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A Spatial Epidemiological Analysis of Stroke in Alberta, Canada, Using GIS.

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by

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Abstract

Stroke is the potentially devastating result of a sudden interruption of blood flow to the brain. It is a leading cause of death and disability world wide and incidence is expected to increase due to an aging population and increased prevalence in risk factors.

Epidemiological research can enhance our understanding of stroke as a health problem in the population with respect to the extent of disease incidence and prevalence, the efficacy of health care delivery for stroke prevention and acute care, and to inform public health policy and planning.

Geographic Information Systems (GIS) technology and spatial methods provide the means to store and retrieve spatially indexed health data, display the spatial information in maps, and conduct analyses examining health service delivery and utilization.

The overall objective of this research is to enrich our current understanding of stroke as a health problem in the province of Alberta, Canada. This thesis is comprised of three studies. The first study utilized GIS-based methods and administrative datasets to identify and locate significant clusters of high and low rates of the major stroke types and in-hospital mortality. Important questions were raised regarding why regional differences exist and how disparities might be mitigated.

The second study expanded upon the cluster analysis with an examination of associations between selected predictors and stroke and mortality hot and cold spots, mortality at the individual level, and recurrent stroke, using multivariable logistic regression. Distance from specialized stroke care was a significant predictor of index and

recurrent stroke and mortality. EMS transport and Comprehensive Stroke Centre care significantly lowered the odds of stroke mortality.

The third study employed spatial methods to evaluate the concordance of GIS predicted versus actual EMS ground transport times and to estimate the proportion of the Alberta population with potential and realized access to stroke care within critical time windows. GIS methods predicted ground transport time with reasonable accuracy and there was expanded access to stroke care over a 5-year time span.

This research highlights the benefits of incorporating spatial methods and GIS in epidemiological research to elucidate how and to what extent place matters to health.

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List of Symbols, Abbreviations and Nomenclature

Symbol	Definition
AIS	Acute Ischemic Stroke
CSC	Comprehensive Stroke Centre
CT	Computerized Tomography
DA	Dissemination Area
DM	Diabetes Mellitus
ED	Emergency Department
EMS	Emergency Medical Services
GIS	Geographic Information Systems
ICH	Intracerebral Hemorrhage
IDDM	Insulin Dependent Diabetes Mellitus (Type 1)
IV	Intravenous
LR	Likelihood Ratio
MAUP	Modifiable Areal Unit Problem
MRI	Magnetic Resonance Imaging
NIDDM	Non-Insulin Dependent Diabetes Mellitus (Type 2)
OTT	Onset-to-Treatment Time
PSC	Primary Stroke Centre
SAH	Subarachnoid Hemorrhage
SC	Stroke Centre
SPC	Stroke Prevention Clinic
TIA	Transient Ischemic Attack
tPA	Tissue plasminogen activator

Contribution of Authors

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Chapter 1: Thesis Overview

1.1 Stroke: A Spatial Epidemiological Perspective

Stroke is the result of a sudden interruption of blood flow to the brain. It is a leading cause of death and disability world wide. Strategies to reduce stroke burden must account for the fact that stroke is a complex and multifactorial disease caused by a combination of risk factors. Strategies to reduce stroke burden include (i) treating first ever and recurrent stroke to reduce case fatality and maximize independence; (ii) reduce the risk of stroke after transient ischemic attack; (iii) seek out and treat those at high risk of stroke; and (iv) reduce the average level of causative risk factors in the whole population (Warlow et al., 2001).

There have been significant advances in treatments for index and recurrent stroke since the pivotal National Institute for Neurological Disorders Trial in 1995 which found the administration of intravenous (IV) thrombolysis (tPA) within 3-hours of onset of ischemic stroke improved clinical outcome at 3-months (NINDS and Stroke r-tPA Stroke Study Group, 1995). Subsequent to this trial, the treatment window for tPA administration has been extended from 3-hours to 4.5-hours in select cases (Hacke et al., 2008). Trials for endovascular treatments (thrombectomy and thrombolysis), neuroprotective agents, and diagnostic testing with high sensitivity and specificity for ischemic stroke are ongoing.

Primary and secondary stroke prevention practices have been informed by findings from research examining the efficacy of behavioural risk factor modification, medical treatments (e.g. anticoagulation, antiplatelet, and lipid lowering), and surgical interventions (e.g. carotid endarterectomy, stenting) on stroke reduction. Risk factors that may be rooted in behaviours that are considered to be self-imposed (Lalonde, 1981; Frohlich, 2008) are identified and managed through high risk identification strategies and individual consultation at primary care offices and prevention clinics with the expectation that adherence to risk reductions strategies will be maintained.

There is increasing evidence that compliance with treatment in 'real life' is considerably less than in randomized control trials and that efforts at health promotion have transient effects (Warlow, 2001; Rothwell, 2005). Many disparities that affect an individual's opportunity to pursue a healthy lifestyle occur beyond individual level characteristics, resources, and behaviours (Holmes et al., 2008); rather they are shaped by the physical, social, geopolitical and other environments within which one lives. Issues relating to environmental justice where negative health impacts resulting from exposure to toxic pollutants are visited on those least able to deal with them (Harvey, 1996; WHO, Dec 2014; Maheswaran et al., 2005); neighbourhood stressors (e.g. crime, poverty); government investment in stroke infrastructure to enhance access to care and improve outcomes (APSS, 2014); and universal health care coverage are examples of structural influences on individual health. A prevention strategy that reduces the average level of causative risk factors for the population complements the individually based 'high risk' strategy (Warlow et al., 2001; Rose, 1985). A population prevention strategy is likely to lower stroke incidence (and prevalence) because most strokes occur in those who are at moderate risk and who comprise a much greater proportion of the population than those at high risk (Rose, 1985). A population approach proposes that the magnitude of stroke as a health problem and on future short and long term population health may be better elucidated as a function of the distribution of the population and health care resources (Rose, 1985; Spasoff, 1999).

A fundamental assumption of epidemiology is that diseases do not distribute randomly in populations but rather distribute in relation to their determinants (Last, 2000). For most non-infectious diseases, a lot is known about the individual characteristics of susceptible individuals but less is known about the determinants of the incidence rate (Rose, 1985). A valuable first step in terms of our understanding of stroke in the population and for public health planning is to examine the characteristics of populations where clusters of modifiable risk factors exist and where higher than expected stroke and stroke mortality rates overlap. Directed and potentially more effective population risk reduction strategies could then be implemented in a more cost effective manner. These strategies might include (i) increasing the availability of healthy and affordable foods in food deserts (CDC, Dec 2014), (ii) mandatory reductions of sodium levels in pre-prepared foods (Mohan, Campbell, & Willis, 2009), (iii) increasing the availability of safe environments for play and exercise (Harvard School of Public Health, Dec 2014), (iv) risk reduction strategies that consider the contextual setting of communities including cultural values and language (including the homeless community), and (v) equitable access to preventive care that includes bringing care to populations where exposure to multiple risk factors and a greater number of comorbidities exist (including the workplace).

Analyses exploring population level risk factors are enhanced by the inclusion of explanatory variables that are spatial, enabling a richer and more comprehensive exploration of 'where' and 'why' questions. Spatial epidemiology is a dynamic body of theory and analytic methods concerned with the study of spatial patterns of disease incidence and mortality (Waller & Gotway, 2004). Spatial epidemiology relates disease patterns to geographic variation in health risks (Lai, So & Chan, 2009), incorporating geographically indexed health data that includes demographic, environmental, behavioural, socioeconomic, genetic, and infectious risk factors (Elliot & Wartenberg, 2004).

Arguably, the most significant contribution that geographers have made to quantitative health research has been to demonstrate that data for both places and individuals can be linked in order to shed light on health outcomes (Gatrell, 2002). Geographic Information Systems (GIS) are a powerful set of tools for collecting, storing, retrieving, transforming, and displaying spatial data from the real world (Lai et al., 2009). GIS have been used increasingly as an evidence-based tool in epidemiological research (Longley, Goodchild, Maguire, & Rhind, 2005) and in stroke research specifically. Epidemiology and GIS are well aligned. GIS offers a unique perspective for examining spatial stroke patterns and processes, is useful for analyzing the effectiveness of health interventions and health care delivery applications, can be a stimulus for generating novel hypotheses of disease causation, and produces maps that inform and educate (Boulos, 2004). To avoid drawing false conclusions from maps, users of GIS technology need to understand and apply epidemiological principles and methods in formulating study questions, testing hypotheses about cause-and-effect relationships, and critically evaluating how data quality, confounding factors, and bias may influence the interpretation of results (Richards, Croner, Rushton, Brown, & Fowler; 1999).

Population based administrative data are useful for epidemiologic studies. In Canada, they have the advantage of providing data for virtually all members of the population that they represent and are therefore highly generalizable and representative of large (geographically) defined populations (Deyo et al., 1994). When linked with more detailed spatial data that are now available, analyses can take 'place' into account, recognizing that where one lives matters to health. These studies may be followed by more focused analyses conducted at larger geographic scales that incorporate qualitative methods.

GIS and spatial methods have been utilized to examine regional disparities in disease risk, incidence and mortality. Regional disparities in stroke are well documented in the literature and persist despite our knowledge of them. It is inevitable that some variation in disease incidence and outcomes will exist, but inequities may be avoidable, and should be capable of being narrowed (Gatrell, 2002). Although regional disparities in stroke are acknowledged to exist in Alberta, no published research exploring disparities using GIS has been carried out. Hence, the focus of this research is to enrich our current understanding of stroke as a health problem in Alberta by exploring spatial patterns of stroke occurrence and mortality and by examining geographic accessibility to specialized stroke care services.

1.2 Thesis Outline

This is a retrospective, population based exploratory study using administrative data and linked ambulance and hospital data and a spatial epidemiological approach integrating GIS examining the geographic distribution of stroke in Alberta and geographic access to specialized stroke care.

This thesis begins with a cursory review of stroke types and treatments, stroke systems of care, a discussion of the integration of GIS in health research, and a summary of selected research papers on stroke utilizing GIS and spatial methods. This is followed by the presentation of Studies I, II, and III. This thesis concludes with a synopsis of research findings, a discussion of the merits and limitations of integrating GIS in stroke research, and suggestions for future research.

The first study employed spatial methods using administrative data to identify and locate geographic clusters of high and low rates of stroke, in-hospital mortality, and stroke risk factors across Alberta, Canada. Findings from the first study raised important questions regarding why regional differences exist and how disparities might be mitigated. The second study expanded upon the cluster analysis with an examination of associations between known and novel predictors of stroke and (i) stroke and mortality hot and cold spots identified in Study I, (ii) mortality at the individual level, and (iii) recurrent stroke, using multivariable logistic regression methods. Taking into account the importance of timely access to specialized stroke care to good outcome, the third study employed spatial methods to estimate the proportion of the Alberta population with predicted geographic access to specialized stroke care by ground transport within critical treatment time windows. The proportion of stroke events with predicted geographic access to stroke care who accessed care at an accredited stroke centre (realized access) was also determined and regions where realized access might be increased were highlighted. This thesis concludes with a summary integrating findings from the three studies, a discussion of the merits and limitations of integrating GIS in stroke research, and suggestions for future research.

Chapter 2: Thesis Purpose

2.1 Study Rationale

Studies examining geographic variations in health care often identify unrecognized problems in clinical decision making, identify populations with inequitable geographic access to health care, inform public health policy, quantify the impact(s) of process and policy changes, may predict future population health care trends and needs (Birkmeyer, 2001), and enhance our understanding of how disparities might be mitigated.

Specific gaps in knowledge pertaining to stroke in Canada have been identified and include (i) the extent to which health services before admission to hospital affect mortality rates, other patient outcomes, and costs (CIHI, 2006), (ii) why regional differences in 30-day in-hospital stroke mortality exist (CIHI, 2006), and (iii) our understanding of why stroke that occurs in women, in children, in rural areas, ethnic minorities and disadvantaged populations persist (Birdsell, Omelchuk, & Skanes, 2007). Efficacious stroke prevention strategies and timely access to specialized care for stroke are necessary components of a strategy to reduce stroke incidence and improve outcomes. Although geographic variability in access to health care experts, technology, and at-risk populations in Alberta has been established, evaluations of stroke services and outcomes in Alberta have been conducted to assess changes in service provision and outcomes over time but have not incorporated a spatial component beyond the stratification of outcomes by health zone (Jeerakathil, Burridge, Thompson, Fang, & Hill, 2010). An analysis of the spatial distribution of stroke types and mortality in Alberta has not previously been undertaken, and the extent to which regional differences in known and novel risk factors for stroke are associated with any disparities in the spatial distribution of stroke in

Alberta has not been fully considered. How much geographic variation exists, where it exists, what populations (rather than persons) are affected, and whether preventable regional disparities have been mitigated with targeted enhancements to stroke services are not known.

There has been extensive research investigating regional disparities in disease incidence and mortality. Geographic variation in traditional stroke risk factors is now thought to play a smaller role in the geographic variation in stroke and mortality than previously thought (Howard et al., 2009). It is estimated that 15% of the population's health is attributable to biology and genetic factors, 10% to the physical environment, 25% to the reparative work of the health care system, and 50% to the social and economic environment (Keon & Pépin, 2009). There is a need to consider alternative causes, in addition to traditional risk factors, that underlie geographic variation in stroke incidence and mortality (Howard et al., 2009).

Although stroke and mortality data have been available within the public domain in table, report, and choropleth rate map formats at multiple scales - international (WHO, Oct 2014), national (WHO, Oct 2014), and provincial and regional for Alberta (PHAC, Oct 2014; AHW, Oct 2014), the availability of spatial incidence and prevalence data at larger geographic scales is inconsistent across disease states and geography within Canada. The availability of geocoded administrative stroke data for Alberta joined with Statistics Canada census data, geocoded and linked ambulance and hospital stroke data, detailed spatial data files, and GIS has facilitated the analyses for Parts I, II, and III of this research project that are designed to address some of these gaps as they pertain to stroke in Alberta.

2.2 Study Hypotheses

It is hypothesized that, after adjusting for age and population distribution, the geographic distribution of stroke in Alberta is neither uniform nor random. There will be geographic areas with populations who are at greater risk for stroke, experience higher than expected rates of stroke, and have worse outcomes after stroke. Variations will exist at the local and regional scale. There may additionally be geographic variations in stroke distribution according to stroke type.

It is expected that strokes will be higher in areas with populations who have higher than expected risk(s) for stroke that include diabetes mellitus, hypertension, atrial fibrillation, and hypercholesterolemia, and where there is a greater proportion of the resident population with low median household income, who are ethnic minorities, non-English speaking, and have less than high school education. It is hypothesized that these predictors may be of less importance to outcome after stroke than geographic proximity, costed by ground travel time, to a Primary Stroke Centre (PSC) or Comprehensive Stroke Centre (CSC).

It is expected that geographic proximity to a Stroke Prevention Clinic (SPC) will be an important predictor of recurrent stroke and that geographic proximity to a Stroke Centre (SC) will be an important predictor of mortality after adjusting for stroke severity. It is also expected that with the increase in the number of PSCs, a greater proportion of the population of Alberta have access to specialized stroke care within acute stroke treatment time windows.

2.3 Study Objectives

The primary objective of this research study is to inform on the role of geography in stroke as a health problem in Alberta. A spatial epidemiological analysis will be carried out in three parts with study objectives as follows:

Study I: to identify geographic variances in stroke occurrence, in-hospital mortality and reported stroke risk factors using GIS based methods and administrative data sets in the province of Alberta. The goal is to identify population clusters with higher or lower rates of the major stroke types and in-hospital mortality;

Study II: to investigate whether (1) distance from a SPC predicts inclusion in a hot or cold spot for stroke and distance from a SC predicts in-hospital mortality after adjusting for selected Dissemination Area level characteristics, (2) drive time (minutes) from a SC predicts in-hospital mortality after stroke, and (3) drive time (minutes) from a SPC predicts admission to hospital for a recurrent stroke event, using multivariable logistic regression; and

Study III: to (1) evaluate the concordance of GIS predicted versus actual Emergency Medical Services (EMS) ground transport times for stroke, (2) estimate the proportion of Alberta population age ≥20 years with potential geographic access to acute stroke care by ground within critical onset-to-treatment (OTT) time windows as defined by parameters in our data (predicted geographic access), (3) identify the proportion of a stroke population with predicted geographic access to stroke care who accessed care at a CSC or PSC (realized access) in 2002 and 2007, and (4) to characterize stroke populations with predicted geographic access within and outside of critical transport time windows.

An overview of stroke types and treatments, stroke systems of care, and a summary of selected studies in the stroke literature utilizing spatial methods and GIS now follows.

Chapter 3: Stroke, Stroke Systems of Care, Outcomes and Geography

3.1 Stroke Types and Treatment

Stroke is the result of a sudden interruption of blood flow to the brain caused either by the occlusion of a blood vessel by a thrombus or atherosclerotic plaque in ischemic stroke or the rupture of a diseased blood vessel in hemorrhagic stroke (AHA, Sept 2014). Neurological deficits reflect the area of the brain that has been affected. Stroke is the fourth leading cause of death in Canada and a leading cause of acquired long-term disability in adults (APSS, 2006). Twenty percent of strokes are fatal and for those who survive, 75% live with some form of disability (APSS, 2006).

Diagnostic imaging (Computed Tomography or CT) is required to identify stroke type and to delineate viable (penumbra) and infarcted tissue. Treatment varies according to the type of stroke. The National Institute for Neurological Disorders and Stroke (NINDS) Trial (1995) was a pivotal study that found treatment with IV tPA within 3-hours after onset of stroke symptoms improved clinical outcome at 3-months (NINDS and Stroke r-tPA Stroke Study Group, 1995). Definitive treatment for Acute Ischemic Stroke (AIS) remains the administration of IV tPA within 3-hours of onset of symptoms and longer (up to 4.5-hours) in selected circumstances (Hacke et al., 2008). The onset-to-treatment (OTT) time with IV-tPA is strongly associated with outcome, with a doubling of the odds of good outcome when administered under 1.5-hours after onset versus 1.5 to 3.0-hours after onset (Hacke et al., 2008; Marler et al., 2000). This relationship holds for all forms of reperfusion therapy (Mazighi et al., 2009; Mazighi et al., 2012; Khatri et al., 2014).

Transient Ischemic Attack (TIA) is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms similar to ischemic stroke but typically lasting less than one hour, and without evidence of acute infarction (Albers et al., 2002) on imaging (Magnetic Resonance Imaging or MRI). After a first TIA, 10% to 20% of patients go on to have an ischemic stroke in the next 90-days (Albers et al., 2002). Therefore, urgent evaluation and treatment to prevent ischemic stroke is recommended. Effective lifestyle changes and treatments for preventing ischemic stroke include blood pressure management, dietary modification, exercise (Davis & Donnan, 2012), surgery for severe carotid-artery stenosis, anticoagulant therapy for high-risk cardioembolic conditions (e.g. atrial fibrillation), and antiplatelet agents for the prevention of noncardioembolic stroke (e.g. atherosclerotic plaque) (Albers et al., 2002).

Intracerebral Hemorrhage (ICH) is bleeding into the parenchyma of the brain (Qureshi et al., 2001). Treatment is time sensitive and may include blood pressure management, intraventricular administration of thrombolytic agents, and surgical evacuation (Qureshi et al., 2001) necessitating admission to a neuro-intensive care unit.

The leading cause of non-traumatic Subarachnoid Hemorrhage (SAH) is rupture of an intracranial aneurysm (80% of cases) leading to the extravasation of blood into the subarachnoid space (Suarez, Tarr, & Selman, 2006). Hypertension and smoking increase the risk of SAH. Treatment for intracranial aneurysms includes observation, craniotomy with clipping of the aneurysm, and endovascular coil-occlusion of the aneurysm (Brisman, Song, & Newell, 2006), also necessitating admission to a neuro-intensive care unit. Treatment is time-sensitive.

3.2 Stroke Systems of Care

A stroke system of care should coordinate and promote patient access to services associated with primary and secondary stroke prevention, community education, notification and response of EMS, acute stroke treatment, subacute stroke treatment and secondary prevention, rehabilitation, reintegration, and continuous quality improvement activities (Schwamm et al, 2005). Fragmentation of the delivery of these services frequently results in suboptimal treatment, safety concerns, and inefficient use of healthcare resources (Schwamm et al, 2005).

Increasing access to acute reperfusion therapy and minimizing OTT are two of the major goals in the implementation of an integrated system of stroke care (Schwamm et al, 2005; Lackland et al, 2014, Acker et al., 2007) (Figure 3.1). Prevention of delays in treatment for stroke requires early stroke recognition, rapid activation of EMS and use of transport protocols for EMS and close geographic proximity of the populace to operational stroke centres. Implementation of a comprehensive system of stroke care has been shown to increase the use of EMS for transport, reduce interfacility transfer delays, reduce OTT times, and increase rates of thrombolysis administration for AIS (Prabhakaran, O'Neill, Stein-Spencer, Walter, & Alberts, 2013; Prabhakaran et al., 2011; Saver et al, 2010).

3.2.1 Stroke Systems of Care in Alberta, Canada

In Alberta, there are 2 Comprehensive Stroke Centres (CSC), located in the two largest cities, and 14 Primary Stroke Centres (PSC). PSCs have CT scan availability, stroke expertise on-site or available by telestroke linkage, and tPA treatment availability.

ONSET	→			DOOR →	CT →	NEEDLE
Symptom Onset to 9-1-1	9-1-1 to Dispatch	Dispatch to Scene	Scene	Scene to PSC/CSC	ED to CT	CT to Treatment
	<90-sec*	<8-min*	<15-min*	Lights & Siren[†]	≤25-min* <20-min[‡]	
< 3.0-hours [Class 1 Recommendation; Level of Evidence A][§]				<60-minutes [Class 1; Level of Evidence A][§]		
3.0 to 4.5-hours [Class 1 Recommendation; Level of Evidence B][§]						

*American Heart Association Guidelines, 2013.
https://www.aan.com/Guidelines/home/GetGuidelineContent/581.
[†]Alberta Health Services Emergency Medical Services.
[‡]Alberta Provincial Stroke Strategy Pre-Hospital Care, 2009.
http://www.strokestrategy.ab.ca/Prehospital%20Nov2409%20Final.pdf.
[§]American Heart Association Target: Stroke. http://www.strokeassociation.org/idc/groups/heart-public/@wcm/@hcm/@gwtg/documents/downloadable/ucm_308277.pdf.

Figure 3.1. Guidelines for symptom onset (time last seen normal) to treatment time intervals.

CSCs have a stroke team, neurosurgical expertise, and neuro-interventionalist expertise on-site in addition to PSC capabilities. Telestroke linkage can increase access to IV-tPA treatment for AIS patients receiving care at SCs without on-site stroke expertise but with tPA treatment availability. The SC connects to a remote neurologist who can access CT imaging and examine a patient via video-link for the purpose of advising the ED physician whether to administer IV-tPA (Bisby & Campbell, 2012). Telestroke linkage can also be used to access specialized care for primary and secondary stroke prevention.

In 2006, the Government of Alberta recognized the need to provide an integrated and accessible health service to best meet the needs of stroke patients regardless of place of residence, noting that 40% of the population resided in rural Alberta (APSS, 2006). Eleven existing regional hospitals with CT scan availability were designated as PSCs, supported by a standardized EMS stroke screen tool, direct EMS transport protocols, and best practice stroke care guidelines instituted at all sites.

EMS modes of transport for acute stroke patients include ground ambulance and rotary or fixed wing aircraft. In Alberta, the Referral Access Advice Placement Information and Destination centre (RAAPID) facilitates critical and urgent transfers or consultations with a tertiary care centres or specialists, ensuring that patients are transferred expeditiously to the appropriate facility (AHS, Oct 2014).

3.3 Conceptual Framework: The Structurationist Approach

The structurationist approach to health geography is selected as a framework for this research because it recognizes the duality of structure and human agency; that humans make their own health but not in conditions of their choosing (Gatrell & Elliott, 2009). Social structure affects agency. Social structures (e.g. health care infrastructure and proximity to specialized care; transportation infrastructure; universal health coverage) together with employment and family commitments; health beliefs, attitudes, values and knowledge; and physical ability may dictate whether a person seeks care, is referred to a specialist, attends preventive care appointments, and is compliant with / can afford recommended therapy(s). Agency may transform structure. Public awareness campaigns regarding abstinence from risk taking behaviours are often ineffective because these behaviours are social and rooted in community life (Rose, 1985; Douglas & Wildavsky, 1983; Frohlich & Potvin, 2008) and roots of these behaviours are not effectively addressed at a structural level. A consequence of a lack of change in risk taking behaviours or of uptake of health care in particular locations may be modifications to how services are delivered.

Andersen's behavioural model (Figure 3.2) (Andersen, 1995) is used as a framework for understanding conditions that either facilitate or impede utilization of health care services and equitable access to health care. It fits within a structurationist framework because it recognizes that both community (structural) and personal enabling resources must be present for utilization of health care services to take place. In Andersen's model, 'perceived need' will help us better understand care-seeking and adherence to a medical regime, and 'evaluated need' will be related to the type and amount of treatment that will be provided. 'Need' and 'demographic' characteristics would dictate hospital services received for an acute health event. Utilization of more discretionary health services would be explained more by social structure, beliefs, and enabling factors. Andersen defines 'equitable' access as occurring when 'demographic' and 'need' variables account for most of the variance in utilization. 'Inequitable' access occurs when 'social structure', 'health beliefs', and 'enabling resources' determine who receives health care. Petersen relates the importance of mutability of variables to the ability to institute policy change(s) that increase access to care. Enabling resources are considered highly mutable. Health beliefs are rated as having medium mutability since they can be altered and sometimes effect behavioural change. Health education may increase or decrease perceived need, and evaluated needs can be altered to influence the medical practitioner's judgment about the patient's evaluated need for health care. This last point ties in with Birkmeyer's model addressing geographic variation in the provision of care.

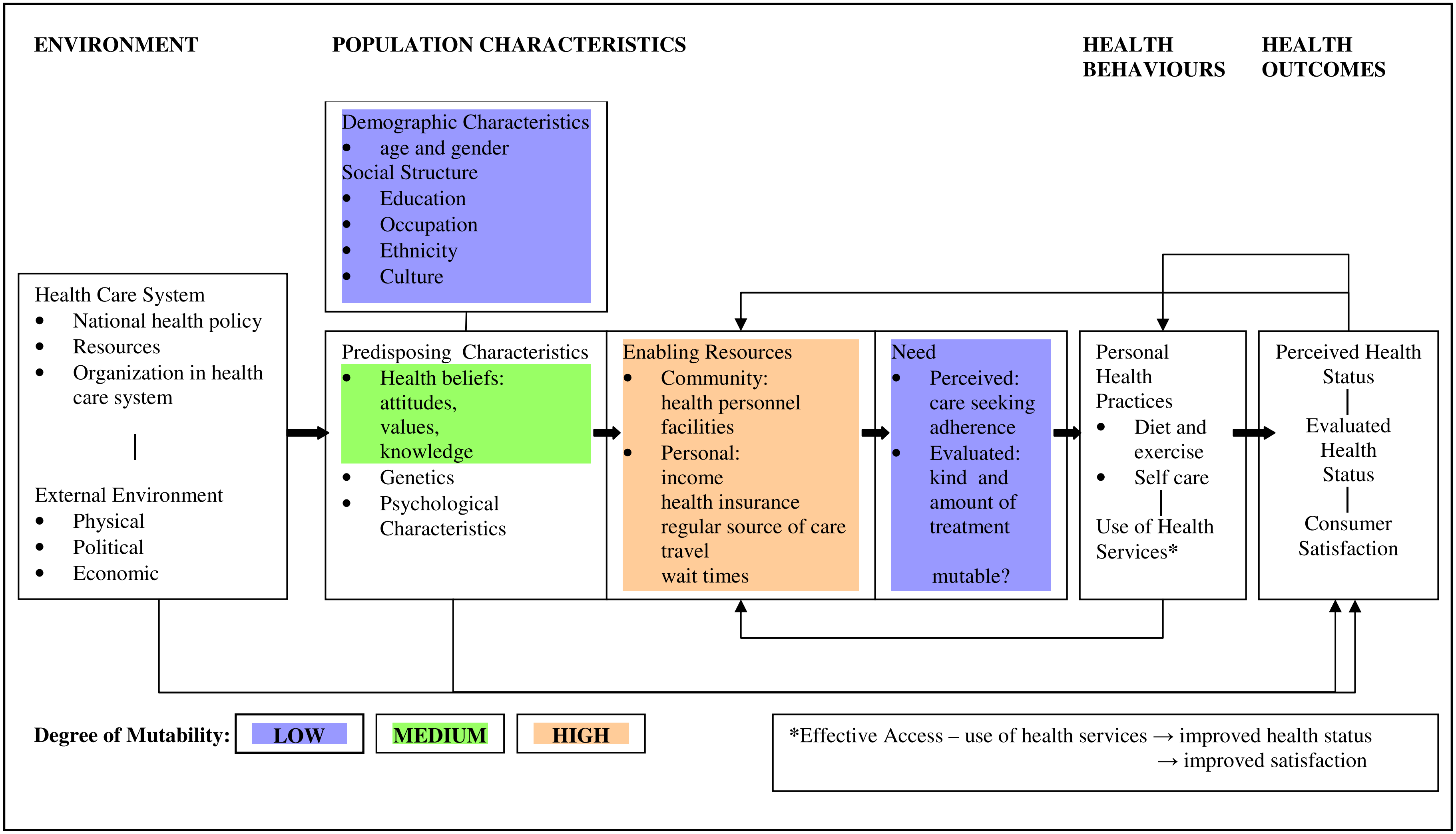


Figure 3.2 An Emerging Behavioural Model of Health Services Use – Phase 4 (Andersen, 1995).

