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Regional Differences in the Care and Outcomes of Acute Stroke Patients: Evidence from the Australian Stroke Clinical Registry (AuSCR)

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ABSTRACT

Background: Access to evidence-based acute stroke care has been reported to be comparatively lower in rural as opposed to urban areas. It remains unclear which aspects of acute stroke care may differ by geographic location, and whether there are corresponding differences in long-term patient outcomes.

Aims: To compare the processes and outcomes of care in patients with stroke treated in urban versus rural hospitals that participate in the Australian Stroke Clinical Registry (AuSCR).

Methods: Data from the AuSCR registry between 2010 and 2015 were analysed using group comparisons; patients were divided into two groups (urban, rural) according to the Australian Standard Geographical Classification Remoteness Area classification. Between-group differences in processes of care, survival analyses up to 180 days and health-related quality of life at 90-180 days were explored using multilevel, multivariable analyses.

Results: Of the 28,115 patients, 8,159 (29%) were admitted to hospitals located within rural areas. Compared to those admitted to urban hospitals, patients in rural hospitals less often received thrombolysis if an ischaemic stroke (urban 12.7% vs rural 7.5%, $p<0.001$) or received treatment in stroke units (urban 82.2% vs 76.5%, $p<0.001$), and fewer were discharged with a care plan (urban 61.3% vs 44.7%, $p<0.001$). No significant differences were found in terms of survival or overall self-reported quality of life.

Conclusions: Rural access to recommended components of acute stroke care was comparatively poorer; however, this did not appear to impact health outcomes at approximately 6 months.

Article Summary

Strengths and Limitations of this Study

- This is the first study in Australia to look at how access to acute stroke care varies between Australia's urban and rural areas, using data from the Australian Stroke Clinical Registry (AuSCR).
- This study also reports on regional differences in patient outcomes, in the form of mortality and health-related quality of life (HRQoL) at up to 180 days post-stroke.
- Patient outcome measures were adjusted for known confounders.
- Hospitals participating in the AuSCR may not be representative of all Australian hospitals.

Introduction

Internationally, evidence suggests that patients with stroke admitted to hospitals located in rural or regional areas have limited access to known evidence-based interventions, such as thrombolysis and stroke unit care, relative to those treated in urban hospitals.[1] There is a paucity of research investigating disparities in other, more elementary processes which define contemporary standards of acute stroke care, such as the prescription of secondary prevention medications. In addition, if there are differences in stroke care between urban and rural regions, determining if there are corresponding differences in patient outcomes warrants attention so as to permit future exploration of organisational, process or patient barriers preventing evidence-based stroke care being received.

Overall, prior research on the rural and urban outcomes of care has yielded inconsistent findings,[1] and is characterised by studies with inadequate risk adjustment,[2-4] or an indirect focus on urban-rural differences in outcomes.[5-7] Previous attempts to explore this issue have also been reliant on 'hard' outcome measures such as rates of mortality and readmission;[8-10] whereas regional differences in patients' quality of life has been rarely investigated.[11, 12] The aim of this study was to compare the processes of care and outcomes for patients with stroke treated in urban compared with rural hospitals.

Methods

Study design

We used data from Australian hospitals that participate in the Australian Stroke Clinical Registry (AuSCR). The AuSCR registry is used to monitor processes of care provided to, and

the outcomes of, individuals hospitalised with acute stroke or transient ischaemic attacks (TIAs) in Australian hospitals.[13] Death information (date and cause) from Australia's National Death Index (NDI) are routinely linked to the AuSCR by the Australian Institute of Health and Welfare (AIHW).[14] For this study, we used data from 50 hospitals submitted to the AuSCR from January 2010 to December 2015, and we excluded patients admitted with TIAs from this analysis. Selection bias is minimised in the AuSCR by use of an "opt-out" approach when recruiting participants, whereby all eligible patients are registered unless they or their next of kin nominates to have their data excluded;[13] during the study period less than 3% of potential participants opted out of the registry. Patients who did not opt out of the registry, and who were discharged from hospital following their stroke, were followed up by trained research staff between 90 and 180 days following their index admission (i.e. the first registered event in AuSCR). This process uses a modified Dillman protocol,[15] whereby two attempts are made to contact patients by post prior to an attempt by telephone.[16]

Collected processes of care in AuSCR up to 2015 were: admission to a stroke unit, thrombolysis (ischaemic stroke only), discharge on anti-hypertensive medication, and the provision of a care plan. Hospitals located in the state of Queensland also collected four additional variables: time to first mobilisation, dysphagia screen, aspirin within 48 hours, and being discharged on antiplatelets or antithrombotics if an ischemic event. Indicator data with responses of no, unknown, or missing were recoded as negative (proportion of missing data ranged from <1% to 5.05%). Regional differences in patient mortality were assessed using intervals of 7, 30, 90 and 180 days.

Participants' health-related quality of life (HRQoL) data were collected at 90-180 day follow-up using the EuroQoL-5 dimension-3 level (EQ-5D-3L) instrument.[17] Respondents were

asked to report their health status in five domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with each domain having three possible responses (no problems, some problems, and extreme problems). Respondents use a Visual Analogue Scale (VAS) to rate their overall perceived health from 0 to 100, with 0 being the worst imaginable health state and 100 the best imaginable health state.[17] The VAS was coded as 0 for individuals who had died within the follow-up period.

Statistical analysis

Hospitals were divided into categories of 'urban' or 'rural' based on their classification under the Australian Standard Geographical Classification Remoteness Area (ASGC-RA) system.[18] Hospitals located in ASGC-RA category 1 (i.e. major cities) were regarded as 'urban', while those in categories 2 or above were regarded as 'rural'. The majority of hospitals (>95%) that contribute data to AuSCR are funded under the public health care scheme. Participants' baseline characteristics were compared between regions using χ^2 tests for categorical data, and Wilcoxon Rank Sum tests for continuous variables. Care processes were expressed as the proportion of eligible patients who received each form of care and were analysed by location (urban or rural) using χ^2 tests. Participants' responses to the EQ-5D-3L instrument were expressed as the number of individuals who encountered problems with each domain, with 'some problems' and 'extreme problems' being recoded into one category. Regional differences within each domain were then analysed using χ^2 tests.

Cox proportional hazards regression analysis was conducted to assess deaths within 7, 30, 90, and 180 days. Logistic regression was used to assess regional differences in each of the EQ-5D-3L domains. Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission (as a validated measure of stroke severity)[19] and socioeconomic

status (SES) using the index of relative socio-economic advantage and disadvantage (IRSAD).[20] Each regression model also accounted for inter-hospital transfers, in-hospital stroke, and whether the individual received treatment in a stroke unit. Patient clustering was adjusted for directly in each of our models, to account for correlation between patients admitted to the same hospital. Data were analysed using Stata/SE 12.[21]

Ethical approval

All participating hospitals have provided ethical and governance approvals for AuSCR data collection and analysis. Ethical approval was obtained from the AIHW to conduct data linkage to the NDI, and from the Tasmanian Human Research Ethics Committee to conduct this data analysis (reference H0017787).

Results

Between 2010 and 2015, 28,115 episodes of care from 50 hospitals were registered in the AuSCR. Of these episodes, 8,159 (29%) were for individuals admitted to hospitals located within rural areas. Compared to those from urban areas, individuals from rural areas were more likely to have been born in Australia, have an indigenous background, and be of a lower SES (Table 1). Rural patients were also more likely than urban patients to be diagnosed with a stroke of 'undetermined' subtype (8.1% vs 3.6%). When compared to urban patients, those treated in rural hospitals had poorer access to several clinical processes of care (Table 2, online supplement 1 for variables collected only in Queensland). Specifically, rural patients were less likely to be admitted to a stroke unit (odds ratio [OR] = 0.70, 95% Confidence Interval [CI] 0.66 to 0.74), receive intravenous thrombolysis in ischaemic stroke (OR = 0.55, 95% CI 0.50 to 0.62), or be provided with a care plan at time of discharge (OR = 0.59, 95% CI 0.54 to 0.64). There were no significant differences between regions in prescribing rates of anti-hypertensive medications at discharge (OR = 0.97, 95% CI 0.91 to 1.03). Regional

differences in the proportion of patients discharged home were not observed, but urban patients were more likely to die in hospital in the unadjusted comparisons (Table 2). The median LOS for rural patients was one day shorter than that of urban patients, and this remained the case after adjustment for potential confounders (coefficient -1, 95% CI -1.97 to -.03).

