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Title

Cost-effectiveness of stroke care in Aboriginal and non-Aboriginal patients in the Northern Territory of Australia over 21 years

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Abstract

Objectives: To assess the cost-effectiveness of stroke care for Aboriginal compared with non-Aboriginal population in Australia.

Design: Cohort-based observational study by following up stroke incidences from 1992 to 2013.

Setting: Aboriginal and non-Aboriginal stroke patients in all public hospitals in the Northern Territory of Australia (NT).

Participants: Individual patient data were extracted and linked from the hospital inpatient and primary care information systems. Survival time was used to measure effectiveness of stroke care, in comparison with the net costs per life-year gained, from a health care perspective.

Outcome measures: Incremental cost-effectiveness ratios were calculated and assessed graphically to determine the efficiency of health care. A marginal structural model was used to adjust for time of treatment, demographics, loss to follow-up and differences in case-mix.

Results: 2,158 patients with incident stroke were included (males: 54%, aged<65 years: 55% and from non-remote areas: 55%, with 47% of Aboriginal origin (28% in the NT population)). Of all cases, 43% were ischaemic and 30% haemorrhagic stroke. Aboriginal patients had 14 years younger age of onset, 71% more hospital bed-days, 7% fewer procedures and 50% greater observed costs than non-Aboriginal patients, over a median follow-up time of 318 days from their incident events. The differential costs and effects for each population were distributed evenly across the incremental cost-effectiveness plane threshold line (set at AUD120,000 per life-year gained), indicating no difference in cost-effectiveness between populations. After further adjustment for time-dependent confounding and censoring, cost-effectiveness appeared greater for Aboriginal than non-Aboriginal patients, but this was not statistically significant (P=0.25).

Conclusions: Stroke care for the NT Aboriginal population is at least as cost-effective as the non-Aboriginal population. Stroke care will present worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher level burden of disease.

Subject headings: Health economics; Neurology; Public health; Health services research

Keywords: Stroke; Health economics; Social medicine

Strengths and limitations of this study

- This study included a large sample size of Aboriginal patients with stroke relative to the non-Aboriginal patients over a 22-year period, using linked patient records across multiple sources of data.
- The methodology informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.
- The results are most relevant to Aboriginal population living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high cost environment.
- The lifetime stroke costs were based on health service use, which did not cover costs associated with the loss of quality of life among stroke survivors.

Introduction

Worldwide, stroke has a substantial impact on the health of populations and on health systems.[1] In 2010, about 16.9 million people suffered first-ever stroke globally, with 5.9 million stroke-related deaths. This was associated with a 68% and 26% increase from 1990 in incidence and mortality respectively.[1] In 2014, approximately 51,000 Australians suffered a new or recurrent stroke, nearly 12,000 people died from stroke and almost 440,000 people lived with the effects of disability caused by stroke.[2] Stroke has been estimated to cost the Australian economy AUD5 billion annually.[2] The lifetime cost of first-ever stroke care in 2010 was estimated at approximately AUD100,000 per patient in Australia.[3-6] In a recent Northern Territory (NT) study, the estimated net lifetime health care cost for non-Aboriginal patients with a haemorrhagic stroke (HS) without significant comorbidities was AUD73,000 in 2012/2013, whereas ischaemic stroke (IS) cost 54% more than HS and Aboriginal patient costs were 44% greater overall.[7]

Over the past 25 years, improvement in stroke prevention and treatment has resulted in substantial increases in stroke survival.[8,9] This improvement was evident for both Aboriginal and non-Aboriginal patients in the NT, albeit much shorter survival in the Aboriginal patients after adjustments for age at onset and other confounders.[10] The Aboriginal patients with stroke had similar survival with younger age at onset and greater prevalence of comorbidity, as compared with non-Aboriginal counterparts.[10] Previous studies provide evidence that patients with stroke who were Aboriginal had less access to the hospital procedures than non-Aboriginal patients.[11,12] In a recent national audit of hospital care, it was identified that Aboriginal patients with stroke received a reduced quality of care in hospital and experienced worse outcomes than non-Aboriginal patients.[13] Cost-effectiveness of stroke care may be monitored using health care utilisation data to determine if there are any treatment biases.[14] One important measure of cost-effectiveness is the marginal changes in health costs over the marginal changes in stroke survival.[15] Cost-effectiveness analyses provide useful information to ensure effective, efficient and equitable use of limited resources.[14] Information on the cost-effectiveness of stroke care and prevention has been published previously.[14,16] However, little is known about the cost-effectiveness of stroke care in Aboriginal compared with non-Aboriginal

patients.[17] It is important to assess if Aboriginal patients with stroke received less stroke care than non-Aboriginal patients, and this may, in part, explain why they experience worse outcomes.[13] The comparative cost-effectiveness design provides a valuable means of evaluation for intervention strategies to prevent, diagnose and treat disease by monitoring health care activities in a real world setting.[18]

The NT is a large, sparsely populated area of northern Australia where a substantial Aboriginal population resides as opposed to other parts of Australia. In 2011, the NT resident population was 211,943 (1% of the Australian population), 28% of whom were Aboriginal Australians (nationally 2.5%).[19] There are five public hospitals, which provided stroke care in the NT, and of which only one (Royal Darwin Hospital) has a specialised stroke unit, which was opened around 2008. In 2006, life expectancy at birth was 21 and 15 years shorter in Aboriginal than non-Aboriginal population for males (60 vs 81 years) and females (70 vs 85 years) respectively.[20] Between 1999-2003, the burden of disease resulting from premature death and disability in the Aboriginal population was 2.8-3.3 times greater than in the non-Aboriginal population in the NT.[21]

The aim of the study was to compare the cost-effectiveness of stroke care for two populations with very different burdens of disease, the Aboriginal and non-Aboriginal Australians to explore whether inequalities in providing health care exist and to determine the efficiency of the health care that is provided. This study draws conclusions and makes recommendations regarding cost-effectiveness of stroke care for Aboriginal patients.

Method

This is an observational cohort study based on data spanning 21 years between 1 July 1992 and 30 June 2013 for Aboriginal and non-Aboriginal patients with first-ever stroke in the NT. Four administrative data sources were used. Individual patient-level data from the hospital inpatient data (HID) between 1982 and 2013 and event data from the primary care information system between 2009 and 2013, were merged using an encrypted unique patient identifier for patient tracking and

survival analysis. Two additional data sources, Medicare and Pharmaceutical Benefits Scheme (PBS) data from 1993 to 2013, were used for calculating non-hospital costs.

Patients with stroke were identified from HID using the International Classifications of Diseases (ICD) version 9 to June 1998 and version 10 thereafter. Stroke was categorised into three types: haemorrhagic stroke (HS) (diagnosis codes 430, 431, 432.9 (ICD-9); I60, I61, I62.9 (ICD-10)), ischaemic (IS) (433, 434; I63) and stroke type undetermined (UND) (436; I64).[22] Transient ischaemic attack (TIA) (435.9; G45.9) was excluded from this study. Incidence of stroke was identified using the first-ever admission with a stroke diagnosis during the study period, and a stroke-free admission in the preceding clearance of at least ten years using data from 1 July 1982. Follow-up time was calculated as the number of days between the first-ever admission date and the discharge date of the subsequent or recurrent admission. Each intervening hospital admission or readmission was regarded as a follow-up. The numbers of ICD coded procedures per hospitalisation were averaged for each patient. Stroke-related death was identified by HID, where the discharge classification was recorded as deceased, and stroke was recorded as a diagnosis at that episode. Follow-up time was censored at: the date of death for patients who died from causes other than stroke, or the discharge date of the last admission (or first admission if only admitted once) for patients discharged alive.

Six main categories of service use were costed from a health care perspective: hospital inpatient care, outpatient, nursing home, primary care (general practitioner (GP) and remote clinic), pharmaceuticals and allied health. Indirect (i.e. loss of productivity), intangible (i.e. loss on quality of life) and external social costs were beyond the scope of this study. Inpatient costs were calculated by multiplying the Australian national/refined diagnosis related group weights times the NT benchmark prices,[23] covering medical, nursing, supplies, imaging, pathology, allied health, pharmacy, critical care, operating room, emergency, prostheses, procedures, and hospital overhead oncosts. The stroke related events (occasions of service) in remote communities were identified using the primary care information system data. The remote clinic costs were obtained by multiplying the number of events by the average cost estimate in the year the service was provided (e.g. AUD36 in 2003).[24] The urban primary care cost was estimated as 3.2% of total NT Medicare benefits for GPs, because 3.2%

of GP patients had a stroke or TIA according to the most recent GP survey.[25] The PBS cost was estimated by the item codes for antihypertensive, antiplatelet and anticoagulant agents. The cost was multiplied by two to cover Section 100 (access to highly specialised drugs by remote Aboriginal people) expenditure and to counterbalance the under-coverage of data for drugs administered in remote areas, because preliminary analysis indicated that Section 100 expenditure was similar to the claimed PBS in the NT Aboriginal setting. A detailed description of the costing methodology has been reported elsewhere.[7] Five percent was applied to represent the present value of costs based on the reference year 2012/2013, because 5% reflected an average level of health inflation.[26]

Health outcome was assessed through measuring survival time after stroke. Univariable analysis was performed using mean, median and the interquartile range to describe demographics, time of incidence, hospital bed-days, number of procedures, costs and survival time. Chi-square significance test and Kaplan-Meier survival curves were used to compare Aboriginal and non-Aboriginal patients. Linear censored regression was used to adjust for loss to follow-up. Estimation of the incremental cost-effectiveness ratio (ICER) was adapted for comparing cost and survival for the Aboriginal and non-Aboriginal populations, based on the notion of maximising health gains with available resources.[27] The bootstrap method with 2000 replications was used to construct the cost-effectiveness plane for assessment of the ICER variability.[27] A threshold statistical value of AUD120,000 per life-year was used to evaluate cost-effectiveness, as recommended by the Australian Safety and Compensation Council.[28] The cost-effectiveness of health care for incident stroke was further analysed by using a marginal structural model (MSM) to account for time-dependent confounding and censoring.[29] A log10 transformation was applied to the costs, because preliminary analysis showed the observed costs resembled a lognormal distribution. The multiplicative cost increment was used as an independent variable and survival as the dependent variable, because survival represents benefits of stroke care as an outcome, and the cost representing the resource use as the input. The hazard ratio (HR) of mortality for a unit of cost increment represents the proportional change in mortality hazard given the percent change in health care costs. A full range of thresholds for the ICER (AUD0-500,000 per life-year) representing different values of willingness-to-pay was tested

for assessing the uncertainty of the ICER. The willingness-to-pay acceptability curves were compared for comparative cost-effectiveness, i.e. saving more life-years cost-effectively. Sensitivity analysis was also performed using 3% and 10% discount rates, with and without log-transformation.

The study was approved by the Human Research Ethics Committee of the NT Department of Health and the Menzies School of Health Research (HREC-2011-1680).

Results

Between 1992 and 2013, 2,889 patients were hospitalised with stroke in the NT, of whom 731 patients with recurrent stroke were excluded, leaving 2,158 incident stroke cases in this study. Among these incident strokes, just over half were male (54%), aged less than 65 years (55%) or from non-remote areas (55%), with 43% being IS, 30% HS, and 46% of Aboriginal origin (Table 1). The total median follow-up time was 318 days with interquartile range 13 to 1,512 days. Aboriginal patients had 14 years younger age of stroke onset, 71% more hospital bed-days and 50% greater observed costs than the non-Aboriginal patients (all $P<0.001$). The average number of procedures per hospitalisation in Aboriginal patients was 7% fewer than that for non-Aboriginal patients (2.7 vs 2.9, $P<0.05$). Number of incident strokes increased over time likely driven by population growth and ageing, despite there being no changes in the proportion between Aboriginal and non-Aboriginal patients. Compared with non-Aboriginal patients, Aboriginal patients were disproportionately more likely to experience HS, attributed to a greater prevalence of hypertension, diabetes and chronic kidney disease (CKD) ($P\leq0.01$). There was no difference in total case fatality between Aboriginal and non-Aboriginal patients with stroke in this study.

