

**Inequities in acute stroke care and outcomes among rural versus urban populations in
Canada: a literature review**

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1. Abstract

In acute stroke evaluation, rapid intervention and rehabilitation is critical. Canada's vast geography innately creates barriers for efficient transport to stroke centres, thus delaying treatment. The purpose of this literature review is to investigate potential inequities in acute stroke care and outcomes, and to understand the causes and consequences of inequities in access to diagnostic investigations, acute stroke care management, and overall post stroke mortality in rural versus urban populations in Canada. A literature search using PubMed database was performed using keywords ischemic stroke, hemorrhagic stroke, Canada, and rural or urban. Three articles met the inclusion criteria and were included in the review. One additional related report was included by consulting primary sources in reference lists of relevant articles. Literature suggests that rural residence is associated with limited access to stroke centres and rehabilitation services, decreased acquisition of neuroimaging, increased hesitancy to treat with tPA, and impeded access to timely revascularization intervention via EVT. These disparities may in part be explained by time required to access appropriate healthcare facilities, variations in resource allocation and level of expertise of treating health care providers. There is contrasting findings regarding usage of tPA and 30-day post stroke mortality rates. Acute stroke care management is substandard in rural compared to urban populations in Canada. This gap in care may be addressed by focusing on minimizing existing barriers including access to stroke centres and rehabilitation services, neuroimaging, comfort administering tPA and timely revascularization intervention. Implementing telestroke and regionalization of stroke care may be of value.

2. Introduction

Canadian stroke epidemiology and possible rural vs. urban disparities in outcome

Stroke is the third leading cause of death and the primary leading cause of adult disability in Canada.(1,2) More than 62,000 Canadians suffer from stroke and transient ischemic attack (TIA) each year.(3) Acute stroke evaluation, rapid assessment, diagnosis, intervention and rehabilitation is critical.(4) Rapid identification and treatment initiation results in better overall patient outcome following stroke, and may have a significant impact on mortality, long-term recovery and quality of life.(4) The goal of stroke care is to minimize brain injury and neurologic impairment, and maximize brain restoration and overall recovery. Canada's vast geography innately creates barriers for efficient transport to stroke centres, and thus delaying treatment. This is particularly true for patients who reside in remote rural areas. Given Canada's geographical distribution, there may be inequities in acute stroke care and outcome for those who live beyond the urban radius of the narrow therapeutic window.

Kapral et al. found an association between rural residence and increased rate of stroke and all-cause mortality among individuals with and without prior stroke in Ontario between 2008 and 2012.(5) This association was attenuated but not eliminated after adjusting for demographic and socioeconomic factors, cardiovascular risk factors and comorbid conditions.(5) These results suggest that enhanced identification and management of vascular risk factors are necessary but insufficient to address disparities in rural stroke morbidity and mortality.(5)

Classification of ischemic vs. hemorrhagic stroke

There are two major types of stroke: ischemic and hemorrhagic. Ischemic strokes account for 87% of all strokes and usually result from occlusion of an artery to a region of the brain.(6) Hemorrhagic strokes account for the remaining 13% of strokes and result from a ruptured blood vessel in the brain.(6) It is presumed that abrupt onset of focal neurological symptoms is vascular

in origin until proven otherwise; however, it is impossible to classify the cause as ischemic or hemorrhagic based on clinical characteristics alone.(7)

Ischemic strokes have different risk factors, treatments, and outcomes as compared to hemorrhagic strokes. A hemorrhagic stroke or the finding of an intracranial hemorrhage on brain imaging in the presence of an acute ischemic stroke are absolute contraindications to tissue plasminogen activator (tPA).(8) Therefore, management cannot be initiated until neuroimaging has been completed and the diagnosis of ischemic or hemorrhagic stroke is established.(8,9)

Neuroimaging is a critical component in the initial assessment and management of acute stroke. Computed tomography (CT) and magnetic resonance imaging (MRI) technology is able to distinguish the type of stroke causing the deficit and rule out hemorrhage.(10) Imaging provides quantitative assessment of the degree of brain injury, and may be able to differentiate irreversible infarcted areas and brain tissue that is potentially salvageable.(10) A non-contrast CT brain is critical in determining intravenous tPA eligibility as it is able to identify hemorrhage and assess ischemic changes.(11) Computed tomography angiography (CTA) of the head and neck is able to identify the vascular lesion responsible for the ischemic insult(10) and determine eligibility for further endovascular thrombectomy (EVT).(12)

AIS treatment

The goal of reperfusion therapy is to restore blood supply to ischemic but potentially salvageable tissue, and thus restore normal cell function to the area of brain at risk of infarction.(13) Intravenous thrombolysis is the primary treatment for acute ischemic stroke (AIS) in patients who present within 4.5 hours of symptom onset.(14) The effectiveness of tPA is highly time-dependent, therefore early recognition and timely intervention of AIS is critical.(15) Rapid treatment with tPA has been reported in many urban stroke centres while hospitals in rural areas frequently struggle to reduce tPA treatment times.(15) Acute stroke treatment is evolving

rapidly as is the standard of care. In Canada, EVT initiated within 6 hours of symptom onset has become the standard of care for AIS with large vessel occlusion.(4,16)

