Regional Differences in Acute Stroke Care and Patient Outcomes

by

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DECLARATION OF ORIGINALITY

This thesis contains no material which has been accepted for a degree or diploma by the University or any other institution, except by way of background information and duly acknowledged in the thesis, and to the best of my knowledge and belief no material previously published or written by another person except where due acknowledgement is made in the text of the thesis, nor does the thesis contain any material that infringes copyright.

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STATEMENT OF ETHICAL CONDUCT

The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University. The research conducted as part of the DMR study described in chapter 3 was approved by the Tasmanian Health and Medical Human Research Ethics Committee (reference H0016053). The research conducted as part of the qualitative study described in chapter 4 was approved by the Tasmanian Health and Medical Human Research Ethics Committee (reference H0017665). The research conducted using data from the Australian Stroke Clinical Registry (AuSCR; Chapter 5) was approved by the Tasmanian Health and Medical Human Research Ethics Committee (reference H0017787. My study proposal was also approved by the AuSCR Research Task Group and its Management Committee in March 2019. Ethical approval was obtained from all participating hospitals in AuSCR and from the Australian Institute of Health and Welfare to conduct data linkage to the National Death Index.

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LIST OF PUBLICATIONS

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LIST OF ABBREVIATIONS

ABS	Australian Bureau of Statistics
ACSQHC	Australian Commission on Safety and Quality in Health Care
AF	Atrial Fibrillation
AIHW	Australian Institute of Health and Welfare
APC NMDS	Admitted Patient Care National Minimum Data Set
ARIA+	Accessibility/Remoteness Index for Australia
ASA	American Stroke Association
ASGC-RA	Australian Standard Geographical Classification Remoteness Area
ASGS	Australian Statistical Geography Standard
ASU	Acute Stroke Unit
AuSCR	Australian Stroke Clinical Registry
CAH	Critical Access Hospital
CI	Confidence Interval
CNC	Clinical Nurse Consultant
COREQ	Consolidated Criteria for Reporting Qualitative Research
CPSS	Cincinnati Prehospital Stroke Scale
CSC	Comprehensive Stroke Centre
CT	Computed Tomography
DALY	Disability-adjusted Life Year
DMR	Digital Medical Record
DVT	Deep Vein Thrombosis
ED	Emergency Department
EMS	Emergency Medical Service
EQ-5D-3L	EuroQoL-5 dimension-3 level
FAST	Face, Arms, Speech, Time test
FIM	Functional Independence Measure
GP	General Practitioner

GWTG-S	Get With The Guidelines - Stroke
HCS	HealthCare Software
HDU	High Dependency Unit
HRQoL	Health-related Quality of Life
ICD-10-AM	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification
ICU	Intensive Care Unit
IRSAD	Index of Relative Socio-economic Advantage and Disadvantage
LGH	Launceston General Hospital
MCH	Mersey Community Hospital
MMM	Modified Monash Model
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
MSA	Metropolitan Statistical Area
MSU	Mobile Stroke Unit
NHMRC	National Health and Medical Research Council
NIHSS	National Institutes of Health Stroke Scale
NUTS3	Nomenclature of Territorial Units for Statistics - Level 3
NWRH	North West Regional Hospital
OR	Odds Ratio
OT	Occupational Therapy
PAR	Population-attributable risk
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses
PROM	Patient-reported Outcome Measure
PROSPERO	International PROSPEective Register Of systematic reviews
PSC	Primary Stroke Centre
PT	Physiotherapy
RA	Remoteness Area
RCT	Randomised Controlled Trial

REGARDS	REasons for Geographic And Racial Differences in Stroke
RHH	Royal Hobart Hospital
ROSIER	Recognition of Stroke in the Emergency Room
RUCA	Rural-Urban Commuting Area
SDAC	Survey of Disability, Ageing and Carers
SES	Socioeconomic Status
StOP	Stroke Outreach Program
SU	Stroke Unit
THS	Tasmanian Health Service
TIA	Transient Ischaemic Attack
TOAST	Trial of ORG 10172 in Acute Stroke Treatment Classification System
TPA	Tissue Plasminogen Activator
USA	United States of America
VAS	Visual Analogue Scale
VST	Victorian Stroke Telemedicine
VTE	Venous Thromboembolism
WHO	World Health Organization

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ABSTRACT

Stroke continues to place a large burden on society, ranking as the third leading cause of death in Australia, and accounting for around 7% of all deaths in the year 2017. The burden of stroke has considerably reduced over time, however, which has been partially attributed to advances made in the field of acute stroke care. Regrettably, such advances (e.g. the advent of acute stroke units, thrombolysis) have not been uniformly distributed throughout our society. Indeed, there is some evidence to suggest that rural areas have comparatively poor access to such interventions. It remains unclear, however, as to what the extent of these care disparities are, and what impact they may be having on patient outcomes. The purpose of this body of work was to characterise and contrast the care provided to, and outcomes of, people with stroke across geographical settings (e.g. with varying degrees of rurality). Doing so will indicate whether patients' hospital care and outcomes contribute to wider geographical disparities in health. Recommendations produced by this thesis will also assist clinicians and policymakers to improve the delivery of stroke services in both urban and rural settings.

In order to address these objectives, a systematic review was conducted as a way of characterising the existing body of literature. Several databases, including CINAHL, PubMed and Scopus were systematically searched for published and unpublished literature until 9th December 2017. Studies were included if they compared the acute care provided to, or outcomes of, patients hospitalised for stroke in urban versus rural settings. A total of 28 studies were included in the review (16 on care, 12 on outcomes). This review showed that with few exceptions, studies addressing the provision of care suggested that rural patients have less access to most aspects of acute stroke care. At the same time, studies reporting urban-rural differences in patient outcomes were inconsistent in their findings.

Capitalising on a number of gaps identified in the systematic review, a study was conducted to describe the regional differences in acute stroke care and outcomes within the

Australian state of Tasmania. This entailed a retrospective case note audit of 395 acute stroke cases from all four of Tasmania's major public hospitals. Sixteen care processes were recorded, which covered time-critical treatment, allied health interventions, and secondary prevention. Outcome measures were assessed using 30-day mortality and discharge destination, both of which were analysed for differences between urban and rural hospitals using logistic regression models. Results of the audit indicated that no patients in rural hospitals were administered thrombolysis, and that these hospitals also did not have acute stroke units. With few exceptions, patients' access to the remaining care indicators was comparable between regions. After adjusting for confounders, there were no significant differences between regions in terms of 30-day mortality (OR = 0.99, 95% C.I. 0.46-2.18) or discharge destination (OR = 1.24, 95% C.I. 0.81-1.91). Overall, the findings from this study indicated that with the exception of acute stroke unit care and thrombolysis, stroke care within Tasmania's urban and rural hospitals was broadly similar. No significant differences were found between regions in terms of patient outcomes.

Upon completion of the medical record audit, the primary researcher had a set of quantitative findings, but little understanding of how the experiences of clinicians delivering care differed between regions. In order to address this, a sequential-explanatory approach was used to understand the local barriers and facilitators to providing care in urban and rural settings. A total of two focus groups and five individual interviews were conducted with Tasmanian clinicians from the subject hospitals (one urban, two rural) used in the initial study. An inductive process of thematic analysis was then used to identify themes and subthemes across the data set. Four major themes were isolated from analysis of the data: systemic issues, clinician factors, additional support, and patient factors. Overall, the findings suggested that acute stroke care within the study's urban hospital was structured and comprehensive, aided by the hospital's acute stroke unit and specialist nursing support. In

contrast, care provided in the study's rural hospitals was somewhat less sophisticated, and often constrained by an absence of infrastructure or poor access to existing resources.

The main limitation of the initial Tasmanian-specific medical record audit was its relatively small sample from only four hospitals. In order to address this limitation, the primary researcher collaborated with the Australian Stroke Clinical Registry (AuSCR) on a study using data from this registry. This study utilised data submitted by 50 hospitals (25 urban, 25 rural) during the period January 2010 to December 2015. Data in relation to four care processes were analysed, and patient outcomes were assessed using mortality at intervals of 7, 30, 90 and 180 days. Data in relation to participants' health-related quality of life (HRQoL) was also collected at follow up using the EuroQoL-5 dimension-3 level (EQ-5D-3L) instrument, while an overall measure of perceived health was obtained using the visual analog scale (VAS). 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. In conclusion, rural access to recommended components of acute stroke care was comparatively poorer; however, as was the case in the initial study, this did not appear to impact health outcomes at approximately 6 months.

This thesis demonstrates that when compared to hospitals located in urban areas, those in rural areas typically provided a basic form of acute stroke care, with reduced access to stroke unit care and thrombolysis. An increased use of telestroke, coupled with a more efficient use of existing resources would greatly help to improve the state of stroke care in rural areas. No regional differences in patient outcomes were reported in either of the

quantitative studies. This finding was consistent with previous research; however, it may have been influenced by methodological limitations, particularly relating to statistical power to detect differences in outcomes. Similarities in patient outcomes between regions should not be taken as that both regions have access to a commensurate level of care, when in fact, the level of care differs markedly between regions. The urban-rural disparity in stroke care must be addressed now, while it is primarily an issue of thrombolysis and stroke unit care, as the disparity can only be expected to grow with the advent of new therapies.

1. CHAPTER ONE: Introduction

Cardiovascular disease is a leading cause of disease burden in Australia, accounting for over one million hospitalisations during 2016-17 (1). Within the broader category of cardiovascular disease is stroke, currently the third leading cause of death in Australia (2) and a condition which disproportionately affects individuals from rural and remote areas (3).

1.1 An Overview of Stroke

The World Health Organization (WHO) defines stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin" (4). In more simple terms, stroke is a form of cerebrovascular disease in which the brain's blood supply is interrupted unexpectedly (5). Individuals who have suffered a stroke commonly experience a weakness or numbness in their extremities, difficulty speaking, and a loss of vision, among other symptoms (6). Stroke can be divided into cases where a blood vessel supplying the brain experiences a blockage (known as an ischaemic stroke or cerebral infarction) or a bleed (known as a haemorrhagic stroke) (7).

Ischaemic Stroke is defined by the American Stroke Association (ASA) as "an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction" (8). Ischaemic strokes account for around 80% of all stroke cases (9) and have an estimated 30-day mortality rate of around 14% (10). Ischaemic strokes are further classified into one of five categories, using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Classification System (11):

- Large artery atherosclerosis
- Cardioembolism
- Small vessel occlusion
- Stroke of other, unusual, determined aetiology
- Stroke of undetermined aetiology

Haemorrhagic Stroke can be further divided into cases of intracerebral haemorrhage (approx. 10-15% of cases) and subarachnoid haemorrhage (approx. 5% of cases) (9). Intracerebral haemorrhage is defined by the ASA as "a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma" (8). Subarachnoid haemorrhage differs from intracerebral haemorrhage in that it refers to bleeding into the subarachnoid space (8). Outcomes for individuals who have suffered a haemorrhagic stroke are considerably worse than that for ischaemic strokes, with intracerebral haemorrhage and subarachnoid haemorrhage being associated with 30-day mortality rates of 44% and 45%, respectively (12, 13).

Transient Ischaemic Attacks (TIAs) have been defined by the ASA as "brief episodes of neurological dysfunction resulting from focal cerebral ischemia not associated with permanent cerebral infarction" (14). Recognising TIAs is of great importance, as their occurrence is associated with an 8% increase in the risk of stroke at seven days and 17.3% at three months (15).

1.1.1 Diagnosing Stroke

Stroke is a clinical diagnosis, meaning that a diagnosis is initially formed based on the patient's presenting symptoms (16). Common symptoms of stroke include: motor impairments, sensory deficits, speech difficulties, hemianopia, dizziness, gait disturbance, convulsion, headache, and difficulty swallowing (17). Most facilities use computed tomography (CT) scans and magnetic resonance imaging (MRI) to distinguish between ischaemic and haemorrhagic strokes, and to determine the location and magnitude of the stroke (18).

1.1.2 Risk Factors for Stroke

An individual's risk profile for stroke is comprised of numerous genetic and lifestyle factors which may be modifiable or non-modifiable (19, 20). Of the non-modifiable risk factors, age

is perhaps the most often cited; on a global scale, the per 100,000 person-year incidence of stroke has been estimated to be 168.75 per in those aged under 75, and 3,113 for those aged 75 and over (21). There are also marked gender differences in the incidence of stroke; a pooled estimate derived from 44 different populations suggested that stroke was 33% more incident in males than in females (22). The INTERSTROKE study was a case-control study undertaken in 22 countries between 2007 and 2010, with the aim of establishing an association between stroke with selected risk factors (23). The findings of INTERSTROKE, which were replicated in 2016 (24), indicated that ten risk factors were associated with 90% of the risk of stroke of any subtype. These factors were hypertension, current tobacco use, obesity (estimated by waist-to hip-ratio measurements), poor diet, physical inactivity, diabetes mellitus, excessive alcohol intake, psychosocial factors (psychosocial stress and depression), cardiac causes of stroke (e.g. atrial fibrillation) and high cholesterol. Of these factors, hypertension, current tobacco use, obesity, poor diet and physical inactivity alone accounted for in excess of 80% of the risk of all stroke (Table 1) (23).

Table 1. Risk of stroke associated with risk factors (23)

Risk Factor	OR†	99% CI	PAR*	99% CI
History of hypertension	2.64	(2.26–3.08)	34.6%	(30.4–39.1)
Current tobacco use	2.09	(1.75–2.51)	18.9%	(15.3–23.1)
Obesity	1.65	(1.36–1.99)	26.5%	(18.8–36.0)
Poor Diet	1.35	(1.11–1.64)	18.8%	(11.2–29.7)
Regular physical activity	0.69	(0.53–0.90)	28.5%	(14.5–48.5)
Diabetes mellitus	1.36	(1.10–1.68)	5.00%	(2.6–9.5)
Alcohol intake (30+ drinks/month)	1.51	(1.18–1.92)	3.8%	(0.9–14.4)
Psychosocial factors	-	-	-	-
Psychosocial stress	1.30	(1.06–1.60)	4.6%	(2.1–9.6)
Depression	1.35	(1.10–1.66)	5.2%	(2.7–9.8)
Cardiac causes**	2.38	(1.77–3.20)	6.7%	(4.8–9.1)
High cholesterol	1.89	(1.49–2.40)	24.9%	(15.7–37.1)

†Odds ratio *Population-attributable risk - the independent contribution of each risk factor to the burden of stroke worldwide **Includes atrial fibrillation, or flutter, previous myocardial infarction, rheumatic valve disease, or prosthetic heart valve. ¶For the protective factor of physical activity, population-attributable risks are provided for the group without this factor

1.2 Defining Rurality

'Rurality' is a term with a number of definitions and methods of measurement (25). In broad terms, 'rural' refers to geographic areas which typically have smaller populations in more isolated settings, or with limited availability of services (26). It should be noted however, that in Australia, the term 'regional' is often used by government sources to describe areas which would typically be regarded as 'rural'. This is a departure from the traditional use of the term 'regional', that refers to something "of, relating to, or characteristic of a region or regions" (27). The way in which rurality is defined has significant implications for planning, policy development and the allocation of resources.

There are multiple geographic classification systems currently in use within Australia, with no universally accepted system (28). The current thesis uses two of these systems to delineate between 'urban' and 'rural' areas of Australia: the Australian Standard Geographical Classification Remoteness Area (ASGC-RA) and the Modified Monash Model (MMM). The ASGC-RA system was developed by the Australian Bureau of Statistics (ABS) in 2001 as a means of allowing quantitative comparisons between 'city' and 'country' areas of Australia (29). Under this system, locations are classified into one of five 'Remoteness Areas' (RAs), namely: Major Cities; Inner Regional; Outer Regional; Remote; and Very Remote. RAs are arranged according to the physical distance of a location from the nearest urban centre (access to goods and services) without taking the area's population into account (30). This results in a series of anomalous classifications. For example, the town of Urana (population 1,500) and city of Townsville (population 170,000) were allocated to the same category, due to their distance from the major cities of Melbourne and Brisbane, respectively (31). The ASGC-RA system remained in use until 2011, when it was superseded by the Australian Statistical Geography Standard (ASGS), from which the MMM is derived (32).

The MMM was developed by Australia's Department of Health in 2015 in order to create a more targeted set of incentives for doctors to relocate to rural areas (33). The MMM achieves this by taking the ASGS framework and further differentiating rural areas based on population, assigning categories ranging from MM1 (major cities) to MM7 (very remote areas) (33). A map of the ASGC Remoteness Areas of Australia, and an overlay of the MMM in the state of Tasmania are shown below in Figures 1 and 2, respectively.

Figure 1. Australian Standard Geographical Classification Remoteness Areas (29)

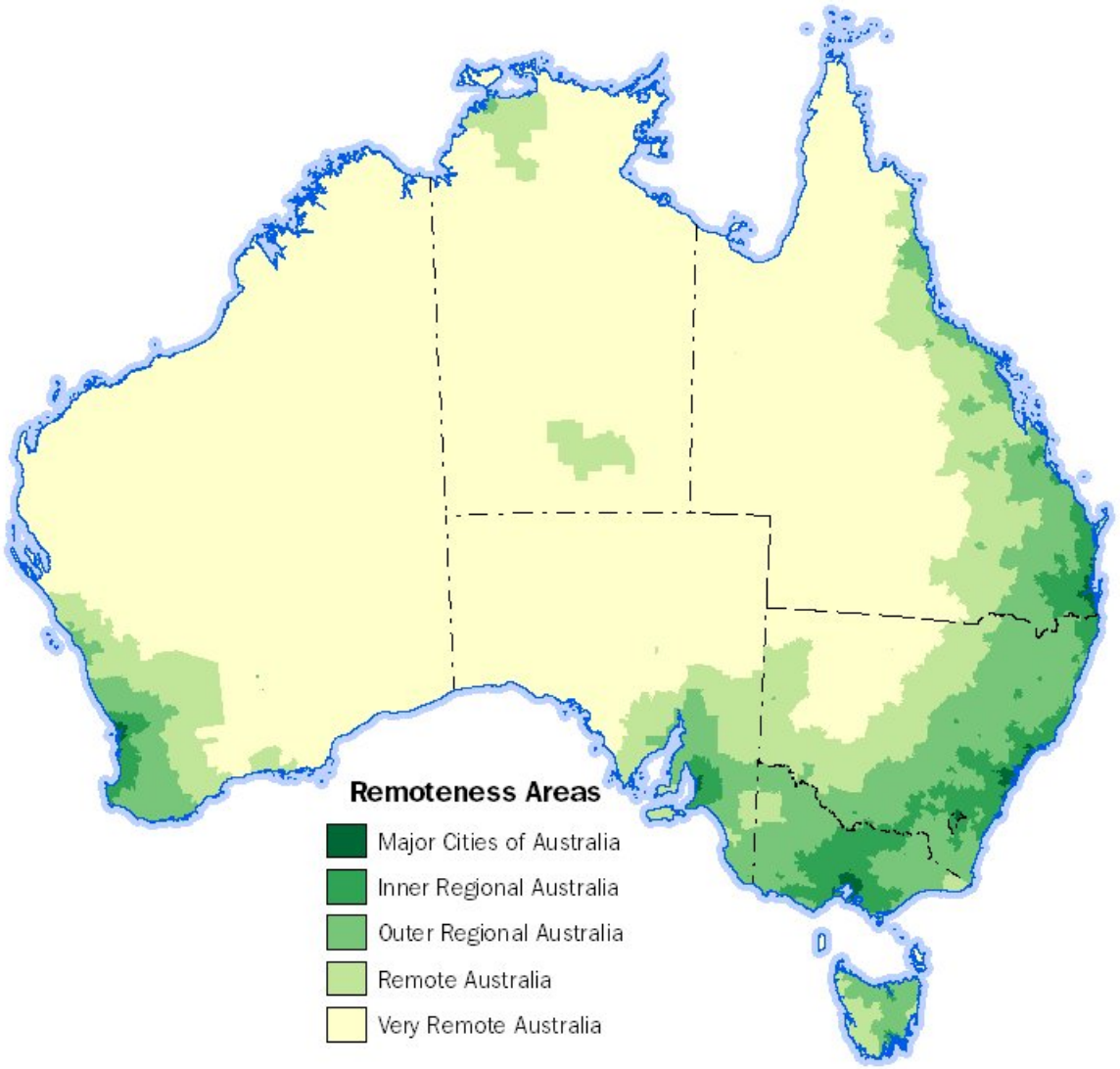
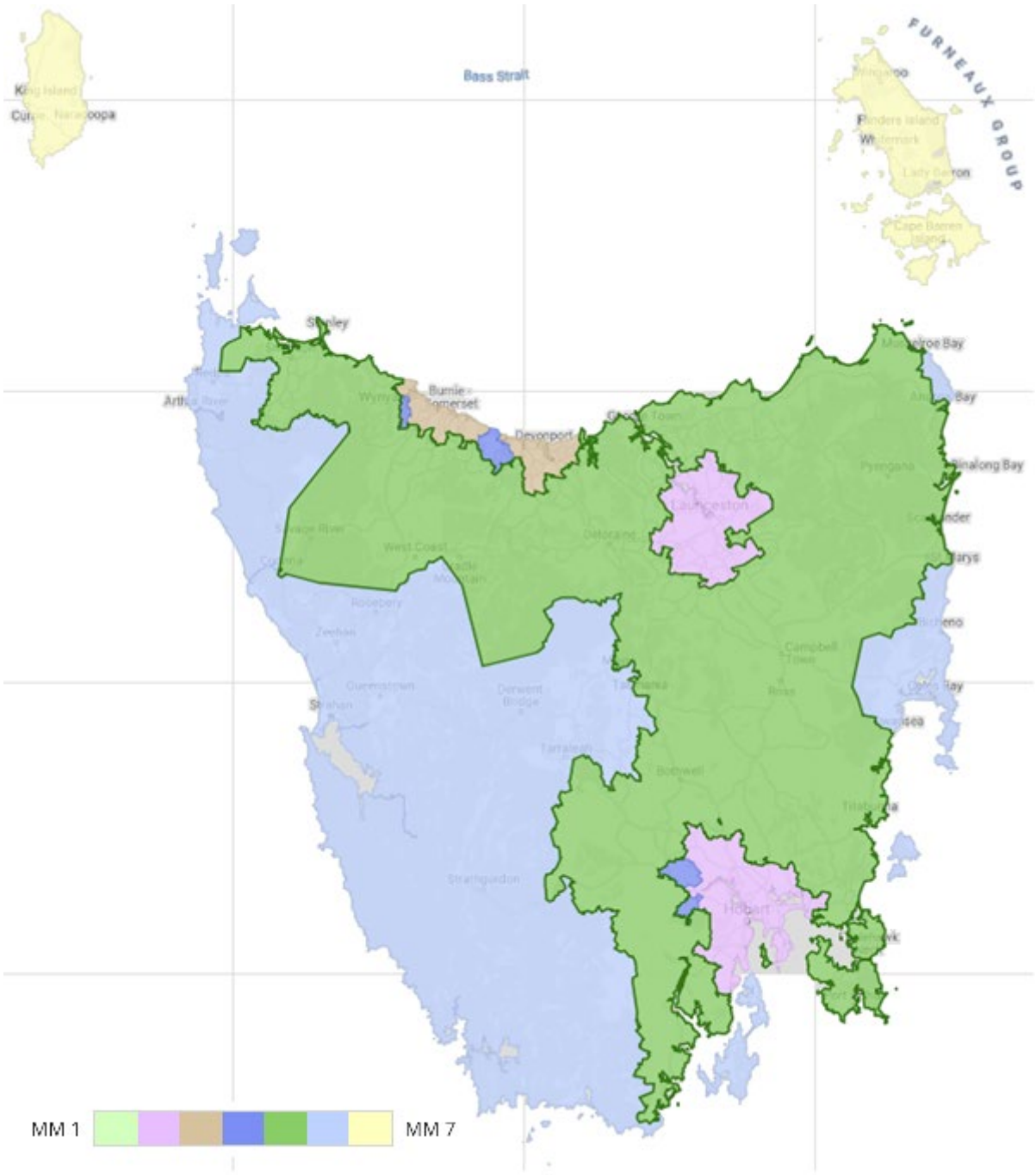


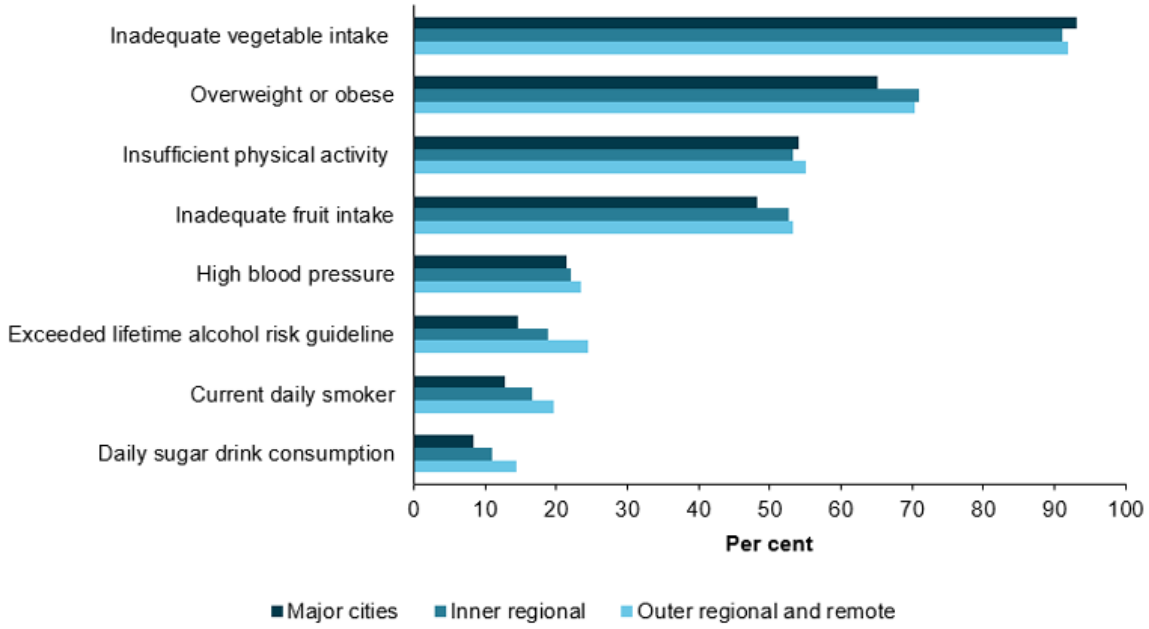
Figure 2. Map of Tasmania - Modified Monash Model Overlay (34)



1.3 Regional Differences in Health Status

Individuals living outside of metropolitan areas often have comparatively poor health outcomes. A report from the Australian Institute of Health and Welfare (AIHW) (35) suggested that, when compared to individuals who resided in major cities, those in 'regional' areas were more likely to have several of the stroke factors identified by INTERSTROKE, as shown in Figure 3 below.

Figure 3. Prevalence of health risk factors, by area of remoteness, 2017–18 (35)



1.4 The Burden of Stroke in Australia

1.4.1 Stroke Incidence and Prevalence

As of 2019, Australia does not have a nationwide system in place to monitor the incidence of stroke. As an alternative, estimates of stroke incidence are often extrapolated from population-specific incidence studies (36), or through the use of algorithms applied to administrative data (37). Using the latter method, the AIHW estimated that there were around 37,800 stroke events during the year 2016, equating to more than 100 events each day (1). The prevalence of stroke in Australia is primarily estimated using self-reported data from the

Australian Bureau of Statistics' *Survey of Disability, Ageing and Carers* (SDAC) (5). An estimate based on the 2015 SDAC indicated that 1.7% of the population had experienced a stroke at some point during their lives (1).

1.5 Regional Differences in Stroke Epidemiology

A recent report commissioned by the Stroke Foundation suggested that stroke incidence rates in 'regional' areas of Australia are 19% higher than that of metropolitan areas (3). As with the incidence of stroke, there are also geographic differences in the prevalence of stroke. A 2017 report by the Stroke Foundation suggested that stroke is 19% more prevalent in 'regional' areas when compared with metropolitan areas, equating to an additional 345 cases for every 100,000 population (3).

1.5.1 Morbidity and Mortality Resulting from Stroke

In Australia, disability resulting from stroke is monitored through the SDAC, with additional analyses being conducted intermittently by state health authorities (38) and in population-specific academic studies (39, 40). Data obtained from the 2015 SDAC identified that of 390,000 individuals who had experienced a stroke, around 40% were currently living with a disability (41). Findings from a previous SDAC showed that the three most common forms of disability were a 'restriction in physical activities', 'incomplete use of feet or legs' and an 'incomplete use of arms or fingers', all of which were reported by more than 35% of survey respondents (6). In terms of disability-adjusted life years (DALYs), the AIHW ranks stroke as the fourth most burdensome condition in Australians aged over 65, sitting behind coronary heart disease, dementia and Chronic Obstructive Pulmonary Disease (42).

In terms of mortality, stroke consistently ranks as one of the top three causes of death among Australians when grouped in the broader category of cerebrovascular disease (43). This is notable, as approximately 78% of deaths within cerebrovascular disease are

attributable to stroke (44). Recent estimates suggest that the stroke mortality rate for individuals in metropolitan areas is 47 per 100,000, while the same figure for rural areas was 19% higher, at 56 per 100,000 (3). A similar pattern can be found in rates of hospitalisation, where rates increase in line with patients' remoteness (as shown Figure 4 below).

Figure 4. Hospitalisations for stroke per 100,000 population, by remoteness (5)

1.5.2 Economic Cost of Stroke

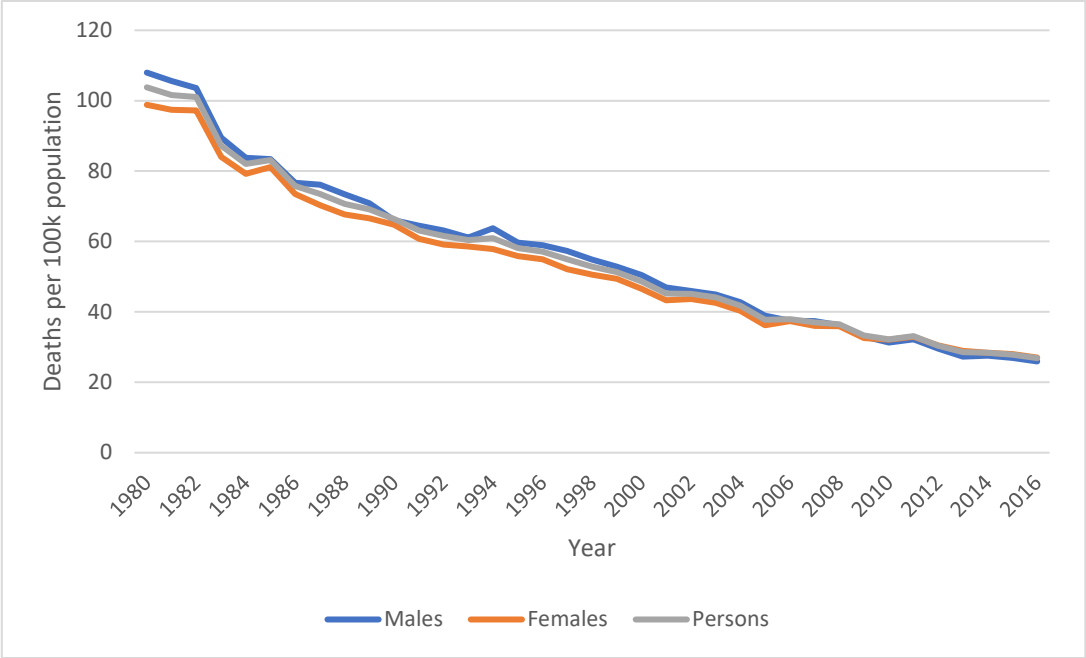
A report commissioned by Australia's Stroke Foundation estimated that the total financial cost associated with stroke in Australia stood at $5 billion during 2012 (45). Of this amount, $3 billion was attributed to a loss of productivity, while health and carer costs were estimated to be $881 million and $222 million, respectively. Putting these financial costs aside, the report noted that the greatest overall cost of stroke was attributed to the loss of healthy life. In terms of DALYs, the total burden of disease cost for stroke in Australia during 2012 was estimated to be $49.3 billion (45).

1.5.3 Temporal Trends in the Burden of Stroke

The incidence of stroke in Australia is an area in which considerable improvements have been made over time. Between 1997 and 2016, the national stroke incidence rate dropped from 186 to 132 per 100,000 population, representing a 29% reduction (1, 5). Age-standardised rates of stroke mortality have also markedly declined over time. From 1980 to

2016, the number of deaths attributed to stroke fell by three-quarters (74%), as shown in Figure 5 below) (41).

Figure 5. Trends in stroke deaths in Australia, by sex, 1980–2016 (41)



As can be expected, the trend in stroke prevalence is somewhat less positive, with the last four iterations of the SDAC all estimating that prevalence rates have remained stable at around 1.5% to 2% of the population (46). The proportion of individuals living with a disability resulting from stroke has also remained static over time, decreasing slightly from 45% to 39% between 1998 and 2012 (46). Improvements in stroke patient outcomes have been attributed to reductions in modifiable risk factors, greater usage of pharmaceutical treatments, and increasingly specialised hospital care, among other factors (5, 47).

1.6 The Tasmanian Context

Two of the studies (i.e. Chapters three and four) contained in this thesis relate to the provision of stroke care and patient outcomes within the Australian state of Tasmania. Tasmania is Australia's only island state, and as of September 2019, had an estimated population of 535,000 (48). The median age of Tasmania's population is 42.3 years, which is the highest of all states and territories in Australia (49). Tasmania also has rates of hypertension, high

cholesterol, and physical inactivity which are above national averages (3). Given its heightened risk profile, it follows logically that the burden of stroke in Tasmania is also disproportionately high. As of 2017, Tasmania's per capita rates of stroke incidence and mortality were 13% and 10% higher than national figures.

1.7 Models of Acute Stroke Care

Stroke care can be viewed through the prism of Donabedian's structure-process-outcome (SPO) model (50). Developed by physician Avedis Donabedian in 1966 (51), the model has had a profound influence on how quality in health care is measured, and is still regarded as a dominant paradigm within its field (52, 53). According to the model (illustrated in Figure 6 below) the elements comprising 'structure' influence the degree to which 'processes' are delivered, while processes, in turn, are said to influence patient outcomes. While the model was not designed to access quality in any specific field (51), it has, over time, been validated in a host of acute settings, including trauma care (54) and bariatric surgery (55) among others (56). Donabedian's model is illustrated in the context of stroke care in Figure 7 (overleaf) from Chimatiro and Rhoda (57).

Figure 6. Donabedian's SPO model (58)

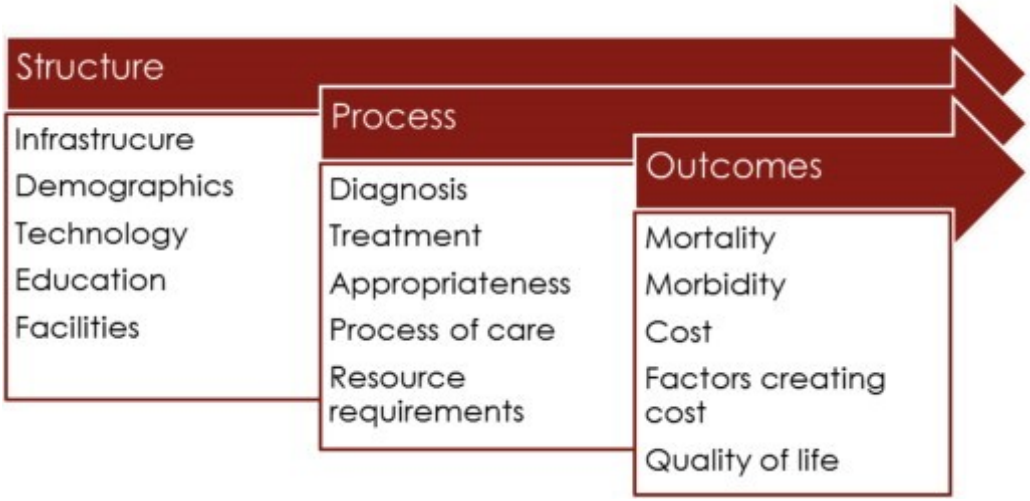
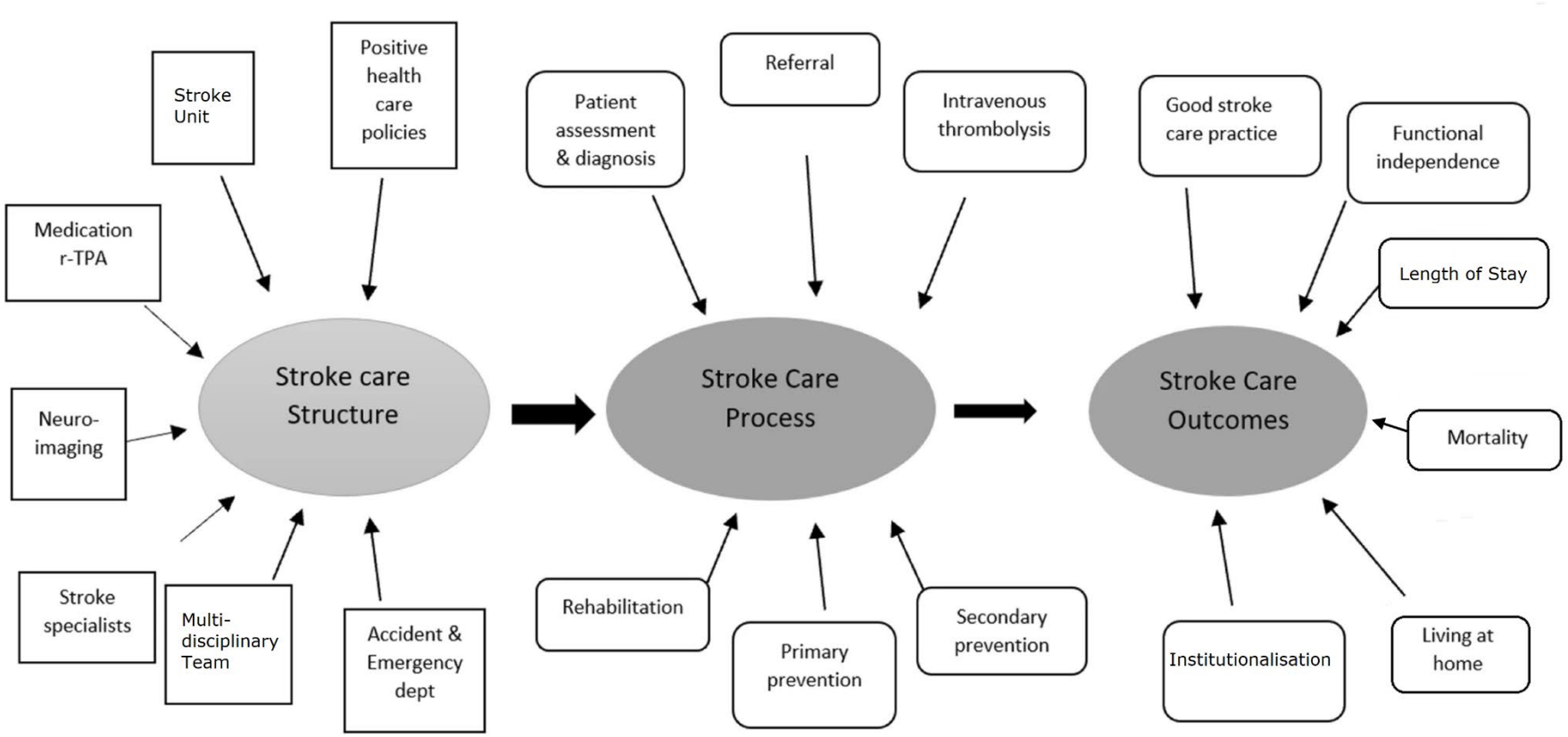


Figure 7. Donabedian's SPO model illustrated in the context of stroke care (57)



The ‘structure’ component of acute stroke care in Australia is described in the *National Acute Stroke Services Framework*. The *Framework* was first developed in 2002 by Australia’s Stroke Foundation with the aim of guiding “the establishment and evaluation of stroke services to support equitable delivery of best practice care” (59). The most recent iteration of this document delineates between three different categories of hospital: comprehensive stroke centres (CSCs), primary stroke centres (PSCs) and general hospitals (59). The characteristics which separate these three types of hospital are numerous and varied (Table 2). In essence, however, CSCs are located in large, tertiary care centres which see high volumes of stroke patients (e.g. in excess of 350 cases annually), while PSCs are expected in hospitals receiving over 75 stroke admissions annually (59). Hospitals receiving under 75 stroke admissions each year are unlikely to have enough demand for specialist services such as stroke units, clinicians with stroke expertise or advanced neuroimaging. As such, these ‘general hospitals’ are encouraged to transfer patients to larger, better equipped hospitals, or alternatively, to access specialist input via telestroke services (59).