Table 1. Stroke patient characteristics by Aboriginality, Northern Territory, 1993-2013

	Aboriginal		Non-Aboriginal		Significance	Total	
Male	464	(47%)	707	(61%)	P<0.001	1,171	(54%)
Age of onset<65 years	704	(71%)	474	(41%)	P<0.001	1,178	(55%)
Remote	735	(74%)	231	(20%)	P<0.001	966	(45%)
Median (IQR)							
Age of onset (years)	51	(41-63)	65	(54-75)	P<0.001	59	(47-71)
Follow-up days	507	(25-1,642)	201	(8-1,367)	P<0.001	318	(13-1,512)
Total bed-days	36	(10-94)	21	(5-73)	P<0.001	28	(7-82)
Average procedures (n)	2.7	(2.5-2.8)	2.9	(2.8-3.0)	P=0.025	2.8	(2.7-2.9)
Observed costs (AUD'000)	50.4	(15.2-123.8)	33.7	(10-89.1)	P<0.001	41.9	(11.2-102.6)
Time period					P=0.066		
1993-1999	236	(24%)	329	(28%)		565	(26%)
2000-2006	336	(34%)	372	(32%)		708	(33%)
2007-2013	420	(42%)	465	(40%)		885	(41%)
Type					P<0.001		
Haemorrhagic	340	(34%)	304	(26%)		644	(30%)
Ischaemic	404	(41%)	516	(44%)		920	(43%)
Undetermined	248	(25%)	346	(30%)		594	(28%)
Comorbidity							
Hypertension	596	(60%)	636	(55%)	P=0.010	1,232	(57%)
Diabetes	446	(45%)	276	(24%)	P<0.001	722	(33%)
IHD	227	(23%)	305	(26%)	P=0.079	532	(25%)
CKD	334	(34%)	200	(17%)	P<0.001	534	(25%)
Depression	25	(3%)	57	(5%)	P=0.004	82	(4%)
COPD	139	(14%)	159	(14%)	P=0.801	298	(14%)
Cancer	53	(5%)	149	(13%)	P<0.001	202	(9%)
Atrial fibrillation	153	(15%)	220	(19%)	P=0.035	373	(17%)
Case fatality	259	(26%)	305	(26%)	P=0.979	564	(26%)
Total	992	(46%)	1,166	(54%)	P<0.001	2,158	(100%)

CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. IHD, ischaemic heart disease. IQR, interquartile range.

Figure 1 (a) shows that there appeared to be slightly better survival in Aboriginal patients with stroke despite the log-rank test indicating statistical insignificance. Aboriginal patients were significantly younger. Age stratified analysis in Figures 1(b)-(d) shows a slightly greater Aboriginal survival in the aged 65+ group (P<0.05), but there were no significant Aboriginal survival differences in the other age groups.

(Insert Figure 1 here)

Details of the average survival time and costs by stroke type comparing Aboriginal and non-Aboriginal patients are provided in Table 2. Aboriginal patients tended to have better survival and greater costs than non-Aboriginal patients, especially after an IS ($P<0.05$). Overall, stroke costs were 40% more in Aboriginal than non-Aboriginal patients ($P<0.001$). The ICER of stroke care for Aboriginal patients compared with that for non-Aboriginal patients was an average of AUD110,965 per survival year, ranging from AUD69,163 in UND to AUD130,376 in HS (see bottom line in Table 2). Figure 2 shows a great degree of uncertainty in both survival and costs, especially in UND, followed by IS and then HS, when comparing cost-effectiveness between Aboriginal and non-Aboriginal patients. It is unlikely that the greater uncertainty in UND was caused by the smaller sample size, because the bootstrap adjusts for sample size by resampling.[27] The differential costs and effects were divided evenly across the threshold line, indicating that stroke care in Aboriginal patients was as cost-effective as in non-Aboriginal patients. Figure 3 provides the probability of whether the stroke care in Aboriginal patients would result in longer survival than in non-Aboriginal patients. The acceptability of achieving optimised stroke care in Aboriginal patients increased progressively with willingness-to-pay. At the threshold price (dotted line in Figure 3), the probability of achieving an optimal cost-effectiveness in Aboriginal patients with UND was 0.76, followed by HS (0.69) and IS (0.42).

Table 2. Average survival time and cost by stroke type and incremental cost-effectiveness ratio comparing Aboriginal and non-Aboriginal patients

		HS	IS	UND	Total
n		644	920	594	2,158
Survival (years)	Aboriginal	6.1	11.4	11.0	9.1
	Non-Aboriginal	5.9	9.9	9.7	8.6
	P-value	0.662	0.023	0.081	0.148
Average cost (AUD)	Aboriginal	192,675	448,451	404,800	331,340
	Non-Aboriginal	166,743	337,732	310,011	275,045
	P-value	0.091	<0.001	0.002	<0.001
Net cost per life-year gained (ICER)		130,376	74,343	69,163	110,965

HS, haemorrhagic stroke. ICER, incremental cost-effectiveness ratio. IS, ischaemic stroke. UND, stroke type undetermined.

(Insert Figures 2 and 3 here)

After further adjustments for time-dependent confounders (time, age and comorbidities), time-independent confounders (sex and remoteness) and dependent censoring by using MSM (Table 3), Aboriginal patients with stroke were 34% more likely to die of stroke than non-Aboriginal patients (P=0.008). Overall, HS was more than twice as likely to cause death as IS (P<0.001), whereas there was no difference in survival between IS and UND. Stroke mortality increased with age at onset (2% for every additional year of age, P<0.001), compounded by CKD (P<0.001) or cancers (P=0.011). The stroke mortality was reduced over time (3% reduction annually, P<0.001), and negatively correlated with residing in remote areas or having hypertension (both P<0.01). In particular, stroke mortality was negatively associated with greater health care costs. A 10-fold increase in health costs was associated with a reduction in stroke mortality by 40% (HR=0.60, P<0.001). The stratified MSM by Aboriginality found that the HR was smaller among Aboriginal patients than in non-Aboriginal patients (0.53 vs 0.64), indicating a slightly greater mortality reduction in Aboriginal, though statistically insignificant (P=0.25).

Table 3. Marginal structural proportional hazard model hazard ratio and confidence interval by Aboriginality

	Aboriginal		Non-Aboriginal		All stroke	
	HR	95%CI	HR	95%CI	HR	95%CI
Cost increment	0.53	0.41 - 0.68	0.64	0.51 - 0.8	0.60	0.5 - 0.71
Aboriginal	-	-	-	-	1.34	1.08 - 1.67
Ischaemic	1.00	-	1.00	-	1.00	-
Haemorrhagic	2.64	1.9 - 3.68	1.78	1.38 - 2.3	2.06	1.69 - 2.51
Undetermined	1.13	0.75 - 1.71	0.92	0.7 - 1.21	0.97	0.78 - 1.22
Time (year-1993)	0.98	0.96 - 1	0.96	0.95 - 0.98	0.97	0.96 - 0.98
Age at onset (years)	1.01	1.01 - 1.02	1.03	1.02 - 1.04	1.02	1.02 - 1.03
Female	0.82	0.63 - 1.07	1.06	0.85 - 1.32	0.98	0.83 - 1.16
Remoteness	0.83	0.63 - 1.09	0.73	0.53 - 1	0.75	0.62 - 0.92
Hypertension	0.70	0.53 - 0.93	0.73	0.58 - 0.91	0.70	0.59 - 0.83
Diabetes	0.80	0.58 - 1.11	1.01	0.77 - 1.33	0.90	0.73 - 1.11
CKD	1.62	1.18 - 2.21	1.48	1.09 - 2.02	1.51	1.21 - 1.88
IHD	1.03	0.67 - 1.59	0.72	0.52 - 1	0.84	0.65 - 1.09
COPD	1.02	0.6 - 1.74	0.99	0.73 - 1.35	1.01	0.77 - 1.33
Cancer	1.30	0.52 - 3.22	1.53	1.09 - 2.16	1.50	1.1 - 2.06
Depression	-	-	0.45	0.15 - 1.32	0.40	0.13 - 1.22
Atrial fibrillation	1.20	0.75 - 1.92	0.99	0.7 - 1.39	1.10	0.84 - 1.44

CI, confidence interval. CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. HR, hazard ratio. IHD, ischaemic heart disease. Cost increment represents percent change in log(Cost).

Sensitivity analysis provided evidence that the ICER was not dominant in favour of the Aboriginal population until the willingness-to-pay threshold was increased close to AUD200,000 per life-year gained (P>0.7, Figure 3). Probabilistic analyses confirmed that treating HS and UND were likely to be more cost-effective in Aboriginal patients than treating IS, likely related to underdiagnoses of stroke

in remote areas. The average cost relativities were insensitive to differing discount rates. Log-transformation would generate more robust cost estimates. Without log-transformation, the magnitude of average costs might be affected, but the sign of difference between Aboriginal and non-Aboriginal patients remained consistent.

Discussion

In terms of survival outcome, to our knowledge, this is the first comparative cost-effectiveness evaluation providing evidence that stroke care among Aboriginal patients is as efficient as among the non-Aboriginal patients within the Australian context. Reports on the economic analysis of cost-effectiveness among Aboriginal and non-Aboriginal populations are rare.[30,31] In our sample almost half (46%) were Aboriginal. Overall, this incidence number was disproportionate to the population proportion for the NT (28% in 2011), reflecting the large impact stroke has in the Aboriginal population. Stroke care in the Aboriginal population may be even more beneficial because of the 14 years younger age at onset of stroke, resulting in more life-years potentially saved from the additional costs of providing care. There have been several estimates of the long-term cost of stroke in Australia in the past two decades, up to AUD100,000,[3-6,32] mainly based on the North East Melbourne Stroke Incidence Study.[3] These cost estimates were based on cohort studies conducted in urban areas and were likely to understate the NT patient lifetime costs, because of attrition bias caused by loss to follow-up and inability to account for the costs related to remote areas.[33] In 2012/2013 Australian dollars, the estimated lifetime cost for an incident stroke in NT was AUD302,538 per patient between 1992 and 2013 after adjusting for loss to follow-up.[7] Stroke cost was found to be 44% greater for Aboriginal patients.[7]

Accurate cost estimates are required for cost-effectiveness assessment related to improvements in stroke survival.[34,35] Cost-effectiveness can be evaluated by comparing costs against outcomes between the alternative treatments.[27] Understanding the cost drivers in stroke treatments informs health service decisions for cost-effective care. Most cost-effectiveness studies for stroke care were focused on specific procedures,[16,36] for example pharmaceuticals,[37,38] surgery,[39,40]

prevention,[41,42] and rehabilitation;[43] or evaluating alternative models of care,[44] for example telemedicine,[45] and specialised stroke unit.[46,47] Hunter and colleagues evaluated the introduction of centralised stroke care, finding the service reduced mortality by 12% and saved more than £811 per patient-year.[48] In Canada, comprehensive stroke care can reduce hospital admissions (3%), bed-days (26%), death (15%) and nursing home care (13%), as well as save costs of over CAD11,000 per stroke.[49]

Comparative cost-effectiveness is an emerging approach to comparing the costs and monitoring health outcomes of interventions and strategies to prevent, diagnose and treat diseases in real world practice for informing clinical and policy decisions.[50,51] Previous reports suggested an effect of institutional bias in clinical decisions, which favoured stroke care in non-Aboriginal patients.[11,12] Despite these reports, the cost-effectiveness of stroke care among different patient populations has not been investigated. Our study confirmed that the uptake of hospital procedures by Aboriginal stroke patients with an incident stroke was 7% less than the non-Aboriginal patients. Univariable analysis showed that stroke care in Aboriginal patients is as cost-effective as in non-Aboriginal patients. The differential costs and effects were divided quite evenly across the willingness-to-pay threshold line. After taking into account the effects of patient-level confounders, time and loss to follow-up using MSM, we found that an increase in stroke care costs was associated with a slightly better health outcome for Aboriginal than non-Aboriginal patients with stroke, despite failing to reach statistical significance. Baker and colleagues evaluated cost-effectiveness of blood pressure control in kidney and cardiovascular disease treatment in an Aboriginal community.[30] It was found that 3-year perindopril treatment was effective in delaying 1.5 years of haemodialysis per patient with a net annual cost of AUD1,200, in comparison with a modelled historical control of the same Aboriginal population. Stroke was not identified in their study and non-Aboriginal controls were not compared.[30] Grieve and colleagues compared stroke care costs and survival among different European countries and different ways of providing stroke care.[52] The authors found that the cost-effectiveness may be related to specialised stroke care, which is required to coordinate different medical professions at various time points after stroke. Our analysis directly compared cost-

effectiveness of stroke care for both Aboriginal and non-Aboriginal patients. This study is also complemented by the use of MSM, which is more appropriate than conventional methods for managing censoring issues in analysing survival and costs.[29]

Strengths of this study include the large sample size of Aboriginal patients relative to the non-Aboriginal patients, access to data to ensure capture of incident cases and the ability to confidently link patient records across multiple sources of data. Further, the methodology in this study informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.[50,51] Several limitations should be noted. First, the results in this study are most relevant to Aboriginal population living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high cost environment.[53,54] The stroke care cost-effectiveness results may be relevant to other disadvantaged populations. Second, our cost estimates may not be precise. In this study we used administrative HID to identify stroke cases and did not include minor and low-cost cases managed solely by outpatient department, GP or remote clinics. These low-cost cases would comprise a small proportion of stokes (previously estimated at 12% in 1997).[3] A top-down approach was applied to calculate the GP, nursing home and allied health costs, which might lead to over- or under-estimation of the true costs. Various statistical methods were used to assess the robustness of the point estimates. More research is needed to further explore the cost-effectiveness of stroke care using prospective patient-level costing data. Third, another potential source of uncertainty in cost-effectiveness evaluation was the lack of non-NT or non-stroke controls, assuming stroke care as a whole is cost-effective in the NT, and stroke survival was independently associated with costs of stroke care and perceived confounders. Fourth, we were unable to measure levels of disability and quality of life among stroke survivors. It might be that there were important differences in levels of stroke-related disabilities between Aboriginal and non-Aboriginal patients. Finally, the joint effects of multiple comorbidities and their interactions were not considered in this study due to limited sample sizes.

