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Short title: Driving time and Thrombectomy

Access to Endovascular Thrombectomy: Does Driving Time to Comprehensive Stroke Center Matter More than Rurality?

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Abstract

Background: Acute stroke treatments are highly time-sensitive, with geographical disparities affecting access to care. This study examined the impact of driving distance to the nearest comprehensive stroke center (CSC) and rurality on the use of thrombectomy or thrombolysis in Ontario, Canada.

Methods: This retrospective cohort study used administrative data to identify adults hospitalized with acute ischemic stroke between 2017 and 2022. Driving time from patients' residences to the nearest CSC was calculated using the Ontario Road Network File and postal codes. Rurality was categorized using postal codes. Multivariable logistic regression, adjusted for baseline differences, estimated the association between driving distance and treatment with thrombectomy (primary outcome) or thrombolysis (secondary outcome). Driving time was modeled as a continuous variable using restricted cubic splines.

Results: Data from 57,678 patients (median age 74 years, IQR 64-83) were analyzed. Increased driving time was negatively associated with thrombectomy in a non-linear fashion. Patients living 120 minutes from a CSC were 20% less likely to receive thrombectomy (adjusted odds ratio [aOR] 0.80, 95%CI 0.62-1.04), and those 240 minutes away were 60% less likely (aOR 0.41, 95%CI 0.28-0.60). Driving time did not affect thrombolysis rates, even at 240 minutes (aOR 1.0, 95%CI 0.70-1.42). Thrombectomy use was similar in medium urban areas (aOR 0.80, 95%CI 0.56-1.16) and small towns (aOR 0.78, 95%CI 0.57-1.06) compared to large urban areas.

Conclusion: Thrombolysis access is equitable across Ontario, but thrombectomy access decreases with increased driving distance to CSCs. A multifaceted approach, combining healthcare policy innovation and infrastructure development, is necessary for equitable thrombectomy delivery.

Keywords: Ischemic stroke; thrombectomy; thrombolysis; geographic disparities; driving distance

Highlights

- Increased driving time to a comprehensive stroke center is associated with significantly lower rates of thrombectomy, with no similar effect observed for thrombolysis.
- Patients residing over 120 minutes from a stroke center have a 20% reduction in odds of receiving thrombectomy, underscoring critical geographical barriers to care.
- Efforts to enhance equitable access to thrombectomy should focus on improving service delivery in regions with extended travel times to stroke centers.

Introduction

Acute stroke revascularization treatments such as endovascular thrombectomy and thrombolysis require rapid initiation to be most effective.[1,2] However, these treatments also require stroke expertise and resources that are still not widely available.[3–5] Despite global efforts to improve stroke recognition and treatment, significant geographic disparities in access to urgent stroke treatments and patient outcomes persist.[6,7]

Concerns about geographical disparities in timely access to stroke treatments are very relevant in Ontario, Canada's most populous province with 15 million people residing in an expansive area of 1.08 million km^2 (about twice the size of France) with highly variable population density. Most comprehensive stroke centers (CSC) with thrombectomy services are in urban regions of southern Ontario. Reduced access to thrombectomy among rural residents compared to urban-dwellers has been previously described,[8–12] but we hypothesized that receipt of thrombectomy is more likely influenced by distance to CSC rather than rurality as rural residents living in close proximity to a CSC should still have timely access to care.

With the overall aim of identifying critical gaps in access to timely stroke care, we undertook a population-based analysis to evaluate the association between driving time between a patient's home residence and the nearest CSC and treatment with thrombolysis or thrombectomy in Ontario, Canada. Driving distance is commonly used as a proxy for access to stroke care, as it provides an objective measure of geographic barriers to timely treatment. Using this metric allows us to evaluate disparities in access across different regions. [11,13] We hypothesized that treatment with thrombolysis would not be affected by driving time because the systems of stroke

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care in Ontario developed over two decades ago were designed for the efficient delivery of thrombolytics[14], but that longer driving time would be associated with reduced thrombectomy because it is still not widely available.

