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Article type : Original Article

Sex differences in quality of life after stroke were explained by patient factors, not clinical care: evidence from the Australian Stroke Clinical Registry

Running title: **Sex differences in quality of life after stroke**

Word counts: 3,394 (Introduction, Method, Results and Discussion)

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ENE.14531](https://doi.org/10.1111/ENE.14531)

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Abstract: 249 words

Background: Women may receive stroke care less often than men. We examined the contribution of clinical care on sex differences and health-related quality of life (HRQoL) after stroke.

Methods: We included first-ever strokes registered in the Australian Stroke Clinical Registry (2010-2014) with HRQoL assessed between 90-180 days after onset (EQ-5D-3L instrument) that were linked to hospital administrative data (up to 2013). Study factors included sociodemographics, comorbidities, walking ability on admission (stroke severity proxy) and clinical care (e.g. stroke unit care). Responses to the EQ-5D-3L were transformed into a total utility value (-0.516 'worse than death' to 1 'best' health). Quantile regression models, adjusted for confounding factors, were used to determine median differences (MD) in utility scores by sex.

Results: Approximately 60% (6,852/11,418) of stroke survivors had an EQ-5D-3L assessment (median 139 days; 44% female). Compared with men, women were older (median age 77.1 vs men 71.2) and fewer could walk on admission (37.9% vs men 46.1%, $p<0.001$). Women had lower utility values than men and the difference was explained by age and stroke severity, but not clinical care ($MD_{adjusted} -0.039$, 95% CI -0.056, -0.021). Poorer HRQoL was

observed in younger men (aged <65 years), particularly those with more comorbidities, and in older women (aged ≥ 75 years).

Conclusion: Stroke severity and co-morbidities contribute to the poorer HRQoL in young men and older women. Further studies are needed to understand age-sex interaction to better inform treatments for different sub-groups and ensure evidence-based treatments to reduce the severity of stroke are prioritized.

Introduction

Women have been reported to have poorer health-related quality of life (HRQoL) after stroke than men,¹ but there is uncertainty over explanatory factors.^{2,3} Often sex-specific outcomes are either not reported or the prediction models used (e.g. using the step-wise approach) have not been focused on sex differences. Another explanation may be related to the sex differences in stroke treatment since, in some studies, women have been reported to receive evidence-based care less often than men.^{4,5} A few studies specifically focused on sex differences in HRQoL lacked details of the clinical care provided.^{3,6,7} Therefore, the contribution of differences in clinical care between men and women on women's poorer HRQoL remains unclear. While women appear to experience poorer HRQoL after stroke than men, women without stroke also report poorer health status than men of all ages.⁸ Therefore, it is also uncertain whether the sex difference in HRQoL is caused by stroke or is due to other differences between sexes.

The aims of the study were to (i) quantify sex differences in HRQoL between 90-180 days after stroke using data from the ongoing prospective, national, Australian Stroke Clinical Registry (AuSCR), (ii) identify contributing factors, including evidence-based clinical care, which may contribute to the difference, and (iii) compare sex differences in HRQoL between those with and without stroke by using data from the AuSCR and population HRQoL norms derived from an Australian general population survey.

Methods

The AuSCR is a nation-wide prospective collection of data on stroke care,⁹ with involving 74 public hospitals across Australia. The registry includes a limited range of information on patient characteristics, evidence-based in-hospital clinical care, and clinical outcomes. This study involved patients registered with first-ever strokes at 39 hospitals (2010-2014). Where

additional data were available for the cohort from linkage with hospital administrative data as part of the Stroke123 study these were used (described below).

This study was approved by the Tasmanian Health and Medical Human Research Ethics Committee (H0015287). Our research proposal was also approved by the AuSCR Research Task Group and its Management Committee (August 2016). Appropriate ethics and/or governance approvals were obtained for all participating hospitals in AuSCR. Opt-out method of consent is used in the AuSCR. The processes involved in the AuSCR are described elsewhere.¹⁰

Study factors

A wide range of patient characteristics and in-hospital evidence-based clinical care variables were investigated to explain sex differences.¹¹ They were grouped according to: (i) socio-demographics: *age, country of birth, state of residence, socioeconomic position*;¹² (ii) behavioral risk factors, comorbidities; (iii) stroke-related factors: *stroke severity* (ability to walk on admission),^{9,13} *stroke type* (acute ischemic stroke, intracerebral hemorrhage [ICH], undetermined stroke), *time from stroke onset to hospital arrival, being transferred from another hospital*; (iv) evidence-based clinical care (or quality indicators) recommended in Australian clinical guidelines:^{10,14} *stroke unit access, intravenous thrombolysis, use of antihypertensive agent(s) at discharge, receipt of a discharge care plan*; (v) discharge information: *length of stay, discharge destination*; and (vi) 90-180 days status: *survival, recurrent stroke, living alone, HRQoL (see below) and proxy assessment by caregivers* (when required).