In conclusion, stroke care for Aboriginal patients is at least as cost-effective as for non-Aboriginal patients managed within a sparsely populated but geographically large region of Australia, where

health care resources are limited. Stroke care was found to present worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher level burden of disease. These data may provide useful information for other countries with Indigenous populations living in regions with similar geographical and resource constraints.

Figure legends

Figure 1. Survival by age and Aboriginality

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

Contributorship statement

YZ designed the study, collected costing data, undertook data linkage and statistical analysis, and wrote the first draft of the manuscript. ¶ SG, H Falhammar, H Flavell and DC participated in the literature review, methodology development, discussion and revision of the manuscript, and contributed equally to this work.

Competing interests

The authors declare that they have no competing interests relevant to the manuscript.

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Data sharing statement

We will share the data via a publicly accessible repository.

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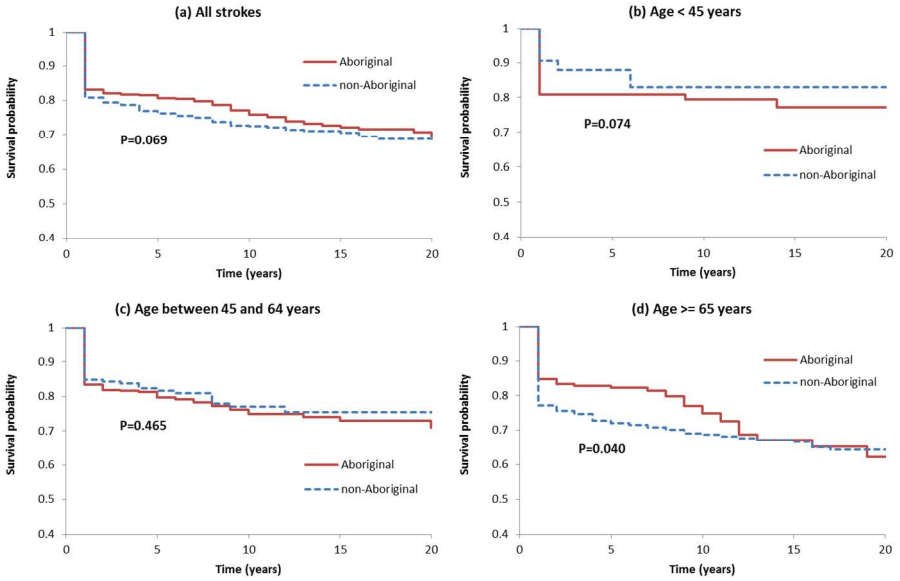

Figure 1. Survival by age and Aboriginality

297x209mm (300 x 300 DPI)

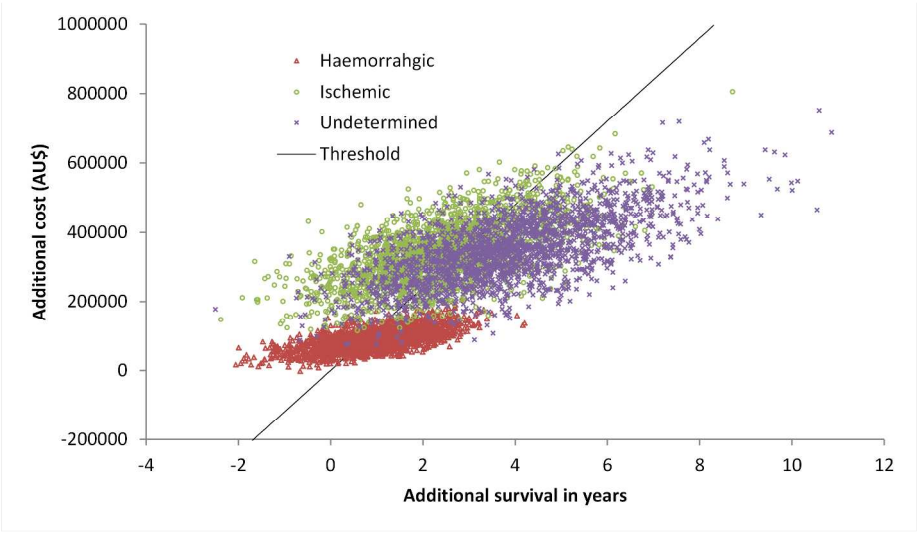

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

297x209mm (300 x 300 DPI)

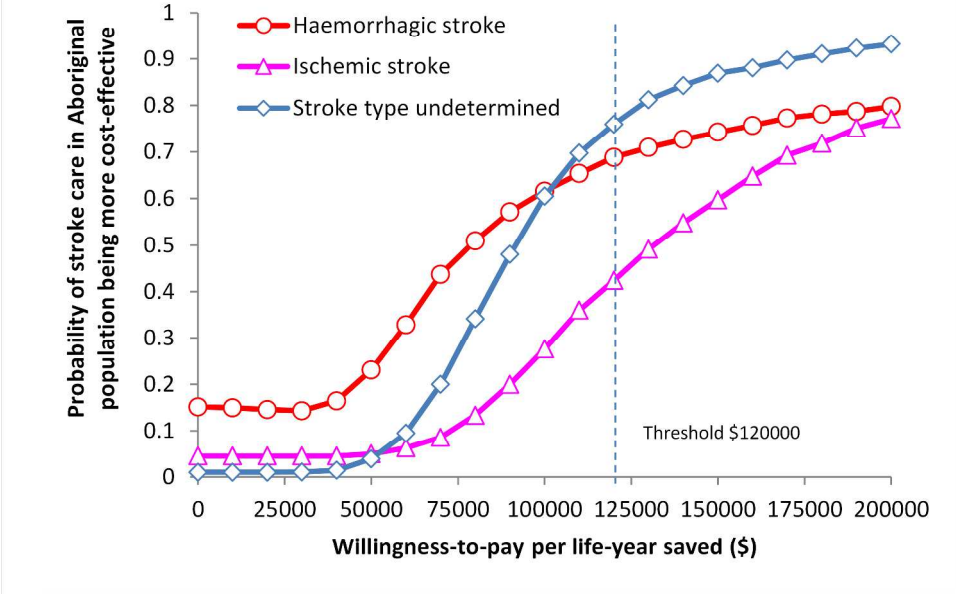

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

297x209mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	6

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cost-effectiveness of stroke care in Aboriginal and non-Aboriginal patients: an observational cohort study in the Northern Territory of Australia

Abstract

Objectives: To assess cost-effectiveness of stroke care for Aboriginal compared with non-Aboriginal patients in the Northern Territory (NT), Australia.

Design: Cost effectiveness analysis using data from a cohort-based follow-up study of stroke incidences.

Setting: Public hospitals in the NT from 1992 to 2013.

Participants: Individual patient data were extracted and linked from the hospital inpatient and primary care information systems.

Outcome measures: Incremental cost-effectiveness ratios were calculated and assessed graphically. Survival time was used to measure effectiveness of stroke care, in comparison with the net costs per life-year gained, from a health care perspective, by applying multivariable models to account for time-dependent confounding.

Results: 2158 patients with incident stroke were included (1171 males, 1178 aged<65 years and 966 from remote areas). 992 patients were of Aboriginal origin (46.0%, disproportionately higher than the population proportion of 28%. Of all cases, 42.6% were ischaemic and 29.8% haemorrhagic stroke. Average age of stroke onset was 51 years in Aboriginal, compared with 65 years in non-Aboriginal patients (P<0.001). Aboriginal patients had 71.4% more hospital bed-days, and 7.4% fewer procedures than non-Aboriginal patients. Observed health costs averaged AUD50 400 per Aboriginal compared with AUD33 700 per non-Aboriginal patient (P<0.001). The differential costs and effects for each population were distributed evenly across the incremental cost-effectiveness plane threshold line, indicating no difference in cost-effectiveness between populations. After further adjustment for

confounding and censoring, cost-effectiveness appeared greater for Aboriginal than non-Aboriginal patients, but this was not statistically significant (P=0.25).

Conclusions: Stroke care for the NT Aboriginal population is at least as cost-effective as the non-Aboriginal population. Stroke care presents worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher level burden of disease. These findings are relevant for health care planning and policy development regarding equal access to stroke care for Aboriginal population.

Subject headings: Health economics; Neurology; Public health; Health services research

Keywords: Stroke; Health economics; Social medicine

Strengths and limitations of this study

- This study included a large sample size of Aboriginal patients with stroke relative to the non-Aboriginal patients over a 21-year period, using linked patient records across multiple sources of data.
- The methodology informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.
- The results are most relevant to Aboriginal population living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high income country.
- The lifetime stroke costs were based on health service use, which did not cover costs associated with the loss of quality of life among stroke survivors.

Introduction

Worldwide, stroke has a substantial impact on the health of populations and on health systems, and about 16.9 million people suffered first-ever stroke, with 5.9 million stroke-related deaths in 2010.[1] Approximately 51 000 Australians experience a new or recurrent stroke each year, and stroke is a national priority since it is a leading cause of death and disability.[2] The lifetime cost of first-ever stroke care are approximately AUD100 000 per patient in Australia.[3-6] In a recent Northern Territory (NT) study, the estimated net lifetime health care cost for Aboriginal patients were 44% greater than for non-Aboriginal patients.[7]

Over the past 25 years, improvement in stroke prevention and treatment has resulted in substantial increases in stroke survival.[8,9] Although Aboriginal populations experience stroke at younger ages and have a higher prevalence of comorbidities, this improvement in survival was evident for Aboriginal and non-Aboriginal patients in the NT, albeit with much shorter survival in the Aboriginal patients after adjustments for age at onset and other confounders.[10] Nationally, it has been recognised in the clinical guidelines that Aboriginal patients require access to general and stroke-specific care in rural and remote areas, consistent with their non-Aboriginal counterparts.[11] However, in previous studies patients with stroke who were Aboriginal had less access to the hospital procedures or medications to prevent stroke than non-Aboriginal patients.[12,13] Further, it has been identified in a national audit that Aboriginal patients with stroke received less access to recommended care, e.g., none received intravenous thrombolysis or timely allied health assessments, they were less likely to be treated in a stroke unit, and subsequently experienced worse outcomes than non-Aboriginal patients.[14] Further research is needed to understand the implications of these findings and verify, if in fact, disparities across the whole continuum of care exist, to inform policy and planning.

Cost-effectiveness of stroke care may be monitored using health care utilisation data to identify potential treatment biases.[15] One important measure of cost-effectiveness is the marginal changes in health costs over the marginal changes in stroke survival.[16] Cost-effectiveness analyses provide useful information to guide effective, efficient and equitable use of limited resources.[15] Information

on the cost-effectiveness of stroke care and prevention has been published previously.[15,17] However, little is known about the cost-effectiveness of stroke care in Aboriginal compared with non-Aboriginal patients.[18] The intuitive way in which cost-effectiveness analysis can handle both costs and effects simultaneously makes it a powerful tool for the evaluation of health policy and practice at a population level.[19] The comparative cost-effectiveness design provides a valuable means to describe health care activities in a real world setting relative to the outcome achieved.[20]

The NT is a large, sparsely populated area of northern Australia where a substantial Aboriginal population resides as opposed to other parts of Australia. In 2011, the NT resident population was 211943 (1% of the Australian population), 28% of whom were Aboriginal Australians (nationally 2.5%).[21] There are five public hospitals, which provided stroke care in the NT, and of which only one (Royal Darwin Hospital) has a specialised stroke unit, which was opened around 2008. Primary care for non-Aboriginal patients was generally provided by general practitioners (GPs) located in urban areas (herein referred to as urban-based primary care), whereas most of Aboriginal patients were from remote communities where primary care services were provided in remote clinics by nurses and Aboriginal health practitioners. In 2006, life expectancy at birth was 21 and 15 years shorter in Aboriginal than non-Aboriginal population for males (60 vs 81 years) and females (70 vs 85 years) respectively in the NT.[22] Between 1999-2003, the burden of disease resulting from premature death and disability in the Aboriginal population was 2.8-3.3 times greater than in the non-Aboriginal population.[23] The Aboriginal NT residents are more likely than their non-Aboriginal counterparts to suffer haemorrhagic stroke (HS) and comorbidities and die from a stroke.[24] Despite there being significant improvements in stroke survival between 1992 and 2013, the hospital mortality was still 56% higher in Aboriginal than non-Aboriginal patients, after age adjustment.[10] However, there was a lack of comprehensive assessments comparing Aboriginal and non-Aboriginal patients with stroke in terms of cost-effectiveness of stroke care including stroke specific procedures as recommended in clinical guidelines.[11]

The aim of the study was to compare the cost-effectiveness of stroke care for two populations with very different burdens of disease, the Aboriginal and non-Aboriginal Australians to explore whether

inequalities in providing health care exist and to determine the efficiency of the health care that is provided. The study was designed to draw conclusions and make recommendations regarding cost-effectiveness of stroke care for Aboriginal patients.