Survival rate following stroke is in part reflected by the quality of acute care received including access to timely thrombolytic intervention and improved intravenous tPA and EVT rates.(17,18) Medical treatment of AIS with alteplase is generally available at both primary stroke centres (PSCs) and comprehensive stroke centres (CSCs).(19) The recent establishment of EVT places even greater demand on systems of care as it is generally performed at CSCs, therefore fewer centres are able to offer this form of treatment for patients with AIS.(19) A study conducted by Mulder et al. found that there was a 7.7% decreased probability of functional independence for every hour that successful reperfusion therapy is delayed.(20)

Stroke standard of care in Canada and rural vs. urban access to acute stroke care centres

The Canadian Stroke Best Practice Recommendations for Acute Stroke Management advise that patients who present to the emergency department (ED) with suspected stroke or TIA undergo rapid assessment and immediate neuroimaging via non-contrast CT or MRI, non-invasive vascular imaging via CTA or magnetic resonance angiography (MRA), and prompt treatment with tPA or EVT when indicated.(4) As per the Canadian Stroke Best Practice Recommendations, intravenous thrombolysis with alteplase should be initiated generally within 4.5 hours of onset of symptoms for disabling acute ischemic strokes and endovascular thrombectomy within 6 hours of onset of symptoms for strokes with large-vessel occlusion.(4)

Most strokes occur at home, and many stroke patients fail to recognize the signs of stroke or try to rationalize their symptoms.(6) This delays initiation of treatment, resulting in increased morbidity and mortality.(6) Majority of stroke patients are not eligible for treatment as they present too late or have medical contraindications to standard treatment interventions.(19) Rural populations within Canada have additional barriers to attain timely definitive stroke intervention.

Many rural hospitals do not have access to CT or MRI required to properly classify the type of stroke or rapid access to a stroke centre nearby. Therefore, additional transportation time must be accounted for as these individuals need to be flown in by medivac or driven by emergency medical services (EMS) to the nearest stroke centre which may amount to several hours in delayed treatment initiation. The delay in treatment intervention may lead to poorer health outcomes and increased morbidity and mortality.

A substantial portion of the Canadian population live in rural areas. In 2020, 18.44% of the total population of Canada lived in a rural area.(21) The proportion of the Canadian population who live within a 4.5 hour drive to a stroke centre via road EMS varies by province.(19) Eswaradass et al. found that Newfoundland and Labrador had the lowest percent population within this 4.5 hour threshold, being 47.1%, whereas Ontario had the highest proportion being 96.4%.(19) These results indicate that there is a significant portion of the Canadian population that do not have access to acute stroke care within the timeframe needed to treat.

Most rural hospitals do not have appropriate resources to treat patients with acute stroke, thus making rapid access to endovascular therapy a challenge.(19,22) Canadian acute stroke patients who reside in rural areas are generally geographically further from acute stroke centres compared to patients residing in urban centers, potentially limiting access to time-sensitive treatment and creating inequities in acute stroke care and outcomes.

3. Objectives and research question

This literature review aims to shed light on potential inequities in acute stroke care and overall outcomes in rural communities based on geographic location to stroke centres in Canada. An additional aspect of this literature review is to understand the causes and consequences of inequities in access to diagnostic investigations, acute stroke care management, and overall post stroke mortality in rural versus urban areas. The primary research question is as follows: do

inequities in access to acute stroke care and outcomes exist among urban versus rural populations in Canada?

4. Methods

Study inclusion criteria and characteristics

Inclusion criteria included primary research, records published in English, data sets restricted to populations within Canada, and studies comparing rural versus urban access to acute stroke care services and acute stroke outcomes. Primary research studies of any methodology were examined. Records were excluded if they did not specifically investigate acute stroke care and/or outcomes or did not directly compare data from rural versus urban populations in any part of Canada.

Search strategy

A literature review using a mix of MeSH and keywords in relation to the topics stroke, Canada and rural care was conducted using the PubMed database on December 18, 2021. Keywords included: ischemic stroke, hemorrhagic stroke, Canada, and rural or urban. The searches were designed and built as follows: ("Ischemic Stroke"[Mesh] OR "ischemic stroke" OR "hemorrhagic stroke" OR "acute stroke") AND ("Canada"[Mesh] OR Canad*) AND ("Rural" OR "Urban"). This search criteria generated 50 individual papers.

Study selection

Records were screened by title and abstract based on relevance to the research question and patient population. Full text articles were then screened to ensure all studies included addressed some aspect of acute stroke care and/or outcomes among rural versus urban areas including access to imaging, treatment and overall outcome. There were a total of three generated results obtained from the literature search that were of direct relevance to the research question.

One additional related report was included by consulting primary sources in reference lists of relevant articles.