1.7.1 Stroke Units

As noted within Table 2, CSCs and PSCs should be equipped with stroke units (SUs). Australia’s Stroke Foundation notes that SUs should have the following characteristics (39):

1. Dedicated hospital beds located within a geographically defined unit.
2. Multidisciplinary team care by staff with an interest in stroke and/or stroke rehabilitation. ‘Multidisciplinary’ in this instance refers to medical, nursing and allied health staff (including occupational therapists, physiotherapists, speech therapists).
3. Multidisciplinary team meetings, which occur at least once weekly.
4. Regular education of staff in matters pertaining to stroke care. This may be in the form of a stroke in-service program, and/or access to stroke conferences.

Table 2. Features of hospital stroke services (59)

Element of service	Comprehensive Stroke Centre	Primary Stroke Centre	General Hospital (in regional and rural settings where not bypassed)
Receive pre-notification and prepare to rapidly accept potential stroke patient from pre-hospital services	✓	✓	✓
Coordinated emergency department systems (includes use of validated screening tools; agreed triage categories; rapid imaging; rapid referral and involvement of stroke team, protocols for IV thrombolysis and ECR intervention/transfer)	✓ including code stroke activation and possible direct transport to CT	✓ including code stroke activation and possible direct transport to CT	✓ initial assessment and thrombolysis via telestroke followed by transfer
Stroke unit	✓	✓	×
Rapid access to onsite CT brain (24/7) including CT perfusion and aortic arch to cerebral vertex angiography	✓	✓	✓ plain CT ✓/× CTP/CTA highly preferable
Delivery of intravenous thrombolysis	✓24/7#	✓24/7#	✓ With telestroke support followed by transfer
On-site endovascular stroke therapy	✓24/7#	Optional¥	×
On-site neurosurgical services (e.g. for hemicraniectomy due to large middle cerebral artery infarcts)	✓	Optional¥	×
Ability to provide acute monitoring (telemetry and other physiological monitoring) for at least 72 hours	✓	✓	×
Acute stroke team	✓	✓	Optional
Dedicated stroke coordinator position	✓	✓	Optional
Dedicated medical lead	✓^	✓	×
Access to HDU / ICU (for complex patients)	✓	✓	×
Rapid (within 48 hours) Transient Ischaemic Attack (TIA) assessment clinics/services (including early access to carotid and advanced brain imaging)	✓	✓	initial assessment and referral
Use of telestroke services for acute assessment and treatment	✓ (providing advice)	Optional (if required for 24/7 service)	✓
Standardised processes that ensure ALL stroke patients are assessed for rehabilitation. This includes use of standardised tools to determine individual rehabilitation needs and goals (ideally within 48 hours of admission).	✓	✓	✓*
Coordination with rehabilitation service providers (this should include a standardised process, and/or a person, used to assess suitability for further rehabilitation).	✓	✓	Optional*
Routine involvement of patients and carers	✓	✓	✓
Routine use of guidelines, care plans and protocols	✓	✓	✓
Regular data collection and stroke specific quality improvement activities	✓	✓	Optional
Access and collaboration with other specialist services (cardiology, palliative care, vascular)	✓	Optional onsite	Referral

SUs are favoured over conventional ward care, as they have a demonstrable link with improved access to the specific processes of acute stroke care, which in turn is associated with improved patient outcomes (60, 61). Indeed, SU care is regarded as being the single most important intervention available to stroke patients (59). Regrettably, the findings of recent Stroke Foundation audits suggest that hospitals in Australia's rural areas are less likely to be equipped with SUs. For example, in 2017, 77% of urban patients and 47% of rural patients received stroke unit care, and in 2019 this disparity had widened to 79% and 35%, respectively (62, 63).

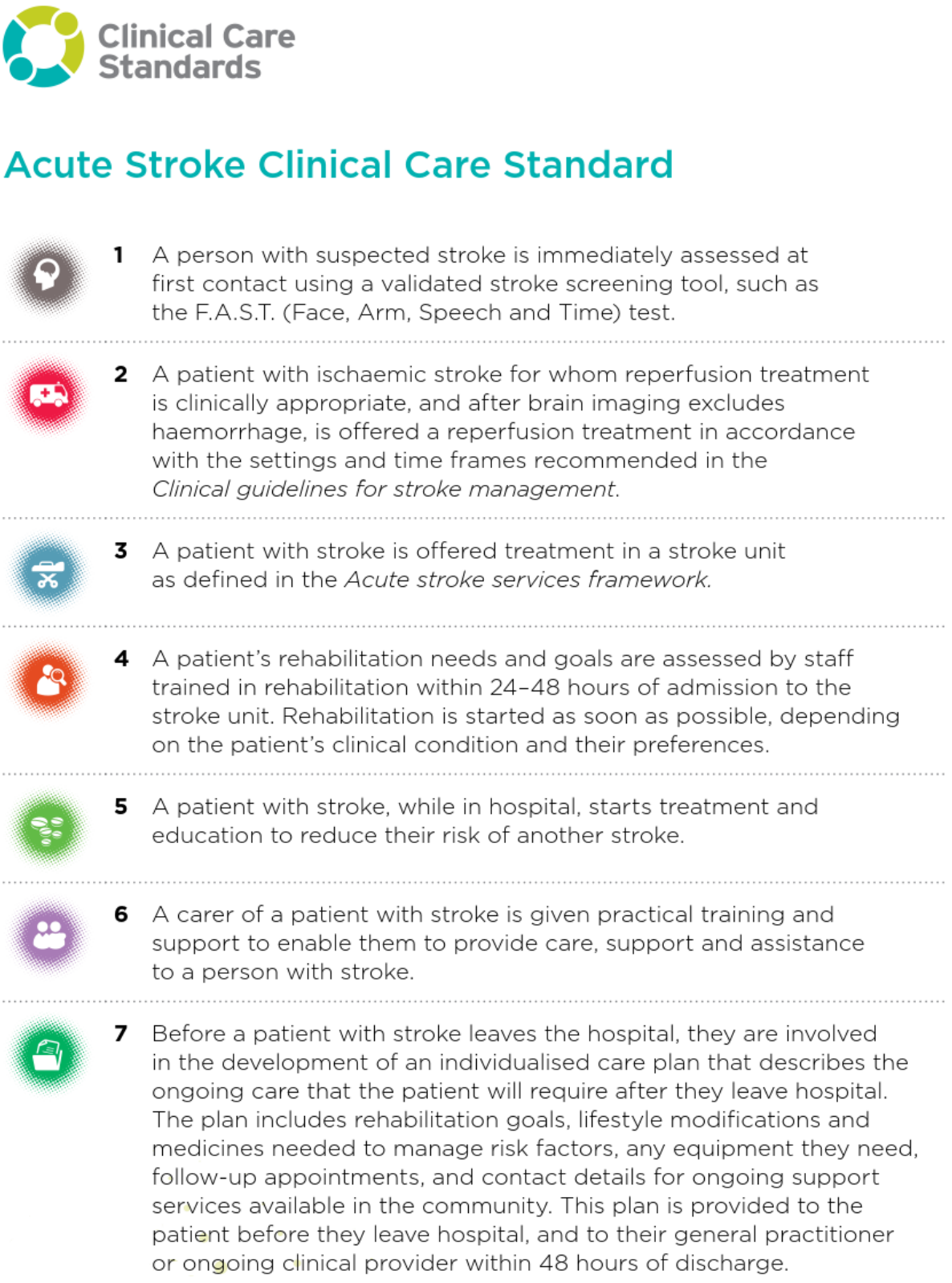
1.8 Acute Stroke Care

Referring once again to Donabedian's triad (50), the 'process' component of acute stroke care is embodied by numerous studies sets of guidelines which detail the gold standard of acute stroke care. In Australia, the Stroke Foundation's *Clinical Guidelines for Stroke Management* (herein referred to as the *Clinical Guidelines*) are the pre-eminent source of research-based evidence for acute stroke care. The *Clinical Guidelines* exist as a set of 'living guidelines' which are regularly updated with recommendations for and against a wide range of interventions (64).

1.9 Acute Stroke Clinical Care Standard

With the formation of the Australian Commission on Safety and Quality in Health Care (ACSQHC) in 2006, efforts were made to create a concise set of clinical guidelines for acute stroke. These guidelines, which would become known as the *Acute Stroke Clinical Care Standard*, detail the essential aspects of acute stroke care using the abovementioned *Clinical Guidelines* as their main source of evidence. The *Clinical Care Standard* is comprised of seven 'quality statements', each of which relate to a set of specific care processes (Figure 8).

Figure 8. Quality Statements of the ACSQHC Acute Stroke Clinical Care Standard (65)



1.9.1 Evidence Base for Clinical Care Standard Items

1.1.1.1 Quality statement 1 – Early assessment

- Assessment by ambulance services

The *Clinical Guidelines* (64) recommend that individuals with suspected stroke should be immediately assessed for stroke using a validated stroke screening tool. Several studies (66-68) have demonstrated that providing hospitals with early notification of suspected stroke patients reduces the time to administration for reperfusion therapies in eligible candidates.

- Assessment in the emergency department (ED)

The *Clinical Guidelines* (64) recommend that individuals with suspected stroke, who have been pre-notified to the hospital's stroke or ED team, should be assessed by these teams upon arrival to the hospital. Early assessment for stroke within the ED has been associated with improved thrombolysis rates (69, 70).

1.1.1.2 Quality statement 2 – Time-critical therapy

- Transport to a hospital able to provide thrombolysis

The *Clinical Guidelines* (64) recommend that individuals who have a confirmed diagnosis of ischaemic stroke, and who appear to be candidates for thrombolysis, should be transported via ambulance to a hospital capable of administering thrombolysis. One study (71) reported an association between ambulance crews' prioritisation of stroke patients and improved rates of thrombolysis administration.

- Thrombolysis in ischaemic stroke / Presentation and intravenous thrombolysis within 4.5 hours of symptom onset

The *Clinical Guidelines* (64) state that individuals with potentially disabling ischaemic strokes should be administered thrombolysis, unless contraindicated. Numerous studies have found an association between the provision of thrombolysis and a reduction in the odds of

death or dependency at 3-6 months post-stroke (72). Thrombolysis is most effective when administered within 4.5 hours of symptom onset (72).

- Thrombolysis within 60 minutes of hospital arrival / Time from onset of symptoms to thrombolysis

As mentioned above, the *Clinical Guidelines* (64) recommend the use of thrombolysis for ischaemic stroke patients. The findings of multiple clinical trials have indicated that the benefits of thrombolysis are most pronounced with earlier intervention (72).

1.1.1.3 Quality statement 3 – Stroke unit care

- Admission into a stroke unit

The *Clinical Guidelines* (64) regard stroke units as being "the single most important recommendation for improving stroke management". Numerous clinical trials have reported an association between stroke unit care and significant reductions in the odds of death or dependency (60).

- 90% of acute hospital admissions on a stroke unit

Whilst not featuring in the *Clinical Guidelines*, this indicator was adopted from the United Kingdom's National Health Service (73). This indicator complements the previous indicator by measuring the proportion of patients who spent the majority of their time in hospital on a stroke unit.

1.1.1.4 Quality statement 4 – Early rehabilitation

- Assessment for rehabilitation by a physiotherapist within 24–48 hours

The *Clinical Care Standard* (65) states that individuals admitted for stroke should be assessed by a physiotherapist within 24-48 hours of their presentation to hospital. The *Clinical Care Standard* (65) further notes that this early assessment is an important starting

point to the acute care management, rehabilitation, and discharge planning process, which should improve the appropriateness of the patient's ongoing management.

- Rehabilitation therapy within 48 hours of initial assessment / Treatment for a rehabilitation goal commencing during an acute hospital admission

This indicator measures the proportion of stroke patients who commence rehabilitation therapy within 48 hours of their initial assessment, and those who commence therapy at any point during their acute admission. Participation in active rehabilitation programs of this kind generally means that patients spend less time in bed and more time standing, walking and being active, which is itself associated with improved patient outcomes (60, 74, 75).

1.1.1.5 Quality statement 5 – Minimising risk of another stroke

- Discharge on statin, antihypertensive and antithrombotic medications (ischaemic stroke) or discharge on antihypertensive medication (haemorrhagic stroke)

The *Clinical Guidelines* (64) recommend that patients with either haemorrhagic or ischaemic stroke should be discharged on medication aimed at lowering their blood pressure. The findings of a meta-analysis of 10 randomised controlled trials (RCTs) (76) indicated that the use of blood pressure lowering agents was associated with a reduced likelihood of secondary stroke and cardiovascular events. For those with ischaemic stroke, the *Clinical Guidelines* (64) recommend that patients should be discharged on statin, antihypertensive and antithrombotic medications. Use of these medications has been found to be independently associated with a reduced risk of secondary stroke (76-78).

- Discharge on oral anticoagulants for atrial fibrillation

The *Clinical Guidelines* (64) recommend that stroke patients with comorbid atrial fibrillation should be prescribed an anticoagulant medication at discharge. A recent systematic review and meta-analysis of 16 RCTs (79) suggested that oral anticoagulants were more effective

than placebo and antiplatelet medications at reducing the risk of all forms of secondary stroke.

- Risk factor modification advice before leaving the hospital

The *Clinical Guidelines* (64) recommend stroke patients are given tailored advice and education about lifestyle modification and medications prior to being discharged from hospital. The findings of a Cochrane Review (80) suggested that providing such information was associated with significant improvements in patient and carer knowledge, and aspects of patient satisfaction.

1.1.1.6 Quality statement 6 – Carer training and support

- Carer support needs assessment and Carer Training

The *Clinical Guidelines* (64) recommend that carers of individuals who have experienced a stroke be given adequate training on how to provide ongoing care in the community. The findings of one RCT suggested that providing carers with such training was associated with reduced costs, caregiver burden and improved psychosocial outcomes in care givers and patients at one year (81).

1.1.1.7 Quality statement 7 – Transition from hospital care

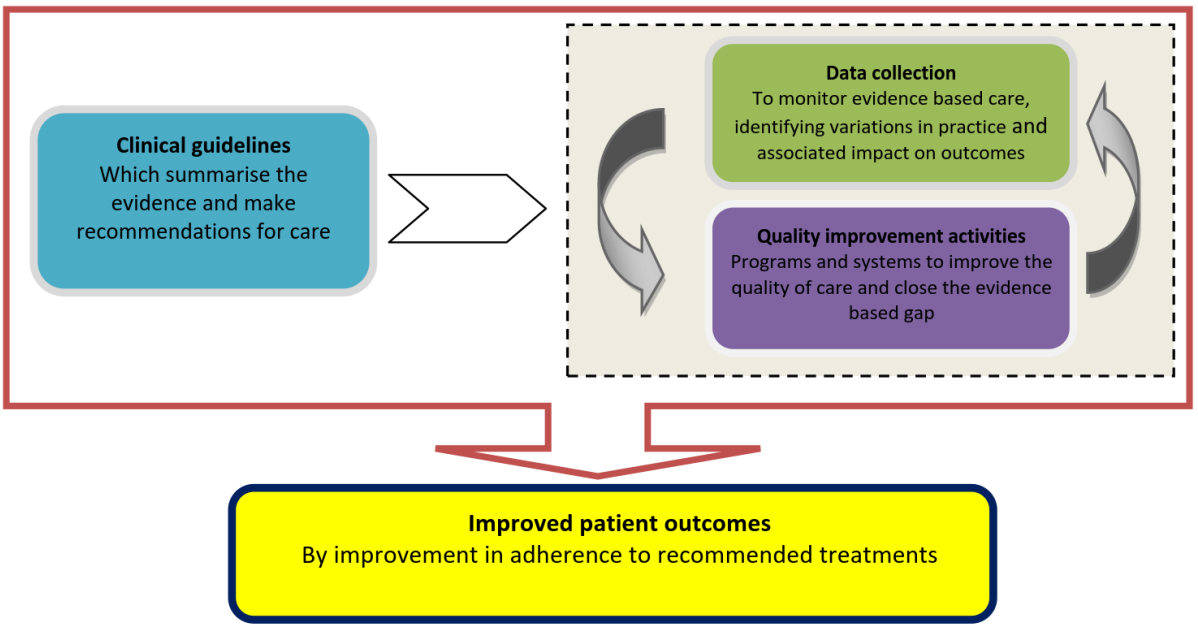
- Written care plan

The *Clinical Guidelines* (64) recommend that patients who are being discharged home are provided with a plan to guide the individual's care once they have returned to the community. The *Clinical Care Standard* (65) notes that such plans should include rehabilitation goals, lifestyle modifications and contact details for ongoing support services, among other items. A recent Cochrane review (82) found that providing patients with a discharge plan may result in a small reduction in hospital length of stay, whilst also reducing the risk of readmission within three months.

1.9.2 Monitoring Adherence to Acute Stroke Care Processes

The *Clinical Care Standard* described above provides clinicians with a set of essential processes of care which should be provided to all patients admitted for stroke in Australian hospitals. Of course, the presence alone of the *Clinical Care Standard* cannot ensure that it is adhered to by policymakers, or by clinicians working in the field. Indeed, in order for this to happen, it is necessary to collect data on provision of care within the hospital, and feed it back to clinicians (83). These data can, in turn, be used as part of quality improvement initiatives (Figure 9) (84). In Australia, the provision of evidence-based acute stroke care is primarily monitored through two data collection programs: the Stroke Foundation's Acute Audits and the Australian Stroke Clinical Registry (AuSCR).

Figure 9. Processes required to ensure delivery of evidence based clinical care (84)



1.9.3 Stroke Foundation Acute Audits

The Stroke Foundation's Acute Audits are comprised of an organisational survey and a clinical audit, both of which are conducted every second year (63). The organisational survey assesses 'structure' as defined by Donabedian (50), providing information about the resources available to deliver acute stroke care, such as the availability of stroke units, imaging services and interdisciplinary staff (63). The clinical audit, on the other hand, is concerned with Donabedian's 'process' (50), taking 40 random cases per hospital and measuring each site's adherence to 18 care processes derived from the ACSQHC's *Clinical Care Standard* (63). These audits have a large scope, capturing data on over 35,000 admissions from 120 hospitals during the most recent 2019 audit (63). Unfortunately, the utility of the *Acute Audits* as a vehicle for investigating regional variations in acute stroke care and outcomes is somewhat limited. This is primarily because the variables needed in order to calculate risk-adjusted patient outcomes (e.g. patient age/sex, measures of stroke severity) are either not collected in the audits, or are only available to researchers in a summary form.

1.9.4 The Australian Stroke Clinical Registry

The AuSCR is a national, non-government clinical registry established in 2009 to monitor the care and outcomes of patients admitted for acute stroke in Australia (85). As of 2017, the AuSCR had recorded over 30,000 episodes of care recorded from a total of 59 sites (86). The AuSCR collects data in relation to four care process measures: intravenous thrombolysis, stroke unit care, discharged on antihypertensive medication, and the provision of a discharge care plan. A further four variables (i.e. dysphagia, hyperacute aspirin, mobilisation, and anti-thrombotic medication at discharge) are collected only in hospitals located in the state of Queensland (87). The registry is also capable of reporting on patient mortality following stroke, as it is routinely linked to the Australian Government's National Death Index (88). Unlike the Stroke Foundation's audits, the AuSCR's data collection is continuous, and

participating hospitals also have the ability to benchmark their performance against peers using a web-based dashboard (85).

The principal limitation of using the AuSCR to examine regional differences in care and outcomes relates to the representativeness of its data. There are significant upfront and ongoing costs associated with participation in the AuSCR. As such, hospitals subscribing to the registry are likely to be larger sites (i.e. with an ample number of stroke admissions each year) and sites with specialist staff who are committed to improving stroke care. Notwithstanding, the AuSCR represents the most comprehensive set of data on acute stroke care in Australia at present.

1.10 Unwarranted Variation

Data collected by the AuSCR and the *Acute Audits* are primarily used by individual hospitals to benchmark their delivery of acute stroke care against that of their peers. Neither of these initiatives yield much information about broader, system-wide patterns in access to care and patient outcomes, such as the disparity between urban and rural areas. This process is known as the study of 'geographic variation', or more commonly 'unwarranted variation' (89). Unwarranted variation can be defined as "wide variations that cannot be explained by illness severity or patient preference" (89). Unwarranted variation distinguishes between 'good' variation which can be explained by differences in clinical need, and 'bad' or unwarranted variation which cannot, and hence should be reduced (90). As noted in a report by the Australian Commission on Safety and Quality in Health Care (91) , there are a host of reasons why detecting and addressing Unwarranted variation should be of interest to clinicians and policymakers:

- It may reflect structural factors that mean some have less access to health care than others.

- It may mean that factors other than patients' need or preferences are driving treatment decisions, particularly for discretionary interventions.
- In some cases, variation may reflect evidential uncertainty as to which medical intervention is best.
- Variation in medical practice may mean some people are having unnecessary (and potentially harmful) tests or treatments. Or, conversely, that some people are missing out on tests and treatments that might be helpful.
- Variation in practice may also mean that scarce health resources are not being put to best use.

1.11 Synopsis

Stroke is a leading cause of death and disability in Australia; this is particularly the case in the country's rural areas where it is more prevalent. Reductions in the burden of stroke over the past half century have been attributed to increasingly specialised hospital care, among other factors. Despite a well-established link between these models of care and improved patient outcomes, it is apparent that hospitals in Australia's rural areas are relatively under-resourced. What remains uncertain, however, is whether this difference in resourcing has resulted in regional differences in access to acute stroke care, and if so, whether there are any corresponding disparities in patient outcomes. There is impetus to use the resources available to researchers (e.g. the AuSCR) to address the issue of Unwarranted variation in acute stroke care within Australia.

1.12 Critical Appraisal of Existing Studies

Where stroke is concerned, it remains unclear as to whether differences in the quality of acute care (and in turn, differences in hospitalisation outcomes) serve to exacerbate existing geographical health disparities. O'Neill and Godden (92) examined patterns of healthcare

utilisation and outcomes in Scotland, concluding that when compared with stroke patients in urban areas, those from rural and remote areas were not relatively disadvantaged. Interestingly, the authors noted that factors including diagnostic uncertainty, and mortality occurring prior to hospital notification may have unduly influenced their findings (92).

In Australia, the Stroke Foundation has previously reported that patients admitted to rural hospitals were less likely to receive certain care processes, although no patient outcome measures were reported alongside these findings (93). Read and Levy (94) audited the medical records of 150 stroke patients from hospitals located in rural and metropolitan areas of Queensland. The authors noted that rural patients were less likely to receive a host of care processes, including swallow assessments, CT scans with 24 hours of admission, and allied health consultations. At the same time, there were no significant differences in patient outcomes between regions. Critically, the authors failed to employ any risk adjustment in their analyses. Given the need to adjust for case-mix variables (95) (and in particular, stroke severity) when comparing stroke patient outcomes, this raises some doubts about the validity of the study's findings.

More recently, Cadilhac and colleagues (96) observed that stroke patients treated in rural Australian hospitals had a relatively high risk of in-hospital mortality, when compared to those treated in metropolitan centres. Notably, the authors found that this risk was nullified in cases where rural patients received treatment in a SU. One limitation of this study, however, is that measures of in-hospital mortality fail to account for patients transferred elsewhere for palliation (i.e. referral bias) (97). As such, rates of in-hospital mortality reported in this study may have been influenced by metropolitan hospitals' ability to transfer their palliative patients to external facilities. Further, whilst this study reported a positive associated between stroke unit care and patient outcomes, it gives no mention to the magnitude of this effect. As such, it is possible that the apparent 'protective' effect of stroke

unit care in this study may have been negligible. The inconsistent findings of previous studies, coupled with their methodological shortcomings, provides impetus for further research on geographic differences in the quality of acute stroke care, and the associated outcomes.

1.13 Factors Influencing the Delivery of Care

As mentioned above, several studies have described geographic differences in the quality of acute stroke care (93, 94, 96). Comparatively little is known about the factors influencing clinicians' ability to deliver care in different geographic settings. Brems and colleagues (98) surveyed 1,500 healthcare professionals working within either urban or rural settings, to determine whether they faced different barriers to the provision of care. The authors noted that whilst both groups had many barriers in common, the number of barriers perceived by clinicians increased in line with their remoteness (98).

Where acute stroke care is concerned, much of the existing literature has focussed on factors influencing the administration of thrombolysis, a treatment for which approximately one third of patients qualify (99). Of those studies which have addressed the delivery of acute stroke care more comprehensively, time and resourcing constraints were cited as barriers to providing care (100, 101). A thorough search identified one study (102) which had addressed barriers and facilitators to providing stroke care within a rural setting. Given the limited utility of existing studies, coupled with an overall paucity of literature, it remains unclear as to whether clinicians working in urban and rural settings encounter similar issues when providing care to acute stroke patients.

1.14 Aim and specific objectives of the thesis

The purpose of this body of work is to characterise and contrast the care provided to, and outcomes of, people with stroke across geographical settings (e.g. with varying degrees of rurality). Doing so will indicate whether patients' hospital care and outcomes contribute to wider geographical disparities in health. Recommendations produced by this thesis will also assist clinicians and policymakers to improve the delivery of stroke services in both urban and rural settings.

The specific objectives of the thesis are to:

I. Identify, critique and synthesise literature pertaining to urban-rural differences in both the quality of care and outcomes of acute stroke patients.

II. Describe the regional differences in acute ischaemic stroke care and outcomes within the Australian state of Tasmania.

III. Interview clinicians located in urban and rural settings, to determine which factors influence their ability and willingness to provide guideline-recommended acute stroke care.

IV. 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).

1.15 Research Design

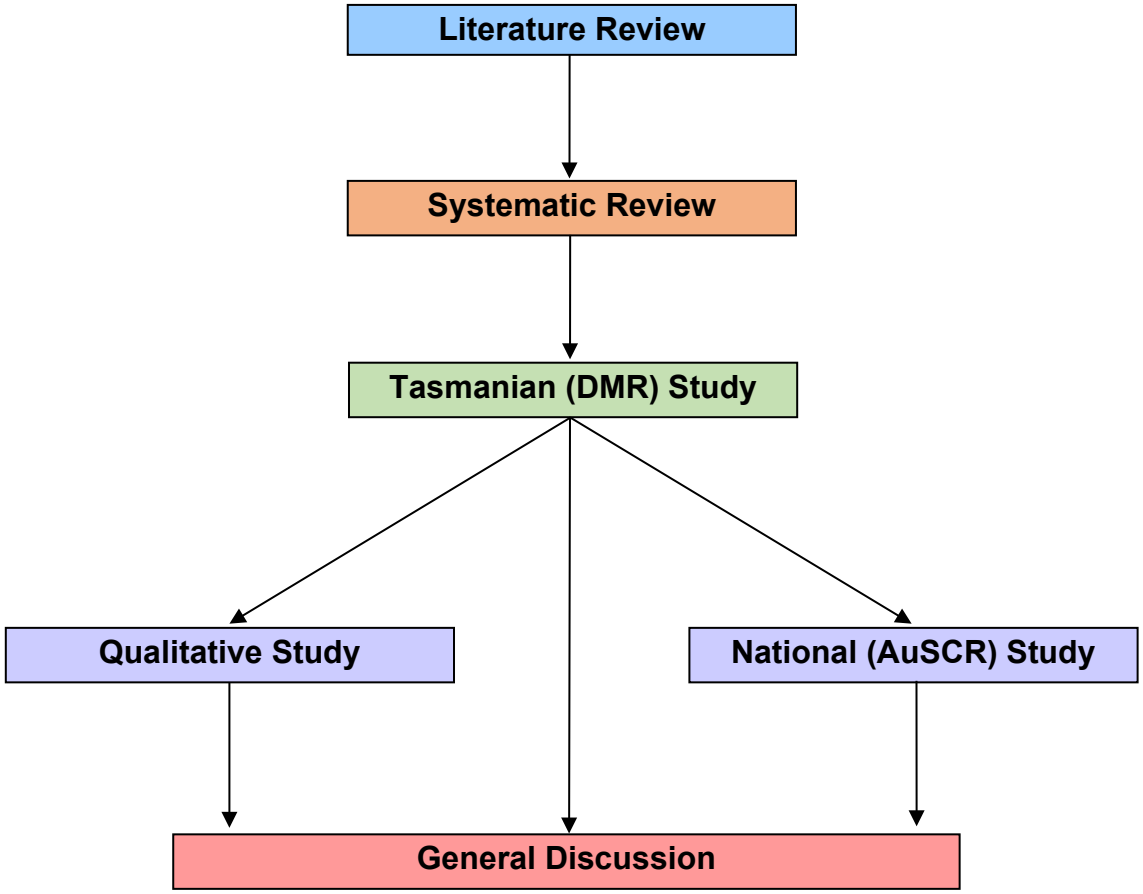
Informed by the desire to achieve a pragmatic outcome from the research, a multi-phase, sequential-explanatory mixed methods design, as described by Creswell and Plano Clark (103), was selected to address the research objectives. This involved two distinct phases of data collection (i.e. quantitative followed by qualitative). Phase one was a case note audit of stroke patients admitted to urban and rural hospitals in Tasmania, Australia. Phase two involved a series of focus groups and interviews with clinicians from the subject hospitals used in phase one. An additional quantitative study was then conducted using data from the AuSCR, with a view to addressing limitations of the initial case note audit. Lastly, phase three was an integration and explanation of the results stemming from the two former phases.

1.16 Thesis Structure

Chapter one has summarised the literature, defined key knowledge gaps, and provided a rationale for the research approach. **Chapter two** presents a systematic review on urban-rural differences in the quality of care and outcomes of acute stroke patients. **Chapter three** describes the findings of a case note audit on regional differences in acute ischaemic stroke care and outcomes within the Australian state of Tasmania. **Chapter four** reports the findings of a qualitative study which aimed to determine which factors influenced urban and rural clinicians' ability and willingness to provide guideline-recommended acute stroke care. **Chapter five** contains a retrospective study comparing the processes and outcomes of care in patients with stroke treated in urban versus rural hospitals across Australia, using data from the AuSCR. **Chapter six** discusses the overall findings of the studies included in the thesis in the context of the extant literature, before addressing limitations and providing suggestions for future research and changes to clinical practice.

Chapters one and four are written using the passive voice. Chapters two, three, and five are written in the first-person plural, while chapter six is written in the first-person singular. The flow of this thesis is illustrated in Figure 9 below.

Figure 10. Thesis flow diagram



2. CHAPTER TWO: Urban-rural differences in the care and outcomes of acute stroke patients: Systematic review

This chapter reports a systematic review conducted with the aim of identifying, critiquing and synthesizing literature relating to urban-rural differences in the quality of care and outcomes of acute stroke patients.

This work was published in *The Journal of the Neurological Sciences*:

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Review Article

Urban-rural differences in the care and outcomes of acute stroke patients: Systematic review

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ABSTRACT

Objective: To describe literature pertaining to urban-rural differences in both the quality of care and outcomes of acute stroke patients.

Methods: We systematically searched CINAHL, PubMed, ProQuest Dissertations & Theses, and Scopus for published and unpublished literature until 9th December 2017. Studies were included if they compared the acute care provided to, or outcomes of, patients hospitalised for stroke in urban versus rural settings. Abstract, full-text review, and data extraction were conducted in duplicate. Findings are presented in the form of narrative syntheses.

Results: A total of 28 studies were included in the review (16 on care, 12 on outcomes). With few exceptions, studies addressing the provision of care suggested that rural patients have less access to most aspects of acute stroke care. Studies reporting urban-rural differences in patient outcomes were inconsistent in their findings, however, few of these studies were primarily focused on the issue of urban-rural disparities. Overall, study findings did not appear to differ in line with study quality ratings, stroke subtypes included, or how inter-facility patient transfers were accounted for.

Conclusions: There is convincing, albeit not unanimous, evidence to suggest that stroke patients in rural areas receive less acute care than their urban counterparts. Despite this, the available data and methodology have largely not been used to study urban-rural differences in patient outcomes.

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1. Introduction

Individuals living in rural areas are likely to have worse risk factor profiles [1,2] and higher incidence rates [3–5] for stroke than their urban counterparts. Evidence from other disease-specific groups suggests that rural populations also have comparatively limited access to acute care services than urban populations [6–8]. Similar disparities have previously been reported in relation to acute stroke care [9]. Much of this literature, however, has focused on specific care processes that are clearly impacted by geographical factors (e.g. pre-hospital care, time-critical therapies) [10,11]. Less is known about how acute stroke care in its entirety differs between urban and rural settings [12].

If there is variation in care delivery between urban and rural settings, the critical issue is whether this results in corresponding differences in patient outcomes, as reflected by measures including mortality and readmission rates. Literature in relation to urban-rural differences in outcomes of acute stroke patients remains equivocal [13–15]. This may be due, in part, to the methodological shortcomings of some studies (e.g. poor risk adjustment) [16]. Given that rates of stroke-related mortality remain higher in rural areas [17–19], there is impetus to determine whether patients' clinical care and outcomes may be contributing to this divide. The aim of this systematic review was to identify, critique and synthesize literature pertaining to urban-rural differences in both the quality of care and outcomes of acute stroke

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patients.

2. Methods

2.1. Design and study selection

A literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines [20]. The review addressed literature pertaining to 1) urban-rural differences in the provision of evidence-based acute stroke care, and 2) urban-rural differences in the outcomes of acute stroke patients. This review was registered with PROSPERO (CRD42017073262).

2.2. Eligibility criteria

2.2.1. Types of participants

This review considered studies that compared the care provided to, or outcomes of, individuals admitted to hospitals located in urban and rural settings following an acute episode of stroke. The authors recognise that definitions of 'rural' and 'urban' settings (and their various synonyms) differ markedly between countries; as such, we assumed that these classifications were meaningful within the context of each study. No restrictions were imposed on how urban/rural status was defined or on the unit of analysis used (e.g. patient-level or hospital-level). The review considered articles that defined stroke using generic terms (e.g. stroke, cerebrovascular disease, brain attack etc.) and terms used to describe the following specific diagnoses: transient ischaemic attack, subarachnoid haemorrhage, intracerebral haemorrhage, and cerebral infarction. Articles focussing on the broad category of 'cardiovascular disease' and its synonyms were only considered if they made specific reference to 'stroke' or its sub-classifications.

2.2.2. Types of intervention(s)/phenomena of interest

This review considered studies that explicitly compared the care provided to, or outcomes of, patients within the abovementioned groups.

2.2.3. Study designs

The current review considered quantitative studies that employed observational study designs, including ecological studies, cross-sectional studies, case-control studies, and cohort studies.

2.2.4. Outcomes

This review considered studies that reported care process measures commonly used during episodes of acute hospitalisation for stroke. These included stroke unit treatment, thrombolysis, venous thromboembolism (VTE) prophylaxis, secondary prevention medications (e.g. anti-hypertensives, anticoagulants) and allied health interventions. These care processes may have been provided in pre-hospital, emergency department or inpatient settings. In terms of clinical outcome measures, this review considered studies that reported rates of mortality and readmissions, and patients' discharge destinations following their acute episode of care. Functional measures were also considered; these included patients' scores on the following indices: Modified Rankin Scale (mRS), Barthel Index, and Functional Independence Measure (FIM).

2.3. Exclusion criteria

We excluded articles which reported variations in the care provided to (or outcomes of) acute stroke patients between facilities or regions, without classifying such facilities or regions as being rural or urban (or their synonyms). We also omitted articles reporting differences in the outcomes of urban-rural individuals who experienced a stroke, which were not linked to the individuals' episode of acute hospitalisation (e.g., population-level studies comparing stroke deaths between regions). Where outcome measures were concerned, we excluded studies reporting outcome measures that were not risk-adjusted. Articles published in languages other than English, and articles with no full text available were excluded.