Table 1. Patient characteristics by region

Characteristics	Urban *n* (%)	Rural *n* (%)	p-value
No. of sites	25 (50)	25 (50)	
No. of cases	19,956 (71)	8,159 (29)	
Female	9,095 (45.6)	3,770 (46.2)	0.335
Age (years)			
<65	4,910 (24.6)	2,095 (25.7)	0.030
65-74	4,468 (22.4)	1,887 (23.1)	
75-84	6,141 (30.8)	2,469 (30.3)	
85+	4,431 (22.2)	1,707 (20.9)	
Median age in years (Q1, Q3)[a]	76.1 (65.2, 84.2)	75.4 (64.7, 83.6)	0.003
State			
New South Wales	3,252 (16.3)	805 (9.9)	<0.001
Queensland	6,675 (33.4)	4,401 (53.9)	
Tasmania	-	1,118 (13.7)	
Victoria	9,133 (45.8)	1,835 (22.5)	
Western Australia	896 (4.5)	-	
Born in Australia	11,916 (59.7)	6,282 (77)	<0.001
Aboriginal/Torres Strait Islander	174 (0.9)	262 (3.2)	<0.001
Index of Relative Socio-economic Advantage and Disadvantage			
Quintile 1 (most disadvantaged)	2,367 (12.3)	2,557 (34.4)	<0.001
Quintile 2	2,764 (14.3)	1,932 (26)	
Quintile 3	3,335 (17.3)	1,603 (21.6)	
Quintile 4	4,837 (25.1)	1,092 (14.7)	
Quintile 5 (most advantaged)	5,986 (31)	244 (3.3)	
Able to walk on admission (stroke severity)	6,055 (32.7)	2,439 (34.6)	0.003
Stroke subtype			
Intracerebral haemorrhagic	3,247 (16.3)	1,177 (14.4)	<0.001
Ischaemic	15,962 (80.1)	6,313 (77.5)	
Undetermined	709 (3.6)	658 (8.1)	
Transfer from other hospitals	2,191 (11.2)	1,739 (21.6)	<0.001
In-hospital stroke	1,156 (5.9)	407 (5.1)	0.008
Length of stay, median (Q1, Q3)[a] days	6 (3-10)	5 (2-8)	<0.001
Died in hospital[b]	2,216 (11.3)	720 (9.5)	<0.001
Discharge destination			
Home	7,353 (41.4)	2,899 (39)	0.092
Rehabilitation	6,234 (35.1)	2,137 (28.7)	<0.001
Aged care	1,057 (6)	326 (4.4)	<0.001
Other	3,096 (17.5)	2,077 (27.9)	<0.001

EQ-5D-dimensions			
Mobility			
No problems	4,171 (47.1)	1,791 (48.4)	
Some problems	4,056 (45.8)	1,714 (46.4)	
Extreme problems	631 (7.1)	193 (5.2)	<0.001
Self-care			
No problems	5,784 (65.2)	2,499 (67.4)	
Some problems	2,012 (22.7)	872 (23.5)	
Extreme problems	1,069 (12.1)	339 (9.1)	<0.001
Usual activities			
No problems	3,445 (38.9)	1,448 (39.1)	
Some problems	3,590 (40.6)	1,571 (42.3)	
Extreme problems	1,809 (20.5)	688 (18.6)	0.034
Pain/discomfort			
No problems	4,401 (50)	1,876 (50.9)	
Some problems	3,955 (44.9)	1,622 (44)	
Extreme problems	446 (5.1)	190 (5.1)	0.621
Anxiety/depression			
No problems	4,632 (52.8)	1,948 (52.9)	
Some problems	3,630 (41.3)	1,527 (41.5)	
Extreme problems	518 (5.9)	208 (5.6)	0.860

[a]Q1: 25th percentile; Q3: 75th percentile
[b]<5% missing/not documented data.

Table 2. Processes of care by region

	Urban *n* (%)	Rural *n* (%)	p-value
Evidence-based therapies (all states)			
Treated in a stroke unit	16,408 (82.2)	6,241 (76.5)	<0.001
Intravenous thrombolysis for ischaemic stroke	2,007 (12.7)	463 (7.5)	<0.001
Discharged on antihypertensives	12,184 (70.6)	4,895 (69.9)	0.315
Care plan on discharge to community	4,871 (61.3)	1,441 (44.7)	<0.001

There were no significant differences between geographical groups in terms of survival up to 180 days (Table 3). In relation to HRQoL, no regional differences were observed in four of the EQ-5D domains, namely Anxiety/Depression, Mobility, Self-care, and Usual Activities (Table 4). Rural patients were, however, significantly less likely to have reported symptoms of pain or discomfort during the follow up period (OR = 0.88, 95% CI 0.79 to 0.97, p = 0.015). Rural patients also had marginally higher perceived health, as measured by VAS, than their urban counterparts (70 vs 68, p<0.001).

Table 3. Survival analysis of rural stroke patients as compared to urban stroke patients

	Urban	Rural		Model*	
Time to death	***n* (%)**	***n* (%)**	**p-value**	**HR**	**95% CI**
Up to 7 days	1,750 (8.8)	769 (9.4)	0.081	0.98	(0.79-1.21)
8 to 30 days	1,242 (6.2)	491 (6)	0.608	1.02	(0.87-1.20)
31 to 90 days	745 (3.7)	265 (3.2)	0.055	0.88	(0.73-1.06)
91 to 180 days	526 (2.6)	202 (2.5)	0.439	0.88	(0.69-1.11)

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Table 4. Outcomes at 90-180 day follow-up of rural patients as compared to urban patients

				Model		
EQ-5D-dimensions	**Urban *n* (%)**	**Rural *n* (%)**	**p-value**	**OR**	**95% CI**	**p-value**
Mobility	4,687 (52.9)	1,907 (51.6)	0.169	1.02	(0.92-1.13)	0.717
Self-care	3,081 (34.8)	1,211 (32.6)	0.023	0.92	(0.80-1.06)	0.235
Usual activities	5,399 (61)	2,259 (60.9)	0.910	0.95	(0.85-1.06)	0.376
Pain/discomfort	4,401 (50)	1,812 (49.1)	0.376	0.88	(0.79-0.97)	0.015
Anxiety/depression	4,148 (47.2)	1,735 (47.1)	0.890	0.98	(0.87-1.10)	0.759
Median VAS (Q1, Q3)	68 (40, 80)	70 (50, 83)	<.001	-	-	-

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Discussion

The primary aim of this study was to assess whether there are differences in the quality of care and outcomes for patients treated in urban and rural locations. We found that patients admitted to rural hospitals in Australia were less likely to receive some key care processes that are recommended in our national stroke clinical guidelines.[22] However, for the most part, we did not observe corresponding differences in patient 90-180 day outcomes.

Patients admitted to rural hospitals were significantly less likely to receive treatment in a stroke unit (76.5% vs 82.2%) despite only one rural hospital not being equipped with a stroke unit (n=30 episodes of care). This finding suggests that while nearly all rural sites had facilities which met the minimum criteria for stroke units,[23] many were unable to utilise their stroke unit's full potential. As observed by Dwyer et al.,[24] hospitals without 'quarantined' stroke unit beds may be unable to offer specialist care to stroke patients at times when there is demand for beds from other medical specialties. Such hospitals may benefit from using clinical coordinators to facilitate organisational change, as recommended by Cadilhac and colleagues.[25]

It should be noted that during the study period only 45% of patients located in Australia's 'regional' areas received treatment in a stroke unit, and only 3.3% of all stroke unit beds were located in regional areas.[26, 27] Taken together, these statistics indicate that access to stroke units within rural hospitals participating in the AuSCR was markedly better than the national average. Given that there is a well-established link between stroke unit admission and access to key aspects of acute stroke care,[28] future efforts should focus on increasing the number of stroke units within Australia's regional areas, and improving access to existing stroke units.

Consistent with other studies, rural patients remained less likely than urban patients to be administered thrombolysis. The provision of thrombolysis is known to be influenced by a host of patient, clinician and system-related factors.[29] Of these factors, patients' distance to hospitals, accessing brain imaging after-hours, and obtaining specialist input are among the most pertinent issues encountered by clinicians providing thrombolysis in rural areas.[30-32] Rural-based clinicians in the Australian state of Victoria have been able to obtain specialist input and improve thrombolysis rates through the use of a telemedicine program.[33] The use of

such technology in all regional areas of the country is urgently needed in order to increase rates of thrombolysis administration.[34]

We did not observe differences by location in rates of prescription for antihypertensive medications at hospital discharge. As has been noted previously,[35] this may reflect the fact that the management of patients' blood pressure for primary or secondary prevention is not necessarily specific to stroke, and does not require any additional resources. In any case, the rates of prescription for antihypertensive medications at discharge from both regions were substantially less than expected based on previous AuSCR data, indicating that more work needs to be done to improve this aspect of evidence-based care.[36]

Despite marked differences in access to stroke unit care and thrombolysis, we did not observe any regional differences in rates of survival at up to 180 days post-stroke. This may be because access to acute stroke care, when considered in its entirety, was reasonably comparable between the study's urban and rural hospitals. This notion is supported by the fact that the study's rural hospitals, by virtue of their participation in the registry, are likely to be highly motivated to monitor and improve their provision of stroke care, and perhaps are better resourced than other rural sites. Furthermore, there is evidence that within the state of Queensland (online supplement 1) patients in rural hospitals were provided evidence-based therapies more often than those in urban hospitals. These differences warrant further research.