5. Results

Four articles were included in the literature review from the comprehensive search using PubMed database including reports that met the study objectives regarding acute stroke care and outcome among rural versus urban areas in Canada. Five notable themes were identified in the analyzed reports: 1. access to stroke centres and rehabilitation services, 2. access to timely neuroimaging, 3. access to revascularization treatment via thrombolysis and 4. endovascular therapy, and 5. inequities in post stroke mortality rates. Table 1 of the appendix outlines a summary of the study, methodology, objective, population, sample size, outcomes measured, conclusion and limitations for each of the articles included in the literature search.

Access to stroke centres and rehabilitation services

Koifman et al. conducted a cohort study in 2016, examining 15,713 patients from data obtained via the Ontario Stroke Registry from April, 2008 to March, 2011.(23) They defined rural areas as populations less than 10,000, medium urban area as populations between 10,000-99,000, and large urban areas as population greater than or equal to 100,000.(23) Koifman et al. revealed that patients who had a stroke or TIA and lived in a rural area were less likely than their counterparts from medium and large urban areas to receive care at a district or regional stroke centre (48%, 65%, 71% respectively), transfer to an inpatient rehabilitation facility (16%, 20%, 21%), be admitted to a stroke unit (36%, 34%, 51%), and receive consultation from neurology (36%, 25%, 65%), physiotherapy (71%, 73%, 77%), occupational therapy (52%, 63%, 72%) and speech language pathology (42%, 48%, 57%).(23) The disparities in rural-urban stroke unit care remained substantial throughout the entire study period.(23)

Access to neuroimaging

Koifman et al. found that stroke or TIA patients from rural areas were less likely than their counterparts from medium and large urban areas to receive CT or MRI brain imaging within 24 hours of arrival to the facility (62%, 74%, 85% respectively).(23) Their study also revealed that of those with AIS or TIA, rural patients were less likely to undergo carotid imaging compared to those from medium and large urban areas, which remained substantial throughout the entire study period (62%, 66%, 73% respectively).(23)

Fleet et al. conducted a cohort study in 2018 using Canadian Institute for Health Information (CIHI) data from 310 acute care hospitals in Canada, excluding Quebec and the Territories, from 2007 until 2011.(24) Rural hospitals were defined as hospitals located in rural towns providing 24/7 emergency physician coverage with inpatient beds.(24) Urban hospitals were defined as academic centres designated as level 1 or 2 trauma centres.(24) Fleet et al. revealed that all urban hospitals with the designation of a level 1 or 2 trauma centre had access to 24/7 in-hospital CT and MRI capabilities, whereas only 11% of rural hospitals had access to in-hospital CT scanners and 1% had MRI services.(24)

Access to thrombolysis

In 2021, Bulmer et al. conducted a qualitative analysis through structured interviews with 23 health care professionals at one urban hospital and two rural hospitals involved in thrombolysis treatment in Nova Scotia, Canada from September to October, 2020.(15) The urban site was a level 1 trauma centre with neurologists and CT technologists always available and was the only hospital in Nova Scotia to provide EVT.(15) The included rural hospitals were located in a small town with ED providers primarily responsible for thrombolysis and did not have neurologists on site.(15) Of the 2 rural and 1 urban sites included in Bulmer et al.'s study, each site triaged acute ischemic stroke as the highest or urgent priority and all health care providers acknowledged the

necessity to administer tPA rapidly.(15) Majority of health care providers interviewed reported that tPA should be initiated within 4.5 hours of symptom onset, however is generally preferred within 3 hours of symptom onset.(15) There was more hesitancy to treat with tPA among rural health care providers compared to urban providers, noting how comfort is in part fostered by higher stroke treatment frequency.(15) Some of the largest obstacles identified included the time sensitive nature of tPA treatment, the uncertainty of diagnosis of acute ischemic stroke, reservations regarding the strength of evidence for tPA and subsequent risks.(15)

All three sites included in Bulmer et al.'s study acknowledged existing urban-rural treatment disparities identified as differences in level of expertise and comfort initiating tPA, EMS availability, distance of patients to the nearest hospital, availability of CT scanners, a critical component in determining tPA eligibility, and access to EVT following thrombolysis.(15) EMS in rural areas also cover larger geographical areas, thus cannot respond to AIS patients as quickly.(15) In addition, rural patient often live a greater distance from hospitals, further hindering the narrow therapeutic window.(15)

Koifman et al.'s study revealed that the use of tPA for patients with AIS who arrived to the stroke facility within 4.5 hours was highest in large urban areas (30.5%) compared to medium urban (21.7%) and rural areas (26.9%), however these differences diminished over time and were no longer significant by the end of the study period.(23)