Method

In undertaking this study we adhered to the international guidelines for cost-effectiveness analysis.[25] This is an observational cohort study based on data from 1 July 1992 to 30 June 2013 for Aboriginal and non-Aboriginal patients with first-ever stroke. Four administrative data sources were used. Individual patient-level data from the hospital inpatient data (HID) between 1982 and 2013 and event data from the primary care information system (PCIS) between 2009 and 2013, were merged using an encrypted unique patient identifier for patient tracking and survival analysis. Two additional data sources, Medicare and Pharmaceutical Benefits Scheme (PBS) data from 1993 to 2013, were used for calculating non-hospital costs.

Patients with stroke were identified from HID using the International Classifications of Diseases (ICD) version 9 to June 1998 and version 10 thereafter. Stroke was categorised into three types: HS (diagnosis codes 430, 431, 432.9 (ICD-9); I60, I61, I62.9 (ICD-10)), ischaemic stroke (IS) (433, 434; I63) and stroke type undetermined (UND) (436; I64).[26] Transient ischaemic attack (TIA) (435.9; G45.9) was excluded from this study. Incidence of stroke was identified using the first-ever admission with a stroke diagnosis during the study period, and a stroke-free admission in the preceding clearance of at least ten years using data from 1 July 1982. Follow-up time was calculated as the number of days between the first-ever admission date and the discharge date of the subsequent or recurrent admission. Each intervening hospital admission or readmission was regarded as a follow-up. Procedures including imaging, surgical, pharmaceutical, rehabilitation and other non-stroke specific procedures were defined by using the Australian Classification of Health Intervention (ACHI) block numbers (the mapping table available from data depository).[27] The numbers of ACHI coded procedures per hospitalisation were averaged for each patient. Follow-up time was censored at: the date of death for patients who died from causes other than stroke, or the discharge date of the last admission (or first

admission if only admitted once) for patients discharged alive. Truncation was not used for censoring at the beginning nor the end of this study,[28] because truncation might overestimate survival when resources were not available for vigorous follow-up and search using the national death index.

Six main categories of service use were costed from a health care perspective: hospital inpatient care, outpatient, nursing home, primary care (GP and remote clinic), pharmaceuticals and allied health. Indirect (i.e. loss of productivity), intangible (i.e. loss on quality of life) and external social costs were beyond the scope of this study. Inpatient costs were calculated by multiplying the Australian national/refined diagnosis related group weights times the NT benchmark prices,[29] covering medical, nursing, supplies, imaging, pathology, allied health, pharmacy, critical care, operating room, emergency, prostheses, procedures, and hospital overhead oncosts. The stroke related events (occasions of service) in remote communities were identified using PCIS data. The remote clinic costs were obtained by multiplying the number of events by the average cost estimate in the year the service was provided (e.g. AUD36 in 2003).[30] Since we did not have access to unit record GP data, the urban primary care cost was estimated as 3.2% of total NT Medicare benefits for GPs, because 3.2% of GP patients had a stroke or TIA according to the most recent GP survey.[31] The PBS cost was estimated by the item codes for antihypertensive, antiplatelet and anticoagulant agents. The cost was multiplied by two to cover Section 100 (access to highly specialised drugs by remote Aboriginal people) expenditure and to counterbalance the under-coverage of data for drugs administered in remote areas, because preliminary analysis indicated that Section 100 expenditure was similar to the claimed PBS in the NT Aboriginal setting. Hospital costing methodology complies with the national guidelines for cost data collection [29] and the cost estimate breakdowns have been reported elsewhere.[7] Five percent was applied to represent the present value of costs based on the reference year 2012/2013, because 5% reflected an average level of health inflation.[32]

Case fatality was defined by using HID, where separation mode was recorded as deceased and stroke was recorded as a diagnosis at that episode. Health outcome was assessed through measuring survival time after stroke. Univariable analysis was performed using mean, median and the interquartile range to describe demographics, time of incidence, hospitalisations, bed-days, numbers of procedures, costs

and survival time. Chi-square significance test and Kaplan-Meier survival curves were used to compare Aboriginal and non-Aboriginal patients. Linear censored regression was used to adjust for loss to follow-up. Estimation of the incremental cost-effectiveness ratio (ICER) was adapted for comparing cost and survival for the Aboriginal and non-Aboriginal populations, based on the notion of maximising health gains with available resources.[33] The bootstrap method with 2000 replications was used to construct the cost-effectiveness plane for assessment of the ICER variability.[33] A threshold statistical value of AUD120 000 per life-year was used to evaluate cost-effectiveness, as recommended by the Australian Safety and Compensation Council.[34] The cost-effectiveness of health care for incident stroke was further analysed by using a marginal structural model (MSM) to account for time-dependent confounding and censoring.[35] A log10 transformation was applied to the costs, because preliminary analysis showed the observed costs resembled a lognormal distribution. The multiplicative cost increment was used as an independent variable and survival as the dependent variable, because survival represents benefits of stroke care as an outcome, and the cost representing the resource use as the input. The hazard ratio (HR) of mortality for a unit of cost increment represents the proportional change in mortality hazard given the percent change in health care costs. A full range of thresholds for the ICER (AUD0-500 000 per life-year) representing different values of willingness-to-pay was tested for assessing the uncertainty of the ICER. The willingness-to-pay acceptability curves were compared for comparative cost-effectiveness, i.e., saving more life-years cost-effectively. Sensitivity analysis was also performed using 3% and 10% discount rates, with and without log-transformation.

The study was approved by the Human Research Ethics Committee of the NT Department of Health and the Menzies School of Health Research (HREC-2011-1680).

Results

Between 1992 and 2013, 2889 patients were hospitalised with stroke in the NT, of whom 731 patients with recurrent stroke were excluded, leaving 2158 incident stroke cases in this study. Among incident cases, just over half were male (54.3%), aged less than 65 years (54.6%) or from non-remote areas

(55.2%), with 42.6% being IS, 29.8% HS, and 46.0% of Aboriginal origin (Table 1). The total median follow-up time was 318 days with interquartile range 13 to 1512 days. Aboriginal patients had 14 years younger age of stroke onset, 71.4% more hospital bed-days and 49.6% greater observed costs than non-Aboriginal patients, driven by a higher level of hospitalisations (median 4 vs 3) (all $P<0.001$). The average number of procedures per hospitalisation in Aboriginal patients was 6.9% fewer than that for non-Aboriginal patients (2.7 vs 2.9, $P<0.05$). In particular, Aboriginal patients had significantly less imaging and rehabilitation procedures, but more other non-stroke specific procedures than the non-Aboriginal patients (all $P<0.01$). Average numbers of surgical and pharmaceutical procedures were slightly fewer in the Aboriginal than non-Aboriginal patients with non-statistical significance (0.36 vs 0.41 and 0.14 vs 0.16, respectively; both $P>0.05$). Number of incident strokes increased over time likely driven by population growth and ageing, despite there being no changes in the proportion between Aboriginal and non-Aboriginal patients. Compared with non-Aboriginal patients, Aboriginal patients were disproportionately more likely to experience HS, attributed to a greater prevalence of hypertension, diabetes and chronic kidney disease (CKD) ($P\leq0.01$). There was no difference in total case fatality between Aboriginal and non-Aboriginal patients with stroke over the study period.

Table 1. Stroke patient characteristics (%) by Aboriginality, Northern Territory, Australia, 1993-2013

	Aboriginal		Non-Aboriginal		Significance	Total	
Male	464	(46.8%)	707	(60.6%)	P<0.001	1171	(54.3%)
Age of onset<65 years	704	(71.0%)	474	(40.7%)	P<0.001	1178	(54.6%)
Remote	735	(74.1%)	231	(19.8%)	P<0.001	966	(44.8%)
Median (IQR)							
Age of onset (years)	51	(41-63)	65	(54-75)	P<0.001	59	(47-71)
Hospitalisations per patient	4	(2-11)	3	(1-7)	P<0.001	3	(1-8)
Follow-up days	507	(25-1642)	201	(8-1367)	P<0.001	318	(13-1512)
Total bed-days	36	(10-94)	21	(5-73)	P<0.001	28	(7-82)
Procedures per hospitalisation (n)	2.7	(2.5-2.8)	2.9	(2.8-3.0)	P=0.023	2.8	(2.7-2.9)
Procedure type							
Surgical (n)	0.36	(13.6%)	0.41	(14.3%)	P=0.103	0.39	(14%)
Imaging (n)	0.42	(15.9%)	0.60	(20.7%)	P<0.001	0.52	(18.6%)
Rehabilitation (n)	1.23	(46.1%)	1.42	(49.3%)	P=0.003	1.33	(47.9%)
Pharmaceutical (n)	0.14	(5.4%)	0.16	(5.7%)	P=0.181	0.15	(5.5%)
Other (n)	0.51	(19.0%)	0.29	(10.0%)	P<0.001	0.39	(14.0%)
Observed costs (AUD'000)	50.4	(15.2-123.8)	33.7	(10.0-89.1)	P<0.001	41.9	(11.2-102.6)
Time period					P=0.066		
1993-1999	236	(23.8%)	329	(28.2%)		565	(26.2%)
2000-2006	336	(33.9%)	372	(31.9%)		708	(32.8%)
2007-2013	420	(42.3%)	465	(39.9%)		885	(41.0%)
Stroke type					P<0.001		
Haemorrhagic	340	(34.3%)	304	(26.1%)		644	(29.8%)
Ischaemic	404	(40.7%)	516	(44.3%)		920	(42.6%)
Undetermined	248	(25.0%)	346	(29.7%)		594	(27.5%)
Comorbidity							
Hypertension	596	(60.1%)	636	(54.5%)	P=0.010	1232	(57.1%)
Diabetes	446	(45.0%)	276	(23.7%)	P<0.001	722	(33.5%)
IHD	227	(22.9%)	305	(26.2%)	P=0.079	532	(24.7%)
CKD	334	(33.7%)	200	(17.2%)	P<0.001	534	(24.7%)
Depression	25	(2.5%)	57	(4.9%)	P=0.004	82	(3.8%)
COPD	139	(14.0%)	159	(13.6%)	P=0.801	298	(13.8%)
Cancer	53	(5.3%)	149	(12.8%)	P<0.001	202	(9.4%)
Atrial fibrillation	153	(15.4%)	220	(18.9%)	P=0.035	373	(17.3%)
Case fatality	259	(26.1%)	305	(26.2%)	P=0.979	564	(26.1%)
Total	992	(46.0%)	1166	(54.0%)	P<0.001	2158	(100%)

CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. IHD, ischaemic heart disease. IQR, interquartile range.

Figure 1 (a) shows that there appeared to be slightly better survival in Aboriginal patients with stroke despite the log-rank test indicating statistical insignificance. Aboriginal patients were significantly younger. Age stratified analysis in Figures 1(b)-(d) shows a slightly greater Aboriginal survival in the aged 65+ group (P<0.05), but there were no significant Aboriginal survival differences in the other age groups.

(Insert Figure 1 here)

Details of the average survival time and costs by stroke type comparing Aboriginal and non-Aboriginal patients are provided in Table 2. Aboriginal patients tended to have better survival and greater costs than non-Aboriginal patients, especially after an IS (P<0.05). Overall, stroke costs were 20.5% more in Aboriginal than non-Aboriginal patients (P<0.001). The ICER of stroke care for Aboriginal patients compared with that for non-Aboriginal patients was an average of AUD110 965 per survival year, ranging from AUD69 163 in UND to AUD130 376 in HS (see bottom line in Table 2). Figure 2 shows a great degree of uncertainty in both survival and costs, especially in UND, followed by IS and then HS, when comparing cost-effectiveness between Aboriginal and non-Aboriginal patients. It is unlikely that the greater uncertainty in UND was caused by the smaller sample size, because the bootstrap adjusts for sample size by resampling.[33] The differential costs and effects were divided evenly across the threshold line, indicating that stroke care in Aboriginal patients was as cost-effective as in non-Aboriginal patients. Figure 3 provides the probability of whether the stroke care in Aboriginal patients would result in longer survival than in non-Aboriginal patients. The acceptability of achieving optimised stroke care in Aboriginal patients increased progressively with willingness-to-pay. At the threshold price (dotted line in Figure 3), the probability of achieving an optimal cost-effectiveness in Aboriginal patients with UND was 0.76, followed by HS (0.69) and IS (0.42).

Table 2. Average survival time and cost by stroke type and incremental cost-effectiveness ratio comparing Aboriginal and non-Aboriginal patients

		HS	IS	UND	Total
n		644	920	594	2158
Survival (years)	Aboriginal	6.1	11.4	11.0	9.1
	Non-Aboriginal	5.9	9.9	9.7	8.6
	P-value	0.662	0.023	0.081	0.148
Average cost (AUD)	Aboriginal	192 675	448 451	404 800	331 340
	Non-Aboriginal	166 743	337 732	310 011	275 045
	P-value	0.091	<0.001	0.002	<0.001
Net cost per life-year gained (ICER)		130 376	74 343	69 163	110 965

HS, haemorrhagic stroke. ICER, incremental cost-effectiveness ratio. IS, ischaemic stroke. UND, stroke type undetermined.