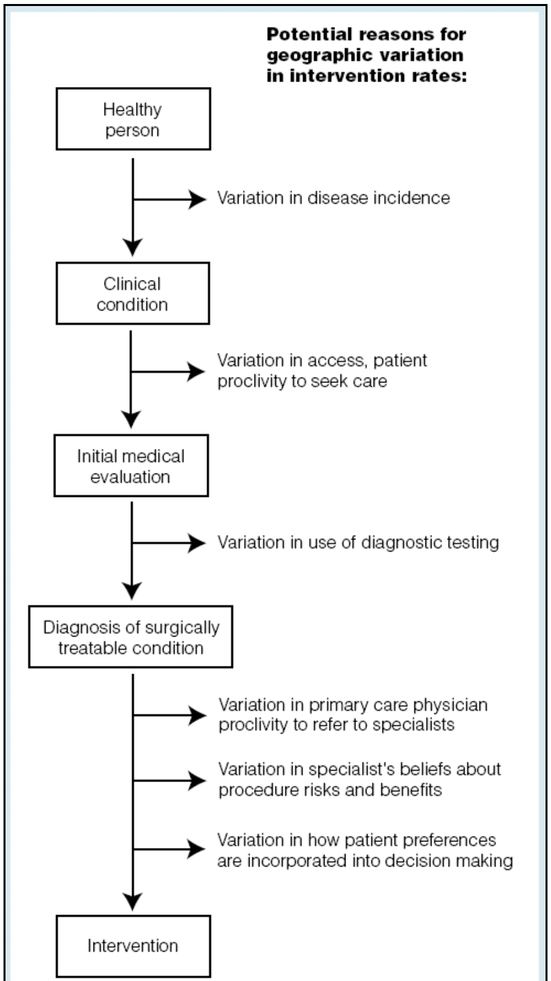


FIGURE 2. **Process by which a healthy person becomes a patient and ultimately receives a medical intervention and potential reasons for geographic variation in intervention rates.**

Figure 3.3. Birkmeyer's model of potential reasons for geographic variation in intervention rates (Birkmeyer, 2001).

Birkmeyer's model (Figure 3.3) (Birkmeyer, 2001) encapsulates potential reasons for geographic variation in the provision of care (intervention rates in his model) emphasizing 'evaluated' need. Reasons for geographic variation in the utilization and provision of health care include (i) disease prevalence in relation to risk factors, (ii) access to care related to regional differences in socioeconomic status, insurance, geographic proximity to health care, and patient proclivity to seek medical care, (iii) the decision on the part of the physician to test, and (iv) the decision to treat, and the propensity to refer the patient to a specialist and the specialist's beliefs regarding the risks and benefits of a given treatment. As Birkmeyer's model pertains to stroke, it highlights the support that is necessary on behalf of healthcare providers working at sites that care for a smaller number of stroke patients in the provision of best practice stroke care. Support is currently available in Alberta via Strategic Clinical Networks, continuing education programs (including interprovincial rounds), RAAPID, telestroke linkages (AHS – Telestroke, 2014), and the TIA Hotline (Coutts & Jeerakathil, 2014).

This research will consider predictors for stroke and mortality that are tied to human agency and are potentially mutable (e.g. hypertension), are structural and have low mutability (e.g. ethnicity), and are structural and mutable (e.g. geographic proximity to specialized stroke care) via government health care policy initiatives and investment.

3.4 Integration of Spatial Methods and Geographic Information Systems in Stroke Research

3.4.1 Spatial Methods and Geographic Information Systems

GIS technology serves two main functions: (i) the production of maps to promote the visualization of spatial information (e.g. disease atlases), and (ii) the analysis of spatial information including exploratory spatial data analysis (e.g. buffer analysis, cluster analysis of high and low risk, network analysis), modeling of health data in a spatial setting (e.g. assessing disease incidence and associations with explanatory variables), and multi-level modeling (Lai et al, 2009; Longley et al., 2005; Gatrell et al., 2009). Multi-level modeling helps to establish whether health variations from place to place are due to compositional effects (because different sorts of people live in different places) or due to contextual effects (because attributes of places themselves differ), thereby contributing to our understanding of how the interaction of human agency and the environment impact health (Gatrell et al., 2009). This research paper will utilize exploratory spatial data analysis and logistic regression techniques.

3.4.2 Defining Access to Care

Dimensions of “access” to health care include (i) availability – the relationship of existing services to the clients’ volume and types of needs, (ii) accessibility – the relationship between the location of supply and the location of clients, taking client transportation resources, travel time, distance and cost into account, (iii) accommodation – the relationship between the manner in which the supply resources are organized to accept clients and the clients’ ability to accommodate to these factors and the clients’ perception of their appropriateness, (iv) affordability – the relationship of prices of services and providers’ insurance, ability to pay, and existing health insurance (e.g. in the Canadian context – supplemental costs including ambulance transport, prescription medications, travel and accommodation, rehabilitation), and (v) acceptability – the relationship of clients’ attitudes about personal and practice characteristics of providers to the actual characteristics of existing providers, as well as to provider attitudes about acceptable personal characteristics of clients (Penchansky & Thomas, 1981). In the case of acute stroke, a potentially life-threatening emergency, availability and accessibility are germane.

Spatial accessibility is a measure of the number of services in comparison to the number of potential users. The extent to which inequalities in access to health care exist is a product of the spatial arrangement of the health care delivery system, the location and distribution of the population within a region, characteristics of the transportation infrastructure (Delamater, Messina, Shortridge, & Grady, 2012), and associated costs. Therefore, the location and number of healthcare services is an important health policy issue. Location-allocation analysis in GIS can support health policy decision making as it considers accessibility and availability in the locating of facilities that makes it possible to reach the most people within a defined time frame (ESRI – Location-Allocation, 2014), imperative for adverse health events including stroke that have critical treatment time windows, and avoids duplication of services.

'Potential' access to health care exists when a needy population coexists in a space and time with a willing and able healthcare delivery system and 'realized' care occurs when all barriers to provision are overcome (Guagliardo, 2004). 'Potential' and 'realized' access are not necessarily equivalent. Gomez et al. (2013) found that a discrepancy existed between the availability of trauma services care (potential access) and realized access to care at a trauma centre, concluding that the availability of services does not ensure their utilization.

3.4.3 Stroke Research Utilizing Spatial Methods and GIS

There has been extensive choropleth mapping of stroke, risk factors, and stroke mortality in the U.S., however geographic mapping of stroke in Canada (WHO, 2014) and Alberta (AHW - IHDA, 2014; AHW, 2007) has been limited. Data are most often presented in table and graphic formats and, if spatial data are available, they are provided at smaller geographic scales (e.g. health region/zone or province).

Spatial methods and GIS have been used to identify patterns of stroke and locate regions where disparities in incidence and mortality exist. In the U.S., the concept of a stroke belt, a broad band of excess mortality from stroke encompassing much of the southeastern U.S., was introduced in 1995 (Lanska & Lewis, 1995). Since this time, choropleth maps of incidence and mortality have been constructed and assessed for associations with spatial distributions of known and novel risk factors including hypertension, ethnicity, and poverty (Tenenbaum & Waters, 2011). More recently Xu, Ma, Liu & Hankey (2013) used GIS to create choropleth maps displaying a newly identified stroke belt of high incidence in China. Differences in risk factor distributions between the stroke belt and other regions were compared using one-way ANOVA. Pedigo, Aldrich, & Odoi (2011) performed a cluster analysis using the spatial scan statistic to identify and locate statistically significant clusters of stroke mortality in the East Tennessee Appalachian Region of the U.S. Logistic modeling was utilized to identify potential associations between neighbourhoods located within a high risk cluster and selected neighbourhood socioeconomic and demographic predictors. GIS have been used to support analyses investigating novel risk factors for stroke. For example, Maheswaran et al. (2005) used GIS to interpolate modeled air pollution data to census enumeration districts in their analysis examining the association between exposure to elevated levels of air pollution and increased risk for stroke mortality and hospital admissions for stroke.

Buffer analysis was used by Scott, Temovsky, Lawrence, Guidaitis & Lowell (1998) in their evaluation of the proportion of the Canadian population with potential geographic access to IV tPA for AIS. Census population data were attached to Enumeration Area (EA) centroids. Census data were then extracted from the EAs located within specified areas around hospitals identified as having the capability to provide care for AIS. These areas were created based upon travel distances and times deemed clinically significant in the treatment of AIS. Proportions of the Canadian population considered to have timely access to stroke care were calculated. Similar methods were used in Suzuki et al.'s (2004) work assessing the proportion of the U.S. population with access to intra-arterial therapies for AIS. The availability of more detailed representations of geographic accessibility (e.g. street network data) incorporating transportation infrastructure (roads for travel distances), travel impedance (speed limits and distance for travel time), and various modes of travel (e.g. public transportation) (Delamater et al., 2012) have enabled more accurate calculations of scene-to-healthcare destination travel times. Acharya et al. (2011) used GIS network analysis to calculate a network distance from each patient's home to the hospital. Patients were grouped by distance into quintiles and a multivariate model was created to identify whether patients living in close proximity to the hospital (arrival within 3-hours of symptom onset) were more likely to receive thrombolysis for AIS. Network analysis was also used by Pedigo & Odoi (2010) in their investigation of neighbourhood disparities in travel time to emergency stroke and myocardial infarction care in East Tennessee.

Study I, the first of three studies exploring stroke as a population health problem in Alberta, now follows. This study will elucidate the geographic distribution of stroke events, mortality, and risk factors occurring from 2002 to 2007 inclusive in Alberta.

Study I. An Analysis of Spatial Clustering of Stroke Types, In-hospital Mortality, and Reported Risk Factors in Alberta, Canada, Using GIS.

Chapter 4: Study I. An Analysis of Spatial Clustering of Stroke Types, In-hospital Mortality, and Reported Risk Factors in Alberta, Canada, Using GIS.

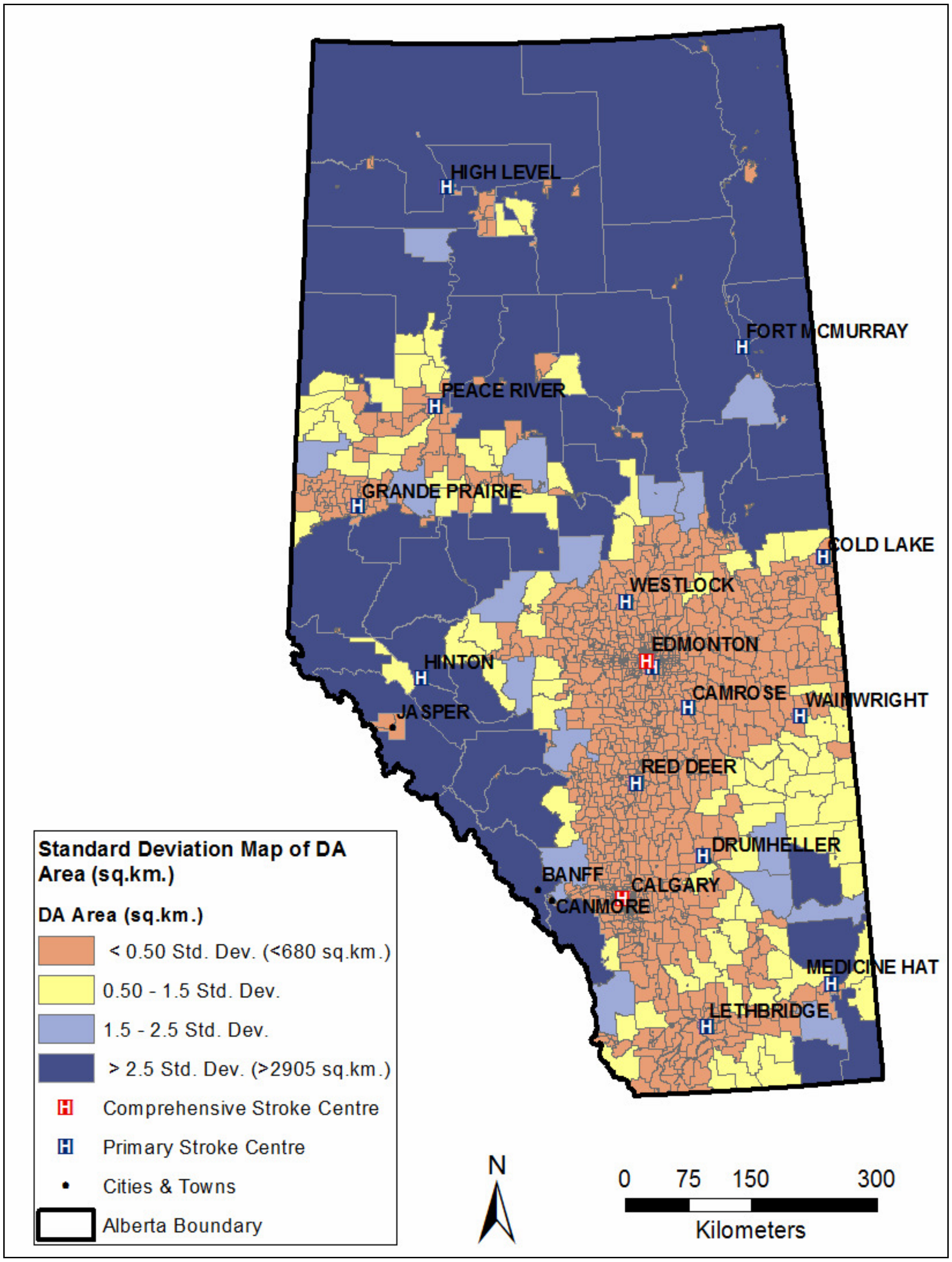
4.1 Background

Alberta is a Canadian province with diverse topography spanning 640,000 square kilometres and a population of 3,645,000 (Statistics Canada – Population and Dwelling Counts, 2014). Population density varies greatly. Two-thirds of the population resides in two major urban centres and the remainder in rural and smaller urban centres (Statistics Canada – Population Urban and Rural, 2014). Stroke expertise is concentrated in the two Comprehensive Stroke Centres (CSC) located in Edmonton and Calgary. There are fourteen Primary Stroke Centres (PSC) with thrombolysis protocols and telestroke access in place (Jeerakathil et al., 2010) strategically located throughout the province (Map 4.1). In 2011, there were 6,951 incident stroke cases (AHW – IHDA, 2014) and approximately 36,000 stroke survivors in Alberta (Michael D. Hill, unpublished data, 2013).

4.2 Study Purpose

Major advances have been made to the quality and delivery of specialized stroke care but regional disparities in stroke incidence and mortality persist (Prabhakaran et al., 2013; Sarti, Rastenyte, Zygimantas & Tuomilehto, 2000). Documenting existing trends and identifying the reason(s) for these variances is fundamental to the design of rational health care planning, distribution of resources and program development (Wennberg & Gittelsohn, 1973). The aim of this investigation was to identify geographic variances in stroke occurrence, in-hospital mortality (henceforth known as mortality) and reported stroke risk factors using Geographic Information Systems (GIS) based methods and administrative data sets in the province of Alberta. The goal was to identify population clusters with higher and lower rates of the major stroke types and in-hospital stroke mortality.

Map 4.1 Standard deviation map of Dissemination Area size (km^2).



4.3 Methods

4.3.1 Study Design

This study employed a spatial epidemiological approach using population-based administrative data, collected over 6-years, integrating GIS. GIS have been used increasingly as an evidence-based tool in epidemiological research (Boulos, 2004), and in stroke research specifically (Pedigo et al., 2011; Han et al., 2005). The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary.

4.3.2 Data

4.3.2.1 Administrative Data

Using administrative data has advantages: (1) there are data for all stroke types and all geographic regions of Alberta, presenting to most or all health care facilities, and (2) these data are more representative than data obtained from small sample size research, or where there are strict eligibility criteria.

Alberta, like other provinces in Canada, has a provincially administered government funded universal health care insurance system covering approximately 97% of permanent residents. Exceptions include Registered First Nations persons, prison inmates, and members of the military and the Royal Canadian Mounted Police who have similar coverage federally (Health Canada, 2013). All persons diagnosed with stroke who accessed the health care system in Alberta are included in our database. Stroke was considered by type – ischemic stroke, transient ischemic attack (TIA), intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Alberta Inpatient Discharge Abstract data (CIHI – DAD, 2013) and Ambulatory Care data (CIHI – NACRS, 2013) that includes Emergency Department (ED) visits for fiscal years 2002/03 to 2007/08 inclusive were linked and all personal identifiers removed. Subjects included had an administrative data diagnosis of stroke. Patients selected for inclusion had an ICD-10 (WHO – ICD-10, 2013) diagnosis of I63 (cerebral infarction), H34 (retinal arterial occlusion), I64 (stroke not specified as hemorrhage or infarction); I60 (subarachnoid hemorrhage - SAH); I61 (intracerebral hemorrhage - ICH); or G45 (transient ischemic attack - TIA). ICD-10 I64 (not specified as hemorrhage or infarction) was coded with I63 and H34 as ischemic stroke based on the assumption that 87% of strokes are ischemic and 13% are hemorrhagic (CDC – Stroke Facts, 2014). ICD-10 codes G454 (transient global amnesia) and I676 (venous thrombosis) were excluded. Patients under 20-years of age were excluded as mechanisms for stroke in children differ from those in adults. Persons without a health care number and/or a valid Alberta postal code were also excluded.

A new stroke event was identified as follows. If multiple visits for the same patient occurred within 48-hours, the most serious event was selected (ICH > SAH > ischemic > TIA). If multiple visits within 48-hours were of the same stroke type, the first event was selected because any treatment(s) received during the first health encounter could alter the patient's risk profile prior to the second encounter (Jeerakathil et al., 2010).

Known risk factors included for examination had an ICD-10 code of E10 (Type 1 or Insulin Dependent Diabetes Mellitus - IDDM), E11-E14 (Type 2 or Non-Insulin Dependent Diabetes Mellitus - NIDDM), I48 (atrial fibrillation), I10-I15 (hypertension), and E780, E781, E784, E785, E788, E789 (hypercholesterolemia).

4.3.2.2 Spatial Data

For the spatial analysis, shapefiles including health care facilities, cities, and Dissemination Area (DA) and Alberta boundaries were obtained from Spatial and Numeric Data Services (SANDS), University of Calgary (University of Calgary, 2013).

4.3.3 Non-Spatial Methods

Administrative data were linked with Statistics Canada 2006 census population data and age standardized rates, using 10-year age categories, were calculated using the direct method in order to preserve consistency for comparisons across geographic areas (Lai et al., 2009; Beyer, Tiwari & Rushton, 2009). Five-year, 10-year, and 20-year (Johansen, Wielgosz, Nguyen & Fry, 2006) age-categories were considered and 10-year categories chosen because they capture differences in age distribution (Buescher, 1998) and are comparable to other epidemiological studies (Klein & Schoenborn, 2001). No adjustment was made for sex to avoid spreading the data too thinly and because age generally has a much stronger impact on stroke incidence and mortality (Buescher, 1998). The date of designation of a health care facility as PSC was not considered in this analysis. STATA/IC 12.1 (StataCorp, 2013) software was used for the non-spatial portion of the analysis.

4.3.4 Spatial Methods

4.3.4.1 Spatial Unit of Analysis

Dissemination Area (DA), as defined by Statistics Canada, was selected as the geographic unit of analysis. DAs are small, relatively stable geographic units with a population of between 400 and 700 persons (Statistics Canada – PCCF, 2013), designed to be socio-economically relatively homogeneous. DA was selected because it is the smallest geographical unit for which Statistics Canada census data is available, cover all of the territory of Canada, and may be demographically more homogenous than larger units. This may facilitate examination of broad regional and local patterns as well as associations with risk factors. DAs have similar population numbers but often vary widely in area. Our DAs ranged in area from 0.005 square kilometres (km^2) in urban centres to 42,640 km^2 in rural regions. Hence, visualization of DA rates and patterns using choropleth maps (i.e. area based) was difficult and potentially misleading as attention may be drawn to DAs with the greatest area (Monmonier, 1991).

Statistically, rates for geographic areas with small populations may be unstable. High rates may be attributable to either underlying high risk or to high variance due to small population numbers (Buescher, 1998). This was addressed in part as (i) DA population numbers are relatively uniform, and (ii) stroke events for fiscal years 2002/03 to 2007/08 were aggregated and annualized mean rates were calculated. Data were not aggregated into larger geographic units as this would obscure local level information.

4.3.4.2 Definition of Rural

Postal codes were used to identify rural and urban geographic areas. Postal code location has been found to closely approximate the location of residence in urban areas; however these findings cannot be generalized to rural areas where single postal codes cover a large geographic territory (Bow et al., 2004). The use of postal code as proxy for location of residence sufficed for this research study. Depending on the definition, Canada's rural population may vary between 22% and 38% of the total population (23% for PC) (du Plessis, Beshiri, Bollman, & Clemenson, 2002). Postal codes were converted to latitude and longitude coordinates using the 2006 and 2011 Postal Code Conversion Files (Statistics Canada – PCCF, 2013). Data were imported into ArcGIS ArcMap 10 (ESRI – ArcMap 10.0, 1999-2010). There were no unmatched postal codes in our dataset. Individual events were aggregated according to DA. Statistics Canada 2006 Census data were suppressed for 15 DAs of 3757 DAs with stroke events due to reserve land, unreliable census data, or small population numbers (<100 for 6-character postal code (Statistics Canada – Data Quality, 2013).

4.3.4.3 Annualized Rates

Annualized mean age-standardized stroke and mortality rates were calculated for each DA and used for our cluster analysis. DAs with suppressed data were assigned a rate of "0" for the cluster analysis if no strokes were reported during the 6-year time span.

4.3.4.4 Spatial Statistics

Data were projected to NAD1983, 10-degree Transverse Mercator, because this best maintains area accuracy (ESRI – Transverse Mercator, 2013). Two widely used statistical methods were employed in GIS, the Getis-Ord Gi* (ESRI – Hot Spot Analysis, 2013) statistic in ArcGIS and spatial scan statistic (Kulldorff, 2013) in SaTScan (SaTScan, 2013) to identify 'hot spots' and 'cold spots' of stroke occurrence and mortality. The Getis-Ord Gi* statistic delineates clusters with rates significantly higher or lower than the overall study area mean. Rates for each DA and its neighbouring DAs are summed and divided by the sum of all values in the data set (Mitchell, 2009). When the observed local sum is larger (or smaller) than the expected, the output is a statistically significant z-score (Mitchell, 2009). The spatial scan statistic, developed by Kulldorff & Nagarwalla (1995), imposes a circular scanning window of varying sizes for each set of DA centroid coordinates across the study area. The window with the maximum Likelihood Ratio (LR), where there is elevated (or reduced) risk within the window as compared to outside, constitutes the most likely cluster. A *p*-value is obtained through Monte Carlo hypothesis testing (Kulldorff, 2013). Secondary clusters are also identified and are ordered according to their LR statistic. Those clusters that do not overlap with the most likely cluster may offer important additional information and are included in our analysis. Age-standardized rates using the direct method were used for the Getis-Ord Gi* analysis and age-standardized rates using the indirect method were used for the spatial scan statistic analysis.

Statistical significance for hot spots was set as DAs with a Gi* Z-score of >1.96, and spatial scan statistic RR >1.0 and p-value <0.05. Statistical significance for cold spots was defined as DAs with a Gi* Z-score <-1.96, and a spatial scan statistic RR <1.0 and p-value <0.05. 999 Monte Carlo simulations were used for the spatial scan statistic. Proportions of stroke patients with known risk factors for stroke were calculated for each DA and comparisons made (1) within and external to the cluster boundary, and (2) between hot and cold clusters.

Getis-Ord Gi Statistic.* Distance band was selected as the method for conceptualization of spatial relationships because of the large variation in DA area (ESRI – Conceptualization of Spatial Relationships, 2013). A spatial weights matrix file was created using (i) a fixed distance band calculation, based on DAs with an area <2.58 SD (Figure 1), that reflected maximum spatial autocorrelation as indicated by the peak Z-score (ESRI – Selecting a Fixed Distance Band Value, 2013), and (ii) a minimum number of 8 neighbors to ensure a reliable Z-score (ESRI – Hot Spot Analysis, 2013). To verify findings, Getis-Ord Gi* analyses were conducted based on two differing conceptualizations. First, a fixed distance band calculated to include all DAs and 8 neighbours was used. Cluster patterns for high and low values were similar for all stroke types and mortality. Second, a K-nearest neighbors conceptualization was used with a minimum number of neighbours set at 15. Cluster patterns for high values were similar for stroke types and mortality although clusters of low values were only starting to emerge.

Spatial Scan Statistic. A purely spatial, discrete Poisson model was used for the analysis. Areas were scanned simultaneously for statistically significant high and low rates. The circular scanning window was set to a maximum size of 40% (the default is 50%) of the population at risk based on the population of the largest DA (Walsh & DeChello, 2001) and a size considered sufficiently large to ensure that small and large clusters could be included (Kulldorff, 2013).

4.4 Results

4.4.1 Study Population

Characteristics of the study population by fiscal year are presented in Table 4.1. Ischemic stroke and TIA accounted for 86.8% of all strokes. Stroke types were evenly divided amongst men and women except for SAH which occurred more often in women

Table 4.1. Study population characteristics.

Fiscal Year	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08
Stroke Total (n)	3673	3678	3724	3619	3665	3527
Age, mean (years)	72.8	72.6	72.4	72.0	72.3	71.8
Female (%)	52.6	49.5	49.7	49.3	49.3	50.2
Comorbidities (% of strokes)						
IDDM*	1.4	1.4	1.4	0.8	0.8	1.0
NIDDM†	19.6	18.8	17.6	18.0	20.8	21.8
Atrial Fibrillation	16.4	16.6	15.9	16.6	17.4	16.9
Hypertension	54.3	56.0	53.4	53.7	56.7	58.5
Hypercholesterolemia	16.8	18.8	17.2	16.9	18.7	20.7
Stroke Type (%)						
Ischemic Stroke	61.7	61.0	60.5	62.3	62.4	64.2
TIA	24.9	26.2	26.4	24.1	23.8	23.5
ICH	9.2	7.9	8.0	8.4	8.2	6.9
SAH	4.3	4.9	5.2	5.2	5.7	5.5
Urban‡ (%)	72.5	74.0	73.9	75.0	73.8	74.9
EMS Transport (%)	59.0	60.9	64.2	65.4	99.9	100.0
Transport Destination (%)						
CSC§	42.4	46.9	46.8	49.7	49.1	47.2
Urban	49.4	54.9	52.8	56.1	55.5	53.7
Rural	23.9	24.0	29.7	30.7	30.8	27.8
PSC‖	16.8	16.3	17.1	15.2	18.5	22.3
Urban	17.7	16.6	17.2	15.2	19.0	21.6
Rural	14.3	15.5	16.7	15.0	17.1	23.9
Other	40.9	36.8	36.2	35.1	32.4	30.6
Urban	32.9	28.5	30.0	28.7	25.5	24.7
Rural	61.8	60.5	53.6	54.3	52.1	48.3
Disposition (%)						
Transfer						
Inpatient	17.8	18.9	19.5	18.0	15.0	15.7
Long Term Care	8.1	8.1	7.9	7.0	12.1	9.9
Other	1.8	1.1	0.7	1.1	1.4	1.2
Discharge						
Home	48.6	48.9	47.3	48.2	44.8	48.4
Home with support	10.0	9.5	10.4	12.1	12.9	11.7
Against Medical Advice	0.3	0.5	0.4	0.5	0.7	0.7
Died	13.4	13.1	13.8	13.2	13.1	12.5

*Insulin Dependent Diabetes Mellitus
†Non-insulin Dependent Diabetes Mellitus
‡Postal Code definition.
§CSC - CT Scan, tPA, on-site: stroke team, neurosurgical/neuro-interventional expertise, acute stroke unit.
‖PSC - CT Scan, tPA, stroke expertise on-site or available by telehealth, acute stroke care provision.