Access to endovascular therapy

A retrospective cohort study conducted by Yan et al. in 2021 evaluated the efficiency of EVT services including EVT rates, onset-to-CTA time and onset-to-groin puncture time in the 195 patients who underwent EVT in Manitoba between January, 2018 and December, 2019.(25) They defined 3 regions, zone I-urban, zone II-within 1 hour drive distance from the CSC, and zone III-greater than 1 hour drive distance from the CSC.(25) AIS patients from zone I are covered directly

by the CSC, whereas those from zone II and III are primarily covered by telestroke sites that function as PSCs under the provincial stroke registry plan.(25) Yan et al. found that the EVT rate in zone I was 8.6, as compared to 5.1 in zone II, and 7.5 in zone III, per 100,000 population/year.(25) The mean onset-to-CTA time was 19 minutes longer in zone II (133 min) and 103 minutes longer in zone III (217 min), compared to their urban counterparts in zone I (114 min).(25) The mean onset-to-groin puncture time was 22 minutes longer in zone II (231 min) and 163 minutes longer in zone III (372 min), compared to zone I (209 min).(25)

Post stroke mortality

Koifman et al. found that the 30-day post stroke mortality was similar in those from rural, medium and large urban areas (9.4% rural, 9.4% medium urban, 9.2% large urban), as was the 30-day post stroke mortality or disabled at discharge defined as a modified Rankin score of 3 to 5 (39.8% rural, 42.1% medium urban, 42.3% large urban).(23) The adjusted hazard ratio (HR) correcting for stroke type, severity, age, sex, income, and comorbid conditions for 30-day post stroke mortality was 1.14 (95% confidence interval (CI) 0.99-1.32) in those from rural compared to large urban areas.(23)

Contrary to the findings above, Fleet et al. reported that the 30-day in-hospital mortality following stroke was significantly higher in rural versus urban hospitals and higher than the Canadian average for every year from 2007 to 2011 with the exception of 2008.(24) The rural hospital average 30-day in-hospital mortality rate following stroke ranged between 18.26 to 21.04 per 100 first stroke admission episodes, compared to urban hospitals with an average rate of 14.11 to 16.78.(24) There was no statistical difference between the 30-day in-hospital mortality rate following stroke in urban areas compared to the Canadian average.(24)

6. Discussion

The current research available suggests that rural residence is associated with limited access to stroke centres and rehabilitation services, decreased acquisition of neuroimaging, increased hesitancy to treat with tPA, and impeded access to timely revascularization intervention via EVT. These disparities may in part be explained by time required to access appropriate healthcare facilities, variations in resource allocation in rural compared to urban hospitals and level of expertise of treating health care providers. There is contrasting findings regarding the usage of tPA and 30-day post stroke mortality rates in rural compared to urban regions in Canada.

Bulmer et al. highlighted that the main differences in the thrombolysis process in urban and rural regions stem from resource availability including access to CT scanners, health care provider expertise, and frequency treating patients with AIS.(15) In the rural hospitals, emergency medicine physicians make the decision to administer tPA, as opposed to neurologists who specialize in acute stroke care at CSCs.(15) Rural health care providers generally treat AIS patients with tPA more infrequently compared to urban sites, which can lead to lower comfort and confidence initiating treatment, as well as, less familiarity with acute stroke care protocols.(15)

The Canadian guidelines recommend that patients with AIS be treated with tPA within 30 minutes from their hospital arrival, which is referred to the door-to-needle (DTN) time.(4) The infrequency rural hospitals have in treating AIS patients with tPA is an additional element contributing to lengthier DTN times.(15) Another barrier Bulmer et al. identified among rural hospitals was access to rapid neuroimaging interpretation from radiology.(15) This difference in stroke care and thrombolysis process presents some inequalities as to how rapidly treatment is initiated in rural versus urban regions in Nova Scotia,(15) and possibly generalized to all of Canada.

The urban-rural disparities highlighted in Bulmer et al.'s study are consistent with previous quantitative studies that showed rural acute ischemic stroke patients are less likely to receive thrombolysis(26) and have lengthier DTN times(27) compared to their urban counterparts. Facilitating a more efficient system by providing rural ED providers with support in treatment decisions from a neurologist who specializes in stroke care may aid to address these deficiencies.(15) Neurology consultation that supports treatment decisions through a centralized telestroke system has been a proven method to alleviate disparities in rural hospital AIS treatment.(28–30)

Although Bulmer et al. interviewed health care providers from only three hospitals from a single Canadian province, the challenges highlighted in the study including lack of comfort with tPA treatment and lack of resources in rural hospitals have been identified in other jurisdictions.(31–33) Implementing clear protocols, addressing system delays and promoting continuing education to improve rural provider comfort treating AIS patients with tPA are critical in attempt to reduce treatment delays, improve DTN times and ensure consistent access to acute stroke care.(15)