Methods

Cohort identification

In this retrospective population-based cohort study, we utilized validated linked administrative datasets to define the study cohort, exposure, covariates, and outcomes. We identified community-dwelling adults, aged 18 to 104 years, who were hospitalized in Ontario, Canada between April 1, 2017, and March 31, 2022, with acute ischemic stroke as their most responsible diagnosis identified using International Classification of Diseases, 10th Revision, Canada (ICD-10-CA) codes I63 (except I63.6), I64, and H34.1. This case definition has been shown to have high accuracy for stroke hospitalization[15]. We created episodes of care using the entire care trajectory, from the initial admission through to discharge, including any transfers to avoid double counting transfers as separate events. We excluded individuals without a valid Ontario health insurance number (non-residents as they cannot be linked to evaluate outcomes), those with errors in birth or death records, or those who suffered a stroke while hospitalized for a different condition. Additionally, we excluded patients whose discharge date was after June 30, 2022 (n=12, 0.02%). For patients with multiple admissions for stroke during the accrual period, only the first admission was included in the analysis. An additional small number of individuals were excluded due to incomplete data on rurality (n=175, 0.3%), missing driving time (n=19, 0.03%), socioeconomic status (n=450, 0.7%), or emergency department triage scores (n=93, 0.1%). The process of cohort selection is in Supplemental Figure 1.

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Overview of Ontario's Stroke Systems of Care

Ontario’s stroke system of care includes CSCs equipped to provide a full range of acute stroke treatments, including thrombectomy, intravenous thrombolysis, vascular neurosurgery, primary stroke centres (PSC) with capacity for acute stroke imaging and thrombolysis, and non-designated centres (NDC) without ability to give thrombolysis or thrombectomy treatment. [16]

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In Ontario's tele-stroke system, when a patient with suspected acute ischemic stroke presents at a non-CSC site, they undergo an initial assessment and imaging. If EVT is considered necessary, the local healthcare team contacts a stroke neurologist from a CSC via CritiCall [17] for a remote consultation. Based on the neurologist's evaluation, if the patient is a suitable candidate for EVT, an urgent transfer to the nearest CSC is arranged, typically via ground or air ambulance. This ensures timely access to EVT, even in regions without direct access to a CSC.[18]

Exposures

The main exposure was driving time from patients' residences to the nearest CSC. We used the Postal Code Conversion File to identify the patients' primary residence postal codes, which were used to determine their geographical coordinates (latitude and longitude) using ArcGIS version 10.2 by the Environmental Systems Research Institute. We repeated these steps to obtain the geographical coordinates of all 11 CSCs across Ontario. We used network analysis to calculate travel time by car from each patient's geocoded location to the nearest CSC through all existing roads while accounting for the posted speed limits using the 2017 Ontario Road Network (ORN) Road Net Element File from Land Information Ontario.

In a secondary parallel analysis, we evaluated whether rurality of the patient residence was associated with acute stroke treatment without accounting for driving time. Using Statistics Canada's classification, rurality was defined based on the population size of their residential locality into three categories: large urban areas (with population exceeding 100,000), medium urban areas (population between 10,000 and 100,000), and small towns (population less than 10,000). [19]

Outcomes

The primary outcome of our study was treatment with thrombectomy, with or without intravenous thrombolysis. We also conducted a secondary analysis on the use of thrombolysis alone. Routine reporting of the use of thrombectomy and thrombolysis to the Canadian Institute for Health Information is mandatory in Ontario throughout the study period.[20,21]

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Standard Protocol Approvals, Registrations, and Patient Consents

Datasets were linked deterministically using unique encoded identifiers and analyzed at ICES (formerly the Institute for Clinical Evaluative Sciences). The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act and did not require research ethics board approval.

Data sharing statement

This study's dataset is securely stored in an encoded format at ICES. While the dataset is not publicly accessible due to data sharing agreements, confidential access may be permitted for qualified individuals through a detailed application process.