In relation to HRQoL, we observed that with the exception of the pain/discomfort domain, there were no significant regional differences in any of the EQ-5D domains or VAS scores. These findings stand in contrast to multiple surveys conducted by the Australian government, in which rural residents had an overall lower self-reported health status.[37, 38] The disparity between regions in terms of self-reported pain/discomfort may point towards regional

differences in attitudes towards pain management. Indeed, literature on cancer patients in Australia has highlighted that a culture of stoicism and self-reliance within rural areas can make individuals less likely to report symptoms of pain[39] and delay seeking medical assistance.[40] There are other demographic factors which may partially explain this finding. For instance, previous researchers using the AuSCR data have found that patients with stroke requiring an interpreter are more likely to report symptoms of pain.[41] Given that urban patients in this study were far less likely to have been born in Australia (i.e. 59.7% vs 77%), the impact of the respondents' English-speaking ability on our findings cannot be discounted. Previous research using the AuSCR data has also highlighted that, other factors remaining equal, younger people from a lower SES are more likely to report symptoms of anxiety/depression.[42] We also found that rural patients had a significantly higher perceived health status than urban patients (70 vs 68 via VAS); however, it is unlikely that this difference represents a clinically relevant finding.[43]

Our study design and data have several limitations. Firstly, the distribution of urban and rural patients in this study (71% vs 29%) may not reflect that of the broader Australian hospital population, which recently stood at 64% and 36%, respectively.[44] We also did not use any data in relation to participants' residential addresses. It is therefore possible that some individuals who were admitted to urban hospitals resided in rural areas, and vice versa. A further limitation is that our HRQoL data did not factor in patients' health prior to their stroke, meaning it is possible that some individuals' HRQoL deficits may relate to pre-existing conditions. Despite these limitations, our study is the first of its kind in Australia to comprehensively examine urban-rural differences in access to acute stroke care and the associated patient outcomes. To the best of the authors' knowledge, it is also among the first in the world to report on urban-rural differences in patients' quality of life post-stroke.

Conclusions

This is the largest study to date examining geographic disparities in processes of stroke care, and providing a benchmark for the development and testing of interventions that may have the potential to reduce the differences between rural and urban patients with acute stroke. Interestingly, while we identified disparities in processes of care, we did not observe any association between geographic region and patient outcomes in terms of mortality or HRQoL. There are clear opportunities to better understand why the impact of these process of care variables on stroke outcomes are more pronounced in urban areas. Our findings underscore the importance of understanding how geographical area influences HRQoL; continued efforts to determine the impact of stroke care post-discharge are important. Future work in this field should also focus on redressing the resourcing disparities, in particular increasing the number of rural hospitals which meet the minimum criteria for stroke unit care.

Declaration of competing interests

DAC is the data custodian for the Australian Stroke Clinical Registry and is supported by a National Health and Medical Research Council fellowship (1154273). She has received grants paid to her institution from Stroke Foundation, Melbourne Health, Victorian government, Queensland government, Tasmanian government, South Australian government, Western Australian government, Boehringer Ingelheim, Medtronic, Pfizer, Amgen and Shire. NAL is the Chair of the Management Committee of the Australian Stroke Clinical Registry, and a member of the Stroke Foundation Clinical Council. NAL is supported by National Heart Foundation of Australia (GNT102055).

Author Contributions

HC, MD, GP, SG, KMF, KF and DC contributed to the study design and concept. JK and DC contributed towards the statistical analyses. HTP, HC, LW, RW, FR, and LA participated in the manuscript preparation, editing and revision and agreed upon the final version of the paper. NL contributed to the interpretation of results and was heavily involved in the final preparation of the paper.

Data sharing statement: contact can be made with the corresponding author for queries relating to unpublished data.

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Online Supplement 1 – Queensland Specific Care Processes

Care Process	Urban *n* (%)	Rural *n* (%)	p-value
Mobilised during admission	2,876 (69.3)	1,950 (80.1)	<0.001
Swallow screen or assessment	4,952 (74.2)	3,676 (83.5)	<0.001
Aspirin within 48h, if ischaemic	3,393 (68.2)	2,843 (75.8)	<0.001
Discharged on antithrombotic medication, if ischaemic	3,823 (80.1)	2,694 (86.7)	<0.001

Online Supplement 2 - Co-investigators and other contributors to the Australian Stroke Clinical Registry

The following people are acknowledged for their contribution to collecting hospital data on the patients registered in AuSCR or their participation on various governance committees between 2010 and 2015:

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

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	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
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	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7-8
		(*e*) Describe any sensitivity analyses	NA
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	8
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	-
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	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11
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	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-14
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	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	2

*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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Regional Differences in the Care and Outcomes of Acute Stroke Patients in Australia: an Observational Study using Evidence from the Australian Stroke Clinical Registry (AuSCR)

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Regional Differences in the Care and Outcomes of Acute Stroke Patients in Australia: an Observational Study using Evidence from the Australian Stroke Clinical Registry (AuSCR)

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ABSTRACT

Objectives: To compare the processes and outcomes of care in patients with stroke treated in urban versus rural hospitals in Australia.

Design: Observational study using data from a multicentre national registry.

Setting: Data from 50 acute care hospitals in Australia (25 urban, 25 rural) which participated in the Australian Stroke Clinical Registry during the period 2010 to 2015.

Participants: Patients were divided into two groups (urban, rural) according to the Australian Standard Geographical Classification Remoteness Area classification. Data pertaining to 28,115 stroke patients were analysed, of whom 8,159 (29%) were admitted to hospitals located within rural areas.

Primary and Secondary Outcome Measures: Regional differences in processes of care (admission to a stroke unit, thrombolysis for ischaemic stroke, discharge on anti-hypertensive medication, and the provision of a care plan). Survival analyses up to 180 days and health-related quality of life at 90-180 days.

Results: Compared to those admitted to urban hospitals, patients in rural hospitals less often received thrombolysis (urban 12.7% vs rural 7.5%, p<0.001) or received treatment in stroke units (urban 82.2% vs 76.5%, p<0.001), and fewer were discharged with a care plan (urban 61.3% vs 44.7%, p<0.001). No significant differences were found in terms of survival or overall self-reported quality of life.

Conclusions: Rural access to recommended components of acute stroke care was comparatively poorer; however, this did not appear to impact health outcomes at approximately 6 months.

Article Summary

Strengths and Limitations of this Study

- This is the first study in Australia to look at how access to acute stroke care varies between Australia's urban and rural areas, using data from the Australian Stroke Clinical Registry (AuSCR).
- This study also reports on regional differences in patient outcomes, in the form of mortality and health-related quality of life (HRQoL) at up to 180 days post-stroke.
- Patient outcome measures were adjusted for known confounders.
- Hospitals participating in the AuSCR may not be representative of all Australian hospitals.

Introduction

Internationally, evidence suggests that patients with stroke admitted to hospitals located in rural or regional areas have limited access to known evidence-based interventions, such as thrombolysis and stroke unit care, relative to those treated in urban hospitals.[1] There is a paucity of research investigating disparities in other, more elementary processes which define contemporary standards of acute stroke care, such as the prescription of secondary prevention medications. In addition, if there are differences in stroke care between urban and rural regions, determining if there are corresponding differences in patient outcomes warrants attention so as to permit future exploration of organisational, process or patient barriers preventing evidence-based stroke care being received.

Overall, prior research on the rural and urban outcomes of care has yielded inconsistent findings,[1] and is characterised by studies with inadequate risk adjustment,[2-4] or an indirect focus on urban-rural differences in outcomes.[5-7] Previous attempts to explore this issue have also been reliant on 'hard' outcome measures such as rates of mortality and readmission;[8-10] whereas regional differences in patients' quality of life has been rarely investigated.[11,12] Given this knowledge gap, the aim of this study was to compare the processes of care and outcomes for patients with stroke treated in urban compared with rural hospitals.