(62%). Similar to previous reports, SAH also occurred at a younger age (56.7 years versus ischemic – 73.2 years and ICH – 70.7 years). Median DA study population size was 410 persons (IQR 345, 525). From 2002 to 2007, ICH rates decreased from 9.2% to 6.9% and SAH rates increased from 4.3% to 5.5%. Over this time span, the proportion of the study population (by DA) with documented NIDDM, hypertension, and hypercholesterolemia increased. There was a trend to increased use of EMS for transport and a greater proportion of patients were transported to either a PSC or CSC by 2007. Mortality decreased from 13.4% in 2002 to 12.5% in 2007.

Of 5357 DAs in Alberta, 3757 DAs reported ≥1 stroke event. A near equal proportion of urban and rural DAs had rates of "0" for ischemic stroke (~11%), ICH (~71%), SAH (~75%), and mortality (~57%). TIA was reported more frequently in rural DAs as having a rate of "0" (48% vs. 31%).

4.4.2 Clusters of Stroke Types and Mortality

Statistically significant spatial clusters of stroke types and mortality are presented in Maps 4.2 – 4.6. Spatial mean centre, the point constructed from the average x and y coordinates for DA centroids (ESRI – Mean Center, 2013), of the Gi* and spatial scan statistic most likely clusters are also plotted. A summary of spatial scan statistic clusters is presented in Table 4.2. Characteristics of confirmed clusters using the two methods are summarized in Table 4.3.

A non-contiguous hot spot of ischemic stroke was located diagonally across the centre of the province in rural DAs northeast of Westlock extending southward to east of Calgary (Map 4.2). TIA hot spots exhibited a similar spatial pattern (Map 4.3). Contrary

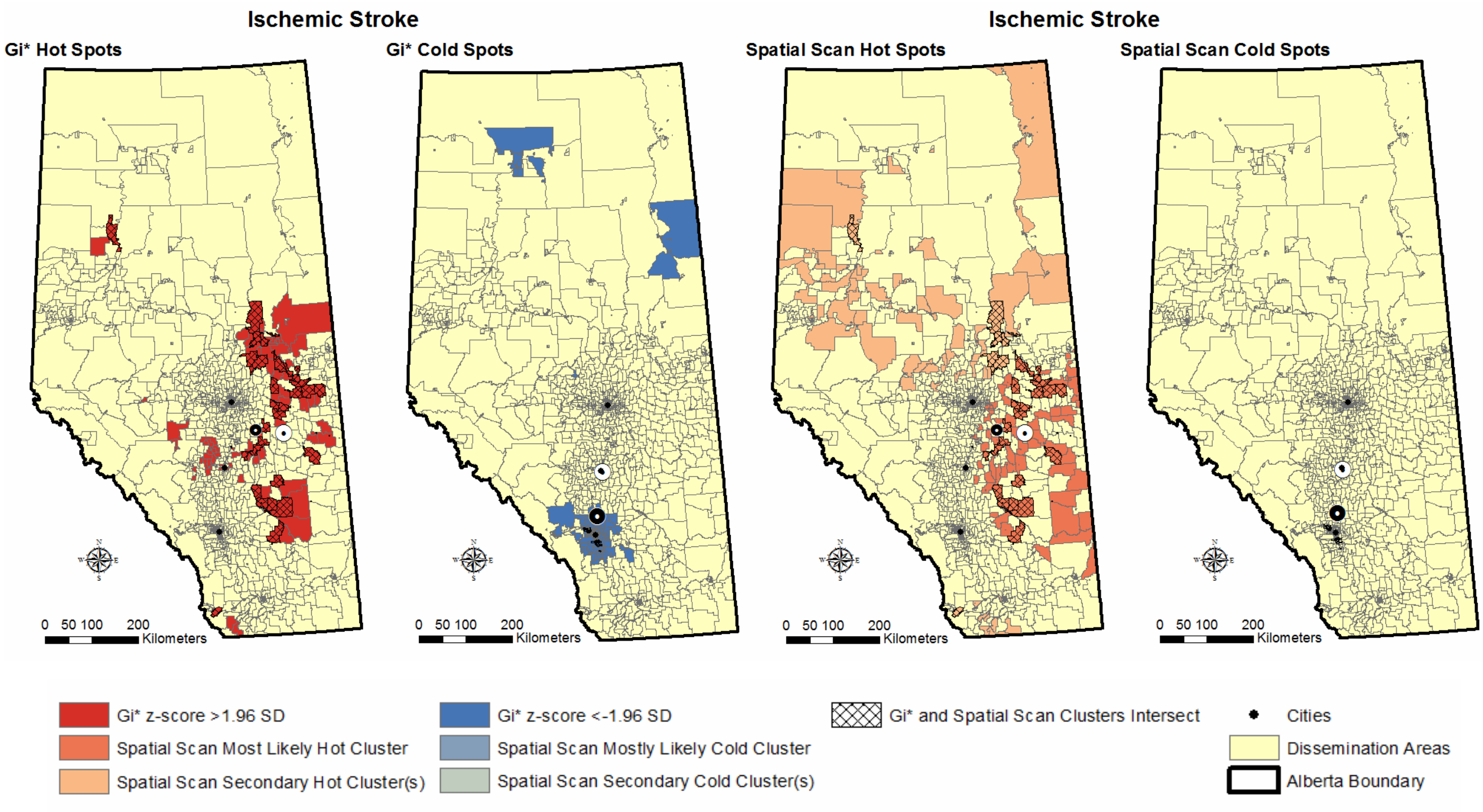
to what would be expected from epidemiological data, ischemic stroke and TIA hot spots had DAs with lower proportions of stroke patients with documented risk factors of atrial fibrillation, hypertension, and hypercholesterolemia (Table 4.4). DAs within ischemic stroke and TIA cold spots had the highest levels of documented stroke risk factors.
ICH and SAH hot spots were identified in the northernmost of the two major urban centres (Map 4.4 and Map 4.5). DAs within the ICH and SAH hot spots had a higher proportion of strokes with documented atrial fibrillation, hypertension, and hypercholesterolemia as compared with DAs outside cluster boundaries (Table 4.4). ICH and SAH were the two stroke subtypes with a higher proportion of hypertension within the hot spot boundaries.

A non-contiguous mortality hot spot was identified in east central Alberta, in a similar geographic distribution to the hot spot for ischemic stroke (Map 4.6). Characteristics of DAs in mortality clusters are shown in Table 4.5. DAs within the mortality hot spot had lower proportions of stroke patients with documented diabetes mellitus (DM), atrial fibrillation, hypertension, and hypercholesterolemia compared with DAs external to the cluster boundary and within the mortality cold spot. Within the mortality hot spot, CSC was less often the transport destination for all stroke types (Table 4.6).

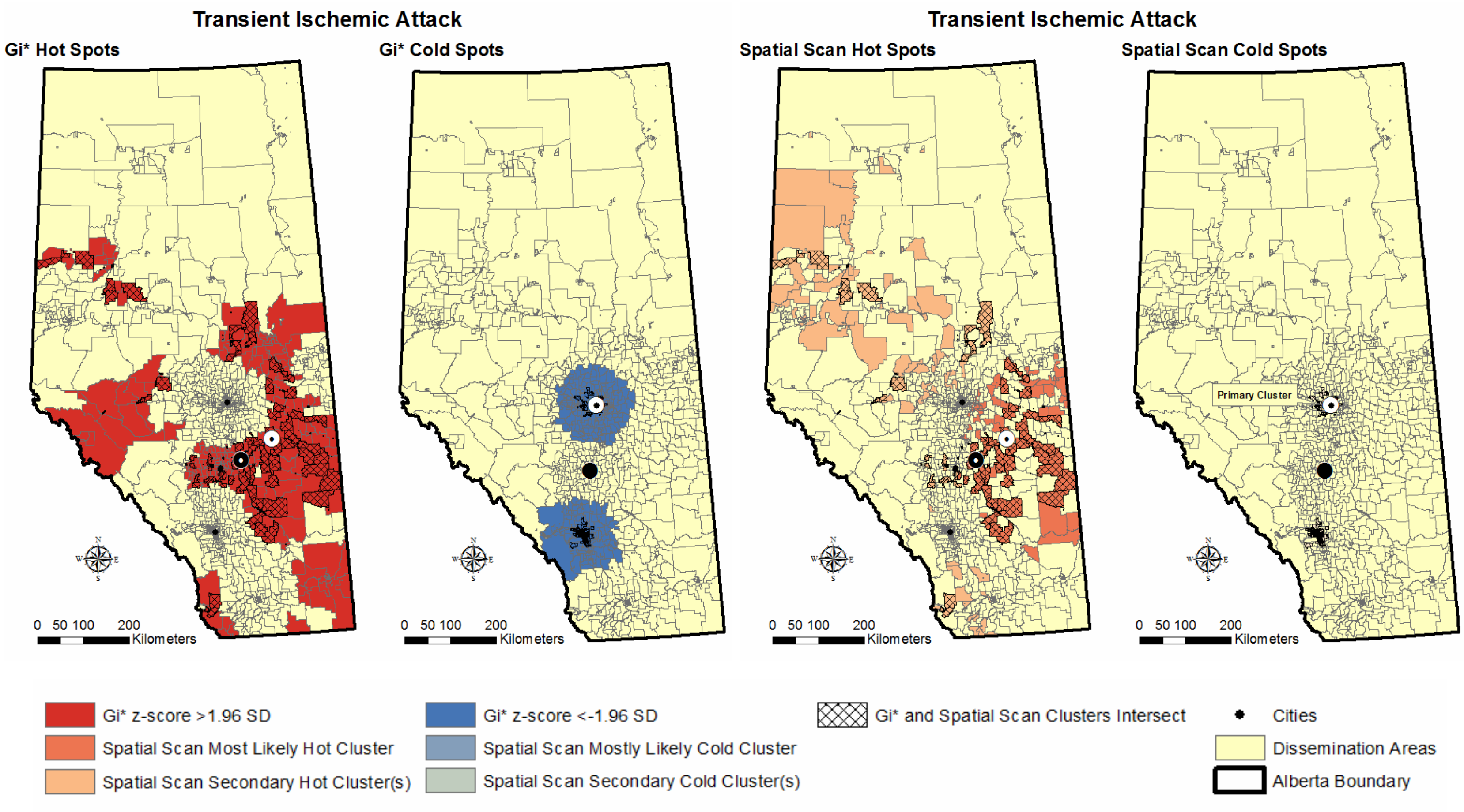
4.4.3 Clusters of Risk

A cluster analysis of risk factors identified hot spots in the two large urban centres with CSCs (Calgary – RR 2.59, p <0.001 and Edmonton – RR 2.43, p <0.001) and one of the urban PSCs (Medicine Hat - p <0.05) (Map 4.7). There was an inverse relationship

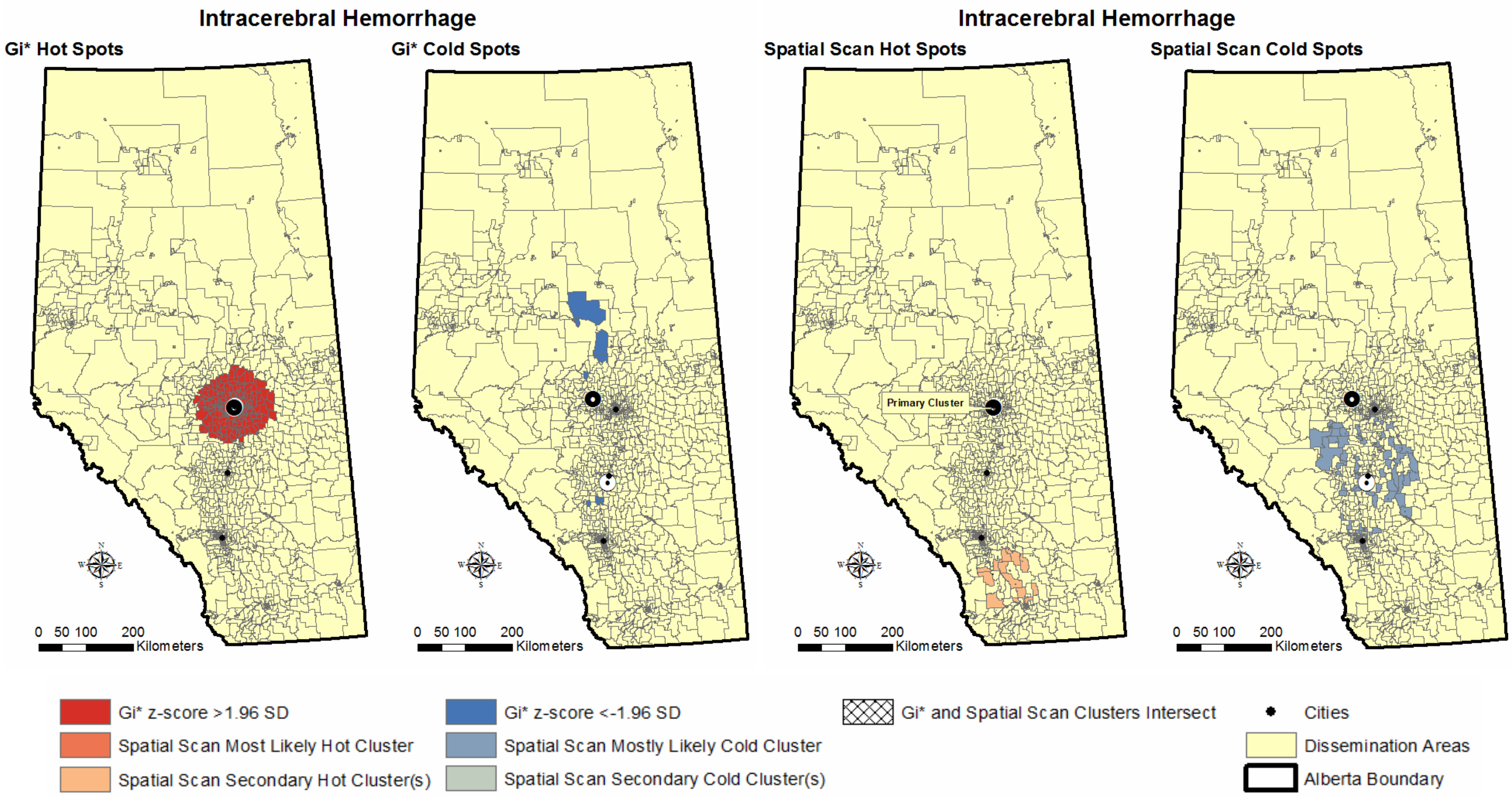
Map 4.2 Hot and cold clusters of Ischemic Stroke identified using the Getis-Ord Gi* and Spatial Scan statistics.



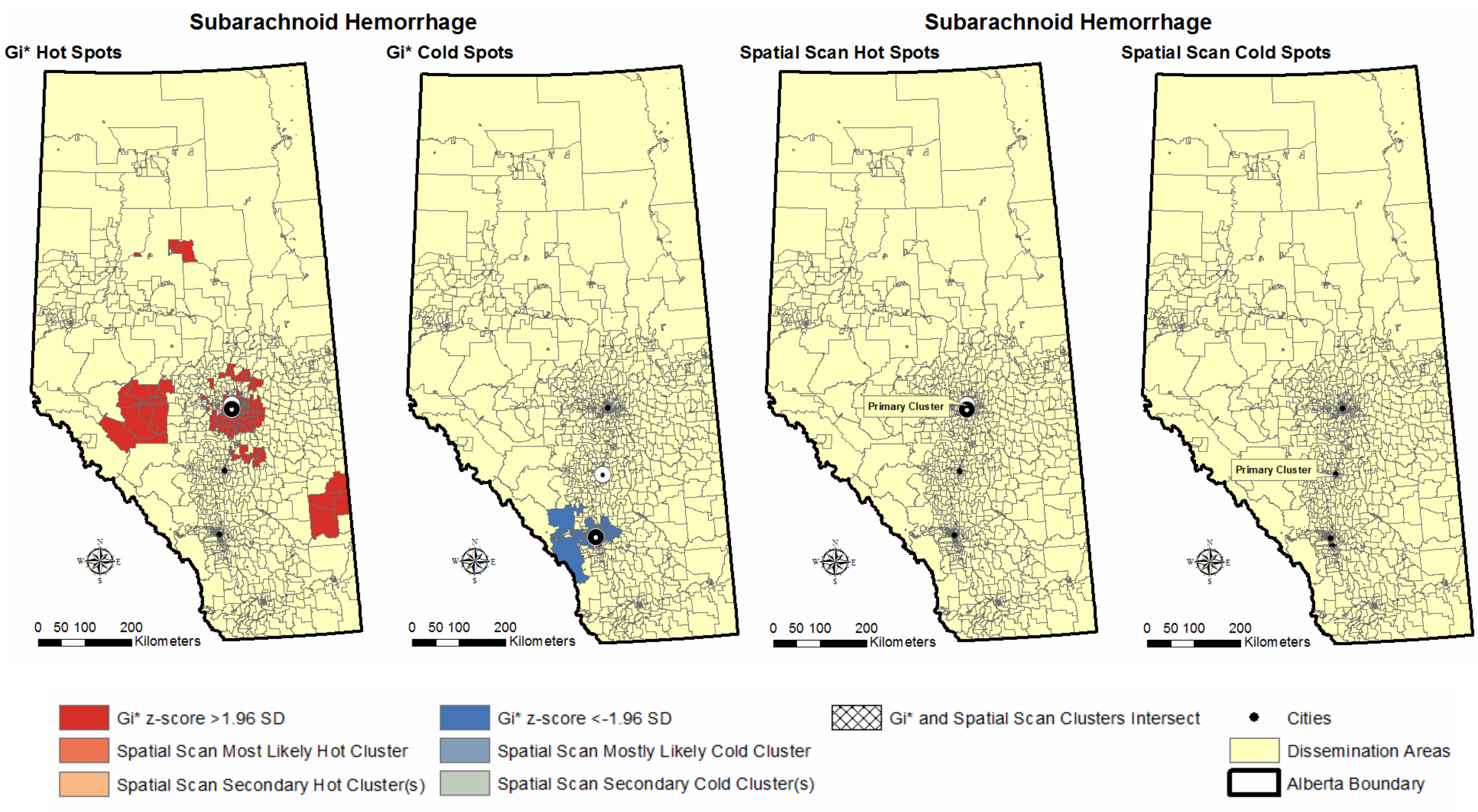
Map 4.3. Hot and cold clusters of Transient Ischemic Attack identified using the Getis-Ord Gi* and Spatial Scan statistics.



Map 4.4. Hot and cold clusters of Intracerebral Hemorrhage identified using the Getis-Ord Gi* and Spatial Scan statistics.



Map 4.5 Hot and cold clusters of Subarachnoid Hemorrhage identified using the Getis-Ord Gi* and Spatial Scan statistics.



Map 4.6. Hot and cold clusters of in-hospital mortality identified using the Getis-Ord Gi* and Spatial Scan statistics.

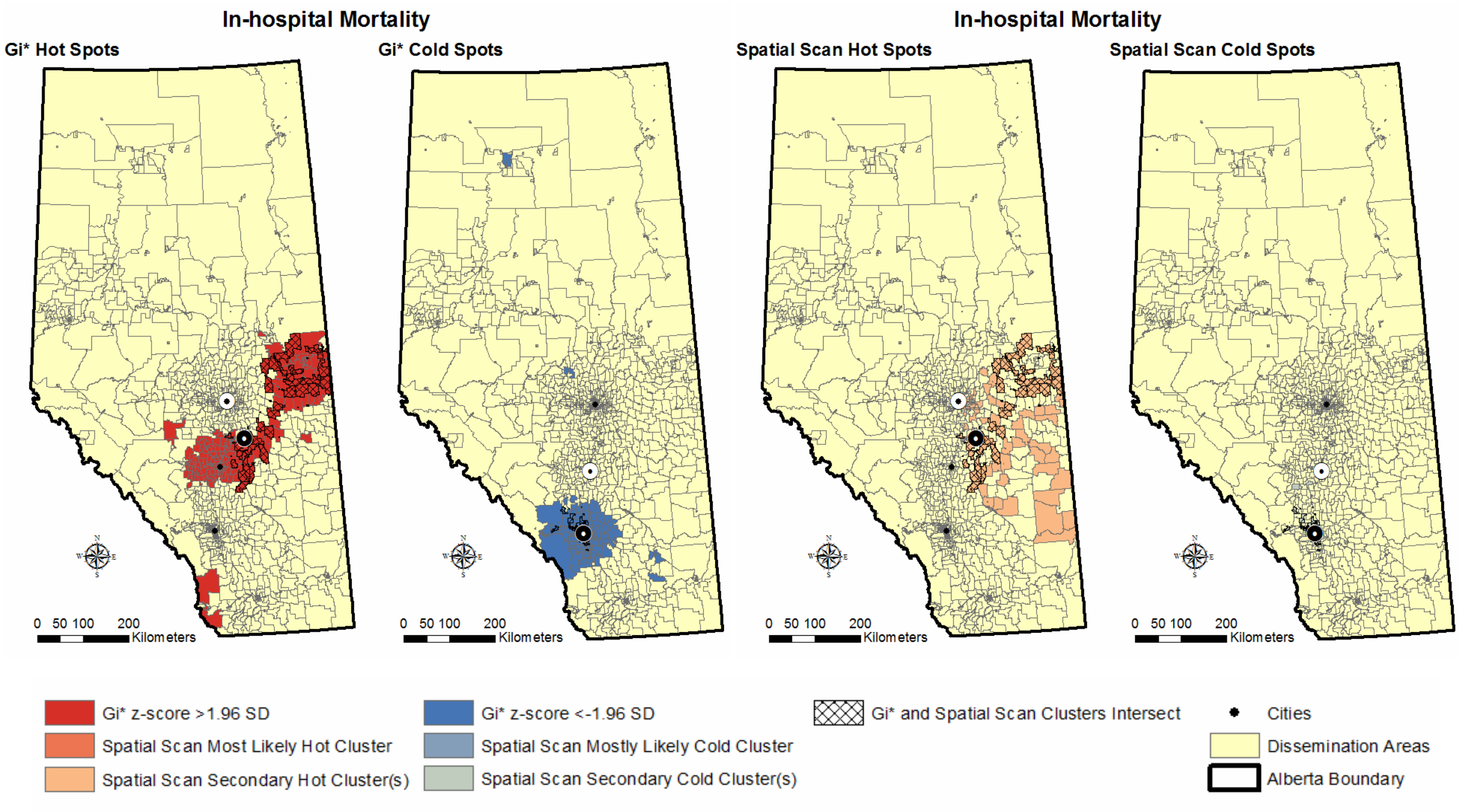


Table 4.2. Characteristics of Dissemination Areas (DAs) within statistically significant high and low clusters of stroke types and in-hospital mortality identified using the spatial scan statistic in SaTScan.

Clusters	DA (n)	Cluster Population (n)	Cluster Cases (n)	Annual Cases per 100,000	Cluster Radius (km)	Cluster Risk*	*P*-value
Ischemic High							
Cluster 4	269	1109230	1609	142.8	228.70	1.43	<0.0001
Cluster 7	273	648575	952	147.0	4.96	1.45	<0.0001
Cluster 9	238	852020	1151	136.4	311.87	1.35	<0.0001
Cluster 12	99	163615	271	165.3	3.36	1.61	<0.0001
Cluster 13	13	123505	207	164.7	69.43	1.60	<0.0001
Cluster 15	90	221050	317	143.2	3.29	1.39	0.0022
Ischemic Low							
Cluster 1	5	423185	41	9.6	2.11	0.09	<0.0001
Cluster 2	26	291215	79	27.3	5.47	0.26	<0.0001
Cluster 3	46	378130	145	38.4	13.13	0.36	<0.0001
Cluster 5	9	154650	38	25.8	2.28	0.25	<0.0001
Cluster 6	114	514315	290	58.0	12.00	0.55	<0.0001
Cluster 8	5	81680	12	15.5	1.41	0.15	<0.0001
Cluster 10	7	85400	18	21.1	7.84	0.20	<0.0001
Cluster 11	2	82155	28	33.0	0.53	0.32	<0.0001
Cluster 14	1	45080	13	27.7	0.49	0.27	0.0001
Cluster 16	4	41355	11	29.0	2.33	0.28	0.0062
TIA High							
Cluster 2	304	1279275	1083	82.6	220.21	2.25	<0.0001
Cluster 3	229	918080	713	78.2	325.50	2.03	<0.0001
Cluster 6	93	328725	263	78.5	62.99	1.95	<0.0001
Cluster 7	40	241560	205	82.3	117.06	2.03	<0.0001
TIA Low							
Cluster 1	1170	3717370	818	22.2	32.04	0.46	<0.0001
Cluster 4	8	426120	19	4.4	2.24	0.10	<0.0001
Cluster 5	1275	3790225	1100	29.2	29.96	0.63	<0.0001
ICH High							
Cluster 1	812	2038560	442	21.7	10.15	1.81	<0.0001
Cluster 4	618	1466235	275	18.9	8.30	1.47	0.0013
Cluster 5	33	131030	41	31.4	59.62	2.35	0.047
ICH Low							
Cluster 2	559	2808105	236	8.5	131.83	0.57	<0.0001
Cluster 3	122	533935	29	5.3	12.26	0.38	<0.0001
SAH High							
Cluster 2	737	1891970	232	12.9	9.52	1.64	<0.0001
SAH Low							
Cluster 1	7	424320	2	0.5	2.18	0.06	<0.0001
Cluster 3	46	378130	4	1.1	13.13	0.13	<0.0001
Cluster 4	131	580940	27	3.8	22.97	0.43	0.020
Mortality High							
Cluster 4	712	1796870	541	29.9	9.33	1.44	<0.0001
Cluster 5	278	1114250	380	31.7	227.17	1.51	<0.0001
Cluster 7	21	32085	25	70.2	1.76	3.20	0.042
Mortality Low							
Cluster 1	6	423550	10	2.2	1.83	0.10	<0.0001
Cluster 2	219	976455	110	11.3	53.39	0.49	<0.0001
Cluster 3	46	378130	25	6.5	13.13	0.29	<0.0001
Cluster 6	128	544675	50	10.3	12.39	0.46	<0.0001

Table 4.3. Characteristics of Getis-Ord Gi* and spatial scan statistic cluster intersects.

Cluster Intersect	DA (n)	Distance* (km)	Urban (%)	CSC (Mean %)	PSC (Mean %)	Other (Mean %)	Primary Location
Ischemic Stroke							
High	64	59.2	39.1	20.4	24.6	5	Non-contiguous band extending NE of Westlock to E of Calgary
Low	127	96.4	97.6	80.7	1.7	17.6	NW & S Calgary
Transient Ischemic Attack							
High	287	85.1	63.1	22.7	29.2	48.1	Non-contiguous band extending from NE of Westlock S to Red Deer & Drumheller; Peace River region
Low	2445	143.1	98.4	70.0	4.9	25.1	Edmonton & Calgary & surrounding areas
Intracerebral Hemorrhage							
High	813	3.4	98.4	58.7	8.9	32.4	Edmonton (excluding sections E/NE)
Low	0	-	-	-	-	-	-
Subarachnoid Hemorrhage							
High	369	9.7	99.2	30.6	15.0	18.7	Edmonton (excluding regions in NW & E/SE)
Low	88	135.0	97.7	75.0	1.7	23.3	S of Calgary
In-Hospital Mortality							
High	108	92.0	53.7	27.4	22.4	54.3	Non-contiguous band from Cold Lake to SE of Red Deer
Low	329	133.9	95.7	83.2	1.4	15.5	N & S Calgary; Okotoks

Spatial mean distance: Euclidean or straight-line distance between Gi and spatial scan most-likely cluster spatial mean centres.

Table 4.4. High and low clusters of stroke types and in-hospital mortality and proportion with risk factor(s).