2.4. Information sources

Four databases (CINAHL, PubMed, ProQuest Dissertations & Theses, and Scopus) were searched for relevant white and grey literature, with additional articles identified via a 'snowballing' process. The reference sections of publications were also screened manually for other relevant articles.

2.5. Search strategy and study selection

One search strategy was developed for each of the four databases, with the assistance of a research librarian. The same strategies were used across both of the review's objectives. All four strategies aimed to find both published and unpublished studies, published until 9th December 2017. A copy of the search strategy used in the PubMed database can be found in Appendix A. The reviewers used Covidence [21], a web-based tool developed by the Cochrane Collaboration tool to screen article titles and abstracts in accordance with the criteria listed above. Three independent reviewers (with the same two per review objective) were used during the screening process; discrepancies between these reviewers were resolved through discussion.

2.6. Data extraction and quality appraisal

Two reviewers independently extracted data from each of the included studies into a standardised electronic form. This included descriptive data (name of first author, publication year), study design (country of origin, sample size, covariates used, care processes and/or patient outcomes of interest), study results and their postulated causes. Risk of bias within the included studies was assessed using a modified version of the Newcastle-Ottawa Scale [22], a tool widely used for the appraisal of non-randomised studies. The tool uses a 'star' system in which a maximum of nine 'stars' may be awarded to each study. The tool assesses three aspects of the study: selection of study groups, comparability of study groups and ascertainment of outcome of interest. Two independent reviewers (MD, SR) assessed the quality of the selected literature, before resolving discrepancies via discussion. Studies assigned ratings of 7–9, 4–6, and 1–3 were considered to be "high", "fair" and "low" quality studies, respectively. No articles were excluded from the review on the basis of their low quality scores.

2.7. Data synthesis

We assessed heterogeneity using the I^2 statistic [23], and found that in light of significant heterogeneity, it was impractical to calculate pooled estimates of urban-rural care disparities. This objective's findings are presented as a narrative synthesis, where results have been categorized according to the domain of acute care they relate to. The researchers attempted to conduct a meta-analysis of studies reporting urban-rural differences in rates of 30-day mortality; however, a scarcity of the necessary data rendered this form of analysis infeasible. Accordingly, this objective's findings are also presented as a narrative synthesis, in which results have been grouped together based on the outcome measure being reported.

3. Results

We illustrate the flow of articles through the review screening process in Fig. 1. Sixteen studies met our inclusion criteria for objective one (care), while 12 studies were included in objective two (outcomes). Study findings did not appear to differ with study quality rating, stroke

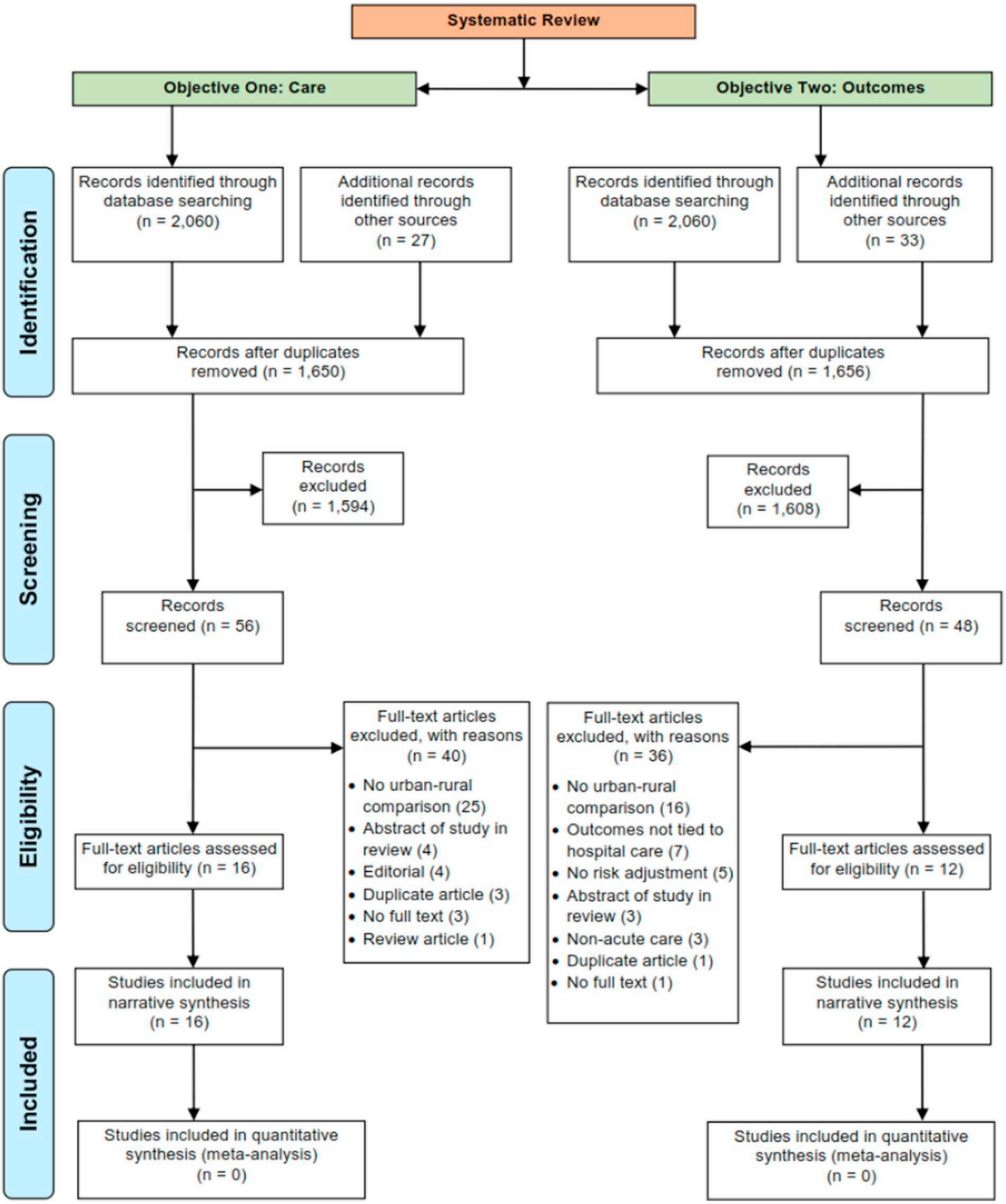

Fig. 1. Study flow diagram.

subtypes included, or how inter-facility patient transfers were accounted for.

3.1. Study characteristics

Of the 16 studies relating to care provision (Table 1), nine (56%) were from the USA, four (25%) were from Australia, two (12.5%) were from Canada, and one study was across Finland and Germany. A clear majority of studies (69%) examined 'stroke' generally, while the remaining studies restricted their analyses to ischaemic stroke. Studies describing urban-rural differences in care used a number of different study designs, of which cross-sectional and cohort studies were the most prevalent. Of the 12 studies on patient outcomes (Table 2), five (42%) were from the USA, three (25%) were from Canada, two (17%) were from Australia, and there was one study each from Iran and Taiwan. Studies describing urban-rural differences in patient outcomes used either ecological (n = 5) and cohort (n = 7) study designs. Across both review objectives, urban-rural status was predominantly defined by the location of the treating hospital, with a minority of studies using patients' residential addresses, or the catchment areas of emergency services.

Table 1
Characteristics of studies examining urban-rural differences in stroke patient care.

Study	Country	Sample size	Urban-rural distinction	Processes measured	Quality
35	Australia	2254 participants from 32 hospitals	Hospitals were classified as either 'metropolitan' or 'rural' based on their New South Wales Area Health service categorization.	Stroke Care Unit access	High
29	USA	185,997 participants from 1563 sites	Patients' residential addresses were classified as 'urban' or 'rural' using an undisclosed methodology.	Ambulance transport to hospital	High
30	USA	914,500	Hospitals were regarded as either 'rural' or 'urban' based on their classification in the National Inpatient Sample (NIS)	Provision of thrombolysis	High
24	USA	566 participants	Patients were classified as either 'urban' or 'rural', based on the location of their residential address, using classifications from the US Census Metropolitan Statistical Areas (MSA)	Ambulance transport to hospital	High
25	Canada	100 participants	Distinctions were made between 'urban' and 'rural' Emergency Medical Service (EMS) providers, based on their catchment areas. Both EMS providers served the same urban based stroke centre.	11 indicators relating to prehospital care by EMS providers.	Fair
26	Finland/ Germany	14,976 participants across two networks	Classifications made using the European Union's Nomenclature of Territorial Units for Statistics - level 3 (NUTS3) system. The Finnish network (HUCH) analysed in this study was deemed to be 'urban', while the German areas (TEMPiS) were classified as 'rural'.	Provision of thrombolysis, pre-hospital/in-hospital/overall delays to thrombolysis.	Fair
31	USA	495,186 participants from 4750 hospitals	Hospitals were classified as 'urban' or 'rural' using US Census data.	Provision of thrombolysis	Fair
27	Canada	15,713 participants from 153 hospitals	Patients' residential addresses classified as 'large urban' (population ≥ 100,000), 'medium urban' (population 10,000 to 99,999) and 'rural or small town' (population < 10,000) using the Canada Census database.	18 process indicators, covering prehospital care, hyperacute therapies, allied health interventions, medications.	High
38	Australia	741 participants from 5 hospitals	Hospitals deemed to be 'rural' were located in areas classified as 'rural' or 'regional' by the Australian Standard Geographical Classification (ASGC) system.	Access to physiotherapy (PT) and occupational therapy (OT)	Fair
36	USA	1000 participants	Patients' residential addresses were classified as 'urban' or 'nonurban' areas. Areas were considered to be 'urban' if they were situated in a US Census tract comprised of > 75% urban addresses.	Evaluation at a Primary Stroke Centre (PSC)	High
12	USA	3889 participants from 128 hospitals	Patients' residential addresses were grouped into 'urban' and 'rural' categories using the Rural-Urban Commuting Areas (RUCA) system. All patients residing outside urban areas (i.e. in areas classified as 'large rural', 'small rural', or 'isolated') were allocated to the 'rural' group.	14 process indicators addressing thrombolysis, secondary prevention, and allied health interventions.	High
37	USA	963,525 participants from 1675 hospitals	Hospitals were classified as 'urban' or 'rural' using an undisclosed methodology.	Provision of 'comfort measures only' care on day 0 or 1 of admission	High
32	Australia	150 participants from 4 hospitals	Hospitals were designated as 'metropolitan' or 'regional' based on their geographic location, bed capacity, and annual number of stroke admissions.	19 process indicators, covering investigations, acute interventions, and secondary prevention strategies.	Fair
33	USA	2758 hospitals	Hospitals were categorized as large metropolitan, medium-metropolitan, small metropolitan, or non-metropolitan, based on their US Department of Agriculture Rural–Urban Continuum Code.	Eight process indicators, covering hyperacute therapy, secondary prevention, and rehabilitation.	Fair
28	Australia	4192 participants from 117 hospitals	Hospitals were classified as either 'metropolitan' or 'regional' using the Modified Monash Model (MMM) system.	37 process indicators, covering prehospital care, hyperacute therapy, secondary prevention, carer involvement.	Fair
34	USA	213 hospitals	Hospitals located in 4/5 states surveyed were asked to self-identify as being 'urban' or 'rural'. In Montana, hospitals located in nonmetropolitan counties with a city of > 10,000 population were categorized as 'urban', while those in a nonmetropolitan counties without a city of > 10,000 population were categorized as 'rural'.	Provision of thrombolysis	Low

Table 2
Characteristics of studies examining urban-rural differences in stroke patient outcomes.

Study	Country	Sample size	Urban-rural distinction	Outcomes measured	Quality
41	Iran	16,351 from one hospital	Patients' residential addresses were classified as urban or rural using an undisclosed methodology	In-hospital mortality	Fair
35	Australia	2254 participants from 32 hospitals	Hospitals were classified as either 'metropolitan' or 'rural' based on their New South Wales Area Health service categorization.	In-hospital mortality, functional status at discharge, clinical complications.	High
48	USA	99,513 participants from an undisclosed number of hospitals	Patients' residences were classified as 'urban' or 'rural' based on their population. Areas with a population of > 25,000 were classified as 'urban', while those with a population < 2500 were deemed to be rural.	Discharge destination	High
42	Canada	208 hospitals (185 rural, 23 urban)	Hospitals were classified as 'rural' if they were outside the commuting zone of centres with a population exceeding 10,000. No corresponding definition was offered for urban areas.	30-day in-hospital mortality	High
43	Taiwan	1583 participants from an undisclosed number of hospitals.	Hospitals were classified as major medical centres or regional hospitals.	In-hospital mortality, for ischaemic and haemorrhagic stroke patients	Fair
39	USA	8233 participants from 234 hospitals	Rural hospitals were identified using the Office of State-wide Health Planning and Development database. No definition was provided for the comparator group.	In-hospital mortality	High
46	USA	50,579 participants from 131 hospitals	Hospitals were classified as 'metropolitan' or 'non-metropolitan' using the Rural-Urban Commuting Area (RUCA) classification system	12-month mortality	High
47	Australia	4139 participants from 35 hospitals	Hospitals classified as rural or urban using an undisclosed methodology	30-day readmission	High
27	Canada	15,713 participants from 153 hospitals	Patients' residential areas were classified as large urban (population ≥ 100,000), medium urban (population 10,000 to 99,999) or rural (population < 10,000).	30-day mortality, disability at discharge	High
45	USA	310,381 participants from 4546 hospitals	Hospitals were classified as Critical Access Hospitals (CAHs) or non-critical access hospitals. CAHs were defined as being > 35 miles from the closest hospital, having < 25 inpatient beds, averaging a length of stay of under 96 h, and providing 24/7 emergency care services.	30-day mortality, 30-day readmission	High
40	Canada	26,676 participants from 606 hospitals	Hospitals were classified as rural or urban using an undisclosed methodology	In-hospital mortality (7-day), in-hospital mortality (at discharge)	Fair
44	USA	459,756 participants from 1680 hospitals	Hospitals were classified as 'urban' or 'rural' based on their designation within the Get With The Guidelines - Stroke (GWTG-S) registry	30-day mortality, 30-day readmission	High

3.2. Methodological quality

The median study quality score was 6.5/9 (IQR 4.75–7) for studies addressing care, and 7/9 (IQR 7–8) for studies addressing outcomes. Most studies used either registry data or trained abstractors to review medical records, and, as such, generally scored well in the 'selection' and 'outcome' domains. A number of studies had reduced quality scores due to an absence of sample size calculations and undisclosed definitions of urban-rural status.

3.3. Urban-rural differences in acute stroke care

Table 3 summarises the urban-rural differences in care found within the included studies; the following narrative synthesis describes differences found within specific domains of acute stroke care.

3.3.1. Pre-hospital care

The provision of pre-hospital care was addressed by six studies [24–29]. There were eight instances in which no association was found between hospital location and patients' likelihood of receiving certain interventions [24,25]. Five studies [25–29] reported one instance each where urban hospitals had higher levels of adherence on measures of ambulance transport and pre-hospital assessment.

3.3.2. Hyperacute care

Nine studies [12,26–28,30–34] investigated urban-rural disparities in the provision of hyperacute therapies, of which thrombolysis was by far the most commonly mentioned. Each of these studies contained some evidence to suggest that rural patients either i) experienced greater delays when being administered thrombolysis, or ii) were less likely to receive thrombolysis. Notwithstanding this, there were instances where rural hospitals provided hyperacute care that was commensurate with that of urban hospitals [12,26,27,32]. Studies that employed multi-level analyses to control for hospital characteristics produced conflicting findings [12,30,31]. Seabury and colleagues [33] also found that disparities in rates of thrombolysis administration between metropolitan and non-metropolitan settings were markedly reduced in cases where both sites were equipped with certified stroke centres.

3.3.3. Investigations

Five studies [12,25,27,28,32] examined variation in hospitals' use of investigations for acute stroke, which centred on the use of medical imaging and blood tests. Around half of the urban-rural comparisons made suggested that rural patients received fewer investigations than their urban counterparts, while the remaining comparisons found no difference.

3.3.4. General acute care

Seven studies [12,27,28,32,35–37] discussed urban-rural differences in 'general' aspects of acute hospital care, covering dysphagia screening, acute stroke unit care, and post-discharge planning, among other factors. A majority (76%) of comparisons made suggested that rural hospitals had a lower adherence to the care processes measured. Phipps et al. [12] noted that there were no significant urban-rural differences with control for hospital characteristics. Additionally, Prabhakaran et al. [37] noted that rural patients were more likely to have 'comfort measures only' care enacted by their second day of hospitalisation, after controlling for potential confounders.

3.3.5. Secondary prevention

Five studies [12,27,28,32,33] addressed secondary stroke prevention, which primarily related to the provision of medications (e.g. anti-thrombotics, anti-hypertensives). There were, however, instances where smoking cessation advice [12] and stroke education [33] were also measured. In a small majority of cases (55%), there was either no

Table 3
Findings of studies examining urban-rural differences in stroke patient care.

Study	Urban-rural differences in care	Postulated causes of disparities
35	• Patients in non-metropolitan areas were less likely to be treated in a Stroke Care Unit (77% vs 3%, $p < .05$).	• Metropolitan hospitals were more likely than regional hospitals to be equipped with a SCU
29	• Rural patients were less likely than those in urban areas to be transported to hospital via ambulance (OR = 0.85, 95% CI 0.74–0.97, $p < .05$). • Findings adjusted for age, race, comorbidities, insurance status, arrival time, stroke severity, US Census region, and hospital characteristics.	• Disparities in the use of ambulance transport may be attributed to patient factors (e.g. fears of medical bills). • Disparities may also be due to differences in stroke education (i.e. symptom recognition).
30	• Patients treated in urban hospitals were more likely to receive thrombolysis (OR = 2.11, 95% CI 1.97–2.27, $p < .0001$). Findings controlled for year, patient age, race, sex, insurance status, US census region, and hospital characteristics. • The proportion of urban patients receiving thrombolysis quadrupled during the study period (range 1.17%–4.87%) compared to rural hospitals (range 0.87%–1.59%).	• Hospitals located in rural areas are less likely to be certified as Primary Stroke Centers (PSCs) • Many rural hospitals cannot afford the accreditation process associated with becoming a PSC. • There may be fewer neurologists operating in rural areas. • Rural areas may have lower rates of preventative health care, making contraindication for thrombolysis more likely. • Patients in rural areas may have relatively less knowledge of stroke symptoms, causing delays to the treatment process. • Rural patients may also need to travel further to the nearest hospital, causing delays to the treatment process.
24	• Univariate analysis revealed no association between patients' ambulance transport and their urban/rural status (OR = 1.02, 95% CI = 0.59–1.77). • No association was found between patients' ambulance transport and their urban/rural status after adjusting for confounders (OR = 1.36, 95% CI = 0.82–2.24).	• No explanation offered
25	• Urban patients were more likely to be assessed with Cincinnati Prehospital Stroke Scale (CPSS) (70.3% vs 31.8%, $p < .05$). • No significant between group differences were found in the remaining indicators.	• High compliance rates observed in both urban and rural settings may be partially attributed to the fact that both regions had developed similar acute stroke protocols and prehospital algorithms with the accepting stroke centre. • Lower rates of CPSS use in rural settings may be attributed to regional differences in documentation.
26	• Rates of in-hospital thrombolysis were significantly higher in the urban network (26.9% vs 15.4%, $p < .001$). • Median prehospital delays were longer in the urban network (88 mins vs 65 mins, $p < .001$), while in-hospital delays were longer in the rural network (18 mins vs 40 mins, $p < .001$). • There were no significant differences in the overall proportion of individuals receiving thrombolysis in each network • There were no significant differences between regions with respect to overall delays.	• Rates of in-hospital thrombolysis were higher in the urban network, as this hospital only received ambulance transfers for patients who were potential thrombolysis candidates. In contrast, patients in the rural network were transferred to nearby hospitals regardless of their eligibility for thrombolysis. • Differences in pre-hospital delays were attributed to relatively short travel times inside the rural network. • Small hospitals in the rural network may have been less accustomed to providing thrombolysis than the urban hospital.
31	• Hospitals in areas with a population density exceeding 500 persons per square mile administered thrombolysis at three times the rate of hospitals in areas with a population density of < 50 persons/sq. mile (2.7% vs 0.9%). • Population density was significantly associated with thrombolysis rates after adjustment for hospital size, census region.	• Rural hospitals may see few eligible thrombolysis cases annually, making it difficult to maintain treatment protocols. • Patients initially treated in rural hospitals may have been transferred to larger centres in order to receive thrombolysis. • The study's age group of 65 and over is likely to have excluded some patients who received thrombolysis.
27	• Compared with urban hospitals, rural hospitals scored significantly lower on all but five of the care processes measured. • No significant regional differences were found with respect to patients' onset to presentation times, thrombolysis rates, and secondary prevention medications (i.e. statins, antiplatelets, anticoagulants). • Rural hospitals performed a greater proportion of telestroke consults.	• Findings may reflect the limited resources in smaller or remote settings. This is supported by the fact that interventions not requiring additional resources (e.g. secondary prevention medications) were comparable in both settings. • Comparable rates of thrombolysis administration may be partially explained by efforts made during the study period to improve i) the transportation of patients to regional stroke centres and ii) the use of telemedicine for thrombolysis.
38	• Rural patients received more direct OT sessions; however, these sessions were shorter than that of metropolitan patients. • Metropolitan patients received more indirect OT sessions, but there were no regional differences in session duration. • Rural patients received significantly more direct physiotherapy sessions, but fewer indirect physiotherapy sessions.	• The referral process for allied health interventions may be a barrier to timely care (however, this issue was not necessarily worse in either metropolitan or rural hospitals).
36	• Compared with urban patients, those in nonurban areas were less likely to be evaluated at a PSC (9.1% vs 23.9%, $p < .001$). • This disparity remained after adjusting for patient demographics and comorbidities (OR = 0.39, 95% CI 0.22–0.67).	• Nonurban patients' geographic access to PSC care is likely to have been lower than that of urban patients. 'Geographic access' incorporates the time, distance, and cost associated with seeking a given treatment.
12	• In univariate analyses, rural patients received significantly fewer of the following interventions: DVT prophylaxis, secondary prevention medications, NIHSS assessments, and smoking cessation counselling. • Rural patients had more assessments for fall risks and rehabilitation, and were more likely to be given stroke education. • No regional differences were found with respect to thrombolysis rates, atrial fibrillation management, dysphagia screening, early ambulation, and assessments for the risk of pressure ulcers. • After adjustment for patient and facility level characteristics, rural patients were significantly less likely to receive DVT prophylaxis (OR = 0.35, 95% CI 0.15–0.81), but more likely to receive rehabilitation assessments (OR = 2.8, 95% CI 1.3–5.9). • There were no significant regional differences among the remaining care processes.	• Similarities in the quality of care delivered across settings may be partially explained by the fact that the Veteran's Affairs health care system is a national organization, which implements system-wide quality improvement initiatives. • Rural patients may have been relatively more complex, therefore having a greater need for rehabilitation services.

(*continued on next page*)

Table 3 (*continued*)

Study	Urban-rural differences in care	Postulated causes of disparities
37	• After controlling for patient and facility level characteristics, patients in rural hospitals were more likely than those in urban hospitals to receive early 'comfort measures only' care (OR = 1.18, 95% CI 1.05–1.31, p = .004).	• The size and location of the hospital, and its annual volume of stroke patients. • Variations in patient and/or physician attitudes towards end-of-life decisions
32	• Metropolitan patients received a greater proportion of swallowing and speech pathology assessments, and DVT prophylaxis interventions. • Regional patients were less likely to have their lipid and glucose levels tested, or to undergo an echocardiogram. • No differences were found in rates of hyperacute aspirin therapy, or in assessments by social workers, physiotherapists, or occupational therapists. • No differences were found in rates of antithrombotic therapy, or in the management of hypertension, dyslipidaemia, or atrial fibrillation.	• Variation in staffing levels, the lack of stroke care protocols, and a lack of local resources or equipment.
33	• Patients in non-metropolitan hospitals were less likely to receive each of the eight care processes measured. • Among non-certified stroke centres, 38.3% of eligible patients arriving with two hours of symptom onset in non-metropolitan areas were given thrombolysis, while the same figure for large metropolitan hospitals was 73%. The divide between metropolitan and non-metropolitan certified stroke centres was considerably smaller (83.2% vs 86.2%).	• The lack of protocols for acute stroke care • Deficits in access to neurological services (measured by the number of neurologists per capita). • Absence of decision support systems (e.g. telemedicine).
34	• The proportion of urban hospitals which had administered thrombolysis during the preceding 12 months was significantly higher than that of rural hospitals (88% vs 53%, p < .001)	• Comparatively less access to stroke personnel and written stroke protocols. Both factors affect hospitals' ability to "drip and ship" patients (i.e. transfer patients to larger hospitals after they have been administered thrombolysis).
28	• Regional hospitals were found to have relatively lower compliance in all but nine care process measures. • No between group differences were found in the proportion of patients involved in the development of their care plans, time taken for social worker/dietitian/physiotherapy assessments, and anticoagulant therapy for atrial fibrillation. • Regional hospitals showed higher rates of adherence to the following care process measures: lipid-lowering therapy, stroke education, rehabilitation assessments, and assessment within emergency departments.	• Presentation of findings only - no explanations offered

association, or a slight positive association, found between rural location and the provision of secondary prevention care. The remaining comparisons suggested that patients treated in rural hospitals received relatively fewer interventions aimed at reducing the risk of secondary stroke.

3.3.6. Allied health

Six studies [12,27,28,32,33,38] examined differences in the provision of allied health care across urban and rural settings. Studies referred to care provided by dietitians, occupational therapists, psychologists, physiotherapists, speech pathologists, and social workers, focussing on patients' initial assessments and their ongoing rehabilitation care. Sixty percent of comparisons made suggested that rural patients received comparatively less allied health care than their urban counterparts. Three studies [12,28,38] identified seven instances in which rural patients received a greater amount of allied health care than urban patients. Three studies [12,28,32] identified nine cases in which urban and rural hospitals provided a commensurate level of allied health care.

3.4. Urban-rural differences in stroke patient outcomes

Table 4 summarises the urban-rural differences in patient outcomes found within the included studies; the following synthesis describes variations found within specific outcome measures.

3.4.1. Mortality

Ten studies measured risk-adjusted mortality rates, of which in-hospital mortality was the most commonly used measure, appearing on 10 occasions within six studies [35,39–43]. A majority (70%) of these comparisons found no association between hospital location and a patient's likelihood of in-hospital mortality. The remaining three comparisons each found evidence of higher rates of in-hospital mortality within rural hospitals [35,42,43]. Several studies examined mortality in the post-discharge period; within these studies, there were three instances [27,44] in which no significant differences were found between urban and rural settings. Lastly, the studies by Lichtman et al. [45] and Ido et al. [46] found evidence of higher mortality rates in rural settings at 30 days and 12 months post-discharge, respectively.

3.4.2. Readmission

Three studies [44,45,47] analysed urban-rural differences in readmission rates within one month of discharge, all of which found no association between hospital location and a patient's risk of readmission.

3.4.3. Other outcome measures

The remaining outcome measures related to patients' functional independence at discharge, their discharge destination, and the presence of severe complications during their admission. Cadilhac et al. [35] identified four instances in which rural patients were more likely than their urban counterparts to be functionally dependent at discharge. The same paper produced conflicting findings with respect to patients' risk of experiencing severe complications during their admission. Lastly, Davis [48] reported that urban patients were less likely than rural patients to be discharged to assisted living facilities, but more likely to be discharged to inpatient rehabilitation facilities (deemed to be the least desirable outcome).

4. Discussion

We aimed to identify urban-rural differences in the care and outcomes of acute stroke patients. Most studies addressing acute stroke care provided some evidence to suggest that when compared to urban patients, those in rural areas had comparatively less access to evidence-based acute stroke care. In contrast, studies describing urban-rural differences in patient outcomes were inconsistent in their findings.

The most frequently mentioned disparities in care related to the provision of thrombolysis [12,26–28,30,31,33,34]. Gonzales et al. [30] summarised the potential causes of these disparities, citing barriers relating to structure (i.e. provider, facility, and organizational characteristics, ability to access care), processes (i.e. diagnosis, treatment) and patient attributes (i.e. thrombolysis eligibility, disease severity). Leira et al. [10] noted in an earlier review that rural hospitals may also

Table 4
Findings of studies examining urban-rural differences in stroke patient outcomes.

Study	Covariates	Urban-rural differences in outcomes	Postulated causes of disparities
41	• Age, sex, SES	• There was no significant association between patients' rural residence and their odds of in-hospital mortality (OR = 1.17, 95% CI 0.99–1.39, p = .065)	• None stated
35	†Age, sex, country of birth, hypertension, hyperlipidaemia, ability to walk on admission and incontinence within 72 h of presentation. ‡Stroke unit care, age, sex, Australian born, living alone, history of hypertension, diabetes or hyperlipidaemia, walk on admission and incontinence within 72 h. *Clustering of patients in hospitals, stroke unit care, age, sex, Australian-born, living alone, history of hypertension, diabetes or hyperlipidaemia, walking ability on admission and incontinence within first 72 h.	†Rural patients' in-hospital mortality was higher (OR = 1.46; 95% CI, 1.03–2.05). †Rural patients were more likely to be dependent following their discharge (OR, 1.75; 95% CI, 1.35–2.28). †Rural patients were more likely to experience a severe complication during their admission (OR, 1.66; 95% CI, 1.16–2.38). ‡Rural patients were less likely to be independent following their discharge from hospital (OR = 0.55, 95% CI 0.32–0.96) ‡Rural patients were more likely to be dependent following their discharge from hospital (OR = 1.82, 95% CI 1.23–2.70) ‡No between group differences were found in the odds of in-hospital mortality (OR = 1.00, 95% CI 0.62–1.61) or severe complications (OR = 1.23, 95% CI 0.74–2.05) *Rural patients were more likely to be dependent following their discharge from hospital (OR = 1.82, 95% CI 1.03–3.19) *No between group differences were found in the odds of in-hospital mortality (OR = 1.00, 95% CI 0.53–1.87) or severe complications (OR = 1.23, 95% CI 0.61–2.49).	• Lower levels of dependency found among patients treated in metropolitan hospitals may be because the rural SCU surveyed had only been recently established. • Rural patients generally had fewer comorbidities, and were more likely to be able to walk at admission. • Rural patients were more likely to have been born in Australia (which is understood to bias such patients towards improved outcomes). • Other aspects of care in rural hospitals may be responsible for the observed disparities in outcomes.
48	• Age, stroke subtype, insurance status, race	• Urban patients were less likely to be discharged to an assisted living facility (OR = 0.68, 95% CI 0.66–0.71, p < .001) • Urban patients were more likely require care at an inpatient rehabilitation facility (deemed to be the most severe outcome) (OR = 1.18, 95% CI 1.13–1.24, p < .001)	• Rural patients may be more likely to require assisted living facilities, as their strokes were more severe. • Rural patients may be less likely to be discharged to inpatient rehabilitation facilities (deemed to be the most severe outcome) because such facilities are not readily available in rural areas.
42	• Age, sex, heart failure or pulmonary oedema, cancer, renal failure, ischaemic heart disease.	• During each of the five years studied, rates of risk-adjusted 30-day in-hospital mortality were significantly higher in rural than urban hospitals. • Rates of in-hospital mortality in rural hospitals were also higher than the national average for each year of the study period except one.	Several factors not measured as part of the study: • The presence or absence of an organized stroke team • Geographic factors (e.g. patient proximity to EDs) • Inter-facility transfer capability • Support from academic centres • Rural patient characteristics.
43	• Age, sex, triage score, Charlson Comorbidity Index score.	• The odds of in-hospital mortality for ischaemic stroke patients admitted to major medical centres were 0.4 times that of their counterparts in regional hospitals. • No regional differences were noted in terms of haemorrhagic stroke outcomes.	• Major medical centres may have more "manpower" to allocate. • Variation in outcomes for haemorrhagic stroke is likely to reflect underlying disease severity, as opposed to hospitals' acute interventions.
39	• Age, sex, race, insurance status, hospital trauma centre designation, patient intubation or mechanical ventilation, hospital do-not-resuscitate rate, hospital craniotomy rate, hospital intracerebral haemorrhage volume, teaching hospital status.	• No significant association was found between patients' treatment in a rural hospital and their odds of in-hospital mortality (OR = 0.81, 95% CI 0.60–1.08, p = .16)	• None stated
46	• Age, sex, race, insurance status, length of stay in hospital, hospital size, hospital participation in registry (y/n), calendar year.	• Patients treated in non-metropolitan hospitals were more likely to have died within 1 year of their admission for stroke (RR = 1.11, 95% CI 1.03–1.21, p = .009).	• None stated
47	• Age, sex, premorbid independence, diabetes, heart disease, arm weakness, impaired speech, walking ability at admission, incontinence within 72 h of admission, brain imaging in first 24 h, provision of a discharge strategy, neurologist management, and any complications.	• No significant association was found between patients' treatment in a rural hospital and their odds of readmission within 28 days (OR = 1.21, 95% CI 0.73–2.00, p = .46)	• None stated
27	• Age, sex, income, smoking history, diabetes, hypertension, hyperlipidaemia, prior stroke, atrial fibrillation, coronary artery disease, peripheral vascular disease, dementia, stroke severity and subtype.	• There was a non-significant trend towards higher 30-day mortality in rural compared to urban patients (HR = 1.14, 95% CI 0.99–1.32) • No association was found between patients' rural residence and their combined risk of 30-day mortality and disability at discharge (HR = 1.03, 0.92–1.16).	• None stated

(*continued on next page*)

Table 4 (*continued*)

Study	Covariates	Urban-rural differences in outcomes	Postulated causes of disparities
45	• Age, sex, cardiovascular disease/stroke history (i.e. congestive heart failure, acute myocardial infarction, unstable angina, chronic atherosclerosis, cardiopulmonary–respiratory failure, peripheral vascular disease, cerebrovascular disease), and 20 other comorbid illnesses.	• The risk standardised 30-day mortality ratio of CAHs was significantly higher than that of non-CAHs (11.9% ± 1.4% vs 10.9% ± 1.7%; p < .001). • No differences were found between CAHs and non-CAHs with respect to 30-day readmission rates.	• Stroke patient volume; the relatively low number of cases seen by CAHs may be insufficient for staff to maintain their skillsets. • Patients treated in CAHs potentially have longer travel times, and hence may arrive at CAHs in a more deteriorated condition. • Rural patients may have less knowledge of stroke warning signs. • Rural patients may decline to be transferred to larger urban hospitals.
40	• Age, sex, Charlson Comorbidity Index score, facility type, most responsible physician, ICU admission, neighbourhood income, weekend admission, hospital stroke patient volume.	• There were non-significant associations between rural hospitals and patients' odds of 7-day in-hospital mortality (OR = 0.97, 95% CI 0.85–1.12) and mortality at discharge (OR = 1.12, 95% CI 0.99–1.25)	• None stated
44	• Age, sex, race, comorbid illnesses (atrial fibrillation, previous ischaemic stroke/TIA, previous myocardial infarction, diabetes, hypertension, smoking) and hospital characteristics (e.g. patient volume, staffing levels, and teaching hospital status, among other factors).	• No significant association was found between hospitals' rural location and their rates of 30-day mortality or 30-day readmission.	• Between region differences in stroke severity (not measured)

experience difficulty in adapting and implementing models of care for thrombolysis, which are often developed in well-resourced urban hospitals. That being said, three recent studies [12,26,27] all found little overall effect of urban-rural status on thrombolysis administration rates. Each of these hospital networks had previously been subject to quality improvement initiatives, and two [26,27] had made extensive use of telemedicine. This suggests that with adequate investment, rural networks can administer thrombolysis at rates comparable to urban hospitals. Future researchers are encouraged to describe their experiences of adapting models of care for use in rural settings, as done by Slivinski et al. [49].

The greatest similarities in acute stroke care were found within the domain of secondary prevention, which Koifman et al. [27] attributed to the fact that such interventions do not typically require any additional resourcing. The issue of resourcing constraints in rural areas was mentioned in several studies, often with reference to stroke units [27, 30, 35] and staffing levels [27,30,32–34]. An absence of care protocols in rural areas was another often cited cause of care disparities [32–34], with two authors [26,31] speculating that rural hospitals' low patient volumes could make it untenable to maintain such protocols. Taken together, these findings may be indicative of a threshold effect of patient volume on stroke care quality, a phenomenon which has been described previously [50].

Of the 'care' studies which were deemed to be of high methodological quality, all but two were conducted in the US, which operates a 'user pays' healthcare system. Accordingly, patients' insurance status, and their perceptions of the financial costs associated with seeking healthcare were noted to have influenced the findings of several studies [24,29,36,37]. The extent of acute stroke care provided to American patients also appears to be contingent on the certification status of the admitting hospital. Indeed, hospital certification (e.g. as a Primary or Comprehensive Stroke Center) has been described as an essential step towards improving the quality of stroke care [51]. The cost of certification is borne by hospitals individually and, as Gonzales et al. [30] note, factors including hospital size and casemix can make this process financially unviable for smaller hospitals. For these reasons, the findings of, and conclusions drawn by, US-based studies may not be generalizable to universal healthcare contexts.

As mentioned above, the findings of studies reporting urban-rural differences in patient outcomes were largely inconsistent. There were, however, some patterns to emerge from the data. Several studies [35,39,40,47] found no significant association between urban/rural status and patient outcomes after adjusting for both patient (e.g. patient age) and facility-level (e.g. stroke patient volume) characteristics. Of the four studies which did report higher rates of mortality in rural areas, three [42,43,45] did not adjust for patients' baseline stroke severity. Given that stroke severity is a strong predictor of stroke patients' 30-day outcomes [52], the presence of residual confounding in these studies cannot be discounted. Future research utilising multi-level modelling to adjust for patient and facility-level factors is needed to reveal more about the nature of urban-rural differences in stroke patient outcomes.