Yan et al. shed light on the disparities that exist in Manitoba regarding access to EVT in rural compared to urban areas.(25) In comparison to urban areas, access to EVT in rural areas is substantially poorer with considerably longer onset-to-groin puncture times and onset-to-CTA times.(25) It is also important to note that zone III, which includes regions greater than 1 hour from the nearest CSC, had a minimum distance of 61.8km, median distance of 156.6km and a maximum distance of 924.7km to the CSC.(25) These disparities that exist are of great concern and should be addressed through quality improvement initiatives and enhanced guidelines. Similar discrepancies based on geographical area were seen in Catalonia, demonstrating that accessibility

from remote regions is impeded by lower EVT rates and longer time to receive EVT compared to regions covered directly by CSCs.(34)

Yan et al.'s study was conducted over a two year period, and although not significant, their study results showed an increase in EVT procedures per capita in 2019 as compared to 2018.(25) This trend is promising and indicates the need for ongoing data collection and quality improvement initiatives to enhance the proportion of AIS patients with large vessel occlusions who receive EVT.(25)

Most jurisdictions use a pre-hospital AIS triage system where EMS transfers patients with suspected acute stroke to the nearest PSC or CSC for a neurological assessment, neuroimaging, and to administer tPA if indicated.(25) At the PSC, suspected AIS patients are assessed by a neurologist and undergo neuroimaging including a plain CT head and CTA of the head and neck.(25) Patients who have evidence of large vessel occlusion on CTA may be transferred to the CSC for EVT.(25) Transferring patients from a PSC to a CSC for EVT is time-consuming, potentially reducing effectiveness of EVT.(13,35) Canada's vast geography creates barriers for prompt transport to PSC and CSC hospitals. The efficacy of EVT is contingent on an optimal structured acute stroke system.(35) Making CTA available at every PSC may be one potential initiative to enhance onset-to-CTA time and onset-to-groin time.(25) Another potential initiative may be to transfer all suspected AIS patients directly to the nearest CSC for comprehensive assessment and management, however this may increase initial transport time and overall demand on the CSC.

Koifman et al. found that stroke and TIA patients from rural areas were less likely than those from medium and large urban areas to receive numerous interventions including stroke unit care, brain imaging within 24 hours, carotid imaging, transfer to inpatient rehabilitation facility, be admitted to a stroke unit, and receive consultation from neurology, physiotherapy,

occupational therapy and speech language pathology.(23) In addition, Koifman et al. also observed a 14% increase in adjusted HR for 30-day post stroke mortality in those from rural compared to large urban regions, however not of statistical significance.(23)

Discrepancies in acute stroke care and outcomes observed by Koifman et al. reflect the limited resources available in rural areas, which include access to stroke units, neuro and carotid imaging, allied health consultation, and rehabilitation facilities.(23) Enhancing availability of acute stroke care resources, implementing telemedicine and regionalization of stroke care with clinical coordinators are all strategies that should be considered to address geographic barriers that lead to gaps in care and outcomes.(36–41)

Fleet et al. observed that the 30-day in-hospital post stroke mortality rates in Canada were higher in rural compared to urban hospitals and higher than the Canadian average for every year from 2007 to 2011 with the exception of 2008.(24) Fleet et al. also found that fewer rural hospital had access to in-hospital ICUs, CT scanners, MRI imaging, laboratory and basic radiology compared to hospitals in urban areas.(24) 89% of rural Canadian hospitals lacked in-hospital CT scanners, while 99% did not have MRI machines.(24) The results of their study suggest that there may be an association between a lack of crucial stroke services and higher mortality rates following stroke in rural regions in Canada.(24) Disparities in rural-urban acute stroke care and outcomes are of great concern and should be addressed on a national level, as universally accessible health care is a fundamental feature of the Canadian universal healthcare system.

In order to reduce inequities in acute stroke care in rural areas within Canada, Fleet et al. recommended reflecting on the rural hospital system established in the United States.(24) The United States created the Critical Access Hospital (CAH) designation by the Medicare Rural Hospital Flexibility Program of the 1997 Balanced Budget Act with the intent to improve access to medical care and imaging services in rural regions.(42) An acute care hospital can be

designated as a CAH if the facility is located in a rural area, is located greater than 35 miles from the nearest hospital or is certified as being a necessary provider of health care services, provides 24-hour emergency service care services, and has no more than 25 inpatient beds providing care that does not exceed an average length stay of 96 hours.(42) A recent report showed that of all CAHs, 78% had access to CT and 67% had access to MRI.(43) Nonetheless, stroke mortality gaps among rural populations continue to persist in the United States. A study analyzing United States populations by Lichtman et al. observed that the 30-day risk standardized mortality rate following stroke at CAHs were higher than non-CAH, mainly urban, hospitals (19.9% compared to 10.9%).(44)

In February 2017, the College of Family Physicians of Canada presented a strategic road map to improve access to care for rural residents and indigenous peoples of Canada.(45) Outlined is an initiative to develop specific resources, infrastructure, and networks of care to address access issues in rural communities.(45) It also proposed development strategies to guide the implementation of coordinated distance technology to improve access to quality health care in rural areas.(45) Expanding on this initiative, enhancing access to CT scanners in rural hospitals may improve timely diagnosis of AIS, and therefore allow for rapid intervention and potential consultation via telestroke.(24) An additional consideration is enhanced utilization of mobile stroke units, which allow for more rapid delivery of tPA and more efficient transport to EVT centres for eligible AIS patients, reducing additional time delays.(46)