Information on *risk factors for stroke and comorbidities* were only available up to 2013, obtained from administrative hospital records through a parallel data linkage project (Stroke123).¹⁵ These were based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision codes associated with emergency department presentations and hospital admissions using available data for 5-years prior to, and including, the stroke event registered in the AuSCR. A Charlson comorbidity index (CCI) score was also calculated for each patient from their specific comorbidities.¹⁶

Outcome measure

The collection of patient-reported outcomes occurred 90-180 days after the index event using survey methods by post or telephone.⁹ HRQoL was assessed using the European Quality of

Life-5 Dimensions (EQ-5D-3L) instrument,¹⁷ which has been validated for stroke.¹⁸ For each of the 5 dimensions of the EQ-5D-3L: mobility, self-care, usual activities, depression/anxiety, and pain, there are three response categories: no problem, some/moderate, and extreme problem. The EQ-5D-3L information was collected from patients or proxy respondents for those patients unable to complete the survey.

Statistical analysis

All analyses were performed using Stata 12.1 (StataCorp Texas, 2011).¹⁹ Two-sided p values ≥ 0.05 were considered as statistically significant. Responses to the EQ-5D-3L were transformed into a total utility value for each respondent using Australian population-based methods based on the discrete choice experiment.²⁰ The EQ-5D-3L score ranges from a negative score (worse than death) to 1 (perfect health). Only those patients alive during the follow-up (90-180 days after stroke) were included in analyses. The EQ-5D-3L often has a bimodal distribution or, as in this study, is highly skewed. Among survivors of stroke, quantile regression was used to generate median differences in the EQ-5D-3L utility score calculated for women compared to men. This method is based on minimizing least absolute deviations and its estimates are more robust compared to linear regression.²¹ We used random-effects in the quantile regression to account for hospital-level correlations in case mix, patient volume, performance or processes of care among facilities (e.g. better quality of care and survival in high-volume facilities),²² which potentially affect sex differences in care and patient outcome. Multivariable modelling was performed to examine the covariates (sociodemographics, stroke-related factors, evidence-based clinical care) that would potentially contribute to sex differences in EQ-5D-3L at 90-180 days after stroke. The model-building procedures were based on the purposeful selection of covariates²³ chosen according to three criteria of being confounders (Supplemental Methods). Statistical interaction was assessed by a test of statistical significance of a sex x covariate product term. In further analyses of sub-domain scores of EQ-5D-3L, the women:men relative risk (RR) of having any problem within each dimension was performed using log-binomial regression. Factors potentially associated with the sex differences in each sub-domain were further examined in multivariable models. Any interaction effect of age and number of comorbidities (CCI score) for each EQ-5D-3L domain was also tested, separately for men and women.

Sensitivity analyses assessed the effect of missing data using multiple imputation by chained equations (m=50 imputations) and inverse probability weighting²⁴ assuming data were missing at random. The missing individual domain scores of the EQ-5D-3L were initially

imputed and subsequently converted into overall utility scores. This approach is more reliable in a large dataset (>500 cases) than directly imputing the overall utility score.²⁵

In analyses comparing the AuSCR with population-level EQ-5D-3L data, mean utility scores for survivors of stroke were calculated within sex and age groups (<55, 55-64, 65-74 and ≥ 75 years). The corresponding EQ-5D-3L utility scores of the general population were obtained from the data of South Australian population-based Health Omnibus Survey.⁸ The survey provided mean EQ-5D-3L utility scores of the Australian general population that are current and available by age and sex strata. We then calculated the weighted mean difference scores between AuSCR stroke registrants and the general population within each age group, separately for men and women.

