, Incremental Cost-Effectiveness Ratios (ICERs) were calculated where applicable. For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost). The differences between groups in terms of costs and benefits (i.e. QALYs) were compared regardless of the statistical significance of the difference.²³ Cost-effectiveness acceptability curves were plotted to show the probability of VEM being the optimal choice. The ICERs were compared with a common benchmark in Australia of ≤AUD50,000 per QALY.²⁴ All the analyses were performed using the STATA 14.0 statistical package (StataCorp. 2015. Release 14. StataCorp LP.)

Sensitivity analyses

To investigate the impact of using country-specific costs, a country dummy variable was added to the GLM analysis to adjust for country effect.²⁵ Subgroup analysis on the basis of individual countries were also conducted to explore the difference in costs and benefits across countries.

Multiple imputation was performed to test the sensitivity of results to the missing data assumption. The missing patterns were explored with the use of logit regression to investigate if any of the other variables predicted whether a given variable was missing²⁶ (Supplementary document 4).

Secondary analyses were undertaken to assess the robustness of the base case results. Subgroup analyses were performed at the country-specific level to test for differences in efficacy and costs.

Patient and Public involvement

 No patient and public were involved.

Results

Between July 2006 and October 2014, 2,104 patients (VEM 1,054; UC 1,050) were recruited across 58 sites from Australia (N=1,054, 24 sites), New Zealand (N=189, 1 site), United Kingdom (N=610, 29 sites), Singapore (N=128, 1 site) and Malaysia (N=123, 1 site). At recruitment, over 80% of patients had no prior history of stroke; NIHSS was greater than 7 points (indicating a moderate to severe stroke) for around 45% of patients; 26% aged over 80 years and 24% had received recombinant tissue plasminogen activator prior to randomisation¹⁰. Baseline characteristics were similar between the two treatment groups¹⁰.

Outcomes

There was no difference between VEM and UC groups in terms of favourable mRS outcome and quality of life (as measured by AQoL-4D) at month 12. Specifically, a comparable percentage of patients from both treatment groups achieved a favourable outcome at 12 months after stroke (between-group difference in probability: 0.030, 95%CI:-0.021 to 0.082, adjusted for baseline age and NIHSS). Likewise, for the outcome of AQoL-4D at 12 months, no between-group difference was observed (-0.013, 95%CI:-0.043 to 0.017). The detailed mRS outcomes are presented in Supplementary document 5: Table I.

Resource use and costs

The proportion of patients reporting use of a specific resource varied from item to item (Table 1). In relation to the healthcare resource items, nearly half of patients experienced rehabilitation hospital admission and more than a quarter of patients had a stroke-related rehospitalisation, rehabilitation service use (outpatient/provided at home or nursing facility) and ambulant transfers whereas only a small proportion of patients (less than 10%) recorded the use of private physiotherapy and/or respite care. Regarding non-health-related resource use, the majority of patients (>50%) used some form of special aids or equipment during the 12 months after their index stroke, whilst nearly 40% of patients received informal care, and around 27% reported the use of community services and home modifications. Only 16% (VEM) and 17% (UC) of patients respectively, experienced accommodation changes due to the index stroke. For maid's service use in the home in Singapore and Malaysia, a small proportion (less than 10%) of patients hired a maid both before and after the index stroke.

With respect to productivity, nearly one in four patients were employed prior to their stroke; this proportion fell to only one in eight patients at 12 months follow up. Generally, resource use was comparable between VEM and UC groups (p > 0.05) across all items (Table 1).

The median total medical cost was marginally higher in the UC group (\$20,411, IQR: \$7,238 to \$63,835) than in the VEM group (\$19,271, IQR: \$6,294 to \$52,637), primarily due to the higher rehabilitation admission cost in UC. In both groups, the major cost component was acute hospitalisation which accounted for around 30% of medical costs. The median non-medical cost was also marginally higher in the UC group (\$438, IQR: \$0 to \$4,561) than in the VEM group (\$358, IQR: \$0 to \$3,334). The median productivity cost was zero for both treatment groups given that less than one quarter of patients were in paid employment before the index stroke. Overall, the median total cost (including productivity cost and non-medical costs) were nominally higher in the UC group (\$27,042, IQR: \$7,257 to \$63,824) compared to the VEM group (\$25,675, IQR: \$6,766 to \$63,617). The detailed costs of each resource item and

summary costs are presented in Table 2. The costs for VEM and UC interventions are summarised in Supplementary document 5: Table II.

Generally, the cost from VEM and UC groups were comparable: the differences between VEM and UC groups was \$1082 (95%CI: -\$2399, \$4563) for the total medical cost (Supplementary document 6: Table I) and \$3 (95%CI: -\$5, \$12) for the productivity cost per person at 12 months; the between-group difference in the total non-health care cost was -\$1300 (95%CI: -\$3361, \$760) over the same period of time.

Cost-effectiveness analysis

The between group difference in both efficacy and cost outcomes generated from the GLM model are presented in Supplementary document 6: Table I.

In the base case health sector perspective analysis, the VEM yielded comparable total medical costs (\$1082, 95%CI: -\$2520 to \$4685, p=0.544) and QALY gains (-0.013, 95%CI: -0.041 to 0.016) at 12 months. When a societal perspective was adopted, the VEM entailed, again, similar costs with the UC group (\$102, 95%CI: -\$6907 to \$7111, p=0.982, including productivity costs) or (-\$6, 95%CI: -\$5476 to \$5463, p=0.933, excluding productivity costs) (Table 3).

The cost-effectiveness planes and cost-effectiveness acceptability curves from the two perspectives are shown in Supplementary document 7: Figures I to V.

Sensitivity analyses

Inclusion of a country dummy variable in the analysis produced similar results to the base case (Supplementary document 6: Table II).

The analysis from imputed data including all randomised participants produced consistent results with regard to the incremental cost and effectiveness between treatment groups. For example, from a health sector perspective, VEM was associated with similar costs (\$940, 95%CI: \$-4622 to \$4682) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) over 12 months. (Supplementary document 6: Table III and Supplementary document 7: Figures VI-VIII)

The country-specific analysis showed similar results in the between-group differences for both costs and QALYs, indicating that VEM and UC yielded comparable results within each participating countries (Table 4).

When a societal perspective was assumed, again, the point estimate of difference in costs between groups across countries varied substantially, with the 95% confidence intervals mostly Discussion overlapping (Table 4).

The 12 months within-trial cost-effectiveness analysis showed that VEM was unlikely to be cost-effective than UC in patients with stroke. Between-group differences in costs and benefits (probability of achieving a favourable outcome of mRS and differences in QALYs) over the one year study period were comparable from a health sector perspective. The findings from this economic evaluation is also underpinning an adapted version of trial underway to investigate the effectiveness of optimal rehabilitation in patients with mild to moderate stroke

(i.e. AVERT-DOSE, National Health and Medical Research Council Australia, project grant #1139712).

Our earlier economic evaluation of the phase II AVERT trial which consisted of only 71 patients (38 VEM and 33 UC) from two Australian centres reported that VEM was likely to be a cost-effective intervention with both less cost and more benefit when compared to UC.²⁷ Since it was a national pilot study with a limited sample, the direct comparison between the results from this and our current economic evaluation is problematic. In addition, inconsistent with the pilot study, no service shifting was observed in the current study. Across all resource use components, the proportion of patients consuming specific types of resources were comparable between the two groups in this study. On the contrary, in the Phase II AVERT trial, patients from VEM group were more likely to be discharged earlier from hospital than their UC counterparts; those discharged early tended to use more care provided in the outpatient setting, which incurred lower costs; and informal care was not costed. In the current study, the LoS for acute hospitalisation and rehabilitation were similar between treatment groups (median: VEM 16 vs UC 17 days). These differences between the two studies highlight the importance of large, adequately powered studies to inform health care policy.

In this study, resources used were valued on the basis of country-specific unit costs sourced for each participating country. To counteract any concern arising from the adoption of this approach, extensive sensitivity analyses were performed to test the robustness of the results. The conduct of incorporation of a country dummy variable into the model or country-specific analysis did not alter the outcomes substantially, with the resultant 95% confidence intervals overlapping to a great extent. Ramsey et al. 2015 suggest that a country-specific costing approach is likely to yield few qualitative differences in summary measures of cost-effectiveness among countries with similar levels of economic development.²⁵ Therefore, it was believed that any differences in economic status of the participating countries (as reflected

 by the unit costs applied in our study) are unlikely to bear a major influence on the results of the cost-effective analysis.

This multinational trial also revealed that in managing patients post-stroke, practice of stroke care varied from country to country. Although 100% of patients with stroke were hospitalised for the initial acute care, the LoS differs significantly greatly, ranging from 4 days (Malaysia) to 25 days (New Zealand), which might be attributable to the different severity of stroke and/or differences in clinical practice care processes. Moreover, in Malaysia, patients tended to receive rehabilitation services in an outpatient (i.e. up to 52% of patients received the outpatients rehabilitation program services) rather than inpatient (i.e. only up to 2% patients were admitted to rehabilitation hospital) setting; and patients were less likely to utilise ambulant transfer and apply home modifications, as compared to participants from other countries. This might be a signal for future study around stroke care in Malaysia, research potentially could be helpful to improve the service delivery for outpatient rehabilitation program. Patients from western countries consumed more community services and rehabilitation services that provided at home/nursing home than their Asian counterparts, which reflects the difference in social welfare and healthcare systems.

Economic evaluations have been conducted for other types of stroke rehabilitation interventions including early-supported discharge service, community- or home-based rehabilitation. ²⁸⁻³⁶ Generally, these interventions trended towards being cost-saving measured against usual practice. In regards to health-related quality of life (HRQoL) outcomes measured by a series of quality of life instruments (including SF-36, WHOQoL-Bref, Nottingham Health Profile, Sickness Impact Profile and EQ-5D), most studies did not detect an overall significant effect. ²⁸⁻³² ³⁴ ³⁵ ³⁷ Only one study reported a significant difference improvement in the overall

 HRQoL score.³⁶ The conclusions drawn from these economic evaluations of stroke rehabilitation interventions were fairly consistent; the interventions were likely to cost less,³³ ^{34 37-42} although the difference in costs was statistically significant in only one study.⁴¹ None of these studies evaluated the costs and benefits, particularly benefits measured in terms of QALYs, in an aggregated manner, and all were limited by small sample sizes. Another study using a Markov model explored the increased intensity of physiotherapy for stroke patients from a health system perspective, concluding that increased physiotherapy could be cost-effective by improving health outcomes and reducing costs due to the resultant shorter stay in rehabilitation facilities.⁴³

Given that it is not practical to obtain a baseline utility value from patients with stroke, in this study, the baseline AQoL value was mapped from mRS score at baseline. Whilst the mapping exercise was carried out using the baseline mRS score and AQoL values at 3 and 12 months, the significant variation in the mapped baseline utility values for patients falling within the same category of mRS hampered its application to the current economic evaluation. Instead, only the 12-month utility values were compared to approximate the difference in QALY gains over one year between the two treatment groups. Comprehensive sensitivity analyses were undertaken surrounding this assumption. It was observed that there was no noticeable difference among approaches examining the annual QALY gain difference between VEM and UC.

Whilst the results from the clinical study showed that there were no significant differences in either costs or effects between treatment groups, the cost-effectiveness analysis was still performed to investigate the possible ICER of the VEM intervention. It is possible to have greater confidence in the joint outcome of costs and QALYs than looking at them individually.⁴⁴

To the best of our knowledge, this study evaluated the cost-effectiveness of the largest international acute stroke rehabilitation trial ever conducted. The cost-effectiveness analysis was performed alongside the randomised controlled trial, where the costs and benefits data were collected prospectively. Moreover, the Cost CRF was completed by trained and blinded assessors via interviews with individual patients/carers and accessing medical records, which provides for greater accuracy than resource use questionnaires or diaries completed by participants themselves. Since the trial was designed in a pragmatic manner, with close resemblance to real clinical practice, it is believed that the assessment of its cost and cost-effectiveness under this setting reflects the real-life resource use (health and non-health).

This study provides some insights for future economic evaluation alongside multi-country, multi-centre clinical trials. It is important to note that given the large number of centres involved (56 stroke units across five geographical jurisdictions), it was not practical or reasonable to collect centre-specific unit costs which probably leads to huge variations even within a single country. Country-level unit costs were therefore applied to the valuation of resource uses across the trial sites. However, the heterogeneity in the resource utilisation and unit cost among the included countries undermines confidence in the conclusion. A country-specific economic evaluation might be more appropriate in this regard but the lacking of statistical power poses another concern. The current study made a trade-off between them both approaches by presenting both the aggregated (i.e. base case of pooling all countries) and disaggregated (i.e. sensitivity analysis of individual countries) form of results. The resource utilisation, costs and benefits were also tabulated across all sites and individually to allow close scrutiny from various perspectives. ²⁸ It is believed that this practice can be recommended to other multi-country studies.

A couple of limitations of the study are acknowledged. Firstly, the missing data on total costs from a societal perspective was around 24%, and related mainly to the missing information on

community services (10.9%) and productivity loss (10.7%). The base case analysis was based on the ITT population with an assumption of missing pattern being MAR. To account for this, the sensitivity analysis using multiple imputation was undertaken and yielded the identical conclusion (i.e. comparable results in costs and benefits between treatment groups). Secondly, unit costs originating from individual countries were assigned to value resource use. The differences in health care systems and cost structures among the five participating countries may potentially confound the cost comparisons between groups. However, analysis by country produced results consistent with the base case, which overcomes any concern that the latter were heavily weighted towards Australia, the largest sample country.

Conclusions

This economic evaluation alongside a phase III RCT evidenced that based on the ITT population, the VEM intervention for patients with stroke was unlikely to be cost-effective compared to UC. The sensitivity analyses based on the multiple imputation and subgroup analyses by each country separately yielded fairly consistent results. Overall, the VEM intervention was demonstrated to be comparable with UC in terms of both benefits and costs at one-year, however given its poorer outcomes at 3 months, VEM cannot be recommended to clinicians, patients or policymakers.

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Authors' Contribution

Conception/design, revising and final approval: LG, LS, LC, OW, MM, JC, FE, JB, HD, MMoodie. Methodology: LG, MM, LS, LC, MMoodie, OW. Data analysis: LG, LS, MM, LC. Drafting: LG, MMoodie.

Competing Interests Statement

All authors confirm that there is nothing to declare.

Data Availability Statement

No additional data available

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Tables

					BMJ Oper	l		d by copyright, including	bm jopen-2018-026230			Paç
ables								ht, inc	118-026			
ble 1. Quantity of	f resource us AU (N=1054		nths (ITT) (median, IQR NZ (N=189)		UK (N=610)		SG (N=128)		• MA (N=123)		All Countries	
	VEM	UC	VEM	UC	VEM	UC	VEM	UC uses	NEM NEM	UC	VEM	UC
Acute hospitalisation								Ses	Tay			
% of patients using	100	100	100	100	100	100	100	100 00	2 100 2 100	100	100	100
LoS (days)	21(6-42)	22(7-46)	23(6-57)	25(8-48)	12(4-45)	13(5-4)	16(4-25)	18(4-25)	5(3-8)	4(2-8)	16(4-41)	17(5-41)
Stroke-related rehospita	alisation							⊥ ö i	D 5(3-8)			
% of patients using	30	29	28	33	28	23	20	20 20 20	18 18 16 16 16 17 10 11 11 11 12 12	23	28	27
No. readmission/s	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	2(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)
Admission to rehabilita	tion hospital [†]			P ₀				ata S	P D			
% of patients using	62	56	60	65	35	34	45	56	9 0	2	50	47
No. of admission/s	1(0-1)	1(0-1)	1(0-1)	1(0-1)	0(0-1)	0(0-1)	0(0-1)	1(0-1) &	0(0-0)	0(0-0)	0(0-1)	1(1-1)
Outpatient rehabilitatio	on program				* ()			25 ng	jo pe			
% of patients using	40	39	23	19	12	10	19	25	52	48	30	28
No. of services	15(6-29)	12(6-28)	16(7-28)	17(12-34)	12(6-21)	7(4-14)	32(20-77)	29(3-116)	15(7-24)	16(4-22)	15(6-28)	12(6-27)
Rehabilitation provided	at home/nursing	facility						<u>s</u>	₹ •			
% of patients using	30	33	57	52	50	46	3	2 iii	2	2	35	34
No. of services	9(4-22)	10(4-25)	18(8-29)	16(9-30)	12(6-28)	12(6-30)	81(63-99)	9(9-9)	104(104-104)	8(8-8)	12(5-27)	12(5-28)
Ambulance transfer								hno	4 3			
% of pts using	51	53	34	48	41	38	36	9(9-9) technologies	2025	8	43	44
No. of trips	2(1-3)	2(1-3)	2(1-3)	1(1-3)	2(1-3)	2(1-3)	1(1-2)	1(1-2)	→ 2(2-3)	2(1-3)	2(1-3)	2(1-3)
Individual allied health	therapy								genc			
% of pts using	N/A	N/A	N/A	N/A	19	15	-	2	20 E. 20	25	-	-
No. of services	N/A	N/A	N/A	N/A	8(2-12)	8(4-15)	-	2(2-2)	8(3-10)	16(8-31)	-	-
Private physiotherapy)g raphi			

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% of pts using	9	8	11	1	5	5	8	right,	201	2	8	6
No. of services	5(3-19)	6(4-19)	13(6-18)	3(3-3)	12(6-33)	7(1-14)	18(16-24)	14(7-24 算	R 12(11-13)	8(8-8)	15(4-20)	24(3-19)
Respite care								14(7-24 2 44ding	<u>&</u>			
% of pts using	3	2	3	2	2	3	-	- 0	on	2	2	2
No. of services	21(10-43)	15(11-35)	12(10-20)	7(5-8)	24(9-40)	21(12-80)	-	- use		30(N/A)	18(9-39)	18(9-41)
Accommodation moves								s reig	23 223			
% of pts using	18	17	19	28	13	14	11	20 6 9	23	10	16	17
No. of moves	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1) to text and data	1(1-2)	2(1-2)	1(1-1)	1(1-1)
Community Services used	 prior to having	a stroke over the	past year					ext a	Poad Service S			
% of pts using	13	17	6	7	5	5	-	- G	<u> </u>	-	9	11
No. of services	26(26-52)	26(26-52)	52(39-88)	46(14-52)	52(25-104)	40(15-131)	-	- ta	<u>.</u> ≥8 -	-	27(26-52)	26(26-52)
Community services used	over 12 months	after stroke		404				minin	n s Op			
% of pts using	30	35	32	28	31	28	-	3 6 .	6	-	27	28
No. of services	28(18-72)	32(12-78)	130(47-233)	48(17-256)	42(12-185)	90(12-310)	-	3(3-3) training	6(3-73)	-	39(14-119)	39(12-124)
Home modifications under	taken over 12 n	nonths				7		<u>a</u> .	n.b			
% of pts using	27	30	20	17	36	33	16	19 6	3 .3	10	27	28
No. of mods	2(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	1(1-2)	1(1-1)	1(1-1)	1(1-2)	2(1-2)
Aids and appliances used of	over 12 months							similar te	9 ,			
% of pts using	46	47	55	63	58	51	44	45	5 8	59	51	50
No. of aids/appliance used	2(1-5)	2(1-4)	3(2-6)	2(1-4)	4(2-6)	4(2-6)	2(2-3)	2(1-3) hnolog og og s	2(1-3)	2(1-3)	3(1-5)	3(1-5)
Working prior to stroke	1					1		olog	202			
% of patients	24	23	38	34	19	21	52	52	25 24 45	33	27	26
Hrs worked/week	40(27-50)	40(30-50)	40(37-40)	40(37-40)	40(25-48)	37(25-40)	48(40-56)	45(36-50)	42(40-56)	45(32-50)	40(30-50)	40(30-50)
Proportion working at 12	months	1	1	1	<u> </u>	ı	1	1	p ce	1	1	
% of patients	15	12	20	16	7	9	25	22	₽ 24	15	14	12
Hrs worked/week	38(18-40)	25(12-40)	40(20-40)	40(38-40)	35(26-40)	30(24-37)	39(16-46)	35(23-44)	40(32-47)	45(30-50)	38(20-41)	30(16-40)

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6 of patients	-	-	-	-	-	-	19	16	cluc	3 5	10	-	-
No. of maids	-	-	-	-	-	-	1(1-1)	16	ing	35 1(1-1)	1(1-1)	-	-
atients from Singapo	ore and Malaysia who	had a maid at 12	months follow	ving stroke					<u> </u>	•			
6 of patients	-	-	-	-	-	-	23	22	En:	5	7	-	-
lo. of maids	-	-	-	-	-	-	1(1-1)	1(1-1)	seig	1(1-1)	1(1-1)	-	-
Receipt of informal ca	are at 12 months								nem ated)			
6 of patients	35	39	37	33	41	40	30	36	ent :	5 1(1-1) 42 22(10-38) hours; mod:	44	37	39
lo. of hrs/week	15(6-34)	12(4-31)	8(3-21)	14(6-30)	21(9-34)	17(7-35)	35(13-46)	16(4-3	Sub Sub	22(10-38)	16(5-26)	18(7-35)	14(5-32)
: Intention-to-treat; A re expressed as media:	AU: Australia; NZ: New n and interquartile rans	v Zealand; UK: Ur ge (IQR); †includes	nited Kingdom; s any admission	SG: Singapore; National SG: Singapore; National SG: Singapore; National SG:	MA: Malaysia; L hospital followi	oS: length of sta	ay; pts: patients; stroke;	No.: num	المجازة جياج جياج	hours; mod:	modification; -:	no such resourc	e use; all nur
									aining, an				
	15(6-34) AU: Australia; NZ: Nev n and interquartile rang				30				aining, and similar technologies.				

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Page 31 of 8	31 of 82					BMJ Open		;	វ by copyright	bm jopen-2018-024 (N=123)			
1 2 Table 2 (Cost of all the	resources use	d over 12 mont	ths (AUD)				e	ight,	2018-			!
b	AU (N=1054)	TOOUT COS ESC.	NZ (N=189)	ns (rice)	UK (N=610)		SG (N=128)	.	<u>ਵ</u> ਨ ਅ	N=123)		All Countries	
5	VEM	UC	VEM	UC	VEM	UC	VEM		ud V	VS M	UC	VEM	UC
1	7 251.2		7 101,1			lealth care cost (AU			₹	0		, Eliz	'
Acute hospit	italisation						,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		→	9			
Median,	\$6294	\$6294	\$6104	\$6104	\$2763	\$3109	\$1493	\$1493		8 13 63	\$1363	\$6294	\$6294
/ IQR	(6294, 9553)	(6294, 9553)	(4370, 6104)	(4370, 6104)	(1382, 6563)	(1727, 6563)	(1493, 1809)	(1493, 1493)	ն년	i ≤ 63, 1572)	(1363, 1572)	(2279, 9535)	(2418, 9553)
8 Mean, SD	\$9883 (9484)	\$10010(10508)	\$6635 (3244)	\$6549 (3555)	\$5714(7876)	\$5885 (7101)	\$1721 (547)	\$1676 (432)	8 3	3 € 482 (212)	\$1472 (200)	\$7369 (8469)	\$7521 (8916)
	ted rehospitalisation								seigne relate	20.			
10Median,	\$0	\$0	\$0	\$0	\$227	\$227	\$111	\$111	ate me	,66	\$68	\$111	\$111
1 1 QR	(0, 3850)	(0, 3850)	(0, 325)	(0, 2243)	(227, 1401)	(227, 227)	(111, 111)	(111, 111)	Ճ ∃€	(6 6 , 68)	(68, 68)	(0, 1401)	(0, 610)
12Mean, SD	\$6030 (17114)	\$6473 (21590)	\$651 (1371)	\$1507 (2828)	\$4524 (13968)	\$3494(11349)	\$2756 (7565)	\$1679 (3465)			\$603 (1479)	\$4610 (14518)	\$4551 (16707)
	to rehab hospital		~						tex L	<u> </u>			
14 Median,	\$13134	\$13134	\$11262	\$11262	\$0	\$0	\$0	\$1298	t a	<u>6</u>	\$0	\$0	\$1136
IQR	(0, 36371)	(0, 38391)	(0, 30983)	(0, 26486)	(0, 29788)	(0, 29788)	(0, 2921)	(0, 3570)	집쿲	Jp (0)	(0, 0)	(0, 29788)	(0, 29788)
Mean, SD	\$25667 (38892)	\$26648(38315)	\$16871(18536)	\$15573(16848)	\$12539(19682)	\$11758 (18390)	\$1815 (2759)	\$1298 (0, 3570) \$2798 (5082)	fûr (A data	(0) (학 (교	\$43 (234)	\$18197 (31241)	\$18458 (30811)
	rehab program								a n) 			
18 _{Median,}	\$0 (0, 2451)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	3 3	3	\$0	\$0	\$0
1 9 QR		(0, 1913)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,36)	\mathbf{z}	(0.265)	(0, 249)	(0, 478)	(0, 239)
2 M ean, SD	\$2081 (4183)	\$1934 (5316)	\$821 (2236)	\$721 (1991)	\$266 (1026)	\$155 (676)	\$364 (1090)	\$562 (1478)	\$	§ 4 (286)	\$126 (206)	\$1246 (3244)	\$1142 (3976)
	ided at home/nursi								<u>+</u>	<u> </u>			
2 Median,	\$0	\$0	\$1168	\$212	\$922	\$0	\$0	\$0	<u>a</u> \$	S 6 (0)	\$0	\$0	\$0
QR	(0, 717)	(0, 956)	(0, 4299)	(0, 3821)	(0, 11064)	(0, 11064)	(0, 0)	(0, 0)	<u> </u>	<u>克</u> 0)	(0, 0)	(0, 1913)	(0, 1913)
Mean, SD	\$1382 (4069)	\$1551 (4252)	\$3171 (4960)	\$3111 (5754)	\$12085 (28516)	\$11051 (26723)	\$93 (570)	_ , ,		S 27 (719)	\$7 (53)	\$4447 (16294)	\$4180 (15203)
	allied health visit	т	т	.	т.	т.			<u>a</u>	. <u>c</u>	T .	-	
Median,	N/A	N/A	N/A	N/A	\$0	\$0	\$0		a \$0		\$0	N/A	N/A
26QR	37/4	1	1		(0,0)	(0,0)	(0,0)	(0,179)	<u> </u>	1	(0,0)	37/4	37/4
2 Mean, SD	N/A transfers	N/A	N/A	N/A	\$375 (1144)	\$329 (1291)	\$432 (1521)		-C)	SP (0)	\$0.2 (2)	N/A	N/A
28Ambulance		¢500	60	T 60	T 60	T 60				unge	T 60	\$0	1 00
2 9 Median,	\$508 (0, 1015)	\$508 (0, 1015)	\$0 (0, 646)	\$0 (0, 646)	\$0 (0, 1150)	\$0 (0, 575)	\$0 (0, 265)	\$0 (0, 265)		(12 0)	\$0 (0, 0)	(0, 611)	\$0 (0, 610)
Mean, SD	\$671 (1057)	\$623 (946)	\$543 (1082)	\$605 (928)	\$790 (3209)	\$701 (3150)	\$164 (348)			S(26)	\$14 (64)	\$627 (1920)	\$578 (1838)
Private phys	` /	\$023 (370)	\$343 (1002)	\$005 (320)	\$190 (3207)	\$/01 (3130)	\$104 (340)		olog	8(20)	\$14 (U+)	\$027 (1920)	\$3/0(1030)
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0		ges \$	025 (A)	\$0	\$0	\$0
Back Barry	$\begin{vmatrix} 30 \\ (0,0) \end{vmatrix}$	$\begin{pmatrix} \mathfrak{s0} \\ (0,0) \end{pmatrix}$	(0,0)	$\begin{pmatrix} \mathfrak{so} \\ (0,0) \end{pmatrix}$	(0,0)	(0,0)	(0,0)	(0,0)	is ((<u>r</u> .0)	$\begin{pmatrix} 30 \\ (0,0) \end{pmatrix}$	(0,0)	(0,0)
	\$70 (375)	\$124 (797)	\$245 (1308)	\$4 (36)	\$128 (780)	\$174 (2102)	\$238 (1096)	\$333 (1938)	+	9 (19)	\$1 (9)	\$109 (693)	\$132 (1336)
35Respite care		Ψ (, , ,	Ψ= (, -,	, 4.(5.)	_ \$120 (7.5.7)		Ψ=== (,	, , , , , , , , , , , , , , , , , , ,		<u> </u>	, 4 - (-)	()	()
B6Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	<u> </u>	<u></u>	\$0	\$0	\$0
₽ †QR	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(1	(P)	(0,0)	(0,0)	(0,0)
Mean, SD	\$48 (355)	\$20 (182)	\$7 (46)	\$2 (15)	\$9 (95)	\$58 (686)	\$0(0)	\$0 (0)	\$	5 (0)	\$1 (8)	\$27 (259)	\$27 (386)
39	AU (N=1054)	1	NZ (N=189)	+	UK (N=610)		SG (N=128)		N'	V (N=123)		All Countries	
40	VEM	UC	VEM	UC	VEM	UC	VEM	UC		√8 M	UC	VEM	UC
40									$\overline{}$				