Statistical methods

Baseline patient characteristics, including categorical variables such as sex and presence of comorbidities, were analyzed using the Chi-square test and the means of continuous variables were compared using the Kruskal-Wallis test. We compared these baseline characteristics across groups defined by categories of driving time distances to CSCs (<20, 20-60, >60 minutes) and by the population size of the patient's residence (large urban, medium urban, small towns). For all baseline comparisons, statistical significance was designated using a conventional p-value cutoff of $p<0.05$. We used multivariable logistic regression models to determine the association between driving time and outcomes, summarizing the results as adjusted odds ratio (aOR) and 95% confidence intervals (CI). Statistical significance was defined as a 95% confidence interval not crossing 1. These models were estimated using generalized estimating equation methods to account for clustering within the first hospital in the episode of care.[22] Driving time beyond 20 minutes was modeled as a continuous variable using restricted cubic splines with five knots (45 55 65 75 and 95 percentiles) to allow for non-linear associations. [23] All patients with driving times under 20 minutes had their driving time set to 20 minutes, the reference, because we expected that all individuals within this short driving time would have similar access to treatment and that patient characteristics would be the main drivers of differences in treatment. We then compared the odds of the outcome for each driving time to the reference. Covariates were determined based on clinical relevance and included age (modeled as a continuous variable using restricted cubic splines to account for potential non-linear associations with outcomes), sex, prior

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stroke, atrial fibrillation, diabetes, hypertension, dyslipidemia, coronary artery disease, peripheral vascular disease, material deprivation quintiles[24], stroke severity using the Passive Surveillance Stroke Severity indicator[25], and frailty using the hospital frailty risk score[26]. In a secondary analysis, we compared the effects of residing in large urban, medium urban, and small towns on treatment without accounting for driving time. With 'large urban' areas serving as the reference group, we used multivariable logistic regression models to determine the association between community sizes and odds of thrombectomy or thrombolysis, adjusting for covariates. All administrative data case definitions are in Supplemental Table 1. All analyses were conducted using SAS Enterprise Guide version 7.1 (SAS Institute Inc.).

Results

A total of 57,687 patients were included in the analyses, the median age was 74 years (interquartile range: 64-83 years), 45.8% were female, and 25,180 patients (43.6%) resided within 20 minutes of driving time from a CSC. Supplemental Figure 2 shows the distribution of driving times from patients' residences to the nearest Comprehensive Stroke Center (CSC). Compared to those living within 20 minutes driving distance, those living farther were less likely to have hypertension, diabetes, dyslipidemia, and atrial fibrillation, but more likely to have a history of coronary artery disease (Table 1). Table 2 shows baseline characteristics by population size of residence, with 44,444 (77.0%) of the cohort residing in large urban areas. In large urban areas, median driving time to the nearest CSC was 18 minutes and almost no one lived beyond 120 minutes driving time, but driving time was more variable for patients living in medium urban areas or small towns (Figure 1). In the overall cohort, 4,150 (7.2%) patients received thrombectomy and 8,285 (14.4%) were treated with thrombolysis. Table 3 shows the proportion of patients treated by driving time and community size categories.

Driving time and stroke treatments

In multivariable analysis, the odds of thrombectomy declined with increasing driving time from the nearest CSC. The difference became statistically significant from 120 minutes driving time or longer (Figure 2). Patients living 120 minutes away from the nearest had a 20% decrease in the odds of receiving thrombectomy compared to the reference group (aOR 0.80, 95% CI [0.62, 1.04]). This reduction becomes more pronounced at 180 minutes (aOR 0.57, 95% CI [0.43,

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0.76]) and 240 minutes (aOR 0.41 95% CI [0.28, 0.60]). Conversely, the odds of receiving thrombolysis remained relatively stable across most driving times (Figure 2). Even for patients living 690 minutes away from the nearest CSC, the aOR for the receipt of thrombolysis was 0.46, 95% CI [0.11, 1.87]). We performed a sensitivity analysis with 30 minutes as the reference and the results were similar (Supplemental Figure 3). Figure 3 shows the median driving time to the nearest CSC across the province, calculated by dissemination area, the smallest area for which population characteristics are reported to the Canadian Census, typically consisting of 400 to 700 people.