The minimal clinically important difference represents the minimum benefits from treatment or other acute therapies in the practice.²⁶ The minimally important difference for EQ-5D-3L utility scores reported in stroke populations range from 0.08-0.12 units.²⁷ Thus, any difference in utility ≥ 0.08 between sexes was considered clinically meaningful.

Results

Over a median follow-up of 139 days (IQR 123-161), there were 2,700 deaths out of 14,118 registered cases of stroke. Approximately 60% (6,852/11,418) of survivors completed the EQ-5D-3L; 44% being female (Table 1). The proportions of women were similar between those with and without a completed survey (44%; Supplementary Table 1). However, compared to those who did not provide EQ-5D-3L responses, survivors of stroke who responded were older, had less severe strokes (indicated by the ability to walk independently on admission), and had fewer ICH (Supplemental Table 1). Those providing a response (n=6,852; 39 hospitals) more often received evidence-based clinical care (Supplemental Table 1).

Among those providing EQ-5D-3L responses (n=6,852), compared to men, women registrants were 6 years older ($p < 0.001$), and were less often able to walk independently at the time of admission ($p < 0.001$; Table 1). More women with stroke, compared to men, had pre-existing dementia, hypertension, atrial fibrillation, heart disorders (2010-2013 data only; Table 1). Despite the sex differences in the individual comorbidities and stroke risk factors, the distribution of CCI score was similar for both sexes (Table 1). No significant differences in evidence-based clinical care were observed (Table 2). Women were more often discharged

to aged care, and less often discharged directly home from acute care than men (Table 2). At median 139 days after stroke, women were more likely to live alone (25.3% vs 16.4%, $p<0.001$; Supplemental Table 2) but were less likely live at home than men (Table 2). It was also noted that, proxy results for the EQ-5D-3L were obtained among 44% of these registrants with a greater proportion for women than for men (46.3% vs 41.7%, $p<0.019$; Table 2), and proxy-reported EQ-5D-3L scores were skewed towards positive evaluations compared to patient-reported results (median difference; $MD_{unadjusted}$ 0.13, 95% CI 0.11-0.15), even after accounting for sex, age, and severity ($MD_{adjusted}$ 0.12, 95 % CI 0.10-0.14).

Sex difference in EQ-5D-3L domain responses among survivors

Women more often reported problems in four out five EQ-5D-3L domains (self-care, usual activity, pain/discomfort and anxiety/depression) than men and the sex differences were slightly attenuated by stroke severity, and more by age (Table 3). The estimates for women were statistically significant in those aged >75 years in all four domains than men (Supplemental Table 3).

Sex difference in overall utility scores among survivors

Based on AuSCR data, the utility scores ranged from -0.516 (worse than death) to 1 (perfect health) with mean score being 0.64 (SD 0.33). Women had poorer HRQoL compared to men in unadjusted analysis (MD -0.082; Table 3). Age and stroke severity accounted for about 50% of the sex differences and the adjusted MD (-0.039) was below the clinically significant threshold (Table 3). Other factors, such as indicators of evidence-based clinical care, confounded the sex difference in EQ-5D-3L utility in the multivariable models.

Sex difference in EQ-5D-3L utility scores between women and men survivors differed by age group ($p_{interaction}<0.001$) and severity of stroke ($p_{interaction}<0.001$). In the younger age group (<65 years), we did not observe a significant difference between sex regardless of stroke severity (Supplemental Table 4, 'complete-case analysis'). Conversely, women aged ≥ 75 years with a severe stroke had lower utility scores after stroke than elderly men and the difference was clinically relevant (MD -0.103, Supplemental Table 4). Among survivors with a less severe stroke, older women also experienced poorer HRQoL than men with the magnitude of the difference being about two times greater in the 65-74 age group than the oldest group (≥ 75 years; Supplemental Table 4). In the analyses of interaction effects between age and CCI score for each EQ-5D-3L domain, a statistically significant interaction was identified only for pain/discomfort (men; $p_{interaction}=0.008$; women; $p_{interaction}=0.002$; Figure 1).

However, there was a visual trend that younger men with more comorbidities were more likely to have problems compared to women across all EQ-5D-3L dimensions (Figure 1; Supplemental Figures 1-3).

Sensitivity analyses to account for missing data on EQ-5D-3L (40% of survivors) using multiple imputation produced similar results when compared with complete-case analysis (Supplemental Table 4, 'imputed analysis').