Only half of the studies reporting outcomes explicitly measured the impact of urban-rural status on patient outcomes [27,35,42–45] and only two studies [27,35] measured both care and outcomes. This provides scope for future studies to directly address the issue of urban-rural disparities in stroke, whilst incorporating measures of care and outcomes. Such methods are available, and have previously been used to describe disparities in care and outcomes between in-hospital vs community onset stroke [53] and with socioeconomic status [54]. It is conceivable that with an established link between urban-rural differences in care and corresponding differences in patient outcomes, policymakers would be compelled to address the issue.

Our review contains several limitations. Firstly, it is likely that not all of the care disparities reported in this review represent clinically relevant differences in care quality. Secondly, whilst most of the care processes mentioned in this review have demonstrable links with patient outcomes [55], others may not, and could therefore be considered to lack validity as process indicators [56]. It is plausible, however, that such care processes are a marker of overall care quality. Thirdly, we cannot discount the influence of publication bias in this review. We attempted to counter this by including unpublished findings [48]; however, we also recognise that emphasising urban-rural differences in care quality and outcomes has long been the primary concern of rural health researchers [57]. Lastly, and as mentioned above, many of the review's findings were indirect; this was particularly the case where outcomes were concerned.

Despite these limitations, this review makes several meaningful contributions. Our review is, to the best of the authors' knowledge, the first to address the topic of urban-rural differences in stroke care and outcomes in a systematic manner. We note that whilst an urban-rural divide in care quality still exists, these differences are not necessarily pervasive, as has been suggested previously [10]. We also emphasise the importance of considering health system context when interpreting studies of care disparities. Lastly, we note that much of the available data surrounding urban-rural differences in stroke patient outcomes

originates from studies with varying objectives, highlighting the need for future studies to address the issue directly.

In conclusion, interventions for acute stroke are differentially distributed between urban and rural settings, and this is particularly the case where thrombolysis is concerned. It is reasonable to surmise that this is affecting patient outcomes, and yet, the data and methodology available to researchers are, for the most part, not being utilised to address differences in patient outcomes. It is hoped that future researchers can employ these resources to highlight the societal burden associated with urban-rural disparities in stroke care, and in doing so, prompt policymakers to address the issue.

References

[1] R.F. Gillum, D.D. Ingram, Relation between residence in the southeast region of the United States and stroke incidence: the NHANES I Epidemiologic Followup Study, Am. J. Epidemiol. 144 (1996) 665–673.
[2] M.S. Eberhardt, E.R. Pamuk, The importance of place of residence: examining health in rural and nonrural areas, Am. J. Public Health 94 (2004) 1682–1686.
[3] M. Lemesle, M. Giroud, M. Menassa, C. Milan, R. Dumas, Incidence and case-fatality rates of stroke in Burgundy (France). Comparison between a rural (Avallon) and an urban (Dijon) population, between 1989 and 1993, Eur. J. Neurol. 3 (1996) 109–115.
[4] Y. Wang, C.R. Levi, C.A. D'Este, J.R. Attia, J. Fisher, Variation of stroke attack rates in rural, urban, and coalfields areas of the Hunter Region, Australia, 1995-2000, J. Stroke Cerebrovasc. Dis. 12 (2003) 103–110.
[5] M. Correia, M.R. Silva, I. Matos, et al., Prospective community-based study of stroke in Northern Portugal: Incidence and case fatality in rural and urban populations, Stroke 35 (2004) 2048–2053.
[6] K. Sheikh, C. Bullock, Urban-rural differences in the quality of care for medicare patients with acute myocardial infarction, Arch. Intern. Med. 161 (2001) 737–743.
[7] K.E. Joynt, Y. Harris, E. Orav, A.K. Jha, Quality of care and patient outcomes in critical access rural hospitals, JAMA 306 (2011) 45–52.
[8] S.M. Hameed, N. Schuurman, T. Razek, et al., Access to trauma systems in Canada, J. Trauma Acute Care Surg. 69 (2010) 1350–1361.
[9] J. Joubert, L.F. Prentice, T. Moulin, et al., Stroke in rural areas and small communities, Stroke 39 (2008) 1920–1928.
[10] E.C. Leira, D.C. Hess, J.C. Torner, H.P. Adams, Rural-urban differences in acute stroke management practices: a modifiable disparity, Arch. Neurol. 65 (2008) 887–891.
[11] M.A. Pervez, G. Silva, S. Masrur, et al., Remote supervision of IV-tPA for acute ischemic stroke by telemedicine or telephone before transfer to a regional stroke center is feasible and safe, Stroke 41 (2010) e18–e24.
[12] M.S. Phipps, H. Jia, N.R. Chumbler, et al., Rural-urban differences in inpatient quality of care in US veterans with ischemic stroke, J. Rural. Health 30 (2014) 1–6.
[13] G. Howard, D.O. Kleindorfer, M. Cushman, et al., Contributors to the excess stroke mortality in rural areas in the United States, Stroke 48 (2017) 1773–1778.
[14] P. Sobolewski, W. Szczuchniak, A. Sobota, M. Grzesik, Are there differences between rural and urban populations in long-term outcome after systemic cerebral thrombolysis in a hospital located in an agricultural region, Rural Remote Health 14 (2014).
[15] N. O'Neill, D. Godden, Stroke outcomes in Northern Scotland: does rurality really matter, Rural Remote Health 3 (2003) (243–243).
[16] G.C. Fonarow, M.J. Alberts, J.P. Broderick, et al., Stroke outcomes measures must be appropriately risk adjusted to ensure quality care of patients, Stroke 45 (2014) 1589–1601.
[17] N. Nishi, H. Sugiyama, F. Kasagi, et al., Urban-rural difference in stroke mortality from a 19-year cohort study of the Japanese general population: NIPPON DATA80, Soc. Sci. Med. 65 (2007) 822–832.
[18] R. Kalediene, D. Rastenyte, Trends and regional inequalities in mortality from stroke in the context of health care reform in Lithuania, Medicina 52 (2016) 244–249.
[19] A.V. Sergeev, Racial and rural-urban disparities in stroke mortality outside the Stroke Belt, Ethn. Dis. 21 (2011) 307.
[20] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, The PRISMA Group. Preferred re-porting items for systematic reviews and meta-analyses: the PRISMA Statement, PLoS Med. 6 (2009) e1000097.
[21] Veritas Health Innovation, Covidence Systematic Review Software, (2018).
[22] G. Wells, B. Shea, D. O'Connell, et al., The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. Ottawa Hospital Research Institute, (2016).
[23] J.P. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, Stat. Med. 21 (2002) 1539–1558.
[24] P. Govindarajan, R. Gonzales, J.H. Maselli, et al., Regional differences in emergency medical services use for patients with acute stroke (findings from the National Hospital Ambulatory Medical Care Survey Emergency Department Data File), J. Stroke Cerebrovasc. Dis. 22 (2013) e257–e263.
[25] G. Hansen, S. Bal, K.L. Schellenberg, S. Alcock, E. Ghrooda, Prehospital manage-ment of acute stroke in rural versus urban responders, J. Neurosci. Rural Pract. 8 (2017) 33–36.
[26] G.J. Hubert, A. Meretoja, H.J. Audebert, et al., Stroke thrombolysis in a centralized and a decentralized system (Helsinki and Telemedical Project for Integrative Stroke Care Network), Stroke 47 (2016) 2999–3004.
[27] J. Koifman, R. Hall, S. Li, et al., The association between rural residence and stroke care and outcomes, J. Neurol. Sci. 363 (2016) 16–20.
[28] Stroke Foundation, National Stroke Audit Acute Services Report, [online]. Available at https://informme.org.au/en/stroke-data/Acute-audits, (2017) (Accessed 1st March 2018).
[29] O.J. Ekundayo, J.L. Saver, G.C. Fonarow, et al., Patterns of emergency medical services use and its association with timely stroke treatment, Circulation 6 (2013) 262.
[30] S. Gonzales, M.T. Mullen, L. Skolarus, D.P. Thibault, U. Udoeyo, A.W. Willis, Progressive rural–urban disparity in acute stroke care, Neurology 88 (2017)
[31] D. Kleindorfer, Y. Xu, C.J. Moomaw, P. Khatri, O. Adeoye, R. Hornung, US geographic distribution of rt-PA utilization by hospital for acute ischemic stroke, Stroke 40 (2009) 3580–3584.
[32] S. Read, J. Levy, Differences in stroke care practices between regional and metropolitan hospitals, Intern. Med. J. 35 (2005) 447–450.
[33] S. Seabury, K. Bognar, Y. Xu, C. Huber, S.R. Commerford, D. Tayama, Regional disparities in the quality of stroke care, Am. J. Emerg. Med. 35 (2017) 1234–1239.
[34] W. Shultis, R. Graff, C. Chamie, et al., Striking rural-urban disparities observed in acute stroke care capacity and services in the pacific northwest, Stroke 41 (2010) 2278–2282.
[35] D.A. Cadilhac, M.F. Kilkenny, M. Longworth, M. Pollack, C.R. Levi, Metropolitan–rural divide for stroke outcomes: do stroke units make a difference? Intern. Med. J. 41 (2011) 321–326.
[36] M.T. Mullen, S. Judd, V.J. Howard, et al., Disparities in evaluation at certified primary stroke centers: reasons for geographic and racial differences in stroke, Stroke 44 (2013) 1930–1935.
[37] S. Prabhakaran, M. Cox, B. Lytle, et al., Early transition to comfort measures only in acute stroke patients: analysis from the get with the Guidelines-Stroke registry, Neurol. Clin. Pract. 7 (2017) 194–204.
[38] J. Merchant, G. Kitsos, S. Ashby, A. Kitsos, I.J. Hubbard, Occupational therapy and physiotherapy in acute stroke: do rural patients receive less therapy? Stroke Res. Treat. 2016 (2016).
[39] J.C. Hemphill 3rd, J. Newman, S. Zhao, S.C. Johnston, Hospital usage of early do-not-resuscitate orders and outcome after intracerebral hemorrhage, Stroke 35 (2004) 1130–1134.
[40] G. Saposnik, A. Baibergenova, M. O'Donnell, et al., Hospital volume and stroke outcome does it matter, Neurology 69 (2007) 1142–1151.
[41] A. Borhani-Haghighi, R. Safari, S.T. Heydari, et al., Hospital mortality associated with stroke in southern Iran, Iran. J. Med. Sci. 38 (2013) 314.
[42] R. Fleet, S. Bussières, F.K. Tounkara, et al., Rural versus urban academic hospital mortality following stroke in Canada, PLoS ONE 13 (2018) e0191151.
[43] D. Harnod, W.-M. Choi, R.-E. Chang, C.-H. Chang, M.-C. Yang, Are major medical centers better for stroke and myocardial infarction patients in Taiwan? A nationwide population-based study, Int. J. Gerontol. 4 (2010) 137–142.
[44] M.P. Thompson, X. Zhao, K. Bekelis, et al., Regional variation in 30-day ischemic stroke outcomes for medicare beneficiaries treated in get with the Guidelines–Stroke hospitals, Circulation 10 (2017).
[45] J.H. Lichtman, E.C. Leifheit-Limson, S.B. Jones, Y. Wang, L.B. Goldstein, 30-day risk-standardized mortality and readmission rates after ischemic stroke in critical access hospitals, Stroke 43 (2012) 2741–2747.
[46] M.S. Ido, R. Bayakly, M. Frankel, R. Lyn, I.S. Okosun, Administrative data linkage to evaluate a quality improvement program in acute stroke care, Georgia, 2006-2009, Prev. Chronic Dis. 12 (2015) E05.
[47] M.F. Kilkenny, M. Longworth, M. Pollack, C. Levi, D.A. Cadilhac, Factors associated with 28-day hospital readmission after stroke in Australia, Stroke 44 (2013) 2260–2268.
[48] E.M. Davis Jr., Association between Stroke-Related Hospital Discharge Status, Socio-Demographic Characteristics, Insurance Status and Urban-Rural Residence in Tennessee [M.S.], Meharry Medical College, Ann Arbor, 2010.
[49] A. Slivinski, R. Jones, H. Whitehead, V. Hooper, Improving access to stroke care in the rural setting: the journey to acute stroke ready designation, J. Emerg. Nurs. 43 (2017) 24–32.
[50] M.L. Svendsen, L.H. Ehlers, A. Ingeman, et al., Higher stroke unit volume associated with improved quality of early stroke care and reduced length of stay, Stroke. 00392499, 43 (2012) 3041–3045.
[51] R. El Khoury, R. Jung, A. Nanda, et al., Overview of key factors in improving access to acute stroke care, Neurology 79 (2012) S26–S34.
[52] G.C. Fonarow, W. Pan, J.L. Saver, et al., Comparison of 30-day mortality models for profiling hospital performance in acute ischemic stroke with vs without adjustment for stroke severity, JAMA 308 (2012) 257–264.
[53] E. Cumbler, H. Wald, D.L. Bhatt, et al., Quality of care and outcomes for in-hospital ischemic stroke: findings from the national get with the guidelines-stroke, Stroke 45 (2014) 231–238.
[54] V. Langagergaard, K.H. Palnum, F. Mehnert, et al., Socioeconomic differences in quality of care and clinical outcome after stroke: a nationwide population-based study, Stroke 42 (2011) 2896–2902.
[55] E.E. Smith, J.L. Saver, D.N. Alexander, et al., Clinical performance measures for adults hospitalized with acute ischemic stroke performance measures for healthcare professionals from the American Heart Association/American Stroke Association, Stroke 45 (2014) 3472–3498.
[56] J. Mant, Process versus outcome indicators in the assessment of quality of health care, Int. J. Qual. Health Care 13 (2001) 475–480.
[57] T.F. Borders, Advancing the field of rural health research: moving beyond simply documenting rural vs urban differences, J. Rural. Health 33 (2017) 3–4.

3. CHAPTER THREE: Regional differences in access to acute ischaemic stroke care and patient outcomes

The previous chapter provided a summary of existing body of literature describing urban-rural differences in acute stroke care and patient outcomes. Recognising the limitations of the existing literature, the current chapter seeks to describe the regional differences in acute ischaemic stroke care and outcomes within the Australian state of Tasmania.

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Regional differences in access to acute ischaemic stroke care and patient outcomes

In spite of falling incidence rates in recent years (5), stroke continues to place a large burden on society. Stroke is the third leading cause of death in Australia, accounting for around 7% of all deaths in the year 2017 (104). The reduction of Australia's stroke burden has been attributed to, among other factors, advances made in the field of acute stroke care (5). Chiefly among these are the advent of acute stroke unit (ASU) care (60), and the increasing use of thrombolysis for ischaemic stroke (72). Unfortunately, the benefits of these interventions have not been uniformly distributed throughout the population. Several reports commissioned by Australia's Stroke Foundation (3, 62, 105) have highlighted that, when compared to individuals in urban areas, those in rural areas have poorer access to acute stroke care. Whilst these reports employed large samples from a broad range of hospitals, they have tended not to provide risk-adjusted data on patient outcomes.

At the same time, other Australian studies which have addressed regional differences in acute stroke outcomes (94, 96) have had some methodological limitations. Read and Levy's study (94) reported several between-region differences in care, but did not apply any risk adjustment to its outcome measures, and hence may have been vulnerable to residual confounding. The study by Cadilhac et al. (96) accounted for a host of potential confounders; however, its utility was somewhat limited by only measuring in-hospital mortality. For instance, in-hospital mortality figures may be influenced by patients being transferred to separate facilities for palliation (106, 107). Given that the overall burden of stroke is known to be significantly higher in rural areas (3), there is reason to investigate whether the care that stroke patients receive in rural settings, and the associated outcomes, are contributing to this apparent urban-rural divide. Accordingly, the aim of this study was to describe the regional differences in acute ischaemic stroke care and outcomes within the Australian state of Tasmania.

Materials and Methods

We conducted a retrospective study of the management and outcomes of patients admitted with acute ischaemic stroke to Tasmania's four major public hospitals.

Setting

Tasmania is Australia's only island state, and as of June 2018, had an estimated population of 528,000 (48). The majority of the state's population is concentrated in three regions: Hobart, Launceston, and the North West Coast, primarily in the cities of Devonport and Burnie. This study was limited to four hospitals, which are regarded by the Tasmanian Department of Health as being the state's only major public hospitals (108). Other, smaller sites were omitted from the analyses, as stroke patients who present to these sites are invariably transferred to one of the major public hospitals. The Royal Hobart Hospital (RHH) is the state's largest centre, serving a population of approximately 250,000 and with a maximum capacity of 470 beds (109). The Launceston General Hospital (LGH) is a 300-bed centre serving much of the state's north and north east (110). Both the LGH and RHH are equipped with specialist staff in neurology; however, acute stroke care at the LGH is managed by the hospital's General Medical team. The RHH has offered endovascular clot retrieval to eligible patients since 2016; however, this is not a 24-hour service.

The Mersey Community Hospital (MCH) and North West Regional Hospital (NWRH) are located approximately 60 kilometres apart in the state's north west, and have capacities of 100 and 160 beds, respectively (111). The catchment area of these two hospitals spans the entire north west of Tasmania, including King Island (111). In Australia, regions are classified in terms of their remoteness using the Accessibility/Remoteness Index for Australia 2011 (ARIA+) system, which groups areas based on their access to services (112). Under this system the LGH and RHH are situated in 'inner regional' areas, while the MCH and NWRH are in 'outer regional' areas. For the purpose of the current study, the RHH and LGH were classified as 'urban' hospitals, and the MCH and NWRH as 'rural' hospitals.

Sample

This study included patients admitted to one of the four major public hospitals with a principal diagnosis of acute ischaemic stroke (ICD-10-AM codes I63.x, I64) between 1st January 2015 to 8th March 2017. We then excluded those cases which, despite being coded as 'acute ischaemic stroke', were found to be related to other neurological complaints (e.g. Bell's palsy). We also excluded all non-acute episodes of care (e.g. admissions for palliation, rehabilitation), in-hospital strokes, and episodes of care lasting less than 24 hours. Patients who had been transferred between the four hospitals were also excluded, to avoid attributing care and outcomes to a different hospital. We aimed to recruit a convenience sample of 100 cases from each of the four hospitals, giving 200 cases per sub-group (urban/rural). Screening cases by their ICD codes yielded the following sub-samples (RHH = 619, LGH = 390, MCH = 112, NWRH = 196). Cases were then randomly drawn without replacement, using the 'Sample' package in R (113) from these sub-samples until there were 100 eligible cases each from the RHH, LGH and NWRH (i.e. 300 in total from these hospitals) which met the inclusion criteria. A total of 95 cases were included for the MCH, which represented all eligible cases during the study period.

Outcome Variables

This study's key variables were care processes and outcome measures. The care processes of interest were a sub-set of 13 indicators from the *Acute Stroke Clinical Care Standard* (65). This standard was developed by the Australian Commission on Safety and Quality in Health Care, and covers the recognition of stroke, rapid assessment, early management and early initiation of rehabilitation care. The researchers adhered to the *Clinical Care Standard's Indicator Specification* document (114), which stipulates the inclusion and exclusion criteria to be used for each indicator. For example, individuals with documented hypotension are contraindicated for antihypertensive medication, and would therefore be excluded from this indicator. Six of the care processes featured in the *Clinical Care Standard* were excluded

from the audit. Indicators 1A and 1B, which relate to the transport and assessment of stroke patients by ambulance crews, were omitted due to the absence of a reliable operational definition for these variables. Indicator 5A was excluded as it specifically relates to haemorrhagic stroke patients. Indicators 6A, 6B, and 7A relate to ongoing rehabilitation care, and were not collected as we focussed exclusively on episodes of acute care. In addition, two indicators relating to the management of dysphagia, obtained from the National Stroke Data Dictionary (115), were added to the analyses because dysphagia management is regarded as an important component of acute stroke care (116). Patient outcome measures were assessed using 30-day mortality and discharge destination (i.e. usual place of residence vs other).

Data Collection

Data from the Admitted Patient Care National Minimum Data Set (APC NMDS) (117) were obtained via the Tasmanian Health Service (THS). The APC NMDS provides the timestamps of each admission, along with patient demographics (i.e. age, sex) and discharge destination. Admission details were then used to access patients' digital medical records. National Institutes of Health Stroke Scale (NIHSS) (118) scores were retrospectively calculated for each case using the algorithm described by Williams et al. (119). NIHSS scores are routinely used to assess the neurological impairment resulting from stroke, and are also a strong predictor of post-stroke outcomes (120). Mortality data were obtained from the Tasmanian Department of Health, which routinely links patients' unique reference numbers to the National Death Index (88).

Data relating to care process were extracted from medical records and entered into a database using standardised worksheets (121). Error checks were incorporated into the tool to prevent the collection of illogical data. In each instance where a patient was ineligible for a given care process (e.g. due to contraindication), this was checked by a second researcher.

Two abstractors completed half of the MCH and NWRH cases each, while all of the LGH and RHH cases were abstracted by the main researcher (MD). Data abstracted from medical records was reviewed for completeness by MD; missing data were added in a second round of data abstraction.

Data Analysis

In order to test for regional differences in patient characteristics, categorical variables were compared between regions using chi-square tests, while mean ages and median length of stay (LOS) were compared using an independent samples t-test and a Mann-Whitney U-test, respectively. Care processes were expressed as the proportion of eligible patients from each region who received each form of care and analysed using Fisher's Exact test. LOS was calculated by subtracting each case's discharge timestamp from the timestamp of the patient's admission to hospital (i.e. as opposed to their presentation to an ED).

Logistic regression models were used to quantify urban-rural differences in 30-day mortality and patient discharge destination. Outcome measures used individual-level data but were analysed at the level of the region (i.e. urban or rural). Hospital variation was accounted for by using a cluster variable for each hospital in the models. We adjusted for patient characteristics which may have accounted for regional differences in outcomes; these factors were purposefully selected because they were associated with the outcome and the exposure. NIHSS scores were dichotomised into Mild (NIHSS $\leqslant$7) and Moderate/Severe (NIHSS 8+) for the purpose of reporting and analyses, as has been done previously (75, 122, 123). A forward stepwise procedure was then used to determine the final regression model that included the review of nested models and analysis of likelihood ratio tests. Data were analysed using R (113). Ethical approval to conduct this study was obtained from the Human Research Ethics Committee of Tasmania (application H0016053).

Results

The study sample consisted of 395 patients, of whom 195 (49%) were admitted to rural hospitals. Baseline characteristics of study patients are shown in Table 1. Patients admitted to rural hospitals were more likely to have a comorbid diagnosis of atrial fibrillation (AF; 27.2% vs 16.5%, p = .01) but less likely to be tobacco users (8.7% vs 15.5%, p = .045). There were no statistically significant differences between regions on any of the other measures.

Table 1. Patient Characteristics

	Overall	**Urban (n=200)**	**Rural (n=195)**	**P value**
	%	n (%)	n (%)	
Mean Age (SD), years	71.4	70.9 (13.9)	71.9 (13.2)	.45
Female	39	82 (41)	72 (36.9)	.47
Stroke Risk Factors				
Atrial Fibrillation	21.8	33 (16.5)	53 (27.2)	.01*
Ischaemic Heart Disease	5	10 (5)	10 (5.1)	1.00
Diabetes	23.8	51 (25.5)	43 (22.1)	.49
Hypertension	45.8	83 (41.5)	98 (50.2)	.10
Tobacco Use	12.1	31 (15.5)	17 (8.7)	.05*
Previous Stroke	9.4	18 (9)	19 (9.7)	.80
rNIHSS Score				
Mild (NIHSS ≤7)	82.8	161 (80.5)	166 (85.1)	.28
Moderate/Severe (NIHSS 8+)	17.2	39 (19.5)	29 (14.9)	-
Discharged Home	50.1	94 (47)	104 (53.3)	.21
In-hospital Mortality	9.1	16 (8)	20 (10.3)	.55
30-day Mortality	10.6	22 (11)	20 (10.3)	.94
Median LOS[1] (IQR), days	5.9 (3.0-9.8)	6.0 (3.1-9.4)	5.9 (3.0-9.8)	1.00

[1]LOS = length of stay
*p<.05

Data collected in relation to care processes are presented in Table 2 (Appendix); national average figures obtained from the Stroke Foundation's 2017 National Stroke Audit Acute Services Report (62) and the Australian Stroke Clinical Registry (AuSCR), where applicable (86). No patients admitted to the state's rural hospitals received thrombolysis, nor did any receive treatment in an ASU. Patients admitted to rural hospitals were, overall, less likely to receive risk factor modification advice and secondary prevention medication prescription on discharge. These differences were most pronounced in the number of patients prescribed oral anticoagulants, when not contraindicated, for AF (65.3% vs 96.9%, p<.001), and the number

of individuals given documented advice about risk factor modification prior to discharge (45.3% vs 70.2%, p<.05). Patients admitted to rural hospitals were also less likely to be prescribed the combination of statins, antihypertensives and antithrombotic medications (68.9% vs 82.3%, p<.05). It should be noted, however, that there was significant variation between the rural hospitals in terms of prescriptions for antihypertensives. Overall, both regions were comparable in terms of dysphagia screening; however, there was significant variation between the two urban hospitals on these measures.

There were no significant regional differences in terms of patients' discharge destinations after adjustment for age, sex, and NIHSS score (OR = 1.24, 95% C.I. 0.81-1.91). There were also no significant differences between regions in terms of 30-day mortality, after adjustment for age, sex, NIHSS score and Charlson Comorbidity Index score (OR = 0.99, 95% C.I. 0.46-2.18). The presence of a diagnosis of AF was not independently associated with either of the two outcome measures; hence this variable was not included as a covariate in either model.

Discussion

The primary aim of this study was to describe the regional differences in acute ischaemic stroke care within Tasmania. We found that thrombolysis was not administered to any patients admitted to the rural hospitals during the study period. Suboptimal access to thrombolysis in rural areas has been reported numerous times both within Australia (62, 105) and internationally (124, 125), and is acknowledged to be the product of multiple structural and patient-related factors (126). Notwithstanding, progress has been made in this area elsewhere in Australia (127), primarily through the introduction of 'telestroke' services (128). The absence of such a facility in Tasmania would appear to be an obvious impediment to providing thrombolysis in the state's rural areas.

No patients admitted to the study's rural hospitals received care in an ASU, as neither of the study's rural hospitals were equipped with these units. This is a concerning finding, as unlike the case of thrombolysis, all stroke patients may benefit from admission to an ASU (129). Australia's Stroke Foundation (59) recommends that hospitals receiving over 75 acute stroke admissions annually should be equipped with an ASU – a figure which, when combined, this study's nearby rural hospitals would easily surpass (130). The centralisation of acute stroke services has been implemented elsewhere with moderate success (131, 132). Both the Stroke Foundation (133) and a local clinical advisory group (130) have lobbied unsuccessfully to have NW Tasmania's acute stroke services centralised in an ASU located at the NWRH.

We found that patients admitted to the rural hospitals were less likely to receive secondary prevention on discharge; this was particularly the case for patients requiring anticoagulants for AF. It is worth noting, however, that the average among urban hospitals for this indicator (96.9%) was substantially higher than the national average of 70%. Similarly, although the study's rural hospitals were less likely to provide patients with the combination of statins, antihypertensives and antithrombotics on discharge, their performance was almost identical to the national average, and considerably higher than the average among AuSCR hospitals. These findings likely reflect the combined benefit of ASU care and the presence of specialist nursing and neurology staff within the study's urban hospitals.

The secondary aim of this study was to describe urban-rural differences in ischaemic stroke patient outcomes within Tasmania. Despite differences in access to ASU care and thrombolysis, it was pleasing that we did not observe any significant differences between urban and rural patients in terms of 30-day mortality or discharge destination. It is possible that a longer follow-up period is required to detect any differences in mortality outcome

relating to variation in care. For instance, the AuSCR reports risk-adjusted rates of mortality at up to 180 days post-stroke (134).

Our study has several limitations. Firstly, this study was limited to a relatively small sample from only four hospitals, all of which are situated in either 'inner regional' or 'outer regional' areas. The absence of data from large metropolitan centres, and equally, from small remote hospitals, prevents us from drawing conclusions about how stroke care and outcomes differ between these two extremes. Secondly, the study was reliant on the quality of documentation within patients' case notes. Some forms of care (e.g. patient education on risk factors) may be informal in nature, and therefore less likely to be documented than more systematic processes, such as the prescription of medications. The observed regional differences for such indicators may therefore reflect differences in documentation rather than underlying care processes.

Thirdly, when abstracting data on care process measures from patients' medical records, the researchers did not calculate a measure of inter-rater reliability. As an alternative means of maintaining inter-rater reliability, the data abstractors consulted the main researcher with any ambiguities prior to inputting data into the collection tool. A further limitation relates to the absence of a measure of patients' functioning at the time of discharge. The use of a validated measure, such as the mRS, would have provided further information about regional differences in patient outcomes, whilst allowing for comparisons with previous Australian studies which also used the measure (96). Nonetheless, patients' discharge destination has been found to be highly predictive of mRS scores at three months post-stroke (135), and hence may be an appropriate surrogate marker.

Lastly, because patient deaths were relatively infrequent within the follow-up time frame, we were likely underpowered to detect a difference in this outcome measure during hospitalisation or at 30-days post-stroke. In spite of these limitations, our study is the first to

take an in-depth look at the state of acute stroke care and its associated outcomes within Tasmania. These findings will provide a useful baseline to future researchers and policymakers who are seeking to improve the delivery of acute stroke care within the state (e.g. via the potential expansion of new telehealth initiatives).

Conclusion

With the exception of thrombolysis and ASU care, patients treated for stroke in Tasmania's rural hospitals received a standard of care comparable to that of the state's urban hospitals. This is an encouraging finding. Further research is needed, however, to determine which factors influence clinicians' ability to provide acute stroke care in both settings. In addition, we did not observe any significant regional differences in terms of patient outcomes. Future research in this area should employ larger datasets, which capture a broad sample of large metropolitan sites and smaller rural sites.

4. CHAPTER FOUR: Health care providers' perceptions of factors that influence the provision of acute stroke care in urban and rural settings: A qualitative study

Chapter three sought to describe the regional differences in acute ischaemic stroke care and outcomes within the Australian state of Tasmania. The current chapter sought to contextualise these quantitative findings by interviewing clinicians from the subject hospitals, to determine which factors influenced their ability and willingness to provide guideline-recommended acute stroke care.

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Health care providers' perceptions of factors that influence the provision of acute stroke care in urban and rural settings: A qualitative study

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Abstract

Objectives: Individuals living in rural areas have comparatively less access to acute stroke care than their urban counterparts. Understanding the local barriers and facilitators to the use of current best practice for acute stroke may inform efforts to reduce this disparity.

Methods: A qualitative study featuring semi-structured interviews and focus groups was conducted in the Australian state of Tasmania. Clinical staff from a range of disciplines involved in acute stroke care were recruited from three of the state's four major public hospitals (one urban and two rural). A semi-structured interview guide based on the findings of an earlier quantitative study was used to elicit discussion about the barriers and facilitators associated with providing acute stroke care. An inductive process of thematic analysis was then used to identify themes and subthemes across the data set.

Results: Two focus groups and five individual interviews were conducted. Four major themes were identified from analysis of the data: systemic issues, clinician factors, additional support and patient-related factors. Acute stroke care within the study's urban hospital was structured and comprehensive, aided by the hospital's acute stroke unit and specialist nursing support. In contrast, care provided in the study's rural hospitals was somewhat less comprehensive, and often constrained by an absence of infrastructure or poor access to existing resources.

Conclusion: The identified factors help to characterise acute stroke care within urban and rural hospitals and will assist quality improvement efforts in Tasmania's hospitals.

Keywords

Neurology, nursing, acute stroke, emergency medicine

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Introduction

Stroke continues to place a heavy burden on our society. On a global scale, stroke accounts for 5.5 million deaths annually, and personally affects one in four people during their lifetime.[1] Within Australia, stroke is the third leading cause of death,[2] costing the Australian economy in the order of $5 billion annually.[3] Thankfully, the management of acute stroke has evolved from an era of therapeutic nihilism[4] to one in which numerous evidence-based interventions are readily available. Indeed, contemporary models of acute stroke care typically involve a host of different nursing, medical and allied health professionals, beginning with the delivery of hyperacute therapies and concluding with the patient's rehabilitation.[5,6] In many developed nations, these treatment modalities have been collated into sets of guidelines, in an effort to bridge the divide between evidence and clinical practice.[7] A key example of this is the Australian Commission on Safety and Quality in Health Care's *Acute Stroke Clinical Care Standard*, which outlines the care that patients with stroke should expect to receive within Australian hospitals.[8]

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Regrettably, the care processes which comprise the *Clinical Care Standard* are not used ubiquitously, with individuals in Australia's rural areas seemingly having inferior access to acute stroke care.[9,10] In order to begin to address this disparity, it is necessary to understand the factors which may influence clinicians' ability to provide care in line with what is considered current best practice.[11] Moloczij et al.[12] interviewed nursing and medical staff in a regional Victorian hospital, finding that the clinicians' main barrier to using telemedicine consults with metropolitan centres was their scepticism of the use of thrombolysis. This study and several others in the area of acute stroke[13] have been exclusively concerned with the delivery of thrombolysis. Very few studies have examined the factors influential to acute stroke management in its entirety,[14] and fewer still have looked at how such factors may differ between urban and rural contexts. The aim of this study was to interview clinicians located in urban and rural settings, to determine which factors influence their ability and willingness to provide guideline-recommended acute stroke care.

Methods

Study design

This qualitative study was undertaken as part of a broader, mixed method sequential explanatory study. Semi-structured interviews and focus groups were used to explore with clinicians the barriers and facilitating factors they experience when providing acute stroke care, and whether there are differences between urban and rural settings.

Participants and settings

This study took place in the Australian state of Tasmania, which has an estimated population of 528,000.[15] Tasmania has four tertiary level health care centres, the largest of which is the Royal Hobart Hospital (RHH), with a maximum capacity of 470 beds.[16] The Launceston General Hospital (LGH), with 300 beds, serves much of the state's north and north east.[17] Both the LGH and RHH have neurology staff on-site. The Mersey Community Hospital (MCH) and North West Regional Hospital (NWRH) are smaller rural hospitals with capacities of 100 and 160 beds, respectively.[18] Acute stroke cases presenting to the MCH and NWRH are handled by general medical physicians. In Australia, regions are classified in terms of their remoteness using the Accessibility/Remoteness Index for Australia 2011 (ARIA+) system, based on access to services.[19] According to this system, the MCH and NWRH are in 'outer regional' areas, while the LGH and RHH are situated in 'inner regional' areas. For the purpose of this study, the MCH and NWRH were regarded as 'rural' hospitals, while the RHH is referred to as an 'urban' hospital.

Participants were purposefully selected clinical staff from the RHH, MCH and NWRH. Clinicians from the LGH were not recruited for this study; the researchers were primarily concerned with describing the contrast between urban and rural settings, as opposed to the experience of acute stroke care within all four of Tasmania's hospitals. In order to be considered for recruitment, clinicians were required to be involved in the delivery of 'acute stroke care' as defined by the Australian Commission on Safety and Quality in Health Care's *Acute Stroke Clinical Care Standard*.[8] These included clinicians from a range of health professions, including general medicine, neurology, nursing, pharmacy and physiotherapy.

Staff specialists at all three hospitals were contacted via email and asked for details of a regular meeting in their hospitals which would be an appropriate forum for conducting a focus group. Staff specialists were also asked to nominate potential participants to be involved in individual interviews. Those nominated were contacted and asked to participate in interviews, and to nominate any other clinicians with relevant experience in the provision of acute stroke care. Participants were given the option of participating in a focus group, interview or both. Those who agreed to participate in either a focus group or interview provided their written consent after being provided with an information sheet outlining the aims of the study. All focus groups and interviews were conducted in meeting rooms inside the participants' place of work. No individuals other than the researcher and participants were present during focus groups and interviews.

Data collection

A semi-structured interview guide was used to elicit discussion in both focus groups and interviews (Supplemental Material 1). The interview guide was based on the care processes which comprise the abovementioned *Clinical Care Standard*,[8] and are detailed in Table 1.[20] For each care process, the lead researcher (M.D., a male PhD candidate) asked participants for an explanation of how the process worked, and a description of the factors that helped or hindered this. All interviews and focus groups were audio recorded and transcribed verbatim by a third party. The lead researcher used field notes and memos written following focus groups and interviews to advance and contextualise data analysis. Data collection ceased once data saturation was achieved (i.e. when the barriers or facilitators that emerged from the data became repetitive and there were no more new findings). Reporting of the data was guided by the consolidated criteria for reporting qualitative research (COREQ) (Supplemental Material 2).

Data analysis

The researchers used an inductive approach to thematic analysis, in accordance with the six phases described by Braun et al.[21] This began with the lead researcher reading and re-reading the transcripts making initial analytical observations about the data. Coding was data-driven and the initial coding helped to organise the data into meaningful groups. Coding was through the software programme NVivo version 12.[22] The codes were then sorted to form themes and subthemes.

Table 1. Care processes discussed during focus groups and interviews.

- Transport to a hospital able to provide thrombolysis
- Thrombolysis in ischaemic stroke (with exclusions)
- Presentation and intravenous thrombolysis within 4.5 h of symptom onset
- Thrombolysis within 60 min of hospital arrival
- Time from onset of symptoms to thrombolysis
- Admission into a stroke unit
- 90% of acute hospital admission episode time spent on a stroke unit
- Assessment for rehabilitation by a physiotherapist within 48 h of admission
- Rehabilitation therapy within 48 h of initial assessment
- Treatment for a rehabilitation goal commencing during an acute admission
- Discharge on statin, antihypertensive and antithrombotic medications
- Discharge on oral anticoagulants for atrial fibrillation
- Risk factor modification advice before leaving the hospital
- Dysphagia screening within 24 h
- Dysphagia screen passed before first oral intake of fluids, nutrition or medications

Themes were reviewed and refined and then named and defined. Two other researchers (K.F. and K.M.F.) cross-checked the outcomes of this process.

Ethical considerations

Ethical approval to conduct this study was obtained from the Human Research Ethics Committee of Tasmania (application number H0017665).