Rurality and stroke treatments

We found no significant difference in the odds of thrombectomy based on rurality categories measured by population size (aOR 0.81, 95% CI [0.56, 1.16] for medium urban areas and aOR 0.78, 95% CI [0.57, 1.06] for small towns compared to large urban areas). Similarly, for thrombolysis, no significant difference was observed among these groups (aOR 1.15, 95% CI [0.88, 1.52] for medium urban areas and aOR 1.18, 95% CI [0.94, 1.48] for small towns compared to large urban areas).

Discussion

This study shows that the geographic disparities in access to acute ischemic stroke treatment are nuanced. First, increasing distance to CSC, measured by driving time, negatively impacted the odds of treatment with thrombectomy, but this was not the case for thrombolysis. Second, rurality measured by community size was not associated with treatment. This suggests that strategies to mitigate inequities in stroke treatments should be focused on certain rural regions, namely those situated >120 minutes from the nearest CSC.

Using driving time introduces novel insights into geographic disparities by allowing us to study this parameter in a graded fashion. Previous research in geographic disparities in stroke care primarily focused on population size as the definition of rurality.[10,27,28] We did not find differences in treatment by rurality categories. Disparities emerged only when we considered driving time to CSCs, suggesting that proximity, rather than population size, is the critical factor in accessing specialized healthcare services for acute stroke care. Small communities located

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close to CSCs appear to have similar access to comprehensive stroke care compared to those living in large urban regions, but remote communities, even if medium in size, are at risk of reduced access.

The significance of incorporating driving time as a measure to understand geographic disparities has been shown elsewhere. In a study conducted in Manitoba, Canada, researchers found that patients living in rural areas, particularly those more than an hour's drive from CSCs, faced longer delays in thrombectomy treatment compared to those living in the urban setting.[29] Similarly, in the United States, a study found that longer driving times were significantly associated with reduced odds of receiving thrombolysis treatment for ischemic stroke.[11] Similar observations extend to non-stroke medical emergencies. For instance, a Swiss population-based study linked mortality from acute myocardial infarction to driving time to the nearest university hospital, a relationship not evident with general hospital proximity.[13]

One explanation of why driving distance is critical may lie in the pathophysiology of stroke and the importance of time. It is conceivable that some patients with stroke due to large vessel occlusion were no longer eligible for thrombectomy due to infarct progression after long inter-hospital transfer times. While the recent publications demonstrating the effectiveness of thrombectomy even in the setting of a large infarct core[30–32] may increase thrombectomy treatment rates across the province, it is nevertheless critical to lower the barriers to thrombectomy access because faster treatment leads to better outcomes.[2] It is also possible that patients living in close proximity to a CSC are more likely to be treated outside strict guideline indications (low ASPECT score or medium vessel occlusion).

We showed that use of thrombolysis was not associated with proximity to a CSC, a success that is likely at least partly due to the strategic establishment of PSCs with capacity to administer thrombolysis in addition to CSCs, thus covering larger parts of the province. This success can be attributed, in part, to the strategic establishment of PSCs with capacity to administer thrombolysis in addition to CSCs, thus covering most parts of the province.[33] There is a pressing need for strategies to broaden access to thrombectomy, including increasing the number of CSCs and/or expanding the Ontario Telestroke Network.[34] The successful implementation

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of thrombolysis across the province can provide a roadmap for targeted strategies to expand access to thrombectomy in underserved regions. While it is neither possible nor necessary for every hospital to offer thrombectomy, our study shows that regions where individuals are more than 120 minutes away from a CSC are most vulnerable and stand the benefit the most from enhanced service distribution. One potential solution is the expansion of the Ontario Telestroke Network, which would allow neurologists at CSCs to remotely assess stroke patients in hospitals located far from these centers, facilitating quicker decision-making and transfer for thrombectomy. Additionally, enhancing air ambulance services in remote areas could significantly reduce transport delays and improve access to timely thrombectomy.