Cluster Intersect (Gi* and SS)	High		Low	
% of Strokes by DA* With Risk Factor(s) (SD)	Cluster	Not Cluster	Cluster	Not Cluster
Ischemic Stroke				
IDDM†	3.8 (13.8)	1.1 (7.2)	1.9 (10.8)	1.1 (7.2)
NIDDM‡	17.7 (20.9)	19.7 (25.7)	15.9 (26.5)	19.8 (25.5)
Atrial Fibrillation	10.4 (15.6)	15.8 (23.5)	12.6 (19.1)	15.9 (23.5)
Hypertension	46.6 (29.2)	57.5 (32.3)	67.1 (31.9)	56.9 (32.3)
Hypercholesterolemia	12.7 (7.9)	21.3 (27.0)	21.4 (28.5)	21.1 (26.9)
Transient Ischemic Attack				
IDDM	2.7 (13.5)	1.0 (6.6)	1.0 (6.6)	1.5 (8.6)
NIDDM	15.5 (20.7)	20.0 (25.9)	20.2 (26.7)	18.7 (23.3)
Atrial Fibrillation	10.4 (17.3)	16.2 (23.8)	17.2 (24.8)	13.1 (20.3)
Hypertension	45.1 (29.9)	58.3 (32.3)	60.7 (32.9)	50.9 (30.3)
Hypercholesterolemia	13.6 (21.9)	21.8 (27.2)	24.5 (28.4)	14.9 (22.5)
Intracerebral Hemorrhage				
IDDM	1.1 (7.4)	1.2 (7.4)	-	-
NIDDM	21.2 (26.2)	19.2 (25.4)	-	-
Atrial Fibrillation	18.8 (25.1)	14.9 (22.8)	-	-
Hypertension	60.0 (32.4)	56.5 (32.2)	-	-
Hypercholesterolemia	30.3 (29.1)	18.6 (25.7)	-	-
Subarachnoid Hemorrhage				
IDDM	1.2 (8.5)	1.2 (7.2)	1.0 (5.8)	1.2 (7.4)
NIDDM	19.4 (24.9)	19.7 (25.7)	16.0 (27.9)	19.7 (25.5)
Atrial Fibrillation	17.6 (23.5)	15.6 (23.4)	13.3 (21.8)	15.8 (23.4)
Hypertension	57.8 (33.1)	57.2 (32.2)	65.7 (34.7)	57.1 (32.2)
Hypercholesterolemia	29.2 (28.7)	20.3 (26.6)	19.9 (28.4)	21.1 (26.9)
In-hospital Mortality				
IDDM	1.3 (5.7)	1.2 (7.4)	1.2 (7.7)	1.2 (7.3)
NIDDM	15.0 (19.5)	19.8 (25.7)	15.9 (25.8)	20.0 (25.5)
Atrial Fibrillation	9.8 (14.7)	15.9 (23.6)	17.1 (26.2)	15.6 (23.1)
Hypertension	41.8 (26.7)	57.7 (32.4)	62.7 (35.0)	56.8 (32.0)
Hypercholesterolemia	14.6 (21.8)	21.3 (27.0)	18.4 (27.5)	21.4 (26.9)

*Dissemination Area (n=3757)
†Insulin Dependent Diabetes Mellitus
‡Non-insulin Dependent Diabetes Mellitus

Table 4.5. Characteristics of high and low clusters of in-hospital mortality.

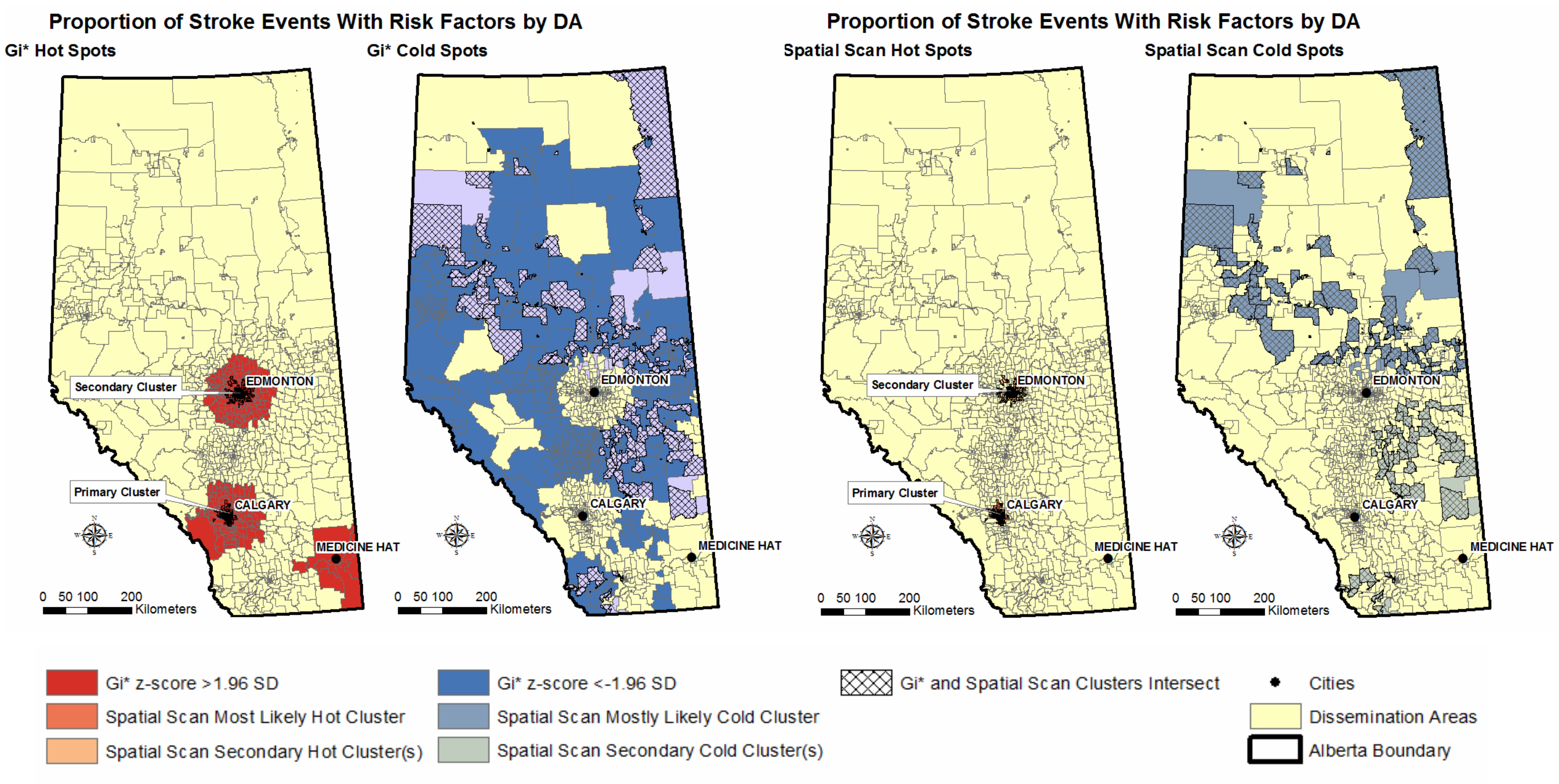
In-hospital Mortality	High				Low				
Statistic Cluster Number	Gi*	Spatial Scan 4	5	7	Gi*	Spatial Scan 1	2	3	6
Gi* Z-score	>1.96				<-1.96				
Cluster Risk		1.438	1.507	3.205		0.070	0.494	0.291	0.456
P-value	<0.05	<0.001	<0.001	0.042	<0.05	<0.001	<0.001	<0.001	<0.001
Age, mean (years)	74.1	71.9	74.8	76.5	71.3	72.1	71.4	71.6	70.2
Female (%)	49.0	48.5	49.4	57.0	49.5	40.6	59.5	53.2	47.4
Comorbidity (%)									
IDDM*	1.7	0.9	1.3	0	1.0	2.9	1.2	1.1	1.0
NIDDM†	15.9	21.7	16.4	28.4	19.5	18.8	15.2	16.5	17.8
Atrial Fibrillation	12.8	20.9	12.7	29.6	18.7	15.9	19.8	26.1	18.0
Hypertension	44.5	61.8	46.0	59.3	62.6	42.0	59.8	65.4	62.0
Hypercholesterolemia	12.6	28.8	12.8	16.1	18.6	17.4	16.9	28.2	18.0
Stroke Type									
Ischemic	58.8	67.4	57.8	64.2	63.5	60.9	61.4	77.1	65.4
TIA	31.0	14.5	33.1	19.8	21.9	27.5	25.1	11.7	23.0
ICH	6.0	11.7	5.5	11.1	9.2	8.7	8.1	9.0	6.0
SAH	4.2	6.4	3.7	4.9	5.4	2.9	5.4	2.1	5.6
EMS Transport (%)	70.7	78.6	70.1	76.5	40.4	79.7	75.5	77.7	81.6
Destination									
CSC‡	20.2	56.9	25.3	12.3	76.5	10.1	76.9	68.1	69.4
PSC§	31.9	7.7	20.9	84.0	2.1	87.0	1.2	11.7	1.4
Other	47.9	35.4	53.8	3.7	21.4	2.9	21.3	20.2	29.2

*Insulin Dependent Diabetes Mellitus
†Non-insulin Dependent Diabetes Mellitus
‡CSC - CT Scan, tPA, stroke team, neurosurgical/neuro-interventional expertise, acute stroke unit..
§PSC - CT Scan, tPA, stroke expertise on-site or available by telehealth, acute stroke care provision.

Table 4.6. In-hospital mortality hot spot and transport destination, by stroke type. Higher proportions of stroke events outside the in-hospital mortality hot spot were transported to a CSC and fewer events were transported to 'Other' healthcare facility.

In-hospital Mortality	Events Within Hot Spot				Events Outside Hot Spot			
Destination (%)	CSC	PSC	Other	Total	CSC	PSC	Other	Total
Ischemic	26.3	16.3	57.4	59.7	48.7	18.3	33.0	62.1
TIA	9.6	14.3	76.1	31.3	35.8	20.7	43.5	24.4
ICH	35.9	14.1	50.0	5.3	62.5	13.8	23.7	8.3
SAH	71.1	4.4	24.5	3.7	80.8	4.4	14.8	5.2

Map 4.7. Cluster analysis of the proportion of stroke patients with ≥ 1 reported risk factor(s) by DA.



between risk factor hot spots and hot spots for ischemic stroke, TIA and stroke mortality (Table 4.4).

4.5 Discussion

4.5.1 Principal Findings

Significant hot and cold spots of stroke types and mortality were identified and located (Maps 4.2 - 4.6). There was overlap of clusters across statistical methods and, in relation to the geographical expanse of the province, spatial mean centres of high clusters calculated for each statistic were not far apart in distance (Table 4.3). Only slight variation in Gi* clusters was found when using different conceptualizations of spatial relationships.

4.5.2 Ischemic Stroke and Transient Ischemic Attack

DAs within ischemic stroke and TIA hot spots had lower proportions of stroke patients with documented DM, atrial fibrillation, hypertension, and hypercholesterolemia compared with DAs outside of the hot spot and DAs within cold spots (excluding DM) (Table 4.4). This is contrary to the established link between stroke risk factors and stroke occurrence (Lackland et al., 2014). The most likely explanation is a lower incidence of recognition and reporting of stroke risk factors in these clusters with high rates of ischemic stroke and TIA. Furthermore, the high rates of reported stroke risk factors in cold spots for ischemic stroke and TIA suggests a strong and potentially causal link between recognition/documentation of stroke risk factors and occurrence of ischemic stroke and TIA. These findings serve to emphasize the importance of primary prevention.

Clusters with lower proportions of documented risk factors may be indicative of populations with decreased access to primary care and/or that are less amenable to seeking and receiving preventive care. Forty percent of TIAs have MRI evidence of infarction (Kidwell et al., 1999). Differences in access to MRI and extent of investigation as well as urban-rural differences in the coding accuracy of TIA versus ischemic stroke (Kokotailo & Hill, 2005) may partially explain the urban bias for TIA cold spots located in Edmonton and Calgary.

4.5.3 Intracerebral Hemorrhage and Subarachnoid Hemorrhage

ICH and SAH hot spots had DA populations with higher proportions of documented hypercholesterolemia and hypertension compared to DAs outside of cluster boundaries (Table 4.4). Under diagnosis or under treatment of hypertension may be an important factor in addition to other risk factors. The SAH hot spot had a lower proportion of DAs with documented hypertension than did the SAH cold spot which is consistent with the fact that hypertension is less important as a risk factor for SAH compared to ICH. Data relating to incidence of smoking, a major risk factor for SAH, were not available.

4.5.4 In-hospital Mortality

DAs within the mortality hot spot had lower proportions of documented NIDDM, atrial fibrillation, hypertension, and hypercholesterolemia (Table 4.4) and higher occurrence of ischemic stroke and TIA. This finding raises questions regarding access to and efficacy of prevention programs and in-hospital stroke care in this region. Transport destination may have contributed to this finding as mortality hot spots had lower proportions of patients transported to a CSC and cold spots had a higher proportion of transports to a CSC (Table 4.6). Time from symptom onset to recanalization (NINDS and Stroke r-tPA Stroke Study Group, 1995; Hacke et al., 2008; Mazighi et al., 2009)) and specialized stroke care (Stroke Unit Trialists' Collaboration, 1997) are crucial factors in morbidity and mortality after stroke. Prolonged transport times, suboptimal transport destination (Schwamm et al., 2005; Prabhakaran, 2011), quality of care issues (i.e. percentage receiving tPA), or other unmeasured differences in stroke systems of care could account for mortality hot spots. Stroke severity, an important risk factor for mortality after stroke, could not be assessed due to a lack of clinical data.

4.5.5 Risk Factors

Hot spots of risk factors were identified and located using cluster analysis in Calgary, Edmonton, and Medicine Hat (Map 4.7). These cities have well established stroke prevention programs in place. This supports findings stemming from the cluster analyses of stroke types and mortality suggesting that identification and reporting of risk factors is positively associated with significantly lower stroke occurrence and mortality. Risk factors appeared to be less important in the spatial distribution of ICH and SAH.

4.6 Study Implications

This study highlights the power of using GIS to understand regional variability in stroke occurrence, risk factors and outcomes. These types of analyses can be particularly useful in identifying gaps in service, in planning and evaluation of health systems and health care delivery, and in (re)allocation of resources (Wennberg & Gittelsohn, 1973).

Strengths of this research study include that spatial analyses were performed by stroke type and that clusters were confirmed using two statistical methods. A broad regional analysis was conducted but the geographic unit of analysis was sufficiently small to permit a more refined delineation of cluster boundaries and a later, more detailed examination of explanatory variables including local population characteristics and geography using linked census data and shape files. A polygon analysis removed spatial autocorrelation of events between DAs due to underlying population density. The small numbers problem resulted in greater variation of rates in DAs with smaller populations but this was mitigated, in areas of overlap, by the use of the spatial scan statistic (Tables 4.1 and 4.2). Findings were validated in that ischemic stroke and TIA had similar geographical distributions and that risk factor hot spots were located in regions with well established stroke prevention programs and acute care health service provision in place.

4.7 Study Limitations

Potential limitations of this study include those associated with the use of administrative data: (1) lack of clinical detail, (2) regional differences with ICD-10 coding of stroke type, (3) regional differences in documentation of risk factors, (4) inaccurate documentation of postal code, and (5) errors associated with the collection of Statistics Canada census data including under or over coverage of specific populations (Statistics Canada – Population Coverage Error, 2013). An important potential limitation in our study was that the postal code documented on the clinical health record may not accurately represent location of residence or stroke or risk exposure. Residential mobility was not taken into account. Limitations associated with the spatial data analysis include: (1) position error, (2) DAs limited capacity to reveal what is happening in rural areas (greater heterogeneity in larger DAs; greater number of PCs per DA in rural areas), (3) Modifiable Area Unit Problem (rates change with a change in the geographic unit of analysis) (Openshaw, 1983), (4) small numbers problem (greater variability in rate estimates with smaller geographic unit of analysis), and (5) ecological and atomistic fallacy. It remains a useful but high level tool for evaluation of disease incidence and outcomes.

4.8 Conclusion

Using whole population administrative data for a large geographic region of Canada integrated with GIS, significant regional variations in ischemic stroke, TIA, ICH, SAH and in-hospital mortality were found. Risk factor hot spots were identified in regions with significantly low ischemic, TIA, and in-hospital mortality rates. ICH and SAH did not have this same inverse association. Spatial regression and other tools in GIS may be used in future research to examine whether regional variations in incidence and outcomes identified in this study reflect disparities in access to and/or the provision of best practice primary and secondary preventive stroke care and care for acute stroke.

Future research might include a more localized investigation of the mortality hot spot that incorporates additional novel predictors (e.g. ethnicity, economic, environmental, and preventive, pre-hospital and in-hospital service provision). Future research might also entail conducting a cluster of analysis of smoothed age-standardized annual stroke (by type), recurrent stroke, and mortality rates to permit an examination of spatial migration of clusters over time and associations with enhancements to pre-hospital and SC care. Findings may inform public health policy and health service provision.

Study II. Multivariable Regression Analysis of Stroke and In-hospital Mortality Hot Spots and Cold Spots in Alberta, Canada.

Chapter 5: Study II. Multivariable Regression Analysis of Stroke and In-hospital Mortality Hot Spots and Cold Spots in Alberta, Canada.

5.1 Background

Stroke is the potentially devastating result of a sudden interruption of blood flow to the brain (CIHI, 2006) and is a leading cause of acquired disability (Davis & Donnan, 2012) and death worldwide (van der Worp & van Gijn, 2007). Overall 30-day in-hospital mortality following admission with a new stroke in Canada is approximately 19% and has remained stable since 1999-2000 (CIHI, 2006). There are four stroke types, each differing with respect to causal mechanisms, severity, treatment, and outcomes. Eighty-seven percent of strokes are caused by ischemia due to arterial occlusion and 13% are caused by hemorrhage (CDC – Stroke Facts, 2014).

5.1.1 Stroke Types

5.1.1.1 Ischemic Stroke

Ischemic stroke occurs when there is occlusion of a blood vessel by a thromboembolism resulting in brain tissue injury and death. Definitive treatment for acute ischemic stroke (AIS) is the administration of IV thrombolysis or tPA within 3-hours of onset of symptoms (NINDS and Stroke r-tPA Stroke Study Group, 1995) and longer (up to 4.5-hours) in selected circumstances (Hacke et al, 2008). The symptom onset-to-treatment (OTT) time with IV-tPA is strongly associated with outcome, with a doubling of the odds of good outcome when administered under 1.5-hours after onset versus 1.5 to 3.0-hours after onset (Marler et al., 2000; Hacke et al., 2008). Thirty-day stroke mortality ranges from 2% in patients with lacunar infarct to 78% in patients with large hemispheric lesions (van der Worp & van Gijn, 2007).

5.1.1.2 Transient Ischemic Attack

Transient Ischemic Attack (TIA) is a brief episode of focal ischemia with symptoms similar to ischemic stroke but typically lasting less than one hour and without evidence of acute infarction on imaging (Magnetic Resonance Imaging or MRI) (Albers et al., 2002). Because clinical symptoms resolve, a TIA diagnosis may be missed in persons who do not seek medical attention. If medical attention is sought, accuracy of the diagnosis depends on the clinical experience, skills, and judgment of the evaluating physician (Albers et al., 2002). Milder strokes that were once diagnosed as TIA are now diagnosed as ischemic stroke as a result of diagnostically competent physicians and more sensitive brain imaging (Warlow et al., 2001). After a first TIA, 10% to 20% of patients have an ischemic stroke within the next 90 days, and in 50% of these patients, the stroke occurs in the first 24 to 48-hours after the TIA (Albers et al., 2002). TIA offers a valuable opportunity to initiate early and aggressive risk factor management to prevent ischemic stroke and therefore time to expert diagnosis and treatment is important to good outcome (Davis & Donnan, 2012).

5.1.1.3 Intracerebral Hemorrhage

Intracerebral Hemorrhage (ICH) is bleeding into the parenchyma of the brain (Qureshi et al., 2001). ICH accounts for 10% to 15% of all strokes and is associated with the highest mortality rate with only 38% of patients surviving the first year (Qureshi et al., 2001). Primary ICH accounts for 78% to 88% of ICH and originates from the spontaneous rupture of small blood vessels damaged by chronic hypertension or amyloid angiopathy (Qureshi et al., 2001). Treatment may include blood pressure management, intraventricular administration of thrombolytic agents, and surgical evacuation (Qureshi et al., 2001). Treatment is also time sensitive.

5.1.1.4 Subarachnoid Hemorrhage

Subarachnoid Hemorrhage (SAH) accounts for 2% to 5% of all new strokes (Suarez et al., 2006). The leading cause of non-traumatic SAH is rupture of an intracranial aneurysm (80% of cases) leading to the extravasation of blood into the subarachnoid space (Suarez et al., 2006). Hypertension and smoking increase the risk of SAH. SAH has a 30-day mortality rate of 45% (Brisman et al., 2006) and case-fatality rate of 51% (Suarez et al., 2006). An estimated 30% (Brisman et al., 2006) to 46% (Suarez et al., 2006) of survivors will have moderate-to-severe disability. Treatment for intracranial aneurysm includes observation, craniotomy with clipping of the aneurysm, and endovascular coil-occlusion of the aneurysm (Brisman et al., 2006). Similar to other stroke types, treatment is time sensitive.

5.1.1.5 Recurrent Stroke

Risk of recurrent stroke is dependent upon stroke type, age, adherence to secondary prevention risk factor management, and lifestyle change. Risk of recurrent stroke is also affected by differences in geography, race and ethnicity, socioeconomic status, and type of care (Lackland et al., 2014). The 30-day case fatality rate is almost double for recurrent stroke compared with index stroke, and age plays a significant role (Lackland et al., 2014).

5.1.2 Individual Predictors of Stroke and Stroke Mortality

The risk of stroke doubles with each decade increase in age (Mohr et al., 2004) and the risk of dying is two times higher for those aged 65 to 74 years and four times higher for those aged ≥75 years as compared to those <50 years (CIHI, 2006). Hypertension is the most important modifiable risk factor for both primary and secondary stroke (Davis & Donnan 2012; Lackland et al., 2014). Diabetes mellitus, atrial fibrillation, and dyslipidemia are strong risk factors for stroke and stroke mortality. Success of risk factor management varies according to multiple socioeconomic and geographic factors (Albers et al., 2002; Davis & Donnan, 2012; Qureshi et al., 2001; Suarez et al., 2006; Lackland et al., 2014; van der Worp & van Gijn, 2007; Abbott, Donahue, MacMahon, Reed & Yano, 1987; Kneeland & Fang; 2014).

5.1.3 Geographic Predictors of Stroke and Stroke Mortality

5.1.3.1 Sociodemographic Dissemination Area Level Characteristics

Socioeconomic status, minority status, and less than high school education are predictors associated with stroke and mortality. Non or limited proficiency in the English language may diminish the effectiveness of public awareness campaigns, understanding of the importance of risk reduction strategies including compliance with medication regimes and maintenance of therapeutic levels (Rodriquez et al., 2013), awareness to dial

9-1-1 for onset of stroke symptoms, and may result in delays in clinical assessment and treatment for stroke in the acute setting.

There is evidence at an international level that education is linked to health and to determinants of health including health behaviours, risky health behaviours, and use of preventive health services, and that the effects of education on health are at least as great as the effect of income (Han et al., 2005; Feinstein, Sabates, Anderson, Sorhaindo, & Hammond, 2006). Explanations for this link include differential use of tobacco and alcohol, receipt of primary and preventive care, referral to a specialist (Feinstein et al., 2006), and access to inpatient rehabilitation services after stroke (Ado et al., 2012). Workers in manual positions have been found to have higher rates of mortality after stroke than non-manual workers, with differences decreasing with age (Martinez, Pampalon, & Hamel, 2003).

Stroke has a disproportionate effect on minority and underserved populations and this has been identified as a critical health disparities issue (NINDS, 2002). Disparities may be related to genetic predisposition, racial and ethnic variations in lifestyle, access to healthcare including proclivity to seek care, the quality of healthcare received, differences in health beliefs, religiosity, health literacy, adherence to prescribed therapy, stress, and exposure to environmental toxins (NINDS, 2002). Studies of migrants have shown the tendency to acquire the risk of the country they migrate to, rather than retaining the risk of the country that they came from (Ebrahim & Harwood, 1999) emphasizing the importance of neighbourhood and community to health.

Poverty has been linked to increased stroke risk (Howard & Feigin, 2008) and to more severe deficits after stroke (Ado et al., 2012). Socioeconomic status has been associated with inequalities in the delivery of care across the stroke pathway, within countries with universal health care (Ado et al., 2012). Han et al. (2005) found that the relationship between cerebrovascular disease and median ZIP code level income was non-linear, with both low and high observed disease rate areas associated with higher income. Because mortality (versus morbidity) data were used in their analysis, it was thought that residents in higher income areas survive longer with cerebrovascular disease than those in lower income areas and that deaths are not as prevalent (making disease rates higher). In Canada, for every $10,000 increase in median neighbourhood income, the risk of death at 30-days after stroke dropped by 9% (CIHI, 2006). People with lower incomes, or from lower-income neighbourhoods, are less likely to be admitted to a high volume hospital following a stroke or be treated by a physician specializing in stroke care (CIHI, 2006), have less access to specialized care following a stroke and are more likely to die from stroke than those living in wealthier neighbourhoods (CIHI, 2006, Martinez et al., 2003).

5.1.3.2 Distance and Access to Care

The use of EMS for pre-hospital transport and care is associated with significantly shorter transport times (Prabhakaran et al., 2013; Moser et al., 2006) and is a powerful determinant of arrival to hospital within the first 60-minutes of stroke onset (Saver et al., 2010). Delays in transport result in prolonged ischemia and a greater likelihood of not meeting criteria for thrombolysis for AIS. Paramedics initiate protocols for patient stabilization and provide early notification of arrival to the stroke centre.

Direct transport to a CSC is associated with a better response to thrombolytic treatment, a greater probability of neurologic improvement at 24-hours, and better long term functional outcome after adjustment for baseline neurologic condition (Pérez de la Ossa et al., 2009). U.S. data have shown that PSCs may have lower rates of mortality at discharge and beyond compared with non-stroke centres (Lackland et al., 2014).

Geographic variation in traditional stroke risk factors plays a smaller role in the geographic variation in stroke and mortality (Howard et al., 2009) than previously thought. As location of residence is associated with the type and quality of primary and secondary preventive stroke care available, and with geographic proximity to accredited stroke centres for acute care, distance to a SPC was included as a predictor for recurrent stroke and distance to a SC was included as a predictor for in-hospital mortality in our logistic regression models.

5.2 Study Purpose

Research objectives for this study were to investigate whether (1) drive time from a SPC / SC predicts inclusion in a hot or cold spot for stroke / in-hospital mortality after adjusting for DA level sociodemographic characteristics, (2) drive time (minutes) from a SC predicts in-hospital mortality after stroke, and (3) drive time (minutes) from a SPC predicts admission to hospital for a recurrent stroke event, using multivariable logistic regression.

5.3 Methods

5.3.1 Study Design

This is a population-based, retrospective cohort study employing multivariable logistic regression techniques, using administrative data, integrating GIS. The aims of this study were to investigate associations between (1) (a) previously identified stroke hot spots/cold spots and predicted drive time from a SPC, adjusting for DA level sociodemographic predictors, (b) previously identified in-hospital mortality (henceforth referred to as 'mortality') hot spots/cold spots and predicted drive time to an accredited SC, adjusting for DA level sociodemographic predictors, (2) mortality and predicted drive time to an accredited SC and individual level predictors, and (3) predicted drive time to a SPC and admission to hospital with a recurrent stroke event and individual level predictors. The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary.