Methods

Study design

We undertook a multicentre observational cohort study of adults admitted to hospital with acute stroke using linked data from the Australian Stroke Clinical Registry (AuSCR) (see protocol[13] and www.auscr.com.au).The AuSCR is used to monitor processes of care provided to, and the outcomes of, individuals hospitalised with acute stroke or transient ischaemic

attacks (TIAs) in Australian hospitals primary for quality improvement and benchmarking activities.[13] Cases are entered prospectively in the AuSCR based on clinical diagnosis of stroke during the admission. Case ascertainment is checked annually using International Classification of Diseases (ICD)-10 discharge codes obtained from the hospital administrative system and compared to the cases entered in the registry at each hospital. A complete list of co-investigators and other contributors to the AuSCR is contained in online supplement 1. Death information (date and cause) from Australia's National Death Index (NDI) are routinely linked to the AuSCR by the Australian Institute of Health and Welfare (AIHW).[14] For this study, we used data from all 50 hospitals who submitted data to the AuSCR from January 2010 to December 2015. Patients diagnosed with TIAs were excluded from the analyses, as these individuals are unlikely to require the care processes of interest in this study. As at 2015, the 50 hospitals covered by the AuSCR accounted for approximately 46% of all Australian hospitals receiving n≥50 stroke admissions per annum.[15] Selection bias is minimised in the AuSCR by use of an "opt-out" approach when recruiting participants, whereby all eligible patients are registered unless they or their next of kin nominates to have their data excluded.[13] The proportion of cases who opt-out from the registry is <3% in urban and rural hospitals. Patients who did not opt out of the registry, and who were discharged from hospital following their stroke, were followed up by trained research staff between 90 and 180 days following their index admission (i.e. the first registered event in AuSCR). This process uses a modified Dillman protocol,[16] whereby two attempts are made to contact patients by post prior to an attempt by telephone.[17]

Process of care data collected in AuSCR up to 2015 were: admission to a stroke unit, thrombolysis (ischaemic stroke only), discharge on anti-hypertensive medication, and the provision of a care plan. Care plans are developed with the patient and family if discharged from acute care directly to the community (i.e., to a home setting or institutional residential

aged care and not transferred to another hospital, that is, for rehabilitation). This is not the discharge summary written by hospital clinicians for the primary care doctor; the discharge care plan should include information to improve the transition to home, such as arrangements for community support services, information on risk factor management, equipment to be purchased, and follow-up appointments. Hospitals located in the state of Queensland also collected four additional variables: time to first mobilisation, dysphagia screen, aspirin within 48 hours, and being discharged on antiplatelets or antithrombotics if an ischemic event. Indicator data with responses of no, unknown, or missing were recoded as negative (proportion of missing data ranged from <1% to 5.05%). Regional differences in patient mortality were assessed using intervals of 7, 30, 90 and 180 days.

Participants' health-related quality of life (HRQoL) data were collected at 90-180 day follow-up using the EuroQoL-5 dimension-3 level (EQ-5D-3L) instrument.[18] Respondents were asked to report their health status in five domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with each domain having three possible responses (no problems, some problems, and extreme problems). Respondents use a Visual Analogue Scale (VAS) to rate their overall perceived health from 0 to 100, with 0 being the worst imaginable health state and 100 the best imaginable health state.[18] The VAS was coded as 0 for individuals who had died within the follow-up period.

Statistical analysis

The primary exposure variable of interest was classification of hospital (urban versus rural), and the primary outcomes were survival analyses up to 180 days was health related quality of life as assessed on the EQ-5D-3L. Hospitals were divided into categories of 'urban' or 'rural' based on their classification under the Australian Standard Geographical Classification

Remoteness Area (ASGC-RA) system.[19] The ASGC-RA system classifies areas into five categories: major cities, inner regional, outer regional, remote or very remote.[19] For the purpose of this study, hospitals located in ASGC-RA category 1 (i.e. major cities) were regarded as 'urban', while those in categories 2 or above were regarded as 'rural'. Interactive maps with overlays of the RA categories can be accessed via the Australian Bureau of Statistics website.[20] The majority of hospitals (>95%) that contribute data to AuSCR are funded under the public health care scheme. Participants' baseline characteristics were compared between regions using χ^2 tests for categorical data, and Wilcoxon Rank Sum tests for continuous variables. Care processes were expressed as the proportion of eligible patients who received each form of care and were analysed by location (urban or rural) using χ^2 tests. Participants' responses to the EQ-5D-3L instrument were expressed as the number of individuals who encountered problems with each domain, with 'some problems' and 'extreme problems' being recoded into one category. Regional differences within each domain were then analysed using χ^2 tests.

Cox proportional hazards regression analysis was conducted to assess deaths within 7, 30, 90, and 180 days. Logistic regression was used to assess regional differences in each of the EQ-5D-3L domains. Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission (as a validated measure of stroke severity)[21] and socioeconomic status (SES) using the index of relative socio-economic advantage and disadvantage (IRSAD).[22] Each regression model also accounted for inter-hospital transfers, in-hospital stroke, and whether the individual received treatment in a stroke unit. Patient clustering was adjusted for directly in each of our models, to account for correlation between patients admitted to the same hospital. A sensitivity analysis was undertaken using datasets where inter-hospital transfers were excluded, to assess the potential impact of this variable on patient outcomes. Data were analysed using Stata/SE 12.[23]

Ethical approval

All participating hospitals have provided ethical and governance approvals for AuSCR data collection and analysis. Ethical approval was obtained from the AIHW to conduct data linkage to the NDI, and from the Tasmanian Human Research Ethics Committee to conduct this data analysis (reference H0017787).

Results

Between 2010 and 2015, 28,115 episodes of care from 50 hospitals were registered in the AuSCR. Of these episodes, 8,159 (29%) were for individuals admitted to hospitals located within rural areas. Compared to those from urban areas, individuals from rural areas were more likely to have been born in Australia, have an indigenous background, and be of a lower SES (Table 1). Rural patients were also more likely than urban patients to be diagnosed with a stroke of 'undetermined' subtype (8.1% vs 3.6%). When compared to urban patients, those treated in rural hospitals had poorer access to several clinical processes of care (Table 2, online supplement 2 for variables collected only in Queensland). Specifically, rural patients were less likely to be admitted to a stroke unit (odds ratio [OR] = 0.70, 95% Confidence Interval [CI] 0.66 to 0.74), receive intravenous thrombolysis in ischaemic stroke (OR = 0.55, 95% CI 0.50 to 0.62), or be provided with a care plan at time of discharge (OR = 0.59, 95% CI 0.54 to 0.64). There were no significant differences between regions in prescribing rates of anti-hypertensive medications at discharge (OR = 0.97, 95% CI 0.91 to 1.03). Regional differences in the proportion of patients discharged home were not observed, but urban patients were more likely to die in hospital in the unadjusted comparisons (Table 2). The median LOS for rural patients was one day shorter than that of urban patients, and this

remained the case after adjustment for potential confounders (coefficient -1, 95% CI -1.97 to -.03).

Table 1. Patient characteristics by region

Characteristics	Urban *n* (%)	Rural *n* (%)	p-value
No. of sites	25 (50)	25 (50)	
No. of cases	19,956 (71)	8,159 (29)	
Female	9,095 (45.6)	3,770 (46.2)	0.335
Age (years)			
<65	4,910 (24.6)	2,095 (25.7)	0.030
65-74	4,468 (22.4)	1,887 (23.1)	
75-84	6,141 (30.8)	2,469 (30.3)	
85+	4,431 (22.2)	1,707 (20.9)	
Median age in years (Q1, Q3)[a]	76.1 (65.2, 84.2)	75.4 (64.7, 83.6)	0.003
State			
New South Wales	3,252 (16.3)	805 (9.9)	<0.001
Queensland	6,675 (33.4)	4,401 (53.9)	
Tasmania	-	1,118 (13.7)	
Victoria	9,133 (45.8)	1,835 (22.5)	
Western Australia	896 (4.5)	-	
Born in Australia	11,916 (59.7)	6,282 (77)	<0.001
Aboriginal/Torres Strait Islander	174 (0.9)	262 (3.2)	<0.001
Index of Relative Socio-economic Advantage and Disadvantage			
Quintile 1 (most disadvantaged)	2,367 (12.3)	2,557 (34.4)	<0.001
Quintile 2	2,764 (14.3)	1,932 (26)	
Quintile 3	3,335 (17.3)	1,603 (21.6)	
Quintile 4	4,837 (25.1)	1,092 (14.7)	
Quintile 5 (most advantaged)	5,986 (31)	244 (3.3)	
Able to walk on admission (stroke severity)	6,055 (32.7)	2,439 (34.6)	0.003
Stroke subtype			
Intracerebral haemorrhagic	3,247 (16.3)	1,177 (14.4)	<0.001
Ischaemic	15,962 (80.1)	6,313 (77.5)	
Undetermined	709 (3.6)	658 (8.1)	
Transfer from other hospitals	2,191 (11.2)	1,739 (21.6)	<0.001
In-hospital stroke	1,156 (5.9)	407 (5.1)	0.008
Length of stay, median (Q1, Q3)[a] days	6 (3-10)	5 (2-8)	<0.001
Died in hospital[b]	2,216 (11.3)	720 (9.5)	<0.001
Discharge destination			
Home	7,353 (41.4)	2,899 (39)	0.092
Rehabilitation	6,234 (35.1)	2,137 (28.7)	<0.001
Aged care	1,057 (6)	326 (4.4)	<0.001
Other	3,096 (17.5)	2,077 (27.9)	<0.001
EQ-5D-dimensions			
Mobility			
No problems	4,171 (47.1)	1,791 (48.4)	
Some problems	4,056 (45.8)	1,714 (46.4)	

Extreme problems	631 (7.1)	193 (5.2)	<0.001
Self-care			
No problems	5,784 (65.2)	2,499 (67.4)	
Some problems	2,012 (22.7)	872 (23.5)	
Extreme problems	1,069 (12.1)	339 (9.1)	<0.001
Usual activities			
No problems	3,445 (38.9)	1,448 (39.1)	
Some problems	3,590 (40.6)	1,571 (42.3)	
Extreme problems	1,809 (20.5)	688 (18.6)	0.034
Pain/discomfort			
No problems	4,401 (50)	1,876 (50.9)	
Some problems	3,955 (44.9)	1,622 (44)	
Extreme problems	446 (5.1)	190 (5.1)	0.621
Anxiety/depression			
No problems	4,632 (52.8)	1,948 (52.9)	
Some problems	3,630 (41.3)	1,527 (41.5)	
Extreme problems	518 (5.9)	208 (5.6)	0.860

[a]Q1: 25th percentile; Q3: 75th percentile
[b]<5% missing/not documented data.