Early stroke identification and protocol initiation that facilitate rapid patient transport via EMS to stroke centres have resulted in reduced delay in treatment and interfacility transfer, and increased rates of thrombolysis administration.(47,48) Implementing a comprehensive system for acute stroke care has increased the role of EMS to transport patients to stroke centres.(19)

Physician assistants are medical generalists trained to perform complete and appropriate patient assessments and implement effective management plans in collaboration with physicians that include preventive and therapeutic interventions.(49) Enhancing utilization of physician assistants in rural hospital emergency departments may be an additional strategy to address gaps in acute stroke care as this would allow for additional health care providers to rapidly identify acute stroke and initiate appropriate treatment or facilitate transfer to an appropriate acute stroke care facility.

There are apparent implications for service delivery and equitable access to given stroke interventions.(19) It is important that efforts are made to enhance public awareness of the signs of stroke and contact EMS without delay to maximize eligibility for treatment and minimize neurological deficits given the time-sensitive nature of stroke care.(19) Triaging stroke patients directly to designated stroke centres has shown favourable benefit over initial transport to hospitals that are closer in proximity but not equipped to manage stroke.(6) The American Heart Association recommends that receiving hospitals should define their capability for treating patients with acute stroke and inform the EMS system and community in an effort to enhance optimal patient outcome.(6) Transporting patients to stroke centres with dedicated stroke teams can continue to improve the quality of treatment offered to patients who arrive within evidence-based time windows.(19)

Optimal acute stroke care requires access to urgent neuroimaging, thrombolysis, endovascular revascularization, and rehabilitation; however, access to these resources is often not available in rural areas.(50) Geospatial analysis of access to specific stroke services may aid in decision making for additional stroke centre sites, resource allocation to maximize population access, and to identify gaps in stroke service accessibility across geographic regions in Canada.(19) Continued development and evolution of coordinated systems of care and

ambulance bypass agreements should be considered to optimize access to time-sensitive acute stroke services.(19)

Health care providers, hospital facilities, communities and policy makers must continue to develop efficiencies within systems in place that will improve effectiveness of acute stroke care.(6) Improving access, care and overall outcomes for stroke in rural communities should be a priority.(26)

7. Limitations and future directions

This review was set forth mainly to identify inequities in acute stroke care and outcomes among rural versus urban centres in Canada. A limitation of this study is that healthcare is within provincial jurisdiction, therefore the majority of the articles analyzed data from a single province. Some of the outcomes cannot be standardized to the entire country, however the findings do paint a picture of where Canada is at on a national level and adds to the growing body of evidence highlighting inequities among rural versus urban acute stroke care and outcomes. Another limitation of this study is that each report obtained from the literature search used specific criteria to define rural versus urban areas within their article. There was no clear consistency or standard definition of rurality among the included reports. Additional limitations noted from the individual studies are highlighted in Table 1 of the appendix.

The 30-day mortality rate was found to be significantly different in only one of the two reports analyzed, therefore this literature review did not reveal irrefutable evidence to suggest a significantly different 30-day mortality rate among rural versus urban populations in Canada. Further research is needed to confirm if morbidity and mortality rates are negatively affected in rural areas.

Future studies that evaluate the long-term functional outcomes for AIS patients that compare pre-hospital triage systems that transfer patients to a PSC or bypass the closest PSC and

go directly to the CSC offering EVT, would be of value.(25) Given the known benefits of rapid revascularization with tPA(51) and EVT in appropriately selected patients(20), stroke unit care and rehabilitation(52–56), future studies and initiatives should focus on understanding the reasons for these differences in management of AIS care. Future studies should also focus on developing targeted interventions to address these gaps in an effort to minimize disparities in stroke care and outcomes among rural residents in Canada.

Research on implementing telestroke and mobile stroke units in rural acute care hospitals is sparse. Further research in this area may be of benefit as these initiatives might be an effective way to create efficiencies and reduce delays in AIS treatment initiation. Further research should be done to guide and recommend a systemic approach that healthcare systems and medical providers can implement in rural communities to optimize patient outcome and minimize neurological deficits for acute stroke patients.

8. Conclusion

Acute stroke care management is substandard in rural compared to urban populations in Canada. As a result, this creates an unacceptable health disparity in acute stroke care and overall outcomes among rural versus urban Canadians. This gap in care may be addressed by focusing on minimizing existing barriers including access to stroke centres and rehabilitation services, neuroimaging, comfort initiating tPA treatment and timely revascularization intervention. In addition, implementing new strategies such as telestroke and regionalization of stroke care may be of value.