5.3.2 Data

5.3.2.1 Administrative Data

All persons diagnosed with stroke who accessed the health care system in Alberta are included in the database. Alberta Inpatient Discharge Abstract data (CIHI – DAD, 2013) and Ambulatory Care data (CIHI – NACRS, 2013) that includes ED visits for fiscal years 2002/03 to 2007/08 inclusive were linked and all personal identifiers removed. New stroke events aged ≥ 20-years with an ICD-10 (WHO – ICD-10, 2013) diagnosis of I63 (cerebral infarction), H34 (retinal arterial occlusion), I64 (stroke not specified as hemorrhage or infarction); I60 (subarachnoid hemorrhage - SAH); I61 (intracerebral hemorrhage - ICH); or G45 (Transient Ischemic Attack - TIA) were included (n = 21,886). ICD-10 I64 (not specified as hemorrhage or infarction) was coded with I63 and H34 as ischemic stroke based on the assumption that 87% of strokes are ischemic and 13% are hemorrhagic (CDC – Stroke Facts, 2014). A new stroke event was identified as follows. If multiple visits for the same patient occurred within 48-hours, the most serious event was selected (ICH > SAH > AIS > TIA). If multiple visits within 48-hours were of the same stroke type, the first event was selected because any treatment(s) received during the first health encounter could alter the patient's risk profile prior to the second encounter (Jeerakathil et al., 2010). A stroke event was considered a 'recurrent' event if it occurred >48-hours after the 'index' event. Persons <20-years of age, without a health care number and/or a valid Alberta postal code were excluded.

5.3.2.2 Spatial Data

Spatial shapefiles including healthcare centres, cities, street network data, and Dissemination Area and Alberta boundaries were obtained from Spatial and Numeric Data Services, University of Calgary (University of Calgary, 2013). These data were joined with Statistics Canada 2006 census demographic data that is based on a 20% sample (Statistics Canada – 20% Sample, 2014), by DA. DAs are defined by Statistics Canada as small, relatively stable geographic units with a population of between 400 and 700 persons (Statistics Canada – Census Dictionary, 2014).

5.3.3 Analysis

Predicted drive time service areas were generated at 30-minute intervals to 180-minutes, from SCs (for 2005, 2007, and 2010 stroke infrastructure) (Jeerakathil et al., 2010) and SPCs (for 2005 and 2010 stroke infrastructure) (Jeerakathil et al., 2010) using

Street Network data (DMTI 2011, 2014) and ArcGIS ArcMap Network Analyst Service Area analysis (Mitchell, 1999). An interval of 30-minutes was selected arbitrarily as it was thought to be sufficiently sensitive to capture changes in the estimate of effect with increased distance while limiting the number of categories. A service area includes all streets that can be reached within a specified period of travel distance or time from the SC or SPC (Mitchell, 1999).

DA and individual level predictors for the multivariable regression models were selected based upon (i) known risk factors for stroke, and (ii) available predictors which enabled an examination of the research objectives. STATA/IC 12.1 (StataCorp, 2013) software was used for the regression analysis.

Rotary and fixed wing transport were not considered for this analysis as these transports currently comprise only a small proportion of transports for acute stroke events. Research indicates that air transport does not necessarily reduce dispatch-to-arrival times for stroke and incurs greater cost and risk (Hesselfeldt, Gyllenborg, Steinmetz, Do & Rasmussen, 2014; Olson & Rabinstein, 2012). Patel et al. (2007) conducted an analysis of air versus ground travel times for acute myocardial infarction in Alberta, Canada, using GIS.

5.3.3.1 (1a) Stroke and Predicted Drive Time to a SPC. (1b) Mortality and Predicted Drive Time to a SC. Adjusted for DA Level Sociodemographic Predictors.

DA (Statistics Canada – PCCF, 2013) was selected as the geographic unit of analysis for the cluster analysis as previously described (van Rheenen, Watson, Alexander & Hill, May 2014). Hot spots and cold spots of stroke types and mortality were identified and located using the Getis-Ord Gi* statistic (ESRI – Hot Spot Analysis, 2013) in ArcGIS and Spatial Scan Statistic (Kulldorff, 2013) in SaTScan. DA centroids were 'selected by location' in ArcMap and identified as positioned within or outside Gi* and SSS hot spot and cold spot boundaries. Data were imported into ArcGIS ArcMap 10 (ESRI – ArcMap 10.0, 1999-2000) and joined with Statistics Canada 2006 census demographic data.

Binary outcomes of interest were: (i) DA within hot spot of stroke type (=1) or outside hot spot (=0), (ii) DA within hot spot of mortality (=1) or outside hotspot (=0), (iii) DA within cold spot of stroke type (=1) or outside cold spot (=0), and (iv) DA within cold spot of mortality (=1) or outside cold spot (=0). The primary predictor of interest was drive time, at 30-minute intervals to 180-minutes, from a SPC for stroke and from a SC for mortality. Highly correlated variables included 'urban' and 'drive time to a SC' (-0.4030 for 2005 and -0.3996 for 2010) and 'drive time to a SPC'(-0.4050 for 2005 and -0.4390 for 2010), therefore 'urban' was excluded from the models. Quartile cutpoints from the distribution of DA level sociodemographic predictors were used to dichotomize variables as follows: proportion with English language (1 = lowest quartile), visible minority status (1 = highest quartile), high school or less education (1 = highest quartile). Median household income was modeled as a continuous variable. Models were created based on 2005 and 2010 stroke infrastructure for comparison.

5.3.3.2 Mortality and Predicted Drive Time to an Accredited SC and Individual Level Predictors.

Postal codes of individual stroke events (Bow et al., 2004) (proxy for place of residence and location of stroke) were geocoded using the 2006 and 2011 Postal Code Conversion Files (Statistics Canada – PCCF, 2013) and imported into ArcGIS ArcMap 10.0 (ESRI – ArcMap10.0, 1999-2000). Stroke point data were 'selected by location' and positioned within their corresponding 30-minute drive time from SC service area for examination. SC service areas based on 2005 infrastructure were used for stroke events occurring in fiscal years 2002/03, 2003/04, 2004/05, and 2005/06. SC service areas based on 2007 infrastructure were used for stroke events occurring in fiscal years 2006/07 and 2007/08.

Unadjusted estimates were performed using the chi-square test for dichotomous variables and 'logistic' function in Stata for continuous (age, median household income), ordinal (distance from SC), and categorical (stroke type, transport destination) data to determine the association between mortality and predictors. The primary predictor of interest was drive time, at 30-minute intervals to 180-minutes, from a SC. Variables 'drive time to a SC' and 'urban' were highly correlated (-0.4471 for 2005 and -0.4919 for 2007), therefore 'urban' was excluded from the model. Individual patient predictors included age, sex, stroke type, EMS transport, transport destination (PSC, CSC, or 'Other' healthcare facility), and known risk factors including Type 1 or insulin dependent diabetes mellitus (IDDM), Type 2 or non-insulin dependent diabetes mellitus (NIDDM), hypertension, atrial fibrillation, and hypercholesterolemia. Two-way interaction terms were created to assess for effect modification. Adjusted estimates for predictors were obtained using backwards selection and variables with non-significant associations ($p>$

0.05) were removed. If no effect modification was found, an assessment for confounding would be carried out.

5.3.3.3 Recurrent Stroke Events and Predicted Drive Time to a SPC and Individual Level Predictors.

Postal codes of individual stroke events (proxy for place of residence and location of stroke) were geocoded using the 2006 and 2011 Postal Code Conversion Files and imported into ArcGIS ArcMap 10. Stroke point data were 'selected by location' and positioned within their corresponding 30-minute drive time from SPC service area for examination. SPC service areas based on 2005 infrastructure were used for recurrent stroke events occurring in fiscal years 2002/03, 2003/04, 2004/05, and 2005/06. SPC service areas based on 2010 infrastructure were used for recurrent stroke events occurring in fiscal years 2006/07 and 2007/08. An identical approach to multivariable modeling was taken as was for mortality. The primary predictor of interest was drive time, at 30-minute intervals to 180-minutes, to a SPC and individual patient predictors included age, sex, stroke type, transport destination (PSC, CSC, or 'Other' healthcare facility), and known risk factors including IDDM, NIDDM, hypertension, atrial fibrillation, and hypercholesterolemia.

5.4 Results

Predictors of DA hot and cold spots (see footnote[1]) after adjustment for proportion English speaking, visible minority, high school or less education, and median household income varied by stroke type (Table 5.1). For ischemic stroke, for every 30-

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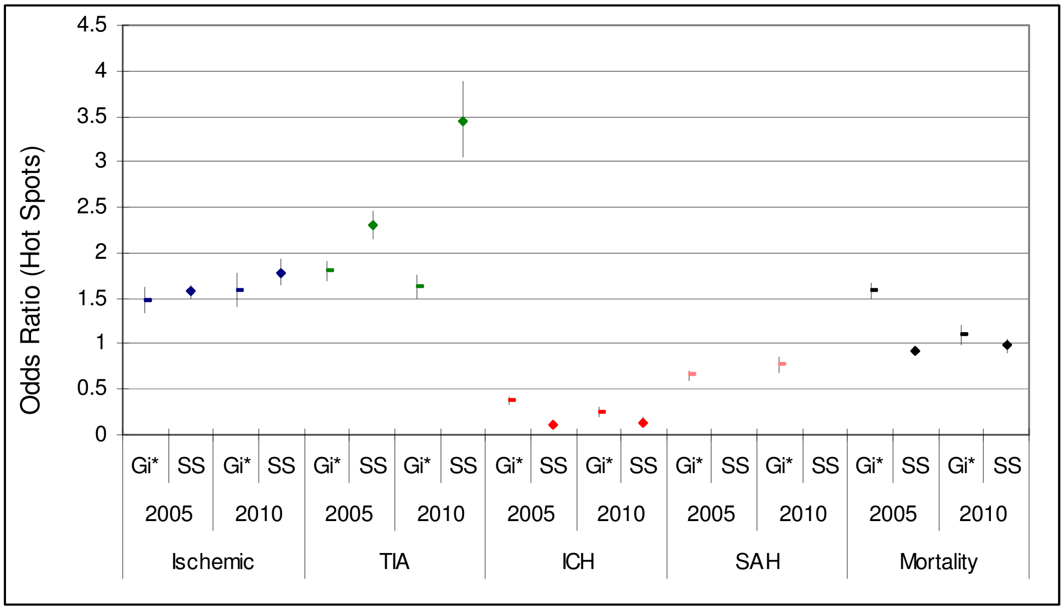
[1] † denotes Getis-Ord Gi* statistic. ‡ denotes Spatial Scan statistic.

minute increase (to 180-minutes) in drive time from a SPC (Map 5.1), there was a 1.47[†] (95% CI 1.34, 1.62) / 1.57[‡] (95% CI 1.50, 1.64) increased odds of DA classification in an ischemic stroke hot spot (Figure 5.1(a)). A comparison of ORs using 2005 and 2010 stroke infrastructure demonstrated a stronger association over time. Odds of DA classification in an ischemic stroke cold spot decreased (OR 0.60[†], 95% CI 0.56, 0.65 / OR 0.44[‡], 95% CI 0.32, 0.59) with increased distance from a SPC (Figure 5.1(b)). The direction of effect was similar for TIA hot spots (OR 1.80[†]; 95% CI 1.70, 1.90) / (OR 2.31[‡]; 95% CI 2.16, 2.46) and TIA cold spots (OR 0.15[†], 95% CI 0.13, 0.17 / OR 0.04[‡], 95% CI 0.03, 0.05).

Table 5.1. Adjusted* estimates for drive time distance, at 30-minute intervals to 180-minutes[†], to a SPC / SC and inclusion in a stroke/ mortality hot or cold spot.

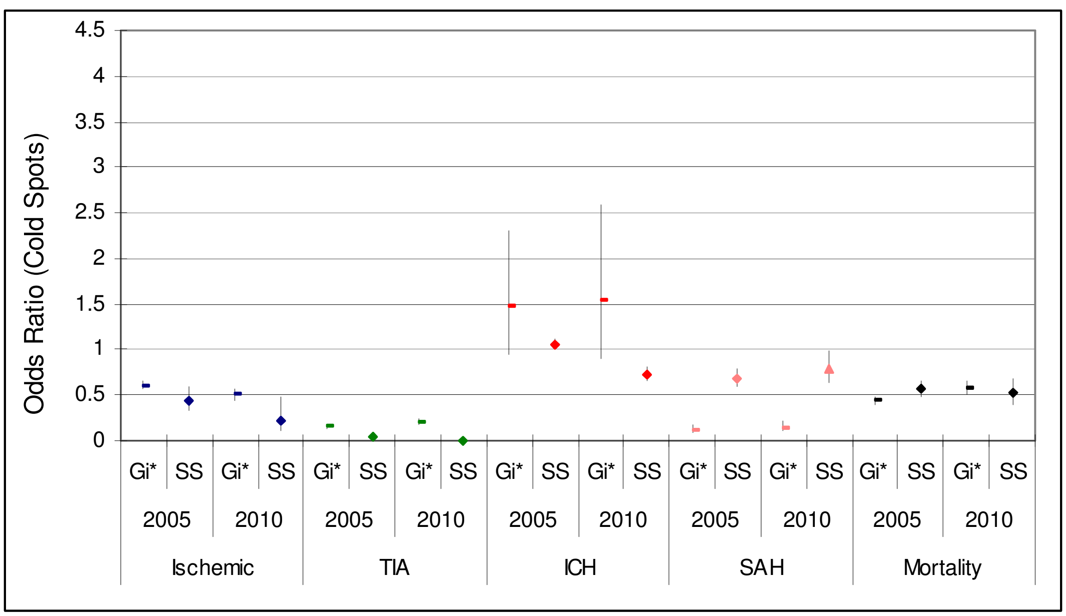
	Hot Spots				Cold Spots			
Infrastructure Year	2005		2010		2005		2010	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Ischemic Stroke – Stroke Prevention Clinic								
Gi*[‡]	1.47	1.34, 1.62	1.58	1.41, 1.78	0.60	0.56, 0.65	0.51	0.44, 0.58
SSS[§]	1.57	1.50, 1.64	1.78	1.64, 1.94	0.44	0.32, 0.59	0.23	0.10, 0.49
Transient Ischemic Attack – Stroke Prevention Clinic								
Gi*	1.80	1.70, 1.90	1.63	1.50, 1.76	0.15	0.13, 0.17	0.20	0.17, 0.24
SSS	2.31	2.16, 2.46	3.44	3.05, 3.88	0.04	0.03, 0.05	0.01	0.01, 0.02
Intracranial Hemorrhage – Stroke Prevention Clinic								
Gi*	0.37	0.33, 0.42	0.25	0.19, 0.31	1.48	0.95, 2.31	1.53	0.90, 2.59
SSS	0.11	0.08, 0.15	0.14	0.10, 0.20	1.06	1.01, 1.11	0.73	0.65, 0.82
Subarachnoid Hemorrhage – Stroke Prevention Clinic								
Gi*	0.66	0.60, 0.71	0.76	0.68, 0.86	0.12	0.08, 0.18	0.14	0.10, 0.21
SSS	-	-	-	-	0.69	0.59, 0.80	0.80	0.64, 0.99
In-hospital Mortality – Stroke Centre								
Gi*	1.57	1.49, 1.66	1.08	0.98, 1.20	0.44	0.40, 0.49	0.57	0.51, 0.65
SSS	0.93	0.88, 0.97	0.98	0.91, 1.06	0.56	0.48, 0.65	0.52	0.40, 0.68

* Proportion English speaking, visible minority, high school or less education, median household income.
[†] Predicted 30-minute drive time intervals (minutes): 0-30, 31-60, 61-90, 91–120, 120–150, 151–180, ≥180.
[‡]Getis-Ord Gi* statistic.
[§]Spatial Scan Statistic.



* Proportion English speaking, visible minority, high school or less education, median household income.
† Predicted 30-minute drive time intervals (minutes): 0-30, 31-60, 61-90, 91–120, 120–150, 151–180, ≥180.

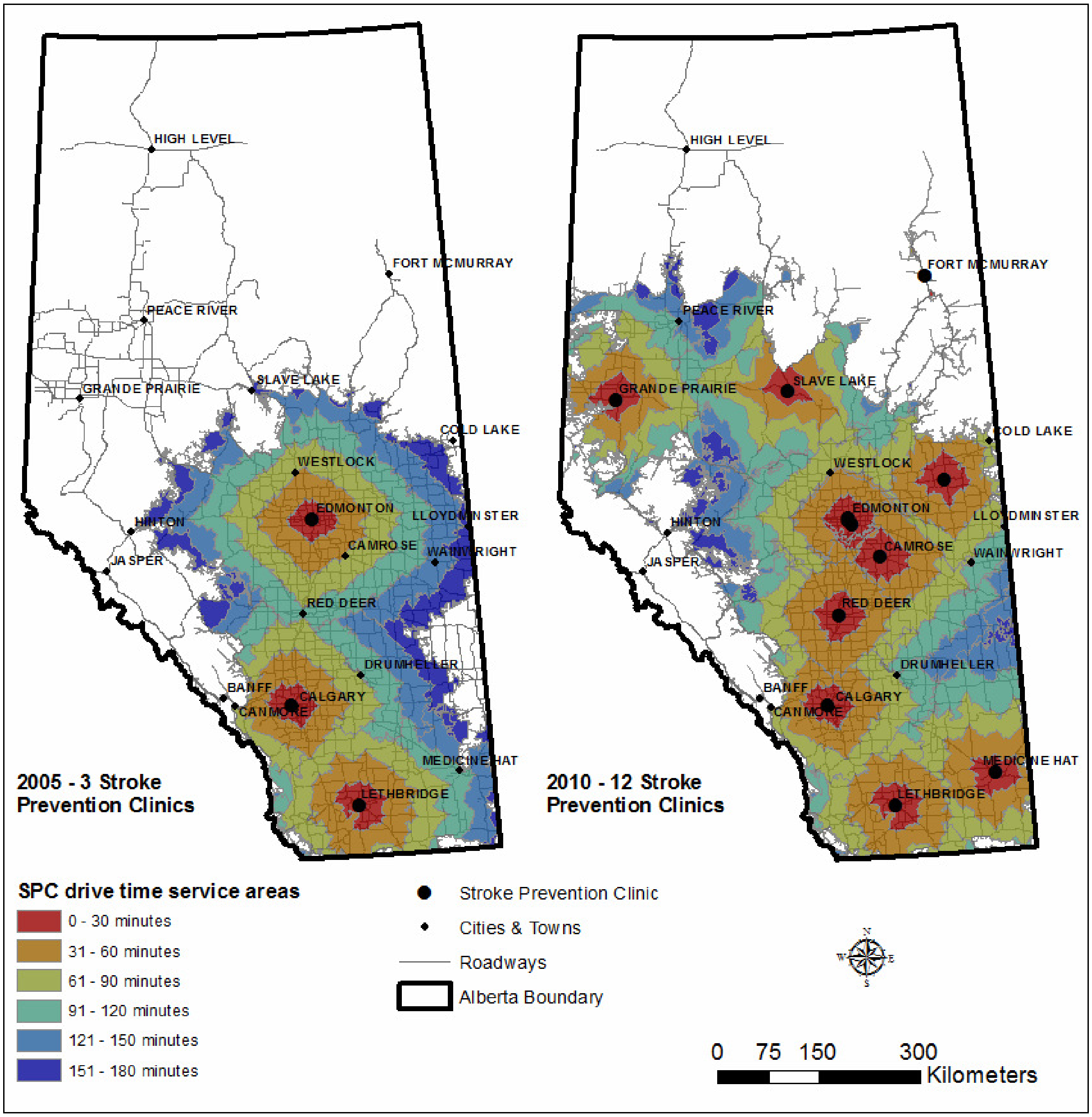
Figure 5.1(a). Adjusted* estimates for drive time distance, at 30-minute intervals to 180-minutes†, to a SPC / SC and inclusion in a stroke/ mortality hot spot.



* Proportion English speaking, visible minority, high school or less education, median household income.
† Predicted 30-minute drive time intervals (minutes): 0-30, 31-60, 61-90, 91–120, 120–150, 151–180, ≥180.

Figure 5.1(b). Adjusted* estimates for drive time distance, at 30-minute intervals to 180-minutes†, to a SPC / SC and inclusion in a stroke/ mortality cold spot.

Map 5.1. Predicted Stroke Prevention Clinic drive time (minutes) service areas; 2005 and 2010 infrastructure.



The effect was opposite for hemorrhagic forms of stroke. In ICH, for every 30-minute increase (to 180-minutes) in drive time from a SPC (Map 5.1), odds of DA classification in an ICH hot spot decreased by 63%† (OR 0.37; 95% CI 2) / 89%‡

(OR 0.11; 95% CI 0.08, 0.15) (Table 5.1; Figure 5.1(a)). This association became stronger from 2005 to 2010 for the Gi* statistic and weaker for the Spatial Scan statistic. Odds of DA classification in an ICH cold spot increased by 1.48[†] (95% CI 0.95, 2.31) / 1.06[‡] (95% CI 1.01, 1.11) for every 30-minute increase (to 180-minutes) in drive time to a SPC (Figure 5.1(b)). The association became stronger for the Gi* statistic and weaker for the Spatial Scan statistic over time. Similarly, for SAH, for every 30-minute increase (to 180-minutes) in drive time from a SPC (Map 5.1), odds of DA classification in a SAH hot spot decreased by 34%[†] (OR 0.66; 95% CI 0.60, 0.71) (Figure 5.1(a)). An estimate for the Spatial Scan statistic was not obtained because there were no SAH events included within the Spatial Scan SAH hot spot beyond the 30-minute drive time service area. For every 30-minute increase in drive time from a SPC, the OR for DA classification in a SAH cold spot decreased by 88%[†] (OR 0.12; 95% CI 0.08, 0.18) / 31%[‡] (OR 0.69; 95% CI 0.59, 0.80) (Figure 5.1(b)). From 2005 to 2010, the association weakened for the Gi* statistic and strengthened for the Spatial Scan statistic.

The distance effect on in-hospital mortality paralleled the effect for ischemic stroke (Table 5.1). For every 30-minute increase (to 180-minutes) in drive time from a SC (Map 5.2), there was a 1.57[†] (95% CI 1.49, 1.66) increase in odds of DA classification in a mortality hot spot for the Gi* statistic and a 7% decreased odds[‡] (OR 0.93; 95% CI 0.88, 0.97) for the Spatial Scan statistic. From 2005 to 2010 the associations weakened and by 2010 neither statistic was statistically significant. For every 30-minute increase in drive time from a SC, odds of DA classification in a mortality cold spot decreased 56%[†] (OR 0.44; 95% CI 0.40, 0.49) / 44%[‡] (OR 0.56; 95%

CI 0.48, 0.65). From 2005 to 2010, the association weakened for the Gi* statistic and strengthened for the Spatial Scan statistic.

Adjusted analysis of individual events confirmed this direction of effect (Table 5.2). Every 30-minute increase in drive time from a SC (to 180-minutes) (Map 5.2) was associated with increased odds of mortality (OR 1.11; 95% CI 1.04, 1.05) after adjusting for age, sex, stroke type, risk factors, EMS transport, and transport destination. Stroke type was significantly associated with mortality. As expected, with ischemic stroke as the referent category, ICH (OR 3.95; 95% CI 3.51, 4.44) and SAH (OR 4.12; 95% CI 3.49, 4.87) had higher odds of mortality and TIA had lower odds (OR 0.02; 95% CI 0.02, 0.04). Advanced age (OR 1.04; 95% CI 1.04, 1.05), NIDDM (OR 1.13; 95% CI 1.01, 1.26), and atrial fibrillation (OR 1.36; 95% CI 1.23, 1.52) were associated with higher odds of mortality. Hypertension (OR 0.64; 95% CI 0.58, 0.70) and hypercholesterolemia (OR 0.48; 95% CI 0.41, 0.56) had lower odds of mortality.

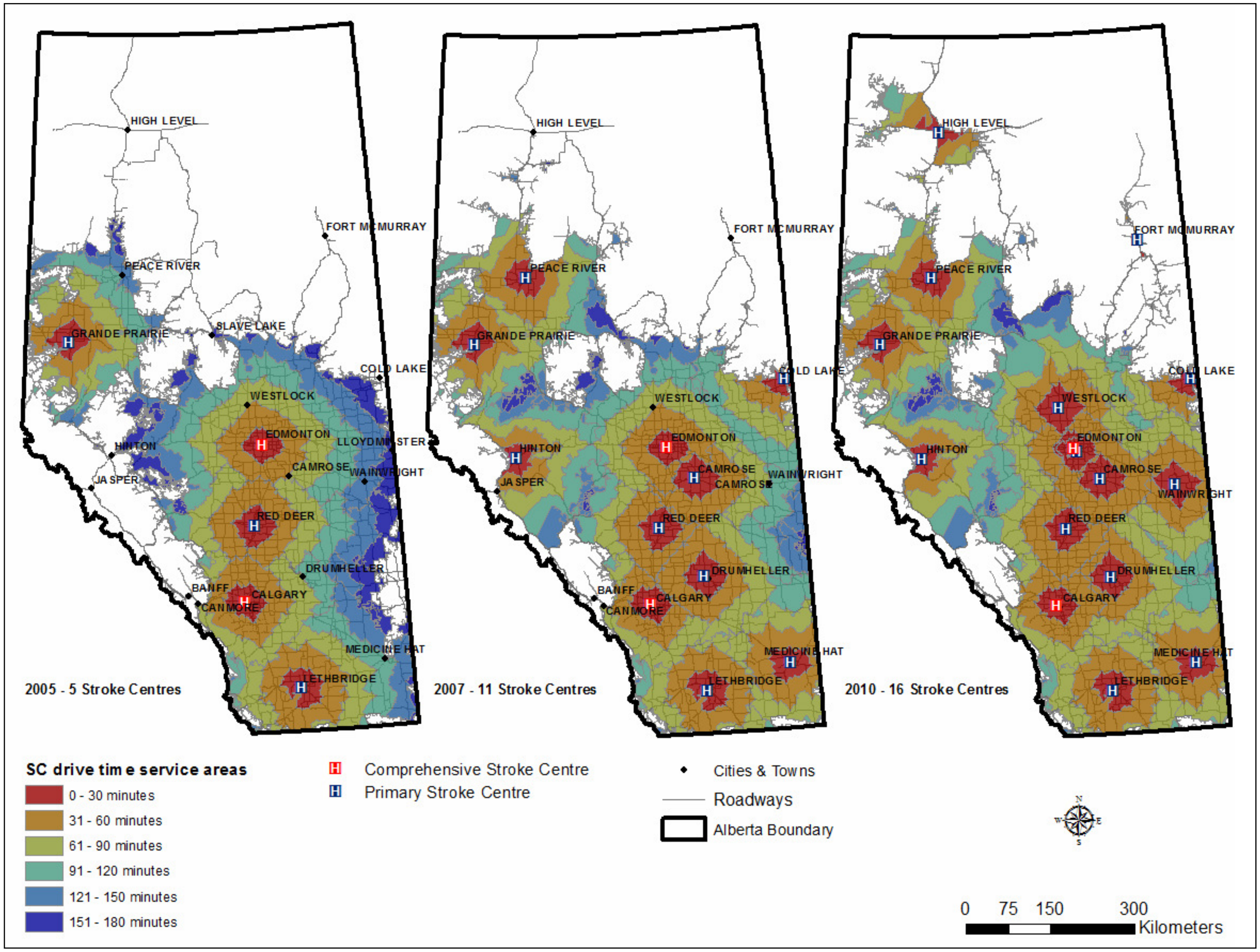
Effect modification of EMS transport on drive time from a SC was found. Increased drive time from a SC and non-EMS transport was significantly associated with mortality (OR 1.11; 95% CI 1.03, 1.19) whereas increased drive time from a SC and transport by EMS was not (OR 0.98; 95% CI 0.94, 1.01). Transport destination was associated with mortality. With PSC as the referent category, transport to a CSC was associated with a 37% reduction in mortality (OR 0.63; 95% CI 0.56, 0.71). Transport to ‘Other’ healthcare facility was not significantly associated with mortality (OR 0.91; 95% CI 0.80, 1.02).

Table 5.2. Drive time distance, at 30-minute intervals to 180-minutes*, to a Stroke Centre (SC) and in-hospital mortality after stroke†. Main effects and effect modification (EM) of EMS transport on distance to a Stroke Centre.