Table 2. Processes of care by region

	Urban *n* (%)	Rural *n* (%)	p-value
Evidence-based therapies (all states)			
Treated in a stroke unit	16,408 (82.2)	6,241 (76.5)	<0.001
Intravenous thrombolysis for ischaemic stroke	2,007 (12.7)	463 (7.5)	<0.001
Discharged on antihypertensives	12,184 (70.6)	4,895 (69.9)	0.315
Care plan on discharge to community	4,871 (61.3)	1,441 (44.7)	<0.001

There were no significant differences between geographical groups in terms of survival up to 180 days (Table 3). In relation to HRQoL, no regional differences were observed in four of the EQ-5D domains, namely Anxiety/Depression, Mobility, Self-care, and Usual Activities (Table 4). Rural patients were, however, significantly less likely to have reported symptoms of pain or discomfort during the follow up period (OR = 0.88, 95% CI 0.79 to 0.97, p = 0.015). Rural patients also had marginally higher perceived health, as measured by VAS, than their urban counterparts (70 vs 68, p<0.001). The sensitivity analysis that excluded transferred patients did not influence the results.

Table 3. Survival analysis of rural stroke patients as compared to urban stroke patients

	Urban	Rural		Model*	
Time to death	***n* (%)**	***n* (%)**	**p-value**	**HR**	**95% CI**
Up to 7 days	1,750 (8.8)	769 (9.4)	0.081	0.98	(0.79-1.21)
8 to 30 days	1,242 (6.2)	491 (6)	0.608	1.02	(0.87-1.20)
31 to 90 days	745 (3.7)	265 (3.2)	0.055	0.88	(0.73-1.06)
91 to 180 days	526 (2.6)	202 (2.5)	0.439	0.88	(0.69-1.11)

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Table 4. Outcomes at 90-180 day follow-up of rural patients as compared to urban patients

				Model		
EQ-5D-dimensions	**Urban *n* (%)**	**Rural *n* (%)**	**p-value**	**OR**	**95% CI**	**p-value**
Mobility	4,687 (52.9)	1,907 (51.6)	0.169	1.02	(0.92-1.13)	0.717
Self-care	3,081 (34.8)	1,211 (32.6)	0.023	0.92	(0.80-1.06)	0.235
Usual activities	5,399 (61)	2,259 (60.9)	0.910	0.95	(0.85-1.06)	0.376
Pain/discomfort	4,401 (50)	1,812 (49.1)	0.376	0.88	(0.79-0.97)	0.015
Anxiety/depression	4,148 (47.2)	1,735 (47.1)	0.890	0.98	(0.87-1.10)	0.759
Median VAS (Q1, Q3)	68 (40, 80)	70 (50, 83)	<.001	-	-	-

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Discussion

The primary aim of this study was to assess whether there are differences in the quality of care and outcomes for patients treated in urban and rural locations. We found that patients admitted to rural hospitals in Australia were less likely to receive some key care processes that are recommended in our national stroke clinical guidelines.[24] However, for the most part, we did not observe corresponding differences in patient 90-180 day outcomes.

Patients admitted to rural hospitals were significantly less likely to receive treatment in a stroke unit (76.5% vs 82.2%) despite only one rural hospital not being equipped with a stroke unit (n=30 episodes of care). This finding suggests that while nearly all rural sites had facilities which met the minimum criteria for stroke units,[25] many were unable to utilise their stroke unit's full potential. As observed by Dwyer et al.,[26] hospitals without 'quarantined' stroke unit beds may be unable to offer specialist care to stroke patients at times when there is demand for beds from other medical specialties. Such hospitals may benefit from using clinical coordinators to facilitate organisational change, as recommended by Cadilhac and colleagues.[27]

It should be noted that during the study period only 45% of patients located in Australia's 'regional' areas received treatment in a stroke unit, and only 3.3% of all stroke unit beds were located in regional areas.[28,29] Taken together, these statistics indicate that access to stroke units within rural hospitals participating in the AuSCR was markedly better than the national average. Given that there is a well-established link between stroke unit admission and access to key aspects of acute stroke care,[30] future efforts should focus on increasing the number of stroke units within Australia's regional areas, and improving access to existing stroke units. Adherence rates in the current study were, for the most part, representative of that of more recent stroke care audits in Australia.[31,32] The main exception was in rates of care plan provision; on average 53% of patients in the current study received this form of care, which was substantially lower than that of AuSCR data from 2018 (69%)[32] and data from the Stroke Foundation's 2019 Acute Audit (65%).[31]

Consistent with other studies, rural patients remained less likely than urban patients to be administered thrombolysis. The provision of thrombolysis is known to be influenced by a host of patient, clinician and system-related factors.[33] Of these factors, patients' distance to

hospitals, accessing brain imaging after-hours, and obtaining specialist input are among the most pertinent issues encountered by clinicians providing thrombolysis in rural areas.[34-36] Rural-based clinicians in the Australian state of Victoria have been able to obtain specialist input and improve thrombolysis rates through the use of a telemedicine program.[37] Such a system was implemented in the state of Victoria for a small part of the study period,[37] and as such, may have influenced adherence rates in this group of hospitals. The use of telemedicine technology in all regional areas of the country is urgently needed in order to increase rates of thrombolysis administration.[38]

We did not observe differences by location in rates of prescription for antihypertensive medications at hospital discharge. As has been noted previously,[39] this may reflect the fact that the management of patients' blood pressure for primary or secondary prevention is not necessarily specific to stroke, and does not require any additional resources. In any case, the rates of prescription for antihypertensive medications at discharge from both regions were substantially less than expected based on previous AuSCR data, indicating that more work needs to be done to improve this aspect of evidence-based care.[40]

Despite marked differences in access to stroke unit care and thrombolysis, we did not observe any regional differences in rates of survival at up to 180 days post-stroke. This may be because access to acute stroke care, when considered in its entirety, was reasonably comparable between the study's urban and rural hospitals. This notion is supported by the fact that the study's rural hospitals, by virtue of their participation in the registry, are likely to be highly motivated to monitor and improve their provision of stroke care, and perhaps are better resourced than other rural sites. Furthermore, there is evidence that within the state of Queensland (online supplement 2) patients in rural hospitals were provided evidence-based therapies more often than those in urban hospitals. These differences warrant further research.

In relation to HRQoL, we observed that with the exception of the pain/discomfort domain, there were no significant regional differences in any of the EQ-5D domains or VAS scores. These findings stand in contrast to multiple surveys conducted by the Australian government, in which rural residents had an overall lower self-reported health status.[41,42] The disparity between regions in terms of self-reported pain/discomfort may point towards regional differences in attitudes towards pain management. Indeed, literature on cancer patients in Australia has highlighted that a culture of stoicism and self-reliance within rural areas can make individuals less likely to report symptoms of pain[43] and delay seeking medical assistance.[44] There are other demographic factors which may partially explain this finding. For instance, previous researchers using the AuSCR data have found that patients with stroke requiring an interpreter are more likely to report symptoms of pain.[45] Given that urban patients in this study were far less likely to have been born in Australia (i.e. 59.7% vs 77%), the impact of the respondents' English-speaking ability on our findings cannot be discounted. Previous research using the AuSCR data has also highlighted that, other factors remaining equal, younger people from a lower SES are more likely to report symptoms of anxiety/depression.[46] We also found that rural patients had a significantly higher perceived health status than urban patients (70 vs 68 via VAS); however, it is unlikely that this difference represents a clinically relevant finding.[47]

Our study design and data have several limitations. Firstly, the distribution of urban and rural patients in this study (71% vs 29%) may not reflect that of the broader Australian hospital population, which recently stood at 64% and 36%, respectively.[48] We also did not use any data in relation to participants' residential addresses. It is therefore possible that some individuals who were admitted to urban hospitals resided in rural areas, and vice versa. A further limitation is that our HRQoL data did not factor in patients' health prior to their

stroke, meaning it is possible that some individuals' HRQoL deficits may relate to pre-existing conditions. Lastly, although we used patients' baseline walking ability as a validated measure of stroke severity,[21] the study may have benefited from the use of a more recognised scale, such as the NIHSS. Despite these limitations, our study is the first of its kind in Australia to comprehensively examine urban-rural differences in access to acute stroke care and the associated patient outcomes. To the best of the authors' knowledge, it is also among the first in the world to report on urban-rural differences in patients' quality of life post-stroke.