Sex difference in HRQoL between people with and without stroke

Stroke caused substantial health loss for both sexes, generally increasing with age. Mean EQ-5D utility scores were significantly lower for people with stroke compared to the population norms across all age groups (mean difference ranged: 0.15 – 0.27), each of which is above the clinically meaningful threshold (Table 4). However, in analysis between those with and without stroke, younger males were more like to have greater health loss due to stroke than their female counterparts, and vice versa (Table 4).

Discussion

In our study, using data from a large stroke registry, differences between men and women in HRQoL at 90-180 days after stroke were largely explained by age, initial severity of stroke, and the place of residence rather than clinical care factors, discharge destination, living situation, and form of assessment. As there were complex differences in HRQoL depending on age, sex and stroke severity, and differences could not be fully explained based on these measures further studies are needed to better understand these interactions.

Older women had statistically and clinically poorer HRQoL than older men. This difference was particularly evident among those women with severe strokes. The poorer HRQoL is potentially attributable to the increased frailty in older women and larger numbers of health problems at time of stroke than men, which in turn leads to poorer functional outcome.²⁸ This is supported by the finding in our study, where more women than men had dementia and cardiac conditions such as atrial fibrillation. In sub-domain analyses of the HRQoL, elderly women generally had higher levels of pain/discomfort, and anxiety/depression after stroke than elderly men, consistent with previous research.^{29,30} Other researchers have reported disparities between sexes in coping strategies,³¹ and greater social isolation in older women³², both of which may differently effect their life satisfaction.³³ Our findings highlight an

imperative to improve health among the elderly, most of whom are women and promote active healthy aging and survivorship.³⁴

We also found that younger men with stroke had greater impacts across all HRQoL dimensions than younger women, particularly if they had more comorbidities. This could be due to sex differences in various comorbidities such as a higher prevalence of smoking or history of cancer in men. There is also evidence that men who do not return to work at 6 months after stroke have poorer HRQoL than men who are able to work, although this is not the situation for women,³⁵ a factor that may be associated with differences in self-perceptions of role.³⁶ The potential importance and protective nature of role permanence after stroke warrants further investigation. Strategies to reduce risk factors for cardiovascular diseases (CVD), factors that are more prevalent in men, such as smoking cessation, should also be addressed to narrow the gender gap in the younger age group.

Overall, stroke caused a significant health loss for both sexes. Our comparison between people with stroke and population norms appeared to indicate that stroke caused a greater HRQoL loss for younger men than younger women, but that the direction of the association with sex may have been reversed for older people. This suggests that sex differences in HRQoL were not only a result of the stroke but other existing sex disparities may contribute to these findings. For those without stroke, the presence of chronic health conditions or depressive symptoms can have different effects on the HRQoL of women and men in the same age group.³⁷ The fact that Thayabaranathan and colleagues found significant interactions between age and increased number of comorbidities on mental health after stroke may be a potential mechanism for greater health loss among older adults with multimorbidity.³⁸ In future studies, researchers should consider the existing differences between sexes when reporting results of sex differences in HRQoL after stroke and associated factors. Developing more effective primary prevention strategies to reduce health disparities according to age and sex should also be a priority,³⁹ particularly providing more support for those who are more vulnerable to the adverse impacts of stroke.

Walking ability at admission, previously shown to highly correlate with and serve as a good marker of stroke severity,^{9,13} was also found in the current sample to contribute to sex differences in HRQoL. This finding is consistent with our previous research whereby stroke severity (as measured by the National Institute Health Stroke Scale – NIHSS) was an important factor in the association between sex and HRQoL after stroke.¹ When prevention

fails and a stroke occurs, every effort must be made to reduce the impact of stroke. Interventions to reduce the severity of stroke including managing of risk factors/comorbidities and access to reperfusion therapies⁴⁰ for high-risk patients should be prioritized.

The magnitude of the sex difference in EQ-5D-3L overall scores after stroke was small and consistent with previous research with the EQ-5D-3L instrument.⁴¹ Although EQ-5D-3L has been well-validated for use in stroke, the generic instrument of HRQoL may exclude some domains that differ by sex (e.g. family role, importance of work, social interactions, self-perception),⁴²⁻⁴⁴ or are specific to stroke (e.g. communication, sexual function). Therefore, the sex difference in HRQoL might be underestimated when using EQ-5D-3L when compared to stroke-specific instruments (e.g. Stroke-Specific Quality of life).