	Adjusted‡ Estimates					
	Main Effects		EM of EMS Transport on Distance			
			EMS=1		EMS=0	
	(n=21,886)		(n=16,351)		(n=5,535)	
Predictor	OR	95% CI	OR	95% CI	OR	95% CI
Distance from SC* (minutes)	1.11	1.04, 1.18	0.98	0.94, 1.01	1.11	1.03, 1.19
Age, years	1.04	1.04, 1.05	1.04	1.03, 1.04	1.06	1.05, 1.07
Stroke Type						
Ischemic Stroke	Referent		Referent			
Transient Ischemic Attack	0.02	0.02, 0.04	0.02	0.02, 0.04	0.02	0.01, 0.05
Intracerebral Hemorrhage	3.95	3.51, 4.44	3.95	3.48, 4.49	3.69	2.65, 5.12
Subarachnoid Hemorrhage	4.12	3.49, 4.87	4.01	3.37, 4.77	4.30	2.30, 8.04
NIDDM	1.13	1.01, 1.26	1.13	1.01, 1.28	1.10	0.82, 1.49
Hypertension	0.64	0.58, 0.70	0.64	0.58, 0.71	0.62	0.49, 0.80
Atrial Fibrillation	1.36	1.23, 1.52	1.32	1.18, 1.48	1.72	1.28, 2.31
Hypercholesterolemia	0.48	0.41, 0.56	0.46	0.39, 0.54	0.72	0.47, 1.04
EMS Transport	2.58	2.21, 3.01	-			
Transport Destination						
Primary Stroke Centre	Referent		Referent			
Comprehensive Stroke Centre	0.63	0.56, 0.71	0.64	0.56, 0.73	0.52	0.36, 0.75
‘Other’ healthcare facility	0.91	0.80, 1.02	0.91	0.79, 1.04	0.87	0.66, 1.15

*Predicted 30-minute drive time intervals: 0-30, 31-60, 61-90, 91–120, 120–150, 151–180, ≥180.
†2005 SC infrastructure used for stroke events in fiscal years 2002/03, 2003/04, 2004/05, 2005/06 and 2007 SC infrastructure
used for stroke events in fiscal years 2006/07 and 2007/08.
‡Adjusted for distance to Stroke Centre, age, sex, stroke type, IDDM, NIDDM, hypertension, atrial fibrillation, hypercholesterolemia, EMS for transport, transport destination.

Map 5.2. Predicted Stroke Centre drive time (minutes) service areas; 2005, 2007, and 2010 infrastructure.



Distance also predicted recurrent stroke events (Table 5.3). Every 30-minute increase in drive time from a SPC (to 180-minutes) (Map 5.1) was associated with increased odds (OR 1.16; 95% CI 1.13, 1.18) of hospitalization with a recurrent stroke event. With TIA as the referent category, ischemic stroke (OR 0.82; 95% CI 0.76, 0.89), ICH (OR 0.64; 95% CI 0.55, 0.74), and SAH (OR 0.59; 95% CI 0.48, 0.72) had lower odds of being a recurrent event. Advanced age (OR 1.01; 95% CI 1.01, 1.02), male sex (OR 1.22; 95% CI 1.14, 1.31), NIDDM (OR 1.21; 95% CI 1.11, 1.32), and atrial fibrillation (OR 1.25; 95% CI 1.13, 1.40) showed increased odds of recurrent event.

There was effect modification of atrial fibrillation on drive time from a SPC (Table 5.3). Increased drive time from a SPC and no documented atrial fibrillation was associated with increased odds of recurrent stroke event (OR 1.15; 95% CI 1.13, 1.18), whereas documented atrial fibrillation had an OR of 1.09 (95% CI 1.04, 1.15). With PSC as the referent category, transport to 'Other' healthcare facility was associated with increased odds of recurrent stroke event (OR 1.22; 95% CI 1.12, 1.35). The association between transport to a CSC and recurrent stroke event was not statistically significant (OR 0.99; 95% CI 0.89, 1.09).

Table 5.3. Drive time distance, at 30-minute intervals to 180-minutes*, from a Stroke Prevention Clinic (SPC) and admission to hospital with a recurrent stroke event†. Main effects and effect modification (EM) of documented atrial fibrillation on distance to a Stroke Prevention Clinic.

	Adjusted‡ Estimates					
	Main Effects		EM of Atrial Fibrillation on Distance			
			Atrial Fibrillation=1		Atrial Fibrillation=0	
	(n=21,886)		(n=3,642)		(n=18,244)	
Predictor	OR	95% CI	OR	95% CI	OR	95% CI
Distance from SPC* (minutes)	1.16	1.13, 1.18	1.09	1.04, 1.15	1.15	1.13, 1.18
Age, years	1.01	1.01, 1.02	1.01	1.00, 1.02	1.01	1.01, 1.02
Sex (Male=1)	1.22	1.14, 1.31	1.00	0.85, 1.18	1.27	1.18, 1.38
Stroke Type						
Transient Ischemic Attack	Referent		Referent			
Ischemic Stroke	0.82	0.76, 0.89	0.70	0.58, 0.86	0.85	0.78, 0.92
Intracerebral Hemorrhage	0.64	0.55, 0.74	0.57	0.39, 0.81	0.65	0.56, 0.77
Subarachnoid Hemorrhage	0.59	0.48, 0.72	0.85	0.45, 1.60	0.58	0.47, 0.73
NIDDM	1.21	1.11, 1.32	1.26	1.03, 1.52	1.20	1.10, 1.32
Atrial Fibrillation	1.25	1.13, 1.40	-			
Transport Destination						
Primary Stroke Centre	Referent		Referent			
Comprehensive Stroke Centre	0.99	0.89, 1.09	1.18	0.94, 1.49	0.94	0.84, 1.05
‘Other’ healthcare facility	1.22	1.12, 1.35	1.16	0.92, 1.47	1.24	1.12, 1.38

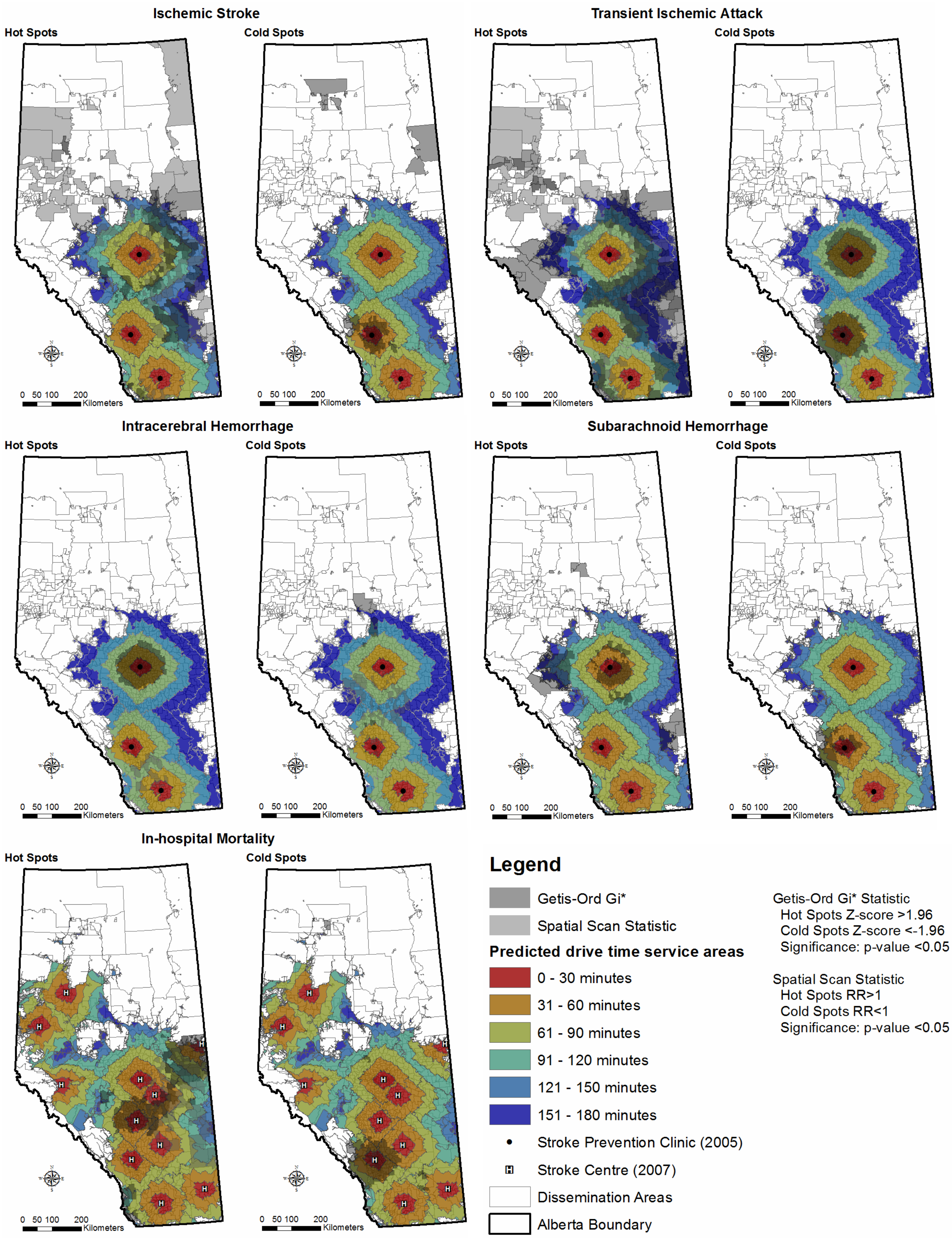
*Predicted 30-minute drive time intervals: 0-30, 31-60, 61-90, 91–120, 120–150, 151–180, ≥180.
†2005 SPC infrastructure used for stroke events in fiscal years 2002/03, 2003/04, 2004/05, 2005/06 and 2010 SPC infrastructure used for stroke events in fiscal years 2006/07 and 2007/08.
‡Adjusted for distance to Stroke Prevention Clinic, age, sex, stroke type, IDDM, NIDDM, hypertension, atrial fibrillation, hypercholesterolemia, transport destination.

5.5 Discussion

In summary, drive time from a SPC and SC were significant predictors of hot spots and cold spots of ischemic stroke, TIA, and mortality in Alberta from 2002/03 to 2007/08 at both DA and individual levels. With increased distance from a SPC, DAs had higher odds of classification in ischemic stroke and TIA hot spots and lower odds of classification in ICH and SAH hot spots. Higher adjusted odds of mortality was associated with increased drive time from a SC, ICH and SAH, NIDDM, atrial fibrillation, and non-EMS transport. Increased odds of hospitalization with a recurrent stroke event was associated with increased drive time from a SPC, male sex, TIA, NIDDM, atrial fibrillation and transport destination 'Other' than SC. Geographic patterns and locations of stroke and mortality hot and cold spots shown in Map 5.3 signify that there are important predictors related to geography, in addition to distance from specialized stroke care.

After adjusting for selected DA sociodemographic characteristics, increased drive time from a SPC was associated with increased odds of DA classification in an ischemic stroke and TIA hot spot (Table 5.1). Factors accounting for this association may include (i) preventive care received at a SPC is effective for stroke prevention, and (ii) a distance decay effect of the influence of SPCs on the medical community, (iii) a higher cost burden associated with increased travel for primary and secondary prevention reduces attendance at a SPC appointment, (iv) reduced number of referrals to a SPC with increased distance, (v) DA characteristics including the type and quality of preventive stroke care available, limited transportation options, employment sector flexibility, (vi)

Map 5.3. Hot and cold spots of stroke and in-hospital mortality and predicted drive time (minutes) service areas.



increased exposure to risks for stroke, and (vii) unique population characteristics including proclivity to seek preventive care and adhere to risk reduction strategies. Box plots of estimated ground travel distance from the recurrent stroke event's documented postal code centroid to the closest SPC, obtained using Network Analyst Route analysis, suggest that there is a proportion of stroke patients who may be required to travel great distances in order to receive secondary preventive care at a SPC (Figure 5.2).

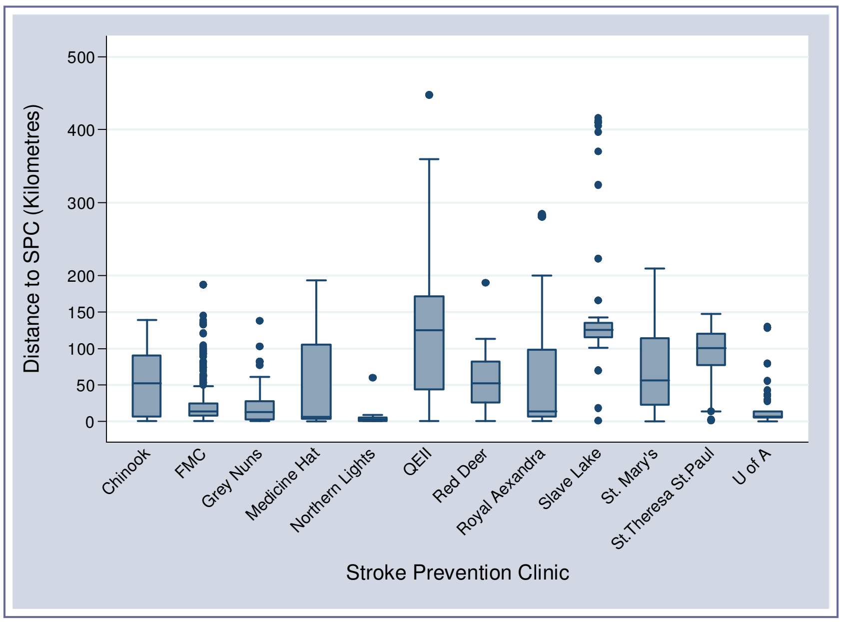


Figure 5.2. Estimated distance from recurrent stroke event postal code centroid to nearest Stroke Prevention Clinic obtained using Network Analyst Route Analysis.

Variations in clinical practice exist around the decision to test, treat and refer patients to specialists. There is variation in specialists' beliefs about the risks and benefits of medications and procedures, and regional variations in the degree to which patient preferences are incorporated into clinical decisions and influence patient outcomes (Birkmeyer, 2001). SPCs work in partnership with primary care, acute care, rehabilitation, long-term care, and community services and other stakeholders to offer prevention to those patients *within their community* (emphasis added) who have been identified as having high risk for stroke, or who have had a TIA and/or stroke (HSF, 2014). They work collaboratively with CSCs and PSCs to guide the primary and secondary stroke prevention plan (i.e. referrals and diagnostic work-ups) and facilitate best practice prevention throughout the community (HSF, 2014). Increased distance from a SPC may be associated with diminished influence on medical practitioners' judgments about stroke care provision.

Drive time from a SPC was also a significant predictor for ischemic stroke cold spots (Table 5.1). The geographic pattern of the ischemic stroke cold spot shown in Map 5.3 suggests that there are factors in addition to distance from a SPC that are uniquely and positively related to this population and/or the way in which preventive stroke care is delivered in this area.

Similar to ischemic stroke, drive time from a SPC was a significant predictor of TIA hot and cold spots (Table 5.1). TIA cold spots were located in and surrounding the cities of Edmonton and Calgary (Map 5.3). Differences in access to MRI, extent of investigation, expertise of the investigator, as well as urban-rural differences in the coding accuracy of TIA versus ischemic stroke (Kokotailo & Hill, 2005) may partially explain the urban bias for TIA cold spots located in Edmonton and Calgary.

Increased drive time from a SPC was associated with decreased odds of DA classification in an ICH or SAH hot spot (Table 5.1). This finding is likely due to differing population risk profiles for ischemic versus hemorrhagic stroke.

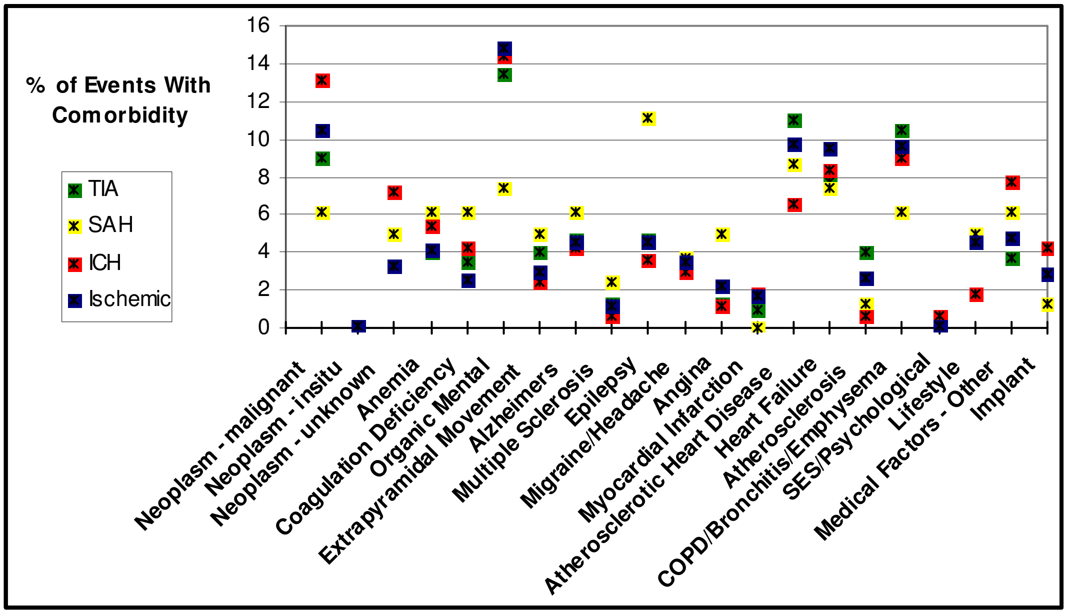


Figure 5.3. Proportion of administrative data stroke events with documented pre-existing medical conditions, by stroke type.

Higher population levels of undiagnosed hypertension, suboptimal treatment of hypertension, comorbidities (e.g. 11.1% of SAH events have documented epilepsy - Figure 5.3), and differential use of tobacco, alcohol, and illicit drugs that varies by geography may be factors in the geographic location of ICH and SAH hot spots (Map 5.3). There is an established link between exposure to fine particulate matter air pollution and stroke (Wellenius et al., 2012; U.S. EPA, 2014). There may be increased exposure to fine particulate matter which occurs with proximity to heavy traffic areas and/or heavy industry, during temperature inversions, and weather systems with associated low wind speeds. Variations in clinical practice and expertise (i.e. recognition, diagnosis, and treatment of cerebral aneurysm) and variations in the delivery of primary and preventive stroke care within this population may also be contributing factors. Alternatively, the association between increased distance from a SPC and decreased risk of ICH and SAH may be spurious.

After adjusting for selected predictors, the association between drive time to a SC and DA classification in a mortality hot spot was inconsistent between the Getis-Ord Gi* and Spatial Scan statistics (Table 5.1). The geographic location and pattern of the mortality hot spot (Map 5.3) suggests that there are important regional level predictors for mortality in this region in addition to distance from a SC. Factors might include a higher at-risk population for mortality, systemic issues resulting in prolonged OTT times, the provision of pre-hospital care (e.g. lack of or underutilization of a stroke screen tool, type of EMS service provider, availability of EMS vehicles, decisions regarding transport destination), and ED and in-hospital care (e.g. timely access to a CT scanner, stroke team care, and stroke unit care). Increased drive time from a SC was significantly associated with decreased odds of DA classification in a mortality cold spot for both statistics (Table 5.1). Decreased drive time from a SC may contribute to reduced mortality from stroke in part due to the increased likelihood of meeting criteria for thrombolysis (87% of strokes are ischemic). The location of the mortality cold spot shown in Map 5.3 suggests that there are factors unique to the population of this area and/or the ways in which stroke care is delivered in this area that contribute to this significant cluster of low mortality.

Effect modification of EMS transport on increased drive time from a SC was found where non-EMS transport and increased drive time from a SC was associated with increased odds of mortality. Patient stabilization by EMS personnel, EMS direct transport protocols where patients are transported to the nearest SC (Greg Vogelaar, unpublished data, 2014), pre-notification to the receiving SC, and transport speed are likely associated with the increasingly significant role that EMS transport has as distance from a SC becomes greater. This is despite the unique challenges for EMS related to the expanse and realities of rural and remote coverage (Health Quality Council of Alberta, 2013). ICH and SAH were both associated with higher odds of mortality (Table 5.2). Stroke severity is the primary predictor of survival at one month after stroke (Brown et al., 2013). Documented hypertension and hypercholesterolemia were associated with reduced odds of mortality (36% and 52% respectively) (Table 5.2). An association between hypertension and mortality has been found at 1-year but not at 30-days (Brown et al., 2013). A lower ratio of TC/HDL is associated with higher mortality at both 30 days and 1 year (Brown et al., 2013) but dyslipidemia is associated with reduced risk for hemorrhagic stroke. It would be expected that hypertension and hypercholesterolemia would be associated with higher risk of mortality, however adherence to treatment regimens (i.e. diagnosed and controlled hypertension equates with reduced mortality risk) may have confounded these associations or there may be a difference in the type and quality of care provided to those individuals with documented hypertension and hypercholesterolemia. NIDDM and atrial fibrillation were associated with increased odds of mortality (Table 5.2). Diabetes mellitus is a risk factor for cardiovascular disease, renal failure, and other serious health problems that can increase overall mortality risk. Cardioembolic clots associated with atrial fibrillation may be more resistant to thrombolysis leading to worsened outcomes. Additionally, risk for atrial fibrillation and mortality both increase with age so age may have confounded this association. With PSC as referent, care at a CSC was associated with a 37% reduction in mortality (Table 5.2). CSC care has been associated with reduced OTT times, increased use of tPA for AIS, reduced mortality related to specialized care on a stroke unit, and availability of neuro-interventional and neuro-intensive care for AIS, ICH and SAH.

Increased drive time from a SPC was associated with increased odds of hospital admission with a recurrent stroke event. This relationship held even after adjustment for individual predictors (Table 5.3). With TIA as the referent category, ischemic stroke, ICH, and SAH all had decreased odds of being a recurrent event. This finding was expected due to the increased risk for ischemic stroke after TIA. As of 2010, 51% of ischemic stroke and TIA patients received a referral to a SPC for secondary prevention (Jeerakathil et al., 2010). Advanced age, male sex (at higher risk for non-adherence to warfarin) (Kneeland & Fang, 2014), NIDDM, and atrial fibrillation were significantly associated with a recurrent stroke event. There was effect modification of atrial fibrillation on distance from a SPC where events with no documented atrial fibrillation had higher odds of being a recurrent event (Table 5.3). The efficacy of secondary prevention of stroke with anticoagulation therapy for atrial fibrillation combined with patient adherence with medication and blood work regimes lowers the odds of recurrent stroke. With PSC as referent, transport to 'Other' than SC healthcare facility was associated with increased odds of a recurrent stroke event. The referral and follow-up process for preventive stroke care provided at a SPC may be more efficacious and streamlined when initiated at CSCs and PSCs, due to the comparatively larger patient volumes. ICH and SAH patients are more likely to be followed by neurosurgeons practicing at CSCs, sites where SPCs are also located. Organized approaches for preventive strategies (e.g. medication adherence interventions) initiated during hospitalization may help support adherence to secondary stroke prevention guidelines after discharge (Schwamm et al., 2005). There should be a smooth transition from inpatient to outpatient care, including timely transfer of hospital discharge information to the subsequent treating physician and a clear method of appropriate follow-up (Schwamm et al., 2005).

5.6 Study Implications

Distance from a SPC and SC to place of residence (proxy for location of stroke) is a significant predictor of index ischemic stroke and TIA, recurrent stroke, and mortality in Alberta. Associations were identified at both the DA and individual levels. EMS transport and CSC care significantly lowered the odds of mortality after stroke.

Strengths of this research study include that associations with known predictors of stroke and mortality were confirmed and significant associations with novel predictors (e.g. distance to stroke care) identified. The analysis was conducted according to stroke type. The spatial unit of analysis (DA) was sufficiently small to control for predictors at a more localized scale and to permit more accurate estimations of distance (e.g. DA centroid to SPC or SC). GIS can be used to predict actual ground transport times with reasonable accuracy (van Rheenen, Hill, Alexander, & Watson, July 2014), therefore predicted 30-minute drive time service areas used in this study were considered a reasonably accurate representation of actual drive times. Multivariable regression modeling identified statistically significant associations between outcomes and predictors of interest, several of which were unexpected. GIS generated maps augmented the analysis by permitting the visualization of the spatial relationship between patterns of hot and cold spots and drive time service areas. In addition to known risk factors for stroke, this study highlights the significance of geographic proximity to specialized stroke care for primary and secondary stroke prevention and for (hyper)acute stroke. It emphasizes the importance of EMS transport and Stroke Centre care to in-hospital mortality and may thus inform future directions in stroke research and underscore the benefit of incorporating GIS based methods.

5.7 Study Limitations

Potential limitations of this study include those associated with the use of administrative data: (1) lack of clinical detail (i.e. stroke severity, INR, blood pressure, BMI), (2) regional differences with ICD-10 coding of stroke type, (3) regional differences in the documentation of risk factors, (4) inaccurate documentation of postal code, and (5) errors associated with the collection of Statistics Canada census data including under or over coverage of specific populations (Statistics Canada – Population Coverage Error, 2013). A limitation of TIA diagnosis is that patients who undergo more extensive diagnostic evaluations may be classified differently from those who undergo less extensive evaluations (Albers et al., 2002). The postal code documented on the clinical health record may not accurately represent location of residence or location of stroke (predicted travel distance from stroke location to care that is associated with outcome may not accurately reflect actual travel distance). The large study sample size would likely negate differential bias. Limitations associated with the use of multivariable logistic regression include residual confounding as it is not possible to have knowledge of or include all possible predictors. There are uncertainties associated with the graphic representation of spatial data including (1) the positional accuracy of DA centroids and events (Longley et al., 2005), (2) the limited capacity of DAs to reveal what is happening in rural areas, (3) the Modifiable Areal Unit Problem for rate and estimate drive time distance calculations, (4) small numbers problem and DA rate stability, and (5) ecological and atomistic fallacy. Misclassification of DA centroids within drive time service areas may occur but likely would be non-differential due to the large sample size.

5.8 Conclusion

Study findings confirm that where you live in relation to a SPC and SC matters with respect to stroke and stroke mortality at both the DA and individual level. At the individual level, stroke type was the most important predictor of in-hospital mortality. The majority of the population in Alberta have potential geographic access to acute stroke care within critical time windows (van Rheenen et al., July 2014), however increased distance from a SC (a component of OTT time) remains a significant predictor for stroke mortality. This fits with the literature that early treatment is crucial to good outcome. Study findings support ongoing public awareness emphasizing the importance of dialing 9-1-1 for symptoms of stroke. Geographic proximity to a SPC is an important predictor of recurrent stroke. At the DA level, there are predictors for ICH and SAH that are unaccounted for in this analysis that warrant further exploration (Map 5.3).

A multi-level spatial analysis utilizing GIS that provides the ability to examine the dual complexity of compositional (individual level) and contextual (neighbourhood level) predictors on stroke and stroke mortality using geographically weighted regression techniques would be both interesting and valuable. Predictors might include population proclivity to seek preventive care, the efficacy of preventive care, and differentials with respect to meeting thrombolysis criteria if geocoded linked EMS, ED, in-hospital, and administrative and pharmaceutical data were available for stroke events assessed at a SPC and/or admitted to hospital with a diagnosis of stroke. Novel predictors might include proximity (exposure to) to environmental pollutants, smoking rates, drug use, crime rates, access to public transportation, access to healthy and affordable foods, access to safe green spaces, and distance to specialized stroke care. Findings would inform and guide future population level stroke prevention strategies.

Study III. An Analysis of Geographic Access to Acute Stroke Care in Alberta, Canada, Using Network Analysis and GIS.

Chapter 6: Study III. An Analysis of Geographic Access to Acute Stroke Care in Alberta, Canada, Using Network Analysis and GIS.

6.1 Background

In Acute Ischemic Stroke (AIS), tissue outcome is determined by the sensitivity to ischemia, severity and duration of ischemia (Jones et al., 1981). Duration of ischemia is a critical factor. The onset-to-treatment (OTT) time with IV tPA is strongly associated with outcome, with a doubling of the odds of good outcome when administered under 1.5-hours after onset versus 1.5 to 3.0-hours after onset (Hacke et al., 2008; Marler et al., 2000). This relationship holds for all forms of reperfusion therapy (Hacke et al., 2008, Mazighi et al., 2012; Mazighi et al., 2009).

Increasing access to acute reperfusion therapy and minimizing OTT time are two of the major goals in the implementation of an integrated system of stroke care (Schwamm et al., 2005; Lackland et al., 2014; Acker et al., 2007). Delays to presentation at a PSC or tertiary stroke centre (CSC) are the main source of lost opportunity for reperfusion therapy. This requires early stroke recognition, rapid activation and transport protocols for EMS and close proximity of the populace to operational stroke centres. Implementation of a comprehensive system of stroke care has been shown to increase the use of EMS for transport, reduce interfacility transfer delays, reduce OTT times, and increase rates of thrombolysis administration for AIS (Prabhakaran et al., 2013; Prabhakaran et al., 2011; Saver et al., 2010). Changes in the organization of stroke care delivery over the past two decades may have had the greatest impact on the decline in stroke mortality (Lackland et al., 2014).