Conclusions

This is the largest study to date examining geographic disparities in processes of stroke care, and providing a benchmark for the development and testing of interventions that may have the potential to reduce the differences between rural and urban patients with acute stroke. Interestingly, while we identified disparities in processes of care, we did not observe any association between geographic region and patient outcomes in terms of mortality or HRQoL. There are clear opportunities to better understand why the impact of these process of care variables on stroke outcomes are more pronounced in urban areas. Our findings underscore the importance of understanding how geographical area influences HRQoL; continued efforts to determine the impact of stroke care post-discharge are important. Future work in this field should also focus on redressing the resourcing disparities, in particular increasing the number of rural hospitals which meet the minimum criteria for stroke unit care.

Declaration of competing interests

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Author Contributions

HC, MD, GP, SG, KMF, KF and DC contributed to the study design and concept. JK and DC contributed towards the statistical analyses. HTP, HC, LW, RW, FR, and LA participated in the manuscript preparation, editing and revision and agreed upon the final version of the paper. NL contributed to the interpretation of results and was heavily involved in the final preparation of the paper.

Data sharing statement: contact can be made with the corresponding author for queries relating to unpublished data.

Patient and Public Involvement: patients and/or the public were not directly involved in the design, recruitment or implementation of the study. Consumer representatives are members of the AuSCR Steering Committee, and regular reviews by consumers of the AuSCR documents (policies and reports) are undertaken.

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Online Supplement 1 - Co-investigators and other contributors to the Australian Stroke Clinical Registry

The following people are acknowledged for their contribution to collecting hospital data on the patients registered in AuSCR or their participation on various governance committees between 2010 and 2015:

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Online Supplement 2 – Queensland Specific Care Processes

Care Process	Urban *n* (%)	Rural *n* (%)	p-value
Mobilised during admission	2,876 (69.3)	1,950 (80.1)	<0.001
Swallow screen or assessment	4,952 (74.2)	3,676 (83.5)	<0.001
Aspirin within 48h, if ischaemic	3,393 (68.2)	2,843 (75.8)	<0.001
Discharged on antithrombotic medication, if ischaemic	3,823 (80.1)	2,694 (86.7)	<0.001

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

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	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
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	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7-8
		(*e*) Describe any sensitivity analyses	NA
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	8
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	-
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	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11
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	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-14
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	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	2

*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.

BMJ Open

Regional Differences in the Care and Outcomes of Acute Stroke Patients in Australia: an Observational Study using Evidence from the Australian Stroke Clinical Registry (AuSCR)

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Regional Differences in the Care and Outcomes of Acute Stroke Patients in Australia: an Observational Study using Evidence from the Australian Stroke Clinical Registry (AuSCR)

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ABSTRACT

Objectives: To compare the processes and outcomes of care in patients with stroke treated in urban versus rural hospitals in Australia.

Design: Observational study using data from a multicentre national registry.

Setting: Data from 50 acute care hospitals in Australia (25 urban, 25 rural) which participated in the Australian Stroke Clinical Registry during the period 2010 to 2015.

Participants: Patients were divided into two groups (urban, rural) according to the Australian Standard Geographical Classification Remoteness Area classification. Data pertaining to 28,115 stroke patients were analysed, of whom 8,159 (29%) were admitted to hospitals located within rural areas.

Primary and Secondary Outcome Measures: Regional differences in processes of care (admission to a stroke unit, thrombolysis for ischaemic stroke, discharge on anti-hypertensive medication, and the provision of a care plan). Survival analyses up to 180 days and health-related quality of life at 90-180 days.

Results: Compared to those admitted to urban hospitals, patients in rural hospitals less often received thrombolysis (urban 12.7% vs rural 7.5%, p<0.001) or received treatment in stroke units (urban 82.2% vs 76.5%, p<0.001), and fewer were discharged with a care plan (urban 61.3% vs 44.7%, p<0.001). No significant differences were found in terms of survival or overall self-reported quality of life.

Conclusions: Rural access to recommended components of acute stroke care was comparatively poorer; however, this did not appear to impact health outcomes at approximately 6 months.

Article Summary

Strengths and Limitations of this Study

- This is the first study in Australia to look at how access to acute stroke care varies between Australia's urban and rural areas, using data from the Australian Stroke Clinical Registry (AuSCR).
- This study also reports on regional differences in patient outcomes, in the form of mortality and health-related quality of life (HRQoL) at up to 180 days post-stroke.
- Patient outcome measures were adjusted for known confounders.
- Hospitals participating in the AuSCR may not be representative of all Australian hospitals.

Introduction

Internationally, evidence suggests that patients with stroke admitted to hospitals located in rural or regional areas have limited access to known evidence-based interventions, such as thrombolysis and stroke unit care, relative to those treated in urban hospitals.[1] There is a paucity of research investigating disparities in other, more elementary processes which define contemporary standards of acute stroke care, such as the prescription of secondary prevention medications. In addition, if there are differences in stroke care between urban and rural regions, determining if there are corresponding differences in patient outcomes warrants attention so as to permit future exploration of organisational, process or patient barriers preventing evidence-based stroke care being received.

Overall, prior research on the rural and urban outcomes of care has yielded inconsistent findings,[1] and is characterised by studies with inadequate risk adjustment,[2-4] or an indirect focus on urban-rural differences in outcomes.[5-7] Previous attempts to explore this issue have also been reliant on 'hard' outcome measures such as rates of mortality and readmission;[8-10] whereas regional differences in patients' quality of life has been rarely investigated.[11,12] Given this knowledge gap, the aim of this study was to compare the processes of care and outcomes for patients with stroke treated in urban compared with rural hospitals.

Methods

Study design

We undertook a multicentre observational cohort study of adults admitted to hospital with acute stroke using linked data from the Australian Stroke Clinical Registry (AuSCR) (see protocol[13] and www.auscr.com.au).The AuSCR is used to monitor processes of care provided to, and the outcomes of, individuals hospitalised with acute stroke or transient ischaemic

attacks (TIAs) in Australian hospitals primary for quality improvement and benchmarking activities.[13] Cases are entered prospectively in the AuSCR based on clinical diagnosis of stroke during the admission. Case ascertainment is checked annually using International Classification of Diseases (ICD)-10 discharge codes obtained from the hospital administrative system and compared to the cases entered in the registry at each hospital. A complete list of co-investigators and other contributors to the AuSCR is contained in online supplement 1. Death information (date and cause) from Australia's National Death Index (NDI) are routinely linked to the AuSCR by the Australian Institute of Health and Welfare (AIHW).[14] For this study, we used data from all 50 hospitals who submitted data to the AuSCR from January 2010 to December 2015. Patients diagnosed with TIAs were excluded from the analyses, as these individuals are unlikely to require the care processes of interest in this study. As at 2015, the 50 hospitals covered by the AuSCR accounted for approximately 46% of all Australian hospitals receiving n≥50 stroke admissions per annum.[15] Selection bias is minimised in the AuSCR by use of an "opt-out" approach when recruiting participants, whereby all eligible patients are registered unless they or their next of kin nominates to have their data excluded.[13] The proportion of cases who opt-out from the registry is <3% in urban and rural hospitals. Patients who did not opt out of the registry, and who were discharged from hospital following their stroke, were followed up by trained research staff between 90 and 180 days following their index admission (i.e. the first registered event in AuSCR). This process uses a modified Dillman protocol,[16] whereby two attempts are made to contact patients by post prior to an attempt by telephone.[17]

Process of care data collected in AuSCR up to 2015 were: admission to a stroke unit, thrombolysis (ischaemic stroke only), discharge on anti-hypertensive medication, and the provision of a care plan. Care plans are developed with the patient and family if discharged from acute care directly to the community (i.e., to a home setting or institutional residential

aged care and not transferred to another hospital, that is, for rehabilitation). This is not the discharge summary written by hospital clinicians for the primary care doctor; the discharge care plan should include information to improve the transition to home, such as arrangements for community support services, information on risk factor management, equipment to be purchased, and follow-up appointments. Hospitals located in the state of Queensland also collected four additional variables: time to first mobilisation, dysphagia screen, aspirin within 48 hours, and being discharged on antiplatelets or antithrombotics if an ischemic event. Indicator data with responses of no, unknown, or missing were recoded as negative (proportion of missing data ranged from <1% to 5.05%). Regional differences in patient mortality were assessed using intervals of 7, 30, 90 and 180 days.

Participants' health-related quality of life (HRQoL) data were collected at 90-180 day follow-up using the EuroQoL-5 dimension-3 level (EQ-5D-3L) instrument.[18] Respondents were asked to report their health status in five domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with each domain having three possible responses (no problems, some problems, and extreme problems). Respondents use a Visual Analogue Scale (VAS) to rate their overall perceived health from 0 to 100, with 0 being the worst imaginable health state and 100 the best imaginable health state.[18] The VAS was coded as 0 for individuals who had died within the follow-up period.