While our study offers significant insights, there are several limitations. While driving time provides an objective measure of geographic accessibility to CSCs, it is a non-physiological proxy for proximity to EVT. Factors such as stroke severity, time of symptom onset, and clinical presentation are also critical in determining eligibility and outcomes for EVT. Additionally, driving time does not account for other real-world factors, such as traffic conditions, weather, or the availability of air transport, which may influence the actual time to treatment. We also acknowledge that driving times may differ for some patients who get transferred using air transportation and this information was not available in our dataset. We also did not have detailed clinical information on stroke severity, last seen normal time, and presence and location of vessel occlusion, which could result in residual confounding. However, the observation that driving time did not influence thrombolysis treatment suggests no major geographic differences in stroke acuity and severity of presentation, and there is no a priori reason to believe that people living far from CSCs are less likely to have large vessel occlusion. Although most patients with stroke are picked up at or near their home, stroke events at another location could introduce some misclassification. Administrative data do not have the level of granularity to address these limitations comprehensively. Additionally, while proximity to PSCs is likely a more direct predictor of thrombolysis access due to the shorter treatment window, our analysis focused on driving time to CSCs, as our primary aim was to examine access to thrombectomy. Future studies should explore the impact of proximity to PSCs on thrombolysis access to further validate these findings. Moreover, the context-specific nature of our research, centered on Ontario's unique healthcare landscape and stroke care network, may limit the applicability of our

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findings to other regions with differing healthcare systems and geographic characteristics, but these findings provide the need to collect critical information on driving times to optimize access to stroke treatments for all. Finally, it is important to note that the large sample size of our study may have contributed to statistically significant differences in baseline characteristics, even when the absolute differences were small.

In conclusion, our study underscores the critical influence of geographic factors on the accessibility of thrombectomy. Addressing these disparities requires a multifaceted approach that combines healthcare policy innovation, infrastructure development, and the adoption of telehealth solutions. By confronting these challenges head-on, we can move closer to achieving equitable healthcare access and improving outcomes for stroke patients across all geographic regions.

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Disclosures The authors report no disclosures.

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Table 1 - Baseline characteristics of patients hospitalized with acute ischemic stroke in Ontario, Canada from April 1, 2017, to March 31, 2022 by driving time (n=57,687 patients)

	<20 minutes n=25,180	**20-60 minutes n=20,029**	**>60 minutes n=12,478**	**p-value**
Median age, years [Q1, Q3]	75 [64, 84]	74 [63, 83]	74 [65,83]	<0.0001
Female sex, n (%)	11,890 (47.2%)	9,064 (45.3%)	5,492 (44.0%)	<0.0001
Hypertension, n (%)	20,804 (82.6%)	16,415 (82.0%)	10,040 (80.5%)	<0.0001
Diabetes, n (%)	10,047 (39.9%)	7,836 (39.1%)	4,553 (36.5%)	<0.0001
Atrial fibrillation, n (%)	7,124 (28.3%)	5,339 (26.7%)	3,365 (27.0%)	0.0002
Dyslipidemia, n (%)	9,699 (38.5%)	6,693 (33.4%)	3,298 (26.4%)	<0.0001
Previous stroke, n (%)	2,154 (8.6%)	1,747 (8.7%)	1,117 (9.0%)	0.43
Coronary artery disease, n (%)	3,595 (14.3%)	3,001 (15.0%)	2,024 (16.2%)	<0.0001
Peripheral vascular disease, n (%)	1,951 (7.7%)	1,443 (7.2%)	981 (7.9%)	0.04
Stroke severity Median PaSSV score [Q1, Q3]	7.5 (6.9-8.8)	7.5 (6.8-8.8)	8.1 (7.0-8.8)	<0.0001

CSC: Comprehensive Stroke Centres; PaSSV: Passive Surveillance Stroke Severity, where lower scores indicates higher stroke severity

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Table 2 - Baseline characteristics of patients hospitalized with acute ischemic stroke in Ontario, Canada from April 1, 2017, to March 31, 2022 by population size of residence (n=57,706 patients*)