Results

A total of five individual interviews and two focus groups were conducted. The researchers deemed that no further focus groups or interviews were required after getting sufficient representation from the various clinical groups (and achieving data saturation) in the initial round. Table 2 provides an overview of the participating clinicians from each region. All of the clinicians who were invited to be interviewed agreed to do so. The first focus group was conducted at the NWRH as part of this hospital's weekly general medical team meeting. Present during this focus group were five members of this hospital's general medical team and one physician based at the MCH. The second focus group was held at the RHH during the hospital's neurology department's weekly meeting, and included six members of the hospital's neurology team, along with one resident medical officer. Individual interviews were conducted with one pharmacist each from the NWRH and RHH, and one physiotherapist each from the NWRH and RHH. In addition, one individual interview was conducted with a senior nurse from the RHH. All sessions lasted between 30 min and 1 h. There were no clinicians who participated in both a focus group and an interview.

Table 2. Participant characteristics.

Interviews	Urban	Rural
Male	–	1
Female	3	1
Pharmacists	1	1
Senior nurse	1	–
Physiotherapists	1	1
Focus groups		
Male	4	5
Female	4	1
General medical physicians	1	6
Neurologists	7	–

Themes

The following four overarching themes were identified from analysis of the focus groups and interview data: systemic issues, clinician factors, additional support and patient-related factors. Each theme was divided into a series of subthemes to provide structure and to demonstrate the hierarchy of meaning within the data.

Systemic issues

This theme refers to the way in which the surveyed hospitals were configured to deliver stroke care. Three subthemes within the theme systemic issues were: protocols, infrastructure and staffing.

Protocols. Several clinicians mentioned the role that established protocols play in their provision of acute stroke care. One urban clinician stated that the use of a discharge checklist covering medications and lifestyle modification advice improved their ability to provide patients with these aspects of care. In contrast, rural clinicians noted that the absence of such a checklist from their hospitals was a barrier to providing recommended medications and lifestyle modification advice. Other clinicians based in the large urban hospital referred to several protocols which they believed facilitated stroke care. These were the use of blanket physiotherapy referrals for stroke, multidisciplinary meetings and the use of sequential screening for dysphagia. Finally, a rural-based speech pathologist commented that the timely assessment of patients for dysphagia was facilitated by a stroke protocol which required speech pathologists to service their hospitals' emergency department (ED).

Infrastructure. It was acknowledged that the smaller rural hospitals did not have an acute stroke unit (ASU). Urban neurologists mentioned that their ability to use computed

tomography (CT) perfusion imaging (as opposed to conventional CT imaging) improved their ability to offer thrombolysis. The urban neurologists also mentioned that the capacity of the wider hospital impacted their ability to admit stroke patients under the hospital's ASU. The RHH ASU is situated inside the hospital's medical specialties ward and does not have any quarantined beds of its own. This, in turn, meant that demand for beds from other medical specialties could prevent stroke patients from reaching the ASU. Similarly, the need for the RHH to clear patients from its ED and intensive care unit (ICU) often resulted in patients becoming medical outliers (i.e. where patients were admitted to wards other than their 'home' ward).[23] An urban physiotherapist noted that such patients may have, in turn, experienced delays to their physiotherapy assessments, given that they were not 'flagged' as stroke patients:

> If we haven't got enough beds here to put people in; they outlie wherever around the hospital wherever there's a bed. So, there's not a lot of thought goes into it. And then it's all driven by ED because you might have someone, say, for example, over on a ward that's been there for three days and you really want to get them to the Stroke Unit, but if there's someone in ED, no matter if they're a stroke or something else, they get priority because it's all about ED. (Senior Nurse, RHH)

Staffing. Staffing constraints were identified as a barrier to the assessment and treatment of dysphagia in the urban hospital. In this hospital, initial assessments for dysphagia were generally conducted by ED nursing staff, with subsequent treatment handled by speech pathology. A shortage of speech pathologists and a lack of ED nursing staff capable of screening patients for dysphagia were both reported by the hospital's neurologists. The issue of staffing in relation to workload was also identified. Physiotherapists at both urban and rural sites cited their excessive workload as being the main reason why they were unable to assess patients in a timely manner. Urban physiotherapists regarded the use of a weekend physiotherapy service and dedicated stroke physiotherapists as being beneficial to providing patients with timely assessment and treatment. Conversely, in the smaller rural hospitals, staffing physiotherapy on weekends was seen to be inadequate and of little benefit to patients recovering from stroke. This was because the rural hospitals' weekend service was staffed with only one physiotherapist, and priority was given to orthopaedic patients.

Clinician factors

This theme captures how the attitudes and beliefs of clinicians influenced the delivery of acute stroke care. Three subthemes were established under the theme of clinician factors; these were prescribing styles, clinician preferences and protocol adherence.

Prescribing styles. There were clear differences between regions in terms of how medications were prescribed. General medical physicians from the rural hospitals held varying perspectives on how aggressively certain risk factors (e.g. hypertension) should be treated in the wake of stroke. This was corroborated by a pharmacist from one of the rural hospitals. The same rural pharmacist noted that rural doctors may have lacked familiarity with certain medicines (e.g. newer generation antithrombotic treatments for atrial fibrillation) causing them to defer the task of prescription to outpatient cardiologists or general practitioners (GPs). Neurologists from the RHH attributed their relatively higher rates of prescription to a handful of reasons. One urban neurologist believed that they were 'vigilant' when it came to prescribing recommended medications, and hesitant to rely upon other clinicians (e.g. GPs) to initiate medications:

> I guess maybe we're cynical and we realise that if we leave decisions for other people to make regarding medications that they don't always happen. (RHH Neurologist)

The same clinician pointed out that urban neurologists often used magnetic resonance imaging (MRI) scans to determine the source of a stroke. This, in turn, made it easier for the neurologists to identify and target specific risk factors. Another urban neurologist speculated that the supervision available to junior clinicians at the RHH from their superiors might be greater than in the rural hospitals, and that this may have facilitated the prescription of recommended medications.

Clinician preferences. Clinicians from all three hospitals generally agreed that some of the care processes featured in the *Acute Stroke Clinical Care Standard* were not appropriate to be measured in their hospitals. This was particularly the case for the variables relating to the pre-hospital and ED assessment of individuals suspected of having a stroke. ED doctors emphasised that the process of assessing stroke patients in an ED was not amenable to a 'tick box' exercise, such as the F.A.S.T. tool,[24] as is suggested in the *Acute Stroke Clinical Care Standard*. ED doctors further noted that stroke cases present with a variety of symptoms, and the process for assessing these patients invariably works through a range of differential diagnoses before arriving at a provisional diagnosis of stroke. On a related note, urban neurologists mentioned that the neurological examinations performed by ED doctors were sometimes inadequate to identify all stroke presentations, leading to a delay in the stroke protocol being activated. One urban nurse also noted that some of the hospital's ED doctors were not entirely supportive of using thrombolysis for acute ischaemic stroke.

Physiotherapists from both regions and one senior nurse from the RHH did not believe it was appropriate to measure 'written care plans' or 'carer needs assessment/training' at their sites. The clinicians agreed that such processes were

more closely aligned with rehabilitation care within the Tasmanian system, which was typically provided on a separate ward. One rural physiotherapist speculated that these indicators were written in the context of larger urban hospitals, which may have less of a demarcation between the acute and rehabilitation care provided to stroke patients. Finally, a senior nurse from the RHH also noted that clinicians involved in hospital bed allocation were at times unaware of the benefits of ASU care over conventional ward care. In her view, this increased the likelihood of stroke patients being allocated to outlying wards instead of the hospital's ASU.

Protocol adherence. Several clinicians mentioned how their colleagues' reluctance to comply with stroke care protocols presented a barrier to delivering best practice care. For instance, speech pathologists from the rural hospitals noted that once patients had been started on the stroke care pathway, it was common to see 'nil by mouth' patients being given food and oral medications. The same phenomenon was reported by an urban neurologist.

Additional support

This theme covers instances where clinicians acted beyond the scope of their usual roles to assist colleagues in providing aspects of acute stroke care. This theme contained subthemes in relation to the role of each hospital's pharmacy department and the RHH's expert clinical nurse consultant (CNC).

Pharmacy. An urban pharmacist highlighted that while it was the primary responsibility of the neurology department to prescribe secondary prevention medications, pharmacists had a facilitating role in this process. By attending ward rounds and multidisciplinary meetings, urban pharmacists had the opportunity to make suggestions about medications which may have otherwise been overlooked by medical staff. The same pharmacist also noted that having the ability to conduct multiple medication reconciliations throughout a stroke patient's admission increased the likelihood of patients being discharged with the necessary and correct medications. A senior physician based at one of the rural hospitals noted that the absence of pharmacists from their ward rounds was a barrier to prescribing the necessary medications for patients. One medical registrar from the NWRH also mentioned that pharmacy would typically only audit patients' medication at admission and discharge, missing opportunities to identify instances where medications had not been charted.

Expert CNC involvement. Clinicians in one of the rural hospitals acknowledged that the absence of an expert CNC and ASU at their site was barriers to providing patients with advice about reducing their risk of another stroke:

> This is why a proper stroke unit or a dedicated unit is really important, because everything is geared towards not just the rehab or the medicine, but patient information and patient education and relatives' education. (NWRH General Medical Physician)

A senior nurse described the facilitating role of the expert CNC in a range of different processes which were not their primary responsibility. This included assisting with allied health referrals, completing dysphagia assessments and ensuring that patients were prescribed all the necessary discharge medications. One urban pharmacist also noted that the hospital's expert CNC engaged with patients and provided them with tailored advice on reducing their risk of secondary stroke.

Patient-related factors

This theme refers to instances where patients' characteristics influenced clinicians' ability to provide the patient with best practice care. Neurologists and a senior nurse from the RHH mentioned how patient behaviour was particularly relevant to the provision of thrombolysis, which requires patients (or their significant others) to identify stroke symptoms and seek medical assistance in a timely manner:

> . . . it's the patient factor, so it's being either witnessed onset or being found early. It's then somebody calling an ambulance you know as soon as they're found. And so, to me that's public education which is hopefully going to improve this year with some extra money. (Urban neurologist)

The same group of clinicians noted that patients who presented with atypical symptoms also presented a challenge to the timely delivery of care. This was particularly the case for posterior circulation strokes, which were often mistaken for more common neurological complaints, and triaged as non-urgent cases as a result. This initial misdiagnosis was associated with delays (and subsequent contraindication) to thrombolysis and delays to dysphagia screening. Finally, one rural clinician reported that providing patients with information on modifying their lifestyle to reduce their risk of stroke was difficult in patients with poor engagement.

Discussion

This study aimed to identify barriers and facilitators to the provision of acute stroke care in urban and rural settings. The overall barriers and facilitating factors are discussed in the context of existing literature below.

Barriers

Bed shortages in the urban hospital were seen to impact clinicians' ability to treat their patients within the hospital's ASU. These findings are consistent with an earlier audit conducted by Australia's National Stroke Foundation. The Foundation's 2017 *Acute Services Report*[9] highlighted that while 75% of surveyed hospitals had stroke units, only 45% of patients spent the majority (i.e. 90% or more) of their

hospital admission in ASUs. Staffing and workload constraints were viewed by rural clinicians as a barrier to treating patients in a timely manner. These findings align with that of Lindsay et al.,[25] who reported that high caseloads and staff shortages were among the main workplace stressors encountered by a cohort of physiotherapists from regional Victoria, Australia. The introduction of a limited weekend physiotherapy service in the smaller rural hospitals to address this issue was seen to be of little benefit, given the emphasis placed on non-stroke patients. This issue of service prioritisation (or rationing) was previously identified by Adams et al.[26] as a major barrier to providing physiotherapy services within Australia's rural areas.

The general medical teams of the rural hospitals were somewhat less accustomed to treating acute stroke patients than their urban counterparts. This is likely due to the specialist nature of the urban hospital's neurology team, and the hospital's relatively higher patient volumes. The rural hospitals, however, are staffed by general medical physicians for whom acute stroke cases represent only a small proportion of their admissions. Previous studies have reported associations between higher stroke patient volumes and improved care[27] and outcomes.[28] This could be achieved in Tasmania by having acute stroke services for both rural hospitals amalgamated into one ASU located in the NWRH,[29] as has been suggested by local clinicians previously. The absence of a stroke CNC within the rural hospitals was viewed as a significant barrier to counselling patients about their lifestyle behaviours. This finding adds to an existing body of literature documenting the beneficial effect of specialist nursing care on the care and outcomes of individuals who have experienced a stroke.[30] It is foreseeable that with an increase in patient volumes, smaller rural sites such as the NWRH could justify employing a stroke CNC. Delays in stroke symptom recognition (e.g. by patients or their significant others) were associated with delays to thrombolysis. Patient symptom recognition is a commonly reported barrier which has been described at length by previous authors.[31–33] Similarly, clinicians' recognition of stroke symptoms was viewed by urban clinicians as being a barrier to providing care. This was particularly the case for patients with posterior circulation strokes undergoing investigation in the hospital's ED. The issue of misdiagnosis in posterior stroke and its impact on patient outcomes have been identified by previous authors.[34–36] An increased use of MRI[37,38] and the use of novel stroke screening tools[39,40] are among the interventions which have been proposed to decrease the rate of misdiagnosis.

Facilitating factors

The management of stroke patients within the large urban hospital was facilitated by a comprehensive, vigilant and team-oriented approach towards patient care. The urban hospital also had a strongly protocol-driven approach towards acute stroke care, central to which was the role of the hospital's expert CNC. These protocols (e.g. multidisciplinary care) are hallmarks of ASU care,[41,42] and therefore likely reflect the beneficial impact of this hospital's ASU on stroke care. In terms of early rehabilitation, the presence of dedicated stroke physiotherapists and an adequate weekend service within the urban hospital facilitated the timely treatment of patients. The level of pharmacy involvement in care planning influenced the extent to which patients received the necessary medications in both regions. This is consistent with the findings of a recent systematic review,[43] which reported that increased pharmacy involvement in stroke care was associated with an increase in the use of evidence-based therapies, medication adherence and risk factor target achievement.

This study contains some limitations which must be addressed. Our study was limited to three hospitals, all of which are located within one state of Australia. Moreover, this study applied definitions of 'urban' and 'rural' to areas of Australia which are technically classified as inner and outer regional areas. Both of the above factors mean that our findings may not be generalisable to other contexts, particularly those in large metropolitan areas and remote areas. Second, although this study sought to involve all clinicians involved in the provision of acute stroke care, this was not achieved in practice. Within both focus groups, the majority of comments were made by senior male clinicians, with relatively little input from junior clinicians. This may reflect the gender distributions within the clinicians' professions, and also the fact that senior clinicians are typically influential people who generally determine clinical practice. The experiences of junior and senior clinicians are likely to differ greatly, meaning that our findings may not be generalisable to all levels of clinicians. Future researchers in this field may consider targeting junior clinicians for individual interviews, as opposed to focus groups held in the company of their superiors. As a final limitation, it should be acknowledged that the interview guide used in this study had not been validated or pilot-tested prior to being used. To the best of the authors' knowledge, this is the first study to interview clinicians in urban and rural settings about the barriers and facilitators they encounter in providing acute stroke care. This information will be useful to policymakers seeking to reduce regional disparities in access to acute stroke care. This study's findings may also assist clinicians to adapting models of acute stroke care from urban hospitals to rural settings.

Conclusion

This study identified barriers and facilitating factors experienced by clinicians responsible for delivering a range of acute stroke care processes in urban and rural settings. Care provided in the study's urban hospital was facilitated by a host of policies and procedures, which centred around the hospital's ASU and the role of its expert CNC. Systemic issues and the misidentification of stroke symptoms – by patients or clinicians – were the primary barriers to patients accessing this pathway. The smaller rural hospitals, in

contrast, were less comprehensive in their delivery of acute stroke care, and would likely benefit increasing patient volumes by merging all acute stroke services into one hospital. Future researchers in this area are encouraged to obtain the perspectives of both junior and senior clinicians.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

Written informed consent was obtained from all subjects before the study.

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Supplemental material

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References

1. World Stroke Organization. Global stroke impact, https://www.world-stroke.org/publications-and-resources/resources/global-stroke-fact-sheet, 2019.
2. Australian Bureau of Statistics. Australia's leading causes of death, 2015, 2016. http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2015~Main%20Features~Australia's%20leading%20causes%20of%20death,%202015~3
3. Deloitte Access Economics. The economic impact of stroke in Australia: scoping cost effective prevention, 2013, https://www2.deloitte.com/au/en/pages/economics/articles/economic-impact-stroke-australia.html
4. Damani R. A brief history of acute stroke care. *Aging* 2018; 10(8): 1797–1798.
5. Smith EE, Saver JL, Alexander DN, et al. Clinical performance measures for adults hospitalized with acute ischemic stroke performance measures for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014; 45(11): 3472–3498.
6. Boulanger J, Lindsay M, Gubitz G, et al. Canadian stroke best practice recommendations for acute stroke management: prehospital, emergency department, and acute inpatient stroke care, update 2018. *Int J Stroke* 2018; 13: 949–984.
7. Jabbour M, Newton AS, Johnson D, et al. Defining barriers and enablers for clinical pathway implementation in complex clinical settings. *Implement Sci* 2018; 13(1): 139.
8. Australian Commission on Safety and Quality in Health Care. Acute stroke clinical care standard, 2017, https://www.safetyandquality.gov.au/our-work/clinical-care-standards/acute-stroke-clinical-care-standard/
9. Stroke Foundation. National stroke audit acute services report, 2017, https://informme.org.au/en/stroke-data/Acute-audits
10. Stroke Foundation. National stroke audit: acute services report, 2015, https://informme.org.au/en/stroke-data/Acute-audits
11. Tavender EJ, Bosch M, Fiander M, et al. Implementation research in emergency medicine: a systematic scoping review. *Emerg Med J* 2016; 33(9): 652–659.
12. Moloczij N, Mosley I, Moss K, et al. Is telemedicine helping or hindering the delivery of stroke thrombolysis in rural areas? A qualitative analysis. *Intern Med J* 2015; 45: 957–964.
13. Paul CL, Ryan A, Rose S, et al. How can we improve stroke thrombolysis rates? A review of health system factors and approaches associated with thrombolysis administration rates in acute stroke care. *Implement Sci* 2016; 11: 51.
14. Baatiema L, de-Graft Aikins A, Sav A, et al. Barriers to evidence-based acute stroke care in Ghana: a qualitative study on the perspectives of stroke care professionals. *BMJ Open* 2017; 7(4): e015385.
15. Australian Bureau of Statistics 3101.0 – Australian demographic statistics, 2018, http://www.abs.gov.au/ausstats/abs@.nsf/mf/3101.0
16. Department of Health and Human Services. Royal Hobart Hospital, 2019, https://www.dhhs.tas.gov.au/hospital/royal-hobart-hospital/information_for_patients_and_visitors2/rhh_patient_information_guide/welcome
17. Department of Health and Human Services. Launceston General Hospital, 2019, https://www.dhhs.tas.gov.au/hospital/launceston-general-hospital
18. Department of Health and Human Services. Tasmanian Health Service – North West Region, 2019, https://www.dhhs.tas.gov.au/career/home/medical/junior_docs/more_information_-_north_west_area_health_service
19. Hugo Centre for Migration and Population Research. Accessibility/Remoteness Index of Australia (ARIA), 2019, https://www.adelaide.edu.au/hugo-centre/services/aria#advantages-of-aria
20. Australian Commission on Safety and Quality in Health Care. Indicator specification: acute stroke clinical care standard, 2015, https://www.safetyandquality.gov.au/publications/acute-stroke-indicator-specification/
21. Braun V, Clarke V, Hayfield N, et al. Thematic analysis. In: Liamputtong P (ed.) *Handbook of research methods in health social sciences*. Singapore: Springer, 2019, pp. 843–860.
22. QSR International. *NVivo qualitative data analysis software*. 10th ed. Melbourne, VIC, Australia: QSR International, 2012.
23. Santamaria JD, Tobin AE, Anstey MH, et al. Do outlier inpatients experience more emergency calls in hospital? An observational cohort study. *Med J Aust* 2014; 200(1): 45–48.
24. Kleindorfer DO, Miller R, Moomaw CJ, et al. Designing a message for public education regarding stroke: does FAST capture enough stroke? *Stroke* 2007; 38(10): 2864–2868.
25. Lindsay R, Hanson L, Taylor M, et al. Workplace stressors experienced by physiotherapists working in regional public hospitals. *Aust J Rural Health* 2008; 16(4): 194–200.

26. Adams R, Jones A, Lefmann S, et al. Rationing is a reality in rural physiotherapy: a qualitative exploration of service level decision-making. *BMC Health Serv Res* 2015; 15: 121.
27. Svendsen ML, Ehlers LH, Ingeman A, et al. Higher stroke unit volume associated with improved quality of early stroke care and reduced length of stay. *Stroke* 2012; 43(11): 3041–3045.
28. Saposnik G, Baibergenova A, O'Donnell M, et al. Hospital volume and stroke outcome does it matter? *Neurology* 2007; 69: 1142–1151.
29. Department of Health and Human Services. Neurology and Stroke Clinical Advisory Group: response to green paper, 2015, https://www.dhhs.tas.gov.au/__data/assets/pdf_file/0007/186541/CAG_-_Neurology_and_Stroke_-_Submission.pdf
30. Paley L, Williamson E, Bray BD, et al. Associations between 30-day mortality, specialist nursing, and daily physician ward rounds in a National Stroke Registry. *Stroke* 2018; 49(9): 2155–2162.
31. Meurer WJ, Majersik JJ, Frederiksen SM, et al. Provider perceptions of barriers to the emergency use of tPA for acute ischemic stroke: a qualitative study. *BMC Emerg Med* 2011; 11: 5.
32. Lecouturier J, Murtagh MJ, Thomson RG, et al. Response to symptoms of stroke in the UK: a systematic review. *BMC Health Serv Res* 2010; 10: 157.
33. Kurz M, Kurz K and Farbu E. Acute ischemic stroke – from symptom recognition to thrombolysis. *Acta Neurol Scand* 2013; 127: 57–64.
34. Merwick Á and Werring D. Posterior circulation ischaemic stroke. *BMJ* 2014; 348: g3175.
35. Sarraj A, Medrek S, Albright K, et al. Posterior circulation stroke is associated with prolonged door-to-needle time. *Int J Stroke* 2015; 10(5): 672–678.
36. Lever NM, Nystrom KV, Schindler JL, et al. Missed opportunities for recognition of ischemic stroke in the emergency department. *J Emerg Nurs* 2013; 39(5): 434–439.
37. Markus HS, van der Worp HB and Rothwell PM. Posterior circulation ischaemic stroke and transient ischaemic attack: diagnosis, investigation, and secondary prevention. *Lancet Neurol* 2013; 12(10): 989–998.
38. Yew KS and Cheng EM. Diagnosis of acute stroke. *Am Fam Physician* 2015; 91: 528–536.
39. Yamada S, Yasui K, Kawakami Y, et al. DEFENSIVE Stroke Scale: novel diagnostic tool for predicting posterior circulation infarction in the emergency department. *J Stroke Cerebrovasc Dis* 2019; 28: 1561–1570.
40. Kuroda R, Nakada T, Ojima T, et al. The TriAGe+ score for vertigo or dizziness: a diagnostic model for stroke in the emergency department. *J Stroke Cerebrovasc Dis* 2017; 26(5): 1144–1153.
41. Langhorne P and Pollock A. What are the components of effective stroke unit care? *Age Ageing* 2002; 31(5): 365–371.
42. Stroke Unit Trialists Collaboration. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev* 2013; 9: CD000197.
43. Basaraba JE, Picard M, George-Phillips K, et al. Pharmacists as care providers for stroke patients: a systematic review. *Can J Neurol Sci* 2018; 45(1): 49–55.

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

Recognising the limitations of the manual case note audit conducted as part of chapter three, the current chapter aimed to build upon this research by employing a much larger sample of data from the Australian Stroke Clinical Registry (AuSCR).

This work was submitted to *BMJ Open* on 13th May 2020, and is currently under review.

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

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 (136). 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 (136), and is characterised by studies with inadequate risk adjustment (137-139), or an indirect focus on urban-rural differences in outcomes (140-142). Previous attempts to explore this issue have also been reliant on 'hard' outcome measures such as rates of mortality and readmission (143-145); whereas regional differences in patients' quality of life has been rarely investigated (146, 147). 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 (85). 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) (134). 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 (85); during the study period less than 3% of potential participants opted out of the registry. Flow charts detailing the number of patients lost to follow-up during each year of the study period are contained in Appendix J. 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 (148), whereby two attempts are made to contact patients by post prior to an attempt by telephone (149).

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. 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 (150). 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 (150). 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 (29). Hospitals located in ASGC-RA category one (i.e. major cities) were regarded as 'urban', while those in categories two 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) (151) and socioeconomic status (SES) using the index of relative socio-economic advantage and disadvantage (IRSAD) (152). 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 (153).

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%). 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 1). 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).

When compared to urban patients, those treated in rural hospitals had poorer access to several clinical processes of care (Table 3). 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).

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

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

Table 2. Health-related quality of life by region

EQ-5D-dimensions	Urban *n* (%)	Rural *n* (%)	p-value
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

Table 3. Processes of care by region

Evidence-based therapies (all states)	Urban *n* (%)	Rural *n* (%)	p-value
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 4). In relation to HRQoL, urban patients were more likely to report 'extreme problems' with their mobility, self-care and usual activities (Table 2). After adjusting for known covariates, there were no regional differences were observed in four of the EQ-5D domains, namely Anxiety/Depression, Mobility, Self-care, and Usual Activities (Table 5). 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 4. 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 5. 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 (64). 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 (59), many were unable to utilise their stroke unit's full potential. As observed by Dwyer et al. (154), 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 (155).

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 (62, 156). 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 (60), 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 (157). 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 (126, 158, 159). 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 (160). The use of such technology in all regional areas of the country is urgently needed in order to increase rates of thrombolysis administration (161). We did not observe differences by location in rates of prescription for antihypertensive medications at hospital discharge. As has been noted previously (125), 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 comparable to those observed in recent studies which also used AuSCR data (162, 163).

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.

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 (164, 165). 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 (166) and delay seeking medical assistance (167).

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 (168). 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 (169). 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 (170).

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 (171). 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.

6. CHAPTER SIX: General Discussion

The purpose of this thesis was to characterise and contrast the care provided to, and outcomes of, people with stroke across geographical settings. As a starting point, a systematic review was conducted to summarise the existing body of literature and identify potential avenues of future research. Based on the gaps identified in the systematic review, a retrospective case note audit was conducted using data from hospitals in Tasmania, Australia. A qualitative study was then undertaken to contextualise these findings and understand how the experiences of clinicians operating in urban and rural settings differed from each other. Recognising the limitations of the initial case note audit, a second study of this kind was conducted using a much larger, more representative sample from the Australian Stroke Clinical Registry (AuSCR). The section is written in the first person as I, the primary researcher, provide a summary of the four discrete study outcomes. The findings arising from these studies are then discussed drawing on current knowledge. Finally, the contribution that these studies make to the literature is established.

6.1 Summary of Study Findings

- The systematic review (Chapter Two) highlighted that of the 28 studies reviewed, most reported that patients in rural areas had comparatively poorer access to stroke care than their urban counterparts. The most commonly cited disparity related to thrombolysis, and the greatest similarities between regions were found in the area of secondary prevention. Overall, however, the literature was American-centric, which limited the generalisability of findings to other settings (e.g. those with universal healthcare).
- The DMR study (Chapter Three) showed that no patients in either of the two rural hospitals were administered thrombolysis during the study period. These hospitals

also did not have acute stroke units. Patients' access to the remaining care indicators was broadly comparable between regions. After adjusting for confounders and acknowledging the relatively small sample, there were no significant differences between regions in terms of 30-day mortality (OR = 0.99, 95% C.I. 0.46-2.18) or discharge destination (OR = 1.24, 95% C.I. 0.81-1.91).

- The qualitative study (Chapter Four) highlighted that acute stroke care within the study's urban hospital was structured and comprehensive, aided by the hospital's acute stroke unit and specialist nursing support. This stood in contrast to the description of care provided in the study's rural hospitals, which was somewhat less comprehensive, and often constrained by an absence of infrastructure or poor access to existing resources.
- The AuSCR study (Chapter Five) indicated that patients in rural hospitals received thrombolysis for ischaemic stroke less often (urban 12.7% vs rural 7.5%, $p<0.001$). Rural patients in this sample were also less likely to receive 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 in overall self-reported quality of life.

6.2 Study Findings in Context of the Literature

6.2.1 Time-critical Therapy

An urban-rural disparity in access to thrombolysis was a consistent theme in both quantitative studies. The two rural hospitals surveyed in the DMR study had never offered thrombolysis before, and this is likely to have been the case with several of the rural hospitals in the AuSCR study. The barriers to delivering thrombolysis in rural areas are numerous and varied (126), and many are discussed in chapter four of this thesis. One factor which has hitherto not been discussed, and which may partially explain my findings, relates to patient transfers

between facilities. Individuals residing in rural areas may be transported, either privately or by ambulance, to urban hospitals in order to receive thrombolysis, as occurred in two studies included in the systematic review (125, 172). If this pattern occurred in the AuSCR study, it would have inflated the number of patients receiving thrombolysis in urban hospitals. Despite evidence of poorer access to thrombolysis in rural areas, it is encouraging to see a growing body of evidence supporting the use of TPA at longer intervals after the onset of stroke (173, 174). This represents a promising opportunity for rural areas, where patients' eligibility for thrombolysis is often hampered by the need to travel long distances to reach a major hospital (158).

6.2.2 Stroke Unit Care

Similar to the issue of thrombolysis, regional disparities in access to stroke unit care was a recurring theme throughout this research. The findings of the qualitative study suggested that there were two main reasons why patients may not receive treatment in a stroke unit. Firstly, and most obviously, there were hospitals which were simply not equipped with stroke units, as was the case for both rural hospitals in the DMR study. Secondly, and as evidenced in both quantitative studies, there were cases where hospitals with stroke units were unable to provide stroke unit care to eligible patients. Participants in the qualitative study attributed this phenomenon to overall bed capacity constraints within their hospital. This finding aligns with previous research by Darehed et al. (175), who found that a patient's likelihood of being admitted to a stroke unit from ED decreased by 1.5% with each 1% increase in hospital bed occupancy above 85%. This is noteworthy, as participants in the qualitative study reported that once stroke patients became medical unit outliers, they were less likely to be transferred to the hospital's stroke unit at any point during their admission. Given the harms associated with medical outlier status (176), and the benefits associated with stroke unit care (60), these

findings highlight that stroke care must be coordinated (e.g. by a stroke CNC) if hospitals are to make the best use of existing resources.

6.2.3 Secondary Prevention

The systematic review suggested that of all the domains of acute stroke care, the provision of secondary prevention medications was generally the most similar between urban and rural areas. This finding was also largely confirmed in both quantitative studies. As noted in the systematic review, this may be because such treatments are familiar to clinicians, given that they are used in the context of many other conditions. The other main aspect of secondary prevention involves providing patients with advice on how to reduce their risk of secondary stroke through lifestyle changes. This care process was not measured in the AuSCR study; however, the DMR study suggested that rural patients were far less likely to be provided with this form of care. Such interventions, unfortunately, have limited efficacy in improving patients' body mass index, blood pressure, lipid profiles and medication adherence (177). Nevertheless, the provision of advice and education is associated with increased patient and carer knowledge, along with aspects of patient satisfaction (80). Therefore, whilst this form of care may not be clearly associated with hard outcomes, it is of importance to patients themselves, and for this reason, should be addressed if we are to improve the patient-centeredness of stroke care.

6.2.4 Outcomes

Despite notable differences in access to care, particularly in relation to stroke units and thrombolysis, I did not observe any consistent regional differences in patient outcomes. This is a seemingly counterintuitive finding in light of several publications which have reported excess stroke mortality (i.e. deaths per 1,000 population due to stroke) rates in Australia's rural areas (3, 5). My findings appear to be consistent with the US-based Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which found no evidence

of an urban-rural divide in stroke mortality following hospitalisation (178, 179). The authors of that study and others (180) have attributed rural areas' excess stroke mortality rates to the fact that these regions have higher stroke incidence rates. Put simply, individuals in rural areas have higher per capita rates of stroke mortality because they are more likely to have strokes in the first place. There is reason to believe that this is also the case in Australia, where stroke incidence and hospitalisation rates are both significantly higher in rural as compared to urban areas (3, 181). Alas, addressing urban-rural disparities in stroke incidence rates is an entirely separate issue with its own potential solutions, and as such, it is beyond the scope of this body of work, which is focused on care and outcomes after a stroke event.

An alternative explanation for these findings is that there was a tenuous association between patient outcomes and the care processes which were maldistributed between regions (i.e. thrombolysis, stroke unit care). This was almost certainly the case for thrombolysis in the context of the DMR study. Given that this drug has a number-needed-to-treat of 14 (182), and only 16 subjects received the drug, any protective effect of thrombolysis on 30-day mortality rates in this study is likely to have been negligible. It is typically expected that the benefit of thrombolysis would manifest as patients' improved functioning in the medium to longer term, as opposed to mortality in the short term (72). It should also be noted that the DMR study was not powered in order to detect regional differences in rates of 30-day mortality, as this would likely have been impractical using a manual case note audit. Indeed, given the small difference between regions on this variable (i.e. 11% vs 10.3%), a sample in excess of 60,000 cases would have been required for the difference to be considered statistically significant (183). Future research in this area should only be conducted using a sufficiently large sample with a follow-up period of at least 180 days.

Where stroke unit care is concerned, it is possible that rural hospitals, seeking to make the most of limited resources, had utilised their hospitals' Intensive Care Units (ICUs) or High Dependency Units (HDUs) as substitutes for stroke units. This practice appears to be commonplace in the state of New South Wales, where successive audits of acute stroke care

have pooled ICU and HDU care together with stroke unit care (184, 185). Whilst this approach is unlikely to be as effective as stroke unit care, it would represent a more specialised form of care than that of a general medical ward, and hence may have had a protective effect on the outcomes of rural patients.

6.3 Strengths and Limitations

This body of work is the first of its kind to describe differences in acute stroke care and outcomes between Australia's urban and rural areas using a large sample. This is an important contribution to the literature base, as much of the pre-existing literature was written from an American-centric perspective. My findings are also strengthened by the use of robust statistical modelling with risk adjustment for patients' stroke severity, the strongest known predictor of stroke patient outcomes in the short term (186, 187). The addition of stroke severity measures to regression models in both quantitative studies not only adds validity to my findings, but also addresses a key limitation of previous studies in the field. The use of a sequential-explanatory mixed methods design allowed the qualitative results to assist in validating and explaining the trends identified in the DMR study. Lastly, this project has also benefited from access to national data and collaboration with subject matter experts from Monash University.

This study also contains methodological limitations which must be addressed. My research used the location of the treating hospital as a proxy measure of rurality when defining 'urban' and 'rural' areas, without considering the patient's residential address. Whilst this approach was underpinned by recognised classification systems (e.g. ASGC-RA, MMM), there is a risk of misclassification bias resulting from patients receiving treatment outside of their native region. This most notably occurs when patients from rural areas travel to urban hospitals to receive thrombolysis, as discussed above. Future researchers are encouraged to incorporate patients' residential addresses and the location of the treating

hospital when conducting studies of this kind. On a related note, by dichotomising urban and rural areas, I was unable to account for the heterogeneity of Australia's rural areas, which vary greatly in their sociodemographic and health indicators (188). This could be overcome by grouping areas along a continuum of rurality using bands designated by one of the abovementioned classification systems.

The use of hospital administrative data in the DMR also carries some limitations. Firstly, the time-consuming nature of medical record abstraction (189) made it impractical to use a large sample. In using a relatively small sample, my study may have been underpowered to detect regional differences in outcomes stemming from disparate access to thrombolysis. The need to adopt a smaller sample also meant that I could ill-afford to include cases of conditions mimicking stroke, which in turn required us to thoroughly screen cases before including them in the study. The time spent acquiring, screening and analysing DMR data also meant that there was a significant gap between the age of my DMR data, and when the qualitative focus groups and interviews took place. This has implications for the sequential-explanatory nature of qualitative study, in that the barriers and facilitators mentioned by clinicians may have been more relevant to their current context than the period when the DMR data occurred.

There are also limitations associated with my use of data from the AuSCR which must be acknowledged. Firstly, the number of care processes collected by the AuSCR (in most hospitals only 4) is limited, and hence does not provide a comprehensive account of acute stroke care in participating hospitals. Secondly, and as touched on in Chapter Five, the rural hospitals participating in AuSCR are unlikely to be representative of all rural hospitals in Australia. All but one of these hospitals was equipped with a stroke unit, and anecdotally, many of these units would have been staffed by neurologists, making them characteristically similar to large urban hospitals. These similarities, coupled with the overall small magnitude

of differences in stroke unit care and thrombolysis, may have further contributed to the absence of an overall urban-rural divide in patient outcomes.

Lastly, there are limitations associated with the representativeness of my findings. Both the DMR and qualitative studies relate specifically to the Australian state of Tasmania. Given that Tasmania's demographics and risk factor profile is markedly different to the rest of Australia (38), my findings may have limited generalisability to other Australian states and indeed, other countries. This body of work also did not seek the input of any stroke patients, which, as discussed in greater detail below, limited my ability to make inferences about care quality from the patient's perspective.

6.4 Future Research

6.4.1 Novel Determinants of Stroke Care and Outcomes

This thesis took a conventional approach towards characterising acute stroke, focussing on the concrete aspects of care and patient outcomes. There is an emerging body of research detailing the role of other, more nebulous factors which were previously unmeasured. For instance, Andrew et al. (190) used a validated survey to describe the effect of certain qualitative factors (e.g. a hospital's culture and social capital), finding that both were linked with an increased use of stroke unit care. Similarly, Bray et al. (191) reported an association between a composite measure of staffing (numbers, type, and training level), facilities (e.g. continuous physiological monitoring) and service level (e.g. 24/7 availability of emergency imaging and thrombolysis) and access to evidence-based care. Additional research is needed in this area, as it may further knowledge of what defines urban and rural stroke care. With a more holistic understanding of what separates both regions, researchers would be better positioned to address disparities in care.