(Insert Figures 2 and 3 here)

After further adjustments for time-dependent confounders (time, age and comorbidities), time-independent confounders (sex and remoteness) and dependent censoring by using MSM (Table 3), Aboriginal patients with stroke were 34.4% more likely to die of stroke than non-Aboriginal patients (P=0.008). Overall, HS was more than twice as likely to cause death as IS (P<0.001), whereas there was no difference in survival between IS and UND. Stroke mortality increased with age at onset (2.4% for every additional year of age, P<0.001), compounded by CKD (P<0.001) or cancers (P=0.011). The stroke mortality was reduced over time (3.2% reduction annually, P<0.001), and negatively correlated with residing in remote areas or having hypertension (both P<0.01). In particular, stroke mortality was negatively associated with greater health care costs. A 10-fold increase in health costs was associated with a reduction in stroke mortality by 40.5% (HR=0.595, P<0.001). The stratified MSM by Aboriginality found that the HR was smaller among Aboriginal patients than in non-Aboriginal patients (0.525 vs 0.642), indicating a slightly greater mortality reduction in Aboriginal, though statistically insignificant (P=0.25).

Table 3. Marginal structural proportional hazard model hazard ratio and confidence interval by Aboriginality

	Aboriginal		Non-Aboriginal		All stroke	
	HR	95%CI	HR	95%CI	HR	95%CI
Cost increment	0.525	0.405 - 0.681	0.642	0.514 - 0.801	0.595	0.502 - 0.706
Aboriginal	-	-	-	-	1.344	1.079 - 1.673
Ischaemic	1.000	-	1.000	-	1.000	-
Haemorrhagic	2.644	1.897 - 3.684	1.778	1.377 - 2.297	2.059	1.687 - 2.512
Undetermined	1.128	0.746 - 1.705	0.922	0.704 - 1.208	0.974	0.776 - 1.222
Time (year-1993)	0.982	0.960 – 1.004	0.961	0.945 - 0.977	0.968	0.955 - 0.981
Age at onset (years)	1.015	1.006 - 1.024	1.033	1.024 - 1.043	1.024	1.018 - 1.030
Female	0.822	0.631 - 1.071	1.059	0.845 - 1.322	0.984	0.834 - 1.161
Remoteness	0.826	0.629 - 1.086	0.727	0.527 – 1.002	0.753	0.615 - 0.921
Hypertension	0.698	0.526 - 0.927	0.726	0.582 - 0.905	0.702	0.591 - 0.834
Diabetes	0.801	0.578 - 1.111	1.013	0.772 - 1.331	0.897	0.725 - 1.109
CKD	1.616	1.184 - 2.207	1.484	1.088 - 2.023	1.509	1.210 - 1.881
IHD	1.033	0.671 - 1.589	0.720	0.520 – 0.997	0.839	0.647 - 1.086
COPD	1.017	0.696 - 1.735	0.989	0.725 - 1.348	1.014	0.773 - 1.330
Cancer	1.299	0.524 - 3.217	1.534	1.090 - 2.158	1.503	1.098 - 2.058
Depression	-	-	0.450	0.154 - 1.318	0.399	0.130 - 1.224
Atrial fibrillation	1.200	0.751 - 1.917	0.989	0.705 - 1.388	1.099	0.841 - 1.437

CI, confidence interval. CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. HR, hazard ratio. IHD, ischaemic heart disease. Cost increment represents percent change in log(Cost).

Sensitivity analysis provided evidence that the ICER was not dominant in favour of the Aboriginal population until the willingness-to-pay threshold was increased close to AUD200 000 per life-year gained (P>0.7, Figure 3). Probabilistic analyses confirmed that treating HS and UND were likely to be more cost-effective in Aboriginal patients than treating IS, likely related to underdiagnosis of stroke in

remote areas. The average cost relativities were insensitive to differing discount rates. Log-transformation would generate more robust cost estimates. Without log-transformation, the magnitude of average costs might be affected, but the sign of difference between Aboriginal and non-Aboriginal patients remained consistent.

Discussion

In terms of survival outcome, to our knowledge, this is the first comparative cost-effectiveness evaluation providing evidence that stroke care among Aboriginal patients is as efficient as among the non-Aboriginal patients within the Australian context. Reports on the economic analysis of cost-effectiveness among Aboriginal and non-Aboriginal populations are rare.[36,37] In our sample almost half (46%) were Aboriginal. Overall, this incidence number was disproportionate to the population proportion for the NT (28% in 2011), reflecting the large impact stroke has on the Aboriginal population. Stroke care in the Aboriginal population may be even more beneficial because of the 14 years younger age at onset of stroke, resulting in more life-years potentially saved from the additional costs of providing care. There have been several estimates of the long-term cost of stroke in Australia in the past two decades, up to AUD100 000,[3-6,38] mainly based on the North East Melbourne Stroke Incidence Study.[3] These cost estimates were based on cohort studies conducted in urban areas and were likely to understate the NT patient lifetime costs, because of attrition bias caused by loss to follow-up and inability to account for the costs related to remote areas.[39] In 2012/2013 Australian dollars, the estimated lifetime cost for an incident stroke in NT was AUD302 538 per patient between 1992 and 2013 after adjusting for loss to follow-up.[7] Stroke cost was found to be 44% greater for Aboriginal patients.[7]

Accurate cost estimates are required for cost-effectiveness assessment related to improvements in stroke survival.[40,41] Cost-effectiveness can be evaluated by comparing costs against outcomes between the alternative treatments.[33] Understanding the cost drivers in stroke treatments informs health service decisions for cost-effective care. Most cost-effectiveness studies for stroke care were focused on specific procedures,[17,42] for example pharmaceuticals,[43,44] surgery,[45,46]

prevention,[47,48] and rehabilitation;[49] or evaluating alternative models of care,[50] for example telemedicine,[51] and specialised stroke unit.[52,53] Hunter and colleagues evaluated the introduction of centralised stroke care, finding the service reduced mortality by 12% and saved more than £811 per patient-year.[54] In Canada, comprehensive stroke care can reduce hospital admissions (3%), bed-days (26%), death (15%) and nursing home care (13%), as well as save costs of over CAD11 000 per stroke.[55]

Comparative cost-effectiveness is an emerging approach to comparing the costs and monitoring health outcomes of interventions and strategies to prevent, diagnose and treat diseases in real world practice for informing clinical and policy decisions.[56,57] Previous reports suggested an effect of institutional bias in clinical decisions, which favoured stroke care in non-Aboriginal patients.[12,13] Despite these reports, the cost-effectiveness of stroke care among different patient populations has not been investigated. Our study found that the uptake of hospital procedures by Aboriginal stroke patients with an incident stroke was 7% less than the non-Aboriginal patients (mainly imaging and rehabilitation). Univariable analysis showed that stroke care in Aboriginal patients is as cost-effective as in non-Aboriginal patients. The differential costs and effects were divided quite evenly across the willingness-to-pay threshold line. After taking into account the effects of patient-level confounders, time and loss to follow-up using MSM, we found that an increase in stroke care costs was associated with a slightly better health outcome for Aboriginal than non-Aboriginal patients with stroke, despite failing to reach statistical significance. Baker and colleagues evaluated cost-effectiveness of blood pressure control in kidney and cardiovascular disease treatment in an Aboriginal community.[36] It was found that 3-year perindopril treatment was effective in delaying 1.5 years of haemodialysis per patient with a net annual cost of AUD1200, in comparison with a modelled historical control of the same Aboriginal population. Stroke was not identified in their study and non-Aboriginal controls were not compared.[36] Grieve and colleagues compared stroke care costs and survival among different European countries and different ways of providing stroke care.[19] The authors found that the cost-effectiveness may be related to specialised stroke care, which is required to provide interdisciplinary care after stroke. Our analysis directly compared cost-effectiveness of stroke care for both Aboriginal

and non-Aboriginal patients. This study is also complemented by the use of MSM, which is more appropriate than conventional methods for managing censoring issues when estimating survival and costs.[35]

Strengths of this study include the large sample size of Aboriginal patients relative to the non-Aboriginal patients, access to data to ensure capture of incident cases and the ability to confidently link patient records across multiple sources of data. Further, the methodology in this study informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.[56,57] This study covered 21 years from 1992 to 2013, largely because of the requirements to identify sufficient incident cases and follow-up for survival analysis. Several limitations should be noted. First, the results in this study are most relevant to Aboriginal population living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high income country.[58,59] The stroke care cost-effectiveness results may be relevant to other disadvantaged populations. Second, our cost estimates may not be precise. PCIS was only available for Aboriginal communities after 2009. PCIS data were only used for costing primary care, which was extrapolated to cover the previous years and adjusted for health inflation. In this study we used administrative HID to identify stroke cases and did not include minor and low-cost cases managed solely by outpatient department, GP or remote clinics. These low-cost cases would comprise a small proportion of stokes (previously estimated at 12% in 1997).[3] A top-down approach was applied to calculate the GP, nursing home and allied health costs, which might lead to over- or under-estimation of the true costs. Various statistical methods were used to assess the robustness of the point estimates. More research is needed to further explore the cost-effectiveness of stroke care using prospective patient-level costing data. Third, another potential source of uncertainty in cost-effectiveness evaluation was the lack of non-NT or non-stroke controls, assuming stroke care as a whole is cost-effective in the NT, and stroke survival was independently associated with costs of stroke care and perceived confounders. Fourth, we were unable to measure levels of disability and quality of life among stroke survivors. It might be that there were important differences in levels of stroke-related disabilities between Aboriginal and non-

Aboriginal patients. Finally, the joint effects of multiple comorbidities and their interactions were not considered in this study due to limited sample sizes.

In conclusion, stroke care for Aboriginal patients is at least as cost-effective as for non-Aboriginal patients managed within a sparsely populated but geographically large region of Australia, where health care resources are limited. Stroke care was found to present worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher burden of disease. These data may provide useful information for other countries with Indigenous populations living in regions with similar geographical and resource constraints.

Figure legends

Figure 1. Survival by age and Aboriginality

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

Contributorship statement

YZ designed the study, collected costing data, undertook data linkage and statistical analysis, and wrote the first draft of the manuscript. SG, H Falhammar, H Flavell and DC participated in the literature review, methodology development, discussion and revision of the manuscript, and contributed equally to this work.

Competing interests

The authors declare that they have no competing interests relevant to the manuscript.

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Data sharing statement

We will share the data via a publicly accessible repository.

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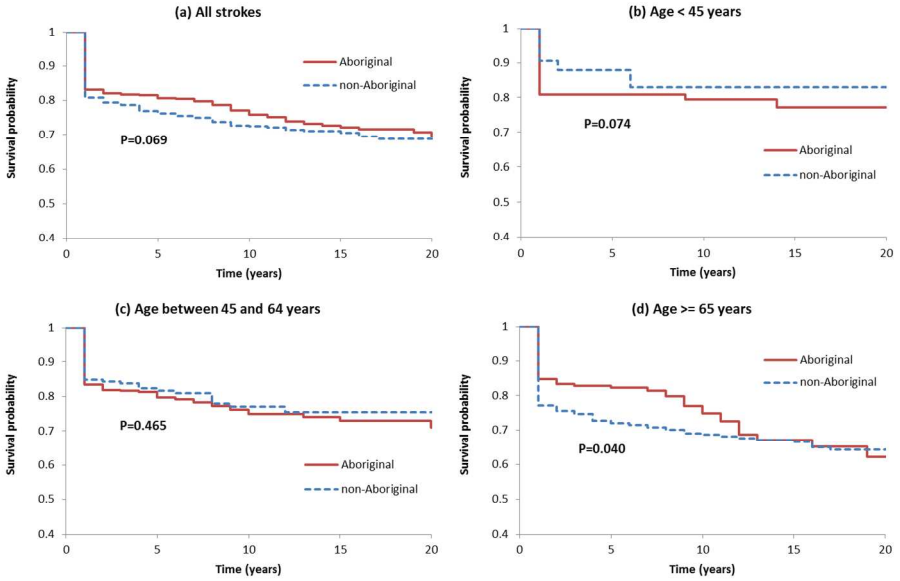

Figure 1. Survival by age and Aboriginality

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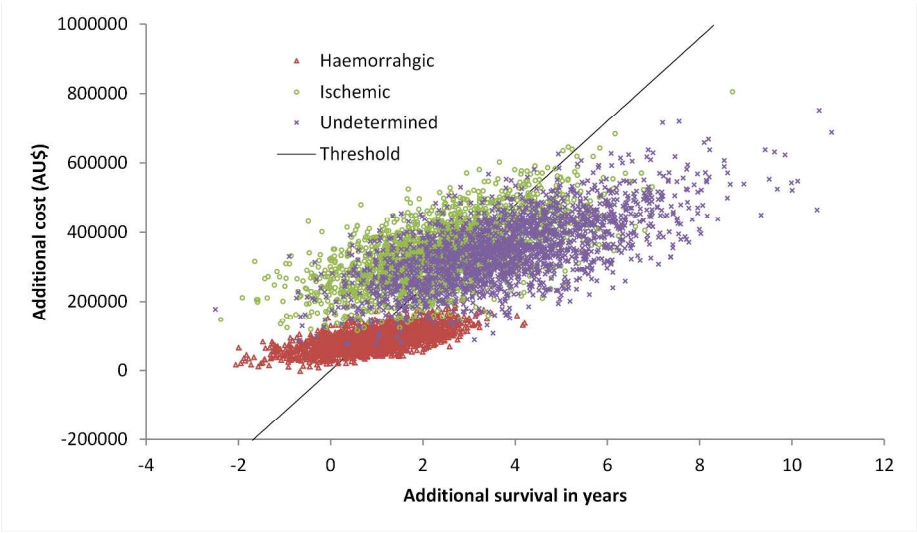