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								yrigh:	n-201			
1								g	201			
2 Sub-total								-	7 P P			
Median	\$29278	\$29441	\$20621	\$23722	\$18896	\$20843	\$4525	\$4687	\$ № 13	\$1746	\$19271	\$20411
(IQR)	(8218, 63622)	(9811, 62489)	(6068, 46909)	(7316, 40162)	(4030, 48999)	(3682, 47908)	(1604, 8668)	(2724, 10926) 	(1 ×1 31, 2532)	(1431, 2348)	(6294, 52637)	(7238, 63835)
Mean	\$45620 (51458)	\$47453(53715)	\$28898 (25011)	\$27986(22676)	\$34863 (42509)	\$32842 (39517)	\$7681 (8828)	\$8358 (8787)	\$2385(1587)	\$2269(1574)	\$36351 (45620)	\$36604 (46309)
5 (SD)	4 10 0 2 0 (0 1 10 0)	417100(00710)	4-00/0 (-000)	+= / > 0 0 (== 0 / 0 /	40 1000 (1207)	(0,017)	4,000 (0020)	9,00	Q	4==== (== , 1)	(10000)	40000 (1000)
6					N	on-health care cos	st	0	23			
7 Accommoda	ation moves											
8 Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0		\$0	\$0	\$0
9 IQR	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)		(0,0)	(0,0)	(0,0)
Mean, SD	\$2089 (8518)	\$2482 (9323)	\$5975 (19614)	\$9135 (26918)	\$2901 (12958)	\$2532 (11125)	\$72 (578)	\$108 (507)	m May (N) (N) (1893)	\$104 (501)	\$2460 (11036)	\$2821 (12212)
Community	\ /	\$2402 (7323)	\$3773 (1701 4)	(20710)	\$2701 (12730)	\$2332 (11123)	\$12 (310)	φ100 (307)	13 D	\$104 (301)	\$2400 (11030)	\$2021 (12212)
	\$0	\$0	\$0	60	\$0	\$0	\$0	\$0 5		\$0	\$0	\$0
1 Median, 1 7QR	(0,0)	(0,0)	(0,0)	\$0 (0, 0)	(0, 430)	(0, 174)	(0,0)	(0,0)	1 1 1 1 1 1 1 1 1 1	(0, 0)	(0,0)	(0,0)
13Mean, SD	\$570 (2681)	\$1091 (8556)	\$238 (950)	\$1022 (4113)	\$22275(294988)	\$10738 (57306)		\$244 (1902)	(110)	\$0(0)	\$6870 (160318)	\$3786 (31893)
	` /	\$1091 (8330)	\$238 (930)	\$1022 (4113)	\$22273(294988)	\$10/38 (3/300)	\$0 (0)	3244 (1902)	ngh (110)	\$0 (0)	\$08/0 (100318)	\$3/80 (31893)
Home modif		**			• •				<u> </u>			4.0
15 _{Median} ,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	28 <u>C</u>	\$0	\$0	\$0
1 6 QR	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0,0)	<u> </u>	(0, 0)	(0, 0)	(0,0)
1 ≯ Mean, SD	\$805 (6338)	\$751 (7715)	\$833 (4862)	\$565 (3204)	\$352 (2133)	\$834 (7091)	\$234 (1079)	\$62 (299)	(369)	\$64 (237)	594 (4840)	\$676 (6734)
18 pecial aids	and equipment							≅	.m d			
₁ Median,	\$0	\$0	\$70	\$103	\$27	\$0	\$0	\$0	3 5	\$36	\$0	\$0
JQR	(0, 332)	(0,318)	(0, 549)	(0, 357)	(0,786)	(0, 846)	(0, 240)	(0, 210)	(0,218)	(0, 186)	(0, 414)	(0, 414)
Mean, SD	\$1986 (7668)	\$2787 (10396)	\$2198 (7993)	\$1798 (7229)	\$1354(3649)	\$1720 (5083)	\$1117 (5843)	\$1079 (5483)	\$53 (252)	\$193 (658)	\$1660 (6426)	\$2141 (8328)
Informal car	re	` '	, ,					5	8			· · · ·
²² Median,	\$24	\$48	\$14	\$0	\$29	\$29	\$0	\$0 5	\$24	\$9	\$24	\$24
2 3 QR	(0, 503)	(0, 455)	(0, 283)	(0, 149)	(0, 471)	(0, 375)	(0, 114)	\$0 (0, 238)	(13 60)	(0, 50)	(0, 407)	(0, 407)
24Mean, SD	\$414 (747)	\$405 (758)	\$236 (536)	\$152 (311)	\$324 (516)	\$324 (645)	\$144 (285)	\$159 (300)	\$43 (57)	\$27 (34)	\$335 (633)	\$322 (660)
25 iving-in ma		\$.00 (700)	\$ 2 55 (655)	ψ10 2 (511)	ψ52 · (€10)	\$52 · (\$ · b)	(200)		6	Ψ=7 (5.)	<i>\$555</i> (655)	Ψ322 (000)
Median,	N/A	N/A	N/A	N/A	N/A	N/A	\$0	\$0 0	1 . 3	\$0	N/A	N/A
J-JQR	IV/A	1 \ //A	1 V /A	IV/A	1 \ // A	IV/A	(0,0)	\$0 (0,0)	(9 0)	(0,0)	IV/A	IV/A
Mean, SD	N/A	N/A	N/A	N/A	N/A	N/A	\$3154 (8146)	\$4268(11338)		\$83 (504)	N/A	N/A
Sub-total	IN/A	IN/A	IN/A	IN/A	1 V /A	IV/A	\$3134 (8140)		\ =	\$65 (504)	IN/A	IN/A
120	0.450	¢772	¢201	0(20	Ф 7 50	¢471	025	© 0104	\$74	0.57	\$250	¢420
Median	\$459 (0, 3334)	\$673 (0, 5209)	\$381 (0, 3674)	\$638	\$758 (0, 5097)	\$471	\$25 (0, 1293)	\$194 (0, 6999)	(9, 285)	\$57	\$358 (0, 3334)	\$438 (0, 4561)
(IGIC)		· · /		(103, 14551)		(0, 4725)	· · /	(0, 6999)	(6, 285)	(0, 318)		
Ivican	\$6104 (15582)	\$6985 (17554)	\$7752 (17751)	\$11981(27676)	\$27892(306917)	\$15345(61750)	\$4802 (10366)	\$6177 (13942)	\$81 (2272)	\$484 (1113)	\$12043 (164026)	\$9360 (36504)
32 (SD)						<u> </u>		<u></u>	5 at			
33						Productivity cost		Ç,	2.7		·	
3 Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$6	\$0	\$0	\$0
35QR	(0,0)	(0, 0)	(0,0)	(0,0)	(0, 0)	(0, 0)	(0,0)	(0,0)	(9 0)	(0,0)	(0,0)	(0,0)
Mean, SD	\$75 (317)	\$84 (391)	\$29 (130)	\$14 (54)	\$17 (152)	\$44 (245)	\$6 (29)	\$8 (35)	\$ 8 (4)	\$0.4(3)	\$46 (246)	\$58 (312)
Total cost									<u> </u>			
Median	\$33203	\$35143	\$29934	\$32216	\$25374	\$30537	\$6960	\$8810	\$ ≅ 16	\$1816	\$25675	\$27042
Median 88(IGR)	(9687, 71902)	(12696, 74070)	(8528, 65781)	(15710, 68292)	(4712, 64285)	(4629, 67012)	(1674, 26187)	(3426, 19493)	(2 61, 3994)	(1537, 3301)	(6766, 63617)	(7257, 63824)
BMean (SD)	\$52456(57264)	\$56408(62536)		\$43901(43170)			\$15036(16921)	\$16340(19650)		\$2938(2350)		\$47627(64249)
40		, ,							3			, , ,
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/1/1				-								

**c only a loss propertion (r.e. fless Para 595s) of patient regarded certain lyges of resource stiffsation, year median and/or 10R are r.
**satisfs includes a patient's immediate admission to resubdilization hospital on discharge from hospital as the rehabilization service s.

revoked.

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	QALYs	Per capita mean cost (AUD)
Health care perspective		
Total medical costs	-0.013	\$1082
	(-0.041, 0.016)	(-\$2520, \$4685)
Societal perspective		
Total medical and non-medical	-0.013	-\$6
costs (excl. productivity cost)	(-0.041, 0.016)	(-\$5476, \$5463)
Total medical and non-medical	-0.013	\$102
costs (incl. productivity cost)	(-0.041, 0.016)	(-\$6907, \$7111)
ITT. Intention to the Avent OALVe Overline address	LUIC M. ALID A. I. II	

ITT: Intention-to-treat; QALYs: Quality-adjusted Life Years; AUD: Australian dollar; excl: excluding; incl: including



Table 4 Results of country-specific analysis of costs and benefits

	AU	NZ	UK	SG	MA
	(N=1054)	(N=189)	(N=610)	(N=128)	(N=123)
Total medical	\$948	-\$2836	\$2937	-\$81	\$137
costs	(-\$4352, \$6248)	(-\$8403, \$2730)	(-\$3635, \$9509)	(-\$2789, \$2627)	(-\$324, \$599)
Total non-	-\$1318	-\$3959	-\$1387	-\$3164	\$200
medical costs	(-\$3038, \$403)	(-\$7769, -\$150)	(-\$7331, \$4557)	(-\$6834, \$505)	(-\$232, \$631)
Total cost	-\$1735	-\$8981	\$1870	-\$2636	\$479
(incl.	(-\$8482, 5013)	(-\$18380, \$418)	(-\$13955, \$17694)	(-\$9233, \$3961)	(-\$487, \$1446)
productivity)					
Total cost	-\$1185	-\$7610	\$2552	-\$1534	\$416
(excl.	(-\$7184, \$4815)	(-\$15302, \$82)	(-\$11377, \$16481)	(-\$6464, \$3395)	(-\$364, \$1196)
productivity)					
QALY gains	-0.036	0.086	-0.010	0.008	0.003
	(-0.076, 0.003)	(-0.003, 0.176)	(-0.064, 0.044)	(-0.106, 0.123)	(-0.126, 0.132)

AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia; QALY: Quality-adjusted Life Year.

^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

Supplementary document 1: Mapping baseline mRS score to utility of AQoL-4D

Methods

Generalized additive model (GAM) with spline smother was used to map AQoL from premorbid mRS, stroke severity, and/ or age group. The performance of the models was evaluated using mean absolute, mean squared errors (MAE and MSE) and R2. 10-fold cross-validation was implemented for model validation. The mapped baseline utility of AQoL-4D was used in the following models.

The analyses are structured as follows:

Model 1:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and pre- morbid mRS as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 2:

- a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input;
- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity as a covariate;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity and age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 3:

a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value as a covariate;

- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 4:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Results

Table I. Difference in utility values between treatment groups by different models

	a	b	c	d		
				1	2	
Model 1	-0.011	-0.015	-0.016	-0.026	0.006	
	(-0.042, 0.020)	(-0.042, 0.011)	(-0.042,0.010)	(-0.062, 0.009)	(-0.030, 0.041)	
Model 2*	-0.001	-0.007	-0.008	-0.007	0.005	
	(-0.046, 0.044)	(-0.047, 0.034)	(-0.048, 0.031)	(-0.062, 0.048)	(-0.050, 0.060)	
Model 3*	-0.008	-0.014	-0.015	-0.014	0.002	
	(-0.043, 0.026)	(-0.043, 0.016)	(-0.043, 0.014)	(-0.052, 0.033)	(-0.050, 0.045)	
Model 4	-0.008	-0.014	-0.015	-0.026	0.006	
			(-0.043, 0.014)	(-0.062, 0.010)	(-0.030, 0.042)	

^{*}models 2 and 3 used the mapped baseline AQol utility to estimate the QALY gains over 12 month for each patient.

utility value to calculate the difference in QALYs between treatment groups (results from models 2 and 3) yielded similar results to the primary analysis (-0.013, 95%CI [-0.043, 0.018]), and the 95% confidence

Supplementary document 2: Cost Case Report Form (CRF)

The Cost CRF was originally developed via pathway analysis during Phase II of AVERT to identify resource items associated with the trial 11. Since the Phase II of AVERT trial was a national project and resource utilisation tools were tailored to the Australian setting, the form was further modified to accommodate international differences in the acute service delivery, rehabilitation and post-acute care. An extensive review of country-specific literature and consultation with international AVERT project team members based in each country were undertaken to tailor the Cost CRF tool to each participating country.



Case Report Form - Cost

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	Research Institige

PATIENT INITIALS

National Strokes:

Research Institute

Note: this one form is to be completed AND faxed following BOTH the 3 and 12 months at 12 months fax all pages 25.36 to the Date Page. When CRF Cost complete at 3 months AND at 12 months, fax all pages 25-36 to the Data Fax.

Instructions to the person responding: These questions are about health care provided as a consequence of the stroke which occurred on (give date of stroke) or as a result of any further stroke. I will be asking about health care such as visits to hospital, rehabilitation, the stroke were provided and their cost.

Subject's stroke date

Subject's stroke date

Obtain from CRE. Severaging Day 0

Obtain fi	rom CRF - Screening Day 0		<u></u>	ext a	nload Supe	
3 MONTH DA	ATE OF ASSESSMENT	//	Assessor initials	nd data	<u> </u>	
PERSON RESPONI	DING	ASSISTANCE FOR IN	NTERVIEW OBTAINED FROM		E IVING ARRANGEMENT O	F RESPONDENT*
Index case	Other relative \square	Index case □	Other relative	9, /	giving with index	
Spouse/partner	Friend/Associate/Neighbour	Spouse/partner 🗆 🧸	Friend/Associate/Neighbour	<u>≥</u>	Not living with index	
Sibling \square	Carer, e.g. nurse □	Sibling 🗌	Carer, e.g. nurse □	<u>a</u> .	Professional carer in nursing ho	ome or hostel \square
Son/Daughter	Other, unspecified \square	Son/Daughter 🗌	Other, unspecified \square	j	S S S S S S S S S S S S S S S S S S S	offic of floorer
Parent		Parent □		g, an	nj.cc	
12 MONTH DA	ATE OF ASSESSMENT	//	Assessor initials	d similar	n/ on Ju	
PERSON RESPOND	DING	ASSISTANCE FOR II	NTERVIEW OBTAINED FROM	tec	्रो।VING ARRANGEMENT O	F RESPONDENT*
Index case □	Other relative \square	Index case □	Other relative \square	hnologies	with index	
Spouse/partner	Friend/Associate/Neighbour	Spouse/partner	Friend/Associate/Neighbour	90	Sot living with index	
Sibling	Carer, e.g. nurse	Sibling 🗌	Carer, e.g. nurse 🗌	gie	জ Professional carer in nursing h	ome or hostel \square
Son/Daughter	Other, unspecified \square	Son/Daughter	Other, unspecified \square	ÿ		offic of flooter 🗖
Parent		Parent □			geno	
					Please note: this is the 'normal' the respondent with respect to the subject is currently in hospital	







Case Report Form - Cost

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I ACCOUNT IN DURING

ATIENT STUDY NUMBER				
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S PATIENT IN	ITIA	LS		

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1) DISCHARGE)26230 o ncluding		
ate of discharge from acute care	Acute discharge des Home Rehabilitation ward/ho Supported residential Hostel Nursing home Other	stination	Date of admission Date of discharge Leave dates BLAN Please note: inpati inclusive of geriatric transitional care.	to inpatient rehable from inpatient reh K if not applicable ent rehabilitation is	ilifation	Discharge destination after Home Rehabilitation hospital Supported residential service Hostel Nursing home Other	
	Unknown	000	transitional care.	c evaluation and	nd from ht ieur (ABE id data m	Unknown Leave BLANK if not app	□ blicable
2) LIVING ARRANGEMENT					tp:// ining		
re-stroke residential address		Residential address at	t 3 months*		Residentia	al address at 12 months*	
Own house, flat – alone		Own house, flat – alone			Ogin higuse	e, flat – alone	
Own house, flat – with family/relative/frie	nd 🗆	Own house, flat – with fa	amily/relative/friend		Q∰m h∰use	e, flat – family/relative/friend	
lome of relative/friend		Home of relative/friend			H ğ me ğ f re	lative/friend	
Supported residential service (SRS)		Supported residential se	ervice (SRS)		S group ted	residential service (SRS)	
lostel		Hostel			Heste E		
lursing home		Nursing home			Nersing ho	me	
Other		Other			Ogen 2		
Jnknown		Unknown			O g known		
			ote if the subject is ir current residentia			t (acute or subacute), address	
	For peer revi	iew only - http://hmione	on hmi com/sito/ah	out/quidalines vhtr	de		





Case Report Form - Cost

32	National Stroke <u>≤</u>
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PATIENT INITIALS	
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3) CHANGE IN LIVING ARRANGEMENTS	026230 o			
As a consequence of your stroke, have you needed to change your place of residence?	3 moRths2	Yes □	No □ U	nknown 🗆
If NO, proceed to question 4. * Please note: if subject has been a hospital inpatient this is NOT a change of residence	ნ ლ ≦ 3-12 წეტებენიs	Yes 🗆	No □ U	nknown 🗆
DATE OF MOVE LOCATION	2019. Do seigneme s related			
Own home or unit Home of relative/friend SRS Hostel Nursing home	ownloaded ent Superie to text and			
Other Own home or unit Home of relative/friend SRS Hostel Nursing home Other	from http://bmj. ur (ABES) . data mining, Al			
3) /	ttp://bmjopen.bmj.com/ on June 13, 202 ES) . iining, Al training, and similar technolog			
Own home or unit Home of relative/friend SRS Hostel Nursing home Other	202 olog			
4) AMBULANCE TRANSFERS: EMERGENCY AND NON-EMERGENCY	5 at A			
As a consequence of your stroke, have you required ambulance transport after your acute admission to hospital?* If NO, please proceed to question 5	* 3 mogsths	s Yes □	No □	Unknown 🗌
	3-12 g	nths Yes 🗆	No □	Unknown 🗌
Count number of ambulance trips (recruitment to 3 months) * Include post-acute transfers (eg - acute Count number of ambulance trips (from 3 to 12 months)	liographique to rehab)			
For near review only - http://hmignen.hmi.com/site/ahout/quideline	de			ı

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Case Report Form - Cost

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RATIENT S	TUDY NUMBER				
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If patient not

discharged at

If NO, proceed to question 6

5) HOSPITALISATION OR EMERGENCY DEP	ARTMENT	ATTENDANCES	0 o			
a) Have you been readmitted to hospital or attended the emr	ergency depar	tment as a consequence of another stroke	of 3 months	Yes 🗆	No 🗆	Unknown 🗆
ONLY include information for admissions and attendances troke-related problems and CRF completion manual for fur			May 2019. Enseigne Ises relate	Yes 🔟	No 🗆	Unknown 🗆
NO, proceed to question 6			Down ment :			
b) If YES, Start with the earliest admission or attendance. If parates BLANK (complete dates at 12 month assessment)		arged at 3 month assessment, leave discharge	ext and data			If patient not discharged a 12 month
Admission or Attendance 1 - Hospital name	Hospital code	Date admitted	from Date of	discharged		assessment cross box.
			http://bi	/		
Admission or Attendance 2 - Hospital name	Hospital code	Date admitted	≥ ₫	discharged		
			ning, /	/		
Admission or Attendance 3 - Hospital name	Hospital code	Date admitted	and si	discharged		
·			Date of June 13, 20	/ 📗		
Admission or Attendance 4 - Hospital name	Hospital code	Date admitted	e 13, 2 Date of	discharged		
Training Training			025 at ogies.]/		
Admission or Attendance 5 - Hospital name	Hospital	Data admitted	Agenc	dicabargad		
Admission or Attendance 5 - Hospital name	code	Date admitted / / / / / / / / / / / / / / / / / / /	© Date	discharged		П
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Stroke related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary catheter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11. Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional pre-lem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting 19. Surgery or procedural management of of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21. Inabies to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26. Pressum sores.

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Case Report Form - Cost

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6)	INPATIENT REHABILITATION ADMISSIO	N					6230 cludi			
	r your stroke on (give date of stroke), were you admitte			-	•	3	moffths S	Yes 🗆	No 🗆	Unknown 🗆
	ere you received rehabilitation treatment? Please includ luation' and 'transitional care'	de adr	nissions with the care	e type 'rehab	oilitation', 'geriatric	3-	12 months	Yes □	No □	Unknown □
If Y	O, proceed to question 7. ES, complete inpatient rehabilitation admission details, state atient NOT discharged at 3 month assessment, leave discharged at 3 month assessment at 3 month as 3 month as 3 month as 3 month as 3 month at 3 month as					sment)	May 2019. Down Enseignement t uses related to t			If patient not discharged at 12 month
	Admission 1- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		Dow d to	Date disch	arged	assessment,
				/	/		nlloade Super text an	//		cross box.
	Admission 2- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		d fro ieur d da	Date disch	arged	
	Admission 2 Renabilitation hospital name				/ 📗		(ABES	//		
	Admission 3- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		ing,	Date disch	arged	
	·				/ 📗		Al tra	//		
7) OUTPATIENT REHABILITATION PROGR	RAM					ning,			
	d you attend or are you attending an outpatient rehabi			nsequence (of your stroke?		3 anong h	ıs Yes 🗆	No [☐ Unknown ☐
Ar loc	 g. with physiotherapy, occupational therapy, speech the noutpatient rehabilitation program is any rehabilitation prograted at a hospital or community facility. 			ends a facilit	y. The program ca	an be	=:	onths Yes 🗆	No [☐ Unknown ☐
If `	NO, proceed to question 8. YES, complete outpatient rehabilitation details, starting from patient NOT discharged at 3 month assessment, leave disc	m you charg	ur first outpatient reha e dates and number	abilitation vis of days atter	it. nded BLANK (com	nplete date	ne 1 tecl	onth assessme	Tota	
	Admission 1 - Outpatient rehabilitation name	Ref	nab facility le	Date admi	tted		o Gate di	ischarged	of Datte	
	Admission 1 - Outpatient renabilitation fiame] / 	/		
	Admission 2 - Outpatient rehabilitation name	Reh	nab facility le	Date admi	itted		ာင္စ Date	ischarged		
			 					7		
52036	Admission 3 - Outpatient rehabilitation name	Rel	nab facility le	Date admi	itted		Date ₹	ischarged		
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Case Report Form - Cost

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No □

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Unknown

8) REHABILITATION SERVICES PROVIDED AT HOME OR IN A NURSING HOME

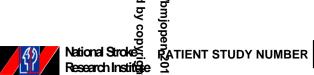
Have you had a rehabilitation program provided to you at home or a nursing home as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech

as a consequence of your stroke? e.g. with	physiotherapy, occupatio	nal therapy, speech		No 🗆 Halmania	
If NO, proceed to question 9. If YES, complete rehabilitation details, starting fr sessions. If patient NOT discharged at 3 month assessment (complete dates at 12 month assessment)	•		S S S S S S S S S S S S S S	No ☐ Unknown	If patient not discharged at
Time 1 - Rehabilitation service name	Rehab service code	Start date	nloadate Superjeur (A Ceand data	Total number of SESSIONS	12 month assessment, cross box.
Time 2 - Rehabilitation service name	Rehab service code	Start date	Cease Cate		
Time 3 - Rehabilitation service name	Rehab service code	Start date	Cease date / and kor		
Time 4 - Rehabilitation service name	Rehab service code	Start date	Cease date / Lech		
			3, 2025 at Age inologies.		





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9) COMMUNITY SERVICES								6230 :Judir		
9a) Did you receive any community services	in the year	PRIOR	to your	stroke?	>			230 on 22 luding for	Yes 🗆	No ☐ Unknown ☐
Community services are individual care self NO, proceed to question 9b. If YES, which service/s did you receive in	the year P	RIOR to	your s	troke?			nabilitation the	erapy. Um many times in the second s	ı	
Community service codes 1 = Nursing Service			∏ 3	☐ 4	. (One st			the past year Harding Downloaded from http://bmjopen.graded to text and data mining, Al training, Al training		
2 = Delivered Meals 3 = Personal Care (Bath/Shower) 4 = Housework help	1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	Superior and		
5 = Gardening/home maintenance 6 = Home respite 7 = Other service, specify	_		□ 3 -	☐ 4	□ 5 —	□ 6 —	□ 7 —	I from July (AE) data i		
7 - Other Service, Specify	☐ 1 If "othe	_	☐ 3 : 7), ple	☐ 4 ase spe	☐ 5 cify	□ 6	□ 7	http://i		
			_ _					, Al tra		
9b) Have you received community services S Community services are individual care s			t home	and do	NOT incl	ude reb	abilitation the	Stany 3 IIIOI Bis 5		D ☐ Unknown ☐
If NO, proceed to question 10.	•		t Home	and do		uue ieii	abilitation the	3-12 months	Yes ☐ No	Unknown 🗆
If YES, which service/s did you receive Al For each service, complete a seperate lin- months, and then add service data for 3-1	e. If a servi	ce is on			th interv	iew, ent	er data for 3	How many m	How many hours	Note: hours per service
	Which	service	did you	receive	? (One s	ervice o	ode per line)		per service?	
Community service codes 1 = Nursing Service	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□7	chnologie		
2 = Delivered Meals 3 = Personal Care (Bath/Shower)		□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	13, 2025 at Agence Bibliographique chnologies.		
4 = Housework help 5 = Gardening/home maintenance 6 = Home respite	□ 1 —	□ 2 -	☐ 3 —	☐ 4 —	□ 5 —	□ 6 □	□ 7 —	\dagger \dagger \q		
7 = Other service, specify	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	e B		
	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	Diliog		
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10) HOME MODIFICATIONS			.026230 includir			
Has your home been modified as a conseque		- 1161	ş Şmontt	n s Yes □	No 🗆	Unknown
e.g. installation of rails, bathroom modification f NO, proceed to question 11	ons, installation of ramp(s), kitchen m	odifications etc	了 2 ~ 表 紹整	onths Yes 🗌	No 🗆	Unknown
If YES, please indicate the type of modifications	, who supplied the modifications and est	imate any personal cost to you	ay 201 nseigi es reli			
Type of modification	SUPPLIERS 1 = Hospital/rehabilitation centre 2 = Patient/family	3 = Veteran's Affairs 4 = Local Council	5 = Ho&s∄nego 5 = Ho&s∄nego 6 = Charte	ommision	7 = Ot	her (specify
(check box for each type supplied)	Who supplied the modification	tion? If supplier is	"other", pl စ္ကာ	ecify		
☐ Rail(s) for steps/stairs	□1 □2 □3 □4 □	5 🗆 6 🗀 7 📗 📗	and and	Cost to you/fa	mily* - \$	
☐ Ramp(s)	_1 _2 _3 _4 _:	5 🗆 6 🗀 7 📗 📗	from data	Cost to you/fa	nmily* - \$	
☐ Platform step(s)	_1 _2 _3 _4 _:	5 🗆 6 🗀 7 📗 📗	ittp://b	Cost to you/fa	mily* - \$	
☐ Shower, bath and toilet rail(s)	1234!	5 🗆 6 🗆 7 📗 📗	Al tra	Cost to you/fa	mily* - \$	
☐ Shower(s) modification	1234 <u></u>	5 🗆 6 🖂 7 📗 📗	ining n.bm	Cost to you/fa	mily* - \$	
☐ Toilet(s) modification	1234 <u></u>	5 🗆 6 🗆 7 📗 📗	and si	Cost to you/fa	mily* - \$	
☐ Remove/modify door(s) from shower/toilet/bath	□1 □2 □3 □4 □	5 🗆 6 🗆 7 📗 📗	imilar t	Cost to you/fa	amily* - \$	
☐ Kitchen modifications	1234!	5 🗆 6 🗆 7 📗 📗	ne 13, techno	Cost to you/fa	amily* - \$	
Other modification (specify below)			2025 a			
Other home modification - 1	<u> </u>	5	at Age	Cost to you/fa	mily* - \$ [
Other home modification - 2	1 2 3 4 5	5)nce B	Cost to you/fa	mily* - \$	
	-' '		_'' _ _	' n overall cost is prov	ided nle	ase indicate
If total costs includes any aids, describe i	in brief below (see also list of aids on	page 33): 	type togal	of modifications abo	ve, and p 'E of any l	rovide the
			- Item	ised costs listed abo Overall Cost		



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Case Report Form - Cost

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11) SELCIAL EQUIFIVILIATI AND A	4103		<u>¥</u> 8		
Have you been given, hired or purchased an	y special equipment, aids or special	food as a consequence of stroke?	T N	Yes 🗌	No ☐ Unknown ☐
			3-12 ខ្លាំ 	Yes 🗌	No ☐ Unknown ☐
Prompt: These may have been provided by an If NO, proceed to question 12	Occupational Therapist or Physiothera	pist. What about a?	May 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 a finseignement Superieur (ABES) . Ses related to text and data mining, Al training, and similar technologies to text and data mining.		
Walking aids	Mobility aids	Eating aids	. Dov ed to		Kitchen aids
☐ Single point stick	☐ Manual wheelchair	☐ Built-up cutlery	vnlo It Su It ex		☐ Tap handles
☐ Three or four point stick	☐ Electric wheelchair/scooter	☐ Plate guard	ade Iperi t an		☐ Chopping board
☐ Walking frame - pick up	☐ Car steering wheel knob	☐ Non-slip mat	d fro d da		☐ Modified knife
☐ Walking frame - wheelie		☐ Special food e.g. NG/PEG	ata n		☐ Vitamiser/blender
☐ Walking frame - gutter (forearm suppt)		If yes, number of days used:	ninir		☐ Non-slip mat
☐ Crutch(es)		3 months	/bn		_ non-enp man
		3-12 months	≱ tra		
			ainir		
			າ <u>ຫ</u> ຼຸ່.		
Lounge and bedroom equipment	Bathroom equipment	Continence aids	and Com		General aids
☐ Chair platform/blocks raise	☐ Over-toilet seat	☐ Urine bottle	y on sim		☐ Long handled aid
☐ Cushion to relieve pressure	☐ Toilet surround	☐ Bedpan	ilar		☐ Blood pressure machine ☐ Treadmill
☐ Special chair (NOT wheelchair)	☐ Bathroom and grooming aids	☐ Commode	ne 1 tech		☐ Stationary bike
☐ Table - bedside/wheelie	☐ Shower chair/stool	☐ Incontinence sheet (bed prote	ctor) 3, 20		☐ Intercom (portable)
☐ Bed platform/block raise	☐ Over bath seat	☐ Incontinence sheet (kylie/blue))25 a		☐ Modified tap handles
☐ Bedstick	☐ Hand held shower	If yes, number of days used - 3 mo			If yes, number supplied
☐ Hospital bed (eg - height/tilt adjust)	☐ Non-slip mat	☐ Incontinence pads 3-12 mg	onths 8		
☐ Mobile hoist/lifter		If yes, number of days used - 3 mo	onths P		☐ Personal alarm If yes, number of days supplied:
Any other aids/equipment, specify		☐ Catheter 3-12 mg	onths 6		3 months
		If yes, number of days used - 3 mo	onths $\frac{3}{2}$		3-12 months
,		3-12 ma	onths 5		

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PATIENT INITIALS

NOTE: this one form is to be completed AND faxed following BOTH the 3 and 12 months region.