Several other limitations should be acknowledged including the response rate of 60% for the follow-up survey and the lack of co-morbidity data after 2013. Compared with those unassessed, assessed patients were older, had fewer intracerebral hemorrhages, less severe strokes, and more often received evidence-based clinical care. Although the results of sensitivity analyses accounting for missing data using imputation showed almost no change, we cannot fully preclude the bias that may have arisen. The generalizability of the study results may be restricted by the fact that patients from the AuSCR hospitals received better care for stroke than the general stroke population.⁴⁵ However, this is less likely to substantially affect our conclusion since sex disparities in access to care did not account for the difference in HRQoL after stroke. The mean score of EQ-5D-3L (0.64, SD 0.33) in the AuSCR dataset was closely similar to those from other developed countries^{41,46,47}, providing evidence that our results may reflect the experience of survivors of stroke in different settings. The lack of detailed data on case-mix adjustment variables including pre-stroke function, social factors (e.g. employment), and psychological factors before stroke prevented us from undertaking more in-depth analyses of these potential contributing factors on HRQoL.⁴⁸ For example, socioeconomic position (SEP) is commonly identified as a contributor to sex differences in outcomes after stroke,⁴⁹ including in Australia (occupation as a marker of SEP),⁵⁰ but this was not the case in the present study. This may be due to the lack of individual patient data on particular aspects of socio-economic advantage and disadvantage including education, occupation, and income.⁵¹ Our use of residential postcode was used to derive a measure of SEP based on the Australian Bureau of Statistics Index of Relative Socio-Economic Advantage and Disadvantage may capture other aspects of SEP not captured

using more conventional sources.¹² Linking data from multiple sources (e.g. medical records, rehabilitation services) may provide a mechanism to provide more granularity in the sex difference in HRQoL. The ability to walk independently on admission was used as a proxy assessment of stroke severity. This marker mostly captures motor deficits and does not account for aphasia as primary stroke deficit. It may also include people with mobility impairment due to pre-stroke functional limitations, rather than the stroke. In addition, our marker of stroke severity is binomial, and it is possible that there was a difference in stroke severity between men and women within our category of “severe” stroke. Adjustment with a more responsive tool such as NIHSS may improve our models, but it is not yet collected consistently enough in our registry to be used.^{13,52}

The study has several strengths. It was based on a large dataset obtained from 39 hospitals across five states of Australia with standardized data collection to ensure data quality and adequate power to test our hypotheses. By using a national registry of clinical care and outcomes linked with administrative data from hospitals, this study significantly adds to the current literature about sex differences in stroke care in Australia and its association with HRQoL. The discrete choice experiment approach was used for analyzing EQ-5D-3L scores,²⁰ instead of Time-Trade-Off technique, as it was more aligned with our stroke cohort. Further comparison of the sex difference in HRQoL between people with and without stroke helps fill a further gap in identifying the loss of HRQoL that occurs following stroke.^{53,54} By determining factors that explain sex differences in HRQoL, we further provide the evidence basis for future development of targeted treatments according to particular patient characteristics, that, in turn, may reduce the impact of stroke.

Conclusion

We found that differences in HRQoL after stroke among older women and younger men, was largely attributable to stroke severity, but was also associated with other sex-related health differences existing in the population such as comorbidities (e.g. depression) and social circumstances. These findings highlight a need for further research to understand the age-sex interactions with HRQoL and associated social and psychological factors. More effective strategies to reduce the severity of stroke, and better targeted post-stroke support, particularly for the more vulnerable population of elderly women and younger men should also be a priority.

Acknowledgements

We acknowledge staff from AuSCR Office who contributed to AuSCR operations during this study period. Staff from The George Institute, the Florey and the Stroke Foundation are acknowledged for their contributions to patient follow-up. Hospital site investigators, data collectors, and members of the steering committee are also acknowledged (online supplement).

Compliance with Ethical Standards

Conflict of interest

All authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study as part of the AuSCR registry.

Disclosure of conflict of interest

DAC, NAL, RSG, MFK, CSA are members of the management committee for AuSCR. DAC reports educational grants from Boehringer Ingelheim, Shire, Ipsen, Amgen, and Medtronic paid to her institution. CSA has research grants from Takeda, paid to his institution, and speaker fees from Takeda unrelated to this work. AGT declares being on the AuSCR Steering Committee and Board of the Stroke Foundation. The other authors do not have any disclosures. No competing financial interests exist.