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Appendix

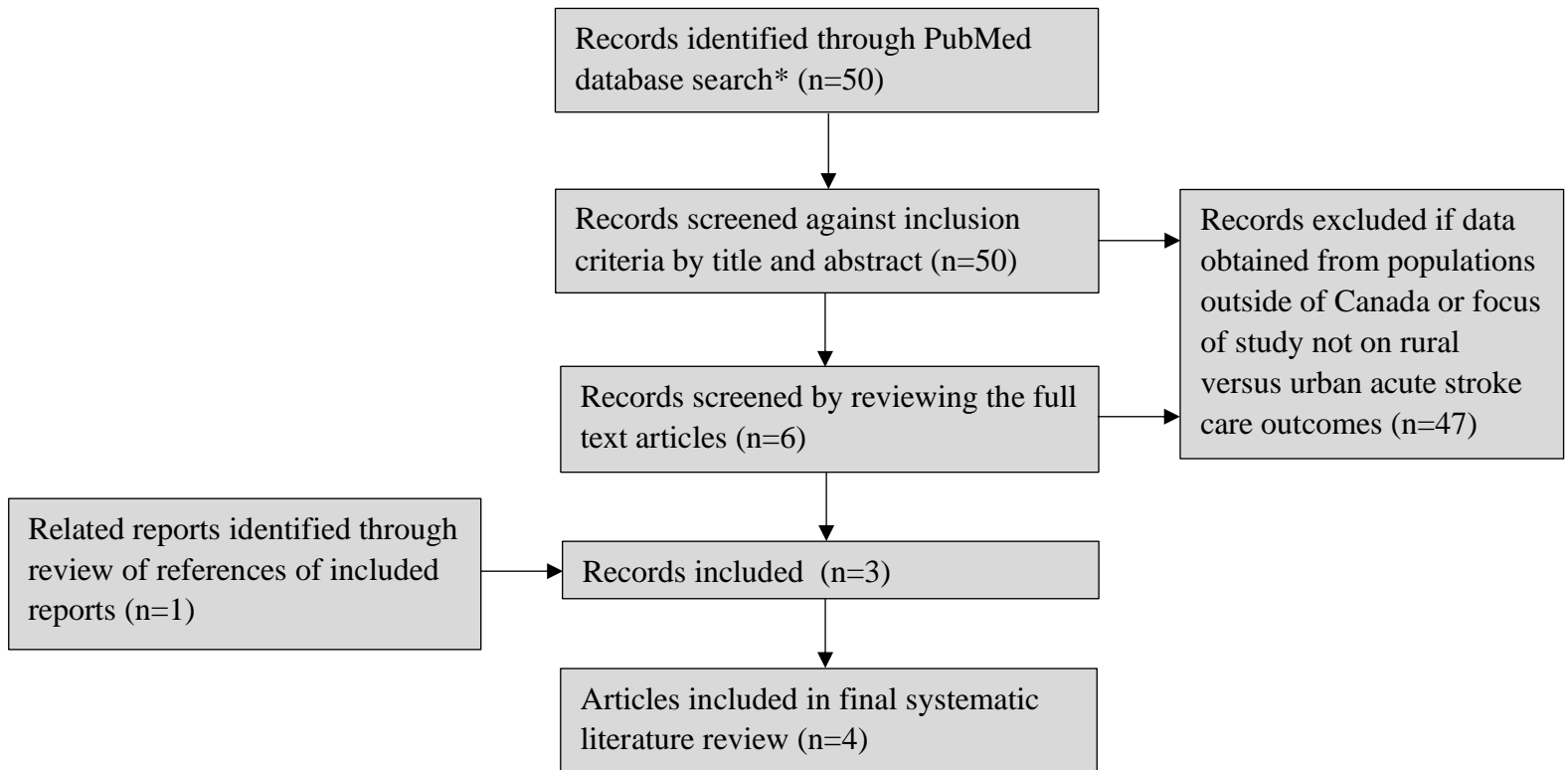


Figure 1: Study selection. Articles included based on relevance of title to research question. Inclusion criteria: acute stroke, Canada, rural vs. urban, primary research. *Search was conducted on December 18, 2020, in the PubMed Database using the following search terms ("Ischemic Stroke"[Mesh] OR "ischemic stroke" OR "hemorrhagic stroke" OR "acute stroke") AND ("Canada"[Mesh] OR Canad*) AND ("Rural" OR "Urban").

Table 1: Summary of the articles used in the literature search including the study, methodology, objective, population and sample size, outcomes measured, conclusion, and limitations.