When CRF Cost complete at 3 months AND at 12 months, fax all pages 25-36 to the Deta Fax.

Instructions to the person responding: These questions are about health care provided as a consequence of the stake which occurred on (give date of stroke) or as a result of any further stroke. I will be asking about health care such as visits to hospital, rehabilitation, the at the community, and to you and your family, I will be asking about how often service were provided and their cost.

	Subject's stroke date rom CRF - Screening Day 0			d to text a	Ownload
3 MONTH DA	TE OF ASSESSMENT	//	Assessor initials	nd data m	fro
PERSON RESPONI	DING	ASSISTANCE FOR IN	ITERVIEW OBTAINED FROM	inin	VIVING ARRANGEMENT OF RESPONDENT*
Index case ☐ Spouse/partner ☐ Sibling ☐ Son/Daughter ☐ Parent ☐	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	Index case ☐ Spouse/partner ☐ Sibling ☐ Son/Daughter ☐ Parent ☐	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	g, Al training, an	Siot living with index Professional carer in nursing home or hostel
12 MONTH DA	ATE OF ASSESSMENT	/ / / / / / / / / / / / /	Assessor initials ITERVIEW OBTAINED FROM	d similar te	S S EIVING ARRANGEMENT OF RESPONDENT
Index case Spouse/partner Sibling Son/Daughter Parent	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	Index case Spouse/partner Sibling Son/Daughter Parent	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	technologies.	Living with index Story Professional carer in nursing home or hostel
					Please note: this is the 'normal' living arrangement of the respondent with respect to the subject, even if the currently in hospital







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1) DISCHARGE				26230 c		
Date of discharge from acute care	Acute discharge des	stination	Date of admission to inp	atient rehabil c ati e	Discharge destination a	after inpatient rehab
	Home			use	Home	
	Rehabilitation ward/h	ospital 🔲		y 20	Rehabilitation hospital	
	Supported residential	service (SRS) 🗆	Date of admission to inp	山山山山島東京。 ubatient tenaemagano	Supported residential ser	vice (SRS) □
	Hostel			Down down to		
	Nursing home		Leave dates BLANK if no	ot applicable $\overset{\leftarrow}{S}$	Nursing home	
	Other		Please note: inpatient reh inclusive of geriatric evalu	nabilitation is and	Other	
	Unknown		transitional care.	ot applicable nabilitation and attain	Unknown	
			 	ata m	Leave BLANK if not a	pplicable
2) LIVING ARRANGEMENT				ttp://		
Pre-stroke residential address		Residential address	at 3 months*	R ≧side n	tial address at 12 months*	
Own house, flat – alone		Own house, flat – alon	ne 🗆	Ogn hogu	se, flat – alone	
Own house, flat – with family/relative/frie	end 🗆	Own house, flat – with	family/relative/friend □	Qan hagu	se, flat – family/relative/frien	d 🗆
Home of relative/friend		Home of relative/friend	d 🗇	H o me o f	relative/friend	
Supported residential service (SRS)		Supported residential	service (SRS)	S supposte	ed residential service (SRS)	
Hostel		Hostel		Heste E		
Nursing home		Nursing home		Norsing h	nome	
Other		Other		Ober 2025 Uniknown		
Unknown		Unknown		U n knowr	1	
			note if the subject is curren eir current residential addre			
		iou oply http://b	nen hmi com/site/ahout/gu	Bibliographique de I		

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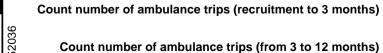
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					includin	0 0 0 0 0	PAHENI INII		!
3) CH	ANGE IN LIVING ARRANGE	MENTS			(0)	•			
	sequence of your stroke, have you r	needed to change your p	place of residence?		3 moRths	Yes □	No 🗆	Unknown 🗆	
	oceed to question 4. note: if subject has been a hospita	I inpatient this is NOT a	change of residence		3-12 (h)	ns Yes □	No 🗆	Unknown 🗆	
	DATE OF MOVE	LOCATION			eignem related	9019			
1)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			ment Superieur (ABES) . ed to text and data mining, Al training, and similar techn	Downloaded fr			
2)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			(ABES) . ata mining, AI t				
3)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			raining, and si	nes hai com/			
4)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other		0,		n line 13 2025			
4) AN	IBULANCE TRANSFERS: E	MERGENCY AND	NON-EMERGENCY		jies.	л 9 +			
As a coi	nsequence of your stroke, have you	required ambulance tra	nsport after your acute adm	nission to hospital	?* 3 mol	D	П МоГ	I Unknown □	

If NO, please proceed to question 5

3 mogths	Yes 🗆	No 🗆	Unknown 🗌
P			
3-12 months	: Yes □	No □	Unknown □





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No □

No □

Unknown

Unknown

If patient not

12 month

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5) HOSPITALISATION OR EMERGENCY DEPARTMENT ATTENDANCES

5a) Have you been readmitted to hospital or attended the emergency department as a consequence of another stroke or for any stroke related problems?

Yes Dounths

Yes Dounths

Yes Dounths

**ses related to text and **

**ses related to text and **

**ses related to text and **

**ses related to text and ** (ONLY include information for admissions and attendances for stroke-related problems (see below for summary list of stroke-related problems and CRF completion manual for further clarification)

If NO, proceed to question 6

5b) If YES, Start with the earliest admission or attendance. If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

Hospital

Admission or Attendance 1 - Hospital name	code	Date admitted	ਕੂ ਨੂੰ Date discharged	cross box.
			http://b	
Admission or Attendance 2 - Hospital name	Hospital code	Date admitted	Al mjop Date discharged	
Admission or Attendance 3 - Hospital name	Hospital code	Date admitted /	and similar to no June discharged	
Admission or Attendance 4 - Hospital name	Hospital code	Date admitted /	on June 13, 2025 at A	
Admission or Attendance 5 - Hospital name	Hospital code	Date admitted /	Date discharged	



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Stroke related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary cataleter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11. Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional pre-lem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting 19. Surgery or procedural management of of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21. Inabies to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26. Pressum sores.

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Yes

Yes □

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RATIEN'	T STUDY NUMBER			
018-026230	PATIENT INITI	ALS		
6230				
0				

No □

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No 🗆

Total

number

Unknown □

Unknown □

Unknown

If patient not

12 month

discharged at

discharged at

After your stroke on (give date of stroke), were you admitted to a Rehabilitation Hospital or other hospital where you received rehabilitation treatment? Please include admissions with the care type 'rehabilitation', 'geriatric evaluation' and 'transitional care'

If NO. proceed to question 7.

If YES, complete inpatient rehabilitation admission details, starting from your first inpatient rehabilitation admission. If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

e you received rehabilitation treatment? Please include ad ation' and 'transitional care'	missions with the care	type 'rehabilitation', 'geriatric	3-12 months	Yes 🗆	No 🗆	Unknown □
proceed to question 7. 5, complete inpatient rehabilitation admission details, starting ent NOT discharged at 3 month assessment, leave discharge			ay 201 nseig es rel			If patient not discharged a 12 month
Admission 1- Rehabilitation hospital name	Rehab hospital code	Date admitted	Dowr nent d to 1	Date discha	ırged	assessment, cross box.
OA			Super Super text ar	//		
Admission 2- Rehabilitation hospital name	Rehab hospital code	Date admitted	∌d fror ieur (ıd dat	Date discha	ırged	
			h http ABES a min	//		
Admission 3- Rehabilitation hospital name	Rehab hospital code	Date admitted	ing, ,	Date discha	rged	
			Noper Al trail	//		
			<u> </u>			

7) OUTPATIENT REHABILITATION PROGRAM

Did you attend or are you attending an outpatient rehabilitation program as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech therapy, etc

An outpatient rehabilitation program is any rehabilitation program where the patient attends a facility. The program can be located at a hospital or community facility.

If NO, proceed to question 8.

If YES, complete outpatient rehabilitation details, starting from your first outpatient rehabilitation visit.

If patient NOT discharged at 3 month assessment, leave discharge dates and number of days attended BLANK (complete dates a 12 fflonth assessment)

Admission 1 - Outpatient rehabilitation name	Rehab facility code	Date admitted	Lance discharged	of DAYS attended	assessment, cross box.
		/] [] / E / [] / []		
Admission 2 - Outpatient rehabilitation name	Rehab facility code	Date admitted	ਨ੍ਹ Date <mark>ਉ</mark> lischarged		
		//			
Admission 3 - Outpatient rehabilitation name	Rehab facility code	Date admitted	ਤੂੰ Dateਕ੍ਰੀischarged		
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8) REHABILITATION SERVICES I	PROVIDED AT HOME	OR IN A NURSING			
Have you had a rehabilitation program provi as a consequence of your stroke? e.g. with			3 months of N	No ☐ Unknow	n 🗆
If NO, proceed to question 9. If YES, complete rehabilitation details, starting sessions. If patient NOT discharged at 3 month assessm	from the first visit since your s	stroke. Count number of	3-12 montures related to te	No □ Unknown	If patient not
(complete dates at 12 month assessment) Time 1 - Rehabilitation service name	Rehab service code	Start date	žť o a Čte o o o o o o o o o o o o o o o o o o o	Total number of SESSIONS	discharged at 12 month assessment, cross box.
Time 2 - Rehabilitation service name	Rehab service code	/ /	dat American		
	Rehab service		g, Alltrair		
Time 3 - Rehabilitation service name	code	Start date /	Cease date /		
Time 4 - Rehabilitation service name	Rehab service code	Start date	Cease date / tech		
			3, 2025 at A mologies.		





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							nt, inc	8-020	PAT	TIENT INITIAL	.s _ _
9) COMMUNITY SERVICES							udin	-026230			
9a) Did you receive any community s	ervices in the year l	PRIOR to you	stroke	?			g for	on 2	Yes □	No □	Unknown 🗌
Community services are individua	al care services pro	vided at home	and do	NOT inc	lude reh	nabilitation th	nerapy. с п	22 M			
If NO, proceed to question 9b. If YES, which service/s did you re	ceive in the year PR	IOR to your s	troke?				How many times				
	-	ervice did you		? (One se	ervice co	ode per line)	the past year Sig receive the serve				
Community service codes		∃2 □3	□ 4	5	□6			Do			
1 = Nursing Service 2 = Delivered Meals		J- LJ	ш-	П	υ	ш,					
3 = Personal Care (Bath/Shower	r)]2	□ 4	□ 5	□ 6	□ 7	ext and	ade			
4 = Housework help 5 = Gardening/home maintenand	ce 🛮 🗘 1	2 3	□ 4	□ 5	□ 6	□ 7		inloaded from			
6 = Home respite 7 = Other service, specify				_ 			data mi) T			
]2	4 ase spe	☐ 5 cify	□ 6	□ 7	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□) -5			
					1 1	1 1 1	ng, /	://bm			
	<u> </u>	_ _ _	_		_		Al tra	jop			
o) Have you received community ser								4			_
				NOT			3 mon∰ns	Yes		No 🗌 Unkı	nown 🗌
Community services are individua If NO, proceed to question 10.			and do	NOT incl	ude reh	abilitation the	erapy. 3 months 3-12 mon	3			nown 🗆
Community services are individua If NO, proceed to question 10. If YES, which service/s did you red	I care services prov ceive AFTER your s	rided at home troke?					erapy. ద	3			
Community services are individua If NO, proceed to question 10.	Il care services prov ceive AFTER your st erate line. If a servic	rided at home troke? e is ongoing a	at 3 mon				erapy. 3-12 mon 3-12 mon Similar How many	ths Yes	□ How many	No □ Unkı	nown □
Community services are individua If NO, proceed to question 10. If YES, which service/s did you rec For each service, complete a sepe	Il care services prov ceive AFTER your st erate line. If a servic a for 3-12 months or	rided at home troke? e is ongoing a	at 3 mon ine.	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12	ths Yes		No □ Unkı Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a sepemenths, and then add service data	Il care services prov ceive AFTER your st erate line. If a servic a for 3-12 months of Which se	rided at home troke? e is ongoing a n a separate li	at 3 mon ine.	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	mtcom/ on Juge 13,	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a sepermenths, and then add service data community service codes 1 = Nursing Service	ceive AFTER your sterate line. If a service a for 3-12 months of Which se	rided at home troke? e is ongoing a n a separate li ervice did you 2 3	at 3 mon ine. ı receive □ 4	th interv e? (One s	iew, ent ervice c □ 6	er data for 3 code per line)	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	mtcom/ on Juge 13,	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a seperation and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals	Il care services proviceive AFTER your sterate line. If a service a for 3-12 months of Which services 1	vided at home troke? e is ongoing a n a separate li ervice did you	at 3 mon ine. ı receive	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12	Yes Yes ? ? Yee 13, 2025	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individual If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showed 4 = Housework help	ceive AFTER your sterate line. If a service a for 3-12 months on Which service 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	rided at home troke? e is ongoing a n a separate li ervice did you 2 3	at 3 mon ine. ı receive □ 4	th interv e? (One s	iew, ent ervice c □ 6	er data for 3 code per line)	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	Yes e e e e e e e e e e e e e	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4	th interv	iew, entervice co	er data for 3 code per line) 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	Yes e e e e e e e e e e e e e	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe 4 = Housework help 5 = Gardening/home maintenan	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4 4	th interv	iew, entervice colored for the	er data for 3 code per line) 7 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	ກະ Ye ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe 4 = Housework help 5 = Gardening/home maintenan 6 = Home respite	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4	th interv	iew, entervice co	er data for 3 code per line) 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	es Ye Mgcom/ on Juge 13, 2025 at Agence Bib	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individual If NO, proceed to question 10. If YES, which service/s did you red For each service, complete a septemonths, and then add service data Community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showeded Housework help) 5 = Gardening/home maintenanded Home respite 7 = Other service, specify	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4 4	th interv	iew, entervice colored for the	er data for 3 code per line) 7 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	es Ye Mgcom/ on Juge 13, 2025 at Agence Bib	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you red For each service, complete a sepe months, and then add service data Community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe 4 = Housework help 5 = Gardening/home maintenan 6 = Home respite 7 = Other service, specify	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. I receive	th interv	iew, entervice compared of the	er data for 3 code per line) 7 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	es Ye Mgcom/ on Juge 13, 2025 at Agence Bib	☐ How many hours	No □ Unkı / Note: ho NOT app	nown □ ours per servic olicable to
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Case Penort Form - Cost

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10) HOME MODIFICATIONS			Research Instiffate 018-026230	
las your home been modified as a conse			amonths	Yes ☐ No ☐ Unknown ☐
f NO, proceed to question 11	ications, installation of ramp(s), kitchen mo		55 12 Boonths	Yes No Unknown
	SUPPLIERS 1 = Hospital/rehabilitation centre 2 = Patient/family	3 = Veteran's Affairs 4 = Local Council	5 = Housing commis 6 = Character	ion 7 = Other (specify)
Type of modification (check box for each type supplied)	Who supplied the modificati	ion? If supplier is	s "other", plage	
☐ Rail(s) for steps/stairs	□1 □2 □3 □4 □5	6 🗆 6 🗆 7 📗 📗	aded peric and	Cost to you/family* - \$
☐ Ramp(s)	□1 □2 □3 □4 □5	6	<u></u>	Cost to you/family* - \$
☐ Platform step(s)	□1 □2 □3 □4 □5	6 🗆 7	nttp://b	Cost to you/family* - \$
☐ Shower, bath and toilet rail(s)	□1 □2 □3 □4 □5	6 🗆 7 📗 📗	_ <u> </u> _ <u></u>	Cost to you/family* - \$
☐ Shower(s) modification	□1 □2 □3 □4 □5	6 07	<u> </u>	Cost to you/family* - \$
☐ Toilet(s) modification	□1 □2 □3 □4 □5	6 6 7		Cost to you/family* - \$
☐ Remove/modify door(s) from shower/toilet/bath	□1 □2 □3 □4 □5	6 6 7	<u> </u>	Cost to you/family* - \$
☐ Kitchen modifications	□1 □2 □3 □4 □5	6 🗆 7 📗 📗	ne 13,	Cost to you/family* - \$
☐ Other modification (specify below) Other home modification - 1			ne 13, 2025 a technologie	
		5	s: Age	Cost to you/family* - \$
Other home modification - 2	12345	6 🗆 7 📗 📗	nce B	Cost to you/family* - \$
If total costs includes any aids, descr	ibe in brief below (see also list of aids on p	page 33):	tyge of mod	all cost is provided, please indicate difications above, and provide the here, INCLUSIVE of any known
			itemised co	osts listed above: Overall Cost \$

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11) SPECIAL EQUIPMENT AND	AIDS		6230) Judin		
lave you been given, hired or purchased an	y special equipment, aids or special	food as a consequence of stroke?	a mogiths	Yes □	No ☐ Unknown ☐
			3-12 gn gn sh	s Yes 🗆	No ☐ Unknown ☐
Prompt: These may have been provided by ar f NO, proceed to question 12	n Occupational Therapist or Physiothera	apist. What about a?	/ 2019. seigner s relate		
Walking aids	Mobility aids	Eating aids	men d to		Kitchen aids
☐ Single point stick	☐ Manual wheelchair	☐ Built-up cutlery	vnlo t Su tex		☐ Tap handles
☐ Three or four point stick	☐ Electric wheelchair/scooter	☐ Plate guard	aded perie t and		☐ Chopping board
☐ Walking frame - pick up	☐ Car steering wheel knob	☐ Non-slip mat	d fro eur d da		☐ Modified knife
☐ Walking frame - wheelie		☐ Special food e.g. NG/PEG	rom h r (ABI lata m		☐ Vitamiser/blender
☐ Walking frame - gutter (forearm suppt)		If yes, number of days used:	http://b BES) . mining,		☐ Non-slip mat
☐ Crutch(es)		3 months	g, A		
		3-12 months	l tra		
			ining		
Lounge and bedroom equipment	Bathroom equipment	Continence aids	Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 (ment Superieur (ABES) . id to text and data mining, Al training, and similar technologie		General aids
☐ Chair platform/blocks raise	Over-toilet seat	☐ Urine bottle	nd si		☐ Long handled aid
☐ Cushion to relieve pressure	☐ Toilet surround	□ Bedpan	mila		☐ Blood pressure machine
☐ Special chair (NOT wheelchair)	☐ Bathroom and grooming aids	☐ Commode	r tec		☐ Treadmill
☐ Table - bedside/wheelie	☐ Shower chair/stool	☐ Incontinence sheet (bed protect	ctor) in 3, 3		☐ Stationary bike
		☐ Incontinence sheet (kylie/blue)	ctor) ologic		☐ Intercom (portable)
☐ Bed platform/block raise	Over bath seat		<u> </u>		☐ Modified tap handles If yes, number supplied
Bedstick	☐ Hand held shower	If yes, number of days used - 3 mo	 	\dashv	
☐ Hospital bed (eg - height/tilt adjust)	☐ Non-slip mat	☐ Incontinence pads 3-12 mg			☐ Personal alarm
☐ Mobile hoist/lifter		If yes, number of days used - 3 mc			If yes, number of days supplied:
Any other aids/equipment, specify		☐ Catheter 3-12 mg	onths E		3 months
		If yes, number of days used - 3 mo	onths 2		3-12 months
		3-12 mg	onthe	7	







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12) PRIVATE PHYSIOTHERAPY					ding				
Have you paid for private physiotherapy sessions after your st	roke? (NOT while	a hospital inpa	tient)		3 months	Yes 🗌	No 🗆	Unknown 🗌	
If no, proceed to question 13					3-12 m om t	s Yes 🗆	No 🗆	Unknown 🗌	
If yes, number of sessions - 3 months					nei ate				
3-12 months					nent :				
13) RESPITE CARE					Supe ext a				
As a consequence of your stroke, have you been admitted to a	respite bed in a r	nursing home o	hospital		~~~	Yes 🗆	No 🗆	Unknown 🗌	
If NO, proceed to question 14					3-12	s Yes 🗆	No 🗆	Unknown 🗌	
f yes, how many days of respite have you received since your s	stroke? 3 month	ns			ining				
	3-12 month	is			g, Al ı				
					pen.k traini				
14) EMPLOYMENT STATUS/ PAID WORK					<u>a</u> <u>c</u>				
Were you working up to the time of your stroke? $\gamma_{es} \square$	No □ L	Jnknown □			om/ o nd sir				
Have you paid for private physiotherapy sessions after your stroke? (NOT while a hospital inpatient) A									
How many	hours did you worl	k each week?			ne 13, 2 techno				
Since the stroke, have you returned to this work?	3 months	Yes 🗆	No □ L	Jnknown 🗌	logie				
	3-12 months	Yes 🗌	No □ L	Jnknown 🗆	,				
Have you returned to normal hours or decreased hours?	3 months	Norma	al 🔲 De	ecreased 🗆	Jence				
	3-12 months	Norma	al 🔲 De	ecreased 🗆	Bib				
How many hours per week of work have you performed since	e the last assessr	ment?			liogra				
2		If more tha	ın 0 but le	ess than 1hi	_ م	1			
Record average amount per week over the period 3	to 12 months	I I							

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15) INFORMAL CARE - 3 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hospital in patients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at home. Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services.

This might include assistance with community tasks (such as help with your bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning)

If the answer is NO, no further questions are required in this section

or assistance with personal care tasks (such as bathing, toileting and feeding)

15b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to question 15c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening; handyman tasks; grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to guestion 15d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

Hours
Hours

Yes

Yes

Hours

Yes

Hours

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16) INFORMAL CARE - 12 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hos⊞ital inpatients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at come. Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member 4 family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon to any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the base, feeding). Supervision of daily activities to ensure safety should also be included as care.

16a) OVER THE LAST WEEK, have you received any assistance with your daily activities from a carer as a result of t This might include assistance with community tasks (such as help with your banking, paying your	he str
This might include assistance with community tasks (such as help with your banking, paying your	nd ried
bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning)	from ur (A data
or assistance with personal care tasks (such as bathing, toileting and feeding)	ā ⊋ă

If the answer is NO, no further questions are required in this section

16b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to guestion 16c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening: handyman tasks: grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to question 16d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

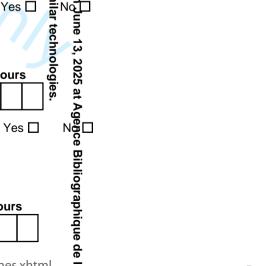
Hours

Yes □

Hours

Hours

End Case Report Form - Cost
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml V 4.0 : 1 Nov 10 (AUS)





Supplementary document 3: Unit costs and valuation of costs

Unit costs for hospitalisation, rehabilitation, non-health sector costs and productivity costs

Acute stroke hospitalisation costing: Unit costs for acute stroke hospitalisation for all countries at baseline were categorised by stroke severity, using the National Institute of Health Stroke Scale (NIHSS) to group patients into three severity levels: mild (0-7), moderate (8-16) and severe (>16). (1)·(2) It was assumed that severity as classified by the NIHSS was consistent with the stroke severity that corresponded to three levels of unit cost for acute hospitalisation. Length of Stay (LoS) together with stroke severity were used to estimate the cost of acute hospitalisation for Australia and New Zealand patients (i.e. the cost of acute hospitalisation was weighted by the LoS). LoS was taken as the difference between the date of hospital discharge and date of hospital admission (plus one day or not) in accordance with country-specific practice. For the other countries, only stroke severity was considered in the assignment of a unit cost to acute stroke hospitalisation due to insufficient health sector data.

Re-hospitalisation and rehabilitation costing: Due to the diversity of causes for patients being readmitted to hospital after the index stroke, the average daily cost of hospitalisation for all disease conditions from individual countries in combination with LoS was used to gauge the cost of readmission for stroke-related causes, while the average cost for an emergency department visit was assigned whenever a patient was hospitalised for one day only. Similarly, the unit cost of rehabilitation hospital admission was taken from the national average cost for all disease conditions. The median cost was used where there was more than one unit cost identified for the same resource item.

Non-health sector costs: Unit costs of non-health sector resource items (e.g. community service, accommodation changes, special aids and equipment) were sourced on a country- specific basis from official websites or published literature where applicable. No unit cost was retrieved for home modification items since the cost of home modifications was generally reported in the Cost CRF.

Productivity cost: Lost productivity was valued based on a human capital approach using average earnings across all occupations up to normal retirement age. The average wage of a

The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

All the unit costs from participating countries are summarised in Table I.

Table I. Unit cost (in Australian dollars) across five countries, 2015 reference year

Resource items		Jnit cost (AU	AUD)			
	AU	NZ	UK	SG	MA	
Healthcare						
Acute hospitalisation*						
Severe (per episode)	\$19157	\$10867	\$15327	\$4371	\$2066	
Moderate (per episode)	\$9553	\$6104	\$8115	\$2126	\$1572	
Mild (per episode)	\$6279	\$4370	\$4272	\$1493	\$1363	
Stroke-related rehospitalisation (per day)	\$1925	\$320	\$701	\$789	\$230	
Emergency department attendance (per attendance)	\$610	\$325	\$227	\$111	\$68	
Rehabilitation hospital admission [†]						
Severe (per episode)	\$1010 [‡]	\$8032	\$19136 [§]	\$157 [‡]	\$1293	
Moderate (per episode)	1	\$5727	\$29788 [§]			
Mild (per episode)	1	\$5727	\$13920 [§]			
Same day (per episode)	1	\$758	N/A			
Outpatient rehab visit (per/session)	\$239	\$164	\$213	\$36	\$17	
Rehab services at home/nursing	\$239	\$212	\$922	\$36	\$51	
facility (per/session)						
Private physiotherapy (per session)	\$64	\$153	\$162	\$116	\$8	
Respite care (per hour)	\$45	\$14	\$26	\$15	\$2	
Individual allied health visit						
Physiotherapy	N/A	N/A	\$243	\$239	\$8	
Occupational therapy	N/A	N/A	\$243	\$36	\$7	
Speech and language therapy	N/A	N/A	\$69	\$36	\$4	
Ambulance transfer	\$508	\$646	\$575	\$265	\$52	
Non-healthcare						
Community services	Not listed	here due to t	the number of	items		
Home modifications	Cost was p	rovided by	individual pat	ients		
Special aids and equipment	Not listed	here due to t	the substantia	l number of ite	ems	
Accommodation changes	Not listed	here due to t	the number of	items		
Professional carer (per hour)	\$24	\$14	\$14	\$10	\$2	
Living-in maid (per month)	N/A	N/A	N/A	\$571	\$103	
Average weekly earnings						
Male	\$1137	\$621	\$1152	\$973	\$137	
Female]		\$957 ¹			

Unit cost for intervention [#]					
Hospital physiotherapist (per	\$33	\$32	\$30	\$21	\$5
hour)					
Hospital nurse (per hour)	\$30	\$25	\$29	\$21	\$5

AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia;

Sources of CPI:

Australian Bureau of Statistics. Consumer price index inflation calculator. Accessed

from: Http://www.Abs.Gov.Au/websitedbs/d3310114.Nsf/home/consumer+price+index+inflation+calculator. 2017

Office for National Statistics. Inflation and price indices. Accessed from:

Https://www.Ons.Gov.Uk/economy/inflationandpriceindices. 2017

Department of Statistics Singapore. Consumer price index. Accessed from: https://data.Gov.Sg/dataset/consumer-price-index-annual. 2017

Statistics New Zealand. Consumer price index, accessed from:

Http://www.Stats.Govt.Nz/browse for stats/economic indicators/cpi inflation/info-releases.Aspx. 2017

Department of Statistics Malaysia OP. Consumer price index malaysia. Accessed from:

Https://www.Dosm.Gov.My/v1/index.Php?R=column/cthemebycat&cat=106&bul_id=zi9pmutpvzixb042mlptt1buellazz09&menu_id=bthzthqxn1zqmvf6a2i4rkzondfkqt09. 2017

*severity was determined by baseline NIHSS score; †severity was classified by baseline mRS score; the hospital survey of Household Income was provided on gender basis, so the weekly earnings for UK patients were assigned corresponding to this; hourly wage of hospital physiotherapist and nurse were assigned; N/A: not applicable. Main sources of unit cost: AU: Independent Hospital Pricing Authority (IHPA), Australia, National Efficient Price Data (2015-16); National Hospital Cost Data collection (https://www.ihpa.gov.au/publications/australian-public-hospitals-cost-report-2013-2014-round-18); Department of Health, Revised residential care subsidies (https://agedcare.health.gov.au/aged-care-funding/aged-care-subsidies-and-supplements); Australian Bureau of Statistics

(http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/E9FF9F13B417A488CA257F630014DF30 ?opendocument

NZ: Ministry of Health (http://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations); World Health Organisation (http://www.who.int/choice/country/nzl/cost/en/); Cost Resource Manual Version 2.2 (https://www.pharmac.govt.nz/assets/pfpa-v2-2-cost-resource-manual.pdf); study by Te Ao et al 2011 (Te Ao BJ et al. Are stroke units cost effective? Evidence from a New Zealand stroke incidence and population-based study. Int. J. Stroke. 2012;7:623-630); Statistics New Zealand

(http://www.stats.govt.nz/browse for stats/income-and-

<u>work/employment_and_unemployment/LabourMarketStatistics_HOTPJun15qtr.aspx</u>); District Health Board, Multi Employer Agreement, New Zealand Nurses Organisation(http://www.bopdhb.govt.nz/media/58613/psa-ronz-allied-meca-2015-2017.pdf);

UK: National Health Service (NHS) reference costs 2014 to 2015, United Kingdom

(https://www.gov.uk/government/publications/nhs-reference-costs-2014-to-2015); NICE Technology Appraisal (Davis,S., Holmes,M., Simpson,E., Sutton,A. Alteplase for the treatment of acute ischaemic stroke [review of technology appraisal 122]: A Single Technology Appraisal. ScHARR, The University of Sheffield 2012, https://www.nice.org.uk/guidance/ta264/documents/stroke-acute-ischaemic-alteplase-review-of-ta122-evidence-review-group-report2); Personal Social Services Research Unit (PSSRU)(http://www.pssru.ac.uk/); Information Services Division, Scotland (http://www.isdscotland.org/); Annual Survey of Hours and Earnings 2015, Office for National Statistics

(https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2015provisionalresults); Payscale UK

(http://www.payscale.com/research/UK/Job=Care_Worker/Hourly_Rate); NHS pay and benefits

 $(\underline{https://www.healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates});$

SG: Ministry of Health, Hospital Bill Sizes, Singapore

(https://www.moh.gov.sg/content/moh_web/home/costs_and_financing/HospitalBillSize/stroke.html.); Outpatient Charges, Singapore General Hospital (https://www.sgh.com.sg/patient-services/charges-payment/pages/outpatient-charges.aspx); Charges, Ren Ci Hospital (http://www.renci.org.sg/patients-guide/charges-2/); Hospital rates and charges, Bright Vision Hospital (http://www.bvh.org.sg/hospital-rate-charge.html); Ministry of Manpower (http://stats.mom.gov.sg/Pages/Occupational-Wages-Tables2014.aspx);

MA: study by Mohd Nordin et al 2012 (Mohd Nordin et al.: Estimating cost of in-patientmedical care for stroke using Casemix data. BMC Health Services Research 2012 12(Suppl 1):P10.); Ministry of Health Malaysia (http://www.moh.gov.my/english.php/pages/view/160); Study by Akhavan Hejazi et al 2015(Akhavan Hejazi SM, et al. Cost of post-stroke outpatient care in malaysia. Singapore Med. J. 2015;56:116-119); Department of Statistics Malaysia

(https://www.dosm.gov.my/v1/index.php?r=column/pdfPrev&id=czRyNkJIbDFyYXJFbU5YTVJ1V1BHZz09).

