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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Methods: We systematically searched CINAHL, PubMed, ProQuest Dissertations & Theses, and Scopus for published and unpublished literature until 9th December 2017.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

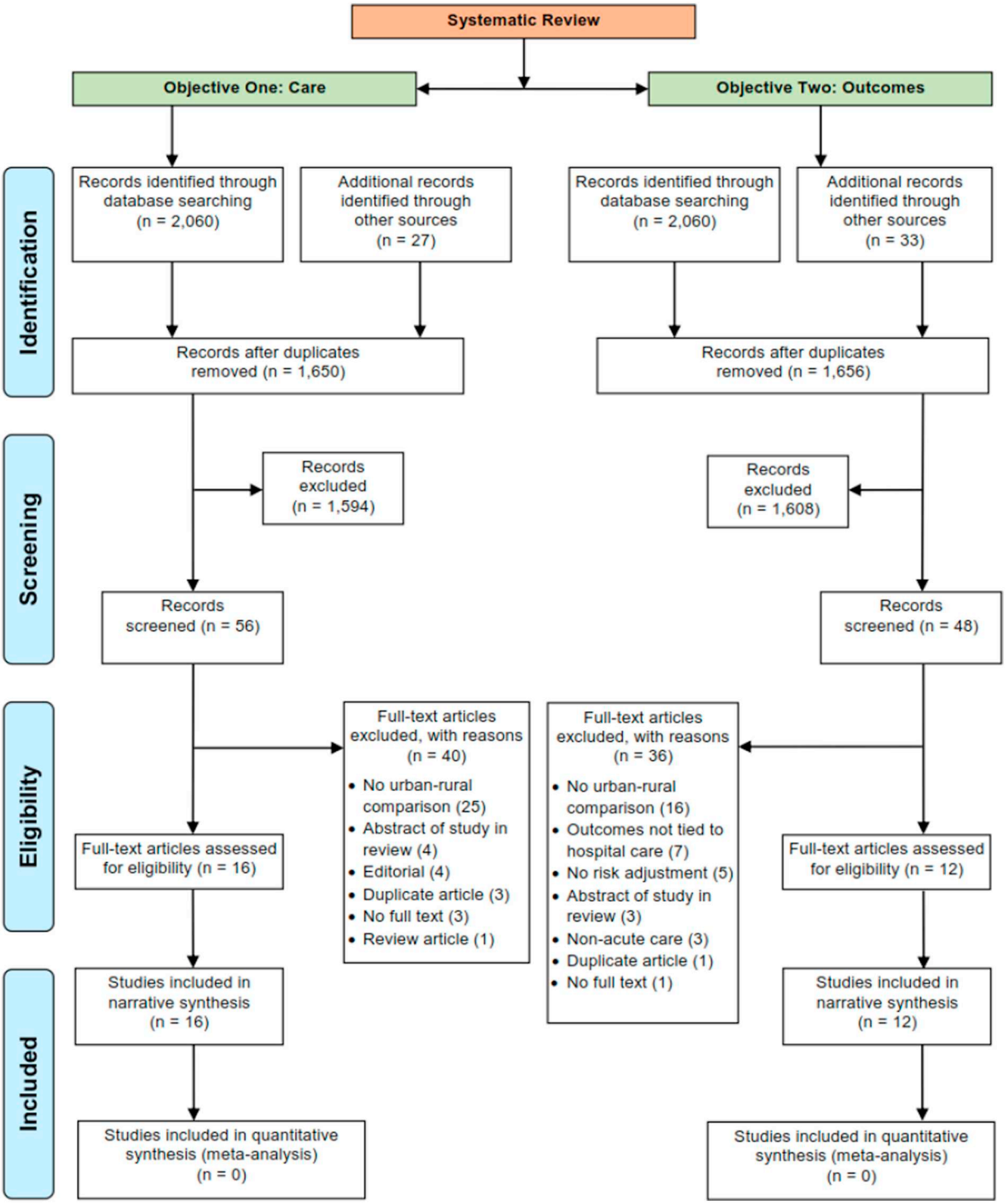

Fig. 1. Study flow diagram.

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. antithrombotics, 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.
37		• 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

(*continued on next page*)

Table 3 (*continued*)

Study	Urban-rural differences in care	Postulated causes of disparities
	• 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).	
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
45			

(*continued on next page*)

Table 4 (*continued*)

Study	Covariates	Urban-rural differences in outcomes	Postulated causes of disparities
	• 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.

Appendix A. PubMed search strategy

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. Authors

Name	Location	Role	Contribution
Mitchell Dwyer	University of Tasmania, Hobart	Author	Conceptualisation of study, article screening, quality assessment, preparation of draft manuscript
Dr Sabah Rehman	University of Tasmania, Hobart	Author	Article screening, quality assessment
Thomas Ottavi	University of Tasmania, Hobart	Author	Article screening, quality assessment
Jim Stankovich, PhD	University of Tasmania, Hobart	Author	Conceptualisation of study
Seana Gall, PhD	University of Tasmania, Hobart	Author	Conceptualisation of study, editing of manuscript
Greg Peterson, PhD	University of Tasmania, Hobart	Author	Conceptualisation of study, editing of manuscript
Karen Ford, PhD	Tasmanian Health Service, Hobart	Author	Conceptualisation of study, editing of manuscript
Leigh Kinsman, PhD	University of Tasmania, Launceston	Author	Conceptualisation of study, editing of manuscript

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