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Secondary Stroke Prevention in Ontario: A Population Based Cohort Study

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Abstract

Background: Secondary stroke prevention can reduce subsequent vascular events, mortality, and accumulation of disability. Current rates of adherence to secondary stroke prevention indicators are unknown. Our aim was to evaluate secondary stroke prevention care in Ontario, Canada.

Methods: A retrospective cohort study using health administrative databases included all adults discharged alive following an ischemic stroke from April 2010 to March 2019. Indicators of secondary stroke prevention, including laboratory testing, physician visits, and receipt of routine influenza vaccinations, were evaluated among survivors in the one year following a stroke event. Use of medication was also assessed among individuals over the age of 65 years, and within subgroups of stroke survivors with diabetes and atrial fibrillation.

Results: After exclusions, 54,712 individuals (mean age 68.4 years, 45.7% female) survived at least one year following their stroke event. In the 90 days following discharge from hospital, most individuals (92.8%) were seen by a general practitioner, while 26.2% visited an emergency department. Within the year following discharge, 66.2% and 61.4% were tested for low density lipoprotein and glycated hemoglobin, respectively; and 39.6% received an influenza vaccine. Among those over the age of 65 years, 85.5% were prescribed a lipid-lowering agent and 88.7% were prescribed at least one antihypertensive medication. In those with diabetes, 70.3% were prescribed an anti-hyperglycemic medication, while 84.9% with atrial fibrillation were prescribed an anticoagulant.

Conclusion: Secondary stroke prevention, especially for important laboratory values, remains suboptimal, despite thorough best practice guidelines. Future studies should explore barriers to better secondary stroke care.

Highlights

- Most individuals post stroke receive anti-hypertensives and lipid-lowering medications
- A significant proportion of individuals do not have their LDL or HbA1C tested within the year post stroke, and even fewer have their values fall within targets
- Almost all individuals see their family doctor within 90 days of discharge post stroke

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Introduction

Global incidence of stroke is increasing(1), and is expected to continue to increase over time(2). Ischemic stroke survivors are at high risk of recurrent stroke, with approximately one in four individuals experiencing another stroke within five years(3). Many risk factors for ischemic stroke are modifiable through management of comorbidities(4). Control of these factors is important for prevention of further stroke, other vascular conditions, accumulation of disability, and mortality.

Guidelines for secondary stroke prevention outline lipid and glucose targets and suggest recommendations for first line antihypertensive and lipid-lowering medications (Table 1) (5). Previous studies have demonstrated that increased adherence to secondary stroke prevention guidelines reduces the risk of subsequent stroke (6–9). Additionally, early visits to primary care after discharge from hospital post stroke have also shown to reduce risk of hospital readmission(10). However, contemporary rates of secondary stroke care and healthcare utilization post stroke at the population level are currently unknown.

Aims and Hypothesis

Our goal was to evaluate secondary stroke prevention indicators in Ontario - the most populous province in Canada, with a population of over 15 million residents(11). An understanding of the current state is essential to identify opportunities to improve adherence to secondary stroke guidelines and inform targeted communication, education, and resource allocation. We hypothesized that care would be suboptimal, based on previous studies assessing acute management of stroke(12), and secondary prevention of other conditions(13–16).

Methods

Study Design and Setting

We conducted a retrospective population-based cohort study using administrative data from Ontario, Canada from April 1st, 2010, to March 31st, 2019. We intentionally stopped our study in 2019 to allow for a 1-year follow-up with minimal influence of the COVID-19 pandemic where care may have been affected. Within the province of Ontario, residents receive access to physician, hospital, and other healthcare services through the single-payer Ontario Health Insurance Plan (OHIP). Reporting followed the Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement(17) (Supplementary Material 1-A).

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Data Sources

Healthcare administrative databases available at ICES (www.ices.on.ca) were used to complete the study. ICES is an independent, non-profit institution housing administrative data in Ontario, Canada. We included several datasets linked using unique encoded identifiers that are outlined in Supplementary Material 1-B. We also used several ICES-derived datasets created using validated case definitions for diabetes(18), hypertension(19), and congestive heart failure(20) (Supplementary Material 1-B). All datasets were linked using unique encoded identifiers and analyzed at ICES.