Declarations

Not applicable

Funding

During the study period AuSCR was supported by grants from the National Health and Medical Research Council (NHMRC:1034415), Allergan, Ipsen, Boehringer Ingelheim, Monash University, Queensland Health, the Stroke Society of Australasia, the Stroke Foundation and consumer donations. HTP was supported by a Merle Weaver Postgraduate Scholarship (University of Tasmania) and the Menzies Research Enhancement Program 2017

- Stimulating National and International Collaborations (obtained by Dr SLG) to undertake the AuSCR analyses at Monash University. SLG and NAL are supported by National Heart Foundation of Australia Future Leader Fellowships (SLG 100446; NAL 102055). The following authors received research fellowship funding from the NHMRC: DAC (co-funded Heart Foundation: 1063761), AGT (1042600) and CSA (1081356).

Data Availability Statement

This study is based on the secondary analysis of data as part of a data linkage study. Qualified investigators can request access to patient-level data, analytic methods, and study materials after ethics clearance and approval by all authors and the data custodians of the primary sources of the data-sets.

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Figure legends and Tables

Figure. Predicted probability of issue with pain or discomfort by Charlson comorbidity index and age among men (top; $p_{\text{interaction}}=0.008$) and women (bottom; $p_{\text{interaction}}=0.002$)

Table 1. Characteristic of AuSCR registrants for first-ever stroke during 2010–2014 providing EQ5D responses at 3 months after stroke (n=39 hospitals; n=6,852)

	Men	Women	p-value
	N (%)*	N (%)*	
Number of cases	3821 (55.8)	3031 (44.2)	<0.001
Age, median (IQR)	71.2 (62.0–79.5)	77.1 (65.7–84.4)	<0.001
Walking independently at admission (proxy for stroke severity)†	1653 (46.1)	1077 (37.9)	<0.001
Comorbidities (only 2010-2013 data)‡			
Number of cases	2321 (51.1)	2223 (48.9)	0.138
Charlson Comorbidity Index score, median (min-max)	3 (0-12)	3 (0-12)	0.954
Individual comorbidities			
Dementia	153 (6.6)	208 (9.4)	0.001
Hypertension	1628 (70.1)	1676 (75.4)	<0.001
Smoking	621 (26.8)	355 (16.0)	<0.001
Hyperlipidemia	348 (15.0)	273 (12.3)	0.008
Atrial fibrillation	735 (31.7)	840 (37.8)	<0.001
Heart failure/myocardial infarction	527 (22.7)	573 (25.8)	0.016
Renal or liver disease	236 (14.1)	234 (14.6)	0.611
Chronic obstructive pulmonary disease	210 (9.1)	205 (9.2)	0.839
Diabetes	482 (20.8)	410 (18.4)	0.049
Cancer	337 (14.5)	223 (10.0)	<0.001

*n (%) unless otherwise indicated

†stroke severity was defined as unable to walk independently on admission

‡available among 4544 cases with EQ5D responses

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Table 2. Processes of care, discharge information and longer term outcomes for first-ever stroke in the AuSCR during 2010-2014 providing EQ5D responses at 3 months after stroke (n=39 hospitals; n=6,852)

	Men	Women	P-value
	N (%)	N (%)	
Processes of care			
Treated in stroke unit	3358 (87.9)	2647 (87.3)	0.835
Intravenous thrombolysis*	436 (13.3)	315 (12.3)	0.298
Discharged on antihypertensives†	2834 (74.9)	2254 (75.1)	0.986
Care plan on discharge to community	1100 (54.7)	782 (52.4)	0.280
Discharged destination			<0.001
Died in hospital	—	—	
Aged care	61 (1.3)	155 (5.1)	
Home	1950 (51.0)	1337 (44.1)	
Rehabilitation	1324 (34.7)	1142 (37.7)	
Hospitals/other	486 (12.7)	397 (13.1)	
Data between 3-6 months (self-reported)			
Current residence			<0.001
Aged care	255 (6.7)	479 (16.0)	
Home	3307 (87.4)	2338 (77.9)	
Rehabilitation	65 (1.7)	29 (1.0)	
Hospitals/other	158 (4.2)	157 (5.2)	
Proxy EQ5D assessment‡	1109 (41.7)	968 (46.3)	0.019
Additional process of acute care indicators			
(Queensland participants only)			
Number of cases	1388 (55.7)	1104 (44.3)	
Mobilisation ≤48 hours if unable to walk on admission	463 (66.2)	404 (63.1)	0.765
Received swallow assessment ≤24 hours	819 (59.0)	602 (54.5)	0.094
Aspirin administration ≤48 hours*	894 (73.1)	643 (66.3)	0.245
Discharged on antiplatelets or antithrombotic*	960 (82.3)	715 (77.4)	0.556