Statistical analysis

The primary exposure variable of interest was classification of hospital (urban versus rural), and the primary outcomes were survival analyses up to 180 days was health related quality of life as assessed on the EQ-5D-3L. Hospitals were divided into categories of 'urban' or 'rural' based on their classification under the Australian Standard Geographical Classification

Remoteness Area (ASGC-RA) system.[19] The ASGC-RA system classifies areas into five categories: major cities, inner regional, outer regional, remote or very remote.[19] For the purpose of this study, hospitals located in ASGC-RA category 1 (i.e. major cities) were regarded as 'urban', while those in categories 2 or above were regarded as 'rural'. Interactive maps with overlays of the RA categories can be accessed via the Australian Bureau of Statistics website.[20] The majority of hospitals (>95%) that contribute data to AuSCR are funded under the public health care scheme. Participants' baseline characteristics were compared between regions using χ^2 tests for categorical data, and Wilcoxon Rank Sum tests for continuous variables. Care processes were expressed as the proportion of eligible patients who received each form of care and were analysed by location (urban or rural) using χ^2 tests. Participants' responses to the EQ-5D-3L instrument were expressed as the number of individuals who encountered problems with each domain, with 'some problems' and 'extreme problems' being recoded into one category. Regional differences within each domain were then analysed using χ^2 tests.

Cox proportional hazards regression analysis was conducted to assess deaths within 7, 30, 90, and 180 days. Logistic regression was used to assess regional differences in each of the EQ-5D-3L domains. Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission (as a validated measure of stroke severity)[21] and socioeconomic status (SES) using the index of relative socio-economic advantage and disadvantage (IRSAD).[22] Each regression model also accounted for inter-hospital transfers, in-hospital stroke, and whether the individual received treatment in a stroke unit. Patient clustering was adjusted for directly in each of our models, to account for correlation between patients admitted to the same hospital. A sensitivity analysis was undertaken using datasets where inter-hospital transfers were excluded, to assess the potential impact of this variable on patient outcomes. Data were analysed using Stata/SE 12.[23]

Patient and Public Involvement

patients and/or the public were not directly involved in the design, recruitment or implementation of the study. Consumer representatives are members of the AuSCR Steering Committee, and regular reviews by consumers of the AuSCR documents (policies and reports) are undertaken.

Ethical approval

All participating hospitals have provided ethical and governance approvals for AuSCR data collection and analysis. Ethical approval was obtained from the AIHW to conduct data linkage to the NDI, and from the Tasmanian Human Research Ethics Committee to conduct this data analysis (reference H0017787).

Results

Between 2010 and 2015, 28,115 episodes of care from 50 hospitals were registered in the AuSCR. Of these episodes, 8,159 (29%) were for individuals admitted to hospitals located within rural areas. Compared to those from urban areas, individuals from rural areas were more likely to have been born in Australia, have an indigenous background, and be of a lower SES (Table 1). Rural patients were also more likely than urban patients to be diagnosed with a stroke of 'undetermined' subtype (8.1% vs 3.6%). When compared to urban patients, those treated in rural hospitals had poorer access to several clinical processes of care (Table 2, online supplement 2 for variables collected only in Queensland). Specifically, rural patients were less likely to be admitted to a stroke unit (odds ratio [OR] = 0.70, 95% Confidence Interval [CI] 0.66 to 0.74), receive intravenous thrombolysis in ischaemic stroke (OR = 0.55, 95% CI 0.50 to 0.62), or be provided with a care plan at time of discharge (OR = 0.59, 95% CI 0.54 to 0.64). There were no significant differences between regions in prescribing rates of anti-hypertensive medications at discharge (OR = 0.97, 95% CI 0.91 to 1.03). Regional

differences in the proportion of patients discharged home were not observed, but urban patients were more likely to die in hospital in the unadjusted comparisons (Table 2). The median LOS for rural patients was one day shorter than that of urban patients, and this remained the case after adjustment for potential confounders (coefficient -1, 95% CI -1.97 to -.03).

Table 1. Patient characteristics by region

Characteristics	Urban *n* (%)	Rural *n* (%)	p-value
No. of sites	25 (50)	25 (50)	
No. of cases	19,956 (71)	8,159 (29)	
Female	9,095 (45.6)	3,770 (46.2)	0.335
Age (years)			
<65	4,910 (24.6)	2,095 (25.7)	0.030
65-74	4,468 (22.4)	1,887 (23.1)	
75-84	6,141 (30.8)	2,469 (30.3)	
85+	4,431 (22.2)	1,707 (20.9)	
Median age in years (Q1, Q3)[a]	76.1 (65.2, 84.2)	75.4 (64.7, 83.6)	0.003
State			
New South Wales	3,252 (16.3)	805 (9.9)	<0.001
Queensland	6,675 (33.4)	4,401 (53.9)	
Tasmania	-	1,118 (13.7)	
Victoria	9,133 (45.8)	1,835 (22.5)	
Western Australia	896 (4.5)	-	
Born in Australia	11,916 (59.7)	6,282 (77)	<0.001
Aboriginal/Torres Strait Islander	174 (0.9)	262 (3.2)	<0.001
Index of Relative Socio-economic Advantage and Disadvantage			
Quintile 1 (most disadvantaged)	2,367 (12.3)	2,557 (34.4)	<0.001
Quintile 2	2,764 (14.3)	1,932 (26)	
Quintile 3	3,335 (17.3)	1,603 (21.6)	
Quintile 4	4,837 (25.1)	1,092 (14.7)	
Quintile 5 (most advantaged)	5,986 (31)	244 (3.3)	
Able to walk on admission (stroke severity)	6,055 (32.7)	2,439 (34.6)	0.003
Stroke subtype			
Intracerebral haemorrhagic	3,247 (16.3)	1,177 (14.4)	<0.001
Ischaemic	15,962 (80.1)	6,313 (77.5)	
Undetermined	709 (3.6)	658 (8.1)	
Transfer from other hospitals	2,191 (11.2)	1,739 (21.6)	<0.001
In-hospital stroke	1,156 (5.9)	407 (5.1)	0.008
Length of stay, median (Q1, Q3)[a] days	6 (3-10)	5 (2-8)	<0.001
Died in hospital[b]	2,216 (11.3)	720 (9.5)	<0.001
Discharge destination			
Home	7,353 (41.4)	2,899 (39)	0.092
Rehabilitation	6,234 (35.1)	2,137 (28.7)	<0.001

Aged care	1,057 (6)	326 (4.4)	<0.001
Other	3,096 (17.5)	2,077 (27.9)	<0.001
EQ-5D-dimensions			
Mobility			
No problems	4,171 (47.1)	1,791 (48.4)	
Some problems	4,056 (45.8)	1,714 (46.4)	
Extreme problems	631 (7.1)	193 (5.2)	<0.001
Self-care			
No problems	5,784 (65.2)	2,499 (67.4)	
Some problems	2,012 (22.7)	872 (23.5)	
Extreme problems	1,069 (12.1)	339 (9.1)	<0.001
Usual activities			
No problems	3,445 (38.9)	1,448 (39.1)	
Some problems	3,590 (40.6)	1,571 (42.3)	
Extreme problems	1,809 (20.5)	688 (18.6)	0.034
Pain/discomfort			
No problems	4,401 (50)	1,876 (50.9)	
Some problems	3,955 (44.9)	1,622 (44)	
Extreme problems	446 (5.1)	190 (5.1)	0.621
Anxiety/depression			
No problems	4,632 (52.8)	1,948 (52.9)	
Some problems	3,630 (41.3)	1,527 (41.5)	
Extreme problems	518 (5.9)	208 (5.6)	0.860

[a]Q1: 25th percentile; Q3: 75th percentile
[b]<5% missing/not documented data.

Table 2. Processes of care by region

	Urban *n* (%)	**Rural *n* (%)**	**p-value**
Evidence-based therapies (all states)			
Treated in a stroke unit	16,408 (82.2)	6,241 (76.5)	<0.001
Intravenous thrombolysis for ischaemic stroke	2,007 (12.7)	463 (7.5)	<0.001
Discharged on antihypertensives	12,184 (70.6)	4,895 (69.9)	0.315
Care plan on discharge to community	4,871 (61.3)	1,441 (44.7)	<0.001

There were no significant differences between geographical groups in terms of survival up to 180 days (Table 3). In relation to HRQoL, no regional differences were observed in four of the EQ-5D domains, namely Anxiety/Depression, Mobility, Self-care, and Usual Activities (Table 4). Rural patients were, however, significantly less likely to have reported symptoms of pain or discomfort during the follow up period (OR = 0.88, 95% CI 0.79 to 0.97, p = 0.015). Rural patients also had marginally higher perceived health, as measured by VAS, than

their urban counterparts (70 vs 68, p<0.001). The sensitivity analysis that excluded transferred patients did not influence the results.