Participants

Individuals with an ischemic stroke (using International Classification of Diseases, 10th revision (ICD-10) codes – Supplementary Material 1-C) as the admission diagnosis, from April 1st, 2010, to March 31st, 2019, were included (Figure 1). Date of discharge from hospital was considered the index date. Use of these codes have been previously validated(21). Hemorrhagic strokes were not included as secondary stroke prevention is different in this population(22). Exclusion criteria (with associated ICD-10 codes in Supplementary Material 1-D) included 1) receiving palliative care in the one year prior to the index date or within thirty days after, as secondary stroke care would be adjusted in these scenarios; 2) previous transient ischemic attack or ischemic stroke, as individuals with previous events may require more advanced secondary stroke care; 3) living in long term care (LTC) within 1 year prior to the index date; 4) hospital encounters lasting over 30 days; or 5) death within one year of hospital discharge. Individuals with missing age, sex, or health card number, or who were not Ontario residents, were also excluded. For outcomes involving medication use, a sub-cohort of individuals aged 66 years and older at time of discharge (medications are covered through ODB for individuals aged 65 years and older) was retained. For outcomes assessing a three year follow-up, individuals accrued on or after April 1st, 2017, were excluded. Post hoc analyses were completed excluding individuals admitted to a LTC facility within the year after the index date.

Indicators of Secondary Stroke Prevention

The following indicators of secondary stroke prevention were assessed at one and three years following the index date: 1) receipt of a low density lipoprotein (LDL) test, and of those tested, rates of falling within target range of ≤1.8 mmol/L (based on Canadian Stroke Best Practice Recommendations(5)), 2) receipt of a glycated hemoglobin (HbA1C) test, and of those

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tested, rates of falling within target range of ≤7%, 3) receipt of an influenza vaccine using physician billing codes (Supplementary Material 1-D) or drug identification number if provided via a pharmacy, 4) receipt of a lipid-lowering agent, 5) receipt of an antihypertensive agent, 6) receipt of an anti-hyperglycemic medication, including insulin, in those with diabetes, and 7) receipt of an anticoagulant in those with atrial fibrillation.

If an individual received more than one laboratory test during the follow-up period, the most recent test was selected. Post hoc analyses also stratified receipt of laboratory values by presence or absence of diabetes and in atrial fibrillation, as guidelines are less clear in cardioembolic strokes. Medications were considered based on receipt of at least one prescription during the follow-up. In another post hoc analysis, participants with continual use of medications, defined by no gaps in prescriptions for more than 14 days, was considered.

Healthcare Utilization

Healthcare utilization was also assessed. This included emergency department visits, and visits to a family physician or CHC, neurologist, or physiatrist, within ninety days after discharge. Data on time spent at home, and not within a health care institution such as hospital, rehabilitation or mental health facility, or LTC was also collected.

Statistical Analysis

Continuous descriptive characteristics were summarized using means and standard deviations (SD), while categorical variables were summarized using frequencies and percentages. All analyses were performed using SAS version 9.4.

Ethics

Use of data through ICES is governed under section 45 of Ontario's Personal Health Information Protection Act and does not require review by a Research Ethics Board or patient consent.

Results

Cohort selection is presented in Figure 1. After exclusions, 54,712 individuals survived at least one year, while 36,506 survived at least three years following their first ischemic stroke. The mean (SD) age was 68.4 years (14.1) and 25,012 (45.7%) were female. A description of the overall cohort is presented in Table 2. Only 3,332 (6.1%) individuals were admitted to a LTC facility within the year after discharge from their ischemic stroke.

One-Year Indicators of Secondary Stroke Prevention

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Secondary stroke prevention indicators are presented in Table 3 for individuals surviving at least one year. Among these, 66.2% received an LDL test within the one year after discharge from hospital, and of those tested, 54.5% fell within target of ≤1.8 mmol/L. Individuals without a history of atrial fibrillation were more likely to have their LDL tested, and were less likely to have their LDL within target range. An HbA1C was checked for 61.4%, with 81.5% falling within the target of ≤7%. Individuals with a history of diabetes were more likely to have their HbA1C checked in the year following discharge, as were those without a history of atrial fibrillation. Influenza vaccinations were recorded for 39.6% of individuals. Results were similar when considering only those who were not admitted to LTC, with results presented in Supplementary Material 2-E.