Use of EMS for pre-hospital transport has been associated with significantly shorter transport times (Prabhakaran et al., 2013; Moser et al., 2006) and is a powerful determinant of arrival to hospital within the first 60 minutes (Saver et al., 2010). EMS transport and travel time by ground from a Stroke Centre (SC) is inversely associated with in-hospital mortality after stroke (van Rheenen, Watson, Alexander & Hill, Oct. 2014). Recommended implementation strategies designed to meet critical treatment time windows for stroke include established targets for onset-to-dispatch, dispatch-to-scene, scene, scene-to-stroke centre, and ED arrival-to-treatment interval times (APSS, 2010; Acker et al., 2007; AHW, 2012) (Figure 3.1).

Stroke care is geographically accessible when it is available in terms of the number of service points (SCs) and in terms of travel impedance (by distance or time) between patient location and service points (Guagliardo, 2004). Access to coordinated stroke care may be problematic in rural areas or areas where there is inadequate access to neurological expertise (Schwamm et al., 2005; Health Quality Council of Alberta, 2013) leading to geographic disparities in access to stroke care, morbidity and mortality. Studies in the U.S. indicate that designated PSCs have lower rates of mortality at and after discharge than non-accredited hospitals (Lackland et al., 2014). Delineation of geographic regions where services can potentially be accessed within a specified time or distance of a healthcare centre can be carried out using GIS. The availability of health care services does not ensure utilization and good outcomes. Therefore, an assessment of only the spatial relationship between SCs and patient or population (DA centroid) locations is incomplete and insufficient to fully understand access (Gomez et al., 2013). Administrative data can be used to identify populations with predicted geographic access who accessed care at a stroke centre. However, a lack of clinical time data precludes an evaluation of whether this access to care is timely.

In 2005, the Government of Alberta funded the implementation of a stroke system of care to enhance geographic access to best-practice stroke care across the province. Extensive educational and training programs resulted in the addition of 11 new PSCs, in addition to the 2 CSCs and 3 preexisting PSCs. This increased the number of hospital sites capable of administering IV-tPA from 5 to 16 by 2010 (Jeerakathil et al., 2010). A standardized EMS stroke screen tool, direct EMS transport protocols, and best practice stroke care guidelines were instituted at all sites.

6.2 Study Purpose

This is a population-based, retrospective cohort study employing spatial methods using matched Alberta Health Services (AHS) EMS and Calgary Stroke Program (CSP) data, Statistics Canada census data, and population-based administrative data integrating GIS. The aims of this study were to (1) evaluate the concordance of GIS predicted versus actual EMS ground transport times for stroke, (2) estimate the proportion of Alberta population age ≥20 years with potential geographic access to acute stroke care by ground within critical OTT time windows as defined by parameters in our data (henceforth referred to as ‘predicted’ geographic access), (3) identify the proportion of a stroke population with predicted geographic access to stroke care who accessed care at a CSC or PSC (henceforth referred to as ‘realized’ access) in 2002 and 2007, and (4) to characterize stroke populations with predicted geographic access within and outside of critical transport time windows. The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary.

6.3 Methods

6.3.1 Concordance of GIS Predicted Versus Observed EMS Ground Transport Times and Generation of Ground Transport Time Service Areas.

6.3.1.1 Data

Demographic, clinical, and spatial data (northings and eastings for scene location of stroke event) for AIS patients transported by AHS EMS and treated at a CSC from April 2010 to March 2013 (n = 367) were matched using a deterministic linkage strategy. Events with missing time data, transfer patients, and inpatients were excluded from the analysis (n = 50). Street network data (DMTI 2011, 2014) and spatial shapefiles including healthcare centres, cities, and Dissemination Area (DA) and Alberta boundaries were obtained from Spatial and Numeric Data Services, University of Calgary (University of Calgary, 2013).

6.3.1.2 Analysis

Median (IQR) time intervals that included symptom onset (time last seen well)-to-dispatch, dispatch-to-scene, scene, transport-to-CSC, and ED arrival-to-treatment were obtained from the AHS EMS - CSP dataset using STATA/IC 12.1 (StataCorp, 2013) software. Predicted ground transport times (scene-to-CSC) were calculated using two methods in ArcGIS ArcMap 10.0 (ESRI – ArcMAP 10.0, 1999-2010): Network Analyst New Route analysis and Network Analyst New Service Area analysis. A network data model was selected for transport time calculations as it has been found to more accurately estimate vehicular-based travel time (Delamater et al., 2012; DMTI 2011, 2014).

In Network Analyst Route Analysis, the GIS uses Dijkstra's algorithm to compute the route between an origin (stroke event) and a destination (SC) that has the lowest impedance (time in minutes) based on street segment edges' assigned distances and speed limits (ESRI – Algorithms, 2014). GIS predicted transport times were compared with EMS observed transport times and outliers examined by month, time of day of transport, and distance from CSC.

Service areas were generated at 5-minute drive time intervals, selected arbitrarily for the purpose of capturing small urban and rural differences in concordance, from the CSC using Street Network data and ArcGIS Network Analyst Service Area analysis. A service area includes all streets that can be reached within a specified period of travel distance or time from the CSC (Mitchell, 1999). Concordance between GIS generated service areas and observed EMS transport times was assessed.

Ground transport time service areas originating from CSCs and PSCs were created based upon stroke infrastructure for years 2002, 2007, and 2010 (Jeerakathil et al., 2010) and time intervals derived from AHS EMS – CSP data. Median (IQR) interval times in minutes for AIS patients who received thrombolysis were (i) symptom onset-to-dispatch - 20 minutes (80), (ii) dispatch-to-scene - 6 minutes (4), (iii) scene - 19 minutes (9), (iv) scene-to-CSC - 14 minutes (10), and (v) ED arrival-to-treatment in accordance with guideline recommended door-to-needle time of <1-hour (Figure 6.1). Calculations incorporating these interval times resulted in scene-to-CSC ground transport times of 15-

minutes for an OTT time of 2.0-hours, 75-minutes for an OTT time of 3.0-hours, and 165-minutes for an OTT time of 4.5-hours:

20 + 6 + 19 + [15] + 60 = 120 minutes / 2.0 hour onset-to-treatment time

20 + 6 + 19 + [75] + 60 = 180 minutes / 3.0 hour onset-to-treatment time

20 + 6 + 19 + [165] + 60 = 270 minutes / 4.5 hour onset-to-treatment time.

	ONSET	**→**		**DOOR**	**→ NEEDLE**
	Symptom Onset to 9-1-1	Dispatch to Scene	Scene	Scene to CSC	ED to Treatment
Median (IQR), minutes	20 (80)	6 (4)	19 (9)	14 (10)	59 (35)

Figure 6.1. AHS EMS – CSP data symptom onset (time last seen normal) to treatment interval times (excluding transfer patients).

6.3.2 Predicted Geographic Access: Regional Data From Statistics Canada 2006 and 2011 Census.

6.3.2.1 Data

Spatial shapefiles including healthcare centres, cities, and Dissemination Area (DA) and Alberta boundaries were obtained from Spatial and Numeric Data Services, University of Calgary (University of Calgary, 2013). These data were joined with Statistics Canada 2006 and 2011 census population data by Dissemination Area. Dissemination Areas (DAs) are defined by Statistics Canada as small, relatively stable geographic units with a population of between 400 and 700 persons (Statistics Canada – Census Dictionary, 2014).

6.3.2.2 Analysis

DA centroids (latitude and longitude coordinates) with joined census population data were selected by location within their corresponding <15-minute, <75-minute, <165-minute, or >165-minute transport time service area in ArcGIS ArcMap for examination. Proportions of the population deemed to have potential geographic access were obtained by summing the total population ≥20-years for each service area and dividing by the total population ≥20-years for Alberta.

6.3.3 Realized Access: Administrative Data Stroke Events

6.3.3.1 Data

Alberta Inpatient Discharge Abstract data (CIHI – DAD, 2013) and Ambulatory Care data (CIHI – NACRS, 2013) that includes ED visits for fiscal years 2002/03 to 2007/08 inclusive were linked and all personal identifiers removed. New stroke events aged ≥ 20-years with an ICD-10 (WHO - ICD-10, 2013) diagnosis of I63 (cerebral infarction), H34 (retinal arterial occlusion), I64 (stroke not specified as hemorrhage or infarction); I60 (subarachnoid hemorrhage - SAH); I61 (intracerebral hemorrhage - ICH); or G45 (Transient Ischemic Attack - TIA) were included (n = 21,886). ICD-10 I64 (not specified as hemorrhage or infarction) was coded with I63 and H34 as ischemic stroke based on the assumption that 87% of strokes are ischemic and 17% are hemorrhagic (CDC – Stroke Facts, 2014). A new stroke event was identified as follows. If multiple visits for the same patient occurred within 48-hours, the most serious event was selected (ICH > SAH > ischemic > TIA). If multiple visits within 48-hours were of the same stroke type, the first event was selected because any treatment(s) received during the first health encounter could alter the patient's risk profile prior to the second encounter

(Jeerakathil et al., 2010). Persons without a health care number and/or a valid Alberta postal code were also excluded.

6.3.3.2 Predicted and Realized Geographic Access to Stroke Care

Documented postal codes of stroke events (proxy for place of residence and location of stroke) were converted to latitude and longitude coordinates using the 2006 and 2011 Postal Code Conversion Files (Statistics Canada – PCCF, 2013) and imported into ArcGIS ArcMap 10.0 (ESRI – ArcMap 10.0, 1999-2000). Stroke event points were selected by location within their corresponding <15-minute, 15 to 75-minute, 75 to 165-minute, or >165-minute transport time service area. These events were considered to have predicted geographic access to acute stroke care within our defined critical OTT times based on the interval times described earlier. Stroke events identified as having predicted geographic access who presented to a CSC or PSC for care were deemed to have realized access and proportions were calculated for each transport time service area. Lack of interval time data in our administrative database precluded an analysis of whether realized access to care was timely.

6.3.4 Characteristics of Populations Within and Outside of Critical Transport Time Service Areas.

Administrative data stroke events for 2002/03 to 2007/08 were selected in ArcGIS ArcMap by location of residence within their corresponding <75-minute, 75 to 165-minute, or >165-minute transport time service area based on 2010 stroke infrastructure. Characteristics of events were then summarized by transport time service area according to stroke type, risk factors, EMS transport, disposition, and urban/rural residence using the postal code definition (du Plessis et al., 2002).

6.4 Results

6.4.1 Concordance of GIS Predicted Versus Observed EMS Ground Transport Times.

GIS-predicted EMS ground transport time using Network Analyst Route analysis was reliably correlated with observed EMS transport times. Predicted time was 70% of actual time plus 2.1 minutes (Figure 6.2). Absolute time differences were small with a median difference in minutes of 1.95 minutes (IQR 5.87). Of EMS transports with a >10-minute difference (n = 33), 63.6% occurred in winter months and 51.5% during peak morning and afternoon rush hour traffic periods. Of patients with EMS transport times shorter than predicted in Network Analyst (n = 6), 5 were transported from towns located outside of Calgary. There was slight discrepancy between GIS Network Analyst Service Area analysis predicted transport time service areas originating from the CSC at 5-minute ground transport time intervals and actual EMS transport times (Figure 6.3). Variation occurred at shorter distances to the CSC and was <6-minutes in 80% of stroke events.

6.4.2 Predicted Geographic Access: Regional Data From Statistics Canada 2006 and 2011 Census.

The increase in geographic extent of transport time service areas based on 2002, 2007, and 2010 stroke infrastructure is shown in Map 6.1. There is overlap of service areas in central and southern Alberta. Based on stroke infrastructure in 2002 and 2007

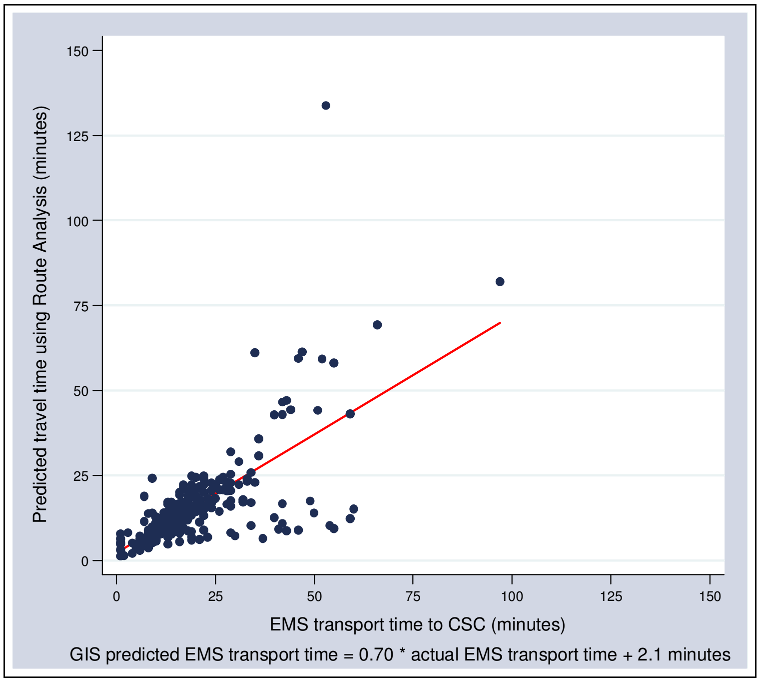


Figure 6.2. Scatter plot of Network Analyst Route Analysis predicted transport times and observed EMS transport times. GIS-predicted EMS transport times were highly linearly related to observed EMS transport times.

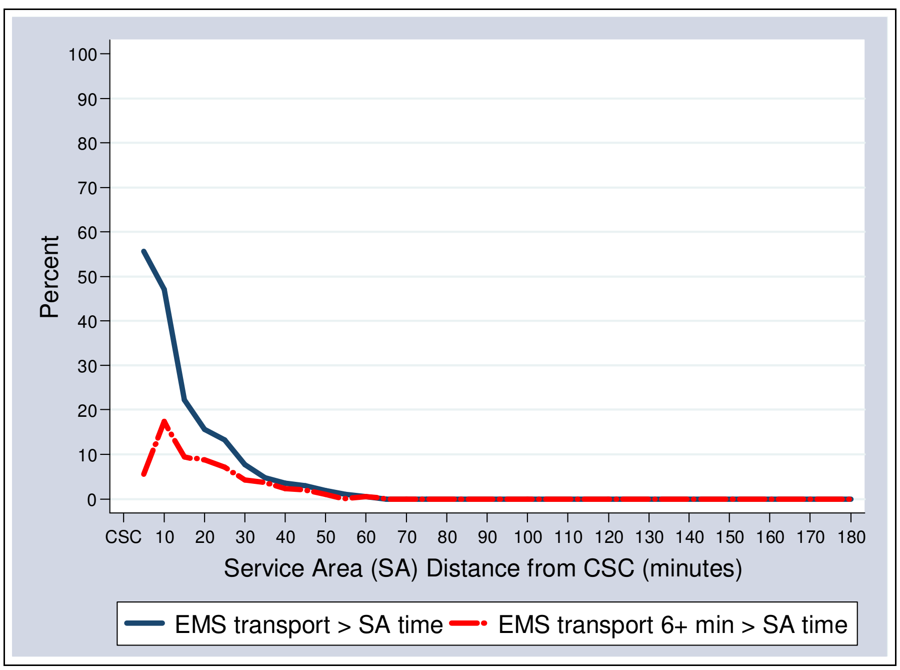


Figure 6.3 Association between actual EMS ground transport times and Network Analyst Service Areas at 5-minute intervals from the CSC. The greatest variation occurred within a 10-minute drive time of CSC.

and Statistics Canada 2006 census data (DA level), and 2010 stroke infrastructure and Statistics Canada 2011 census data, there was an estimated increase from 47.5% to 53.8% in the proportion of Albertans with predicted geographic access by ground transport to a stroke centre in ≤15-minutes, an increase from 84.6% to 93.9% in ≤75-minutes, and an increase from 95.2% to 98.4% in ≤165-minutes (Table 6.1). The proportion of the population ≥165-minute transport time window was reduced from 4.3% in 2002 to 1.6% in 2010.

Table 6.1. Alberta population age ≥20-years with predicted geographic access to stroke care within critical transport time service areas.

Transport time to SC*	<15-minutes			<75-minutes			<165-minutes		
Calculated OTT Service Areas†	<2.0-hours			<3.0-hours			<4.5-hours		
Stroke Infrastructure Year	2002	2007	2010	2002	2007	2010	2002	2007	2010
% AB population‡§	47.5	50.9	53.8	84.6	90.5	93.9	95.2	96.6	98.4
% Stroke Events‖	45.3	51.1	53.1	79.6	89.0	93.4	96.8	98.3	99.1

*Predicted times obtained using Network Analyst Service Area analysis in GIS.
†Onset-to-treatment time calculated using time intervals derived from AHS-EMS – Calgary Stroke Program data.
‡Statistics Canada 2006 census data for stroke infrastructure years 2002 and 2007; Statistics Canada 2011 census data for stroke infrastructure year 2010. Population age≥20-years.
‡Denominator for 2002 and 2007: Alberta census population.
§Denominator for 2010: total DA population in database (missing population data by DA is 16.6%).
‖Administrative Data stroke events for fiscal years 2002/03 to 2007/08.

6.4.3 Predicted and Realized Geographic Access: Administrative Stroke Events.

From 2002 to 2007 there was no change in location or number of CSCs, therefore predicted geographic access to care at a CSC remained unchanged within all transport time service areas. Realized access to care at a CSC increased, most notably in the <15-minute (7.3% increase) and 15 to 75-minute transport time service areas (5.9% increase) (Table 6.2). Predicted geographic access to care at a PSC increased in the <15-minute

Map 6.1. Predicted transport time service areas around Comprehensive and Primary Stroke Centres, 2002 to 2010.

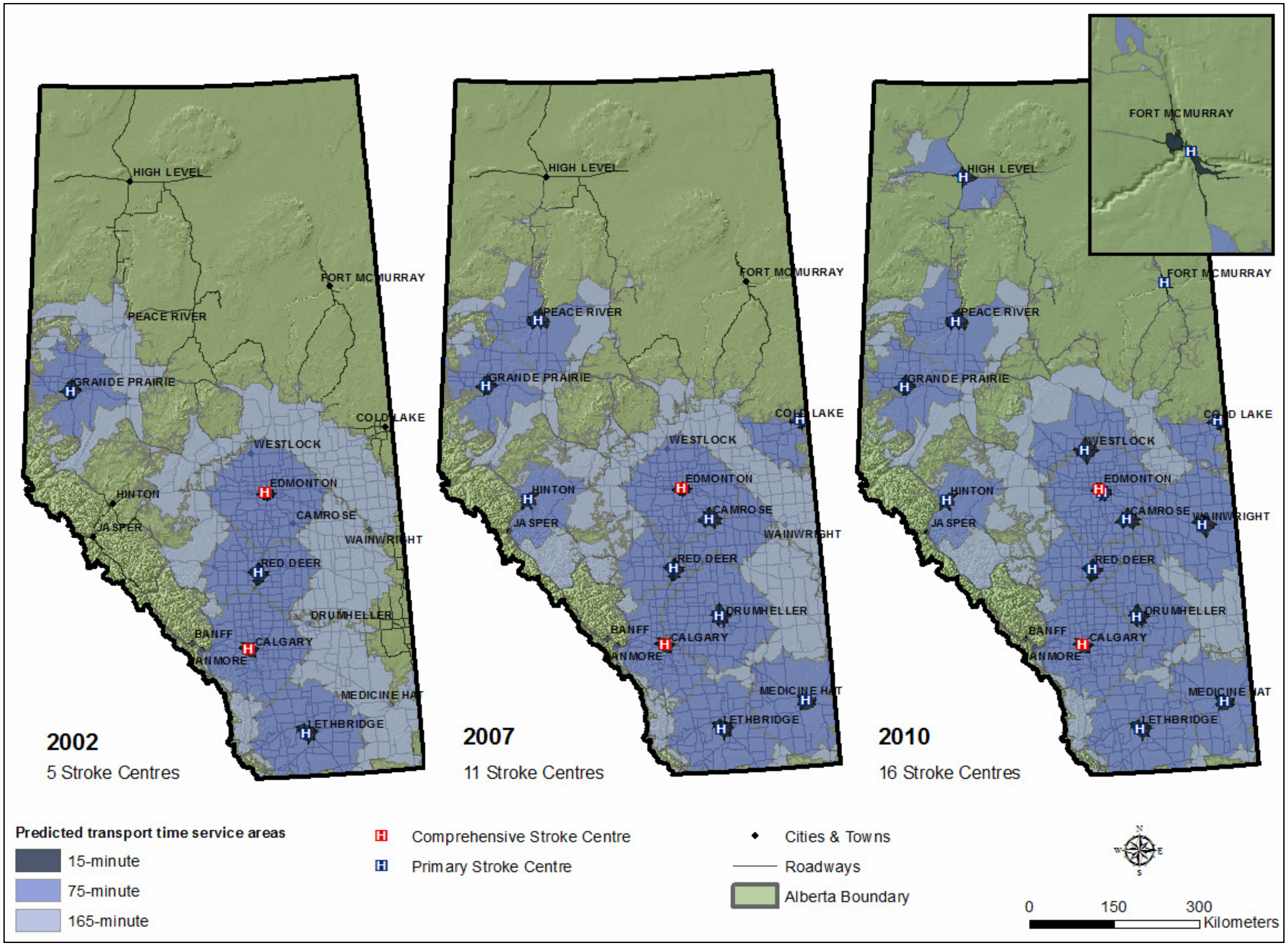


Table 6.2. Proportion of stroke events with predicted geographic access to stroke care within critical transport time service areas treated at a Stroke Centre (realized access), 2002 and 2007.

Transport Time to SC* Calculated OTT Service Areas†	<15-minutes <2.0-hours		15 to 75-minutes 2.0 to 3.0-hours		75 to 165-minutes 3.0 to 4.5-hours	
Stroke Infrastructure Year	2002	2007	2002	2007	2002	2007
Administrative Data Fiscal Year	2002/03	2007/08	2002/03	2007/08	2002/03	2007/08
Total Stroke Events by Year(n)	3673	3527	3673	3527	3673	3527
Comprehensive Stroke Centre‡						
Predicted Geographic Access§ (n)	1405	1349	929	865	910	876
Predicted/Total Events (%)	38.3	38.2	25.3	24.5	24.8	24.8
Realized Access‖ (n)	898	961	431	452	175	190
Realized/Predicted (%)	63.9	71.2	46.4	52.3	19.2	21.7
Primary Stroke Centre#						
Predicted Geographic Access (n)	241	496	528	1661	2561	1313
Predicted/Total Events (%)	6.6	14.1	14.4	47.1	69.7	37.2
Realized Access (n)	199	401	63	278	302	77
Realized/Predicted (%)	82.6	80.8	11.9	16.7	11.8	5.9

*Predicted times obtained using Network Analyst Service Area analysis in ArcGIS.
† Onset-to-treatment time calculated using time intervals derived from AHS-EMS – CSP data.
‡ Comprehensive Stroke Centre: CT Scan, tPA, stroke team, neurosurgical/neuro-interventional expertise, acute stroke unit.
§Potential geographic access: stroke events with residence postal code positioned within critical transport time service areas.
‖Realized access: stroke events with residence postal code positioned within critical transport time service areas treated at a Comprehensive or Primary Stroke Centre. Lack of administrative data interval time data precludes an evaluation of whether realized access was timely.
#Primary Stroke Centre: CT Scan, tPA, stroke expertise on-site or available by telehealth, acute stroke care provision.

transport time (7.5%) and 15 to 75-minute (32.7%) transport time service areas. The proportion with predicted geographic access in the 75 to 165-minute and >165-minute transport time service areas decreased (32.5% and 7.7% respectively). Realized access to care at a PSC decreased slightly in the <15-minute transport time service area (82.6% to 80.8%) and increased from 11.9% to 16.7% in the 15 to 75-minute transport time service area and from 10.0% to 34.4% in the >165-minute transport time service area. For stroke

Table 6.3. Characteristics of Alberta Administrative Data stroke events (2002/03 to 2007/08) within and outside predicted critical transport time service areas using 2010 stroke infrastructure.

Transport Time to SC* Calculated OTT Service Areas†	<75-minutes <3.0-hours	75 to 165-minutes 3.0 to 4.5-hours	>165-minutes >4.5-hours	Total
Stroke Total (n)	20447	1242	197	21886
Stroke Proportion (%)	93.4	5.7	0.9	100.0
Stroke Type (%)				
Ischemic Stroke	62.3	56.9	52.8	62.0
TIA	24.3	31.6	34.0	24.8
ICH	8.2	7.0	7.1	8.1
SAH	5.2	4.5	6.1	5.1
Risk Factors (%)				
Diabetes Mellitus	20.4	22.1	29.4	20.5
Hypertension	56.3	42.4	48.7	55.4
Atrial Fibrillation	17.0	11.1	9.6	16.6
Hypercholesterolemia	18.6	12.6	8.1	18.2
EMS Transport (%)	75.2	68.3	70.1	74.7
Disposition (%)				
Discharged	59.2	60.2	65.0	59.3
Transferred	27.5	28.5	22.3	27.5
In-hospital Death	13.3	11.3	12.7	13.2
Urban‡ (%)	77.7	21.4	17.8	73.4

*Predicted times obtained using Network Analyst Service Area analysis in GIS.
† Onset-to-treatment time calculated using time intervals derived from AHS-EMS – Calgary Stroke Program data.
‡Postal code definition.

events with a rural residence, realized access to care at a PSC increased in all transport time service areas.

6.4.4 Characteristics of Populations Within and Outside of Critical Transport Time Windows.

Given 2010 stroke infrastructure and administrative data stroke events for fiscal years 2002/03 to 2007/08, 93.4% of events had potential access to care at an accredited stroke centre within 75-minutes transport time (Table 6.1, Table 6.3). The >165-minute transport time service area had the highest proportion of documented TIA (34.0% versus 24.8% for the dataset) and SAH (6.1% versus 5.1% for the dataset) (Table 6.2). ICH was highest (8.2%) in the <75-minute transport time service area. The proportion with documented diabetes mellitus (DM) was highest in the >165-minute transport time service area (29.4% versus 20.5% for the dataset), and hypertension, atrial fibrillation, and hypercholesterolemia were highest in the <75-minute transport time service area (56.3%, 17.0%, and 18.6% respectively). EMS transport was highest in the <75-minute transport time service area (75.2%) and lowest in the 75 to 165-minute transport time service area (68.3%). The proportion of strokes discharged from hospital was highest in the >165-minute transport time service area (65.0%), the proportion transferred was highest in the 75 to 165-minute transport time service area (28.5%), and in-hospital mortality was similar across all transport time service areas.

6.5 Discussion

6.5.1 Principal Findings

The principal findings of this study were: (1) GIS methods can be used to predict actual EMS ground transport time, (2) the implementation of a provincial stroke strategy and addition of 6 new PSCs over a 5-year interval resulted in a 40.2% increase in the number of Albertans with shortened transport times and estimated access to tPA in under 3 hours, and (3) there is a marked difference in the potential for early reperfusion therapy between those living in rural versus urban locations. The implications of this work are that potential (predicted) access does not necessarily equate with utilization of services and that maximum utilization of expanded geographic access should be supported by stroke protocols, policies, and education. In 2007, Alberta had near population-wide coverage for acute stroke care access based upon its geography and population distribution. The proportion of stroke patients who had realized access to care at a stroke centre within a 165-minute transport time increased to 68% by 2007. The rural stroke population made significant gains in realized access to CSC and PSC care during this time period.

6.5.2 Concordance of GIS Predicted Versus Observed EMS Ground Transport Times.

Minimal variation was observed between predicted GIS transport times using Network Analyst Route Analysis (Figure 6.2) and Service Area analysis (Figure 6.3) and observed EMS transport times. Dispatch-to-scene, scene, and scene-to-CSC interval times are similar to those in the literature (Kleindorfer et al., 2006; Patel et al., 2012). GIS predicted AHS EMS transport distances ranged from 0.99-kilometres to 201.79-kilometres. Winter season and rush hour traffic times were factors in longer than predicted transport times. Shorter than predicted transport times occurred most often in transports originating outside of Calgary city limits. ‘Lights and Siren’ transport speeds and enhancements to road networks not yet incorporated into Street Network data may have been factors in shorter travel times. Because EMS transports occurred over a period of years, during all seasons and hours of the day, over varied terrain, and because minimal variation between actual EMS transport times and GIS predicted transport time service areas was observed, it was concluded that predicted transport time service areas could be generated around CSCs and PSCs for the province that reflected actual ground transport times with reasonable accuracy.