For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost).



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Supplementary document 4. Missing cost data analyses

Table I. Number of missing data for each cost item

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Table I. Number of missin			cost data	analyses			ight, including for	bmjopen-2018-026230 on			
							or 	22			
Cost variable	Missing Total	AU		NZ		UK	IS En	Ma SG		MA	
	N=2104	VEM	UC	VEM	UC	VEM		No.	UC	VEM	UC
}	N-2104	N=522	N=532	N=94	N=95	VENI N=311	UC lated N=299 days	ων Ε.ΝΙ N=64	N=64	N=62	N=61
Acute hospitalisation	1(0.05%)	1(0.2%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%) 6 5	2 0(0%)	0(0%)	0(0%)	0(0%)
Stroke-related rehospitalisation	51(2.4%)	8(1.5%)	7(1.3%)	0(0%)	0(0%)	17(5.5%)	8(2.7%)	0(0%)	3(4.7%)	7(11.3%)	1(1.6%)
Ambulance transfer	53(2.5%)	8(1.5%)	10(1.9%)	0(0%)	0(0%)	16(5.1%)	7(2.3%)	1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Rehabilitation hospital admission	55(2.6%)	9(1.7%)	9(1.7%)	0(0%)	0(0%)	18(5.8%)	8(2.7%)	0(0%)	3(4.7%)	7(11.3%)	1(1.6%)
Outpatient rehabilitation program	47(2.2%)	0(0%)	0(0%)	0(0%)	0(0%)	23(7.4%)	10(3.3%) ≥	3 0(0%)	3(4.7%)	9(14.5%)	2(3.3%)
Rehabilitation provided at home/nursing facility	67(3.2%)	11(2.1%)	10(1.9%)	0(0%)	0(0%)	23(7.4%)	1(3.7%)	0(0%)	3(4.7%)	7(11.3%)	1(1.6%)
Individual allied health visit§	0(0%)	-	-	- /	-	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Private physiotherapy	76(3.6%)	12(2.3%)	11(2.1%)	0(0%)	1(1.1%)	27(8.7%)	13(4.4%	8 1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Respite care	77(3.7%)	12(2.3%)	11(2.1%)	1(1.1%)	1(1.1%)	27(8.7%)	13(4.4%)	1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Subtotal (medical cost)	94(10.7%)	14(2.7%)	13(2.4%)	1(1%)	1(1.1%)	36(11.6%)	14(4.7%)	1(1.6%)	3(4.7%)	9(14.5%)	2(3.3%)
Accommodation moves	60(2.9%)	15(2.9%)	11(2.1%)	1(1.1%)	1(1.1%)	15(4.8%)	10(3.3%	0(0%)	2(3.1%)	5(8.1%)	0(0%)
Community services	230(10.9%)	63(12.1%)	87(16.4%)	4(4.3%)	5(5.3%)	32(10.3%)	27(9.0% 2 .	1(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Home modifications	13(0.6%)	3(2.6%)	6(1.1%)	0(0%)	1(1.1%)	0(0%)	2(0.7%)	0(0%)	1(1.6%)	0(0%)	0(0%)
Special aids and equipment	48(2.3%)	7(1.3%)	8(1.5%)	1(1.1%)	1(1.1%)	16(5.1%)	14(4.7%	1(1.6%)	0(0%)	0(0%)	0(0%)
Informal care	72(3.4%)	11(2.1%)	12(2.3%)	0(0%)	1(1.1%)	26(8.4%)	10(3.3%	ωl(1.6%)	3(4.7%)	7(11.3%)	1(1.6%)
Living-in maids [‡]	-	-	-	-	-	-	- 6	8 1(1.6%)	3(4.7%)	7(11.3%)	2(3.3%)
Subtotal (non-medical cost)	304(14.5%)	77(14.8)%	97(18.2%)	6(6.4%)	7(7.4%)	54(17.4%)	46(15.4%)	<u>တို</u> 2(3.1%)	5(7.8%)	8(12.9%)	2(3.3%)
Productivity cost	225(10.7%)	50(9.6%)	46(8.7%)	14(14.9%)	10(10.5%)	27(8.7%)	23(7.7%)	17(25.6%)	13(20.3%)	14(22.6%)	11(18.0%)
Total cost (exc. productivity cost)	319(15.2%)	80(15.3%)	97(18.2%)	6(6.4%)	7(7.4%)	61(19.6%)	48(16.1%)	2 2(3.1%)	5(7.8%)	10(16.1%)	3(4.9%)
Total cost	512(24.3%)	124(23.8%)	136(25.6%)	20(21.3%)	16(16.8%)	80(25.7%)	68(22.7%)	⁶ 17(26.6%)	16(25.0%)	22(35.5%)	13(21.3%)

[§]only applicable to UK, Singapore and Malaysia patients; †only applicable to Singapore and Malaysia patients

Table II. Missing pattern analysis based on logit regression

Resource use items with missing data	Predictor of missingness
Stroke-related rehospitalisation	Age (p=0.001)
Rehabilitation hospital admission	Age (p=0.009), NIHSCORE (p=0.037)
Outpatient rehabilitation program	Age (p=-0.003)
Rehabilitation service provided at home/nursing facility	Age (p=0.014),
Community services used prior to stroke	NIHSCORE (p=0.001)
Community services used at 3 months	Age (p=0.003)
Community services used at 12 months	NIHSCORE (p=0.008)
Aids or special equipment uses at 3 months	Age (p=0.012)
Aids or special equipment uses at 12 months	Age (p=0.035), NIHSCORE (p=0.013)
Private physiotherapy uses at 3 months	Age (p<0.0001)
Private physiotherapy uses at 12 months	Age (p=0.006), NIHSCORE (p=0.034)
Respite care use at 3 months	Age (p<0.0001)
Respite care use at 12 months	Age (p=0.017), NIHSCORE (P=0.018)
Informal care use at 3 months	Age (p=0.003)
Informal care use at 12 months	Age (p<0.0001)

If any of the other variables were able to predict the missingness of a given variable representing resource use, the MAR assumption was deemed to be held true. More specifically, multiple imputations were used to replace the missing values (missing mRS, AQoL-4D data or cost categories) with plausible estimates, and generated 30 datasets. Results were provided as pooled estimates of these sets. Identical analyses were carried out to estimate the incremental costs and benefits between groups on the basis of imputed data following the methods outlined in the statistical analysis section above. As the probability of all the resource use items being missing could be predicted by one or more of the other variables, it is likely that the Missing-at-Random (MAR) assumption could be held true. (https://www.ssc.wisc.edu/sscc/pubs/stata mi_decide.htm).

Supplementary document 5. Outcomes

Table I. Results of mRS score at 3 and 12 months follow-up

Modified Rankin Scale Score	UC group n=1050		VEM gro	oup
			n=1054	
	3M	12M	3M	12M
0	96	132	90	137
1	204	231	200	219
2	225	175	190	166
3	218	199	238	186
4	127	95	140	113
5	103	83	92	59
6	72	118	88	139
Total	1045	1033	1038	1019
Missing data	5	17	16	35

Number of patients falling into each category

Since there was no significant intervention effect together with no accepted willingness-to-pay (WTP) per unit increase in probability of achieving a better mRS outcome, further estimation of the ICER was considered not meaningful (i.e. no cost-effectiveness plane or cost-effectiveness acceptability curve could be generated).

Table II. Time and cost associated with delivering VEM and UC (mean, 95%CI)

	VEM		UC		Between group difference	
	Total time (min)	Cost (AUD)	Total time (min)	Cost (AUD)	Total time (min)	Cost (AUD)
Physiotherapist	243 (232, 254)	\$117 (\$111, \$123)	95 (90, 101)	\$48 (\$45, \$51)	147 (135, 159)*	\$69 (\$63, \$75)*
Nurse [†]	494 (456, 532)	\$225 (\$207, \$244)	439 (404, 474)	\$202 (\$185, \$219)	55 (4, 106)*	\$23 (-\$2, \$48)
Total cost	-	\$342 (\$320, \$364)	-	\$250 (\$231, \$269)	-	\$92 (\$63, \$121)*

VEM: very early mobilisation; UC: usual care; CI: confidence interval

Because VEM and UC were supplied by the same group of physiotherapists and nurses, the key difference was that a patient randomised to VEM received early rehabilitation within 24 hours of stroke onset and more out-of-bed mobilisation sessions of early mobilisation.

The total health practitioner (physiotherapist and nurses) time devoted to the delivery of the VEM and UC differed significantly, with the VEM group receiving substantially longer mean service time from both the physiotherapist (VEM: 243 mins, 95%CI: 232 to 254 vs UC: 95 mins, 95%CI: 90 to 101, p<0.0001) and nurse (VEM: 494 mins, 95%CI: 456 to 532 vs UC: 439 mins, 95%CI: 404 to 474, p<0.0001). The resultant difference in costs between groups was significant (\$92, 95%CI: \$63 to \$121, p<0.0001).

^{*}p<0.0001 (adjusted for age, baseline NIHSS and mRS); † nurse's time devoted to delivery of VEM/UC was not recorded in the process of data collection, so the physiotherapist time was used as a proxy

Supplementary document 6. Sensitivity analyses

Generally, the difference in QALY gains between VEM and UC groups were fairly consistent across different get bods.

Table I. Between-group differences based on the Generalised Linear Model_ base case analysis vs. multiple imputation analysis

	ITT (not imputed)		ITT (imputed)		/ 2019.	
	mRS score	QALYs	Cost (AUD)	mRS	QALYs	Case (AUD)
Health Sector Perspec	ctive					wnlo o tex
Total medical costs	0.030	-0.013	\$1082	0.042	-0.019	\$9aded
	(-0.022, 0.082)	(-0.041, 0.016)	(-\$2399, \$4563)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$25.58\$, \$4465)
Societal Perspective			704	l	-1	http BES
Total cost (excl.	0.030	-0.013	-\$6	0.042	-0.019	\$1 3 04 \$
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$5703, \$5690)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$3428; \$8832)
Total cost (incl.	0.030	-0.013	\$102	0.042	-0.019	\$1213
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$6945, \$7149)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$594 0 ; \$8766)

ITT: intention to treatment; mRS: modified Rankin Scale; AUD: Australian dollars

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

Table II. Between-group differences based on the Generalised Linear Model

	Adding country dummies			
	mRS	QALYs	Cost	
Total medical costs	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	\$704 (-\$1968, \$3376)	
Total cost (excl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$335 (-\$4953, \$4283)	
Total cost (incl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$238 (-\$6012, \$5537)	

mRS: modified Rankin Scale; QALYs: Quality-adjusted Life Years

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

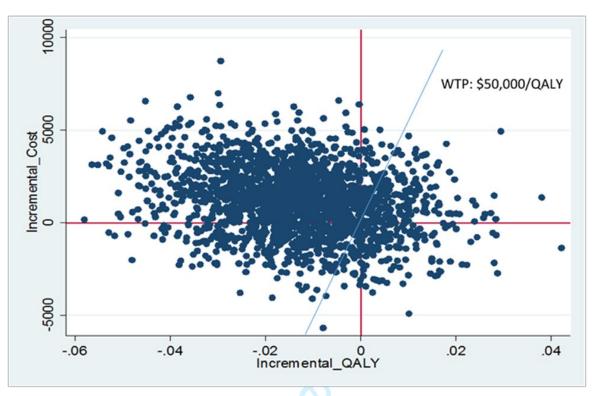
Table III. Cost-utility analysis based on multiple imputation analysis

	Efficacy (QALYs)	Cost (AUD)	Probability of being cost-effective
Health Sector Perspect	ive		
Total medical costs	-0.019	\$940	25%
	(-0.044, 0.005)	(-\$4622, \$4682)	
Societal Perspective			
Total cost (excl.	-0.019	\$1704	20%
productivity cost)	(-0.044, 0.005)	(-\$3817, \$7226)	
Total cost (incl	-0.019	\$1413	23%
productivity cost)	(-0.044, 0.005)	(-\$4044, \$6871)	

QALYs: Quality-adjusted Life Years; AUD: Australian dollar.

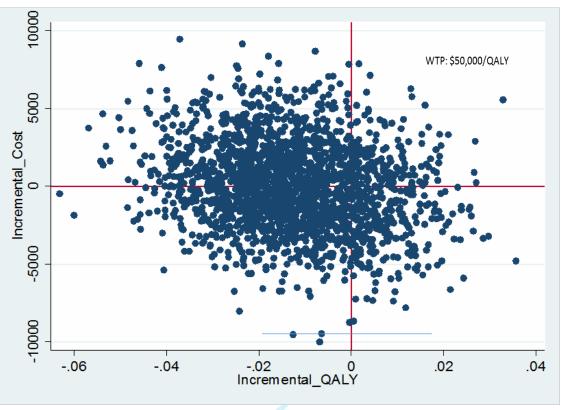
^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

Supplementary document 7: Figures



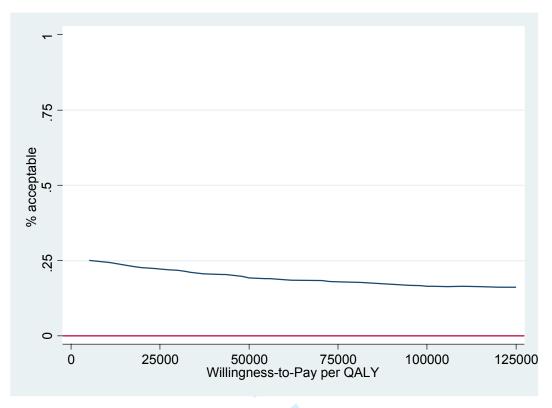
*Probability of VEM being cost-effective is 19%; WTP: willingness-to-pay; QALY: quality adjusted life year

Figure I Cost-effectiveness plane_ health sector perspective



*Probability of VEM being cost-effective is 42%; WTP: willingness-to-pay; QALY: quality-adjusted life year

Figure II Cost-effectiveness plane societal perspective (excl. productivity cost)



Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

Figure III Cost-effectiveness acceptability curve for medical cost

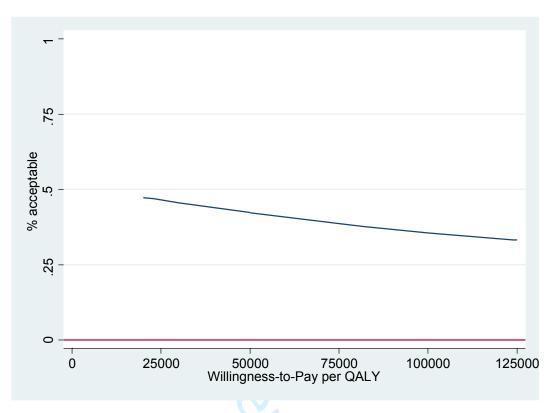


Figure IV Cost-effectiveness acceptability curve for total cost excluding productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

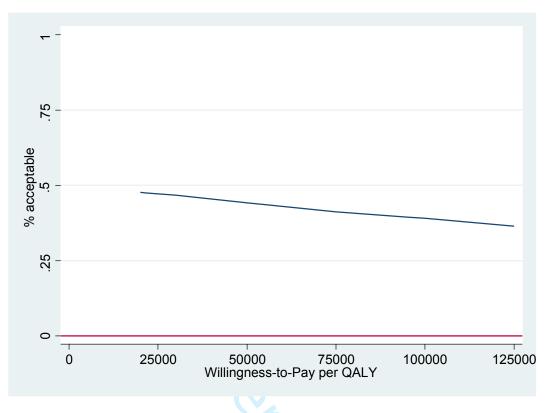


Figure V Cost-effectiveness acceptability curve for total cost including productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

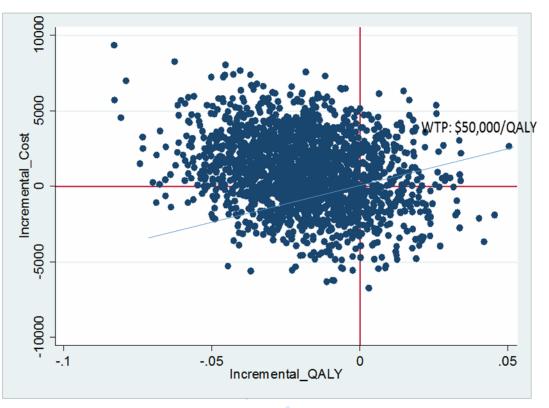


Figure VI Cost-effectiveness plane_ health sector perspective (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

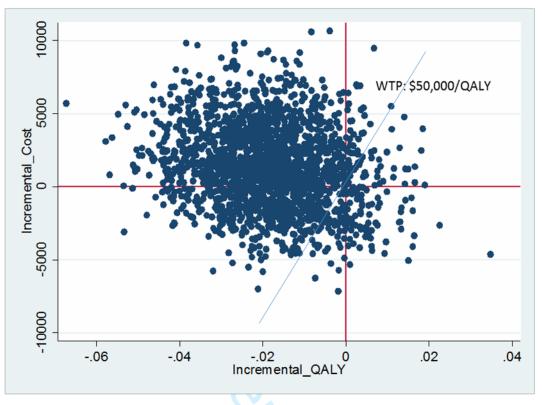


Figure VII Cost-effectiveness plane_ societal perspective including productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

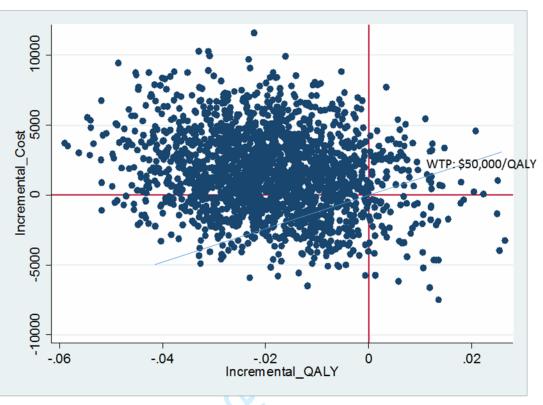


Figure VIII Cost-effectiveness plane_societal perspective excluding productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

- 1. Claesson L, Gosman-Hedstrom G, Johannesson M, Fagerberg B, Blomstrand C. Resource utilization and costs of stroke unit care integrated in a care continuum: A 1-year controlled, prospective, randomized study in elderly patients: the Goteborg 70+ Stroke Study. Stroke 2000;31(11):2569-77.
- 2. Bernhardt J, Dewey H, Thrift A, Collier J, Donnan G. A very early rehabilitation trial for stroke (AVERT) phase II safety and feasibility. Stroke 2008;39(2):390-6.



			Reported of page No/
Section/item	Item No	Recommendation	line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	4-5
ntroduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	7 8
Methods		Present the study question and its relevance for health policy or practice decisions.	0
Farget population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	12
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	9
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	8
Fime horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	11
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	11
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	8-9
Measurement of effectiveness	11a	Single study-based estimates: Describe fully the design features of the single effectiveness stud and why the single study was a sufficient source of clinical effectiveness data.	y 12
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	
Estimating resources and costs	13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	9-10
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resourceuse associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providinga figure to show model structure is strongly recommended.	
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	11-1:
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	N/A
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	14-1
Characterising uncertainty	20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	14
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	
naracterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
Discussion			
udy findings, limitations,	22	Summarise key study findings and describe how they support the conclusions reached. Discuss	

knowledge Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	22

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statementchecklist



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Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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 Title Page

Title

Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT)

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Economic evaluation of AVERT trial

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Abstract

 Objectives While Very Early Mobilisation (VEM) intervention for stroke patients was shown not to be effective at 3 months, 12 -month clinical and economic outcomes remain unknown. The aim was to assess cost-effectiveness of a VEM intervention within a Phase III randomised controlled trial (RCT).

Design An economic evaluation alongside a RCT, and detailed resource use and cost analysis over 12-months post-acute stroke.

Setting Multi-country RCT involved 58 stroke centres.

Participants 2104 patients with acute stroke who were admitted to a stroke unit.

Intervention A very early rehabilitation intervention within 24 hours of stroke onset

Methods Cost-utility analyses were undertaken according to pre-specified protocol measuring VEM against usual care (UC) based on 12 -month outcomes. The analysis was conducted using both health sector and societal perspectives. Unit costs were sourced from participating countries. Details on resource use (both health and non-health) were sourced from Cost Case Report Form. Dichotomised Modified Rankin Scale (mRS) scores (0-2 vs 3-6) and Quality Adjusted Life Years (QALYs) were used to compare the treatment effect of VEM and UC. The base case analysis was performed on an Intention-To-Treat (ITT) basis and 95% confidence intervals (CI) for cost and QALYs were estimated by bootstrapping. Sensitivity analysis were conducted to examine the robustness of base case results.

Results VEM and UC groups were comparable in the quantity of resource use and cost of each component. There were no differences in the probability of achieving a favourable mRS outcome (0.030, 95%CI: -0.022 to 0.082), QALYs (0.013, 95%CI: -0.041 to 0.016) and cost (AUD1082, 95%CI: -\$2520 to \$4685) from a health sector perspective; or AUD\$102, 95%CI:

-\$6907 to \$7111, from a societal perspective including productivity cost). Sensitivity analysis achieved results with mostly overlapped CIs.

Conclusions VEM and UC were associated with comparable costs, mRS outcome and QALY gains at 12 months. Compared with to UC, VEM is unlikely to be cost-effective. The long-term data collection during the trial also informed resource use and cost of care post-acute stroke across five participating countries.

Trial registration Australian New Zealand ClinicalTrials Registry, number ACTRN12606000185561.

Strength and limitations

- This is the first economic evaluation assessing the cost-effectiveness of a very early rehabilitation intervention within the largest Phase III randomised controlled trial in patients with stroke;
- The study assessed the long-term cost and cost-effectiveness of this very early rehabilitation intervention at 12-month;
- The difficulty posed by the multi-country design of the trial and the percentage of missing data may undermine the confidence in the results.

Introduction

Stroke is one of the biggest killers and a leading cause of disability worldwide.¹² 65% of stroke survivors live with some degree of disability that impedes their ability to carry out daily living activities unassisted.³ Therefore, ways of improving the outcomes of patients after stroke is an important focus of research.⁴⁵ Early mobilisation after stroke is believed to contribute to better patient outcomes and clinical trials have been conducted globally.⁶⁻⁹

The short-term efficacy and safety of a very early rehabilitation trial after stroke (AVERT) has been evaluated in a phase III randomised controlled trial (RCT) with 2,104 patients enrolled from Australia, New Zealand, United Kingdom, Singapore and Malaysia. 10 The evidence from this trial indicated that at three months after stroke, very early mobilisation (VEM) of patients was associated with a reduction in the probability of a favourable outcome as defined by a modified Rankin Scale (mRS) score of 0-2 compared to that in the usual care (UC) group. 10 In the research field of stroke, primary endpoint is usually assessed at month 3 after stroke¹¹⁻¹⁴, which means there is a paucity of data in terms of long-term resource use and cost of care for patients with stroke. Given AVERT provided a longer-term (i.e. 12 months) comprehensive measurement of costs relating to stroke care (i.e. direct medical, direct non-medical, and indirect costs), and the broader representativeness of patients across countries and regions (>2000 patients were recruited from both developing and developed world), together with the implications of stroke economic burden sustained beyond the acute phase (i.e., 3 months), holistically examining the cost of stroke care that falls within health and non-health sectors could potentially advance understanding of pattern of resource use post stroke and identify any gaps to improve care for stroke and chances to curb the increasing economic burden of disease.

This examination also benefits healthcare funders (i.e. governments, insurance companies) and the public with addition of substantial knowledge of long-term rehabilitation cost for stroke.

This economic evaluation, which was part of the registered trial protocol (Australian New Zealand Clinical Trials Registry, ACTRN12606000185561) and planned prior to knowledge of outcomes, was conducted alongside the Phase III RCT,¹⁰ The aim of this paper is to assess the cost-effectiveness of very early mobilisation within 24 hours after stroke in terms of improving patient outcomes at 12-months, in comparison to usual care (UC), with a particular focus on examining the resource use and cost of care after stroke.

Methods

The economic analysis was undertaken following the previously published plan.¹⁵ It also conforms to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.¹⁶ Ethics approval was granted by relevant institutions.

Intervention and comparator

The trial design has been reported in detail elsewhere.¹⁰ In brief, patients with confirmed stroke who were admitted to a stroke unit within 24 hours of stroke onset were randomised to receive usual stroke-unit care (UC) alone or VEM in addition to UC in a multinational Phase III trial.

Outcomes

The mRS at 12-months, a secondary outcome of the trial, and Quality-Adjusted life years (QALYs) derived from the Assessment of Quality of Life-4D (AQoL-4D)¹⁷ were used as the effectiveness measures in the economic evaluation. The AQoL-4D instrument is a multi-

attribute utility scale used to assess the health-related quality of life (HRQoL)¹⁸; it was administered at 3 and 12 months.

Outcome of mRS was dichotomised into "favourable" (mRS 0-2) and "poor" (mRS 3-6) based on patients outcomes at 12-month follow up.¹⁰ The difference in the probability of patients achieving a favourable mRS outcome (mRS 0-2) was used to estimate the incremental benefits between treatment groups for the primary efficacy outcome.

Due to the inherent difficulties of administering the AQoL instrument to acute stroke patients (i.e. most of patients were not able to respond to these questions at baseline), the mRS score at baseline¹⁰ was used as a surrogate measure of patient utility during the acute phase. The detailed methods of this work are reported elsewhere¹⁹ and a brief description is supplied in the online Supplementary document 1.

Costs

A societal perspective with a key focus on the health sector was adopted.

Intervention delivery

Intervention delivery costs consisted of the time costs of physiotherapists (PT) and nurses delivering VEM (or UC) to patients. The mean of the total physiotherapist time (recorded by a log documented by each participating PT across whole hospital stay) per patient was calculated. Given insufficient data, physiotherapist's mean time per session was used as a proxy for nurse time spent on delivering either VEM or UC.

Resource use

All resource use during the study period was electronically collated using a validated Cost Case Report Form (Cost CRF) administered and recorded by trained staff at 3- and 12-months using face to face assessments with patients and carers, and medical records. Cost CRF used in Australia is supplied as an example (Supplementary document 2). Cost CRF from other participating countries could be requested from corresponding author.