Receipt of medication was assessed in 32,801 individuals over the age of 65 years. Of these, 85.5% received a lipid-lowering medication in the year post discharge, with the majority of prescriptions (77.1%) occurring within the first 90 days. Similarly, 88.7% of individuals received at least one antihypertensive medication after their stroke, again with the majority in the first 90 days (81.0%). Of the 11,836 individuals over the age of 65 years with diabetes, 70.3% were prescribed an anti-hyperglycemic medication within the year following discharge. Of the 7,262 individuals over the age of 65 years with atrial fibrillation, 84.9% were prescribed an anticoagulant within the year following their stroke. Long term compliance with recurrent prescriptions was reduced for all medications, and is presented in Supplementary Material 2-F.

Three-Year Indicators of Secondary Stroke Prevention

When restricting to individuals who survived three years following their ischemic stroke, marginal increases were observed in most secondary stroke prevention indicators (Supplementary Material 2-G). Apart from the receipt of antihypertensive agents (91.5%) and anticoagulants in those with a history of atrial fibrillation (90.4%) all indicators remained below 90%.

Healthcare Utilization

Over a quarter of patients (26.2%) visited an emergency department within 90 days following their discharge post stroke. Most individuals (92.8%) saw a primary care physician within 90 days of discharge, while nearly half (47.9%) were seen by a neurologist, and 22.6% were seen by a physical medicine and rehabilitation specialist within the same period. The mean (SD) number of days spent at home in the year follow-up was 328.8 (76.5) days.

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Discussion

Secondary stroke prevention is an important part of care post stroke and involves a multimodal approach to risk factor management through lifestyle adjustment, monitoring of comorbidities, and use of medications. Our study found that while some secondary stroke care indicators in Ontario appear to be sufficient, such as prescriptions for antihypertensives, others remain suboptimal, such as LDL and HbA1C testing and achievement of targets for these tests.

The reasons behind low rates in some areas are unknown. Although family physicians provide the majority of long term secondary stroke prevention care(10), they are facing record numbers of burnout (23). Guidelines are also becoming more complex and exist for almost every chronic disease, making it difficult to recall targets and interventions for each patient and each condition. A previous qualitative study on the barriers to use of chronic kidney disease guidelines suggested several reasons for nonadherence from family physicians including cognitive overload, differing priorities, and lack of awareness of the guidelines altogether(24).

Our study found that many individuals do not have their LDL (16%) or HbA1C (20%) checked, even within three years following an ischemic stroke. For many individuals, even when they are checked, the values do not fall within target recommendations. This is despite high levels of lipid-lowering and diabetic medication prescription, and despite many individuals seeing their family physician, on average, once every two months in that first year after stroke. Our findings suggest better glycemic compared to lipid control among those tested with over 80% within target of ≤7% HbA1C versus 54.5% for LDL ≤1.8 mmol/L. This is in contrast to a previous study from Ontario comparing rates in urban versus rural settings of only around 54% for HbA1C(25). Additionally, compliance to important secondary prevention medication over the year follow-up drops, especially for medications like statins and anticoagulants, which each show a reduction in individuals continuing with medications of approximately 50%. As better adherence to guidelines has been associated with a reduced risk of stroke(7), future studies should address barriers to medication use and laboratory monitoring in the post stroke setting to improve secondary stroke risk.

Another important factor that has been recommended for secondary prevention is the receipt of an annual influenza vaccine, which appears unique to the Canadian Stroke Guidelines (5). Our results were found to be suboptimal and significantly lower than the target of 80% of high risk individuals set out by the Public Health Agency of Canada(26). These rates also appear

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lower than previous population averages in the general population, which is typically around 70% in those over the age of 65(27), and lower than in previous studies of individuals with cardiovascular disease(28). Interestingly, despite recommendations in the Canadian guidelines for secondary prevention, most previous research on influenza vaccination is in primary stroke prevention(29–31). Future studies could assess the effect of influenza vaccines on secondary prevention specifically,

Most individuals in our study were prescribed antihypertensives and lipid-lowering medications. It is not prudent for all individuals to be on these therapies, as some will have adequate blood pressure or lipid levels without use of medications, and others still may have allergies or intolerances. Previous studies have shown that use of statins after stroke, even in those with LDL levels within target range, is associated with reduced mortality and vascular outcomes(32,33). Overall, our findings were similar to previous studies. Dalli et al. found that 75% of individuals were prescribed antihypertensives and 84% statins(6), while Kapral et al. found over 80% of individuals with a previous stroke were prescribed antihypertensives(25).