6.5.3 Predicted Geographic Access: Regional Data From Statistics Canada 2006 and 2011 Census.

The addition of 11 PSCs by 2010 for a total of 14 PSCs and 2 CSCs and concomitant extension of stroke centre service area coverage translated into a greater proportion of Albertans having predicted geographic access to care a stroke centre by ground transport within critical transport time windows based on median time intervals derived from the dataset (Table 6.1, Map 6.1). The analysis predicted that given Statistics Canada 2011 census data and 2010 stroke infrastructure, 53.8% of the population would have predicted access to care at stroke centre within the <15-minute transport time service area (OTT time of <2.0-hours) and 98.4% would have predicted geographic access to care within a ≤165-minute transport time (OTT time of <4.5-hours). The region outside of the 165-minute transport time service area is rural and less densely populated, and has a more limited transportation infrastructure. Limited geographic access to stroke prevention services and greater travel distances to stroke centres may be important contributing factors to stroke risk, morbidity, and in-hospital mortality.

Overlap of CSC and PSC transport time service areas was found in central and southern Alberta (Map 6.1). Pre-hospital decision-making regarding transport destination for acute stroke may become more complex when PSCs and CSCs are within close geographic proximity. Recommendations for stroke care include that a patient with stroke presentation be transported to the nearest stroke centre for evaluation (Acker et al., 2007). Rapid interfacility transport protocols should be in place for the subset of stroke population transported to a PSC who do not recanalize with IV thrombolysis and/or who require endovascular treatment in order to avoid delays that may preclude a patient from receiving intra-arterial treatment. Prabhakaran et al. (2011) found that odds of emergent angiography decreased by 3% per minute delay of interfacility transport beyond 46-minutes (lowest limit in their study). In Alberta, EMS practitioners have a specific stroke protocol and screening tool that sanction when to transport to the nearest PSC or CSC. As required, practitioners may consult "Online Medical Control" where a dedicated ED physician assists with decision-making and may authorize the bypass of a healthcare facility if patients do not meet guidelines outlined by protocol (Greg Vogelaar, unpublished data, 2014).

6.5.4 Predicted and Realized Geographic Access: Administrative Data Stroke Events.

The analysis of administrative data stroke events (2002/03 to 2007/08) yielded similar findings to those found using Statistics Canada census data (Table 6.1). From 2002 to 2010, the proportion of stroke events with predicted geographic access in the <15-minute, 15 to 75-minute, and 75 to 165-minute transport time service areas increased. The proportion of stroke events outside the 165-minute transport time service area decreased from 3.2% to 0.9% (Table 6.2).

From 2002 to 2007, predicted geographic access to care at a CSC was unchanged within all transport time service areas yet realized access to care increased, most notably within the <15-minute and 15 to 75-minute service areas (Table 6.2). This increase may have reflected the expanded adoption of a standardized EMS stroke screen tool, direct transport protocols, and stroke education campaigns. From 2002 to 2007, predicted geographic access to care at a PSC increased in the <15-minute and 15 to 75-minute transport time service areas and decreased in the 75 to 165-minute and >165-minute transport time service areas. The addition of 6 stroke centres by 2007 extended <15-minute and 15 to 75-minute transport time service areas incorporating more densely populated regions, and the 75 to 165-minute and >165-minute transport time service areas incorporated less densely populated territory resulting in a reduction in the proportion of the population with predicted geographic access in the latter two transport time service areas. Realized access to care at a PSC in the <15-minute transport time service area decreased from 82.6% to 80.8% likely as a result of increased transports to CSCs or variation in residence of the 2002 and 2007 stroke populations, and increased from 11.9% to 16.7% in the 15 to 75-minute transport time service area. This service area experienced the largest increase in predicted geographic access to care at a stroke centre (from 14.4% to 47.1%) and a disproportionately lower increase in realized access leaving potential for enhanced utilization. Expansion of PSC coverage, increased use of EMS for transport, and direct transport protocols would have important roles in the increased number of Albertans receiving care at an accredited stroke centre over time.

6.5.5 Characteristics of Populations Within and Outside of Critical Transport Time Windows.

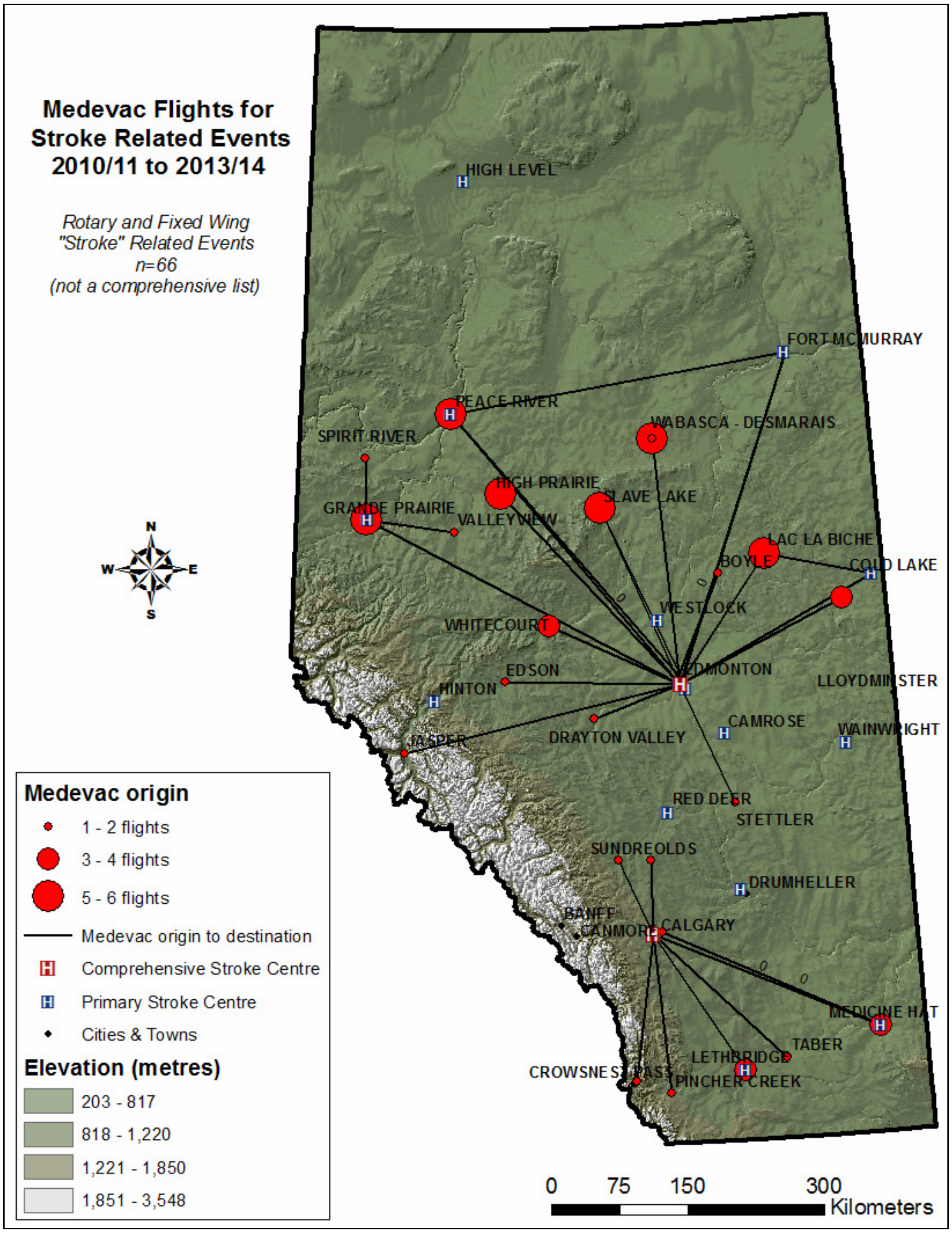
A higher proportion of stroke events in the <15-minute transport time service area were ischemic stroke (Table 6.3) and a higher proportion of stroke events outside of the 165-minute transport time service area were TIA and SAH. Differences in access to MRI (Kidwell et al., 1999), investigator expertise, and extent of investigation as well as urban-rural differences in the coding accuracy of TIA versus ischemic stroke (Kokotailo & Hill, 2005) may partially explain the variation in ischemic stroke versus TIA diagnosis. Stroke events outside of the 165-minute transport time service area were younger, a higher proportion were male, had diabetes mellitus, accessed care at a PSC (compared to the 3.0 to 4.5-hour service area), and were discharged from hospital. Fewer stroke events in this transport time service area had documented hypertension, atrial fibrillation or hypercholesterolemia; conditions which are more likely to occur at a more advanced age.

Air medevacs can reduce transport times for stroke patients residing at greater distances from SC care or at locations that are more difficult to access by ground transport. Air medevac transport patterns for stroke related events are shown in Map 6.2. Of the 66 air medevac origins, 39% were located within the <15-minute transport time service area, 59% within the <75-minute, and 100% within <165-minute transport time service areas. Rotary and fixed wing transports did not service geographically remote events (with respect to access to a SC by ground transport within critical time windows). Rather, they may have serviced events with prolonged onset-to-dispatch times who required reduced transport times in order to meet critical OTT time windows.

6.6 Study Implications

Strengths of this research include the availability of AHS EMS - CSP matched data that enabled the calculation of precise interval times and assessment of the correlation between GIS predicted times and observed EMS transport times. Variation between GIS Network Analyst Service Area analysis predicted transport time service areas and actual EMS transport times was minimal (<6-minutes in 80% of transports) and occurred at shorter distances from the CSC likely due in part to traffic congestion on arterial and collector roads leading to the CSC premises. EMS spatial data included the coordinates of the location of the stroke event, enabling accurate ground transport time to

Map 6.2. Air medevacs for stroke related events, 2010/11 to 2013/14 (n = 66).
Geospatial Modelling Environment software (http://www.spatialecology.com/gme/).



CSC calculations. These types of EMS data for stroke are sparsely available in the literature, and interval times for other acute health events may not be generalizable to acute stroke. Onset-to-dispatch times for stroke may be prolonged due to aphasia, inability to access a phone, or if onset occurs during the night (there is no pain to awaken the patient). Scene times may be prolonged if the patient is physically unable to provide access to health care providers onto the premises. Additional time may be required to obtain vital information (e.g. contraindications to thrombolysis) and to have family member accompaniment to support critical decision-making. The availability of more detailed Street Network data permitted the generation of service areas that more accurately reflected actual transport times in comparison with other spatial methods (i.e. buffer analysis). Because GIS predicted times and observed EMS transport times were well correlated and representative of seasonal and traffic conditions, it was concluded that predicted transport time service areas for CSCs and PSCs in the province reflected actual transport times with reasonable accuracy.

The incorporation of spatial methods added dimension and new perspective to our understanding of the complexities of pre-hospital service provision, of how changes in service provision can enhance access to healthcare services, and to identify potentially vulnerable populations. Regions with increased predicted geographic access and disproportionately low realized access were highlighted. These are regions where supplemental support of current health services or enhancements to health services could result in the increased utilization of specialized stroke care and improved outcomes.

6.7 Study Limitations

Limitations of this study include that AHS EMS – CSP data interval times were obtained for AIS patients who were candidates for and received thrombolytic therapy. If interval times for the Alberta stroke population differed significantly from times in our AHS EMS – CSP stroke population, the size of transport time service areas could be significantly altered. For example, a longer onset-to-dispatch time would decrease time allotted for transport in order to meet critical OTT time windows of 2.0-hours, 3.0-hours and 4.5-hours in our study, thereby reducing CSC and PSC service area coverage. Conversely, service area coverage would expand with decreased interval times (e.g. ED arrival-to-treatment). Delays related to patient or family recognition of stroke systems and limited use of 9-1-1 services are likely much more important than delays that occur because of EMS systems and providers (Kleindorfer et al., 2006). There was remarkably little variation in AHS EMS interval times observed in this study. In this study, the 'symptom onset-to-dispatch' time interval had the greatest variation. The implication of this is that variation in 'symptom onset-to-dispatch' time is more likely to alter CSC and PSC service area coverage and this interval is unaffected by enhancements to pre-hospital and ED care.

Although proportions of the Alberta population with realized access to care at a stroke centre were identified, it could not be concluded that care was received within critical OTT times for good outcome because pre-hospital and interval time data for this population were lacking. Limitations associated with administrative data and the use of postal code as proxy for place of residence and location of stroke including inaccurate documentation of postal code, the postal code may not be current, and the postal code may not accurately represent the location of the stroke event. Limitations also include errors associated with the collection of Statistics Canada census data including under or over coverage of specific populations (Statistics Canada – Population Coverage Error, 2013).

There are uncertainties associated with the graphic representation of spatial data including the positional accuracy of events (Longley et al., 2005). Misclassification of stroke events within transport time service areas may occur but likely would be non-differential due to the large sample size. The position of the DA centroid (with joined census data) may not represent the location of highest population density within the DA resulting in a misclassification of the population at risk within a transport time service area.

6.8 Study Conclusion

IV-tPA administered within 1.5-hours of symptom onset is significantly associated with good outcome. By spatially defining and characterizing populations with predicted and realized geographic access to acute stroke care within critical OTT time windows of 2.0-hours, 3.0-hours and 4.5-hours (based on interval times derived from the study database), an increase in both predicted geographic access and realized access to care at a stroke centre in Alberta from 2002 to 2007 was demonstrated. By 2010, it is estimated that 54% of the Alberta population had predicted geographic access to care at a stroke centre within 2.0-hours of symptom onset. The geographic expansion of stroke centre coverage associated with the addition of 11 PSCs, widened adoption of a standardized EMS stroke screen tool and direct transport protocols, and stroke awareness campaigns have had an important role in the increased utilization of specialized stroke care in Alberta at a population level. Increased utilization has been demonstrated at the individual level where the proportion of patients with a discharge diagnosis of ischemic stroke who received IV thrombolysis increased from 8.6% to 11.3% across Alberta by 2007 (Jeerakathil et al., 2010). Stroke awareness campaigns should be ongoing as it is imperative that EMS services be utilized for stroke and that onset-to-dispatch time intervals be kept to a minimum.

A reanalysis using current data for all ischemic stroke events for the province would more accurately reflect predicted and realized geographic access to (hyper)acute stroke care, utilization of specialized stroke care services, and outcomes. A more accurate assessment of how geographic access has changed in accordance with the provincial initiative to enhance stroke care could be carried out. Future research might also include a location-allocation (optimization technique) analysis of SPCs and SCs to minimize impedance (time and distance), maximize coverage, minimize the number of facilities required, and maximize attendance. An analysis of the spatial distribution of OTT time intervals using density surface or interpolation maps (Map 7.2) would inform potential courses of action to reduce times and increase the number of events who meet critical treatment time windows.

CHAPTER 7: THESIS CONCLUSION

This thesis concludes with a summary integrating findings from the three studies, a discussion of the merits and limitations of integrating GIS, and suggestions for future research.

7.1 Summary of Thesis Findings

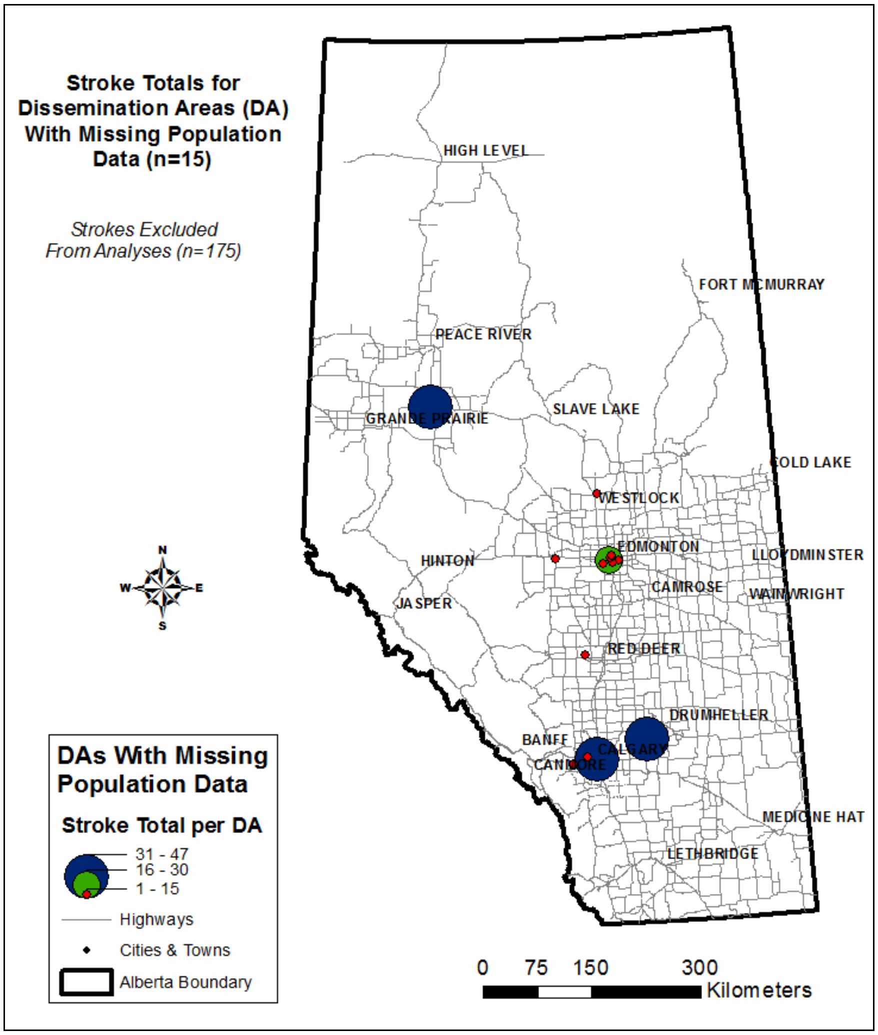
7.1.1 Missing Data

There were 175 stroke events excluded from DA rate calculations, cluster analyses, and DA centroid distance to a Stroke Centre or Stroke Prevention Clinic

Table 7.1. Characteristics of stroke events excluded from DA calculations.

AB Administrative Data 2002/03 to 2007/08	
Stroke Total, n (%)	175 (0.8)
DA, n (%)	15 (0.4)
Urban, n (%)	10 (67.0)
Age, mean (SD)	76.8 (12.5)
Sex, female (%)	58.3
Stroke Type (%)	
Ischemic	60.6
TIA	32.0
ICH	5.7
SAH	1.7
EMS Transport (%)	73.1
Destination (%)	
CSC	44.0
PSC	22.3
Other	33.7
Disposition (%)	
Discharged	57.1
Transfer	31.4
Died	11.4

Map 7.1. Dissemination Areas with strokes and unavailable Statistics Canada census data.



calculations due to unavailable Statistics Canada census data for 15 Dissemination Areas. Characteristics of this population are shown in Table 7.1 and Map 7.1.

7.1.2 Thesis Conclusions

Geographic distributions of stroke and mortality in Alberta from 2002/03 to 2007/08 were not random and varied according to stroke type. Ischemic stroke and TIA hot spots were associated with increased distance from a SPC; in contrast, ICH and SAH hot spots were inversely associated with distance from a SPC. There was higher odds of in-hospital mortality after stroke with longer drive times to a Stroke Centre. ICH and SAH stroke types, NIDDM, atrial fibrillation, and non-EMS transport were also associated with higher odds of mortality. Recurrent stroke was associated with a longer drive time from a SPC. Odds of recurrent stroke were also higher for males, TIA stroke type, NIDDM, atrial fibrillation and transport to a non-Stroke Centre.

Health services before admission to hospital affected outcome. Proximity to a SPC reduced the odds of having a recurrent stroke event. EMS transport and transport to a CSC were associated with reduced odds of mortality. This is despite the unique challenges for EMS related to the geographical expanse of the province and realities of rural and remote coverage and despite CSCs receiving more severe strokes.

It was expected that DAs within high clusters of stroke and mortality would have a higher proportion of documented risk factors but this was not the case for all stroke types. This finding may be related to differing risk distributions, regional differences in the coding of risk factors and the type (a diagnosis bias) and quality of care that is associated with having a documented risk factor.

GIS methods can be used to predict actual EMS ground transport time. The addition of 6 PSCs over a 5-year time period accompanied by the widened adoption of a standardized EMS stroke screen tool and direct transport protocols resulted in a greater proportion of Albertans having predicted geographic access to care at a stroke centre by ground transport within critical time windows based on median time intervals derived from the dataset. This coincides with individual level data demonstrating increased frequency of administration of thrombolysis for AIS.

There was a marked difference between documented risk factors for urban and rural areas (Table 7.2). There was also a marked difference in the potential for early reperfusion therapy between those living in rural versus urban locations. Discrepancy was higher between predicted geographic access and realized access to stroke care at a PSC within the 15 to 75-minute transport time service area. Use of EMS for transport and direct transport protocols would likely increase utilization of PSCs.

Table 7.2 Urban-rural proportions of stroke events with a documented risk factor.

Proportion of Events (%)	Urban	Rural
IDDM	1.07	1.28
NIDDM	19.70	18.63
Hypertension	58.35	47.09
Atrial Fibrillation	17.59	13.95
Hypercholesterolemia	19.99	12.92

Given that the 'symptom onset-to-dispatch' is more likely to alter CSC and PSC service area coverage and that this interval is unaffected by enhancements to pre-hospital and ED care, public stroke awareness campaigns (prevention, recognition of stroke symptoms, dialing 9-1-1 for symptoms of stroke) should be ongoing.

7.2 Merits and Limitations of Integrating GIS in Stroke Research

7.2.1 Merits of Integrating GIS

The merits of incorporating GIS technology in this research included the capacity to join individual level and administrative area level data, data storage and retrieval, the generation of maps and diagrams (e.g. spider), and facilitation of exploratory spatial analyses including cluster analysis, network analysis, and service area analysis.

Available tools used in the analyses included selection, extraction, overlay and proximity. GIS and software capabilities extend far beyond what was used for this research and, providing that spatial data are available, support original evidence-based complex analyses.

The opportunity to visualize patterns of stroke and mortality in map format as they relate to terrain, SPC and SC locations, cities, and transportation infrastructure augments current understanding of stroke as a health problem in Alberta and highlights the complexities of providing pre-hospital and emergent care.

GIS and spatial methods are well suited for analyses that involve adverse health states (including stroke) that are time critical. An assessment of geographic access to care that did not incorporate a spatial component would be incomplete. GIS can be used to assess spatial relationships between geographic access to care, health care utilization, and health outcomes.

Spatial analysis can support a variety of study types in health research including clinical trials, prospective cohort, and case-control studies. Bias as a result of differential losses due to attrition can be assessed spatially; if attrition rates are higher for participants who reside at greater distances from health care, and time to health care is significantly associated with outcome, bias may be introduced into the study. If low income neighbourhoods are under-represented in clinical trials, findings may not be generalizable to a particularly vulnerable population. Cases and controls in a case-control study can be assessed for differences in characteristics with regard to the populations from which they are drawn.

7.2.2 Limitations of Integrating GIS

There are limitations associated with integrating GIS and spatial methods in health research including data quality and availability, data sharing and maintaining the confidentiality of individuals and households (Rushton et al., 2008). Data may only be available in larger geographic units because of concerns regarding the stability of rates (particularly for rare outcomes) and/or confidentiality which can limit investigations relating to healthcare utilization and clinical activity (Boulos, 2004).

Spatial and temporal aggregation of data can preserve data confidentiality and still permit fine-level analyses with reliable results (Boulos, 2004). However, data aggregation creates spatial uncertainty. There can be errors in the positioning of objects (e.g. using area centroids), errors in the attributes associated with the objects, and errors in modelling spatial variation (Boulos, 2004).

There is the potential for the data display to be misleading and for the misinterpretation of data (Monmonier, 1991). Data quality, confounding factors and bias may influence the interpretation of results. Therefore, it is important that robust statistical methods are used to support thematic data layers in order to avoid visual bias. The researcher cannot infer causation from correlation, make inferences about individuals from population data (ecological fallacy), or fail to consider the broader context in which individual behaviour occurs (atomistic fallacy) (Boulos, 2004).

7.3 Future Research Directions

Suggestions for future research include the following:

(1) a cluster analysis of spatially smoothed stroke (by type) and mortality rates over time to assess the spatial migration of clusters and potential associations with enhancements to preventive, pre-hospital, and SC care;

(2) a more localized and detailed examination of the mortality hot spot;

(3) a reanalysis of predicted and realized access to preventive and acute stroke care using current data to inform whether geographic access to acute stroke care is (more) equitable and whether mortality clusters have been reduced in size or eliminated. Potential associations with alterations to the provision of pre-hospital and ED care could be examined;

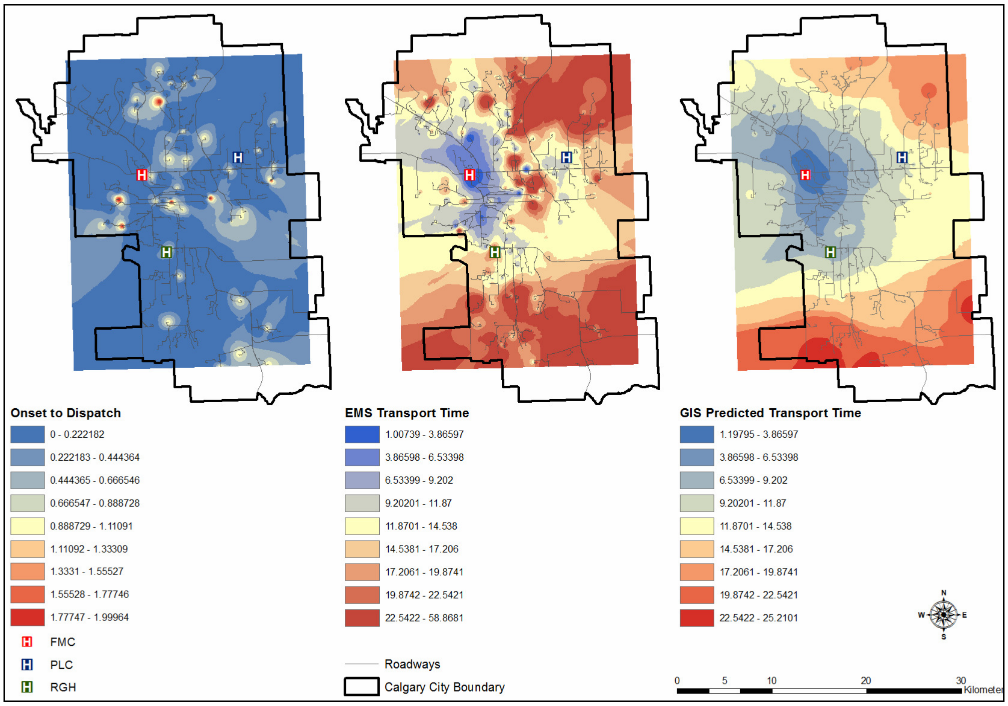
(4) a location-allocation (optimization technique) analysis of SPCs and SCs to minimize impedance, maximize coverage, minimize the number of facilities required, and maximize attendance;

(5) an analysis of the spatial distribution of OTT time intervals using density surface or interpolation maps (Map 7.2) to inform potential courses of action to reduce interval times and increase the number of events who meet critical treatment time windows; and

(6) a multi-level spatial analysis that provides the ability to examine the dual complexity of compositional (individual level) and contextual (neighbourhood level) predictors on stroke and stroke mortality using geographically weighted regression techniques. Predictors might include population proclivity to seek preventive care, the efficacy of preventive care, and differentials with respect to meeting thrombolysis criteria if geocoded linked EMS, ED, in-hospital, and administrative and pharmaceutical data were available for all patients assessed at a SPC and/or admitted to hospital in Alberta with a diagnosis of stroke. Novel neighbourhood predictors might include proximity to

environmental pollutants (particulate matter), smoking rates, drug use, crime rates, public transportation infrastructure, access to healthy foods, access to green spaces, and distance to specialized stroke care. GIS technology enables the linking of individual data with contextual information and aggregated ecologic predictors for the preparation of multi-level spatial models to better evaluate and distinguish biological, contextual and ecological effects (16).

Map 7.2. EMS interval times using Inverse Distance Weighted (IDW) technique.



In this research, the identification of a mortality hot spot, urban-rural differences in clustering of reported risk factors, regional variations in realized access to stroke care, and populations with predicted access to care that is outside of critical transport time areas suggest that there may be inequities that warrant further investigation.

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