	Large urban n=44,444	**Medium urban n=5,766**	**Small town n=7,496**	**p-value**
Median driving time to the nearest CSC (minutes) [Q1, Q3]	17.8 [10.4-33.9]	82.2 [62.1-105.9]	81.2 [56.5-126.4]	<0.0001
Median age [Q1, Q3]	75 [64, 83]	75 [65, 84]	74 [65, 82]	0.0008
Female sex, n (%)	20,574 (46.3%)	2,690 (46.7%)	3,188 (42.5%)	<0.0001
Hypertension, n (%)	36,612 (82.4%)	4,687 (81.3%)	5,976 (79.7%)	<0.0001
Diabetes, n (%)	17,642 (39.7%)	2,137 (37.1%)	2,661 (35.5%)	<0.0001
Atrial fibrillation, n (%)	12,197 (27.4%)	1,667 (28.9%)	1,969 (26.3%)	0.003
Dyslipidemia, n (%)	16,057 (36.1%)	1,593 (27.6%)	2,045 (27.3%)	<0.0001
Previous stroke, n (%)	3,818 (8.6%)	527 (9.1%)	674 (9.0%)	0.24
Coronary artery disease, n (%)	6,489 (14.6%)	947 (16.4%)	1,188 (15.8%)	<0.0001
Peripheral vascular disease, n (%)	3,298 (7.4%)	464 (8.0%)	615 (8.2%)	0.02
Stroke severity Median PaSSV score [Q1, Q3]	7.5 [6.8-8.8]	7.8 [7.0-8.8]	8.1 [7.0-8.8]	<0.0001

CSC: Comprehensive Stroke Centres; PaSSV: Passive Surveillance Stroke Severity, which lower score indicates higher stroke severity. patients were initially identified. *Includes the 19 patients with missing driving time.

Table 3 - Thrombectomy and thrombolysis treatments by driving time distances to CSCs and community size

	<20 minutes n=25,180	**20-60 minutes n=20,029**	**>60 minutes n=12,478**	**p-value***
Thrombectomy, n (%)	2,130 (8.5%)	1,431 (7.1%)	588 (4.7%)	<0.0001
Thrombolysis, n (%)	3,463 (13.8%)	2,975 (14.9%)	1,844(14.8%)	0.0013

	Large urban n=44,444	**Medium urban n=5,766**	**Small town n=7,496**	**p-value***
Thrombectomy, n (%)	3,382 (7.6%)	333 (5.8%)	435 (5.8%)	<0.0001
Thrombolysis, n (%)	6,273 (14.1%)	852 (14.8%)	1,160 (15.5%)	0.005

CSC: Comprehensive Stroke Centres

*p-values presented are based on crude comparisons and do not account for adjustments for potential confounders