This study has several strengths. We obtained a very large sample size of over 50,000 individuals in the largest province in Canada, to capture secondary stroke prevention trends at a population level, resulting in one of the largest studies assessing secondary stroke prevention care indicators. We also were able to incorporate laboratory data to assess rates of meeting recommended secondary stroke prevention targets, which is not available in all administrative database studies. This study also has several limitations. First, administrative data has limits, including capturing that a medication is dispensed, without knowing about compliance, or potential appropriate reasons for nonadherence to guidelines. Additionally, some medications such as low dose aspirin are available over the counter and would not be captured using the ODB. Further, influenza vaccinations may be given by other prescribers under guidance of a physician or pharmacist, such as a nurse practitioner, which may not be captured in our dataset. Other important factors for secondary stroke prevention including blood pressure readings, diet, and smoking status, are also not available through our administrative datasets. Control of these factors is also crucial for secondary stroke prevention. Next, we stopped accrual in 2019 to minimize the effect of the COVID-19 pandemic on secondary stroke prevention care. Because of this, results may not be generalizable to a post-COVID era, and future research may be warranted to assess if the COVID-19 pandemic affected secondary stroke care. Lastly, we only

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recruited patients in Ontario and those not previously living in a LTC facility, which may limit generalizability to other jurisdictions and populations.

In summary, secondary stroke prevention care in Ontario remains suboptimal in many areas. Future work should explore barriers to better care.

Data Availability: The data set from this study is held securely in coded form at ICES. Although data-sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access.

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The authors disclose no competing interests

Statement of Authorship

JLF – Conception, design, analysis, interpretation, drafting, revision, and approval

MKK – Conception, design, analysis, interpretation, drafting, revision, and approval

BC – Design, analysis, interpretation, revision, and approval

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376 **Table 1: Summary of Selected Secondary Stroke Prevention Guidelines from the Canadian**
377 **Stroke Best Practice Recommendations (5)**

Lipids and lipid lowering agents	• Individuals who have had an ischemic stroke or transient ischemic attack should have their serum lipid levels assessed and optimally managed [Evidence level A]. • Lipid levels, including total cholesterol, triglycerides, low-density lipoprotein [LDL] cholesterol, and high-density lipoprotein [HDL] cholesterol, should be measured in patients presenting with ischemic stroke or transient ischemic attack [Evidence Level B]. • Statin pharmacotherapy should be prescribed for secondary prevention of stroke in individuals who have had a non-cardioembolic ischemic stroke or transient ischemic attack, [Evidence Level A]. • A target LDL cholesterol level of < 1.8 mmol/L is recommended [Evidence Level B].
Diabetes and anti-hyperglycemic agents	• Patients with diabetes who have had an ischemic stroke or transient ischemic attack should have their diabetes assessed and optimally managed [Evidence Level A]. • Patients with ischemic stroke or transient ischemic attack should be screened for diabetes with either a fasting plasma glucose, or 2-hour plasma glucose, or glycated hemoglobin (A1C), or 75 g oral glucose tolerance test in either an inpatient or outpatient setting [Evidence Level C]. • In general, A1c values should be targeted to ≤7.0% in patients with either type 1 or type 2 diabetes (and stroke or transient ischemic attack), as this target provides strong benefits for the prevention of microvascular complications [Evidence Level A]. • In patients with stroke and type 2 diabetes in whom glycemic targets are not achieved with standard oral antihyperglycemic medications, an antihyperglycemic agent with demonstrated benefit on major cardiovascular outcomes (for example, SGLT-2 inhibitors or GLP-1