Study	Methodology/ geographic region	Objective	Study population/ sample type	Outcomes	Conclusion	Limitations
Bulmer et al. 2021 (15)	Qualitative study Nova Scotia	Analyze health care professionals views on various acute stroke treatment interventions, and shed light on differences in the thrombolysis process between urban and rural hospitals in Nova Scotia based on presence of neurologists in-hospital and CT availability	Health care professionals involved in AIS treatment at 1 urban CSC and 2 rural hospitals in Nova Scotia from September to October 2020 n = 23 total (8 from an urban site, 15 from two rural sites) Urban site was the only site able to provide EVT and neurologists on site	Differences in tPA administration stem from resource availability including access to CT scanners, health care provider expertise and frequency treating patients with AIS EMS in rural areas also cover larger geographical areas, thus cannot respond to AIS patients as quickly	Implementing clear protocols, addressing system delays, and promoting continuing education to improve rural provider comfort treating with tPA are critical in attempt to reduce treatment delays, improve DTN times, and ensure consistent access to acute stroke care	Limitations: only 3 hospitals were included from a single Canadian province, small sample size, not all providers involved in treatment process were interviewed, cannot eliminate individual bias, relied on self-reported data
Yan et al. 2021 (25)	Retrospective cohort study Manitoba	Examine the efficiency of EVT services including EVT rate, onset-to-CTA time and onset-to-groin puncture time in rural versus urban areas in Manitoba	Patients who underwent EVT in Manitoba between January 1 st , 2018 and December 31 st , 2019 n = 195 total (128 from urban [zone I], 23 from rural < 1 hour from CSC [zone II], 44 from rural ≥ 1 hour from CSC [zone III])	EVT rate: Zone I - 8.6 per 100,000 population Zone II - 5.1 per 100,000 population Zone III - 7.5 per 100,000 population Mean onset-to-CTA time: Zone I – 114 min Zone II – 133 min Zone III – 217 min Mean onset-to-groin puncture time: Zone I – 209 min Zone II – 231 min Zone III – 371 min	In comparison to urban areas, EVT access in rural areas is substantially reduced with considerably longer onset-to-groin puncture times and onset-to-CTA times These findings may aid to modify the patient transfer policy for EVT referral	Limitations: underlying reasons for differences in EVT rate not illustrated, final outcome of EVT patients not accounted for, study limited in its retrospective nature
Koifman et al. 2016 (23)	Cohort study Ontario	Evaluate the association between rural residence and stroke outcomes by comparing those from rural and urban area receiving thrombolysis, stroke unit care,	Patients identified in the Ontario Stroke Registry between April 1, 2008 and March 31, 2011 n = 15,713 total (2560 from rural areas defined as population < 10,000, 1975 from	Patients from rural areas were less likely than those from medium and large urban areas to be treated in a stroke centre (48%, 65%, 71% respectively), receive brain imaging with 24h of arrival (62%,	The findings of this study likely reflect the limited resources in acute stroke care in rural areas including accessible stroke units, imaging, allied health, and	Limitations: rurality was defined based on population size alone, a definition that incorporated distance /accessibility to stroke centres may have better represented

		investigations, consultations treatments, 30-day mortality and disability at discharge in Ontario	medium urban area defined as population 10,000-99,000, 11,178 from large urban areas defined as population \geq 100,000)	74%, 85%), carotid imaging (62%, 66%, 73%), inpatient rehabilitation (16%, 20%, 21%), admission to a stroke unit (36%, 34%, 51%), and consultation from neurology (36%, 25%, 65%), physiotherapy (71%, 73%, 77%), occupational therapy (52%, 63%, 72%) and speech language pathology (42%, 48%, 57%) 30-day mortality was similar in all areas as was disability at discharge	rehabilitation facilities Future initiatives should focus on developing strategies that will increase use of interventions to address gaps in stroke care and outcomes in rural areas	potential disparities, did not include information on long-term patient-centred outcomes
Fleet et al. 2018 (24)	Cohort study All Canadian population excluding Quebec and the Territories	Examine access to in-hospital CT scanners as well as other services, and describe variations in 30-day in-hospital mortality following stroke among rural versus urban academic hospitals in Canada	30-day in-hospital stroke mortality rates using CIHI data from 2007 to 2011 for all acute care hospitals in Canada excluding Quebec and the Territories n = 310 hospitals total (286 rural hospitals defined as hospitals located in rural towns providing 24/7 emergency physician coverage with inpatient beds, 24 urban hospitals defined as academic centres designated as level 1 or 2 trauma centres)	All urban hospitals had access to CT and MRI imaging, in-hospital ICU, laboratory and radiology Of the rural hospitals included in the study, 11% had a CT scanner, 1% had MRI imaging, 21% had in-hospital ICU, 94% had laboratory and 92% had basic radiology Average range of 30-day-in-hospital mortality rates following stroke per 100 first stroke admission episodes: Rural - 18.26 to 21.04 Urban - 14.11 to 16.78 (urban was the same as the Canadian average)	30-day in-hospital mortality rates post stroke were significantly higher in rural versus urban hospitals and higher than the Canadian average for every year from 2007 to 2011 with the exception of 2008 The results of this study suggest that there may be an association between higher stroke mortality rates and lack of in-hospital services in rural emergency departments	Limitations: CIHI data was only available for 65% of rural hospitals and 96% of urban academic hospitals, CIHI does not report data on hospitals with fewer than five stroke cases, did not account for other factors potentially contributing to the mortality difference such as presence or absence of an organized stroke team, inter-facility transfer capability