Healthcare resource use

The quantity of resources used for the following health care resource items was recorded: number of ambulance transfers (emergency and non-emergency), acute hospitalisation (including length of stay, LoS), rehospitalisation (number of occasions and LoS for each occasion), rehabilitation hospital admission (number of occasions and LoS for each occasion), outpatient rehabilitation program (number of occasions and number of days for each occasion), rehabilitation provided at home/nursing facility (number of occasions and number of sessions for each occasion), private physiotherapy (number of sessions), respite care (number of sessions) and individual outpatient (including physiotherapy, occupational therapy, and speech and language therapy) visits (service type and number of sessions) for patients from United Kingdom, Singapore and Malaysia only.

Non-healthcare resource use

The quantity of resources used was recorded for the following non-heath care resource items: accommodation move due to stroke (location moved to and date of move), community service (type of service use and number of service used both for prior to and post-stroke), home modification (type of modification, supplier and cost), special equipment and aids (type of equipment/aids and quantity consumed), informal care (purpose of the care and hours used), live-in maids (number of maids prior to and post stroke) (for Singapore and Malaysia only),

changes to employment (employment status and weekly hours of working both prior to and post-stroke).

Resource use reported at 3 (i.e. resources used between 0 and 3 months) and 12 (i.e. resources used between 4 and 12 months) months was used to calculate the total annual resource use for each participant. Generally, where patients were still using a particular resource at the time of 12-month data collection, the last day of 12 months' follow-up (calculated from the day of index stroke) was used to estimate the duration of that resource utilisation. In the event of a patient dying, resource use data for the period prior to death was ascertained from their carer and medical records, wherever possible.

Unit costing

Costs were computed by applying country-specific unit costs to each resource item utilised. Therefore, five sets of unit costs (one for each of the participating countries) were compiled from the most up-to-date and reliable source (Supplementary document 3). Unit costs from a country with a similar economic status and healthcare system were used where local country-specific unit costs were unavailable.

All costs are expressed in Australian dollars (AUD) for the 2015 reference year value and can be converted to United States dollar (USD) using the Purchasing Power Parity rate 1 USD=1.463 AUD²⁰ (December 2015). The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

The details of unit cost for acute stroke hospitalisation, rehospitalisation, rehabilitation (inpatient and outpatient), non-health sector costs (home modifications, community services, aids etc.) and productivity cost are provided in Supplementary document 3.

Statistical analysis

 All the costs that were attributable to stroke including healthcare costs, non-healthcare costs and productivity costs were accounted for in the economic analysis. Since a 12 month economic evaluation was undertaken, no discounting was applied to either costs or benefits.

Quantity of resource use and costs were summarised using medians and interquartile ranges (IQRs) due the skewness of the raw data. Means and standard deviations (SDs) were also reported. Base case analysis of the economic evaluation was performed based on the Intention-to-Treat (ITT) population²¹ with an assumption for the main analysis that data were Missing At Random (MAR). The difference in costs was analysed using Generalised Linear regression Model (GLM) with gamma family and a log link, with treatment groups as an independent variable, including baseline National Institutes of Health Stroke Scale (NIHSS), baseline mRS¹⁵ and age as treatment covariates.

For the primary outcome, the mRS score at 12 months was compared following the method detailed in the Statistical Analysis Plan.²² While for the secondary effectiveness outcome (i.e. the QALY gains at 12 months), a linear regression model with treatment group as the factor variable and 12 months AQoL-4D utility value as the dependent variable, adjusted for age, baseline mRS was utilised to estimate the difference in QALY gains over 12 months. Non-parametric bootstrap simulations with 2000 replications were used to calculate 95% confidence intervals (CIs) around mean difference in costs and effects for cost-effectiveness analysis. To

 examine the cost-effectiveness of VEM measured against UC, Incremental Cost-Effectiveness Ratios (ICERs) were calculated where applicable. For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost). The differences between groups in terms of costs and benefits (i.e. QALYs) were compared regardless of the statistical significance of the difference.²³ Cost-effectiveness acceptability curves were plotted to show the probability of VEM being the optimal choice. The ICERs were compared with a common benchmark in Australia of ≤AUD50,000 per QALY.²⁴ All the analyses were performed using the STATA 14.0 statistical package (StataCorp. 2015. Release 14. StataCorp LP.)

Sensitivity analyses

To investigate the impact of using country-specific costs, a country dummy variable was added to the GLM analysis to adjust for country effect.²⁵ Subgroup analysis on the basis of individual countries were also conducted to explore the difference in costs and benefits across countries.

Multiple imputation was performed to test the sensitivity of results to the missing data assumption. The missing patterns were explored with the use of logit regression to investigate if any of the other variables predicted whether a given variable was missing²⁶ (Supplementary document 4).

Secondary analyses were undertaken to assess the robustness of the base case results. Subgroup analyses were performed at the country-specific level to test for differences in efficacy and costs.

Patient and Public involvement

 No patient and public were involved.

Results

Between July 2006 and October 2014, 2,104 patients (VEM 1,054; UC 1,050) were recruited across 58 sites from Australia (N=1,054, 24 sites), New Zealand (N=189, 1 site), United Kingdom (N=610, 29 sites), Singapore (N=128, 1 site) and Malaysia (N=123, 1 site). At recruitment, over 80% of patients had no prior history of stroke; NIHSS was greater than 7 points (indicating a moderate to severe stroke) for around 45% of patients; 26% aged over 80 years and 24% had received recombinant tissue plasminogen activator prior to randomisation¹⁰. Baseline characteristics were similar between the two treatment groups¹⁰.

Outcomes

There was no difference between VEM and UC groups in terms of favourable mRS outcome and quality of life (as measured by AQoL-4D) at month 12. Specifically, a comparable percentage of patients from both treatment groups achieved a favourable outcome at 12 months after stroke (between-group difference in probability: 0.030, 95%CI:-0.021 to 0.082, adjusted for baseline age and NIHSS). Likewise, for the outcome of AQoL-4D at 12 months, no between-group difference was observed (-0.013, 95%CI:-0.043 to 0.017). The detailed mRS outcomes are presented in Supplementary document 5: Table I.

Resource use and costs

The proportion of patients reporting use of a specific resource varied from item to item (Table 1). In relation to the healthcare resource items, nearly half of patients experienced rehabilitation hospital admission and more than a quarter of patients had a stroke-related rehospitalisation, rehabilitation service use (outpatient/provided at home or nursing facility) and ambulant transfers whereas only a small proportion of patients (less than 10%) recorded the use of private physiotherapy and/or respite care. Regarding non-health-related resource use, the majority of patients (>50%) used some form of special aids or equipment during the 12 months after their index stroke, whilst nearly 40% of patients received informal care, and around 27% reported the use of community services and home modifications. Only 16% (VEM) and 17% (UC) of patients respectively, experienced accommodation changes due to the index stroke. For maid's service use in the home in Singapore and Malaysia, a small proportion (less than 10%) of patients hired a maid both before and after the index stroke.

With respect to productivity, nearly one in four patients were employed prior to their stroke; this proportion fell to only one in eight patients at 12 months follow up. Generally, resource use was comparable between VEM and UC groups (p > 0.05) across all items (Table 1).

The median total medical cost was marginally higher in the UC group (\$20,411, IQR: \$7,238 to \$63,835) than in the VEM group (\$19,271, IQR: \$6,294 to \$52,637), primarily due to the higher rehabilitation admission cost in UC. In both groups, the major cost component was acute hospitalisation which accounted for around 30% of medical costs. The median non-medical cost was also marginally higher in the UC group (\$438, IQR: \$0 to \$4,561) than in the VEM group (\$358, IQR: \$0 to \$3,334). The median productivity cost was zero for both treatment groups given that less than one quarter of patients were in paid employment before the index stroke. Overall, the median total cost (including productivity cost and non-medical costs) were nominally higher in the UC group (\$27,042, IQR: \$7,257 to \$63,824) compared to the VEM group (\$25,675, IQR: \$6,766 to \$63,617). The detailed costs of each resource item and

summary costs are presented in Table 2. The costs for VEM and UC interventions are summarised in Supplementary document 5: Table II.

Generally, the cost from VEM and UC groups were comparable: the differences between VEM and UC groups was \$1082 (95%CI: -\$2399, \$4563) for the total medical cost (Supplementary document 6: Table I) and \$3 (95%CI: -\$5, \$12) for the productivity cost per person at 12 months; the between-group difference in the total non-health care cost was -\$1300 (95%CI: -\$3361, \$760) over the same period of time.

Cost-effectiveness analysis

The between group difference in both efficacy and cost outcomes generated from the GLM model are presented in Supplementary document 6: Table I.

In the base case health sector perspective analysis, the VEM yielded comparable total medical costs (\$1082, 95%CI: -\$2520 to \$4685, p=0.544) and QALY gains (-0.013, 95%CI: -0.041 to 0.016) at 12 months. When a societal perspective was adopted, the VEM entailed, again, similar costs with the UC group (\$102, 95%CI: -\$6907 to \$7111, p=0.982, including productivity costs) or (-\$6, 95%CI: -\$5476 to \$5463, p=0.933, excluding productivity costs) (Table 3).

The cost-effectiveness planes and cost-effectiveness acceptability curves from the two perspectives are shown in Supplementary document 7: Figures I to V.

Sensitivity analyses

Inclusion of a country dummy variable in the analysis produced similar results to the base case (Supplementary document 6: Table II).

The analysis from imputed data including all randomised participants produced consistent results with regard to the incremental cost and effectiveness between treatment groups. For example, from a health sector perspective, VEM was associated with similar costs (\$940, 95%CI: \$-4622 to \$4682) and QALY gains (-0.019, 95%CI:-0.044 to 0.005) over 12 months. (Supplementary document 6: Table III and Supplementary document 7: Figures VI-VIII)

The country-specific analysis showed similar results in the between-group differences for both costs and QALYs, indicating that VEM and UC yielded comparable results within each participating countries (Table 4).

When a societal perspective was assumed, again, the point estimate of difference in costs between groups across countries varied substantially, with the 95% confidence intervals mostly Discussion overlapping (Table 4).

The 12 months within-trial cost-effectiveness analysis showed that VEM was unlikely to be cost-effective than UC in patients with stroke. Between-group differences in costs and benefits (probability of achieving a favourable outcome of mRS and differences in QALYs) over the one year study period were comparable from a health sector perspective. The findings from this economic evaluation is also underpinning an adapted version of trial underway to investigate the effectiveness of optimal rehabilitation in patients with mild to moderate stroke

(i.e. AVERT-DOSE, National Health and Medical Research Council Australia, project grant #1139712).

Our earlier economic evaluation of the phase II AVERT trial which consisted of only 71 patients (38 VEM and 33 UC) from two Australian centres reported that VEM was likely to be a cost-effective intervention with both less cost and more benefit when compared to UC.²⁷ Since it was a national pilot study with a limited sample, the direct comparison between the results from this and our current economic evaluation is problematic. In addition, inconsistent with the pilot study, no service shifting was observed in the current study. Across all resource use components, the proportion of patients consuming specific types of resources were comparable between the two groups in this study. On the contrary, in the Phase II AVERT trial, patients from VEM group were more likely to be discharged earlier from hospital than their UC counterparts; those discharged early tended to use more care provided in the outpatient setting, which incurred lower costs; and informal care was not costed. In the current study, the LoS for acute hospitalisation and rehabilitation were similar between treatment groups (median: VEM 16 vs UC 17 days). These differences between the two studies highlight the importance of large, adequately powered studies to inform health care policy.

In this study, resources used were valued on the basis of country-specific unit costs sourced for each participating country. To counteract any concern arising from the adoption of this approach, extensive sensitivity analyses were performed to test the robustness of the results. The conduct of incorporation of a country dummy variable into the model or country-specific analysis did not alter the outcomes substantially, with the resultant 95% confidence intervals overlapping to a great extent. Ramsey et al. 2015 suggest that a country-specific costing approach is likely to yield few qualitative differences in summary measures of cost-effectiveness among countries with similar levels of economic development.²⁵ Therefore, it was believed that any differences in economic status of the participating countries (as reflected

 by the unit costs applied in our study) are unlikely to bear a major influence on the results of the cost-effective analysis.

This multinational trial also revealed that in managing patients post-stroke, practice of stroke care varied from country to country. Although 100% of patients with stroke were hospitalised for the initial acute care, the LoS differs significantly greatly, ranging from 4 days (Malaysia) to 25 days (New Zealand), which might be attributable to the different severity of stroke and/or differences in clinical practice care processes. Moreover, in Malaysia, patients tended to receive rehabilitation services in an outpatient (i.e. up to 52% of patients received the outpatients rehabilitation program services) rather than inpatient (i.e. only up to 2% patients were admitted to rehabilitation hospital) setting; and patients were less likely to utilise ambulant transfer and apply home modifications, as compared to participants from other countries. This might be a signal for future study around stroke care in Malaysia, research potentially could be helpful to improve the service delivery for outpatient rehabilitation program. Patients from western countries consumed more community services and rehabilitation services that provided at home/nursing home than their Asian counterparts, which reflects the difference in social welfare and healthcare systems.

Economic evaluations have been conducted for other types of stroke rehabilitation interventions including early-supported discharge service, community- or home-based rehabilitation. ²⁸⁻³⁶ Generally, these interventions trended towards being cost-saving measured against usual practice. In regards to health-related quality of life (HRQoL) outcomes measured by a series of quality of life instruments (including SF-36, WHOQoL-Bref, Nottingham Health Profile, Sickness Impact Profile and EQ-5D), most studies did not detect an overall significant effect. ²⁸⁻³² ³⁴ ³⁵ ³⁷ Only one study reported a significant difference improvement in the overall

 HRQoL score.³⁶ The conclusions drawn from these economic evaluations of stroke rehabilitation interventions were fairly consistent; the interventions were likely to cost less,³³ ^{34 37-42} although the difference in costs was statistically significant in only one study.⁴¹ None of these studies evaluated the costs and benefits, particularly benefits measured in terms of QALYs, in an aggregated manner, and all were limited by small sample sizes. Another study using a Markov model explored the increased intensity of physiotherapy for stroke patients from a health system perspective, concluding that increased physiotherapy could be cost-effective by improving health outcomes and reducing costs due to the resultant shorter stay in rehabilitation facilities.⁴³

Given that it is not practical to obtain a baseline utility value from patients with stroke, in this study, the baseline AQoL value was mapped from mRS score at baseline. Whilst the mapping exercise was carried out using the baseline mRS score and AQoL values at 3 and 12 months, the significant variation in the mapped baseline utility values for patients falling within the same category of mRS hampered its application to the current economic evaluation. Instead, only the 12-month utility values were compared to approximate the difference in QALY gains over one year between the two treatment groups. Comprehensive sensitivity analyses were undertaken surrounding this assumption. It was observed that there was no noticeable difference among approaches examining the annual QALY gain difference between VEM and UC.

Whilst the results from the clinical study showed that there were no significant differences in either costs or effects between treatment groups, the cost-effectiveness analysis was still performed to investigate the possible ICER of the VEM intervention. It is possible to have greater confidence in the joint outcome of costs and QALYs than looking at them individually.⁴⁴

To the best of our knowledge, this study evaluated the cost-effectiveness of the largest international acute stroke rehabilitation trial ever conducted. The cost-effectiveness analysis was performed alongside the randomised controlled trial, where the costs and benefits data were collected prospectively. Moreover, the Cost CRF was completed by trained and blinded assessors via interviews with individual patients/carers and accessing medical records, which provides for greater accuracy than resource use questionnaires or diaries completed by participants themselves. Since the trial was designed in a pragmatic manner, with close resemblance to real clinical practice, it is believed that the assessment of its cost and cost-effectiveness under this setting reflects the real-life resource use (health and non-health).

This study provides some insights for future economic evaluation alongside multi-country, multi-centre clinical trials. It is important to note that given the large number of centres involved (56 stroke units across five geographical jurisdictions), it was not practical or reasonable to collect centre-specific unit costs which probably leads to huge variations even within a single country. Country-level unit costs were therefore applied to the valuation of resource uses across the trial sites. However, the heterogeneity in the resource utilisation and unit cost among the included countries undermines confidence in the conclusion. A country-specific economic evaluation might be more appropriate in this regard but the lacking of statistical power poses another concern. The current study made a trade-off between them both approaches by presenting both the aggregated (i.e. base case of pooling all countries) and disaggregated (i.e. sensitivity analysis of individual countries) form of results. The resource utilisation, costs and benefits were also tabulated across all sites and individually to allow close scrutiny from various perspectives. ²⁸ It is believed that this practice can be recommended to other multi-country studies.

A couple of limitations of the study are acknowledged. Firstly, the missing data on total costs from a societal perspective was around 24%, and related mainly to the missing information on

community services (10.9%) and productivity loss (10.7%). The base case analysis was based on the ITT population with an assumption of missing pattern being MAR. To account for this, the sensitivity analysis using multiple imputation was undertaken and yielded the identical conclusion (i.e. comparable results in costs and benefits between treatment groups). Secondly, unit costs originating from individual countries were assigned to value resource use. The differences in health care systems and cost structures among the five participating countries may potentially confound the cost comparisons between groups. However, analysis by country produced results consistent with the base case, which overcomes any concern that the latter were heavily weighted towards Australia, the largest sample country.

Conclusions

This economic evaluation alongside a phase III RCT evidenced that based on the ITT population, the VEM intervention for patients with stroke was unlikely to be cost-effective compared to UC. The sensitivity analyses based on the multiple imputation and subgroup analyses by each country separately yielded fairly consistent results. Despite substantial differences observed, in resource use and unit costs across the countries, the marginal differences between VEM and UC were consistent. Overall, the VEM intervention was demonstrated to be comparable with UC in terms of both benefits and costs at one-year, however given its poorer outcomes at 3 months, VEM cannot be recommended to clinicians, patients or policymakers.

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Authors' Contribution

Conception/design, revising and final approval: LG, LS, LC, OW, MM, JC, FE, JB, HD, MMoodie. Methodology: LG, MM, LS, LC, MMoodie, OW. Data analysis: LG, LS, MM, LC. Drafting: LG, MMoodie.

Competing Interests Statement

All authors confirm that there is nothing to declare.

Data Availability Statement

No additional data available

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Tables

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ables								ht, inc	118-026			
ble 1. Quantity of	f resource us AU (N=1054		nths (ITT) (NZ (N=189)		(N=610)))	SG (N=128)	luding	• MA (N=123)		All Countri	es
	VEM	UC	VEM	UC	VEM	UC	VEM	UC uses	NEM NEM	UC	VEM	UC
Acute hospitalisation								Ses	Tay			
% of patients using	100	100	100	100	100	100	100	100 00	2 100 2 100	100	100	100
LoS (days)	21(6-42)	22(7-46)	23(6-57)	25(8-48)	12(4-45)	13(5-4)	16(4-25)	18(4-25)	5(3-8)	4(2-8)	16(4-41)	17(5-41)
Stroke-related rehospita	alisation							⊥ ö i	D 5(3-8)			
% of patients using	30	29	28	33	28	23	20	20 20 20	18 18 16 16 16 17 10 11 11 11 12 12	23	28	27
No. readmission/s	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)	2(1-2)	1(1-2)	1(1-2)	1(1-2)	1(1-2)
Admission to rehabilita	tion hospital [†]			P				ata S	P D			
% of patients using	62	56	60	65	35	34	45	56	9 0	2	50	47
No. of admission/s	1(0-1)	1(0-1)	1(0-1)	1(0-1)	0(0-1)	0(0-1)	0(0-1)	1(0-1) &	0(0-0)	0(0-0)	0(0-1)	1(1-1)
Outpatient rehabilitatio	on program				* ()			25 ng	jo pe			
% of patients using	40	39	23	19	12	10	19	25	52	48	30	28
No. of services	15(6-29)	12(6-28)	16(7-28)	17(12-34)	12(6-21)	7(4-14)	32(20-77)	29(3-116)	15(7-24)	16(4-22)	15(6-28)	12(6-27)
Rehabilitation provided	at home/nursing	facility						<u> </u>	¥ .			
% of patients using	30	33	57	52	50	46	3	2 iii	2	2	35	34
No. of services	9(4-22)	10(4-25)	18(8-29)	16(9-30)	12(6-28)	12(6-30)	81(63-99)	9(9-9)	8 104(104-104)	8(8-8)	12(5-27)	12(5-28)
Ambulance transfer								hno	4 3			
% of pts using	51	53	34	48	41	38	36	9(9-9) technologies	2025	8	43	44
No. of trips	2(1-3)	2(1-3)	2(1-3)	1(1-3)	2(1-3)	2(1-3)	1(1-2)	1(1-2)	2(2-3)	2(1-3)	2(1-3)	2(1-3)
Individual allied health	therapy		1						genc			
% of pts using	N/A	N/A	N/A	N/A	19	15	-	2	20 E 20	25	-	-
No. of services	N/A	N/A	N/A	N/A	8(2-12)	8(4-15)	-	2(2-2)	8 (3-10)	16(8-31)	-	-
Private physiotherapy)g raphi			

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% of pts using	9	8	11	1	5	5	8	right,	201	2	8	6
No. of services	5(3-19)	6(4-19)	13(6-18)	3(3-3)	12(6-33)	7(1-14)	18(16-24)	14(7-24 算	R 12(11-13)	8(8-8)	15(4-20)	24(3-19)
Respite care								14(7-24 2 44ding	<u>&</u>			
% of pts using	3	2	3	2	2	3	-	- 0	on	2	2	2
No. of services	21(10-43)	15(11-35)	12(10-20)	7(5-8)	24(9-40)	21(12-80)	-	- use	<u>∏</u> [a]	30(N/A)	18(9-39)	18(9-41)
Accommodation moves								s reig	23 23 23			
% of pts using	18	17	19	28	13	14	11	20 6 6	23	10	16	17
No. of moves	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1)	1(1-1) to text and data	1(1-2)	2(1-2)	1(1-1)	1(1-1)
Community Services used	 prior to having	a stroke over the	past year					ext a	Hoad			
% of pts using	13	17	6	7	5	5	-	- D	- - - - - - -	-	9	11
No. of services	26(26-52)	26(26-52)	52(39-88)	46(14-52)	52(25-104)	40(15-131)	-	- ta	- 	-	27(26-52)	26(26-52)
Community services used	over 12 months	after stroke		101				minin				
% of pts using	30	35	32	28	31	28	-	3 6 .	6	-	27	28
No. of services	28(18-72)	32(12-78)	130(47-233)	48(17-256)	42(12-185)	90(12-310)	-	3(3-3) training	6(3-73)	-	39(14-119)	39(12-124)
Home modifications under	taken over 12 n	nonths				7	I					
% of pts using	27	30	20	17	36	33	16	19 6	3 .3	10	27	28
No. of mods	2(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	2(1-2)	1(1-2)	1(1-2)	1(1-1)	1(1-1)	1(1-2)	2(1-2)
Aids and appliances used of	over 12 months							similar te	9			
% of pts using	46	47	55	63	58	51	44	45	5 8	59	51	50
No. of aids/appliance used	2(1-5)	2(1-4)	3(2-6)	2(1-4)	4(2-6)	4(2-6)	2(2-3)	2(1-3) hnolog og og s	<u>ن</u> 2(1-3)	2(1-3)	3(1-5)	3(1-5)
Working prior to stroke	1						L	olog	202			
% of patients	24	23	38	34	19	21	52	52	5 45	33	27	26
Hrs worked/week	40(27-50)	40(30-50)	40(37-40)	40(37-40)	40(25-48)	37(25-40)	48(40-56)	45(36-50)	42(40-56)	45(32-50)	40(30-50)	40(30-50)
Proportion working at 12	months	1	1	1	1	1	ı	1	Се	1	1	
% of patients	15	12	20	16	7	9	25	22	₽ 24	15	14	12
Hrs worked/week	38(18-40)	25(12-40)	40(20-40)	40(38-40)	35(26-40)	30(24-37)	39(16-46)	35(23-44)	40(32-47)	45(30-50)	38(20-41)	30(16-40)

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6 of patients	-	-	-	-	-	-	19	16	cluc	3 5	10	-	-
No. of maids	-	-	-	-	-	-	1(1-1)	16	ing	35 1(1-1)	1(1-1)	-	-
atients from Singapo	ore and Malaysia who	had a maid at 12	months follow	ving stroke					<u> </u>	•			
6 of patients	-	-	-	-	-	-	23	22	En:	5	7	-	-
lo. of maids	-	-	-	-	-	-	1(1-1)	1(1-1)	seig	1(1-1)	1(1-1)	-	-
Receipt of informal ca	are at 12 months								nem ated)			
6 of patients	35	39	37	33	41	40	30	36	ent :	5 1(1-1) 42 22(10-38) hours; mod:	44	37	39
lo. of hrs/week	15(6-34)	12(4-31)	8(3-21)	14(6-30)	21(9-34)	17(7-35)	35(13-46)	16(4-3	Sub Sub	22(10-38)	16(5-26)	18(7-35)	14(5-32)
: Intention-to-treat; A re expressed as media:	AU: Australia; NZ: New n and interquartile rans	v Zealand; UK: Ur ge (IQR); †includes	nited Kingdom; s any admission	SG: Singapore; National SG: Singapore; National SG: Singapore; National SG:	MA: Malaysia; L hospital followi	oS: length of sta	ay; pts: patients; stroke;	No.: num	توريق چ ا	hours; mod:	modification; -:	no such resourc	e use; all nur
									aining, an				
	15(6-34) AU: Australia; NZ: Nev n and interquartile rang				30				aining, and similar technologies.				