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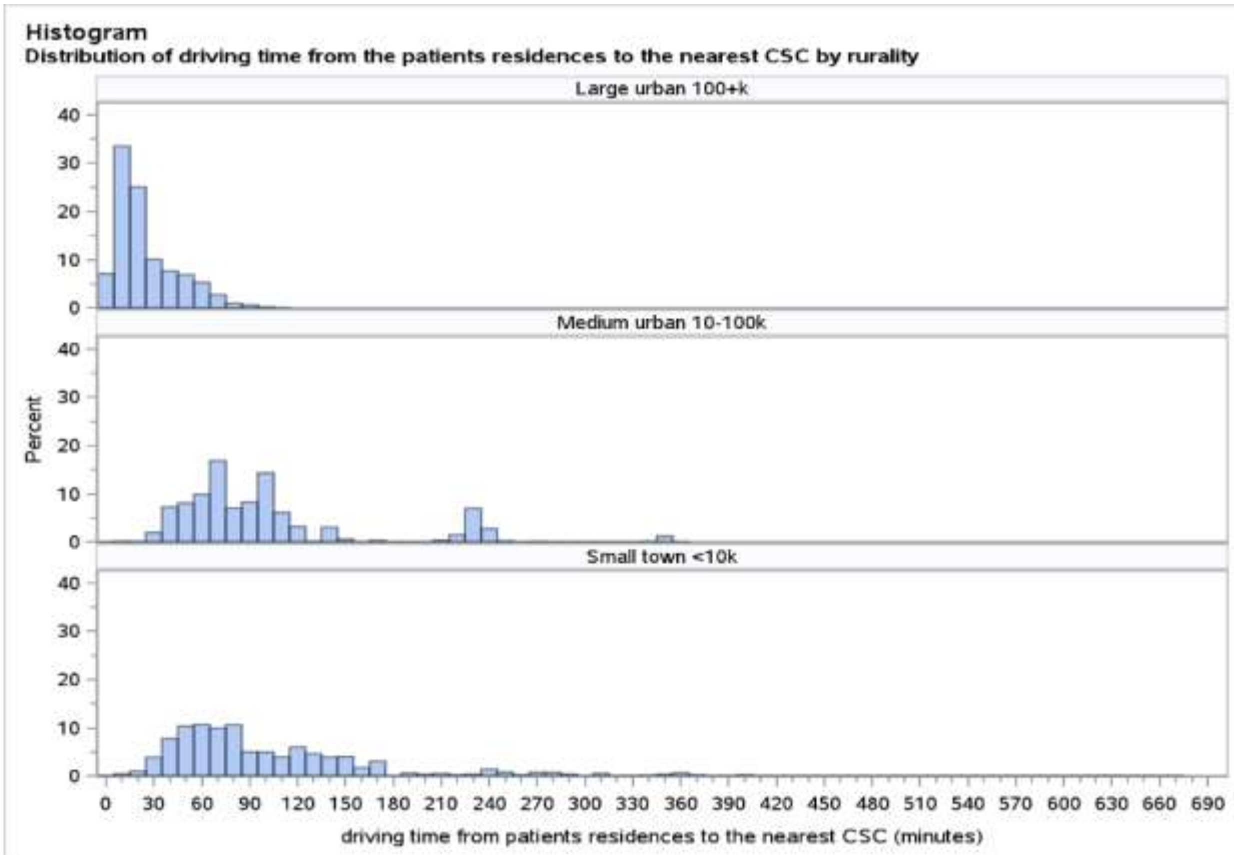

Figure 1 - Histograms showing the distribution of driving times from patients' residences to the nearest CSC, categorized by rurality. The top panel represents large urban areas (>100k population), the middle panel medium urban areas (10-100k population), and the bottom panel small towns (<10k population)

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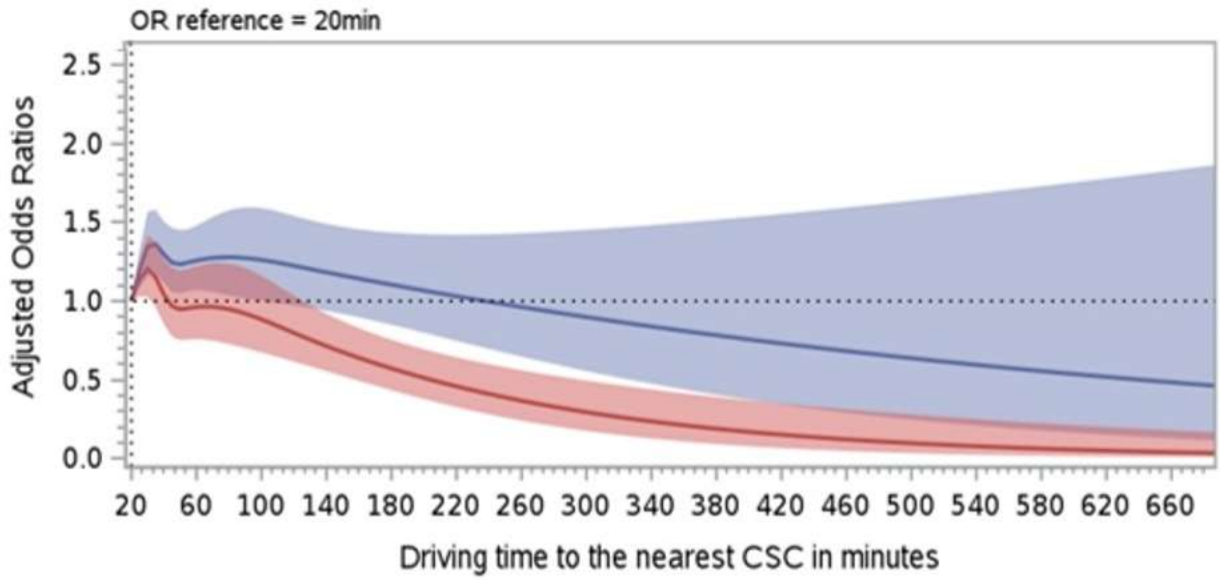