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

297x209mm (300 x 300 DPI)

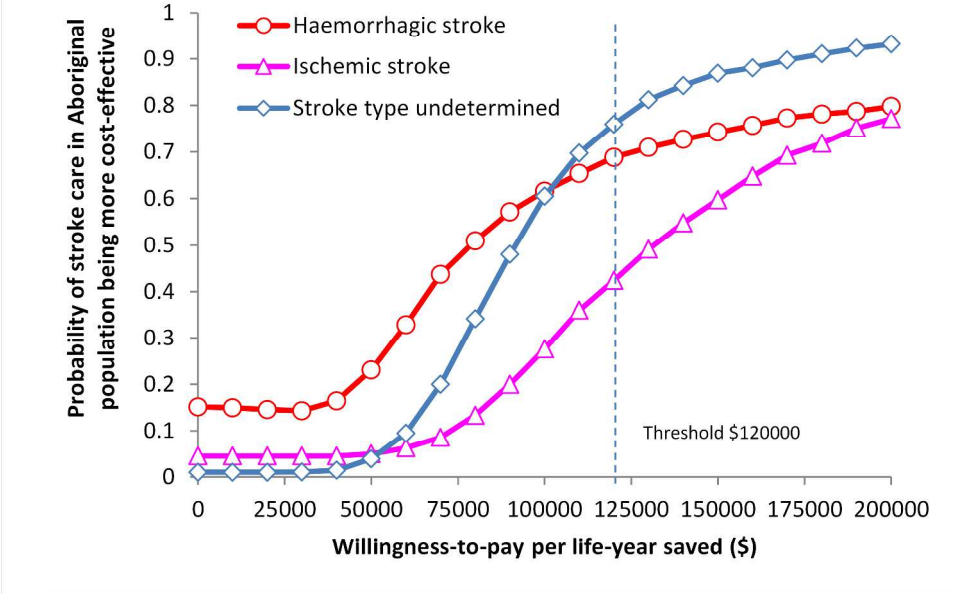

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

297x209mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cost-effectiveness of stroke care in Aboriginal and non-Aboriginal patients: an observational cohort study in the Northern Territory of Australia

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Title

Cost-effectiveness of stroke care in Aboriginal and non-Aboriginal patients: an observational cohort study in the Northern Territory of Australia

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Stroke; Health equity; Efficiency; Social medicine

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Cost-effectiveness of stroke care in Aboriginal and non-Aboriginal patients: an observational cohort study in the Northern Territory of Australia

Abstract

Objectives: To assess cost-effectiveness of stroke care for Aboriginal compared with non-Aboriginal patients in the Northern Territory (NT), Australia.

Design: Cost effectiveness analysis using data from a cohort-based follow-up study of stroke incidences.

Setting: Public hospitals in the NT from 1992 to 2013.

Participants: Individual patient data were extracted and linked from the hospital inpatient and primary care information systems.

Outcome measures: Incremental cost-effectiveness ratios were calculated and assessed graphically. Survival time was used to measure effectiveness of stroke care, in comparison with the net costs per life-year gained, from a health care perspective, by applying multivariable models to account for time-dependent confounding.

Results: 2158 patients with incident stroke were included (1171 males, 1178 aged<65 years and 966 from remote areas). 992 patients were of Aboriginal origin (46.0%, disproportionately higher than the population proportion of 28%. Of all cases, 42.6% were ischaemic and 29.8% haemorrhagic stroke. Average age of stroke onset was 51 years in Aboriginal, compared with 65 years in non-Aboriginal patients (P<0.001). Aboriginal patients had 71.4% more hospital bed-days, and 7.4% fewer procedures than non-Aboriginal patients. Observed health costs averaged AUD50 400 per Aboriginal compared with AUD33 700 per non-Aboriginal patient (P<0.001). The differential costs and effects for each population were distributed evenly across the incremental cost-effectiveness plane threshold line, indicating no difference in cost-effectiveness between populations. After further adjustment for

confounding and censoring, cost-effectiveness appeared greater for Aboriginal than non-Aboriginal patients, but this was not statistically significant (P=0.25).

Conclusions: Stroke care for the NT Aboriginal population is at least as cost-effective as the non-Aboriginal population. Stroke care presents worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher level burden of disease. These findings are relevant for health care planning and policy development regarding equal access to stroke care for Aboriginal patients.

Subject headings: Health economics; Neurology; Public health; Health services research

Keywords: Stroke; Health economics; Social medicine

Strengths and limitations of this study

- This study included a large sample size of Aboriginal patients with stroke relative to the non-Aboriginal patients over a 21-year period, using linked patient records across multiple sources of data.
- The methodology informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.
- The results are most relevant to Aboriginal populations living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high income country.
- The lifetime stroke costs were based on health service use, which did not cover costs associated with the loss of quality of life among stroke survivors.

Introduction

Worldwide, stroke has a substantial impact on the health of populations and on health systems, and about 16.9 million people suffered first-ever stroke, with 5.9 million stroke-related deaths in 2010.[1] Approximately 51 000 Australians experience a new or recurrent stroke each year, and stroke is a national priority since it is a leading cause of death and disability.[2] The lifetime cost of first-ever stroke care are approximately AUD100 000 per patient in Australia.[3-6] In a recent Northern Territory (NT) study, the estimated net lifetime health care cost for Aboriginal patients were 44% greater than for non-Aboriginal patients.[7]

Over the past 25 years, improvement in stroke prevention and treatment has resulted in substantial increases in stroke survival.[8,9] Although Aboriginal populations experience stroke at younger ages and have a higher prevalence of comorbidities, this improvement in survival was evident for Aboriginal and non-Aboriginal patients in the NT, albeit with much shorter survival in the Aboriginal patients after adjustments for age at onset and other confounders.[10] Nationally, it has been recognised in the clinical guidelines that Aboriginal patients require access to general and stroke-specific care in rural and remote areas, consistent with their non-Aboriginal counterparts.[11] However, in previous studies patients with stroke who were Aboriginal had less access to the hospital procedures or medications to prevent stroke than non-Aboriginal patients.[12,13] Further, it has been identified in a national audit that Aboriginal patients with stroke received less access to recommended care, e.g., none received intravenous thrombolysis or timely allied health assessments, they were less likely to be treated in a stroke unit, and subsequently experienced worse outcomes than non-Aboriginal patients.[14] Further research is needed to understand the implications of these findings and verify, if in fact, disparities across the whole continuum of care exist, to inform policy and planning.

Cost-effectiveness of stroke care may be monitored using health care utilisation data to identify potential treatment biases.[15] One important measure of cost-effectiveness is the marginal changes in health costs over the marginal changes in stroke survival.[16] Cost-effectiveness analyses provide useful information to guide effective, efficient and equitable use of limited resources.[15] Information

on the cost-effectiveness of stroke care and prevention has been published previously.[15,17] However, little is known about the cost-effectiveness of stroke care in Aboriginal compared with non-Aboriginal patients.[18] The intuitive way in which cost-effectiveness analysis can handle both costs and effects simultaneously makes it a powerful tool for the evaluation of health policy and practice at a population level.[19] The comparative cost-effectiveness design provides a valuable means to describe health care activities in a real world setting relative to the outcome achieved.[20]

The NT is a large, sparsely populated area of northern Australia where a substantial Aboriginal population resides as opposed to other parts of Australia. In 2011, the NT resident population was 211943 (1% of the Australian population), 28% of whom were Aboriginal Australians (nationally 2.5%).[21] There are five public hospitals, which provided stroke care in the NT, and of which only one (Royal Darwin Hospital) has a specialised stroke unit, which was opened around 2008. Primary care for non-Aboriginal patients was generally provided by general practitioners (GPs) located in urban areas (herein referred to as urban-based primary care), whereas most of Aboriginal patients were from remote communities where primary care services were provided in remote clinics by nurses and Aboriginal health practitioners. In 2006, life expectancy at birth was 21 and 15 years shorter in Aboriginal than non-Aboriginal population for males (60 vs 81 years) and females (70 vs 85 years) respectively in the NT.[22] Between 1999-2003, the burden of disease resulting from premature death and disability in the Aboriginal population was 2.8-3.3 times greater than in the non-Aboriginal population.[23] The Aboriginal NT residents are more likely than their non-Aboriginal counterparts to suffer haemorrhagic stroke (HS) and comorbidities and die from a stroke.[24] Despite there being significant improvements in stroke survival between 1992 and 2013, the hospital mortality was still 56% higher in Aboriginal than non-Aboriginal patients, after age adjustment.[10] However, there was a lack of comprehensive assessments comparing Aboriginal and non-Aboriginal patients with stroke in terms of cost-effectiveness of stroke care including stroke specific procedures as recommended in clinical guidelines.[11]

The aim of the study was to compare the cost-effectiveness of stroke care for two populations with very different burdens of disease, the Aboriginal and non-Aboriginal Australians to explore whether

inequalities in providing health care exist and to determine the efficiency of the health care that is provided. The study was designed to draw conclusions and make recommendations regarding cost-effectiveness of stroke care for Aboriginal patients.

Method

In undertaking this study we adhered to the international guidelines for cost-effectiveness analysis.[25] This is an observational cohort study based on data from 1 July 1992 to 30 June 2013 for Aboriginal and non-Aboriginal patients with first-ever stroke. Four administrative data sources were used. Individual patient-level data from the hospital inpatient data (HID) between 1982 and 2013 and event data from the primary care information system (PCIS) between 2009 and 2013, were merged using an encrypted unique patient identifier for patient tracking and survival analysis. Two additional data sources, Medicare and Pharmaceutical Benefits Scheme (PBS) data from 1993 to 2013, were used for calculating non-hospital costs.

Patients with stroke were identified from HID using the International Classifications of Diseases (ICD) version 9 to June 1998 and version 10 thereafter. Stroke was categorised into three types: HS (diagnosis codes 430, 431, 432.9 (ICD-9); I60, I61, I62.9 (ICD-10)), ischaemic stroke (IS) (433, 434; I63) and stroke type undetermined (UND) (436; I64).[26] Transient ischaemic attack (TIA) (435.9; G45.9) was excluded from this study. Incidence of stroke was identified using the first-ever admission with a stroke diagnosis during the study period, and a stroke-free admission in the preceding clearance of at least ten years using data from 1 July 1982. Follow-up time was calculated as the number of days between the first-ever admission date and the discharge date of the subsequent or recurrent admission. Each intervening hospital admission or readmission was regarded as a follow-up. Procedures including imaging, surgical, pharmaceutical, rehabilitation and other non-stroke specific procedures were defined by using the Australian Classification of Health Intervention (ACHI) block numbers (the de-identified data and mapping table available from data depository with brief technical notes).[27] The numbers of ACHI coded procedures per hospitalisation were averaged for each patient. Follow-up time was censored at: the date of death for patients who died from causes other than stroke, or the

discharge date of the last admission (or first admission if only admitted once) for patients discharged alive. Truncation was not used for censoring at the beginning nor the end of this study,[28] because truncation might overestimate survival when resources were not available for vigorous follow-up and search using the national death index.

Six main categories of service use were costed from a health care perspective: hospital inpatient care, outpatient, nursing home, primary care (GP and remote clinic), pharmaceuticals and allied health. Indirect (i.e. loss of productivity), intangible (i.e. loss on quality of life) and external social costs were beyond the scope of this study. Inpatient costs were calculated by multiplying the Australian national/refined diagnosis related group weights times the NT benchmark prices,[29] covering medical, nursing, supplies, imaging, pathology, allied health, pharmacy, critical care, operating room, emergency, prostheses, procedures, and hospital overhead oncosts. The stroke related events (occasions of service) in remote communities were identified using PCIS data. The remote clinic costs were obtained by multiplying the number of events by the average cost estimate in the year the service was provided (e.g. AUD36 in 2003).[30] Since we did not have access to unit record GP data, the urban primary care cost was estimated as 3.2% of total NT Medicare benefits for GPs, because 3.2% of GP patients had a stroke or TIA according to the most recent GP survey.[31] The PBS cost was estimated by the item codes for antihypertensive, antiplatelet and anticoagulant agents. The cost was multiplied by two to cover Section 100 (access to highly specialised drugs by remote Aboriginal people) expenditure and to counterbalance the under-coverage of data for drugs administered in remote areas, because preliminary analysis indicated that Section 100 expenditure was similar to the claimed PBS in the NT Aboriginal setting. Hospital costing methodology complies with the national guidelines for cost data collection [29] and the cost estimate breakdowns have been reported elsewhere.[7] Five percent was applied to represent the present value of costs based on the reference year 2012/2013, because 5% reflected an average level of health inflation.[32]

Case fatality was defined by using HID, where separation mode was recorded as deceased and stroke was recorded as a diagnosis at that episode. Health outcome was assessed through measuring survival time after stroke. Univariable analysis was performed using mean, median and the interquartile range

to describe demographics, time of incidence, hospitalisations, bed-days, numbers of procedures, costs and survival time. Chi-square significance test and Kaplan-Meier survival curves were used to compare Aboriginal and non-Aboriginal patients. Linear censored regression was used to adjust for loss to follow-up. Estimation of the incremental cost-effectiveness ratio (ICER) was adapted for comparing cost and survival for the Aboriginal and non-Aboriginal populations, based on the notion of maximising health gains with available resources.[33] The bootstrap method with 2000 replications was used to construct the cost-effectiveness plane for assessment of the ICER variability.[33] A threshold statistical value of AUD120 000 per life-year was used to evaluate cost-effectiveness, as recommended by the Australian Safety and Compensation Council.[34] The cost-effectiveness of health care for incident stroke was further analysed by using a marginal structural model (MSM) to account for time-dependent confounding and censoring.[35] A log10 transformation was applied to the costs, because preliminary analysis showed the observed costs resembled a lognormal distribution. The multiplicative cost increment was used as an independent variable and survival as the dependent variable, because survival represents benefits of stroke care as an outcome, and the cost representing the resource use as the input. The hazard ratio (HR) of mortality for a unit of cost increment represents the proportional change in mortality hazard given the percent change in health care costs. A full range of thresholds for the ICER (AUD0-500 000 per life-year) representing different values of willingness-to-pay was tested for assessing the uncertainty of the ICER. The willingness-to-pay acceptability curves were compared for comparative cost-effectiveness, i.e., saving more life-years cost-effectively. Sensitivity analysis was also performed using 3% and 10% discount rates, with and without log-transformation.