6.4.2 Incorporation of Patient-reported Outcome Measures into Clinical Practice

At a basic level, patient-reported outcome measures (PROMs) are a measure of a patient's health which comes directly from the patient themselves, without interpretation by a third party (192). PROMs typically address the patient's functional status, symptom burden, well-being and health-related quality of life (193). PROMs are increasingly being used as a measure of healthcare quality (194), and therefore hold potential to shed light on differences in care quality between regions. Despite the availability of several validated tools which have been endorsed for use with stroke patients (194), we are yet to see PROMs incorporated into routine clinical practice. If we are to increase the patient-centeredness of the care we provide to acute stroke patients, it will be essential to seek the patient's perspective. The need to incorporate PROMs into clinical practice is strengthened by the fact that, as mentioned above, some care processes are not associated with the hard outcomes that are traditionally collected, and hence there is a need for alternative measures of quality.

6.5 Recommendations

6.5.1 An Increased Use of Telestroke

Stroke telemedicine or 'telestroke' refers to the use of audio-visual communication technology to facilitate the remote clinical and radiological evaluation of stroke patients (195). By assessing patients remotely at their presenting hospital, specialists can provide prompt advice around the use of time-critical treatments (e.g. thrombolysis) (196). For this reason, telestroke is often used in so-called 'hub-and-spoke' networks, where larger, predominantly urban hospitals with specialist staff (hubs) provide decision support for smaller rural sites (spokes) (197). Having access to specialist input is a great benefit to clinicians operating in smaller rural hospitals, who may have otherwise been unwilling to administer thrombolysis (161). Telestroke has been successfully trialled in a number of countries, and is acknowledged to be a safe, and cost-effective means of improving access to

thrombolysis (160, 195, 198). Perhaps the most prominent example of telestroke in Australia is the VST, whose implementation has resulted in an increase in the number of patients receiving thrombolysis within 60 minutes of arrival to hospital, whilst also decreasing the number of thrombolysis-related adverse events (160).

The use of telestroke in combination with Mobile Stroke Units (MSUs) may also offer a solution to narrowing urban-rural disparities in access to thrombolysis. In plain terms, MSUs are ambulances equipped with a CT scanner and specialist staff, which would typically include paramedics, a radiographer and neurologist or stroke fellow (199, 200). A MSU was recently implemented in Melbourne, Australia, serving a 20km radius of the city with an estimated catchment of 1.7 million people (199). Whilst there are no data to support their use in rural Australian settings, MSUs have been trialled in rural Alberta, Canada. Shuaib et al. (200) describe a model where rural-based ambulances collect patients and meet MSUs at a predesignated site, where the patients are given a CT scan. The images from the scan are then forwarded to a specialist located in a tertiary care centre for review. The specialist may then choose to administer thrombolysis and transport the patient to a tertiary care centre (i.e. 'drip and ship') or transport the patient to the tertiary care centre for other acute treatment (e.g. endovascular clot retrieval) (200). Patients may also be directed back to their local hospital where deemed necessary (e.g. in the case of stroke mimics), thus reducing the number of costly and unnecessary transfers to tertiary care centres (200, 201).

6.5.2 Increased Access to Stroke Unit Care

As noted above, suboptimal access to stroke unit care can be divided into cases where a given hospital does not have a stroke unit, and cases where the hospital has a stroke unit, but is unable to utilise its full potential. In the latter case, it has been suggested that access can be improved by increasing staff members' recognition of stroke units as significant specialist units (e.g. as being equivalent to a coronary care unit for myocardial infarction) (202). The

use of clinical facilitators in concert with clinical pathways has also been associated with increased access to stroke unit care (203, 204). Taking a broader perspective, the use of clinical networks with ambulance transfer agreements between sites and hospital pre-notification may also improve access to stroke units (205). Models of acute stroke care such as these have been implemented elsewhere in Australia, and in Denmark and the United Kingdom, leading to significant increases in the number of patients receiving stroke unit care (131, 132) and thrombolysis (206, 207). Where there are no pre-existing stroke units, and patient transfers are infeasible, it has been suggested that consultation via telestroke systems, such as those outlined above, may represent the closest alternative to stroke unit care (132, 208, 209).

6.5.3 Expanded Data Collection Infrastructure

There is currently a scarcity of representative data to describe the state of stroke care and patient outcomes in Australia. This was exemplified in the DMR study, where the best available method of data collection was a labour-intensive process of manual case note abstraction, which would be wholly unsustainable as an ongoing means of monitoring stroke care. Whilst the burden of data collection and analysis has undoubtedly been reduced with the advent of the AuSCR (62), the significant financial costs incurred by hospitals participating in the registry could hinder the recruitment of further sites. It is also possible that with the current fiscal outlook (i.e. post-COVID-19), some sites will find it difficult to maintain their subscription to the registry. As an alternative to commercial clinical registries, some government health organisations have developed systems for monitoring stroke care and outcomes (185, 210). In other fields, namely cardiac rehabilitation, registries have been incorporated into administrative data collection, allowing fields to be prepopulated and thus reducing the time needed to enter cases (211). Further development of such state-funded data collection programs may represent a more viable alternative than the AuSCR.

The use of a state-funded, not-for-profit clinical registry with mandatory participation for designated hospitals may also improve the generalisability of data collected. Firstly, by having a large pool of uniform data, it would be possible to apply the same risk adjustment methodology across all cases, thus increasing the ability to monitor and compare patient outcomes. Secondly, by mandating registry participation, there would be opportunities for less-motivated and lower-performing sites to learn from, and benchmark against, the high-performing sites which currently predominate the AuSCR. Providing researchers with access to free or concessionally-priced data from a not-for-profit registry would also remove one of the barriers to conducting research in this field, which may encourage further research. Whilst it is acknowledged that the presence of clinical registry data alone does not ensure quality improvement (212), having a sufficient amount of high-quality data available to clinicians and policymakers would be invaluable. Indeed, as Westert et al. note, public reporting is the first step towards addressing unwarranted variation in medical practice (213).

6.5.4 A Revision of Stroke Data Variables

It is apparent that the set of variables currently collected in Australia through various initiatives (e.g. via the AuSCR, Stroke Foundation Audits etc.) do not cover acute stroke care in its entirety. Of particular note are those relating to dysphagia screening and assessment for stroke in the pre-hospital environment. Dysphagia is common in stroke, affecting 27% to 64% of all patients (214), and patients with dysphagia are significantly more likely to experience pneumonia (207), which is itself associated with an increased risk of mortality in the short term (215, 216). Despite this, and despite featuring in the *Clinical Guidelines* (64) as a consensus-based recommendation, there are no indicators related to dysphagia management in the *Clinical Care Standard* (114). This represents a missed opportunity to utilise the data collection infrastructure of the Stroke Foundation for quality improvement

purposes. This could be addressed by creating a robust operational definition for dysphagia management, and incorporating it into existing stroke data collection initiatives.

With regard to stroke screening, some clinicians interviewed as part of the qualitative study believed that one stroke screening tool recommended by the ACSQHC (i.e. F.A.S.T.) was unfit for purpose, and better suited towards non-clinicians in the community. As a result, F.A.S.T. was seldom, if ever, used by these clinicians. Similar reservations were expressed by clinicians who were consulted about the ACSQHC's *Acute Stroke Clinical Care Standard* prior to its release (202). A similar situation was found in the pre-hospital environment, where, despite Tasmanian guidelines mandating the screening of suspected stroke patients using a validated tool (i.e. the Melbourne Ambulance Stroke Screen) (217), this was not widely adhered to. Despite this, there were clear instances in the DMR study where patients may have been candidates for thrombolysis, had their stroke symptoms been identified earlier. This suggests a need to implement a more clinically-focussed screening tool, such as the Recognition of Stroke in the Emergency Room (ROSIER) Scale (218). This particular tool was recommended by clinicians in the abovementioned consultation paper (202) and therefore may be better received by other clinicians, leading to fewer missed opportunities to administer thrombolysis.

6.5.5 Stroke Follow-up Clinics

Participants in the qualitative study mentioned a host of barriers to providing patients with tailored advice about their lifestyle behaviours while patients are admitted. One solution to this may be an increased use of follow-up services for stroke patients, such as the Stroke Foundation's Stroke Outreach Program (StOP) (219). Under this initiative, consenting stroke survivors are contacted within 21 days of discharge by a multidisciplinary team from the Stroke Foundation to discuss secondary prevention measures. Following the consult, a letter about what was discussed is then generated by the Stroke Foundation's team and sent to the

liaising GP and stroke survivor (219). The use of such follow-up clinics has been associated with a significant reduction in the odds of readmission at 30 days post-discharge (220) and improvements in medication adherence at 12 months (221). Follow-up clinics of this sort would also provide an opportunity to address other unmet needs encountered by patients post-discharge, as suggested by Kjork et al. (222). It is also foreseeable that in the post-COVID-19 world, healthcare providers will implement telehealth initiatives in greater numbers, which may facilitate this kind of follow-up clinic for stroke.

6.6 Recent Developments in Acute Stroke Care in Tasmania

Both the DMR and qualitative studies relate specifically to the provision of stroke care within the Australian state of Tasmania. As of November 2019, there had been several changes made to the delivery of acute stroke care since these studies took place:

6.6.1 Centralisation of Acute Stroke Care

- The MCH was actively reducing the number of acute stroke cases it was handling, instead placing emphasis on becoming a dedicated rehabilitation facility.
- A general medical physician with an interest in stroke who had been working at the MCH during the study period had since transferred to the LGH.
- Unfortunately, however, there were still no protocols in place for ambulances with suspect stroke cases to bypass the MCH and travel directly to the NWRH.

6.6.2 Telestroke

- The NWRH had recently appointed a Stroke CNC, whose first objective was to link the NWRH with the Victorian Stroke Telemedicine (VST) network. As of March 2020, both the LGH and NWRH had joined the VST network.
- It is proposed that the Stroke CNC will eventually spearhead the implementation of a new ASU at the NWRH.

6.6.3 Secondary Prevention

- The RHH had recently obtained funding to modify existing patient management software to include more features tailored towards stroke patients. The project, which has been dubbed ‘My Going Home Plan’, is a checklist containing elements of the Clinical Care Standard (e.g. secondary prevention medications) which aims to reduce the number of patients leaving hospital before receiving adequate care.

6.7 Conclusion

This thesis sought to characterise and contrast the care provided to, and outcomes of, people with stroke across geographical settings. Rural hospitals typically offer a comparatively basic form of acute stroke care, with less access to stroke units and thrombolysis. Central to addressing this disparity will be a reconfiguration of existing resources with an increased use of telestroke services. I did not observe any regional differences in patient outcomes, a finding which, whilst being consistent with previous studies, may have been influenced by a combination of methodological limitations, particularly in relation to sample sizes. Policymakers should note that the apparent similarities in patient outcomes between regions should not be taken as evidence that both groups received a commensurate level of care. Rather, these outcomes belie systemic differences in the way care is provided, which should not be ignored. We must work towards reducing this disparity now, while urban-rural differences in acute stroke care are primarily an issue of thrombolysis and stroke unit care. As Leira et al. (2017) note, this gap will only widen with the increased uptake of more complex procedures (e.g. mechanical thrombectomy) and future interventions.

REFERENCES

1. Australian Institute of Health and Welfare. Cardiovascular disease 2019 [Available from: https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium.
2. Australian Institute of Health and Welfare. Deaths in Australia. 2019.
3. Deloitte Access Economics. Stroke in Australia: No Postcode Untouched: Stroke Foundation; 2017 [Available from: https://strokefoundation.org.au/What-we-do/Research/No-postcode-untouched.
4. Investigators WMPP. The world health organization monica project (monitoring trends and determinants in cardiovascular disease): A major international collaboration. Journal of Clinical Epidemiology. 1988;41(2):105-14.
5. Australian Institute of Health and Welfare. Stroke and its management in Australia: an update 2013 [Available from: http://www.aihw.gov.au/publication-detail/?id=60129543613.
6. Australian Institute of Health and Welfare. How we manage stroke in Australia 2006 [Available from: https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/how-we-manage-stroke-in-australia/contents/table-of-contents.
7. Australian Institute of Health and Welfare. Australia's Health 2014 [Available from: http://www.aihw.gov.au/publication-detail/?id=60129547205.
8. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Culebras A, Elkind MS, et al. An updated definition of stroke for the 21st century a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44(7):2064-89.
9. Sudlow C, Warlow C. Comparing stroke incidence worldwide what makes studies comparable? Stroke. 1996;27(3):550-8.
10. Fonarow GC, Smith EE, Reeves MJ, Pan W, Olson D, Hernandez AF, et al. Hospital-level variation in mortality and rehospitalization for medicare beneficiaries with acute ischemic stroke. Stroke. 2011;42(1):159-66.
11. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1):35-41.

12. Broderick JP, Brott TG, Duldner JE, Tomsick T, Leach A. Initial and recurrent bleeding are the major causes of death following subarachnoid hemorrhage. Stroke. 1994;25(7):1342-7.
13. Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. Stroke. 1993;24(7):987-93.
14. Easton JD, Saver Jeffrey L, Albers Gregory W, Alberts Mark J, Chaturvedi S, Feldmann E, et al. Definition and Evaluation of Transient Ischemic Attack. Stroke. 2009;40(6):2276-93.
15. Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. Bmj. 2004;328(7435):326.
16. Hand PJ, Kwan J, Lindley RI, Dennis MS, Wardlaw JM. Distinguishing between stroke and mimic at the bedside. Stroke. 2006;37(3):769-75.
17. Rodgers H. Chapter 36 - Stroke. In: Barnes MP, Good DC, editors. Handbook of Clinical Neurology. 110: Elsevier; 2013. p. 427-33.
18. Lerner AJ. Diagnostic criteria in neurology: Springer Science & Business Media; 2007.
19. Iribarren C, Darbinian J, Klatsky AL, Friedman GD. Cohort study of exposure to environmental tobacco smoke and risk of first ischemic stroke and transient ischemic attack. Neuroepidemiology. 2004;23(1-2):38-44.
20. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(7):2160-236.
21. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. The Lancet. 2014;383(9913):245-55.
22. Appelros P, Stegmayr B, Terént A. Sex differences in stroke epidemiology a systematic review. Stroke. 2009;40(4):1082-90.
23. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. The Lancet. 2010;376(9735):112-23.

24. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. The lancet. 2016;388(10046):761-75.
25. Meilleur A, Subramanian S, Plascak JJ, Fisher JL, Paskett ED, Lamont EB. Rural residence and cancer outcomes in the United States: issues and challenges. Cancer Epidemiology and Prevention Biomarkers. 2013;22(10):1657-67.
26. Hart LG, Larson EH, Lishner DM. Rural definitions for health policy and research. American journal of public health. 2005;95(7):1149-55.
27. Oxford English Dictionary. "regional, adj. and n.": Oxford University Press.
28. Tham R, Ward B. Rural health systems: Spotlight on equity and access. Understanding the australian health care system. 2016:139-52.
29. Australian Bureau of Statistics. Australian Standard Geographical Classification (ASGC) 2011 [Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/8B8ABC8EC62D8F46CA2570AE000DD3B5?opendocument.
30. McGrail MR, Humphreys JS. Geographical classifications to guide rural health policy in Australia. Australia and New Zealand health policy. 2009;6(1):28.
31. National Rural Health Alliance. Wanted: A uniform system for assessing health workforce shortages and targeting programs to attract health professionals 2012 [Available from: https://www.ruralhealth.org.au/sites/default/files/documents/nrha-policy-document/position/pos-health-workforce-shortages-18-june-12.pdf.
32. Department of Health. Australian Statistical Geographical Classification - Remoteness Area 2019 [Available from: https://www.health.gov.au/health-workforce/health-workforce-classifications/australian-statistical-geographical-classification-remoteness-area.
33. Department of Health. Modified Monash Model 2019 [Available from: https://www.health.gov.au/health-workforce/health-workforce-classifications/modified-monash-model.
34. Department of Health. Health Workforce Locator 2019 [Available from: https://www.health.gov.au/resources/apps-and-tools/health-workforce-locator/health-workforce-locator#hwc-map.
35. Australian Institute of Health and Welfare. Rural & remote health 2019 [Available from: https://www.aihw.gov.au/reports/rural-remote-australians/rural-remote-health.

36. Thrift AG, Dewey HM, Macdonell RA, McNeil JJ, Donnan GA. Stroke incidence on the East Coast of Australia The North East Melbourne Stroke Incidence Study (NEMESIS). Stroke. 2000;31(9):2087-92.
37. Thrift AG, Tong B, Senes S, Waters A-M, Lalor E. No evidence for an epidemic of stroke with the ageing of the population. Neuroepidemiology. 2012;38(4):268-73.
38. Department of Health and Human Services. Health indicators Tasmania 2013 [Available from: https://www.dhhs.tas.gov.au/__data/assets/pdf_file/0019/132283/Health_Indicators_Tasmania_2013.pdf.
39. Katzenellenbogen JM, Vos T, Somerford P, Begg S, Semmens JB, Codde JP. Burden of stroke in indigenous Western Australians a study using data linkage. Stroke. 2011;42(6):1515-21.
40. Katzenellenbogen JM, Begg S, Somerford P, Anderson CS, Semmens JB, Codde JP, et al. Disability burden due to stroke in Western Australia: new insights from linked data sources. International Journal of Stroke. 2010;5(4):269-77.
41. Australian Institute of Health and Welfare. Australia's health 2018 [Available from: https://www.aihw.gov.au/reports/australias-health/australias-health-2018.
42. Australian Institute of Health and Welfare. Older Australia at a glance 2018 [Available from: https://www.aihw.gov.au/reports/older-people/older-australia-at-a-glance.
43. Australian Bureau of Statistics. Australia's leading causes of death, 2015 [Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2015~Main%20Features~Australia's%20leading%20causes%20of%20death,%202015~3.
44. Australian Institute of Health and Welfare. Cardiovascular disease, diabetes and chronic kidney disease series 2014 [Available from: https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/cardiovascular-diabetes-chronic-kidney-prevalence/contents/table-of-contents.
45. Deloitte Access Economics. The economic impact of stroke in Australia: Scoping cost effective prevention 2013 [Available from: https://www2.deloitte.com/au/en/pages/economics/articles/economic-impact-stroke-australia.html.
46. Australian Institute of Health and Welfare. Australia's health 2016 [Available from: http://www.aihw.gov.au/publication-detail/?id=60129555544.

47. Lackland DT, Roccella EJ, Deutsch AF, Fornage M, George MG, Howard G, et al. Factors influencing the decline in stroke mortality a statement from the American Heart Association/American Stroke Association. Stroke. 2014;45(1):315-53.
48. Australian Bureau of Statistics. 3101.0 - Australian Demographic Statistics 2020 [Available from: https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3101.0Main+Features1Sep%202019?OpenDocument.
49. Australian Bureau of Statistics. 3235.0 - Regional Population by Age and Sex, Australia, 2018 [Available from: https://www.abs.gov.au/AUSSTATS/abs@.Nsf/7d12b0f6763c78caca257061001cc588/cdd56c03c2fa5655ca2573210018d999!OpenDocument.
50. Donabedian A. The quality of care: How can it be assessed? JAMA. 1988;260(12):1743-8.
51. Donabedian A. Evaluating the quality of medical care. The Milbank memorial fund quarterly. 1966;44(3):166-206.
52. Ayanian JZ, Markel H. Donabedian's Lasting Framework for Health Care Quality. New England Journal of Medicine. 2016;375(3):205-7.
53. Berwick D, Fox DM. "Evaluating the Quality of Medical Care": Donabedian's Classic Article 50 Years Later. The Milbank Quarterly. 2016;94(2):237-41.
54. Moore L, Lavoie A, Bourgeois G, Lapointe J. Donabedian's structure-process-outcome quality of care model: validation in an integrated trauma system. Journal of Trauma and Acute Care Surgery. 2015;78(6):1168-75.
55. Naranjo LLS, Viswanatha Kaimal P. Applying Donabedian's theory as a framework for bariatric surgery accreditation. Bariatric Nursing and Surgical Patient Care. 2011;6(1):33-7.
56. Gardner G, Gardner A, O'Connell J. Using the Donabedian framework to examine the quality and safety of nursing service innovation. Journal of Clinical Nursing. 2014(1-2):145.
57. Chimatiro GL, Rhoda AJ. Scoping review of acute stroke care management and rehabilitation in low and middle-income countries. BMC Health Services Research. 2019;19(1):789.
58. Lighter DE. How (and why) do quality improvement professionals measure performance? International Journal of Pediatrics and Adolescent Medicine. 2015;2(1):7-11.

59. Stroke Foundation. Acute Stroke Services Framework 2019 [Available from: https://strokefoundation.org.au/-/media/E6682A70FFF0489FA66D28042C0FF472.ashx?la=en.
60. Stroke Unit Trialists Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database of Systematic Reviews. 2013;11(9).
61. Candelise L, Gattinoni M, Bersano A, Micieli G, Sterzi R, Morabito A. Stroke-unit care for acute stroke patients: an observational follow-up study. The Lancet.369(9558):299-305.
62. Stroke Foundation. National Stroke Audit Acute Services Report (2017) [Available from: https://informme.org.au/en/stroke-data/Acute-audits.
63. Stroke Foundation. National Stroke Audit: Acute Services Report 2019 2019 [Available from: https://informme.org.au/-/media/0DAA2643E8F7424C84D384EB16CF0716.ashx?la=en.
64. Stroke Foundation. Clinical Guidelines for Stroke Management 2020 [Available from: https://informme.org.au/en/Guidelines/Clinical-Guidelines-for-Stroke-Management.
65. Australian Commission on Safety and Quality in Health Care. Acute Stroke Clinical Care Standard 2017 [Available from: https://www.safetyandquality.gov.au/our-work/clinical-care-standards/acute-stroke-clinical-care-standard/.
66. De Luca A, Toni D, Lauria L, Sacchetti ML, Rossi PG, Ferri M, et al. An emergency clinical pathway for stroke patients–results of a cluster randomised trial (isrctn41456865). BMC health services research. 2009;9(1):14.
67. Quain DA, Parsons MW, Loudfoot AR, Spratt NJ, Evans MK, Russell ML, et al. Improving access to acute stroke therapies: a controlled trial of organised pre-hospital and emergency care. Med J Aust. 2008;189(8):429-33.
68. O'Brien W, Crimmins D, Donaldson W, Risti R, Clarke TA, Whyte S, et al. FASTER (Face, Arm, Speech, Time, Emergency Response): Experience of Central Coast Stroke Services implementation of a pre-hospital notification system for expedient management of acute stroke. Journal of Clinical Neuroscience. 2012;19(2):241-5.
69. Meretoja A, Weir L, Ugalde M, Yassi N, Yan B, Hand P, et al. Helsinki model cut stroke thrombolysis delays to 25 minutes in Melbourne in only 4 months. Neurology. 2013;81(12):1071-6.
70. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. Neurology. 2012;79(4):306-13.

71. Berglund A, Svensson L, Sjöstrand C, von Arbin M, von Euler M, Wahlgren N, et al. Higher prehospital priority level of stroke improves thrombolysis frequency and time to stroke unit: the Hyper Acute STroke Alarm (HASTA) study. Stroke. 2012;43(10):2666-70.
72. Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database of Systematic Reviews. 2014;7(7).
73. NHS Digital. Clinical Commissioning Group Outcomes Indicator Set (CCG OIS) 2019 [Available from: https://digital.nhs.uk/data-and-information/publications/clinical-indicators/ccg-outcomes-indicator-set.
74. Langhorne P, Pollock A. What are the components of effective stroke unit care? Age and Ageing. 2002;31(5):365-71.
75. Bernhardt J, Chitravas N, Meslo IL, Thrift AG, Indredavik B. Not All Stroke Units Are the Same A Comparison of Physical Activity Patterns in Melbourne, Australia, and Trondheim, Norway. Stroke. 2008;39(7):2059-65.
76. Lakhan SE, Sapko MT. Blood pressure lowering treatment for preventing stroke recurrence: a systematic review and meta-analysis. International archives of medicine. 2009;2(1):30.
77. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Bmj. 2002;324(7329):71-86.
78. Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-Dose Atorvastatin after Stroke or Transient Ischemic Attack. New England Journal of Medicine. 2006;355(6):549-59.
79. Tawfik A, Bielecki JM, Krahn M, Dorian P, Hoch JS, Boon H, et al. Systematic review and network meta-analysis of stroke prevention treatments in patients with atrial fibrillation. Clin Pharmacol. 2016;8:93-107.
80. Forster A, Brown L, Smith J, House A, Knapp P, Wright JJ, et al. Information provision for stroke patients and their caregivers. Cochrane Database of Systematic Reviews. 2012(11).
81. Kalra L, Evans A, Perez I, Melbourn A, Patel A, Knapp M, et al. Training carers of stroke patients: randomised controlled trial. Bmj. 2004;328(7448):1099.
82. Gonçalves-Bradley DC, Lannin NA, Clemson LM, Cameron ID, Shepperd S. Discharge planning from hospital. Cochrane Database of Systematic Reviews. 2016(1).

83. Hinchey JA, editor Measuring and improving the quality of stroke care. Seminars in Cerebrovascular Diseases and Stroke; 2003: Elsevier.
84. Australian Stroke Coalition. National Stroke Data and Quality Discussion Paper 2012 [Available from: https://strokefoundation.org.au/-/media/07379BA57F964EE9B7B12ABB5382A8A2.ashx?la=en.
85. Cadilhac DA, Lannin NA, Anderson CS, Levi CR, Faux S, Price C, et al. Protocol and pilot data for establishing the Australian Stroke Clinical Registry. International Journal of Stroke. 2010;5(3):217-26.
86. Australian Stroke Clinical Registry. Australian Stroke Clinical Registry: Annual Report 2017 [Available from: https://auscr.com.au/about/annual-reports/.
87. Australian Stroke Clinical Registry. AuSCR: Data Dictionary 2017 [Available from: https://strokefoundation.org.au/-/media/D3FDB58A85C740E28D85E98016BE24AA.ashx?la=en.
88. Australian Institute of Health and Welfare. About National Death Index 2019 [Available from: https://www.aihw.gov.au/about-our-data/our-data-collections/national-death-index/about-national-death-index.
89. Wennberg JE. Unwarranted variations in healthcare delivery: implications for academic medical centres. British Medical Journal. 2002;325(7370):961.
90. Appleby J, Raleigh V, Frosini F, Bevan G, HaiYan G, Lyscom T, et al. Variations in health care: the good, the bad and the inexplicable: King's Fund; 2011.
91. Australian Commission on Safety Quality in Health Care. Medical practice variation: background paper 2013 [Available from: https://www.safetyandquality.gov.au/sites/default/files/migrated/SAQ110_Medical_Practice_variation_V10_WEB.pdf.
92. O'Neill N, Godden D. Stroke outcomes in Northern Scotland: does rurality really matter. Rural Remote Health. 2003;3(3):243-.
93. National Stroke Foundation. Acute Services Survey Report 2013: National Stroke Foundation; [Available from: http://www.informme.org.au/-/media/95C36BDF7A4849E8B0E009BDA647ECDD.
94. Read S, Levy J. Differences in stroke care practices between regional and metropolitan hospitals. Internal Medicine Journal. 2005;35(8):447-50.
95. Fonarow GC, Alberts MJ, Broderick JP, Jauch EC, Kleindorfer DO, Saver JL, et al. Stroke outcomes measures must be appropriately risk adjusted to ensure quality care of patients. Stroke. 2014;45(5):1589-601.

96. Cadilhac DA, Kilkenny MF, Longworth M, Pollack M, Levi CR. Metropolitan–rural divide for stroke outcomes: do stroke units make a difference? Internal Medicine Journal. 2011;41(4):321-6.
97. Riggs JE, Libell DP, Hobbs GR. In-Hospital Stroke Mortality, Hospital Transfers, and Referral Bias at a Rural Academic Medical Center. The Journal of Rural Health. 2002;18(2):294-7.
98. Brems C, Johnson ME, Warner TD, Roberts LW. Barriers to healthcare as reported by rural and urban interprofessional providers. Journal of Interprofessional Care. 2006;20(2):105-18.
99. Schwamm LH, Ali SF, Reeves MJ, Smith EE, Saver JL, Messe S, et al. Temporal trends in patient characteristics and treatment with intravenous thrombolysis among acute ischemic stroke patients at Get With The Guidelines–Stroke hospitals. Circulation: Cardiovascular Quality and Outcomes. 2013;6(5):543-9.
100. McCluskey A, Vratsistas-Curto A, Schurr K. Barriers and enablers to implementing multiple stroke guideline recommendations: a qualitative study. BMC health services research. 2013;13(1):1.
101. Drury P, McInnes E, Hardy J, Dale S, Middleton S. Stroke unit Nurse Managers' views of individual and organizational factors liable to influence evidence-based practice: A survey. International journal of nursing practice. 2015.
102. Donnellan C, Sweetman S, Shelley E. Implementing clinical guidelines in stroke: a qualitative study of perceived facilitators and barriers. Health Policy. 2013;111(3):234-44.
103. Creswell JW, Clark VLP. Designing and conducting mixed methods research: Sage publications; 2017.
104. Australian Bureau of Statistics. Australia's leading causes of death, 2017 2018 [Available from: https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2017~Main%20Features~Australia's%20leading%20causes%20of%20death,%202017~2.
105. National Stroke Foundation. National Stroke Audit: Acute Services Report 2015 2015 [Available from: https://informme.org.au/en/stroke-data/Acute-audits.
106. Pouw ME, Peelen LM, Moons KGM, Kalkman CJ, Lingsma HF. Including post-discharge mortality in calculation of hospital standardised mortality ratios: retrospective analysis of hospital episode statistics. British Medical Journal. 2013;347:f5913.

107. Kristoffersen DT, Helgeland J, Clench-Aas J, Laake P, Veierød MB. Comparing hospital mortality - how to count does matter for patients hospitalized for acute myocardial infarction (AMI), stroke and hip fracture. BMC Health Services Research. 2012;12:364-.
108. Department of Health and Human Services. Public Hospitals in Tasmania 2019 [Available from: https://www.dhhs.tas.gov.au/hospital/public_hospitals.
109. Department of Health and Human Services. Royal Hobart Hospital 2019 [Available from: https://www.dhhs.tas.gov.au/hospital/royal-hobart-hospital/information_for_patients_and_visitors2/rhh_patient_information_guide/welcome.
110. Department of Health and Human Services. Launceston General Hospital 2019 [Available from: https://www.dhhs.tas.gov.au/hospital/launceston-general-hospital.
111. Department of Health and Human Services. Tasmanian Health Service - North West Region 2019 [Available from: https://www.dhhs.tas.gov.au/career/home/medical/junior_docs/more_information_-_north_west_area_health_service.
112. Hugo Centre for Migration and Population Research. Accessibility/Remoteness Index of Australia (ARIA): University of Adelaide; 2019 [Available from: https://www.adelaide.edu.au/hugo-centre/services/aria#advantages-of-aria.
113. Team RC. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2019.
114. Australian Commission on Safety and Quality in Health Care. Indicator Specification: Acute Stroke Clinical Care Standard 2015 [Available from: https://www.safetyandquality.gov.au/publications/acute-stroke-indicator-specification/.
115. Stroke Foundation. National Stroke Data Dictionary 2019 [
116. Foley N, Teasell R, Salter K, Kruger E, Martino R. Dysphagia treatment post stroke: a systematic review of randomised controlled trials. Age and Ageing. 2008;37(3):258-64.
117. Australian Institute of Health and Welfare. Admitted patient care NMDS 2016-17: and reference attributes; 2017 [Available from: http://meteor.aihw.gov.au/content/index.phtml/itemId/612171.
118. Brott T, Adams HP, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke. 1989;20(7):864-70.

119. Williams LS, Yilmaz EY, Lopez-Yunez AM. Retrospective assessment of initial stroke severity with the NIH Stroke Scale. Stroke. 2000;31(4):858-62.
120. Adams H, Davis P, Leira E, Chang K-C, Bendixen B, Clarke W, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology. 1999;53(1):126-.
121. FileMaker Inc. FileMaker Pro 13. Santa Clara CA2015.
122. Abilleira S, Ribera A, Permanyer-Miralda G, Tresserras R, Gallofre M. Noncompliance with certain quality indicators is associated with risk-adjusted mortality after stroke. Stroke. 2012;43(4):1094-100.
123. Chang TE, Lichtman JH, Goldstein LB, George MG. Accuracy of ICD-9-CM Codes by Hospital Characteristics and Stroke Severity: Paul Coverdell National Acute Stroke Program. Journal of the American Heart Association. 2016;5(6):e003056.
124. Phipps MS, Jia H, Chumbler NR, Li X, Castro JG, Myers J, et al. Rural-Urban Differences in Inpatient Quality of Care in US Veterans With Ischemic Stroke. The Journal of Rural Health. 2014;30(1):1-6.
125. Koifman J, Hall R, Li S, Stamplecoski M, Fang J, Saltman AP, et al. The association between rural residence and stroke care and outcomes. Journal of the Neurological Sciences. 2016;363:16-20.
126. Moloczij N, Mosley I, Moss K, Bagot KL, Bladin C, Cadilhac DA. Is telemedicine helping or hindering the delivery of stroke thrombolysis in rural areas? A qualitative analysis. Internal Medicine Journal. 2015;45(9):957-64.
127. Bladin C, Molocijz N, Ermel S, Bagot KL, Kilkenny M, Vu M, et al. Victorian Stroke Telemedicine Project: implementation of a new model of translational stroke care for Australia. Internal medicine journal. 2015;45(9):951-6.
128. Cadilhac DA, Moloczij N, Denisenko S, Dewey H, Disler P, Winzar B, et al. Establishment of an effective acute stroke telemedicine program for Australia: protocol for the Victorian Stroke Telemedicine project. International Journal of Stroke. 2014;9(2):252-8.
129. Meretoja A, Kaste M, Tatlisumak T. Burden of Ischemic Stroke and Benefits of Stroke Unit Care and Thrombolytic Therapy. In: Preedy VR, Watson RR, editors. Handbook of Disease Burdens and Quality of Life Measures. New York, NY: Springer New York; 2010. p. 1029-60.
130. Department of Health and Human Services. Neurology and Stroke Clinical Advisory Group: Response to Green Paper, 2015 [Available from:

https://www.dhhs.tas.gov.au/__data/assets/pdf_file/0007/186541/CAG_-_Neurology_and_Stroke_-_Submission.pdf.

131. Hastrup S, Johnsen SP, Terkelsen T, Hundborg HH, von Weitzel-Mudersbach P, Simonsen CZ, et al. Effects of centralizing acute stroke services: A prospective cohort study. Neurology. 2018;91(3):e236-e48.

132. Morris S, Ramsay AIG, Boaden RJ, Hunter RM, McKevitt C, Paley L, et al. Impact and sustainability of centralising acute stroke services in English metropolitan areas: retrospective analysis of hospital episode statistics and stroke national audit data. BMJ. 2019;364:l1.

133. Stroke Foundation. Re: Delivering Safe and Sustainable Clinical Services – Green Paper: Rebuilding Tasmania's Health System 2015 [Available from: https://strokefoundation.org.au/-/media/45876093883E46DB88B8EDC1297DA17E.ashx?la=en.

134. Cadilhac DA, Kilkenny MF, Levi CR, Lannin NA, Thrift AG, Kim J, et al. Risk-adjusted hospital mortality rates for stroke: evidence from the Australian Stroke Clinical Registry (AuSCR). Med J Aust. 2017;206(8):345-50.

135. Qureshi AI, Chaudhry SA, Sapkota BL, Rodriguez GJ, Suri MFK. Discharge destination as a surrogate for Modified Rankin Scale defined outcomes at 3- and 12-months poststroke among stroke survivors. Archives of physical medicine and rehabilitation. 2012;93(8):1408-13.e1.

136. Dwyer M, Rehman S, Ottavi T, Stankovich J, Gall S, Peterson G, et al. Urban-rural differences in the care and outcomes of acute stroke patients: systematic review. Journal of the Neurological Sciences. 2018;397:63-74.

137. Fleet R, Bussières S, Tounkara FK, Turcotte S, Légaré F, Plant J, et al. Rural versus urban academic hospital mortality following stroke in Canada. PloS One. 2018;13(1):e0191151.

138. Harnod D, Choi W-M, Chang R-E, Chang C-H, Yang M-C. Are major medical centers better for stroke and myocardial infarction patients in Taiwan? A nationwide population-based study. International Journal of Gerontology. 2010;4(3):137-42.

139. Lichtman JH, Leifheit-Limson EC, Jones SB, Wang Y, Goldstein LB. 30-day risk-standardized mortality and readmission rates after ischemic stroke in critical access hospitals. Stroke. 2012;43(10):2741-7.

140. Borhani-Haghighi A, Safari R, Heydari ST, Soleimani F, Sharifian M, Kashkuli SY, et al. Hospital mortality associated with stroke in southern Iran. Iranian Journal of Medical Sciences. 2013;38(4):314.
141. Hemphill JC, 3rd, Newman J, Zhao S, Johnston SC. Hospital usage of early do-not-resuscitate orders and outcome after intracerebral hemorrhage. Stroke. 2004;35(5):1130-4.
142. Ido MS, Bayakly R, Frankel M, Lyn R, Okosun IS. Administrative data linkage to evaluate a quality improvement program in acute stroke care, Georgia, 2006-2009. Preventing Chronic Disease. 2015;12:E05.
143. Kilkenny MF, Dewey HM, Sundararajan V, Andrew NE, Lannin N, Anderson CS, et al. Readmissions after stroke: linked data from the Australian stroke clinical registry and hospital databases. Med J Aust. 2015;203(2):102-6.
144. Saposnik G, Baibergenova A, O'Donnell M, Hill M, Kapral M, Hachinski V, et al. Hospital volume and stroke outcome Does it matter? Neurology. 2007;69(11):1142-51.
145. Thompson MP, Zhao X, Bekelis K, Gottlieb DJ, Fonarow GC, Schulte PJ, et al. Regional variation in 30-day ischemic stroke outcomes for medicare beneficiaries treated in Get With The Guidelines–Stroke hospitals. Circulation: Cardiovascular Quality and Outcomes. 2017;10(8).
146. Santos NMF, Tavares DMS, Dias FA. Quality of life comparasion of elderly urban and rural stroke victims. Revista de Pesquisa: Cuidado é Fundamental Online. 2014;6(1):387-97.
147. Nuttaset Manimmanakorn M, Vichiansiri R, Nuntharuksa C, Permsirivanich W, Vilai Kuptniratsaikul M. Quality of life after stroke rehabilitation among urban vs. rural patients in Thailand. J Med Assoc Thai. 2008;9(3):394-9.
148. Dillman DA. The design and administration of mail surveys. Annual review of sociology. 1991;17(1):225-49.
149. Lannin NA, Anderson C, Lim J, Paice K, Price C, Faux S, et al. Telephone follow-up was more expensive but more efficient than postal in a national stroke registry. Journal of clinical epidemiology. 2013;66(8):896-902.
150. Group TE. EuroQol-a new facility for the measurement of health-related quality of life. Health policy. 1990;16(3):199-208.
151. Counsell C, Dennis M, McDowall M, Warlow C. Predicting outcome after acute and subacute stroke. Stroke. 2002;33(4):1041-7.