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Page 31 of 8	12					BMJ Open		;	វ by copyright	bm jopen-2018-024 (N=123)			
1 2 Table 2 (Cost of all the	resources use	d over 12 mont	ths (AUD)				e	ight,	2018-			!
b	AU (N=1054)	TOOUT COS ESC.	NZ (N=189)	ns (rice)	UK (N=610)		SG (N=128)	.	<u>ਵ</u> ਨ ਅ	N=123)		All Countries	
5	VEM	UC	VEM	UC	VEM	UC	VEM		ud V	VS M	UC	VEM	UC
1	7 251.2		7 101,1			lealth care cost (AU			₹	0		, Eliz	'
Acute hospit	italisation						,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		→	9			
Median,	\$6294	\$6294	\$6104	\$6104	\$2763	\$3109	\$1493	\$1493		8 13 63	\$1363	\$6294	\$6294
/ IQR	(6294, 9553)	(6294, 9553)	(4370, 6104)	(4370, 6104)	(1382, 6563)	(1727, 6563)	(1493, 1809)	(1493, 1493)	ն년	i ≤ 63, 1572)	(1363, 1572)	(2279, 9535)	(2418, 9553)
8 Mean, SD	\$9883 (9484)	\$10010(10508)	\$6635 (3244)	\$6549 (3555)	\$5714(7876)	\$5885 (7101)	\$1721 (547)	\$1676 (432)	8 3	3 € 482 (212)	\$1472 (200)	\$7369 (8469)	\$7521 (8916)
	ted rehospitalisation								seigne relate	20.			
10Median,	\$0	\$0	\$0	\$0	\$227	\$227	\$111	\$111	ate me	,66	\$68	\$111	\$111
1 1 QR	(0, 3850)	(0, 3850)	(0, 325)	(0, 2243)	(227, 1401)	(227, 227)	(111, 111)	(111, 111)	Ճ ∃€	(6 6 , 68)	(68, 68)	(0, 1401)	(0, 610)
12Mean, SD	\$6030 (17114)	\$6473 (21590)	\$651 (1371)	\$1507 (2828)	\$4524 (13968)	\$3494(11349)	\$2756 (7565)	\$1679 (3465)			\$603 (1479)	\$4610 (14518)	\$4551 (16707)
	to rehab hospital		~						tex L	<u> </u>			
14 Median,	\$13134	\$13134	\$11262	\$11262	\$0	\$0	\$0	\$1298	t a	<u>6</u>	\$0	\$0	\$1136
IQR	(0, 36371)	(0, 38391)	(0, 30983)	(0, 26486)	(0, 29788)	(0, 29788)	(0, 2921)	(0, 3570)	집쿲	<u>)</u> (1)	(0, 0)	(0, 29788)	(0, 29788)
Mean, SD	\$25667 (38892)	\$26648(38315)	\$16871(18536)	\$15573(16848)	\$12539(19682)	\$11758 (18390)	\$1815 (2759)	\$1298 (0, 3570) \$2798 (5082)	fûr (A data	(0) (학 (교	\$43 (234)	\$18197 (31241)	\$18458 (30811)
	rehab program								a n) 			
18 _{Median,}	\$0 (0, 2451)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	3 13	3	\$0	\$0	\$0
1 9 QR		(0, 1913)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,36)	\mathbf{z}	(0.265)	(0, 249)	(0, 478)	(0, 239)
2 M ean, SD	\$2081 (4183)	\$1934 (5316)	\$821 (2236)	\$721 (1991)	\$266 (1026)	\$155 (676)	\$364 (1090)	\$562 (1478)	\$	§ 4 (286)	\$126 (206)	\$1246 (3244)	\$1142 (3976)
	ided at home/nursi								<u>+</u>	<u> </u>			
2 Median,	\$0	\$0	\$1168	\$212	\$922	\$0	\$0	\$0	<u>a</u> \$	S 6 (0)	\$0	\$0	\$0
QR	(0, 717)	(0, 956)	(0, 4299)	(0, 3821)	(0, 11064)	(0, 11064)	(0, 0)	(0, 0)	<u> </u>	<u>克</u> 0)	(0, 0)	(0, 1913)	(0, 1913)
Mean, SD	\$1382 (4069)	\$1551 (4252)	\$3171 (4960)	\$3111 (5754)	\$12085 (28516)	\$11051 (26723)	\$93 (570)	_ , ,		S 27 (719)	\$7 (53)	\$4447 (16294)	\$4180 (15203)
	allied health visit	т	т	 -	т.	т.			<u>a</u>	. <u>c</u>	T .	-	
Median,	N/A	N/A	N/A	N/A	\$0	\$0	\$0		a \$0		\$0	N/A	N/A
26QR	37/4	1	1		(0,0)	(0,0)	(0,0)	(0,179)	<u> </u>	1	(0,0)	37/4	37/4
2 Mean, SD	N/A transfers	N/A	N/A	N/A	\$375 (1144)	\$329 (1291)	\$432 (1521)		-C)	SP(0)	\$0.2 (2)	N/A	N/A
28Ambulance		¢500	60	T 60	T 60	T 60				unge	T 60	\$0	T 00
2 9 Median,	\$508 (0, 1015)	\$508 (0, 1015)	\$0 (0, 646)	\$0 (0, 646)	\$0 (0, 1150)	\$0 (0, 575)	\$0 (0, 265)	\$0 (0, 265)		(19 0)	\$0 (0, 0)	(0, 611)	\$0 (0, 610)
Mean, SD	\$671 (1057)	\$623 (946)	\$543 (1082)	\$605 (928)	\$790 (3209)	\$701 (3150)	\$164 (348)			S6(26)	\$14 (64)	\$627 (1920)	\$578 (1838)
Private phys	` /	\$023 (370)	\$343 (1002)	\$005 (920)	\$190 (3207)	\$/01 (3130)	\$104 (340)		olog	8(20)	\$14 (U+)	\$027 (1920)	\$3/0(1030)
Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0		ges \$	025 (A)	\$0	\$0	\$0
Back Barry	$\begin{vmatrix} 30 \\ (0,0) \end{vmatrix}$	$\begin{pmatrix} \mathfrak{s0} \\ (0,0) \end{pmatrix}$	(0,0)	$\begin{pmatrix} \mathfrak{so} \\ (0,0) \end{pmatrix}$	(0,0)	(0,0)	(0,0)	(0,0)	is ((<u>r</u> .0)	$\begin{pmatrix} 30 \\ (0,0) \end{pmatrix}$	(0,0)	(0,0)
	\$70 (375)	\$124 (797)	\$245 (1308)	\$4 (36)	\$128 (780)	\$174 (2102)	\$238 (1096)	\$333 (1938)	+	9 (19)	\$1 (9)	\$109 (693)	\$132 (1336)
35Respite care		Ψ (, ,)	Ψ= (, -,	, 4.(5.)	_ \$120 (7.5.7)		Ψ=== (,	, , , , , , , , , , , , , , , , , , ,		<u> </u>	, 4 - (-)	()	()
B6Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	<u> </u>	<u></u>	\$0	\$0	\$0
₽ †QR	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(1	(P)	(0,0)	(0,0)	(0,0)
Mean, SD	\$48 (355)	\$20 (182)	\$7 (46)	\$2 (15)	\$9 (95)	\$58 (686)	\$0(0)	\$0 (0)	\$	5 (0)	\$1 (8)	\$27 (259)	\$27 (386)
39	AU (N=1054)	1	NZ (N=189)	+	UK (N=610)		SG (N=128)		N'	V (N=123)		All Countries	
40	VEM	UC	VEM	UC	VEM	UC	VEM	UC		√8 M	UC	VEM	UC
40									$\overline{}$				

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								yrigh:	n-201			
1								g	201			
2 Sub-total								-	7 P P			
Median	\$29278	\$29441	\$20621	\$23722	\$18896	\$20843	\$4525	\$4687	\$ № 13	\$1746	\$19271	\$20411
(IQR)	(8218, 63622)	(9811, 62489)	(6068, 46909)	(7316, 40162)	(4030, 48999)	(3682, 47908)	(1604, 8668)	(2724, 10926) 	(1 ×1 31, 2532)	(1431, 2348)	(6294, 52637)	(7238, 63835)
Mean	\$45620 (51458)	\$47453(53715)	\$28898 (25011)	\$27986(22676)	\$34863 (42509)	\$32842 (39517)	\$7681 (8828)	\$8358 (8787)	\$2385(1587)	\$2269(1574)	\$36351 (45620)	\$36604 (46309)
5 (SD)	4 10 0 2 0 (0 1 10 0)	417 100 (00710)	4-00/0 (-000)	+= / > 0 0 (== 0 / 0 /	40 1000 (1207)	(0,017)	4,000 (0020)	96	Q	4==== (== , 1)	(10000)	40000 (1000)
6					N	on-health care cos	st	0	23			
7 Accommoda	ation moves											
8 Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0		\$0	\$0	\$0
9 IQR	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)	(0,0)		(0,0)	(0,0)	(0,0)
Mean, SD	\$2089 (8518)	\$2482 (9323)	\$5975 (19614)	\$9135 (26918)	\$2901 (12958)	\$2532 (11125)	\$72 (578)	\$108 (507)	m May (N) (N) (1893)	\$104 (501)	\$2460 (11036)	\$2821 (12212)
Community	\ /	\$2402 (7323)	\$3773 (1701 4)	(20710)	\$2701 (12730)	\$2332 (11123)	\$12 (310)	φ100 (307)	13 D	\$104 (301)	\$2400 (11030)	\$2021 (12212)
	\$0	\$0	\$0	60	\$0	\$0	\$0	\$0 5		\$0	\$0	\$0
1 Median, 1 7QR	(0,0)	(0,0)	(0,0)	\$0 (0, 0)	(0, 430)	(0, 174)	(0,0)	(0,0)	1 1 1 1 1 1 1 1 1 1	(0, 0)	(0,0)	(0,0)
13Mean, SD	\$570 (2681)	\$1091 (8556)	\$238 (950)	\$1022 (4113)	\$22275(294988)	\$10738 (57306)		\$244 (1902)	(110)	\$0(0)	\$6870 (160318)	\$3786 (31893)
	` /	\$1091 (8330)	\$238 (930)	\$1022 (4113)	\$22273(294988)	\$10/38 (3/300)	\$0 (0)	3244 (1902)	ngh (110)	\$0 (0)	\$0870 (100318)	\$3/80 (31893)
Home modif		**			• •				<u> </u>			4.0
15 _{Median} ,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	128	\$0	\$0	\$0
1 6 QR	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0, 0)	(0,0)	<u> </u>	(0, 0)	(0, 0)	(0,0)
1 ≯ Mean, SD	\$805 (6338)	\$751 (7715)	\$833 (4862)	\$565 (3204)	\$352 (2133)	\$834 (7091)	\$234 (1079)	\$62 (299)	(369)	\$64 (237)	594 (4840)	\$676 (6734)
18 pecial aids	and equipment							≅	.m d			
₁ Median,	\$0	\$0	\$70	\$103	\$27	\$0	\$0	\$0	3 5	\$36	\$0	\$0
JQR	(0, 332)	(0,318)	(0, 549)	(0, 357)	(0,786)	(0, 846)	(0, 240)	(0, 210)	(0,218)	(0, 186)	(0, 414)	(0, 414)
Mean, SD	\$1986 (7668)	\$2787 (10396)	\$2198 (7993)	\$1798 (7229)	\$1354(3649)	\$1720 (5083)	\$1117 (5843)	\$1079 (5483)	\$53 (252)	\$193 (658)	\$1660 (6426)	\$2141 (8328)
Informal car	re	` '	, ,					5	8			· · · ·
²² Median,	\$24	\$48	\$14	\$0	\$29	\$29	\$0	\$0 5	\$24	\$9	\$24	\$24
2 3 QR	(0, 503)	(0, 455)	(0, 283)	(0, 149)	(0, 471)	(0, 375)	(0, 114)	\$0 (0, 238)	(0.60)	(0, 50)	(0, 407)	(0, 407)
24Mean, SD	\$414 (747)	\$405 (758)	\$236 (536)	\$152 (311)	\$324 (516)	\$324 (645)	\$144 (285)	\$159 (300)	\$43 (57)	\$27 (34)	\$335 (633)	\$322 (660)
25 iving-in ma		\$.00 (700)	\$ 2 55 (655)	ψ10 2 (511)	ψ52 · (€10)	\$52 · (\$ · b)	(200)		6	Ψ= (() .)	<i>\$555</i> (655)	Ψ322 (000)
Median,	N/A	N/A	N/A	N/A	N/A	N/A	\$0	\$0 0	1 . 3	\$0	N/A	N/A
J-JQR	IV/A	1 \ //A	1 V /A	IV/A	1 \ // A	IV/A	(0,0)	\$0 (0,0)	(9 0)	(0,0)	IV/A	1 V //A
Mean, SD	N/A	N/A	N/A	N/A	N/A	N/A	\$3154 (8146)	\$4268(11338)		\$83 (504)	N/A	N/A
Sub-total	IN/A	IN/A	IN/A	IN/A	1 V /A	IV/A	\$3134 (8140)		\ =	\$65 (504)	IN/A	IN/A
120	0.450	¢772	¢201	0(20	Ф 7 50	¢471	025	© 0104	\$74	0.57	\$250	¢420
Median	\$459 (0, 3334)	\$673 (0, 5209)	\$381 (0, 3674)	\$638	\$758 (0, 5097)	\$471	\$25 (0, 1293)	\$194 (0, 6999)	(9, 285)	\$57	\$358 (0, 3334)	\$438 (0, 4561)
(IGIC)		· · /		(103, 14551)		(0, 4725)	· · /	(0, 6999)	(6, 285)	(0, 318)		
Ivican	\$6104 (15582)	\$6985 (17554)	\$7752 (17751)	\$11981(27676)	\$27892(306917)	\$15345(61750)	\$4802 (10366)	\$6177 (13942)	\$81 (2272)	\$484 (1113)	\$12043 (164026)	\$9360 (36504)
32 (SD)						<u> </u>		<u></u>	5 at			
33						Productivity cost		Ç,	2.7		·	
3 Median,	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$6	\$0	\$0	\$0
35QR	(0,0)	(0, 0)	(0,0)	(0,0)	(0, 0)	(0, 0)	(0,0)	(0,0)	(9 0)	(0,0)	(0,0)	(0,0)
Mean, SD	\$75 (317)	\$84 (391)	\$29 (130)	\$14 (54)	\$17 (152)	\$44 (245)	\$6 (29)	\$8 (35)	\$ 8 (4)	\$0.4(3)	\$46 (246)	\$58 (312)
Total cost									<u> </u>			
Median	\$33203	\$35143	\$29934	\$32216	\$25374	\$30537	\$6960	\$8810	\$ ≅ 16	\$1816	\$25675	\$27042
Median 88(IGR)	(9687, 71902)	(12696, 74070)	(8528, 65781)	(15710, 68292)	(4712, 64285)	(4629, 67012)	(1674, 26187)	(3426, 19493)	(2 61, 3994)	(1537, 3301)	(6766, 63617)	(7257, 63824)
BMean (SD)	\$52456(57264)	\$56408(62536)		\$43901(43170)			\$15036(16921)	\$16340(19650)		\$2938(2350)		\$47627(64249)
40		, ,							3			, , ,
41						32			ique			
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/1/1				-								

**c only a loss propertion (r.e. fless Para 595s) of patient regarded certain lyges of resource stiffsation, year median and/or 10R are r.
**satisfs includes a patient's immediate admission to resubdilization hospital on discharge from hospital as the rehabilization service s.

revoked.

**Approve Bibliographique de label of the properties of the

	_	
	QALYs	Per capita mean cost (AUD)
Health care perspective		
Total medical costs	-0.013	\$1082
	(-0.041, 0.016)	(-\$2520, \$4685)
Societal perspective		
Total medical and non-medical	-0.013	-\$6
costs (excl. productivity cost)	(-0.041, 0.016)	(-\$5476, \$5463)
Total medical and non-medical	-0.013	\$102
costs (incl. productivity cost)	(-0.041, 0.016)	(-\$6907, \$7111)
ITT. Intending to the Avent OALVe Overline address	LUIC M. ALID A. I. II	

ITT: Intention-to-treat; QALYs: Quality-adjusted Life Years; AUD: Australian dollar; excl: excluding; incl: including



Table 4 Results of country-specific analysis of costs and benefits

	AU	NZ	UK	SG	MA
	(N=1054)	(N=189)	(N=610)	(N=128)	(N=123)
Total medical	\$948	-\$2836	\$2937	-\$81	\$137
costs	(-\$4352, \$6248)	(-\$8403, \$2730)	(-\$3635, \$9509)	(-\$2789, \$2627)	(-\$324, \$599)
Total non-	-\$1318	-\$3959	-\$1387	-\$3164	\$200
medical costs	(-\$3038, \$403)	(-\$7769, -\$150)	(-\$7331, \$4557)	(-\$6834, \$505)	(-\$232, \$631)
Total cost	-\$1735	-\$8981	\$1870	-\$2636	\$479
(incl.	(-\$8482, 5013)	(-\$18380, \$418)	(-\$13955, \$17694)	(-\$9233, \$3961)	(-\$487, \$1446)
productivity)					
Total cost	-\$1185	-\$7610	\$2552	-\$1534	\$416
(excl.	(-\$7184, \$4815)	(-\$15302, \$82)	(-\$11377, \$16481)	(-\$6464, \$3395)	(-\$364, \$1196)
productivity)					
QALY gains	-0.036	0.086	-0.010	0.008	0.003
	(-0.076, 0.003)	(-0.003, 0.176)	(-0.064, 0.044)	(-0.106, 0.123)	(-0.126, 0.132)

AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia; QALY: Quality-adjusted Life Year.

^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

Supplementary document 1: Mapping baseline mRS score to utility of AQoL-4D

Methods

Generalized additive model (GAM) with spline smother was used to map AQoL from premorbid mRS, stroke severity, and/ or age group. The performance of the models was evaluated using mean absolute, mean squared errors (MAE and MSE) and R2. 10-fold cross-validation was implemented for model validation. The mapped baseline utility of AQoL-4D was used in the following models.

The analyses are structured as follows:

Model 1:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and pre- morbid mRS as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and pre-morbid mRS + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 2:

- a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input;
- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity as a covariate;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output and group as an input + stroke severity and age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 3:

a) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value as a covariate;

- b) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the difference between utility value at 12 months and baseline mapped utility value as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Model 4:

- a) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value as a covariate;
- b) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity as covariates;
- c) A complete case model with the utility value at 12 months as an output, group as an input, and baseline mapped utility value + stroke severity + age group as covariates;
- d) Sensitivity analyses for the unadjusted model using pattern-mixture models that confirm that there is no statistically significant difference between the groups for the plausible range of changes of a parameter that describes the departure from the assumed "missing-at-random" pattern.

Results

Table I. Difference in utility values between treatment groups by different models

	a	b	c	d	
				1	2
Model 1	-0.011	-0.015	-0.016	-0.026	0.006
	(-0.042, 0.020)	(-0.042, 0.011)	(-0.042,0.010)	(-0.062, 0.009)	(-0.030, 0.041)
Model 2*	-0.001	-0.007	-0.008	-0.007	0.005
	(-0.046, 0.044)	(-0.047, 0.034)	(-0.048, 0.031)	(-0.062, 0.048)	(-0.050, 0.060)
Model 3*	-0.008	-0.014	-0.015	-0.014	0.002
	(-0.043, 0.026)	(-0.043, 0.016)	(-0.043, 0.014)	(-0.052, 0.033)	(-0.050, 0.045)
Model 4	-0.008	-0.014	-0.015	-0.026	0.006
			(-0.043, 0.014)	(-0.062, 0.010)	(-0.030, 0.042)

^{*}models 2 and 3 used the mapped baseline AQol utility to estimate the QALY gains over 12 month for each patient.

utility value to calculate the difference in QALYs between treatment groups (results from models 2 and 3) yielded similar results to the primary analysis (-0.013, 95%CI [-0.043, 0.018]), and the 95% confidence

Supplementary document 2: Cost Case Report Form (CRF)

The Cost CRF was originally developed via pathway analysis during Phase II of AVERT to identify resource items associated with the trial 11. Since the Phase II of AVERT trial was a national project and resource utilisation tools were tailored to the Australian setting, the form was further modified to accommodate international differences in the acute service delivery, rehabilitation and post-acute care. An extensive review of country-specific literature and consultation with international AVERT project team members based in each country were undertaken to tailor the Cost CRF tool to each participating country.



Case Report Form - Cost

An	National Strokes
	Research Institige

PATIENT INITIALS

National Strokes:

Research Institute

Note: this one form is to be completed AND faxed following BOTH the 3 and 12 months at 12 months fax all pages 25.36 to the Date Page. When CRF Cost complete at 3 months AND at 12 months, fax all pages 25-36 to the Data Fax.

Instructions to the person responding: These questions are about health care provided as a consequence of the stroke which occurred on (give date of stroke) or as a result of any further stroke. I will be asking about health care such as visits to hospital, rehabilitation, the stroke were provided and their cost.

Subject's stroke date

Subject's stroke date

Obtain from CRE. Severaging Day 0

Obtain fi	rom CRF - Screening Day 0		<u></u>	ext a	nload Supe	
3 MONTH DA	ATE OF ASSESSMENT	//	Assessor initials	nd data	<u> </u>	
PERSON RESPONI	DING	ASSISTANCE FOR IN	NTERVIEW OBTAINED FROM		E IVING ARRANGEMENT O	F RESPONDENT*
Index case □	Other relative \square	Index case □	Other relative	9, /	giving with index	
Spouse/partner	Friend/Associate/Neighbour	Spouse/partner 🗆 🧸	Friend/Associate/Neighbour	<u>≥</u>	Not living with index	
Sibling \square	Carer, e.g. nurse □	Sibling 🗌	Carer, e.g. nurse □	<u>a</u> .	Professional carer in nursing ho	ome or hostel \square
Son/Daughter	Other, unspecified \square	Son/Daughter 🗌	Other, unspecified \square	j	S S S S S S S S S S S S S S S S S S S	offic of floorer
Parent		Parent □		g, an	nj.cc	
12 MONTH DA	ATE OF ASSESSMENT	//	Assessor initials	d similar	n/ on Ju	
PERSON RESPOND	DING	ASSISTANCE FOR II	NTERVIEW OBTAINED FROM	tec	्रो।VING ARRANGEMENT O	F RESPONDENT*
Index case □	Other relative \square	Index case □	Other relative \square	hnologies	with index	
Spouse/partner	Friend/Associate/Neighbour	Spouse/partner	Friend/Associate/Neighbour	90	Sot living with index	
Sibling	Carer, e.g. nurse	Sibling 🗌	Carer, e.g. nurse 🗌	gie	জ Professional carer in nursing h	ome or hostel \square
Son/Daughter	Other, unspecified \square	Son/Daughter	Other, unspecified \square	ÿ	>	offic of flooter 🗖
Parent		Parent □			geno	
					Please note: this is the 'normal' the respondent with respect to the subject is currently in hospital	







Case Report Form - Cost

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1) DISCHARGE)26230 o ncluding		
ate of discharge from acute care	Acute discharge des Home Rehabilitation ward/ho Supported residential Hostel Nursing home Other	stination	Date of admission Date of discharge Leave dates BLAN Please note: inpati inclusive of geriatric transitional care.	to inpatient rehable from inpatient reh K if not applicable ent rehabilitation is	ilifation	Discharge destination after Home Rehabilitation hospital Supported residential service Hostel Nursing home Other	
	Unknown	000	transitional care.	c evaluation and	nd from ht ieur (ABE id data m	Unknown Leave BLANK if not app	□ blicable
2) LIVING ARRANGEMENT					tp:// ining		
re-stroke residential address		Residential address at	t 3 months*		R æ id e ntia	al address at 12 months*	
Own house, flat – alone		Own house, flat – alone			Ogin higuse	e, flat – alone	
Own house, flat – with family/relative/frie	nd 🗆	Own house, flat – with fa	amily/relative/friend		Q∰m h∰use	e, flat – family/relative/friend	
lome of relative/friend		Home of relative/friend			H ğ me ğ f re	lative/friend	
Supported residential service (SRS)		Supported residential se	ervice (SRS)		S group ted	residential service (SRS)	
lostel		Hostel			Heste E		
lursing home		Nursing home			Nersing ho	me	
Other		Other			Ogen 2		
Jnknown		Unknown			O g known		
			ote if the subject is ir current residentia			t (acute or subacute), address	
	For peer revi	iew only - http://hmione	on hmi com/sito/ah	out/quidalines vhtr	de		





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3) CHANGE IN LIVING ARRANGEMENTS	026230 o			
As a consequence of your stroke, have you needed to change your place of residence?	3 moRths2	Yes □	No □ U	nknown 🗆
If NO, proceed to question 4. * Please note: if subject has been a hospital inpatient this is NOT a change of residence	ნ ლ ≦ 3-12 წეტებენიs	Yes 🗆	No □ U	nknown 🗆
DATE OF MOVE LOCATION	2019. Do seigneme s related			
Own home or unit Home of relative/friend SRS Hostel Nursing home	ownloaded ent Superie to text and			
Other Own home or unit Home of relative/friend SRS Hostel Nursing home Other	from http://bmj. ur (ABES) . data mining, Al			
3) /	ttp://bmjopen.bmj.com/ on June 13, 202 ES) . iining, Al training, and similar technolog			
Own home or unit Home of relative/friend SRS Hostel Nursing home Other	202			
4) AMBULANCE TRANSFERS: EMERGENCY AND NON-EMERGENCY	5 at A			
As a consequence of your stroke, have you required ambulance transport after your acute admission to hospital?* If NO, please proceed to question 5	* 3 mogsths	s Yes □	No □	Unknown 🗌
	3-12 g	nths Yes □	No □	Unknown 🗌
Count number of ambulance trips (recruitment to 3 months) * Include post-acute transfers (eg - acute Count number of ambulance trips (from 3 to 12 months)	liographique to rehab)			
For near review only - http://hmignen.hmi.com/site/ahout/quideline	de			ı

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Case Report Form - Cost

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If patient not

discharged at

If NO, proceed to question 6

5) HOSPITALISATION OR EMERGENCY DEP	ARTMENT	ATTENDANCES	0 o			
a) Have you been readmitted to hospital or attended the emr	ergency depar	tment as a consequence of another stroke	of 3 months	Yes 🗆	No 🗆	Unknown 🗆
ONLY include information for admissions and attendances troke-related problems and CRF completion manual for fur			May 2019. Enseigne Ises relate	Yes 🔟	No 🗆	Unknown 🗆
NO, proceed to question 6			Down ment :			
b) If YES, Start with the earliest admission or attendance. If parates BLANK (complete dates at 12 month assessment)		arged at 3 month assessment, leave discharge	ext and data			If patient not discharged a 12 month
Admission or Attendance 1 - Hospital name	Hospital code	Date admitted	from Date of	discharged		assessment cross box.
			http://bi	/		
Admission or Attendance 2 - Hospital name	Hospital code	Date admitted	≥ ₫	discharged		
			ning, /	/		
Admission or Attendance 3 - Hospital name	Hospital code	Date admitted	and si	discharged		
·			Date of June 13, 20	/ 📗		
Admission or Attendance 4 - Hospital name	Hospital code	Date admitted	e 13, 2 Date of	discharged		
Training Training			025 at ogies.]/		
Admission or Attendance 5 - Hospital name	Hospital	Data admitted	Agenc	dicabargad		
Admission or Attendance 5 - Hospital name	code	Date admitted / / / / / / / / / / / / / / / / / / /	© Date	discharged		П
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Stroke related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary catheter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11. Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional pre-lem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting 19. Surgery or procedural management of of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21. Inabies to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26. Pressum sores.

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6)	INPATIENT REHABILITATION ADMISSIO	N					6230 cludi			
	r your stroke on (give date of stroke), were you admitte			-	•	3	moffths S	Yes 🗆	No 🗆	Unknown 🗆
	ere you received rehabilitation treatment? Please includ luation' and 'transitional care'	de adr	nissions with the care	e type 'rehab	oilitation', 'geriatric	3-	12 months	Yes □	No □	Unknown □
If Y	O, proceed to question 7. ES, complete inpatient rehabilitation admission details, state atient NOT discharged at 3 month assessment, leave discharged at 3 month assessment at 3 month as 3 month as 3 month as 3 month as 3 month at 3 month as					sment)	May 2019. Down Enseignement t uses related to t			If patient not discharged at 12 month
	Admission 1- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		Dow d to	Date disch	arged	assessment,
				/	/		nlloade Super text an	//		cross box.
	Admission 2- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		d fro ieur d da	Date disch	arged	
	Admission 2 Renabilitation hospital name				/ 📗		(ABES	//		
	Admission 3- Rehabilitation hospital name		Rehab hospital code	Date	e admitted		ing,	Date disch	arged	
	·				/ 📗		Al tra	//		
7) OUTPATIENT REHABILITATION PROGR	RAM					ning,			
	d you attend or are you attending an outpatient rehabi			nsequence (of your stroke?		3 anong h	ıs Yes 🗆	No [☐ Unknown ☐
Ar loc	 g. with physiotherapy, occupational therapy, speech the noutpatient rehabilitation program is any rehabilitation prograted at a hospital or community facility. 			ends a facilit	y. The program ca	an be	=:	onths Yes 🗆	No [☐ Unknown ☐
If `	NO, proceed to question 8. YES, complete outpatient rehabilitation details, starting from patient NOT discharged at 3 month assessment, leave disc	m you charg	ur first outpatient reha e dates and number	abilitation vis of days atter	it. nded BLANK (com	nplete date	ne 1 tecl	onth assessme	Tota	
	Admission 1 - Outpatient rehabilitation name	Ref	nab facility le	Date admi	tted		o Gate di	ischarged	of Datte	
	Admission 1 - Outpatient renabilitation fiame			/] / 	/		
	Admission 2 - Outpatient rehabilitation name	Reh	nab facility le	Date admi	itted		ာင္စ Date	ischarged		
			 					7		
52036	Admission 3 - Outpatient rehabilitation name	Rel	nab facility le	Date admi	itted		Date ₹	ischarged		
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No □

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Unknown

8) REHABILITATION SERVICES PROVIDED AT HOME OR IN A NURSING HOME

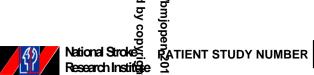
Have you had a rehabilitation program provided to you at home or a nursing home as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech

as a consequence of your stroke? e.g. with	physiotherapy, occupatio	nal therapy, speech		No 🗆 Halmania	
If NO, proceed to question 9. If YES, complete rehabilitation details, starting fr sessions. If patient NOT discharged at 3 month assessment (complete dates at 12 month assessment)	•		S S S S S S S S S S S S S S	No ☐ Unknown	If patient not discharged at
Time 1 - Rehabilitation service name	Rehab service code	Start date	nloadate Superjeur (A Ceand data	Total number of SESSIONS	12 month assessment, cross box.
Time 2 - Rehabilitation service name	Rehab service code	Start date	Cease Cate		
Time 3 - Rehabilitation service name	Rehab service code	Start date	Cease date / and kor		
Time 4 - Rehabilitation service name	Rehab service code	Start date	Cease date / Lech		
			3, 2025 at Age inologies.		