*among ischaemic stroke

†only applies to patients who were discharged

‡missing data 31%

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Table 3. Differences in EQ5D score for women surviving after stroke compared to men

	Unadjusted		Adjusted for					
			Age		Stroke severity*		Age and stroke severity*	
	ES	95% CI	ES	95% CI	ES	95% CI	ES	95% CI
EQ5D utility, MD	-0.082	-0.099, -0.066	-0.041	-0.060, -0.021	-0.026	-0.038, -0.014	-0.039	-0.056, -0.021
Subdomain (any problem with), RR								
Mobility	0.99	0.93, 1.06	1.01	0.94, 1.08	0.99	0.93, 1.06	1.01	0.94, 1.08
Self-care	1.30	1.19, 1.42	1.14	1.05, 1.25	1.21	1.12, 1.33	1.09	0.99, 1.19
Usual activities	1.17	1.10, 1.24	1.12	1.05, 1.19	1.13	1.06, 1.20	1.09	1.02, 1.16
Pain/discomfort	1.14	1.07, 1.23	1.12	1.04, 1.20	1.12	1.04, 1.20	1.08	1.00, 1.16
Anxiety/depression	1.18	1.09, 1.26	1.18	1.09, 1.26	1.16	1.08, 1.24	1.16	1.08, 1.24

ES: effect size; MD: median difference; RR: relative risk

*more severe stroke was defined as unable to walk without assistance on admission

Bold denotes statistically significant results. Of note, differences in utility scores ≥ 0.08 unit were considered clinically meaningful

Table 4. Net mean difference in EQ5D utility scores between AuSCR stroke survivors and the general population norms

	Population norms*		AuSCR utility EQ5D scores (DCE)		Net difference between population norms and AuSCR		
	Male	Female	Male	Female	Male	Female	Female vs Male
Age							

	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	MD (95% CI)	MD (95% CI)	Net difference
<55	948	0.93 [†]	0.12 [†]	944	0.88	0.12	520	0.70	0.27	360	0.73	0.24	0.23 (0.21, 0.25)	0.15 (0.12, 0.18)	-0.08
55–64	217	0.90	0.14	226	0.88	0.15	709	0.68	0.28	356	0.69	0.28	0.22 (0.19, 0.25)	0.19 (0.16, 0.23)	-0.03
65–74	153	0.87	0.16	193	0.87	0.16	1098	0.71	0.29	617	0.66	0.33	0.16 (0.13, 0.19)	0.21 (0.18, 0.24)	0.05
75+	104	0.85	0.16	122	0.82	0.15	1494	0.64	0.34	1698	0.53	0.38	0.21 (0.18, 0.25)	0.27 (0.24, 0.30)	0.06
Total	1422			1483			3821				3031				

MD (95% CI), mean difference (95% Confidence Interval). Differences in utility scores ≥ 0.08 unit were considered clinically meaningful

*from McCaffrey et al (2016)¹

[†]the score for group <55 was used by weighted estimates from age 15–54

Predicted probability of issues with pain & discomfort by age and comorbidities

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Title:

Sex differences in quality of life after stroke were explained by patient factors, not clinical care: evidence from the Australian Stroke Clinical Registry.

Date:

2021-02

Citation:

Phan, H. T., Gall, S. L., Blizzard, C. L., Lannin, N. A., Thrift, A. G., Anderson, C. S., Kim, J., Grimley, R. S., Castley, H. C., Kilkenny, M. F., Cadilhac, D. A. & AuSCR Consortium, Stroke123 Investigators, (2021). Sex differences in quality of life after stroke were explained by patient factors, not clinical care: evidence from the Australian Stroke Clinical Registry.. Eur J Neurol, 28 (2), pp.469-478. <https://doi.org/10.1111/ene.14531>.

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