152. Australian Bureau of Statistics. Socio-Economic Indexes for Areas (SEIFA) 2018 [Available from: https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/2033.0.55.001Main+Features12016?OpenDocument.
153. StataCorp L. Stata data analysis and statistical Software. Special Edition Release. 2007;10:733.
154. Dwyer M. Health care providers' perceptions of factors that influence the provision of acute stroke care in urban and rural settings: a qualitative study [thesis chapter]. Regional Differences in Acute Stroke Care and Patient Outcomes. Hobart, Australia: University of Tasmania; 2020.
155. Cadilhac DA, Purvis T, Kilkenny MF, Longworth M, Mohr K, Pollack M, et al. Evaluation of Rural Stroke Services Does Implementation of Coordinators and Pathways Improve Care in Rural Hospitals? Stroke. 2013;44(10):2848-53.
156. National Stroke Foundation. Clinical Audit: Organisational Survey Report 2013: National Stroke Foundation; 2013 [Available from: https://informme.org.au/-/media/E427FAC31B934527BDA5F35CC7DEB699.ashx?la=en.
157. Baatiema L, Otim ME, Mnatzaganian G, Aikins Ad-G, Coombes J, Somerset S. Health professionals' views on the barriers and enablers to evidence-based practice for acute stroke care: a systematic review. Implementation Science. 2017;12(1):74.
158. Kapral M, Hall R, Gozdyra P, Yu A, Jin A, Martin C, et al. Geographic access to stroke care services in rural communities in Ontario, Canada. The Canadian Journal of Neurological Sciences. 2020;47(3):301-8.
159. Joubert J, Prentice LF, Moulin T, Liaw S-T, Joubert LB, Preux P-M, et al. Stroke in rural areas and small communities. Stroke. 2008;39(6):1920-8.
160. Bladin CF, Kim J, Bagot KL, Vu M, Moloczij N, Denisenko S, et al. Improving acute stroke care in regional hospitals: clinical evaluation of the Victorian Stroke Telemedicine program. Medical Journal of Australia. 2020;212(8):371-7.
161. Lindley RI. Telemedicine is improving outcomes for patients with stroke. The Medical journal of Australia. 2020;212(8):364-5.
162. Kilkenny MF, Lannin NA, Levi C, Faux SG, Dewey HM, Grimley R, et al. Weekend hospital discharge is associated with suboptimal care and outcomes: An observational Australian Stroke Clinical Registry study. Int J Stroke. 2019;14(4):430-8.
163. Cadilhac DA, Kilkenny MF, Lannin NA, Dewey HM, Levi CR, Hill K, et al. Outcomes for Patients With In-Hospital Stroke: A Multicenter Study From the

Australian Stroke Clinical Registry (AuSCR). J Stroke Cerebrovasc Dis. 2019;28(5):1302-10.

164. Australian Institute of Health and Welfare. A snapshot of men's health in regional and remote Australia: Australia Institue of Health and Welfare; 2010.

165. Australian Institute of Health and Welfare. Australia's Health 2012. Australian Institute of Health and Welfare; 2012.

166. Pateman KA, Cockburn NL, Batstone MD, Ford PJ. Quality of life of head and neck cancer patients in urban and regional areas: An Australian perspective. Australian Journal of Rural Health. 2018;26(3):157-64.

167. Emery JD, Walter FM, Gray V, Sinclair C, Howting D, Bulsara M, et al. Diagnosing cancer in the bush: a mixed-methods study of symptom appraisal and help-seeking behaviour in people with cancer from rural Western Australia. Family practice. 2013;30(3):294-301.

168. Kilkenny Monique F, Lannin Natasha A, Anderson Craig S, Dewey Helen M, Kim J, Barclay-Moss K, et al. Quality of Life Is Poorer for Patients With Stroke Who Require an Interpreter. Stroke. 2018;49(3):761-4.

169. Thayabaranathan T, Andrew NE, Kilkenny MF, Stolwyk R, Thrift AG, Grimley R, et al. Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data. Quality of Life Research. 2018;27(12):3145-55.

170. Kim H-Y. Statistical notes for clinical researchers: effect size. Restor Dent Endod. 2015;40(4):328-31.

171. Australian Institute of Health and Welfare. Admitted patient care 2017-18: Australian hospital statistics 2019 [Available from: https://www.aihw.gov.au/reports/hospitals/admitted-patient-care-2017-18/contents/at-a-glance.

172. Hubert GJ, Meretoja A, Audebert HJ, Tatlisumak T, Zeman F, Boy S, et al. Stroke thrombolysis in a centralized and a decentralized system (Helsinki and Telemedical Project for Integrative Stroke Care Network). Stroke. 2016;47(12):2999-3004.

173. Tsivgoulis G, Katsanos AH, Malhotra K, Sarraj A, Barreto AD, Köhrmann M, et al. Thrombolysis for acute ischemic stroke in the unwitnessed or extended therapeutic time window. Neurology. 2020;94(12):e1241-e8.

174. Ma H, Campbell BCV, Parsons MW, Churilov L, Levi CR, Hsu C, et al. Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke. New England Journal of Medicine. 2019;380(19):1795-803.
175. Darehed D, Norrving B, Stegmayr B, Zingmark K, Blom MC. Patients with acute stroke are less likely to be admitted directly to a stroke unit when hospital beds are scarce: A Swedish multicenter register study. European Stroke Journal. 2017;2(2):178-86.
176. Stylianou N, Fackrell R, Vasilakis C. Are medical outliers associated with worse patient outcomes? A retrospective study within a regional NHS hospital using routine data. BMJ Open. 2017;7(5):e015676.
177. Bridgwood B, Lager KE, Mistri AK, Khunti K, Wilson AD, Modi P. Interventions for improving modifiable risk factor control in the secondary prevention of stroke. Cochrane Database of Systematic Reviews. 2018(5).
178. Howard G, Kleindorfer DO, Cushman M, Long DL, Jasne A, Judd SE, et al. Contributors to the Excess Stroke Mortality in Rural Areas in the United States. Stroke. 2017;48(7):1773-8.
179. Elfassy T, Grasset L, Glymour MM, Swift S, Zhang L, Howard G, et al. Sociodemographic Disparities in Long-Term Mortality Among Stroke Survivors in the United States: The REGARDS Study. Stroke. 2019;50(4):805-12.
180. Kapral MK, Austin PC, Jeyakumar G, Hall R, Chu A, Khan AM, et al. Rural-Urban Differences in Stroke Risk Factors, Incidence, and Mortality in People With and Without Prior Stroke: The CANHEART Stroke Study. Circulation: Cardiovascular Quality and Outcomes. 2019;12(2):e004973.
181. Australian Bureau of Statistics. Disability, ageing and carers Australia : First Results, 2015: Australian Bureau of Statistics; 2016 [Available from: https://www.abs.gov.au/ausstats/abs@.nsf/productsbytopic/56C41FE7A67110C8CA257FA3001D080B?OpenDocument.
182. Lees KR, Bluhmki E, von Kummer R, Brott TG, Toni D, Grotta JC, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. The Lancet. 2010;375(9727):1695-703.
183. Select Statistical Services. Comparing Two Proportions - Sample Size - Select Statistical Consultants 2020 [Available from: https://select-statistics.co.uk/calculators/sample-size-calculator-two-proportions/.

184. Agency for Clinical Innovation (NSW). Stroke Clinical Audit Process - Assessing and Addressing Unwarranted Clinical Variation 2016 [Available from: https://www.aci.health.nsw.gov.au/__data/assets/pdf_file/0006/319218/3_UCV_Stroke_Talk.pdf.

185. Bureau of Health Information (NSW). Measuring 30–day mortality following hospitalisation: Bureau of Health Information; 2017 [Available from: http://www.bhi.nsw.gov.au/__data/assets/pdf_file/0010/356428/report-spotlight-30-day-mortality-2017.pdf.

186. Rost NS, Bottle A, Lee JM, Randall M, Middleton S, Shaw L, et al. Stroke Severity Is a Crucial Predictor of Outcome: An International Prospective Validation Study. Journal of the American Heart Association. 2016;5(1):e002433.

187. Fonarow GC, Pan W, Saver JL, Smith EE, Reeves MJ, Broderick JP, et al. Comparison of 30-day mortality models for profiling hospital performance in acute ischemic stroke with vs without adjustment for stroke severity. JAMA. 2012;308(3):257-64.

188. Wakerman J. Defining remote health. Australian Journal of Rural Health. 2004;12(5):210-4.

189. Gregory KE, Radovinsky L. Research strategies that result in optimal data collection from the patient medical record. Applied Nursing Research. 2012;25(2):108-16.

190. Andrew NE, Middleton S, Grimley R, Anderson CS, Donnan GA, Lannin NA, et al. Hospital organizational context and delivery of evidence-based stroke care: a cross-sectional study. Implementation Science. 2019;14(1):6.

191. Bray BD, Ayis S, Campbell J, Hoffman A, Roughton M, Tyrrell PJ, et al. Associations between the organisation of stroke services, process of care, and mortality in England: prospective cohort study. BMJ : British Medical Journal. 2013;346:f2827.

192. National Quality Forum. Patient reported outcomes (PROs) in performance measurement 2013 [Available from: https://www.qualityforum.org/WorkArea/linkit.aspx?LinkIdentifier=id&ItemID=72537.

193. Jenkinson C, Gibbons E, Fitzpatrick R. A structured review of patient-reported outcome measures in relation to stroke 2009 [Available from: https://phi.uhce.ox.ac.uk/pdf/PROMs_Oxford_Stroke_17092010.pdf.

194. Reeves M, Lisabeth L, Williams L, Katzan I, Kapral M, Deutsch A, et al. Patient-reported outcome measures (PROMs) for acute stroke: rationale, methods and future directions. Stroke. 2018;49(6):1549-56.
195. Kepplinger J, Barlinn K, Deckert S, Scheibe M, Bodechtel U, Schmitt J. Safety and efficacy of thrombolysis in telestroke: a systematic review and meta-analysis. Neurology. 2016;87(13):1344-51.
196. Wechsler LR, Demaerschalk BM, Schwamm LH, Adeoye OM, Audebert HJ, Fanale CV, et al. Telemedicine Quality and Outcomes in Stroke: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016.
197. Hess DC, Audebert HJ. The history and future of telestroke. Nature Reviews Neurology. 2013;9(6):340-50.
198. Nelson RE, Saltzman GM, Skalabrin EJ, Demaerschalk BM, Majersik JJ. The cost-effectiveness of telestroke in the treatment of acute ischemic stroke. Neurology. 2011;77(17):1590-8.
199. Zhao H, Coote S, Easton D, Langenberg F, Stephenson M, Smith K, et al. Melbourne Mobile Stroke Unit and Reperfusion Therapy. Stroke. 2020;51(3):922-30.
200. Shuaib A, Jeerakathil T. The mobile stroke unit and management of acute stroke in rural settings. Canadian Medical Association Journal. 2018;190(28):E855.
201. Adams NC, Griffin E, Motyer R, Farrell T, Carmody E, O'Shea A, et al. Review of external referrals to a regional stroke centre: it is not just about thrombectomy. Clinical Radiology. 2019;74(12):950-5.
202. Australian Commission on Safety and Quality in Health Care. Draft Acute Stroke Clinical Care Standard: Consultation Report 2014 [Available from: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/draft-acute-stroke-clinical-care-standard-consultation-report.
203. Purvis T, Moss K, Francis L, Borschmann K, Kilkenny MF, Denisenko S, et al. Benefits of clinical facilitators on improving stroke care in acute hospitals: a new programme for Australia. Internal medicine journal. 2017;47(7):775-84.
204. Purvis T, Kilkenny MF, Middleton S, Cadilhac DA. Influence of stroke coordinators on delivery of acute stroke care and hospital outcomes: An observational study. International Journal of Stroke. 2017;13(6):585-91.

205. Kapral MK, Fang J, Silver FL, Hall R, Stamplecoski M, O'Callaghan C, et al. Effect of a provincial system of stroke care delivery on stroke care and outcomes. Canadian Medical Association Journal. 2013;185(10):E483-E91.
206. Bray JE, Coughlan K, Mosley I, Barger B, Bladin C. Are suspected stroke patients identified by paramedics transported to appropriate stroke centres in Victoria, Australia? Internal Medicine Journal. 2014;44(5):515-8.
207. Bray BD, Smith CJ, Cloud GC, Enderby P, James M, Paley L, et al. The association between delays in screening for and assessing dysphagia after acute stroke, and the risk of stroke-associated pneumonia. Journal of Neurology, Neurosurgery & Psychiatry. 2017;88(1):25.
208. Morris S, Hunter RM, Ramsay AI, Boaden R, McKevitt C, Perry C, et al. Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. British Medical Journal. 2014;349:g4757.
209. Fulop NJ, Ramsay A, Hunter RM, McKevitt C, Perry C, Turner SJ, et al. Evaluation of reconfigurations of acute stroke services in different regions of England and lessons for implementation: a mixed-methods study. Health Services Delivery Research. 2019;7(7).
210. Canadian Stroke Network. The quality of stroke care in Canada 2011 [Available from: http://www.canadianstroke.ca/sites/default/files/resources/QoSC-EN.pdf.
211. Zwisler A-D, Rossau HK, Nakano A, Foghmar S, Eichhorst R, Prescott E, et al. The Danish Cardiac Rehabilitation Database. Clinical epidemiology. 2016;8:451-6.
212. Poffley A, Thomas E, Grace SL, Neubeck L, Gallagher R, Niebauer J, et al. A systematic review of cardiac rehabilitation registries. European journal of preventive cardiology. 2017;24(15):1596-609.
213. Westert GP, Groenewoud S, Wennberg JE, Gerard C, DaSilva P, Atsma F, et al. Medical practice variation: public reporting a first necessary step to spark change. International Journal for Quality in Health Care. 2018;30(9):731-5.
214. Bath PM, Lee HS, Everton LF. Swallowing therapy for dysphagia in acute and subacute stroke. Cochrane Database of Systematic Reviews. 2018(10).
215. Vernino S, Brown Robert D, Sejvar James J, Sicks JoRean D, Petty George W, O'Fallon WM. Cause-Specific Mortality After First Cerebral Infarction. Stroke. 2003;34(8):1828-32.

216. Ouyang M, Boaden E, Arima H, Lavados PM, Billot L, Hackett ML, et al. Dysphagia screening and risks of pneumonia and adverse outcomes after acute stroke: An international multicenter study. International Journal of Stroke. 2019;15(2):206-15.
217. Ambulance Tasmania. Clinical Practice Guidelines for Paramedics & Intensive Care Paramedics 2012 [Available from: https://www.dhhs.tas.gov.au/__data/assets/pdf_file/0018/107334/A00_-_Ambulance_Tasmania_Clinical_Practice_Guidelines_for_Paramedics_and....pdf.
218. Nor AM, Davis J, Sen B, Shipsey D, Louw SJ, Dyker AG, et al. The Recognition of Stroke in the Emergency Room (ROSIER) scale: development and validation of a stroke recognition instrument. The Lancet Neurology. 2005;4(11):727-34.
219. Stroke Foundation. No stroke untreated: A fairer health system, delivering all Australians the opportunity to survive and live well after stroke 2020 [Available from: https://strokefoundation.org.au/-/media/E55B1C38B72F40FE8401EB25DC37ACD8.ashx?la=en.
220. Leppert MH, Sillau S, Lindrooth RC, Poisson SN, Campbell JD, Simpson JR. Relationship between early follow-up and readmission within 30 and 90 days after ischemic stroke. Neurology. 2020;94(12):e1249-e58.
221. Kao A, Lanford J, Wong LK, Ranta A. Do clinical nurse specialist led stroke follow-up clinics reduce post-stroke hospital readmissions and recurrent vascular events? Internal medicine journal. 2019.
222. Kjörk EK, Gunnel C, Lundgren-Nilsson Å, Sunnerhagen KS. Experiences, needs, and preferences for follow-up after stroke perceived by people with stroke and healthcare professionals: A focus group study. PloS one. 2019;14(10).

APPENDICES

Appendix A. PubMed search strategy (Chapter Two)

1. rural[title]
2. region*[title]
3. remote*[title]
4. geographic*[title]
5. provinc*[title]
6. district[title]
7. undeserved[title]
8. frontier[title]
9. non-metropolitan[title]
10. nonmetropolitan[title]
11. non-rural[title]
12. urban[title]
13. non-urban[title]
14. nonurban[title]
15. metropolitan[title]
16. rural-urban[title]
17. urban-rural[title]
18. “Rural Health”[MeSH]
19. “Socioeconomic Factors”[MeSH]
20. “Rural Population”[MeSH]
21. “Urban Health”[MeSH]
22. “Urban Population”[MeSH]
23. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
24. “Stroke/classification”[MeSH]
25. “Stroke/complications”[MeSH]
26. “Stroke/diagnosis”[MeSH]
27. “Stroke/diagnostic imaging”[MeSH]

28. “Stroke/drug therapy”[MeSH]

29. “Stroke/economics”[MeSH]

30. “Stroke/epidemiology”[MeSH]

31. “Stroke/mortality”[MeSH]

32. “Stroke/nursing”[MeSH]

33. “Stroke/organization and administration”[MeSH]

34. “Stroke/prevention and control”[MeSH]

35. “Stroke/statistics and numerical data”[MeSH]

36. “Stroke/therapy”[MeSH]

37. #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36

38. stroke[Title]

39. cerebrovascular[Title]

40. cardiovascular[Title]

41. “cerebral vascular”[Title]

42. “cardio vascular”[Title]

43. CVA[Title]

44. “subarachnoid haemorrhage”[Title]

45. “subarachnoid hemorrhage”[Title]

46. “intracerebral hemorrhage”[Title]

47. “intracerebral haemorrhage”[Title]

48. “cerebral infarct”[Title]

49. “cerebral infarction”[Title]

50. “brain attack”[Title]

51. #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50

52. “Hospitals*”[MeSH]

53. “Health Services Needs and Demand*”[MeSH]

54. “Health Services Research”[MeSH]

55. “National Health Programs”[MeSH]

56. “Emergency Medical Services/standards”[MeSH]

57. “Emergency Medical Services/statistics and numerical data”[MeSH]

58. “Emergency Medical Services/supply and distribution”[MeSH]

59. “Hospitalisation”[MeSH]

60. “Hospitalisation*/trends”[MeSH]

61. “Patient Care”[MeSH]

62. “Secondary Prevention*”[MeSH]

63. “Delivery of Health Care”[MeSH]

64. “Delivery of Health Care/economics”[MeSH]

65. “Delivery of Health Care/methods”[MeSH]

66. “Delivery of Health Care/standards”[MeSH]

67. “Inpatients”[MeSH]

68. “Reperfusion”[MeSH]

69. “Hospital Mortality*”[MeSH]

70. “Quality Indicators, Health Care/economics”[MeSH]

71. “Quality Indicators, Health Care/statistics and numerical data”[MeSH]

72. “Quality Assurance, Health Care”[MeSH]

73. “Outcome and Process Assessment Health Care”[MeSH]

74. #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73

75. #23 and #37 and #51 and #74

Appendix B. Care Process Measures by Region (Chapter Three)

	Urban		Rural		Averages				
	RHH (n=100)	**LGH (n=100)**	**MCH (n=95)**	**NWRH (n=100)**	**Urban**	**Rural**	**P value**	**National[a]**	**AuSCR[b]**
Transport to a hospital able to provide thrombolysis (with exclusions)†	33/38 (86.8%)	22/28 (78.6%)	0%	0%	83.3%	0%	-	71%	76%
Transport to a hospital able to provide thrombolysis (without exclusions)	33/100 (33%)	22/100 (22%)	0%	0%	27.5%	0%			
Thrombolysis in ischaemic stroke (with exclusions)†	7/12 (58.3%)	9/14 (64.3%)	0%	0%	61.5%	0%	-	-	-
Thrombolysis in ischaemic stroke (without exclusions)	7/100 (7%)	9/100 (9%)	0%	0%	8%	0%	-	13%	14%
Presentation and intravenous thrombolysis within 4.5 hours of symptom onset	6/12 (50%)	9/14 (64.3%)	0%	0%	57.7%	0%	-	38%	31%
Thrombolysis within 60 minutes of hospital arrival	1/7 (14.3%)	2/9 (22.2%)	0%	0%	18.8%	0%	-	30%	39%
Time from onset of symptoms to thrombolysis (h:mm) (median)	2:30	2:40	-	-	2:35	-	-	2:36	2:36
Admission into a stroke unit	80/100 (80%)	73/100 (73%)	0%	0%	76.5%	0%	-	69%	73%
90% of acute hospital admission episode time spent on a stroke unit	61/100 (61%)	43/100 (43%)	0%	0%	52.0%	0%	-	45%	-
Assessment for rehabilitation by a physiotherapist within 48 hours of admission	74/95 (77.9%)	66/94 (70.2%)	71/94 (75.5%)	74/99 (74.7%)	74.1%	75.1%	.82	67%	-
Rehabilitation therapy within 48 hours of initial assessment	52/65 (80%)	52/67 (77.6%)	51/64 (79.7%)	48/65 (73.8%)	78.8%	76.7%	.77	86%	-
Treatment for a rehabilitation goal commencing during an acute admission	61/64 (95.3%)	67/67 (100%)	60/65 (92.3%)	60/65 (92.3%)	97.7%	92.3%	.05	90%	-
Discharge on statin, antihypertensive and antithrombotic medications	59/67 (88.1%)	43/57 (75.4%)	50/80 (62.5%)	63/84 (75%)	82.3%	68.9%	.01	69%	49%
Statins	79/82 (96.3%)	72/76 (94.7%)	79/83 (95.2%)	75/86 (87.2%)	95.6%	91.1%	.13	-	77%
Antihypertensives	66/71 (93%)	56/70 (80%)	55/83 (66.3%)	76/86 (88.4%)	86.5%	77.5%	.006	-	70%
Antithrombotics	86/87 (98.9%)	86/86 (100%)	76/83 (91.6%)	84/86 (97.7%)	99.4%	94.7%	<.001	-	88%
Discharge on oral anticoagulants for atrial fibrillation	20/20 (100%)	11/12 (91.7%)	22/29 (75.9%)	10/20 (50%)	96.9%	65.3%	<.001	70%	-
Risk factor modification advice before leaving the hospital	32/45 (71.1%)	27/39 (69.2%)	23/42 (54.8%)	16/44 (36.4%)	70.2%	45.3%	.001	70%	-
Dysphagia screening within 24 hours	75/86 (87.2%)	57/91 (62.6%)	81/93 (87.1%)	68/96 (70.8%)	74.6%	78.8%	.39	49%	80%
Dysphagia screen passed before first oral intake of fluids, nutrition, or medications	64/85 (75.3%)	31/91 (34.1%)	55/92 (59.8%)	51/94 (54.3%)	54%	57%	.14	63%	51%

†Exclusions include presentation >4.5 hours after symptom onset, presence of intracranial haemorrhage, among others (114)
[a] Figures obtained from the Stroke Foundation's 2017 National Stroke Audit Acute Services Report (62)
[b] Figures obtained from the 2017 AuSCR Annual Report (86)

Appendix C. Ethical Approval (Chapter Three)

Office of Research Services
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HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

22 December 2016

Professor Leigh Kinsman
[School of Health Sciences, University of Tasmania]

Sent via email

Dear Professor Kinsman

REF NO: H0016053
TITLE: Acute Stroke Services in Tasmania: Identifying drivers of clinical variation (baseline examination of variability)

Document	***Version***	***Date***
Low Risk Application		
Privacy Form		

The Tasmanian Health and Medical Human Research Ethics Committee considered and approved the above documentation on **13 December 2016** to be conducted at the following site(s):

Royal Hobart Hospital
North West Regional Hospital
HCA - Mersey Community Hospital

Please ensure that all investigators involved with this project have cited the approved versions of the documents listed within this letter and use only these versions in conducting this research project.

This approval constitutes ethical clearance by the Health and Medical HREC. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approvals of other bodies or authorities are required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

All committees operating under the Human Research Ethics Committee (Tasmania) Network are registered and required to comply with the *National Statement on the Ethical Conduct in Human Research* (NHMRC 2007 updated 2014).

Therefore, the Chief Investigator's responsibility is to ensure that:

(1) The individual researcher's protocol complies with the HREC approved

protocol.

(2) Modifications to the protocol do not proceed until **approval** is obtained in writing from the HREC. Please note that all requests for changes to approved documents must include a version number and date when submitted for review by the HREC.

(3) Section 5.5.3 of the National Statement states:

Researchers have a significant responsibility in monitoring approved research as they are in the best position to observe any adverse events or unexpected outcomes. They should report such events or outcomes promptly to the relevant institution/s and ethical review body/ies and take prompt steps to deal with any unexpected risks.

The appropriate forms for reporting such events in relation to clinical and non-clinical trials and innovations can be located at the website below. All adverse events must be reported regardless of whether or not the event, in your opinion, is a direct effect of the therapeutic goods being tested. http://www.utas.edu.au/research-admin/research-integrity-and-ethics-unit-rieu/human-ethics/human-research-ethics-review-process/health-and-medical-hrec/managing-your-approved-project

(4) All research participants must be provided with the current Patient Information Sheet and Consent Form, unless otherwise approved by the Committee.

(5) The Committee is notified if any investigators are added to, or cease involvement with, the project.

(6) This study has approval for four years contingent upon annual review. A *Progress Report* is to be provided on the anniversary date of your approval. Your first report is due **13 December 2017.** You will be sent a courtesy reminder closer to this due date.

(7) A *Final Report* and a copy of the published material, either in full or abstract, must be provided at the end of the project.

Should you have any queries please do not hesitate to contact me on (03) 6226 2764.

Yours sincerely

Camille Kay
Ethics Administrator
Office of Research Services
University of Tasmania
Private Bag 01
Hobart TAS 7001
Phone: (03) 6226 7479
Fax: (03) 6226 2765

Appendix D. Email Script (Chapter Four)

Hi there,

Please find attached an information sheet from Mitchell Dwyer, a PhD student with the University of Tasmania. Under the guidance of his supervision team (Prof Leigh Kinsman, Prof Greg Peterson, Dr Karen Ford and Dr Seana Gall), he is conducting research for a thesis to be titled 'Urban-rural differences in acute stroke care and patient outcomes'.

He is seeking clinicians who are willing to participate in research relating to the care of acute stroke patients within Tasmanian hospitals. Your knowledge and firsthand experiences will provide valuable insights which may assist with improving acute stroke care within Tasmania's hospitals.

If you are willing to participate, could you please email the student directly: mitchell.dwyer@utas.edu.au.

Kind regards,

[Insert Clinician's Name]

Appendix E. Consent Form (Chapter Four)

UNIVERSITY of TASMANIA | DIVISION OF RESEARCH

CONSENT FORM

Health care providers' perceptions of factors influential to the provision of acute stroke care in urban and rural settings: a qualitative study

1. I acknowledge that the nature, purpose and contemplated effects of the project so far as it affects me, have been fully explained to my satisfaction by the research worker and my consent is given voluntarily.

2. The details of the project have also been explained to me, including the anticipated length of time it will take. I understand that my involvement means participation in a focus group (and potentially an interview) to discuss the provision of acute stroke care within either the Royal Hobart Hospital, Mersey Community Hospital, or North West Regional Hospital. Focus groups and interviews will each take approximately 1 hour, and will take place at a venue and time convenient to the participants.

3. I understand that here are no associated risks with participation in this project. There will be a minor inconvenience due to the amount of time taken to participate in the focus group/interview process. I am able to withdraw from the interview and the project at any stage without any effect on my relationship with my employer.

4. Although I understand that the purpose of this research project is to identify factors which health service providers deem to be influential to the provision of the acute stroke care processes in urban and rural areas of Tasmania, it has also been explained that my involvement may not be of any benefit to me.

5. I understand that no information revealing my identity will be published.

6. I understand that my involvement in the project (or my withdrawal from it) will not affect my relationship with my employer.

7. I understand that I will be given a signed copy of this consent form and a participant information sheet. I am not giving up my legal rights by signing this consent form.

8. I understand that the research will be conducted in accordance with the latest versions of the *National Statement on Ethical Conduct in Human Research* and applicable privacy laws.

Name of participant _____

Signature of participant _____ Date _____

I have explained this project and the implications of participation in it to this volunteer and I believe that the consent is informed and that he/she understands the implications of participation.

Name of investigator _____

Signature of investigator _____ Date _____

Appendix F. Participant Information Sheet (Chapter Four)

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Health care providers' perceptions of factors influential to the provision of acute stroke care in urban and rural settings: a qualitative study

PARTICIPANT INFORMATION SHEET

Invitation

You are invited to participate in a research study to explore the perceptions of clinicians providing acute stroke care in Tasmania's tertiary care hospitals.

The study is being conducted by:

- Mitchell Dwyer, PhD Candidate, School of Health Sciences, University of Tasmania
- Professor Gregory Peterson, School of Medicine, University of Tasmania
- Professor Karen Francis, Head – Nursing Discipline, University of Tasmania.
- Dr Seana Gall, Senior Research Fellow, Menzies Institute for Medical Research, University of Tasmania.
- Dr Karen Ford, ADON Research & Practice Development, Tasmanian Health Service

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. 'What is the purpose of this study?'

The purpose of this study is to identify factors which health service providers deem to be influential to the provision of the acute stroke care processes in urban and rural areas of Tasmania.

2. 'Why have I been invited to participate in this study?'

You have been invited to participate in this study, as your professional group is involved in the provision of acute stroke care to patients admitted to Tasmania's tertiary hospitals.

3. 'What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, or to withdraw from the study, it will not affect your relationship with your employer. If you choose to withdraw from the study during the focus group or interview, please inform the researcher. Please note it may not be possible to withdraw your data from the study results.

4. 'What does this study involve?'

If you agree to participate in this study, you may be involved in one of two ways:

Participation in a focus group

- You may volunteer to participate in focus groups with other health care professionals from your workplace who are involved in the provision of acute stroke care.
- The purpose of the focus groups is to identify factors which health service providers deem to be influential to the provision of the acute stroke care processes in urban and rural areas of Tasmania. For the purpose of this study, the Royal Hobart Hospital will be considered an 'urban' area, while the Mersey Community Hospital and North West Regional Hospital will be considered to be 'rural'.
- Each focus group will take 45-60 minutes
- Focus group meetings will be audio recorded to help ensure accurate reporting of the findings.

Participation in an interview

- You may volunteer to participate in a one-to-one interview with one of the researchers, as an alternative to attending a focus group.
- The purpose of these interviews is identical to that of the focus groups.
- Interviews will take 45-60 minutes, and will be audio recorded to help ensure accurate reporting of the findings.

5. 'How is this study being paid for?'

There is no dedicated funding for this research. The PhD candidate, Mitchell Dwyer, is in receipt of an Australian Postgraduate Award scholarship to enable him to complete his studies.

6. 'Are there risks to me in taking part in this study?'

There are no physical risks associated with the study. The focus groups and interviews will ask questions about the nature of acute stroke care within your workplace. You may refuse to answer any of the questions within any focus group or interview you attend, and you may take a break at any time during the study. Because of the nature of a focus group, confidentiality and privacy cannot be guaranteed. However, all the participants will be asked to maintain the confidentiality of what is discussed within the group.

7. 'Will I benefit from the study?'

There are no direct benefits to you for being part of this study. It is hoped that the findings presented to participants, and the discussion occurring during focus groups may prompt a discussion among clinicians about the improving the quality of acute stroke care within their hospital.

8. 'Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything. Your participation in the research is entirely voluntary.

9. 'How will my confidentiality be protected?'

- Given the nature of focus groups, the researchers cannot explicitly maintain confidentiality. However, when the group comes together, agreed ways of working will include maintaining confidentiality about what is discussed within the group.
- Any information that is obtained in connection with participation in the focus groups or workshops will not include identifying information.
- Where interviews are concerned, any identifying information we may hold (e.g. your name, position, employer) will be removed before any reporting or publication of data. Your interview transcript will also be coded with a unique identification number.
- Data will be held securely on a password protected computer at a UTAS office, and only accessible to the research team. Hard copies of interview transcripts will be kept in a locked filing cabinet in the locked office of the researcher, Mitchell Dwyer

10. 'What happens with the results?'

The results will form part of the PhD candidate's final thesis. Results of the study may also be published in peer-reviewed journals or presented at academic conferences. In any publication, information will be provided in such a way that you cannot be identified.

11. 'What should I do if I want to discuss this study further before I decide?'

When you have read this information, you will be provided an opportunity to ask questions and any queries you may have can be answered. If you would like to know more at any stage, please do not hesitate to contact Mitchell Dwyer on 04.....

12. 'Who should I contact if I have concerns about the conduct of this study?'

This study has been approved by the Tasmanian Health and Medical Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 6254 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote H0017665.

Thank you for taking the time to consider this study.

This information sheet is for you to keep.

Appendix G. Ethical Approval (Chapter Four)

12 April 2019

Professor Karen Francis
C/- Nursing, University of Tasmania

Dear Professor Francis

REF NO: H0017665
TITLE: Health care providers perceptions of factors that influence the provision of acute stroke care in urban and rural settings: a qualitative study

Document	*Version*	*Date*
Low Risk Application Form		
Participant Information Sheet		
Consent Form		
Appendix A - Email Script		
Appendix B - Approval Process Flowchart		
Appendix C - Head of Department Approvals		

The Tasmania Health and Medical Human Research Ethics Committee (HREC) considered and approved the above documentation on **03 December 2018** to be conducted at the following site(s):

Royal Hobart Hospital
Launceston General Hospital
HCA - Mersey Community Hospital

Please ensure that all investigators involved with this project have cited the approved versions of the documents listed within this letter and use only these versions in conducting this research project.

This approval constitutes ethical clearance by the Health and Medical HREC. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approvals of other bodies or authorities are required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

In accordance with the National Statement on Ethical Conduct in Human Research, it is the responsibility of institutions and researchers to be aware of both general and specific legal requirements, wherever relevant. If researchers are uncertain they should seek legal advice to confirm that their proposed research is in compliant with the relevant laws. University of Tasmania researchers may seek legal advice from Legal Services at the University.

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All committees operating under the Human Research Ethics Committee (Tasmania) Network are registered and required to comply with the *National Statement on the Ethical Conduct in Human Research* (NHMRC 2007 updated 2018).

Therefore, the Chief Investigator's responsibility is to ensure that:

(1) All investigators are aware of the terms of approval, and that the research is conducted in compliance with the HREC approved protocol or project description.

(2) Modifications to the protocol do not proceed until **approval** is obtained in writing from the HREC. This includes, but is not limited to, amendments that:

(i) are proposed or undertaken in order to eliminate immediate risks to participants;
(ii) may increase the risks to participants;
(iii) significantly affect the conduct of the research; or
(iv) involve changes to investigator involvement with the project.

Please note that all requests for changes to approved documents must include a version number and date when submitted for review by the HREC.

(3) Reports are provided to the HREC on the progress of the research and any safety reports or monitoring requirements as indicated in NHMRC guidance. The appropriate forms for reporting such events in relation to clinical and non-clinical trials and innovations can be located at the website below. All adverse events must be reported regardless of whether or not the event, in your opinion, is a direct effect of the therapeutic goods being tested. http://www.utas.edu.au/research-admin/research-integrity-and-ethics-unit-rieu/human-ethics/human-research-ethics-review-process/health-and-medical-hrec/managing-your-approved-project

(4) The HREC is informed as soon as possible of any new safety information, from other published or unpublished research, that may have an impact on the continued ethical acceptability of the research or that may indicate the need for modification of the project.

(5) All research participants must be provided with the current Participant Information Sheet and Consent Form, unless otherwise approved by the Committee.

(6) This study has approval for four years contingent upon annual review. A *Progress Report* is to be provided on the anniversary date of your approval. Your first report is due **03 December 2019,** and you will be sent a courtesy reminder closer to this due date. Ethical approval for this project will lapse if a Progress Report is not submitted in the time frame provided

(7) A *Final Report* and a copy of the published material, either in full or abstract, must be provided at the end of the project.

(8) The HREC is advised of any complaints received or ethical issues that arise during the course of the project.

(9) The HREC is advised promptly of the emergence of circumstances where a court, law enforcement agency or regulator seeks to compel the release of findings

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or results. Researchers must develop a strategy for addressing this and seek advice from the HREC.

Should you have any queries please do not hesitate to contact me on (03) 6226 6254 or via email Human.ethics@utas.edu.au.