The study was approved by the Human Research Ethics Committee of the NT Department of Health and the Menzies School of Health Research (HREC-2011-1680).

Results

Between 1992 and 2013, 2889 patients were hospitalised with stroke in the NT, of whom 731 patients with recurrent stroke were excluded, leaving 2158 incident stroke cases in this study. Among incident

cases, just over half were male (54.3%), aged less than 65 years (54.6%) or from non-remote areas (55.2%), with 42.6% being IS, 29.8% HS, and 46.0% of Aboriginal origin (Table 1). The total median follow-up time was 318 days with interquartile range 13 to 1512 days. Aboriginal patients had 14 years younger age of stroke onset, 71.4% more hospital bed-days and 49.6% greater observed costs than non-Aboriginal patients, driven by a higher level of hospitalisations (median 4 vs 3) (all $P<0.001$). The average number of procedures per hospitalisation in Aboriginal patients was 6.9% fewer than that for non-Aboriginal patients (2.7 vs 2.9, $P<0.05$). In particular, Aboriginal patients had significantly less imaging and rehabilitation procedures, but more other non-stroke specific procedures than the non-Aboriginal patients (all $P<0.01$). Average numbers of surgical and pharmaceutical procedures were slightly fewer in the Aboriginal than non-Aboriginal patients with non-statistical significance (0.36 vs 0.41 and 0.14 vs 0.16, respectively; both $P>0.05$). Number of incident strokes increased over time likely driven by population growth and ageing, despite there being no changes in the proportion between Aboriginal and non-Aboriginal patients. Compared with non-Aboriginal patients, Aboriginal patients were disproportionately more likely to experience HS, attributed to a greater prevalence of hypertension, diabetes and chronic kidney disease (CKD) ($P\leq0.01$). There was no difference in total case fatality between Aboriginal and non-Aboriginal patients with stroke over the study period.

Table 1. Stroke patient characteristics (%) by Aboriginality, Northern Territory, Australia, 1993-2013

	Aboriginal		Non-Aboriginal		Significance	Total	
Male	464	(46.8%)	707	(60.6%)	P<0.001	1171	(54.3%)
Age of onset<65 years	704	(71.0%)	474	(40.7%)	P<0.001	1178	(54.6%)
Remote	735	(74.1%)	231	(19.8%)	P<0.001	966	(44.8%)
Median (IQR)							
Age of onset (years)	51	(41-63)	65	(54-75)	P<0.001	59	(47-71)
Hospitalisations per patient	4	(2-11)	3	(1-7)	P<0.001	3	(1-8)
Follow-up days	507	(25-1642)	201	(8-1367)	P<0.001	318	(13-1512)
Total bed-days	36	(10-94)	21	(5-73)	P<0.001	28	(7-82)
Procedures per hospitalisation (n)	2.7	(2.5-2.8)	2.9	(2.8-3.0)	P=0.023	2.8	(2.7-2.9)
Procedure type							
Surgical (n)	0.36	(13.6%)	0.41	(14.3%)	P=0.103	0.39	(14%)
Imaging (n)	0.42	(15.9%)	0.60	(20.7%)	P<0.001	0.52	(18.6%)
Rehabilitation (n)	1.23	(46.1%)	1.42	(49.3%)	P=0.003	1.33	(47.9%)
Pharmaceutical (n)	0.14	(5.4%)	0.16	(5.7%)	P=0.181	0.15	(5.5%)
Other (n)	0.51	(19.0%)	0.29	(10.0%)	P<0.001	0.39	(14.0%)
Observed costs (AUD'000)	50.4	(15.2-123.8)	33.7	(10.0-89.1)	P<0.001	41.9	(11.2-102.6)
Time period					P=0.066		
1993-1999	236	(23.8%)	329	(28.2%)		565	(26.2%)
2000-2006	336	(33.9%)	372	(31.9%)		708	(32.8%)
2007-2013	420	(42.3%)	465	(39.9%)		885	(41.0%)
Stroke type					P<0.001		
Haemorrhagic	340	(34.3%)	304	(26.1%)		644	(29.8%)
Ischaemic	404	(40.7%)	516	(44.3%)		920	(42.6%)
Undetermined	248	(25.0%)	346	(29.7%)		594	(27.5%)
Comorbidity							
Hypertension	596	(60.1%)	636	(54.5%)	P=0.010	1232	(57.1%)
Diabetes	446	(45.0%)	276	(23.7%)	P<0.001	722	(33.5%)
IHD	227	(22.9%)	305	(26.2%)	P=0.079	532	(24.7%)
CKD	334	(33.7%)	200	(17.2%)	P<0.001	534	(24.7%)
Depression	25	(2.5%)	57	(4.9%)	P=0.004	82	(3.8%)
COPD	139	(14.0%)	159	(13.6%)	P=0.801	298	(13.8%)
Cancer	53	(5.3%)	149	(12.8%)	P<0.001	202	(9.4%)
Atrial fibrillation	153	(15.4%)	220	(18.9%)	P=0.035	373	(17.3%)
Case fatality	259	(26.1%)	305	(26.2%)	P=0.979	564	(26.1%)
Total	992	(46.0%)	1166	(54.0%)	P<0.001	2158	(100%)

CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. IHD, ischaemic heart disease. IQR, interquartile range.

Figure 1 (a) shows that there appeared to be slightly better survival in Aboriginal patients with stroke despite the log-rank test indicating statistical insignificance. Aboriginal patients were significantly younger. Age stratified analysis in Figures 1(b)-(d) shows a slightly greater Aboriginal survival in the aged 65+ group (P<0.05), but there were no significant Aboriginal survival differences in the other age groups.

(Insert Figure 1 here)

Details of the average survival time and costs by stroke type comparing Aboriginal and non-Aboriginal patients are provided in Table 2. Aboriginal patients tended to have better survival and greater costs than non-Aboriginal patients, especially after an IS (P<0.05). Overall, stroke costs were 20.5% more in Aboriginal than non-Aboriginal patients (P<0.001). The ICER of stroke care for Aboriginal patients compared with that for non-Aboriginal patients was an average of AUD110 965 per survival year, ranging from AUD69 163 in UND to AUD130 376 in HS (see bottom line in Table 2). Figure 2 shows a great degree of uncertainty in both survival and costs, especially in UND, followed by IS and then HS, when comparing cost-effectiveness between Aboriginal and non-Aboriginal patients. It is unlikely that the greater uncertainty in UND was caused by the smaller sample size, because the bootstrap adjusts for sample size by resampling.[33] The differential costs and effects were divided evenly across the threshold line, indicating that stroke care in Aboriginal patients was as cost-effective as in non-Aboriginal patients. Figure 3 provides the probability of whether the stroke care in Aboriginal patients would result in longer survival than in non-Aboriginal patients. The acceptability of achieving optimised stroke care in Aboriginal patients increased progressively with willingness-to-pay. At the threshold price (dotted line in Figure 3), the probability of achieving an optimal cost-effectiveness in Aboriginal patients with UND was 0.76, followed by HS (0.69) and IS (0.42).

Table 2. Average survival time and cost by stroke type and incremental cost-effectiveness ratio comparing Aboriginal and non-Aboriginal patients

		HS	IS	UND	Total
n		644	920	594	2158
Survival (years)	Aboriginal	6.1	11.4	11.0	9.1
	Non-Aboriginal	5.9	9.9	9.7	8.6
	P-value	0.662	0.023	0.081	0.148
Average cost (AUD)	Aboriginal	192 675	448 451	404 800	331 340
	Non-Aboriginal	166 743	337 732	310 011	275 045
	P-value	0.091	<0.001	0.002	<0.001
Net cost per life-year gained (ICER)		130 376	74 343	69 163	110 965

HS, haemorrhagic stroke. ICER, incremental cost-effectiveness ratio. IS, ischaemic stroke. UND, stroke type undetermined.

(Insert Figures 2 and 3 here)

After further adjustments for time-dependent confounders (time, age and comorbidities), time-independent confounders (sex and remoteness) and dependent censoring by using MSM (Table 3), Aboriginal patients with stroke were 34.4% more likely to die of stroke than non-Aboriginal patients (P=0.008). Overall, HS was more than twice as likely to cause death as IS (P<0.001), whereas there was no difference in survival between IS and UND. Stroke mortality increased with age at onset (2.4% for every additional year of age, P<0.001), compounded by CKD (P<0.001) or cancers (P=0.011). The stroke mortality was reduced over time (3.2% reduction annually, P<0.001), and negatively correlated with residing in remote areas or having hypertension (both P<0.01). In particular, stroke mortality was negatively associated with greater health care costs. A 10-fold increase in health costs was associated with a reduction in stroke mortality by 40.5% (HR=0.595, P<0.001). The stratified MSM by Aboriginality found that the HR was smaller among Aboriginal patients than in non-Aboriginal patients (0.525 vs 0.642), indicating a slightly greater mortality reduction in Aboriginal, though statistically insignificant (P=0.25).

Table 3. Marginal structural proportional hazard model hazard ratio and confidence interval by Aboriginality

	Aboriginal		Non-Aboriginal		All stroke	
	HR	95%CI	HR	95%CI	HR	95%CI
Cost increment	0.525	0.405 - 0.681	0.642	0.514 - 0.801	0.595	0.502 - 0.706
Aboriginal	-	-	-	-	1.344	1.079 - 1.673
Ischaemic	1.000	-	1.000	-	1.000	-
Haemorrhagic	2.644	1.897 - 3.684	1.778	1.377 - 2.297	2.059	1.687 - 2.512
Undetermined	1.128	0.746 - 1.705	0.922	0.704 - 1.208	0.974	0.776 - 1.222
Time (year-1993)	0.982	0.960 – 1.004	0.961	0.945 - 0.977	0.968	0.955 - 0.981
Age at onset (years)	1.015	1.006 - 1.024	1.033	1.024 - 1.043	1.024	1.018 - 1.030
Female	0.822	0.631 - 1.071	1.059	0.845 - 1.322	0.984	0.834 - 1.161
Remoteness	0.826	0.629 - 1.086	0.727	0.527 – 1.002	0.753	0.615 - 0.921
Hypertension	0.698	0.526 - 0.927	0.726	0.582 - 0.905	0.702	0.591 - 0.834
Diabetes	0.801	0.578 - 1.111	1.013	0.772 - 1.331	0.897	0.725 - 1.109
CKD	1.616	1.184 - 2.207	1.484	1.088 - 2.023	1.509	1.210 - 1.881
IHD	1.033	0.671 - 1.589	0.720	0.520 – 0.997	0.839	0.647 - 1.086
COPD	1.017	0.696 - 1.735	0.989	0.725 - 1.348	1.014	0.773 - 1.330
Cancer	1.299	0.524 - 3.217	1.534	1.090 - 2.158	1.503	1.098 - 2.058
Depression	-	-	0.450	0.154 - 1.318	0.399	0.130 - 1.224
Atrial fibrillation	1.200	0.751 - 1.917	0.989	0.705 - 1.388	1.099	0.841 - 1.437

CI, confidence interval. CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. HR, hazard ratio. IHD, ischaemic heart disease. Cost increment represents percent change in log(Cost).

Sensitivity analysis provided evidence that the ICER was not dominant in favour of the Aboriginal population until the willingness-to-pay threshold was increased close to AUD200 000 per life-year gained (P>0.7, Figure 3). Probabilistic analyses confirmed that treating HS and UND were likely to be more cost-effective in Aboriginal patients than treating IS, likely related to underdiagnosis of stroke in

remote areas. The average cost relativities were insensitive to differing discount rates. Log-transformation would generate more robust cost estimates. Without log-transformation, the magnitude of average costs might be affected, but the sign of difference between Aboriginal and non-Aboriginal patients remained consistent.