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9) COMMUNITY SERVICES								6230 :Judir		
9a) Did you receive any community services	in the year	PRIOR	to your	stroke?	>			230 on 22 luding for	Yes 🗆	No ☐ Unknown ☐
Community services are individual care self NO, proceed to question 9b. If YES, which service/s did you receive in	the year P	RIOR to	your s	troke?			nabilitation the	erapy. Um many times in the second s	ı	
Community service codes 1 = Nursing Service			∏ 3	☐ 4	. (One st			the past year Harding Downloaded from http://bmjopen.graded to text and data mining, Al training, Al training		
2 = Delivered Meals 3 = Personal Care (Bath/Shower) 4 = Housework help	1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	Superior and		
5 = Gardening/home maintenance 6 = Home respite 7 = Other service, specify	_		□ 3 -	☐ 4	□ 5 —	□ 6 —	□ 7 —	I from July (AE) data i		
7 - Other Service, Specify	☐ 1 If "othe	_	☐ 3 : 7), ple	☐ 4 ase spe	☐ 5 cify	□ 6	□ 7	http://i		
			_ _					, Al tra		
9b) Have you received community services S Community services are individual care s			t home	and do	NOT incl	ude reb	abilitation the	Stany 3 IIIOI Bis 5		D ☐ Unknown ☐
If NO, proceed to question 10.	•		t Home	and do		uue ieii	abilitation the	3-12 months	Yes ☐ No	Unknown 🗆
If YES, which service/s did you receive Al For each service, complete a seperate lin- months, and then add service data for 3-1	e. If a servi	ce is on			th interv	iew, ent	er data for 3	How many m	How many hours	Note: hours per service NOT applicable to
	Which	service	did you	receive	? (One s	ervice o	ode per line)		per service?	
Community service codes 1 = Nursing Service	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□7	chnologie		
2 = Delivered Meals 3 = Personal Care (Bath/Shower)		□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	13, 2025 at Agence Bibliographique chnologies.		
4 = Housework help 5 = Gardening/home maintenance 6 = Home respite	□ 1 —	□ 2 —	☐ 3 —	☐ 4 —	□ 5 —	□ 6 □	□ 7 —	\dagger \dagger \q		
7 = Other service, specify	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	e B		
	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	Diliog		
52036	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	raph		
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	RATIENT STUDY NUMBER						
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10) HOME MODIFICATIONS			.026230 includir			
Has your home been modified as a conseque		- 1161	ş Şmontt	n s Yes □	No 🗆	Unknown
e.g. installation of rails, bathroom modification f NO, proceed to question 11	ons, installation of ramp(s), kitchen m	odifications etc	了 2 ~ 表 紹整	onths Yes 🗌	No 🗆	Unknown
If YES, please indicate the type of modifications	, who supplied the modifications and est	imate any personal cost to you	ay 201 nseigi es reli			
Type of modification	SUPPLIERS 1 = Hospital/rehabilitation centre 2 = Patient/family	3 = Veteran's Affairs 4 = Local Council	5 = Ho&s∄nego 5 = Ho&s∄nego 6 = Charte	ommision	7 = Ot	her (specify
(check box for each type supplied)	Who supplied the modification	tion? If supplier is	"other", pl စ္ကာ	ecify		
☐ Rail(s) for steps/stairs	□1 □2 □3 □4 □	5 🗆 6 🗀 7 📗 📗	and and	Cost to you/fa	mily* - \$	
☐ Ramp(s)	_1 _2 _3 _4 _:	5 🗆 6 🗀 7 📗 📗	from data	Cost to you/fa	nmily* - \$	
☐ Platform step(s)	_1 _2 _3 _4 _:	5 🗆 6 🗀 7 📗 📗	ittp://b	Cost to you/fa	mily* - \$	
☐ Shower, bath and toilet rail(s)	1234!	5 🗆 6 🗀 7 📗 📗	Al tra	Cost to you/fa	mily* - \$	
☐ Shower(s) modification	1234 <u></u>	5 🗆 6 🖂 7 📗 📗	ining n.bm	Cost to you/fa	mily* - \$	
☐ Toilet(s) modification	1234 <u></u>	5 🗆 6 🗆 7 📗 📗	and si	Cost to you/fa	mily* - \$	
☐ Remove/modify door(s) from shower/toilet/bath	□1 □2 □3 □4 □	5 🗆 6 🗆 7 📗 📗	imilar t	Cost to you/fa	amily* - \$	
☐ Kitchen modifications	1234 <u></u>	5 🗆 6 🗆 7 📗 📗	ne 13, techno	Cost to you/fa	amily* - \$	
Other modification (specify below)			2025 a			
Other home modification - 1	<u> </u>	5	at Age	Cost to you/fa	mily* - \$ [
Other home modification - 2	1 2 3 4 5	5)nce B	Cost to you/fa	mily* - \$	
	-' '		_'' _ _	' n overall cost is prov	ided nle	ase indicate
If total costs includes any aids, describe i	in brief below (see also list of aids on	page 33): 	type togal	of modifications abo	ve, and p 'E of any l	rovide the
			Tem liem	ised costs listed abo Overall Cost		



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11) SELCIAL EQUIFIVILIATI AND A	4103		<u>¥</u> 8		
Have you been given, hired or purchased an	y special equipment, aids or special	food as a consequence of stroke?	T N	Yes 🗌	No ☐ Unknown ☐
			3-12 ខ្លាំ 	Yes 🗌	No ☐ Unknown ☐
Prompt: These may have been provided by an If NO, proceed to question 12	Occupational Therapist or Physiothera	pist. What about a?	May 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 a finseignement Superieur (ABES) . Ses related to text and data mining, Al training, and similar technologies to text and data mining.		
Walking aids	Mobility aids	Eating aids	. Dov ed to		Kitchen aids
☐ Single point stick	☐ Manual wheelchair	☐ Built-up cutlery	vnlo It Su It ex		☐ Tap handles
☐ Three or four point stick	☐ Electric wheelchair/scooter	☐ Plate guard	ade Iperi t an		☐ Chopping board
☐ Walking frame - pick up	☐ Car steering wheel knob	☐ Non-slip mat	d fro d da		☐ Modified knife
☐ Walking frame - wheelie		☐ Special food e.g. NG/PEG	ata n		☐ Vitamiser/blender
☐ Walking frame - gutter (forearm suppt)		If yes, number of days used:	ninir		☐ Non-slip mat
☐ Crutch(es)		3 months	/bn		_ non-enp man
		3-12 months	≱ tra		
			ainir		
			າ <u>ຫ</u> ຼຸ່.		
Lounge and bedroom equipment	Bathroom equipment	Continence aids	and Com		General aids
☐ Chair platform/blocks raise	☐ Over-toilet seat	☐ Urine bottle	y on sim		☐ Long handled aid
☐ Cushion to relieve pressure	☐ Toilet surround	☐ Bedpan	ilar		☐ Blood pressure machine ☐ Treadmill
☐ Special chair (NOT wheelchair)	☐ Bathroom and grooming aids	☐ Commode	ne 1 tech		☐ Stationary bike
☐ Table - bedside/wheelie	☐ Shower chair/stool	☐ Incontinence sheet (bed prote	ctor) 3, 20		☐ Intercom (portable)
☐ Bed platform/block raise	☐ Over bath seat	☐ Incontinence sheet (kylie/blue))25 a		☐ Modified tap handles
☐ Bedstick	☐ Hand held shower	If yes, number of days used - 3 mo	 		If yes, number supplied
☐ Hospital bed (eg - height/tilt adjust)	☐ Non-slip mat	☐ Incontinence pads 3-12 mg	onths 🖁		
☐ Mobile hoist/lifter		If yes, number of days used - 3 mo	onths P		☐ Personal alarm If yes, number of days supplied:
Any other aids/equipment, specify		☐ Catheter 3-12 mg	onths 6		3 months
		If yes, number of days used - 3 mo	onths $\frac{3}{2}$		3-12 months
,		3-12 ma	onths 5		

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PATIENT INITIALS

NOTE: this one form is to be completed AND faxed following BOTH the 3 and 12 months region.

When CRF Cost complete at 3 months AND at 12 months, fax all pages 25-36 to the Deta Fax.

Instructions to the person responding: These questions are about health care provided as a consequence of the stake which occurred on (give date of stroke) or as a result of any further stroke. I will be asking about health care such as visits to hospital, rehabilitation, the at the community, and to you and your family, I will be asking about how often service were provided and their cost.

	Subject's stroke date rom CRF - Screening Day 0			d to text a	Ownload
3 MONTH DA	TE OF ASSESSMENT	//	Assessor initials	nd data m	fro
PERSON RESPONI	DING	ASSISTANCE FOR IN	ITERVIEW OBTAINED FROM	inin	VIVING ARRANGEMENT OF RESPONDENT*
Index case ☐ Spouse/partner ☐ Sibling ☐ Son/Daughter ☐ Parent ☐	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	Index case ☐ Spouse/partner ☐ Sibling ☐ Son/Daughter ☐ Parent ☐	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	g, Al training, an	Siot living with index Professional carer in nursing home or hostel
12 MONTH DA	ATE OF ASSESSMENT	/ / / / / / / / / / / / /	Assessor initials ITERVIEW OBTAINED FROM	d similar te	S S EIVING ARRANGEMENT OF RESPONDENT
Index case Spouse/partner Sibling Son/Daughter Parent	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	Index case Spouse/partner Sibling Son/Daughter Parent	Other relative Friend/Associate/Neighbour Carer, e.g. nurse Other, unspecified	technologies.	Living with index Story Professional carer in nursing home or hostel
					Please note: this is the 'normal' living arrangement of the respondent with respect to the subject, even if the currently in hospital







Case Report Form - Cost

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RATIENT :	STUDY NUMBER					
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1) DISCHARGE				26230 c		
Date of discharge from acute care	Acute discharge des	stination	Date of admission to inp	atient rehabil c ati e	Discharge destination a	after inpatient rehab
	Home			use	Home	
	Rehabilitation ward/h	ospital 🔲		y 20	Rehabilitation hospital	
	Supported residential	service (SRS) 🗆	Date of admission to inp	山山山山島東京。 ubatient tenaemagano	Supported residential ser	vice (SRS) □
	Hostel			Down down to		
	Nursing home		Leave dates BLANK if no	ot applicable $\overset{\leftarrow}{S}$	Nursing home	
	Other		Please note: inpatient reh inclusive of geriatric evalu	nabilitation is and	Other	
	Unknown		transitional care.	ot applicable nabilitation and attain	Unknown	
			 	ata m	Leave BLANK if not a	pplicable
2) LIVING ARRANGEMENT				ttp://		
Pre-stroke residential address		Residential address	at 3 months*	Ræsiden	tial address at 12 months*	
Own house, flat – alone		Own house, flat – alon	ne 🗆	Ogn hogu	se, flat – alone	
Own house, flat – with family/relative/frie	end 🗆	Own house, flat – with	family/relative/friend □	Qan hagu	se, flat – family/relative/frien	d 🗆
Home of relative/friend		Home of relative/friend	d 🗇	H o me o f	relative/friend	
Supported residential service (SRS)		Supported residential	service (SRS)	S supposte	ed residential service (SRS)	
Hostel		Hostel		Heste E		
Nursing home		Nursing home		Norsing h	nome	
Other		Other		Ober 2025 Uniknown		
Unknown		Unknown		U n knowr	1	
			note if the subject is curren eir current residential addre			
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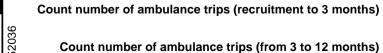
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3) CH	ANGE IN LIVING ARRANGE	MENTS			(0)	•			
	sequence of your stroke, have you r	needed to change your p	place of residence?		3 moRths	Yes □	No 🗆	Unknown 🗆	
	oceed to question 4. note: if subject has been a hospita	I inpatient this is NOT a	change of residence		3-12 (h)	ns Yes □	No □	Unknown 🗆	
	DATE OF MOVE	LOCATION			eignem related	9019			
1)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			ment Superieur (ABES) . ed to text and data mining, Al training, and similar techn	Downloaded fr			
2)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			(ABES) . ata mining, AI t				
3)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other			raining, and si	nes hai com/			
4)		Own home or unit Home of relative/friend SRS Hostel Nursing home Other		0,		n line 13 2025			
4) AN	IBULANCE TRANSFERS: E	MERGENCY AND	NON-EMERGENCY		jies.	л 9 +			
As a coi	nsequence of your stroke, have you	required ambulance tra	nsport after your acute adm	nission to hospital	?* 3 mol	D	П МоГ	I Unknown □	

If NO, please proceed to question 5

3 mogths	Yes 🗆	No 🗆	Unknown 🗌
P			
3-12 months	: Yes □	No □	Unknown □





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Case Report Form - Cost

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PATIENT II	NITIA	LS			

No □

No □

Unknown

Unknown

If patient not

12 month

discharged at

5) HOSPITALISATION OR EMERGENCY DEPARTMENT ATTENDANCES

5a) Have you been readmitted to hospital or attended the emergency department as a consequence of another stroke or for any stroke related problems?

Yes Dounths

Yes Dounths

Yes Dounths

**ses related to text and **

**ses related to text and **

**ses related to text and **

**ses related to text and ** (ONLY include information for admissions and attendances for stroke-related problems (see below for summary list of stroke-related problems and CRF completion manual for further clarification)

If NO, proceed to question 6

5b) If YES, Start with the earliest admission or attendance. If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

Hospital

Admission or Attendance 1 - Hospital name	code	Date admitted	ਕੂ ਨੂੰ Date discharged	cross box.
			http://b	
Admission or Attendance 2 - Hospital name	Hospital code	Date admitted	Al mjop Date discharged	
Admission or Attendance 3 - Hospital name	Hospital code	Date admitted /	and similar to no June discharged	
Admission or Attendance 4 - Hospital name	Hospital code	Date admitted /	on June 13, 2025 at A	
Admission or Attendance 5 - Hospital name	Hospital code	Date admitted /	Date discharged	



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Stroke related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary cataleter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11. Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional pre-lem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting 19. Surgery or procedural management of of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21. Inabies to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26. Pressum sores.

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3 **∃** 2 n**gonths** Yes □

Yes

Yes □

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6230				
0				

No □

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No 🗆

Total

number

Unknown □

Unknown □

Unknown

If patient not

12 month

discharged at

discharged at

After your stroke on (give date of stroke), were you admitted to a Rehabilitation Hospital or other hospital where you received rehabilitation treatment? Please include admissions with the care type 'rehabilitation', 'geriatric evaluation' and 'transitional care'

If NO. proceed to question 7.

If YES, complete inpatient rehabilitation admission details, starting from your first inpatient rehabilitation admission. If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

e you received rehabilitation treatment? Please include ad ation' and 'transitional care'	missions with the care	type 'rehabilitation', 'geriatric	3-12 months	Yes 🗆	No 🗆	Unknown □
proceed to question 7. 5, complete inpatient rehabilitation admission details, starting ent NOT discharged at 3 month assessment, leave discharge			ay 201 nseig es rel			If patient not discharged a 12 month
Admission 1- Rehabilitation hospital name	Rehab hospital code	Date admitted	Dowr nent d to 1	Date discha	ırged	assessment, cross box.
OA			Super Super text ar	//		
Admission 2- Rehabilitation hospital name	Rehab hospital code	Date admitted	∌d fror ieur (ıd dat	Date discha	ırged	
			h http ABES a min	//		
Admission 3- Rehabilitation hospital name	Rehab hospital code	Date admitted	ing, ,	Date discha	rged	
			Noper Al trail	//		
			<u> </u>			

7) OUTPATIENT REHABILITATION PROGRAM

Did you attend or are you attending an outpatient rehabilitation program as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech therapy, etc

An outpatient rehabilitation program is any rehabilitation program where the patient attends a facility. The program can be located at a hospital or community facility.

If NO, proceed to question 8.

If YES, complete outpatient rehabilitation details, starting from your first outpatient rehabilitation visit.

If patient NOT discharged at 3 month assessment, leave discharge dates and number of days attended BLANK (complete dates a 12 fflonth assessment)

Admission 1 - Outpatient rehabilitation name	Rehab facility code	Date admitted	Lance discharged	of DAYS attended	assessment, cross box.
		/] [] / E / [] / []		
Admission 2 - Outpatient rehabilitation name	Rehab facility code	Date admitted	ਨ੍ਹ Date <mark>ਉ</mark> lischarged		
		//			
Admission 3 - Outpatient rehabilitation name	Rehab facility code	Date admitted	ਤੂੰ Dateਕ੍ਰੀischarged		
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Case Report Form - Cost

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8) REHABILITATION SERVICES I	PROVIDED AT HOME	OR IN A NURSING			
Have you had a rehabilitation program provided to you at home or a nursing home as a consequence of your stroke? e.g. with physiotherapy, occupational therapy, speech		3 months of N	No ☐ Unknow	n 🗆	
If NO, proceed to question 9. If YES, complete rehabilitation details, starting sessions. If patient NOT discharged at 3 month assessm	from the first visit since your s	stroke. Count number of	3-12 montures related to te	No □ Unknown	If patient not
(complete dates at 12 month assessment) Time 1 - Rehabilitation service name	Rehab service code	Start date	žť o a Čte o o o o o o o o o o o o o o o o o o o	Total number of SESSIONS	discharged at 12 month assessment, cross box.
Time 2 - Rehabilitation service name	Rehab service code	/ /	dat American		Ш
	Rehab service		g, Alltrair		
Time 3 - Rehabilitation service name	code	Start date /	Cease date /		
Time 4 - Rehabilitation service name	Rehab service code	Start date	Cease date / tech		
			3, 2025 at A mologies.		





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							nt, inc	8-020	PAT	TIENT INITIAL	.s _ _
9) COMMUNITY SERVICES							udin	-026230			
9a) Did you receive any community s	ervices in the year l	PRIOR to you	stroke	?			g for	on 2	Yes □	No □	Unknown 🗌
Community services are individua	al care services pro	vided at home	and do	NOT inc	lude reh	nabilitation th	nerapy. с п	22 M			
If NO, proceed to question 9b. If YES, which service/s did you re	ceive in the year PR	IOR to your s	troke?				How many times				
	-	rvice did you		? (One se	ervice co	ode per line)	the past year Sig receive the serve				
Community service codes		∃2 □3	□ 4	5	□6			Do			
1 = Nursing Service 2 = Delivered Meals		J- LJ	ш-	П	υ	ш,					
3 = Personal Care (Bath/Shower	r)]2	□ 4	□ 5	□ 6	□ 7	ext and	ade			
4 = Housework help 5 = Gardening/home maintenand	ce 🛮 🗘 1	2 3	□ 4	□ 5	□ 6	□ 7		inloaded from			
6 = Home respite 7 = Other service, specify				_ 			data mi) T			
]2	4 ase spe	☐ 5 cify	□ 6	□ 7	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□) -5			
					1 1	1 1 1	ng, /	://bm			
	<u> </u>	_ _ _	_		_		Al tra	jop			
o) Have you received community ser								4			_
				NOT			3 mon∰ns	Yes		No 🗌 Unkı	nown 🗆
Community services are individua If NO, proceed to question 10.			and do	NOT incl	ude reh	abilitation the	erapy. 3 months 3-12 mon	3			nown 🗆
Community services are individua If NO, proceed to question 10. If YES, which service/s did you red	I care services prov ceive AFTER your s	rided at home troke?					erapy. ద	3			
Community services are individua If NO, proceed to question 10.	Il care services prov ceive AFTER your st erate line. If a servic	rided at home troke? e is ongoing a	at 3 mon				erapy. 3-12 mon 3-12 mon Simon How many	ths Yes	□ How many	No □ Unkı	nown □
Community services are individua If NO, proceed to question 10. If YES, which service/s did you rec For each service, complete a sepe	Il care services prov ceive AFTER your st erate line. If a servic a for 3-12 months or	rided at home troke? e is ongoing a	at 3 mon ine.	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12	ths Yes		No □ Unkı Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a sepemenths, and then add service data	Il care services prov ceive AFTER your st erate line. If a servic a for 3-12 months of Which se	rided at home troke? e is ongoing a n a separate li	at 3 mon ine.	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	mtcom/ on Juge 13,	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a sepermenths, and then add service data community service codes 1 = Nursing Service	ceive AFTER your sterate line. If a service a for 3-12 months of Which se	rided at home troke? e is ongoing a n a separate li ervice did you 2 3	at 3 mon ine. ı receive □ 4	th interv e? (One s	iew, ent ervice c □ 6	er data for 3 code per line)	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	mtcom/ on Juge 13,	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a seperation and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals	Il care services proviceive AFTER your sterate line. If a service a for 3-12 months of Which services 1	vided at home troke? e is ongoing a n a separate li ervice did you	at 3 mon ine. ı receive	th interv	iew, ent	er data for 3	erapy. 3-12 mon 3-12	Yes Yes ? ? Yee 13, 2025	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individual If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showed 4 = Housework help	ceive AFTER your sterate line. If a service a for 3-12 months on Which service 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	rided at home troke? e is ongoing a n a separate li ervice did you 2 3	at 3 mon ine. ı receive □ 4	th interv e? (One s	iew, ent ervice c □ 6	er data for 3 code per line)	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	Yes Yes Ngcom/on Jugge 13, 2025 at	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4	th interv	iew, entervice co	er data for 3 code per line) 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	Yes Yes Ngcom/on Jugge 13, 2025 at	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe 4 = Housework help 5 = Gardening/home maintenan	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4 4	th interv	iew, entervice colored for the	er data for 3 code per line) 7 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	ກະ Ye ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ ກະ	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individua If NO, proceed to question 10. If YES, which service/s did you reconstruction for each service, complete a separate months, and then add service data community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showe 4 = Housework help 5 = Gardening/home maintenan 6 = Home respite	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4	th interv	iew, entervice co	er data for 3 code per line) 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	es Ye Mgcom/ on Juge 13, 2025 at Agence Bib	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
Community services are individual If NO, proceed to question 10. If YES, which service/s did you red For each service, complete a septemonths, and then add service data Community service codes 1 = Nursing Service 2 = Delivered Meals 3 = Personal Care (Bath/Showeded Housework help) 5 = Gardening/home maintenanded Home respite 7 = Other service, specify	ceive AFTER your sterate line. If a service a for 3-12 months of Which service	rided at home troke? e is ongoing a n a separate li ervice did you 2	at 3 mon ine. receive 4 4 4 4	th interv	iew, entervice colored for the	er data for 3 code per line) 7 7 7 7	erapy. 3-12 mon 3-12 mon o inc. How many min times did you receive the serv	es Ye Mgcom/ on Juge 13, 2025 at Agence Bib	☐ How many hours	No ☐ Unki / Note: ho NOT app	nown □ ours per servic olicable to
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10) HOME MODIFICATIONS			Research Instiffate 018-026230	
las your home been modified as a conse			amonths	Yes ☐ No ☐ Unknown ☐
f NO, proceed to question 11	ications, installation of ramp(s), kitchen mo		55 12 Boonths	Yes No Unknown
	SUPPLIERS 1 = Hospital/rehabilitation centre 2 = Patient/family	3 = Veteran's Affairs 4 = Local Council	5 = Housing commis 6 = Character	ion 7 = Other (specify)
Type of modification (check box for each type supplied)	Who supplied the modificati	ion? If supplier is	s "other", plage	
☐ Rail(s) for steps/stairs	□1 □2 □3 □4 □5	6 🗆 6 🗆 7 📗 📗	aded peric and	Cost to you/family* - \$
☐ Ramp(s)	□1 □2 □3 □4 □5	6	<u></u>	Cost to you/family* - \$
☐ Platform step(s)	□1 □2 □3 □4 □5	6 🗆 7	nttp://b	Cost to you/family* - \$
☐ Shower, bath and toilet rail(s)	□1 □2 □3 □4 □5	6 🗆 7 📗 📗	_ <u> </u> _ <u></u>	Cost to you/family* - \$
☐ Shower(s) modification	□1 □2 □3 □4 □5	6 07	<u> </u>	Cost to you/family* - \$
☐ Toilet(s) modification	□1 □2 □3 □4 □5	6 6 7		Cost to you/family* - \$
☐ Remove/modify door(s) from shower/toilet/bath	□1 □2 □3 □4 □5	6	<u> </u>	Cost to you/family* - \$
☐ Kitchen modifications	□1 □2 □3 □4 □5	6 🗆 7 📗 📗	ne 13,	Cost to you/family* - \$
☐ Other modification (specify below) Other home modification - 1			ne 13, 2025 a technologie	
		5	s: Age	Cost to you/family* - \$
Other home modification - 2	12345	6 🗆 7 📗 📗	nce B	Cost to you/family* - \$
If total costs includes any aids, descr	ibe in brief below (see also list of aids on p	page 33):	tyge of mod	all cost is provided, please indicate difications above, and provide the here, INCLUSIVE of any known
			itemised co	osts listed above: Overall Cost \$

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Case Report Form - Cost

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11) SPECIAL EQUIPMENT AND	AIDS		6230) Judin		
lave you been given, hired or purchased an	y special equipment, aids or special	food as a consequence of stroke?	a mogiths	Yes □	No ☐ Unknown ☐
			3-12 gn gn sh	s Yes 🗆	No ☐ Unknown ☐
Prompt: These may have been provided by ar f NO, proceed to question 12	n Occupational Therapist or Physiothera	apist. What about a?	/ 2019. seigner s relate		
Walking aids	Mobility aids	Eating aids	men d to		Kitchen aids
☐ Single point stick	☐ Manual wheelchair	☐ Built-up cutlery	vnlo t Su tex		☐ Tap handles
☐ Three or four point stick	☐ Electric wheelchair/scooter	☐ Plate guard	aded perie t and		☐ Chopping board
☐ Walking frame - pick up	☐ Car steering wheel knob	☐ Non-slip mat	d fro eur d da		☐ Modified knife
☐ Walking frame - wheelie		☐ Special food e.g. NG/PEG	rom h r (ABI lata m		☐ Vitamiser/blender
☐ Walking frame - gutter (forearm suppt)		If yes, number of days used:	http://b BES) . mining,		☐ Non-slip mat
☐ Crutch(es)		3 months	g, A		
		3-12 months	l tra		
			ining		
Lounge and bedroom equipment	Bathroom equipment	Continence aids	Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 (ment Superieur (ABES) . id to text and data mining, Al training, and similar technologie		General aids
☐ Chair platform/blocks raise	Over-toilet seat	☐ Urine bottle	nd si		☐ Long handled aid
☐ Cushion to relieve pressure	☐ Toilet surround	□ Bedpan	mila		☐ Blood pressure machine
☐ Special chair (NOT wheelchair)	☐ Bathroom and grooming aids	☐ Commode	r tec		☐ Treadmill
☐ Table - bedside/wheelie	☐ Shower chair/stool	☐ Incontinence sheet (bed protect	tor) in 3, 3		☐ Stationary bike
		☐ Incontinence sheet (kylie/blue)	ctor) ologic		☐ Intercom (portable)
☐ Bed platform/block raise	Over bath seat		<u> </u>		☐ Modified tap handles If yes, number supplied
Bedstick	☐ Hand held shower	If yes, number of days used - 3 mo	 	\dashv	
☐ Hospital bed (eg - height/tilt adjust)	☐ Non-slip mat	☐ Incontinence pads 3-12 mg			☐ Personal alarm
☐ Mobile hoist/lifter		If yes, number of days used - 3 mc			If yes, number of days supplied:
Any other aids/equipment, specify		☐ Catheter 3-12 mg	onths E		3 months
		If yes, number of days used - 3 mo	onths 2		3-12 months
		3-12 mg	onthe	7	







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Case Report Form - Cost

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12) PRIVATE PHYSIOTHERAPY					including				
Have you paid for private physiotherapy sessions after your st	roke? (NOT while	a hospital inpa	tient)		3 months	Yes 🗌	No 🗆	Unknown 🗌	
If no, proceed to question 13					3-12 m om t	s Yes 🗆	No 🗆	Unknown 🗌	
If yes, number of sessions - 3 months					nei ate				
3-12 months					nent : d to t				
13) RESPITE CARE					Supe ext a				
As a consequence of your stroke, have you been admitted to a	respite bed in a r	nursing home o	hospital		3 mongree of	Yes 🗆	No 🗆	Unknown 🗌	
If NO, proceed to question 14					3-12	s Yes 🗆	No 🗆	Unknown 🗌	
f yes, how many days of respite have you received since your s	stroke? 3 month	ns			(ABES) . atamining, Al tra				
	3-12 month	is			g, Al ı				
					njopen.bmj Al training,				
14) EMPLOYMENT STATUS/ PAID WORK					<u>a</u> <u>c</u>				
Were you working up to the time of your stroke? $\gamma_{es} \square$	No □ L	Jnknown □			om/ on Ju nd similar ⊓e □				
If YES, wh	nat was the nature	of this work?	Full time	☐ Part tir	imilar ted				
How many	hours did you worl	k each week?			h 13,				
Since the stroke, have you returned to this work?	3 months	Yes 🗆	No □ L	Jnknown 🗌	2025 ologie				
	3-12 months	Yes 🗌	No □ L	Jnknown 🗆					
Have you returned to normal hours or decreased hours?	3 months	Norma	al 🔲 De	ecreased 🗆	gence				
	3-12 months	Norma	al 🔲 De	ecreased 🗆	Bibliogi				
How many hours per week of work have you performed since	e the last assessr	ment?			liogra				
Record average amount per week over the 3		If more tha	ın 0 but le	ess than 1hi	າ, record a ຂ ຊຸດ ເອ	1			
Record average amount per week over the period 3	to 12 months	I I			Ö				

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Case Report Form - Cost

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RATIENT STUDY NUMBER			
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	PATIENT INITIALS		
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15) INFORMAL CARE - 3 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hospital in patients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at home Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the carer is the person who provides most of this help beyon provided by any formal support services.

15a) OVER THE LAST WEEK, have you received any assistance with your daily activities from a carer as a result of the stroker.

This might include assistance with community tasks (such as help with your banking, paying your

bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning) or assistance with personal care tasks (such as bathing, toileting and feeding)

If the answer is NO, no further questions are required in this section

15b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to question 15c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening; handyman tasks; grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to guestion 15d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

15d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

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Yes

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Yes

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Case Report Form - Cost

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16) INFORMAL CARE - 12 MONTHS

NOTE: This question only applies to patients living at home (ie - excludes subjects in residential care and/or current hos⊞ital inpatients)

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at come. Any assistance provided by an informal carer is over and above the assistance provided by any formal support service. A carer is usually a spouse or other member Ama family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyon to any formal support services. Assistance that a carer may provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with community tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking in the base, feeding). Supervision of daily activities to ensure safety should also be included as care.

16a) OVER THE LAST WEEK, have you received any assistance with your daily activities from a carer as a result of This might include assistance with community tasks (such as help with your banking, paying your	the strន្ទ្រីឌ្គែទ្ធិ
This might include assistance with community tasks (such as help with your banking, paying your	nd ried
bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning)	from ur (A data
or assistance with personal care tasks (such as bathing, toileting and feeding)	a € ×

If the answer is NO, no further questions are required in this section

16b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with COMMUNITY tasks?

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to guestion 16c)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16c) OVER THE LAST WEEK did you receive any assistance with DOMESTIC tasks?

Examples of assistance with domestic tasks include: gardening: handyman tasks: grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to question 16d)

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

16d) OVER THE LAST WEEK did you receive any assistance with PERSONAL CARE tasks?

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions.

If YES, can you estimate how many hours your carer spent helping you with these tasks during the last week?