Yours sincerely

Ailin Ding
Administration Officer

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Appendix H. Co-investigators and other contributors to the Australian Stroke Clinical Registry (Chapter Five)

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:

Steering and Management Committee

Craig Anderson PhD (Royal Prince Alfred Hospital NSW, site investigator, The George Institute for Global Health University of NSW, The George Institute for Global Health at Peking University Health Science Center China); **Dominique Cadilhac** PhD (Stroke and Ageing Research, School of Clinical Sciences at Monash Health, Monash University VIC, Stroke Division, The Florey Institute of Neuroscience and Mental Health VIC, Data Custodian); **Geoffrey Donnan** MD (Stroke Division, The Florey Institute of Neuroscience and Mental Health VIC); **Rohan Grimley** MBBS (Gympie Hospital QLD, Nambour General Hospital QLD, site investigator, Sunshine Coast Clinical School, University of Queensland QLD); **Peter Hand** MBBS, MD, FRACP (Royal Melbourne Hospital VIC, site investigator)

Steering Committee

Julie Bernhardt PhD (The Florey Institute of Neuroscience and Mental Health VIC); **Paul Bew** MPhty (The Prince Charles Hospital QLD); **Christopher Bladin** MD, MBBS, FRACP (Box Hill Hospital VIC, site investigator); **Greg Cadigan** BN (Queensland State-wide Stroke Clinical Network QLD); **Helen Castley** MBBS (Royal Hobart Hospital Tasmania, site investigator); **Andrew Evans** MBBS (Hons), FRACP (Westmead Hospital NSW); **Susan Hillier** PhD (University of South Australia, SA); **Erin Lalor** PhD (Stroke Foundation VIC); **Andrew Lee** MBBS FRACP (Flinders Medical Centre, South Australia); **Richard Lindley** PhD (The George Institute for Global Health NSW); **Mark Mackay** MBBS, FRACP (Royal Children's Hospital VIC, site investigator); **Sandra Martyn** (Health Statistics Centre Queensland Health QLD); **John McNeil** PhD (Monash University VIC); **Sandy Middleton** PhD (Nursing Research Institute, St Vincent's Health Australia NSW, Australian Catholic University NSW); **Michael Pollack** MBBS, FAFRM (RACP), FACRM, FFPM (ANZCA), MMedSci (Clin Epi) (Hunter Stroke Service NSW); **Mark Simcocks** BSc (VIC, Consumer Representative); **Frances Simmonds** MSc(Med), (Australasian Rehabilitation Outcomes Centre NSW); **Amanda Thrift** PhD (Stroke and Ageing Research, School of Clinical Sciences at Monash Health, Monash University VIC); **Andrew Wesseldine** MBBS, FRACP (St John of God Healthcare; Department of Health WA)

Management Committee

Helen Dewey PhD (Austin Hospital VIC, Box Hill Hospital VIC, site investigator, Eastern Health Clinical School, Monash University VIC); **Steven Faux** FAFRM (RACP) (St Vincent's Health Australia NSW); **Kelvin Hill** BAppSci (Stroke Foundation VIC); **Natasha Lannin** PhD (Faculty of Health Sciences, La Trobe University VIC, Occupational Therapy Department, Alfred Health VIC); **Christopher Levi** PhD (Acute Stroke Services, John Hunter Hospital NSW, site investigator); **Christopher Price** BSocW BSc (National Stroke Foundation)

Site Investigators

Lauren Arthurson BSpPath, MHlthServMt (Echuca Regional Health VIC); **Pradeep Bambery** MD, FRCP(G), FRACP (Bundaberg Hospital QLD); **Tim Bates** MBBS, FRACP (Swan District Hospital WA); **Carolyn Beltrame** RN (Div1) (Latrobe Regional Hospital VIC); **David Blacker** MBBS, FRACP (Sir Charles Gairdner Hospital WA); **Ernie Butler** MBBS FRACP (Peninsula Health VIC); **Sean Butler** FIMLS, BM Hons, MRCP(UK), FRACP (Prince Charles Hospital QLD); **Chris Charnley** MBBS (Warrnambool Base Hospital VIC); **Jo Cotterell** BPhysio (Mildura Base Hospital VIC); **Douglas Crompton** MA, PhD, MBBS, FRACP (Northern Hospital VIC); **Vanessa Crosby** Dip Physio (Albury-Wodonga Health VIC); **Carolyn De Wytt** MRCP (UK), MB BCH DUBL, FRACP (Greenslopes Private Hospital QLD); **David Douglas** MBBS, M Admin, FRACGP, FAFRM (RACP) (Ipswich Hospital QLD); **Martin Dunlop** MBBS, FACRM (Cairns Base Hospital QLD); **Paula Easton** BPhty (Hons) (Mackay Hospital QLD); **Sharan Ermel** RN (Div1) (Bendigo Health VIC); **Nisal Gange** MBBS, AMC CERT (Toowoomba Hospital QLD); **Richard Geraghty** MBBS, FRACP (Redcliffe Hospital QLD); **Melissa Gill** BAppSc (SpPath) (Armidale Hospital, NSW); **Graham Hall** MBBS, FRACP (Princess Alexandra Hospital QLD); **Geoffrey Herkes** MBBS, PhD, FRACP (Royal North Shore Hospital NSW); **Karen Hines** BHIM (Caboolture Hospital QLD); **Francis Hishon** RN (Redland Hospital QLD); **James Hughes** BMed, FRACP (Tamworth Hospital NSW); **Joel Iedema** MBBS, FRACP (Redland Hospital QLD); **Martin Jude** MBBS, FRACP (Wagga Wagga Hospital NSW); **Thomas Kraemer** Approbation als Arzt, STATE EXAM MED MUNSTER, FRACP (Ballarat Health Services VIC); **Paul Laird** MBBS, FRACP (Rockhampton Hospital QLD); **Johanna Madden** BPhysio (Goulburn Valley Health VIC); **Graham Mahaffey** RN (Hervey Bay Hospital QLD); **Suzana Milosevic** MD, FRACP, AMC CERT (Logan Hospital QLD); **Peter O'Brien** MBBS, DIP RANZCOG, FRACMA, FACRRM (Warrnambool Hospital VIC); **Trisha Oxley** RN/RM, MANP (Critical Care) (Swan Hill District Health VIC); **Michaela Plante** RN (Div 1) (Rockhampton Hospital QLD); **Juan Rois-Gnecco** Medico Cirujano Javeriana, FAFRM (Ipswich Hospital QLD); **Stephen Read** MBBS, PhD, FRACP (Royal Brisbane and Women's Hospital QLD); **Kristen Rowe** BNurs, Cert NeuroSci Nurs (Austin Health VIC); **Fiona Ryan** BAppSc (SpPath), MHlthSc (Orange Hospital and Bathurst Hospitals NSW); **Arman Sabet** MD, FRACP, BSc (Gold Coast Hospital and Robina Hospital QLD); **Noel Saines** MBBS, FRACP (The Wesley Hospital QLD); **Eva Salud** MD, AMC CERT (Gympie Hospital QLD); **Amanda Siller** MBBS, FRACP (Queen Elizabeth II Jubilee Hospital QLD); **Christopher Staples** MD (Mater Adults QLD); **Amanda Styles** RN (Div 1) (Armidale Hospital NSW); **Judith Walloscheck** MBA (Bendigo Health VIC); **Richard White** MD, FRCP, FRACP. (Townsville Hospital QLD); **Andrew Wong** MBBS, PhD (Royal Brisbane and Women's Hospital QLD); **Lillian Wong** MBBS FRACP (Logan Hospital QLD)

Staff at The Florey Institute of Neuroscience and Mental Health VIC

Robin Armstrong, Leonid Churilov, Alison Dias, Kelly Drennan, Adele Gibbs, Brenda Grabsch, Jen Holland, Monique Kilkenny, Joosup Kim, Charlotte Krenus, Francis Kung, Joyce Lim, Karen Moss, Kate Paice, Enna Salama, Sam Shehata, Sabrina Small, Renee Stojanovic, Steven Street, Emma Tod, Kasey Wallis, Julia Watt

Staff at Monash University VIC
Nadine Andrew

Appendix I. Ethical Approval (Chapter Five)

UNIVERSITY of TASMANIA

13 March 2019

Professor Karen Francis
[ADDRESS]

Sent via email

Dear Professor Francis

REF NO: H0017787
TITLE: Urban-rural differences in the care and outcomes of acute stroke patients

Document	*Version*	*Date*
Low Risk Application Fomr		
Letter of support from Monash University dated October 2018		

The Tasmania Health and Medical Human Research Ethics Committee (HREC) considered and approved the above documentation on **04 February 2019** to be conducted at the following site(s):

Health Science

Please ensure that all investigators involved with this project have cited the approved versions of the documents listed within this letter and use only these versions in conducting this research project.

This approval constitutes ethical clearance by the Health and Medical HREC. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approvals of other bodies or authorities are required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

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Therefore, the Chief Investigator's responsibility is to ensure that:

(1) All investigators are aware of the terms of approval, and that the research is conducted in compliance with the HREC approved protocol or project description.

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(i) are proposed or undertaken in order to eliminate immediate risks to participants;
(ii) may increase the risks to participants;
(iii) significantly affect the conduct of the research; or
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Please note that all requests for changes to approved documents must include a version number and date when submitted for review by the HREC.

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(4) The HREC is informed as soon as possible of any new safety information, from other published or unpublished research, that may have an impact on the continued ethical acceptability of the research or that may indicate the need for modification of the project.

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(7) A *Final Report* and a copy of the published material, either in full or abstract, must be provided at the end of the project.

(8) The HREC is advised of any complaints received or ethical issues that arise during the course of the project.

(9) The HREC is advised promptly of the emergence of circumstances where a court, law enforcement agency or regulator seeks to compel the release of findings or results. Researchers must develop a strategy for addressing this and seek advice from the HREC.

Should you have any queries please do not hesitate to contact me on (03) 6226 6254 or via email Human.ethics@utas.edu.au.

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Yours sincerely

Lisa Hall

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Appendix J. Flow Diagrams of AuSCR Participant Follow-up (2010-2015) (Chapter Five)

SOURCE: 2010 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/06/auscr-final-2010-annual-report-for-distribution.pdf

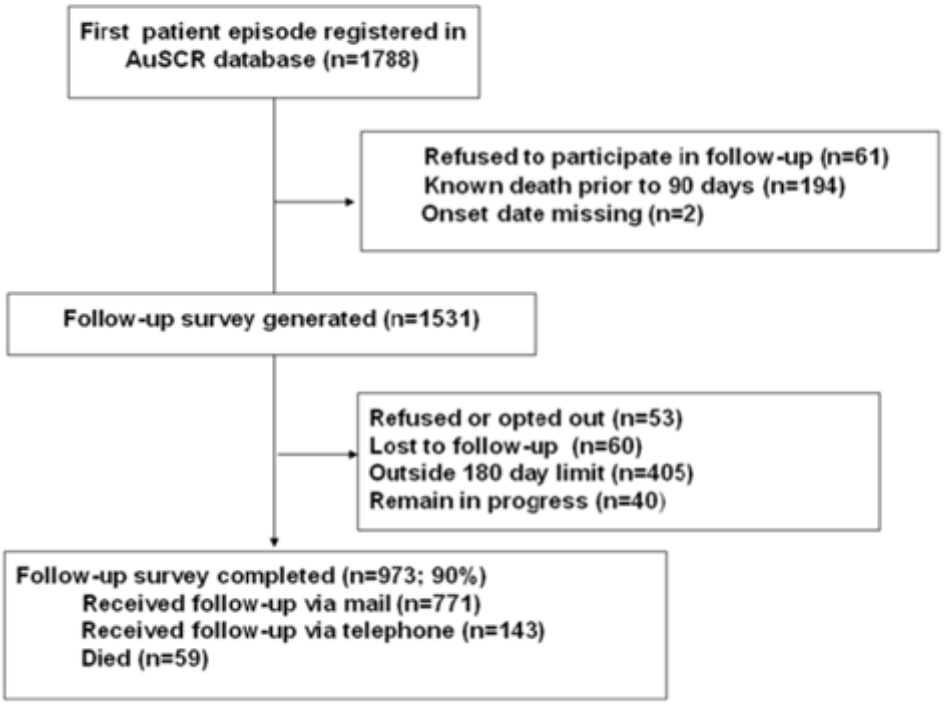


Figure 9: Flow diagram of the follow-up assessments for patients admitted in 2010

Characteristics of the 973 registrants who completed follow-up assessments are summarised in Table 7. The mean age was 72 years and 43% were female; 66% of them had ischemic stroke. This information is consistent with the entire registrant baseline sample characteristics presented in Table 7.

Baseline characteristics for 973 registrants with complete follow-up and 809 registrants without followw-up data in 2010

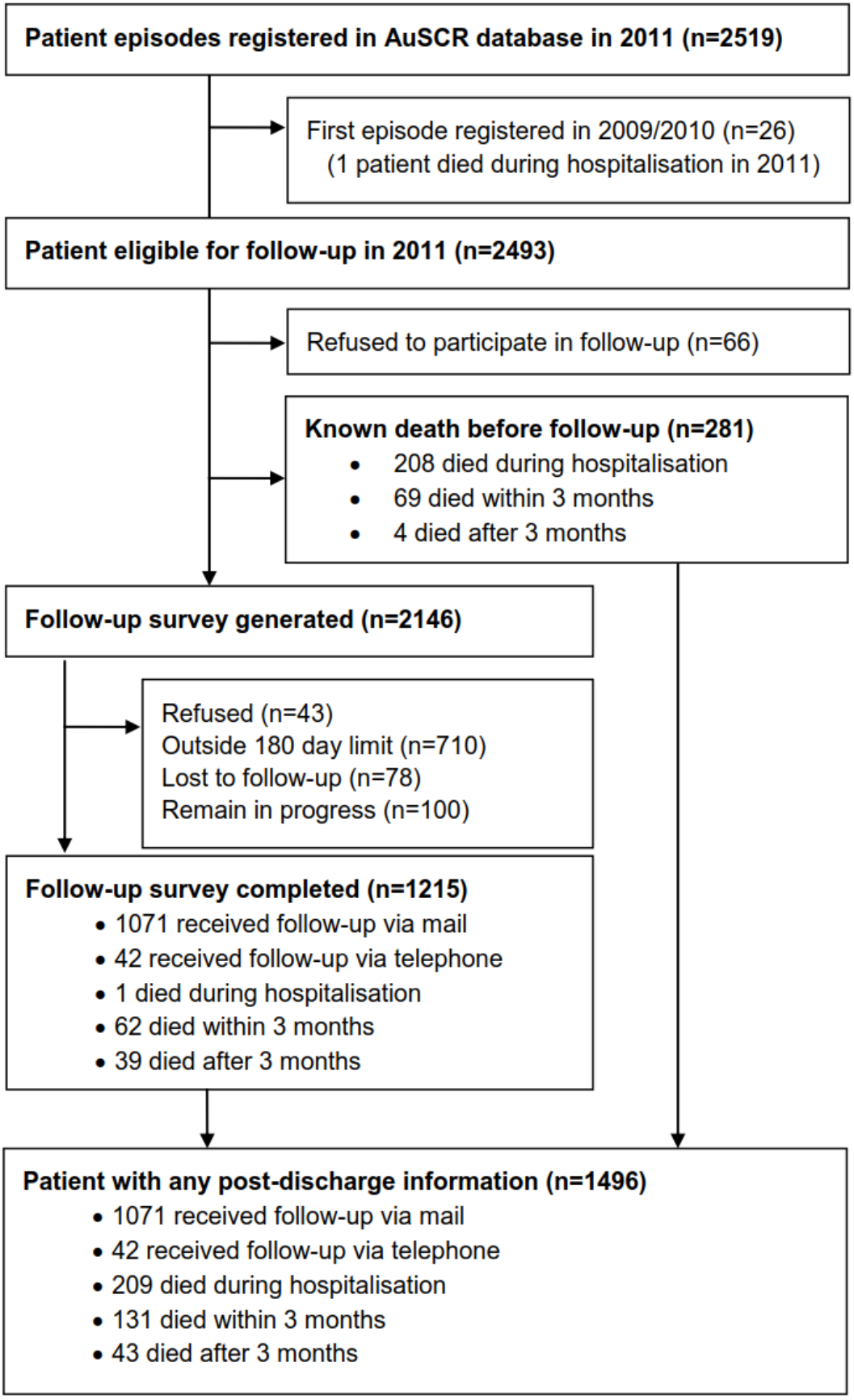
	Patients with complete follow-up (n=973)	Patients without follow-up data (n=809)	p value
Age (years), mean (SD)	72 (14)	72 (15)	0.55
Gender, female, n (%)	408/951 (43%)	362/787 (46%)	0.20
Aboriginal and/or Torres Strait Islander, n (%)	11/972 (1%)	19/800 (2%)	0.04
Type of stroke, n (%)			0.003
Ischaemic	639/971 (66%)	508/807 (63%)	
Haemorrhagic	108/971 (11%)	133/807 (16%)	
TIA	198/971 (20%)	136/807 (17%)	
Undetermined	26/971 (3%)	30/807 (4%)	
Able to walk on admission, n (%)	429/918 (47%)	257/775 (33%)	<0.001
Length of hospital admission (days), median (IQR)	7 (4 to 12)	7 (4 to 14)	0.20
Treated in a stroke unit, n (%)	788/965 (82%)	599 (76%)	0.002

SOURCE: 2011 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/06/2011-auscr-annual-report-final.pdf

Baseline characteristics for 1496 registrants with (and 997 registrants without) any post-discharge information in 2011

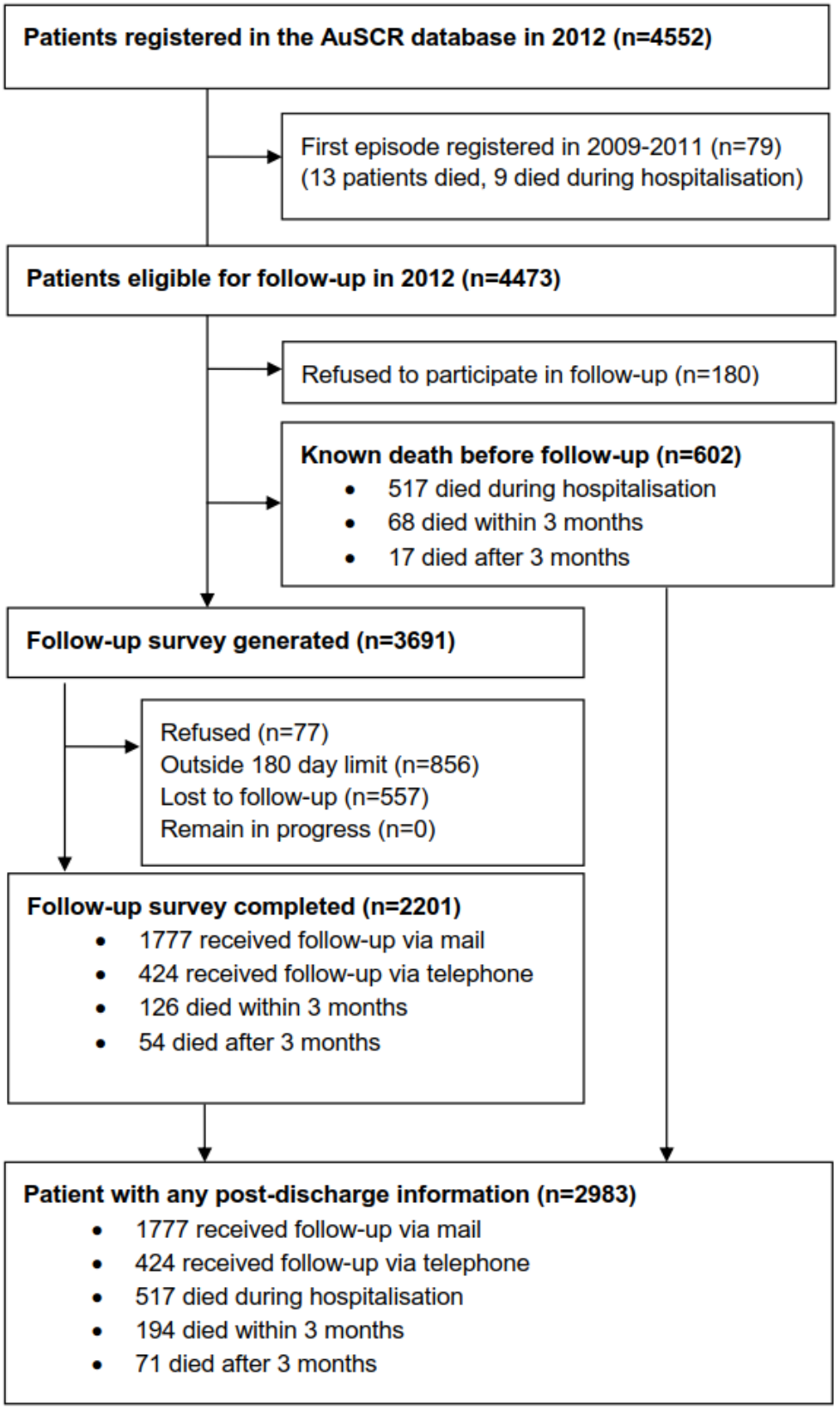
	Patients with any post-discharge information (complete follow-up or death) (n=1496)	**Patients without post-discharge information (refused, lost, after 6 month, or in progress) (n=997)**	***p*-value**
Age (years), mean (SD)	75 (13)	70 (16)	<0.001
Gender, female, n (%)	698/1479 (47%)	470/987 (48%)	0.84
Aboriginal and/or Torres Strait Islander, n (%)	5/1479 (0.3%)	13/988 (1%)	0.005
Type of stroke, n (%)			0.006
Ischaemic	1027/1496 (69%)	658/996 (66%)	
Haemorrhagic	216/1496 (14%)	117/996 (12%)	
TIA	211/1496 (14%)	185/996 (19%)	
Undetermined	42/1496 (3%)	36/996 (4%)	
Able to walk on admission, n (%)	497/1364 (36%)	384/908 (42%)	0.005
Length of hospital admission (days), median (IQR)	7 (4 to 12)	7 (4 to 13)	0.47
Treated in a stroke unit, n (%)	1132/1490 (76%)	779/993 (78%)	0.15

Flow diagram of the follow-up assessments for patients admitted in 2011



SOURCE: 2012 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/06/auscr-annualreport-2012-final.pdf

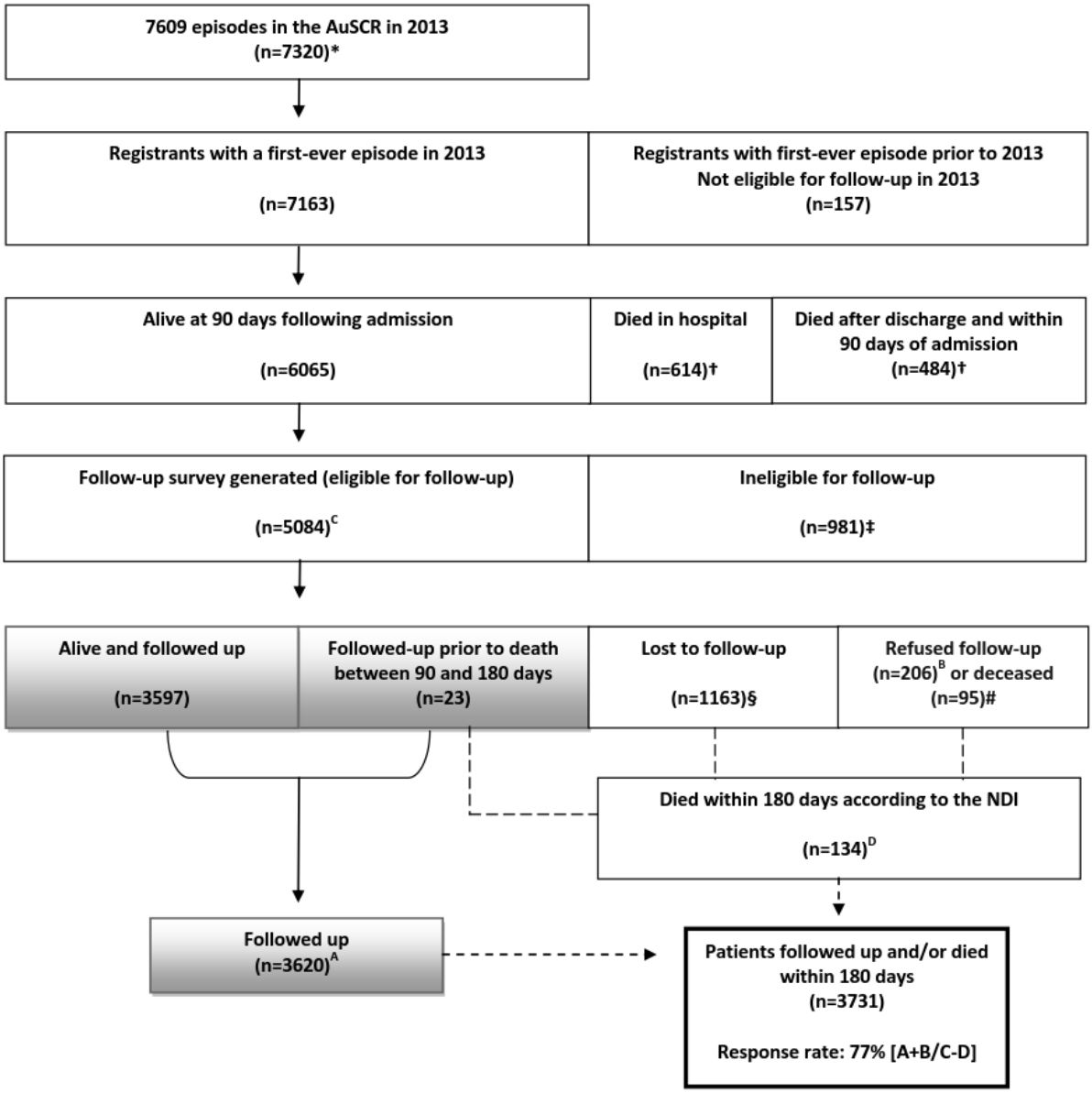
Flow diagram of the follow-up assessments for patients admitted in 2012



Baseline characteristics for 2983 registrants with (and 1490 registrants without) any post-discharge information in 2012

	Patients with any post-discharge information (complete follow-up or death) (n=2983)	Patients without post-discharge information (refused, lost, after 6 month, or in progress) (n=1490)	*p* value
Age (years), mean (SD)	75 (13)	72 (15)	<0.001
Gender, female, n (%)	1430/2963 (48%)	689/1479 (46%)	0.29
Aboriginal and/or Torres Strait Islander, n (%)	16/2983 (1%)	13/1490 (1%)	0.19
Type of stroke, n (%)			0.001
Ischaemic	2006/2981 (67%)	937/1482 (63%)	
Haemorrhagic	432/2981 (15%)	216/1482 (15%)	
TIA	441/2981 (15%)	246/1482 (17%)	
Undetermined	102/2981 (3%)	83/1482 (6%)	
Able to walk on admission, n (%)	1072/2743 (39%)	648/1283 (51%)	<0.001
Length of hospital admission (days), median (IQR)	5 (2 to 9)	5 (3 to 11)	<0.001
Treated in a stroke unit, n (%)	2293/2983 (77%)	1040/1490 (70%)	<0.001

SOURCE: 2013 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/06/auscr-annualreport-2013-final.pdf



Flow diagram of the follow-up assessments for patients admitted in 2013

** Excludes cases admitted to the participating paediatric hospital.*

† There were 45 patients with a missing date of discharge who died within 90 days of their admission.

‡ There were 909 patients who had their data entered into the AuSCR database after 180 days of their admission, 37 patients who opted out of follow-up and 35 who were incorrectly classified as died in hospital. These patients were not followed up.

§ There were 32 patients in this group who died within 180 days of their admission.

 # There were 206 patients in this group who refused follow-up (one who died within 180 days of their admission) and 95 patients who were classified as 'deceased at follow-up' (78 who died within 180 days of their admission).

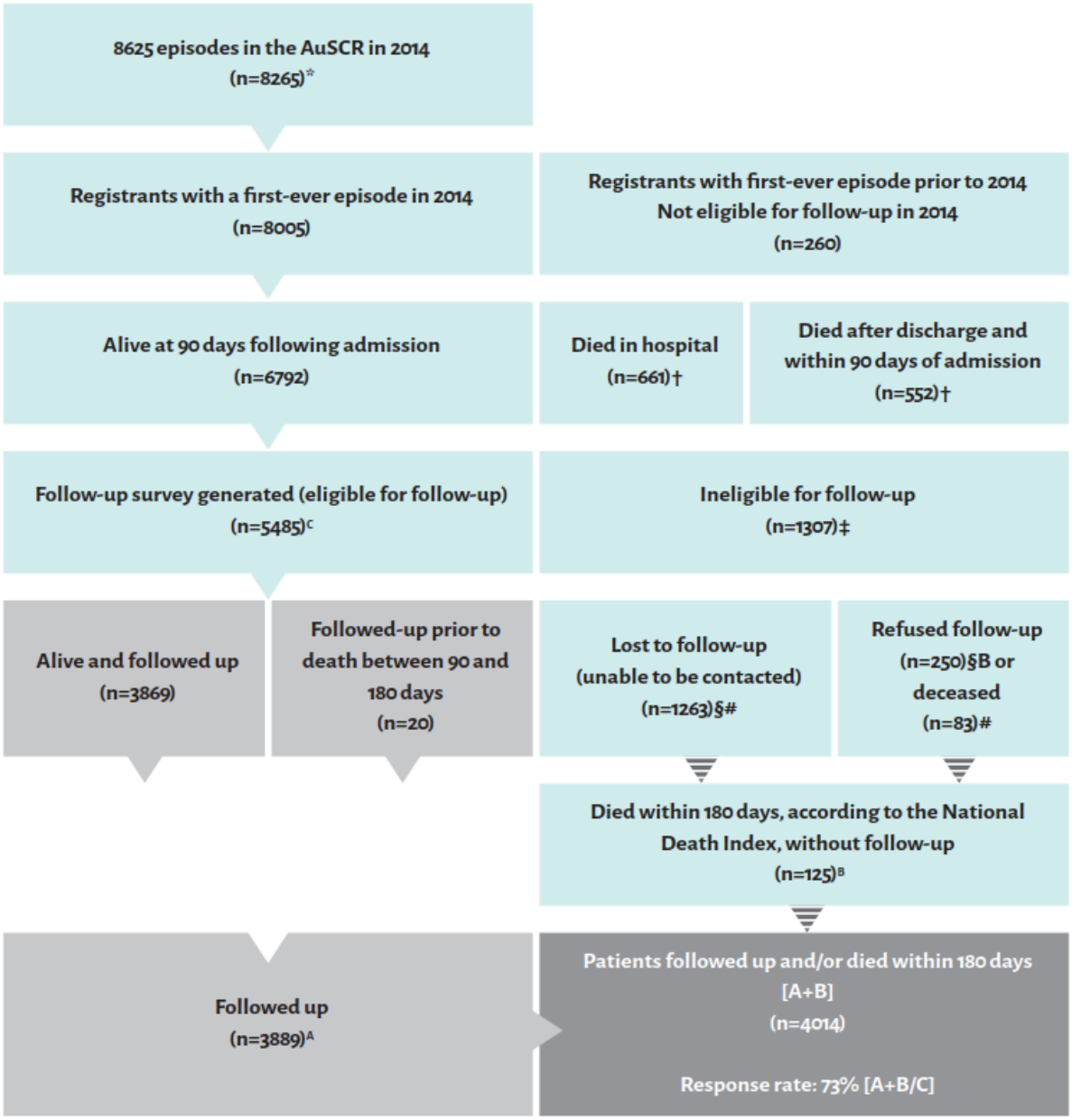
Baseline characteristics for registrants with and without any post-discharge information in 2013

	Patients with any post-discharge information (complete follow-up or death) (n=4865)	Patients without post-discharge information (refused, lost, after 180 days, or in progress) (n=2298)	*p* value
Age (years), mean (SD)	75 (13)	70 (15)	<0.001
Gender, female, n (%)	2200/4837 (45%)	1046/2282 (46%)	0.779
Aboriginal and/or Torres Strait Islander, n (%)			
Type of stroke, n (%)			<0.001
Ischaemic	3064/4853 (63%)	1280/2285 (56%)	
Haemorrhagic	644/4853 (13%)	281/2285 (12%)	
TIA	814/4853 (17%)	572/2285 (25%)	
Undetermined	331/4853 (7%)	152/2285 (7%)	
Able to walk on admission, n (%)	1856/4339 (43%)	994/2007 (50%)	<0.001
Length of hospital admission (days), median (IQR)	4 (2 to 8)	4 (2 to 8)	0.281
Treated in a stroke unit, n (%)	3875/4865 (80%)	1630/2297 (71%)	<0.001

Excludes cases admitted to the participating paediatric hospital

SOURCE: 2014 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/05/auscr-2014annualreport-final.pdf

FLOW DIAGRAM OF THE FOLLOW-UP
ASSESSMENTS FOR PATIENTS ADMITTED IN 2014



* Excludes cases admitted to the participating paediatric hospital
† There were 43 patients with a missing date of discharge who died within 90 days of their admission
‡ There were 1252 registrants who had their data entered into the AuSCR database after 180 days of their admission and 55 who opted out of follow-up
§ There were 40 patients lost to follow-up and two patients who refused follow-up who died within 180 days of their admission
# There were 18 patients who were classified as deceased at follow-up who did not die within 180 days according to the NDI. These patients were reclassified as lost to follow-up

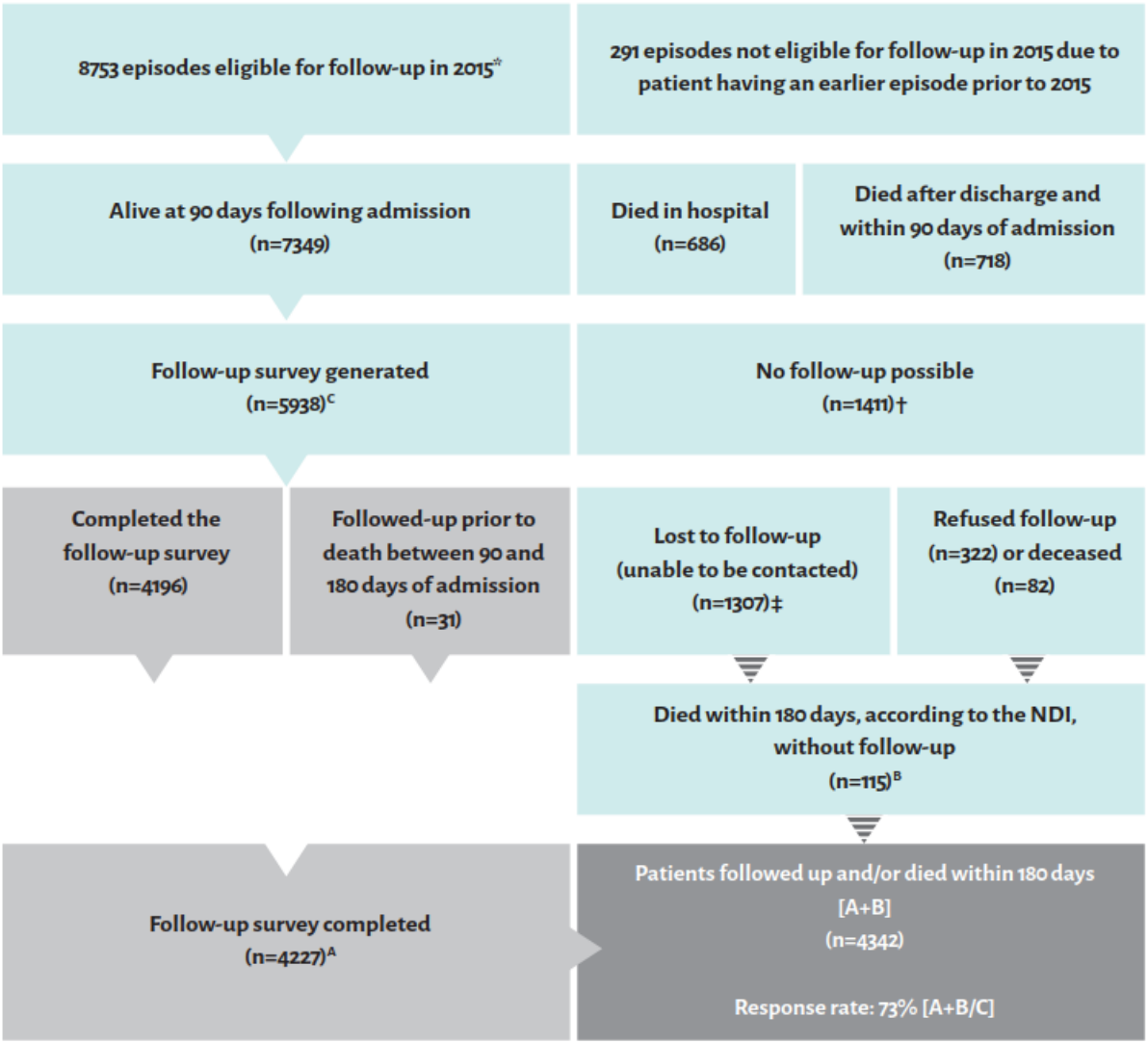
BASELINE CHARACTERISTICS FOR REGISTRANTS WITH AND WITHOUT ANY POST-DISCHARGE INFORMATION IN 2014

		PATIENTS WITH ANY POST-DISCHARGE INFORMATION (COMPLETE FOLLOW-UP OR DEATH) (N=4022)	PATIENTS WITHOUT POST-DISCHARGE INFORMATION (REFUSED OR LOST, AFTER 180 DAYS) (N=1471)	*p* VALUE
Age (years), mean (SD)		72 (14)	69 (15)	<0.001
Female, n (%)		1815/4008 (45%)	618/1471 (42%)	0.041
Aboriginal and/or Torres Strait Islander, n (%)		65/3939 (2%)	51/1459 (4%)	<0.001
Type of stroke, n (%)	Ischaemic	2689/4022 (67%)	933/1471 (63%)	0.046
	Haemorrhagic	328/4022 (8%)	150/1471 (10%)	
	Transient ischaemic attack	838/4022 (21%)	321/1471 (22%)	
	Undetermined	167/4022 (4%)	67/1471 (5%)	
Able to walk on admission, n (%)		1698/3670 (46%)	625/1351 (46%)	0.997
Length of hospital admission (days), median (IQR)		4 (2 to 7)	4 (2 to 7)	0.851
Treated in a stroke unit, n (%)		3437/4022 (85%)	1207/1471 (82%)	0.002

Excludes cases admitted to the participating paediatric hospital SD: standard deviation IQR: inter quartile range

SOURCE: 2015 AuSCR Annual Report - https://auscr2.files.wordpress.com/2017/05/auscr_2015_annual_report_final.pdf

FLOW DIAGRAM OF THE FOLLOW-UP ASSESSMENTS FOR PATIENTS ADMITTED IN 2015



* Includes only adult episodes
† There were 1411 registrants who had their data entered into the AuSCR database after 180 days post their admission
‡ There were 33 patients lost to follow-up who died within 180 days of their admission