Discussion

In terms of survival outcome, to our knowledge, this is the first comparative cost-effectiveness evaluation providing evidence that stroke care among Aboriginal patients is as efficient as among the non-Aboriginal patients within the Australian context. Reports on the economic analysis of cost-effectiveness among Aboriginal and non-Aboriginal populations are rare.[36,37] In our sample almost half (46%) were Aboriginal. Overall, this incidence number was disproportionate to the population proportion for the NT (28% in 2011), reflecting the large impact stroke has on the Aboriginal population. Stroke care in the Aboriginal population may be even more beneficial because of the 14 years younger age at onset of stroke, resulting in more life-years potentially saved from the additional costs of providing care. Given that the majority of NT Aboriginal people live in rural or remote locations, it is important that ongoing efforts to support cardiovascular disease prevention and improve the access to best practice stroke services are prioritised.

There have been several estimates of the long-term cost of stroke in Australia in the past two decades, up to AUD100 000,[3-6,38] mainly based on the North East Melbourne Stroke Incidence Study.[3] These cost estimates were based on cohort studies conducted in urban areas and were likely to understate the NT patient lifetime costs, because of attrition bias caused by loss to follow-up and inability to account for the costs related to remote areas.[39] In 2012/2013 Australian dollars, the estimated lifetime cost for an incident stroke in NT was AUD302 538 per patient between 1992 and 2013 after adjusting for loss to follow-up.[7] Stroke cost was found to be 44% greater for Aboriginal patients.[7]

Accurate cost estimates are required for cost-effectiveness assessment related to improvements in stroke survival.[40,41] Cost-effectiveness can be evaluated by comparing costs against outcomes

between the alternative treatments.[33] Understanding the cost drivers in stroke treatments informs health service decisions for cost-effective care. Most cost-effectiveness studies for stroke care were focused on specific procedures,[17,42] for example pharmaceuticals,[43,44] surgery,[45,46] prevention,[47,48] and rehabilitation;[49] or evaluating alternative models of care,[50] for example telemedicine,[51] and specialised stroke unit.[52,53] Hunter and colleagues evaluated the introduction of centralised stroke care, finding the service reduced mortality by 12% and saved more than £811 per patient-year.[54] In Canada, comprehensive stroke care can reduce hospital admissions (3%), bed-days (26%), death (15%) and nursing home care (13%), as well as save costs of over CAD11 000 per stroke.[55]

Comparative cost-effectiveness is an emerging approach to comparing the costs and monitoring health outcomes of interventions and strategies to prevent, diagnose and treat diseases in real world practice for informing clinical and policy decisions.[56,57] Previous reports suggested an effect of institutional bias in clinical decisions, which favoured stroke care in non-Aboriginal patients.[12,13] Despite these reports, the cost-effectiveness of stroke care among different patient populations has not been investigated. Our study found that the uptake of hospital procedures by Aboriginal stroke patients with an incident stroke was 7% less than the non-Aboriginal patients (mainly imaging and rehabilitation). Univariable analysis showed that stroke care in Aboriginal patients is as cost-effective as in non-Aboriginal patients. The differential costs and effects were divided quite evenly across the willingness-to-pay threshold line. After taking into account the effects of patient-level confounders, time and loss to follow-up using MSM, we found that an increase in stroke care costs was associated with a slightly better health outcome for Aboriginal than non-Aboriginal patients with stroke, despite failing to reach statistical significance. Baker and colleagues evaluated cost-effectiveness of blood pressure control in kidney and cardiovascular disease treatment in an Aboriginal community.[36] It was found that 3-year perindopril treatment was effective in delaying 1.5 years of haemodialysis per patient with a net annual cost of AUD1200, in comparison with a modelled historical control of the same Aboriginal population. Stroke was not identified in their study and non-Aboriginal controls were not compared.[36] Grieve and colleagues compared stroke care costs and survival among different

European countries and different ways of providing stroke care.[19] The authors found that the cost-effectiveness may be related to specialised stroke care, which is required to provide interdisciplinary care after stroke. Our analysis directly compared cost-effectiveness of stroke care for both Aboriginal and non-Aboriginal patients. This study is also complemented by the use of MSM, which is more appropriate than conventional methods for managing censoring issues when estimating survival and costs.[35]

Strengths of this study include the large sample size of Aboriginal patients relative to the non-Aboriginal patients, access to data to ensure capture of incident cases and the ability to confidently link patient records across multiple sources of data. Further, the methodology in this study informs cost-effectiveness analysis for both patients and providers in real world settings, which utilised nonrandomised observational data and focused on more relevant health policy issues.[56,57] It is cost-effective to improve access for Aboriginal patients with suspected and confirmed stroke, especially with respect to imaging for rapid diagnosis and interdisciplinary rehabilitation to reduce the impacts of stroke. Upskilling of doctors and nurses in best practice stroke prevention and management is urgently required as inequities in access to optimal stroke care in different regions impact on the quality of care.[2,58] It is important to develop specialist care in regional centres to improve the overall availability of best practice stroke care in regional and remote areas in Australia.

This study covered 21 years from 1992 to 2013, largely because of the requirements to identify sufficient incident cases and follow-up for survival analysis. Several limitations should be noted. First, the results in this study are most relevant to Aboriginal population living in remote locations, who experience socioeconomic disadvantage and high burden of disease in a high income country.[59,60] The stroke care cost-effectiveness results may be relevant to other disadvantaged populations. Second, our cost estimates may not be precise. PCIS was only available for Aboriginal communities after 2009. PCIS data were only used for costing primary care, which was extrapolated to cover the previous years and adjusted for health inflation. In this study we used administrative HID to identify stroke cases and did not include minor and low-cost cases managed solely by outpatient department, GP or remote clinics. These low-cost cases would comprise a small proportion of stokes

(previously estimated at 12% in 1997).[3] A top-down approach was applied to calculate the GP, nursing home and allied health costs, which might lead to over- or under-estimation of the true costs. Various statistical methods were used to assess the robustness of the point estimates. More research is needed to further explore the cost-effectiveness of stroke care using prospective patient-level costing data. Third, another potential source of uncertainty in cost-effectiveness evaluation was the lack of non-NT or non-stroke controls, assuming stroke care as a whole is cost-effective in the NT, and stroke survival was independently associated with costs of stroke care and perceived confounders. Fourth, we were unable to measure levels of disability and quality of life among stroke survivors. It might be that there were important differences in levels of stroke-related disabilities between Aboriginal and non-Aboriginal patients. Finally, the joint effects of multiple comorbidities and their interactions were not considered in this study due to limited sample sizes.

In conclusion, stroke care for Aboriginal patients is at least as cost-effective as for non-Aboriginal patients managed within a sparsely populated but geographically large region of Australia, where health care resources are limited. Stroke care was found to present worthwhile and equitable survival benefits for Aboriginal patients in remote communities, notwithstanding their higher burden of disease. These data may provide useful information for other countries with Indigenous populations living in regions with similar geographical and resource constraints.

Figure legends

Figure 1. Survival by age and Aboriginality

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

Contributorship statement

YZ designed the study, collected costing data, undertook data linkage and statistical analysis, and wrote the first draft of the manuscript. SG, H Falhammar, H Flavell and DC participated in the literature review, methodology development, discussion and revision of the manuscript, and contributed equally to this work.

Competing interests

The authors declare that they have no competing interests relevant to the manuscript.

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Data sharing statement

We will share the data via a publicly accessible repository.

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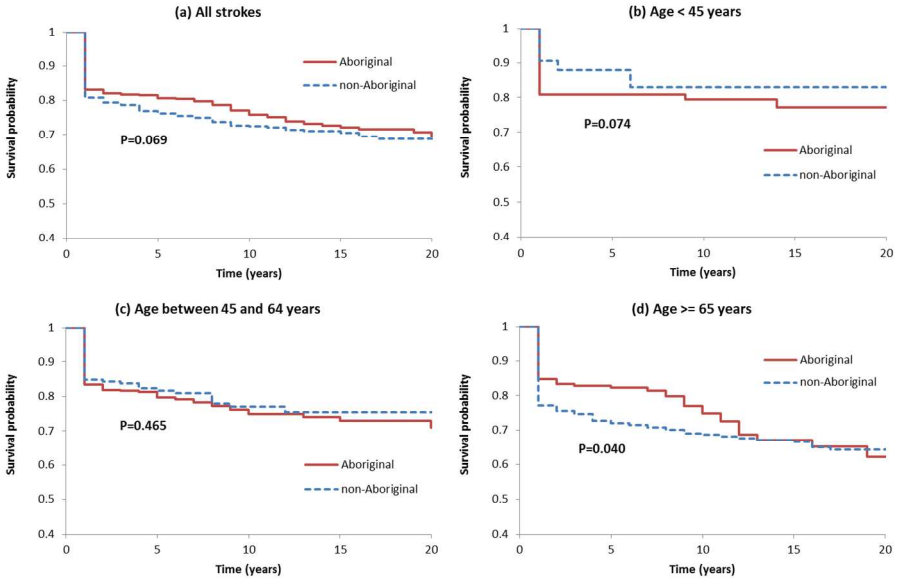

Figure 1. Survival by age and Aboriginality

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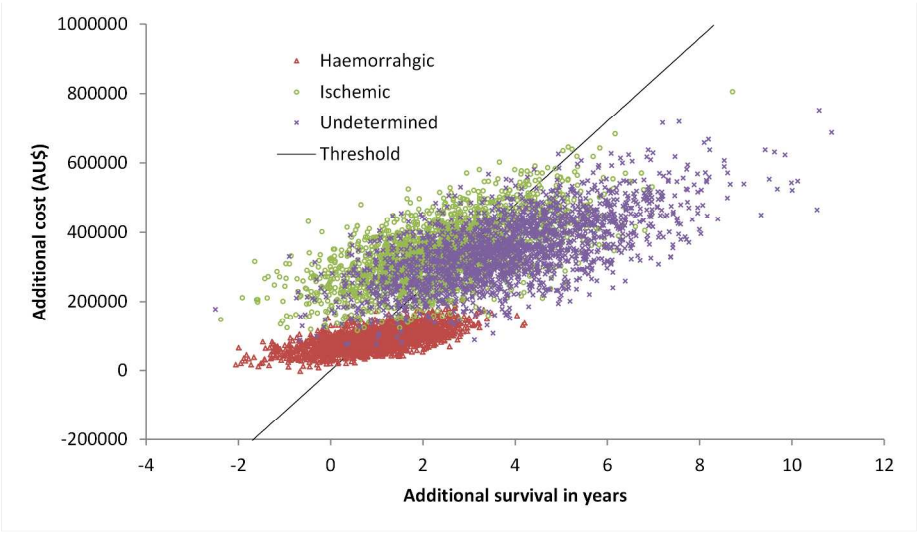

Figure 2. Cost-effectiveness plane comparing Aboriginal with non-Aboriginal patient by stroke type

297x209mm (300 x 300 DPI)

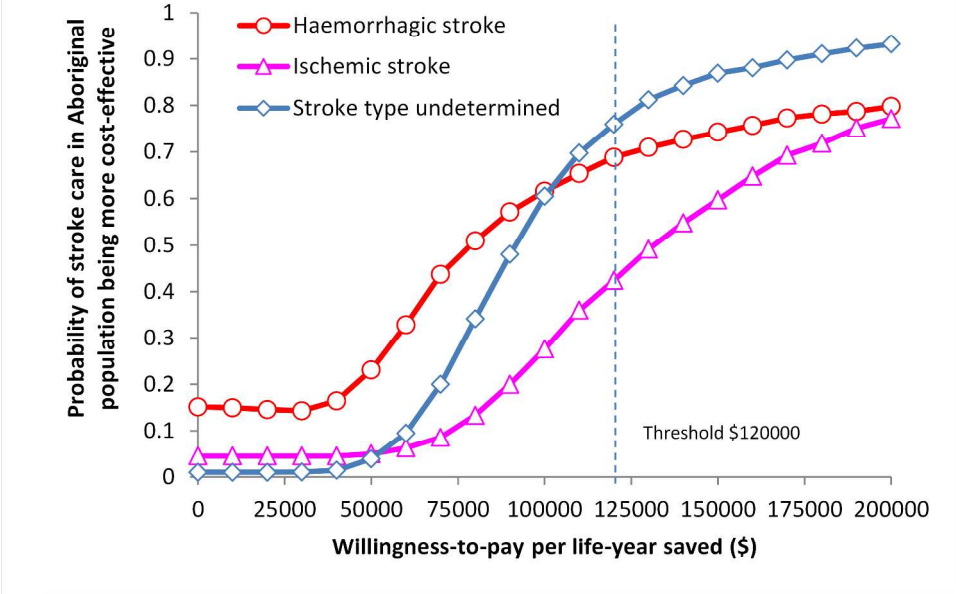

Figure 3. Acceptability curve for comparing cost-effectiveness of stroke care between Aboriginal and non-Aboriginal population

297x209mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.