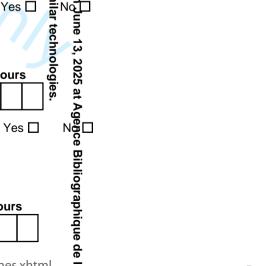
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Supplementary document 3: Unit costs and valuation of costs

Unit costs for hospitalisation, rehabilitation, non-health sector costs and productivity costs

Acute stroke hospitalisation costing: Unit costs for acute stroke hospitalisation for all countries at baseline were categorised by stroke severity, using the National Institute of Health Stroke Scale (NIHSS) to group patients into three severity levels: mild (0-7), moderate (8-16) and severe (>16). (1)·(2) It was assumed that severity as classified by the NIHSS was consistent with the stroke severity that corresponded to three levels of unit cost for acute hospitalisation. Length of Stay (LoS) together with stroke severity were used to estimate the cost of acute hospitalisation for Australia and New Zealand patients (i.e. the cost of acute hospitalisation was weighted by the LoS). LoS was taken as the difference between the date of hospital discharge and date of hospital admission (plus one day or not) in accordance with country-specific practice. For the other countries, only stroke severity was considered in the assignment of a unit cost to acute stroke hospitalisation due to insufficient health sector data.

Re-hospitalisation and rehabilitation costing: Due to the diversity of causes for patients being readmitted to hospital after the index stroke, the average daily cost of hospitalisation for all disease conditions from individual countries in combination with LoS was used to gauge the cost of readmission for stroke-related causes, while the average cost for an emergency department visit was assigned whenever a patient was hospitalised for one day only. Similarly, the unit cost of rehabilitation hospital admission was taken from the national average cost for all disease conditions. The median cost was used where there was more than one unit cost identified for the same resource item.

Non-health sector costs: Unit costs of non-health sector resource items (e.g. community service, accommodation changes, special aids and equipment) were sourced on a country- specific basis from official websites or published literature where applicable. No unit cost was retrieved for home modification items since the cost of home modifications was generally reported in the Cost CRF.

Productivity cost: Lost productivity was valued based on a human capital approach using average earnings across all occupations up to normal retirement age. The average wage of a

The currency of other countries was converted to AUD using the corresponding exchange rate. The country-specific Consumer Price Index (CPI) from the health sector was employed to adjust costs not valued in the year of 2015.

All the unit costs from participating countries are summarised in Table I.

Table I. Unit cost (in Australian dollars) across five countries, 2015 reference year

Resource items	Unit cost (AUD)						
	AU	NZ	UK	SG	MA		
Healthcare							
Acute hospitalisation*							
Severe (per episode)	\$19157	\$10867	\$15327	\$4371	\$2066		
Moderate (per episode)	\$9553	\$6104	\$8115	\$2126	\$1572		
Mild (per episode)	\$6279	\$4370	\$4272	\$1493	\$1363		
Stroke-related rehospitalisation (per day)	\$1925	\$320	\$701	\$789	\$230		
Emergency department attendance (per attendance)	\$610	\$325	\$227	\$111	\$68		
Rehabilitation hospital admission [†]							
Severe (per episode)	\$1010 [‡]	\$8032	\$19136 [§]	\$157 [‡]	\$1293		
Moderate (per episode)	1	\$5727	\$29788 [§]				
Mild (per episode)	1	\$5727	\$13920 [§]				
Same day (per episode)	1	\$758	N/A				
Outpatient rehab visit (per/session)	\$239	\$164	\$213	\$36	\$17		
Rehab services at home/nursing	\$239	\$212	\$922	\$36	\$51		
facility (per/session)							
Private physiotherapy (per session)	\$64	\$153	\$162	\$116	\$8		
Respite care (per hour)	\$45	\$14	\$26	\$15	\$2		
Individual allied health visit							
Physiotherapy	N/A	N/A	\$243	\$239	\$8		
Occupational therapy	N/A	N/A	\$243	\$36	\$7		
Speech and language therapy	N/A	N/A	\$69	\$36	\$4		
Ambulance transfer	\$508	\$646	\$575	\$265	\$52		
Non-healthcare							
Community services	Not listed i	here due to t	the number of	îtems -			
Home modifications	Cost was p	rovided by	individual pat	tients			
Special aids and equipment	Not listed here due to the substantial number of items						
Accommodation changes	Not listed here due to the number of items						
Professional carer (per hour)	\$24	\$14	\$14	\$10	\$2		
Living-in maid (per month)	N/A	N/A	N/A	\$571	\$103		
Average weekly earnings							
Male	\$1137	\$621	\$1152	\$973	\$137		
Female	1		\$957 ¹				

Unit cost for intervention [#]						
Hospital physiotherapist (per	\$33	\$32	\$30	\$21	\$5	
hour)						
Hospital nurse (per hour)	\$30	\$25	\$29	\$21	\$5	

AU: Australia; NZ: New Zealand; UK: United Kingdom; SG: Singapore; MA: Malaysia;

Sources of CPI:

Australian Bureau of Statistics. Consumer price index inflation calculator. Accessed

from: Http://www.Abs.Gov.Au/websitedbs/d3310114.Nsf/home/consumer+price+index+inflation+calculator. 2017

Office for National Statistics. Inflation and price indices. Accessed from:

Https://www.Ons.Gov.Uk/economy/inflationandpriceindices. 2017

Department of Statistics Singapore. Consumer price index. Accessed from: https://data.Gov.Sg/dataset/consumer-price-index-annual. 2017

Statistics New Zealand. Consumer price index, accessed from:

Http://www.Stats.Govt.Nz/browse for stats/economic indicators/cpi inflation/info-releases.Aspx. 2017

Department of Statistics Malaysia OP. Consumer price index malaysia. Accessed from:

Https://www.Dosm.Gov.My/v1/index.Php?R=column/cthemebycat&cat=106&bul_id=zi9pmutpvzixb042mlptt1buellazz09&menu_id=bthzthqxn1zqmvf6a2i4rkzondfkqt09. 2017

*severity was determined by baseline NIHSS score; †severity was classified by baseline mRS score; the hational survey of Household Income was provided on gender basis, so the weekly earnings for UK patients were assigned corresponding to this; hourly wage of hospital physiotherapist and nurse were assigned; N/A: not applicable. Main sources of unit cost: AU: Independent Hospital Pricing Authority (IHPA), Australia, National Efficient Price Data (2015-16); National Hospital Cost Data collection (https://www.ihpa.gov.au/publications/australian-publichospitals-cost-report-2013-2014-round-18); Department of Health, Revised residential care subsidies (https://agedcare.health.gov.au/aged-care-funding/aged-care-subsidies-and-supplements); Australian Bureau of Statistics

(http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/E9FF9F13B417A488CA257F630014DF30 ?opendocument

NZ: Ministry of Health (http://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations); World Health Organisation (http://www.pharmac.govt.nz/assets/pfpa-v2-2-cost-resource-manual.pdf); Study by Te Ao et al 2011 (Te Ao BJ et al. Are stroke units cost effective? Evidence from a New Zealand stroke incidence and population-based study. Int. J. Stroke. 2012;7:623-630); Statistics New Zealand

 $(\underline{http://www.stats.govt.nz/browse_for_stats/income-and-}$

<u>work/employment_and_unemployment/LabourMarketStatistics_HOTPJun15qtr.aspx</u>); District Health Board, Multi Employer Agreement, New Zealand Nurses Organisation(http://www.bopdhb.govt.nz/media/58613/psa-ronz-allied-meca-2015-2017.pdf);

UK: National Health Service (NHS) reference costs 2014 to 2015, United Kingdom

(https://www.gov.uk/government/publications/nhs-reference-costs-2014-to-2015); NICE Technology Appraisal (Davis,S., Holmes,M., Simpson,E., Sutton,A. Alteplase for the treatment of acute ischaemic stroke [review of technology appraisal 122]: A Single Technology Appraisal. ScHARR, The University of Sheffield 2012, https://www.nice.org.uk/guidance/ta264/documents/stroke-acute-ischaemic-alteplase-review-of-ta122-evidence-review-group-report2); Personal Social Services Research Unit (PSSRU)(http://www.pssru.ac.uk/); Information Services Division, Scotland (http://www.isdscotland.org/); Annual Survey of Hours and Earnings 2015, Office for National Statistics

(https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2015provisionalresults); Payscale UK

(http://www.payscale.com/research/UK/Job=Care_Worker/Hourly_Rate); NHS pay and benefits

 $(\underline{https://www.healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates});$

SG: Ministry of Health, Hospital Bill Sizes, Singapore

(https://www.moh.gov.sg/content/moh_web/home/costs_and_financing/HospitalBillSize/stroke.html.); Outpatient Charges, Singapore General Hospital (https://www.sgh.com.sg/patient-services/charges-payment/pages/outpatient-charges.aspx); Charges, Ren Ci Hospital (http://www.renci.org.sg/patients-guide/charges-2/); Hospital rates and charges, Bright Vision Hospital (http://www.bvh.org.sg/hospital-rate-charge.html); Ministry of Manpower (http://stats.mom.gov.sg/Pages/Occupational-Wages-Tables2014.aspx);

MA: study by Mohd Nordin et al 2012 (Mohd Nordin et al.: Estimating cost of in-patientmedical care for stroke using Casemix data. BMC Health Services Research 2012 12(Suppl 1):P10.); Ministry of Health Malaysia (http://www.moh.gov.my/english.php/pages/view/160); Study by Akhavan Hejazi et al 2015(Akhavan Hejazi SM, et al. Cost of post-stroke outpatient care in malaysia. Singapore Med. J. 2015;56:116-119); Department of Statistics Malaysia

(https://www.dosm.gov.my/v1/index.php?r=column/pdfPrev&id=czRyNkJIbDFyYXJFbU5YTVJ1V1BHZz09).

For the ICER from a societal perspective, all the costs from health and non-health sector were summed together, including the productivity cost; for ICER of a health sector perspective, all the costs borne by healthcare system were counted (i.e. excluding non-healthcare costs and productivity cost).



Cost variable

Acute hospitalisation

Ambulance transfer

Stroke-related rehospitalisation

Rehabilitation hospital admission

Outpatient rehabilitation program

Individual allied health visit§

Private physiotherapy

Home modifications

Productivity cost

Special aids and equipment

Subtotal (non-medical cost)

Total cost (exc. productivity cost)

UC

N = 95

0(0%)

0(0%)

0(0%)

0(0%)

0(0%)

0(0%)

1(1.1%)

1(1.1%)

1(1.1%)

1(1.1%)

5(5.3%)

1(1.1%)

1(1.1%)

1(1.1%)

7(7.4%)

7(7.4%)

10(10.5%)

16(16.8%)

NZ

VEM

N=94

0(0%)

0(0%)

0(0%)

0(0%)

0(0%)

0(0%)

0(0%)

1(1.1%)

1(1%)

1(1.1%)

4(4.3%)

1(1.1%)

6(6.4%)

6(6.4%)

14(14.9%)

20(21.3%)

0(0%)

0(0%)

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8(2.7%) 2 2 0(0%)

7(2.3%)

8(2.7%)

10(3.3%) DB0(0%)
1(3.7%) DB0(0%)

30(0%)

21(1.6%)

1(1.6%)

21(1.6%)

60(0%)

1(1.6%)

1(1.6%)

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21(1.6%)

▶17(25.6%)

617(26.6%)

\$2(3.1%)

46(15.4%) (3.1%)

bliographique

[0(0%)]

0(0%)

13(4.4%

13(4.4%)

14(4.7%

10(3.3%

27(9.0%**2**

2(0.7%)

14(4.7%

10(3.3%)

23(7.7%)

48(16.1%)

68(22.7%)

UK

VEM

N = 311

17(5.5%)

16(5.1%)

18(5.8%)

23(7.4%)

23(7.4%)

27(8.7%)

27(8.7%)

36(11.6%)

15(4.8%)

32(10.3%)

16(5.1%)

26(8.4%)

54(17.4%)

27(8.7%)

61(19.6%)

80(25.7%)

0(0%)

0(0%)

0(0%)

MA

VEM

N=62

0(0%)

7(11.3%)

7(11.3%)

7(11.3%)

9(14.5%)

7(11.3%)

7(11.3%)

7(11.3%)

9(14.5%)

5(8.1%)

7(11.3%)

0(0%)

0(0%)

7(11.3%)

7(11.3%)

8(12.9%)

14(22.6%)

10(16.1%)

22(35.5%)

0(0%)

UC

N=61

0(0%)

1(1.6%)

1(1.6%)

1(1.6%)

2(3.3%)

1(1.6%)

0(0%) 1(1.6%)

1(1.6%)

2(3.3%)

1(1.6%)

0(0%)

0(0%)

0(0%)

1(1.6%)

2(3.3%)

2(3.3%)

3(4.9%)

11(18.0%)

13(21.3%)

UC

N = 64

0(0%)

3(4.7%)

3(4.7%)

3(4.7%)

3(4.7%)

3(4.7%)

0(0%)

3(4.7%)

3(4.7%)

3(4.7%)

2(3.1%)

3(4.7%)

1(1.6%)

0(0%)

3(4.7%)

3(4.7%)

5(7.8%)

5(7.8%)

13(20.3%)

16(25.0%)

3 5

2

6

9

Rehabilitation provided at home/nursing

facility

Respite care

Subtotal (medical cost) Accommodation moves 26 Community services

Informal care Living-in maids[‡]

37

41

38 39 40

43 44

46

42

36 Total cost

§only applicable to UK, Singapore and Malaysia patients; †only applicable to Singapore and Malaysia patients

Supplementary document 4. Missing cost data analyses

 \mathbf{AU}

VEM

N = 522

1(0.2%)

8(1.5%)

8(1.5%)

9(1.7%)

11(2.1%)

12(2.3%)

12(2.3%)

14(2.7%)

15(2.9%)

63(12.1%)

3(2.6%)

7(1.3%)

11(2.1%)

77(14.8)%

50(9.6%)

80(15.3%)

124(23.8%)

0(0%)

UC

N=532

0(0%)

7(1.3%)

10(1.9%)

10(1.9%)

11(2.1%)

11(2.1%)

13(2.4%)

11(2.1%)

87(16.4%)

6(1.1%)

8(1.5%)

12(2.3%)

97(18.2%)

46(8.7%)

97(18.2%)

136(25.6%)

9(1.7%)

0(0%)

Table I. Number of missing data for each cost item

Missing

Total

N=2104

1(0.05%)

51(2.4%)

53(2.5%)

55(2.6%)

47(2.2%)

67(3.2%)

76(3.6%)

77(3.7%)

60(2.9%)

13(0.6%)

48(2.3%)

72(3.4%)

304(14.5%)

225(10.7%)

319(15.2%)

512(24.3%)

94(10.7%)

230(10.9%)

0(0%)

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Table II. Missing pattern analysis based on logit regression

Resource use items with missing data	Predictor of missingness
Stroke-related rehospitalisation	Age (p=0.001)
Rehabilitation hospital admission	Age (p=0.009), NIHSCORE (p=0.037)
Outpatient rehabilitation program	Age (p=-0.003)
Rehabilitation service provided at home/nursing facility	Age (p=0.014),
Community services used prior to stroke	NIHSCORE (p=0.001)
Community services used at 3 months	Age (p=0.003)
Community services used at 12 months	NIHSCORE (p=0.008)
Aids or special equipment uses at 3 months	Age (p=0.012)
Aids or special equipment uses at 12 months	Age (p=0.035), NIHSCORE (p=0.013)
Private physiotherapy uses at 3 months	Age (p<0.0001)
Private physiotherapy uses at 12 months	Age (p=0.006), NIHSCORE (p=0.034)
Respite care use at 3 months	Age (p<0.0001)
Respite care use at 12 months	Age (p=0.017), NIHSCORE (P=0.018)
Informal care use at 3 months	Age (p=0.003)
Informal care use at 12 months	Age (p<0.0001)

If any of the other variables were able to predict the missingness of a given variable representing resource use, the MAR assumption was deemed to be held true. More specifically, multiple imputations were used to replace the missing values (missing mRS, AQoL-4D data or cost categories) with plausible estimates, and generated 30 datasets. Results were provided as pooled estimates of these sets. Identical analyses were carried out to estimate the incremental costs and benefits between groups on the basis of imputed data following the methods outlined in the statistical analysis section above. As the probability of all the resource use items being missing could be predicted by one or more of the other variables, it is likely that the Missing-at-Random (MAR) assumption could be held true. (https://www.ssc.wisc.edu/sscc/pubs/stata mi_decide.htm).

Supplementary document 5. Outcomes

Table I. Results of mRS score at 3 and 12 months follow-up

Modified Rankin Scale Score	UC group		VEM group n=1054		
	n=1050	1050			
	3M	12M	3M	12M	
0	96	132	90	137	
1	204	231	200	219	
2	225	175	190	166	
3	218	199	238	186	
4	127	95	140	113	
5	103	83	92	59	
6	72	118	88	139	
Total	1045	1033	1038	1019	
Missing data	5	17	16	35	

Number of patients falling into each category

Since there was no significant intervention effect together with no accepted willingness-to-pay (WTP) per unit increase in probability of achieving a better mRS outcome, further estimation of the ICER was considered not meaningful (i.e. no cost-effectiveness plane or cost-effectiveness acceptability curve could be generated).

Table II. Time and cost associated with delivering VEM and UC (mean, 95%CI)

	VEM		UC		Between group difference		
	Total time (min)	Cost (AUD)	Total time (min)	Cost (AUD)	Total time (min)	Cost (AUD)	
Physiotherapist	243 (232, 254)	\$117 (\$111, \$123)	95 (90, 101)	\$48 (\$45, \$51)	147 (135, 159)*	\$69 (\$63, \$75)*	
Nurse [†]	494 (456, 532)	\$225 (\$207, \$244)	439 (404, 474)	\$202 (\$185, \$219)	55 (4, 106)*	\$23 (-\$2, \$48)	
Total cost	-	\$342 (\$320, \$364)	-	\$250 (\$231, \$269)	-	\$92 (\$63, \$121)*	

VEM: very early mobilisation; UC: usual care; CI: confidence interval

Because VEM and UC were supplied by the same group of physiotherapists and nurses, the key difference was that a patient randomised to VEM received early rehabilitation within 24 hours of stroke onset and more out-of-bed mobilisation sessions of early mobilisation.

The total health practitioner (physiotherapist and nurses) time devoted to the delivery of the VEM and UC differed significantly, with the VEM group receiving substantially longer mean service time from both the physiotherapist (VEM: 243 mins, 95%CI: 232 to 254 vs UC: 95 mins, 95%CI: 90 to 101, p<0.0001) and nurse (VEM: 494 mins, 95%CI: 456 to 532 vs UC: 439 mins, 95%CI: 404 to 474, p<0.0001). The resultant difference in costs between groups was significant (\$92, 95%CI: \$63 to \$121, p<0.0001).

^{*}p<0.0001 (adjusted for age, baseline NIHSS and mRS); † nurse's time devoted to delivery of VEM/UC was not recorded in the process of data collection, so the physiotherapist time was used as a proxy

Supplementary document 6. Sensitivity analyses

Generally, the difference in QALY gains between VEM and UC groups were fairly consistent across different get bods.

Table I. Between-group differences based on the Generalised Linear Model_ base case analysis vs. multiple imputation analysis

	ITT (not imputed)			ITT (imputed)	2019. eigne	
	mRS score	QALYs	Cost (AUD)	mRS	QALYs	Case (AUD)
Health Sector Perspec	ctive					wnlo o tex
Total medical costs	0.030	-0.013	\$1082	0.042	-0.019	\$9aded
	(-0.022, 0.082)	(-0.041, 0.016)	(-\$2399, \$4563)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$25.58\$, \$4465)
Societal Perspective			704	l	-1	http BES
Total cost (excl.	0.030	-0.013	-\$6	0.042	-0.019	\$1 3 04 \$
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$5703, \$5690)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$3428; \$8832)
Total cost (incl.	0.030	-0.013	\$102	0.042	-0.019	\$1213
productivity cost)	(-0.022, 0.082)	(-0.041, 0.016)	(-\$6945, \$7149)	(-0.008, 0.092)	(-0.046, 0.007)	(-\$594 0 ; \$8766)

ITT: intention to treatment; mRS: modified Rankin Scale; AUD: Australian dollars

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

Table II. Between-group differences based on the Generalised Linear Model

	Adding country dummies						
	mRS	QALYs	Cost				
Total medical costs	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	\$704 (-\$1968, \$3376)				
Total cost (excl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$335 (-\$4953, \$4283)				
Total cost (incl. productivity cost)	0.031(-0.021, 0.083)	-0.013(-0.042, 0.015)	-\$238 (-\$6012, \$5537)				

mRS: modified Rankin Scale; QALYs: Quality-adjusted Life Years

^{*}the p-value was >0.05 for the between-group difference in mRS score, QALYs and cost

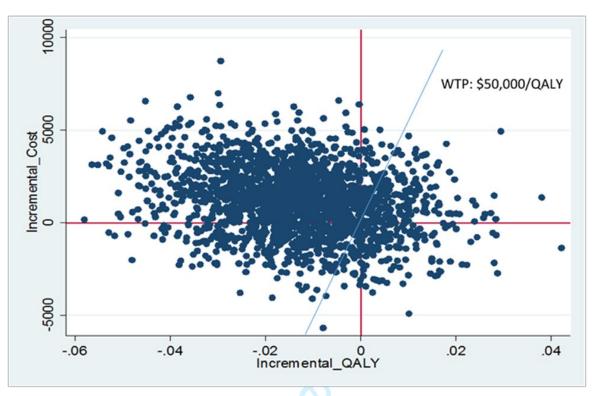
Table III. Cost-utility analysis based on multiple imputation analysis

	Efficacy (QALYs)	Cost (AUD)	Probability of being cost-effective
Health Sector Perspective	ve .		
Total medical costs	-0.019	\$940	25%
	(-0.044, 0.005)	(-\$4622, \$4682)	
Societal Perspective			
Total cost (excl.	-0.019	\$1704	20%
productivity cost)	(-0.044, 0.005)	(-\$3817, \$7226)	
Total cost (incl.	-0.019	\$1413	23%
productivity cost)	(-0.044, 0.005)	(-\$4044, \$6871)	

QALYs: Quality-adjusted Life Years; AUD: Australian dollar.

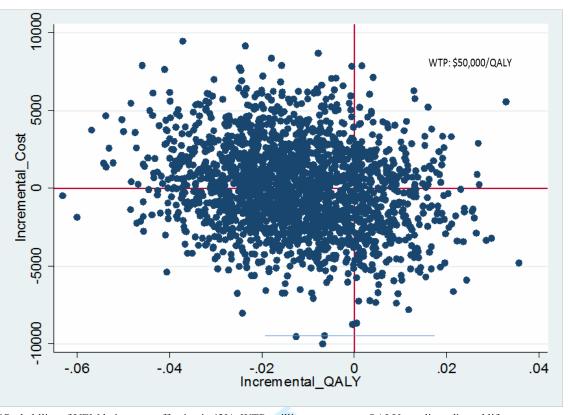
^{*}the p-value was >0.05 for the between-group difference in QALYs and cost

Supplementary document 7: Figures



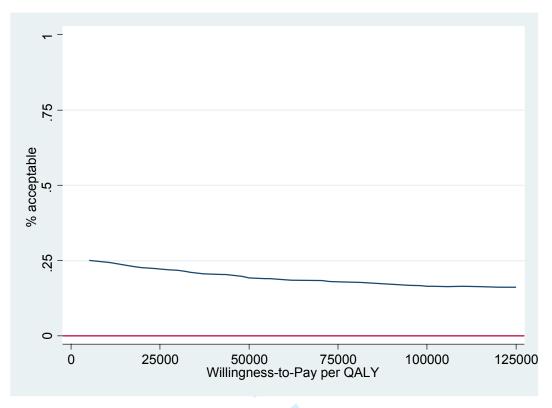
*Probability of VEM being cost-effective is 19%; WTP: willingness-to-pay; QALY: quality adjusted life year

Figure I Cost-effectiveness plane_ health sector perspective



*Probability of VEM being cost-effective is 42%; WTP: willingness-to-pay; QALY: quality-adjusted life year

Figure II Cost-effectiveness plane societal perspective (excl. productivity cost)



Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

Figure III Cost-effectiveness acceptability curve for medical cost

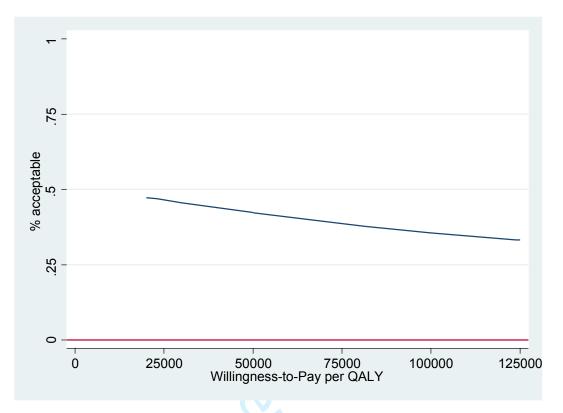


Figure IV Cost-effectiveness acceptability curve for total cost excluding productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

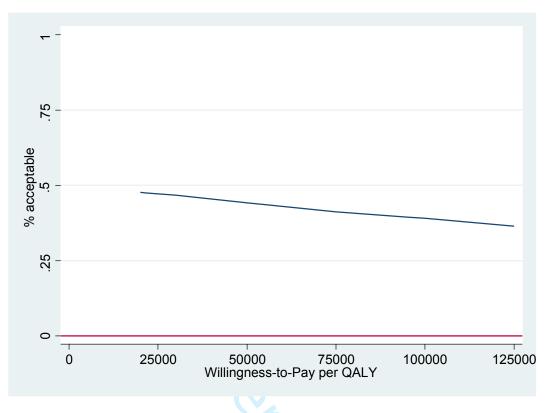


Figure V Cost-effectiveness acceptability curve for total cost including productivity cost

Note: The probability of VEM being cost-effective decreases with the increasing WTP/QALY threshold because the VEM is associated with less costs

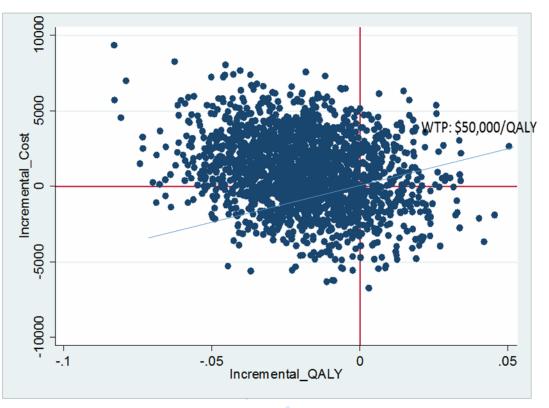


Figure VI Cost-effectiveness plane_ health sector perspective (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

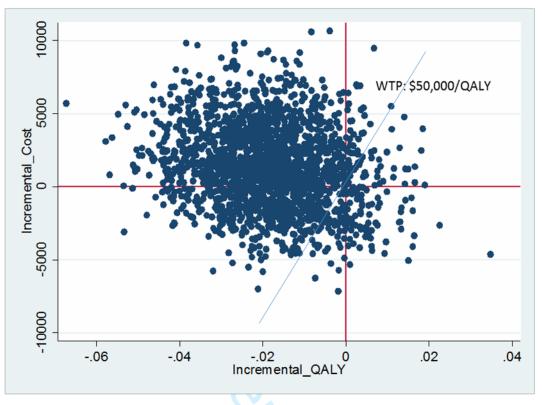


Figure VII Cost-effectiveness plane_ societal perspective including productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

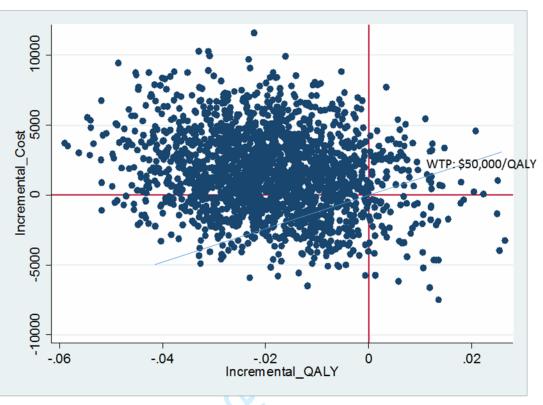


Figure VIII Cost-effectiveness plane_societal perspective excluding productivity cost (multiple imputation analysis)

WTP: willingness-to-pay; QALY: quality-adjusted life year

- 1. Claesson L, Gosman-Hedstrom G, Johannesson M, Fagerberg B, Blomstrand C. Resource utilization and costs of stroke unit care integrated in a care continuum: A 1-year controlled, prospective, randomized study in elderly patients: the Goteborg 70+ Stroke Study. Stroke 2000;31(11):2569-77.
- 2. Bernhardt J, Dewey H, Thrift A, Collier J, Donnan G. A very early rehabilitation trial for stroke (AVERT) phase II safety and feasibility. Stroke 2008;39(2):390-6.



			Reported of page No/
Section/item	Item No	Recommendation	line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	4-5
ntroduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	7 8
Methods		Present the study question and its relevance for health policy or practice decisions.	0
Farget population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	12
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	9
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	
Fime horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	11
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	
Measurement of effectiveness	11a	Single study-based estimates: Describe fully the design features of the single effectiveness stud and why the single study was a sufficient source of clinical effectiveness data.	y 12
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	
Estimating resources and costs	13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	9-10
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resourceuse associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providinga figure to show model structure is strongly recommended.	
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate.	N/A
Incremental costs and outcomes	19	Providing a table to show the input values is strongly recommended. For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	
Characterising uncertainty	20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	14
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	
naracterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
Discussion			
udy findings, limitations,	22	Summarise key study findings and describe how they support the conclusions reached. Discuss	

knowledge			
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	22

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statementchecklist