Table 3. Survival analysis of rural stroke patients as compared to urban stroke patients

	Urban	Rural		Model*	
Time to death	***n* (%)**	***n* (%)**	**p-value**	**HR**	**95% CI**
Up to 7 days	1,750 (8.8)	769 (9.4)	0.081	0.98	(0.79-1.21)
8 to 30 days	1,242 (6.2)	491 (6)	0.608	1.02	(0.87-1.20)
31 to 90 days	745 (3.7)	265 (3.2)	0.055	0.88	(0.73-1.06)
91 to 180 days	526 (2.6)	202 (2.5)	0.439	0.88	(0.69-1.11)

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Table 4. Outcomes at 90-180 day follow-up of rural patients as compared to urban patients

				Model		
EQ-5D-dimensions	**Urban *n* (%)**	**Rural *n* (%)**	**p-value**	**OR**	**95% CI**	**p-value**
Mobility	4,687 (52.9)	1,907 (51.6)	0.169	1.02	(0.92-1.13)	0.717
Self-care	3,081 (34.8)	1,211 (32.6)	0.023	0.92	(0.80-1.06)	0.235
Usual activities	5,399 (61)	2,259 (60.9)	0.910	0.95	(0.85-1.06)	0.376
Pain/discomfort	4,401 (50)	1,812 (49.1)	0.376	0.88	(0.79-0.97)	0.015
Anxiety/depression	4,148 (47.2)	1,735 (47.1)	0.890	0.98	(0.87-1.10)	0.759
Median VAS (Q1, Q3)	68 (40, 80)	70 (50, 83)	<.001	-	-	-

*Models were adjusted for age, sex, year of admission, state, type of stroke, ability to walk on admission, socioeconomic status, inter-hospital transfers, in-hospital stroke, and stroke unit admission

Discussion

The primary aim of this study was to assess whether there are differences in the quality of care and outcomes for patients treated in urban and rural locations. We found that patients

admitted to rural hospitals in Australia were less likely to receive some key care processes that are recommended in our national stroke clinical guidelines.[24] However, for the most part, we did not observe corresponding differences in patient 90-180 day outcomes.

Patients admitted to rural hospitals were significantly less likely to receive treatment in a stroke unit (76.5% vs 82.2%) despite only one rural hospital not being equipped with a stroke unit (n=30 episodes of care). This finding suggests that while nearly all rural sites had facilities which met the minimum criteria for stroke units,[25] many were unable to utilise their stroke unit's full potential. As observed by Dwyer et al.,[26] hospitals without 'quarantined' stroke unit beds may be unable to offer specialist care to stroke patients at times when there is demand for beds from other medical specialties. Such hospitals may benefit from using clinical coordinators to facilitate organisational change, as recommended by Cadilhac and colleagues.[27]

It should be noted that during the study period only 45% of patients located in Australia's 'regional' areas received treatment in a stroke unit, and only 3.3% of all stroke unit beds were located in regional areas.[28,29] Taken together, these statistics indicate that access to stroke units within rural hospitals participating in the AuSCR was markedly better than the national average. Given that there is a well-established link between stroke unit admission and access to key aspects of acute stroke care,[30] future efforts should focus on increasing the number of stroke units within Australia's regional areas, and improving access to existing stroke units. Adherence rates in the current study were, for the most part, representative of that of more recent stroke care audits in Australia.[31,32] The main exception was in rates of care plan provision; on average 53% of patients in the current study received this form of care, which was substantially lower than that of AuSCR data from 2018 (69%)[32] and data from the Stroke Foundation's 2019 Acute Audit (65%).[31]

Consistent with other studies, rural patients remained less likely than urban patients to be administered thrombolysis. The provision of thrombolysis is known to be influenced by a host of patient, clinician and system-related factors.[33] Of these factors, patients' distance to hospitals, accessing brain imaging after-hours, and obtaining specialist input are among the most pertinent issues encountered by clinicians providing thrombolysis in rural areas.[34-36] Rural-based clinicians in the Australian state of Victoria have been able to obtain specialist input and improve thrombolysis rates through the use of a telemedicine program.[37] Such a system was implemented in the state of Victoria for a small part of the study period,[37] and as such, may have influenced adherence rates in this group of hospitals. The use of telemedicine technology in all regional areas of the country is urgently needed in order to increase rates of thrombolysis administration.[38]

We did not observe differences by location in rates of prescription for antihypertensive medications at hospital discharge. As has been noted previously,[39] this may reflect the fact that the management of patients' blood pressure for primary or secondary prevention is not necessarily specific to stroke, and does not require any additional resources. In any case, the rates of prescription for antihypertensive medications at discharge from both regions were substantially less than expected based on previous AuSCR data, indicating that more work needs to be done to improve this aspect of evidence-based care.[40]

Despite marked differences in access to stroke unit care and thrombolysis, we did not observe any regional differences in rates of survival at up to 180 days post-stroke. This may be because access to acute stroke care, when considered in its entirety, was reasonably comparable between the study's urban and rural hospitals. This notion is supported by the fact that the study's rural hospitals, by virtue of their participation in the registry, are likely to

be highly motivated to monitor and improve their provision of stroke care, and perhaps are better resourced than other rural sites. Furthermore, there is evidence that within the state of Queensland (online supplement 2) patients in rural hospitals were provided evidence-based therapies more often than those in urban hospitals. These differences warrant further research.

In relation to HRQoL, we observed that with the exception of the pain/discomfort domain, there were no significant regional differences in any of the EQ-5D domains or VAS scores. These findings stand in contrast to multiple surveys conducted by the Australian government, in which rural residents had an overall lower self-reported health status.[41,42] The disparity between regions in terms of self-reported pain/discomfort may point towards regional differences in attitudes towards pain management. Indeed, literature on cancer patients in Australia has highlighted that a culture of stoicism and self-reliance within rural areas can make individuals less likely to report symptoms of pain[43] and delay seeking medical assistance.[44] There are other demographic factors which may partially explain this finding. For instance, previous researchers using the AuSCR data have found that patients with stroke requiring an interpreter are more likely to report symptoms of pain.[45] Given that urban patients in this study were far less likely to have been born in Australia (i.e. 59.7% vs 77%), the impact of the respondents' English-speaking ability on our findings cannot be discounted. Previous research using the AuSCR data has also highlighted that, other factors remaining equal, younger people from a lower SES are more likely to report symptoms of anxiety/depression.[46] We also found that rural patients had a significantly higher perceived health status than urban patients (70 vs 68 via VAS); however, it is unlikely that this difference represents a clinically relevant finding.[47]

Our study design and data have several limitations. Firstly, we report data only up to 2015. As with clinical quality registries internationally[48], there is a delay in creating aggregate

national samples from local sites due to data sharing, ethics and cleaning delays. Ongoing reporting of the AuSCR data to continue to monitor quality of care and outcomes for patients treated in urban and rural locations will ensure continued monitoring of this issue. Specific to this comparison, we acknowledge that the distribution of urban and rural patients in this study (71% vs 29%) may not reflect that of the broader Australian hospital population, which recently stood at 64% and 36%, respectively.[49] We also did not use any data in relation to participants' residential addresses. It is therefore possible that some individuals who were admitted to urban hospitals resided in rural areas, and vice versa. A further limitation is that our HRQoL data did not factor in patients' health prior to their stroke, meaning it is possible that some individuals' HRQoL deficits may relate to pre-existing conditions. Lastly, although we used patients' baseline walking ability as a validated measure of stroke severity,[21] the study may have benefited from the use of a more recognised scale, such as the NIHSS. Despite these limitations, our study is the first of its kind in Australia to comprehensively examine urban-rural differences in access to acute stroke care and the associated patient outcomes. To the best of the authors' knowledge, it is also among the first in the world to report on urban-rural differences in patients' quality of life post-stroke.

Conclusions

This is the largest study to date examining geographic disparities in processes of stroke care, and providing a benchmark for the development and testing of interventions that may have the potential to reduce the differences between rural and urban patients with acute stroke. Interestingly, while we identified disparities in processes of care, we did not observe any association between geographic region and patient outcomes in terms of mortality or HRQoL. There are clear opportunities to better understand why the impact of these process of care variables on stroke outcomes are more pronounced in urban areas. Our findings underscore

the importance of understanding how geographical area influences HRQoL and, in turn, how population disparities (such as life expectancy, income, and indigenous status) across geographical areas may contribute to these differences; continued efforts to determine the impact of stroke care post-discharge are important. Future work in this field should also focus on redressing the resourcing disparities, in particular increasing the number of rural hospitals which meet the minimum criteria for stroke unit care.

Declaration of competing interests

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Contributorship statement

HC, MD, GP, SG, KMF, KF and DC contributed to the study design and concept. JK and DC contributed towards the statistical analyses. HTP, HC, LW, RW, FR, and LA participated in the manuscript preparation, editing and revision and agreed upon the final version of the paper. NL contributed to the interpretation of results and was heavily involved in the final preparation of the paper.

Data sharing statement: contact can be made with the corresponding author for queries relating to unpublished data.

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Online Supplement 2 – Queensland Specific Care Processes

Care Process	Urban *n* (%)	Rural *n* (%)	p-value
Mobilised during admission	2,876 (69.3)	1,950 (80.1)	<0.001
Swallow screen or assessment	4,952 (74.2)	3,676 (83.5)	<0.001
Aspirin within 48h, if ischaemic	3,393 (68.2)	2,843 (75.8)	<0.001
Discharged on antithrombotic medication, if ischaemic	3,823 (80.1)	2,694 (86.7)	<0.001

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

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	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
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	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7-8
		(*e*) Describe any sensitivity analyses	NA
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	8
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	-
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	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11
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	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-14
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	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	2

*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.