Figure 2 - Adjusted Odds Ratio and 95%Confidence Interval of Receiving Thrombolysis (blue) and Endovascular Thrombectomy (red)

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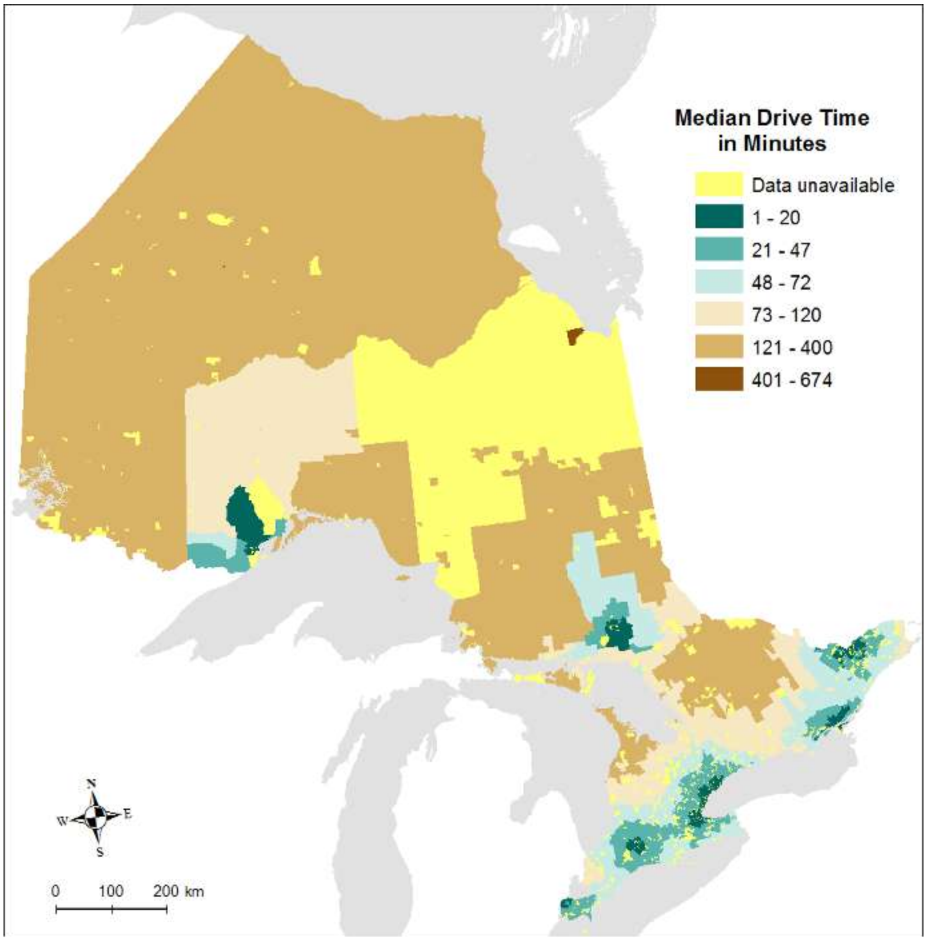

Figure 3 - Geographical distribution of median driving time to nearest CSC in Ontario, Canada

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