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	receptor agonists) should be considered [Evidence Level B].
Antihypertensive agents	• Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of a stroke or transient ischemic attack [Evidence Level A]. • Treatment with an ACE inhibitor and thiazide/thiazide-like diuretic combination is recommended [Evidence Level A]. • Long-acting diuretics may be considered over short-acting [Evidence Level B].
Anticoagulants	• Patients with ischemic stroke or transient ischemic attack *and* atrial fibrillation should receive oral anticoagulant therapy for secondary stroke prevention [Evidence Level A].
Influenza vaccination	• Influenza vaccination is recommended as it has been shown to be associated with a decreased risk of stroke or cardiovascular events, particularly in patients with pre-existing cardiovascular risk factors [Evidence Level B].

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Table 2: Baseline characteristics of individuals hospitalized with an incident stroke between April 1, 2010 and March 31, 2019 and survived one year after discharge.

	N (%) (n = 54,712)
Demographics	
Age, mean (SD)	68.4 (14.1)
Female sex	25,012 (45.7)
Rural residence	7,275 (13.3)
Living in the lowest neighbourhood income quintile	9,349 (17.1)
Comorbidities	
Charlson comorbidity index, mean (SD)	2.0 (1.6)
Alcohol misuse	2,008 (3.7)
Atrial fibrillation	8,752 (16.0)
Congestive heart failure	6,469 (11.8)
Chronic kidney disease	5,229 (9.6)
Coronary artery disease	16,201 (29.6)
Diabetes	18,378 (33.6)
Dyslipidemia	15,477 (28.3)
Hypertension	41,593 (76.0)
Peripheral vascular disease	5,206 (9.5)

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Table 3. Secondary prevention care in the one year following hospital discharge for an incident stroke between April 1, 2010 and March 31, 2019 among individuals who survived one year after discharge

	N (%) (n = 54,712)
Indicators of Secondary Stroke Prevention	
Lipid testing	36,211 (66.2)
Lipid control among individuals tested (LDL ≤ 1.8 mmol/L)	19,741/36,211 (54.5)
Lipid testing among those without atrial fibrillation	30,840 / 45,960 (67.1)
Lipid control among those with LDL testing without atrial fibrillation (LDL ≤1.8 mmol/L)	16,421 / 30,840 (53.2)
HbA1C testing	33,585 (61.4)
Glucose control among individuals tested (HbA1c ≤ 7%)	27,381/33,585 (81.5)
HbA1C testing among those without atrial fibrillation	28,382 / 45,960 (61.8)
Glucose control among those with HbA1C testing without atrial fibrillation	23,022 / 28,382 (81.1)
HbA1C testing among those with diabetes	14,963 / 18,378 (81.4)
Glucose control among those with HbA1C testing with diabetes	9,059 / 14,963 (60.5)
HbA1C testing among those without diabetes	18,622 / 36,334 (51.3)
Receipt of influenza vaccine	21,680 (39.6)
*Pharmacologic risk factor management**	n = 32,801
Lipid-lowering therapy^	28,061 (85.5)
Receipt within 90 days of discharge	25,301 (77.1)
Antihypertensive medications#	29,087 (88.7)
Receipt within 90 days of discharge	26,578 (81.0)
Anti-hyperglycemic medication /Among	8,320 /11,836 (70.3)

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individuals with diabetes	
Anticoagulant medications / Among individuals with atrial fibrillation	6,164/7,262 (84.9)
Healthcare Utilization	
ER visits	
Mean (SD) visits in the one-year follow-up	1.21 (2.3)
Visit within 90 days of discharge	14,361 (26.2)
Primary care	
Mean (SD) visits in the one-year follow-up	6.7 (5.9)
Visit within 90 days of discharge	50,787 (92.8)
Visit to a neurologist within 90 days of discharge	26,208 (47.9)
Visit to a physiatrist within 90 days of discharge	12,355 (22.6)
Home time	
Mean (SD) days at home within 90 days of discharge	73.3 (25.4)
Mean (SD) days at home within 1 year of discharge	328.76 (76.5)

LDL, low density lipoprotein; HbA1C glycated hemoglobin

*Medication information only available for the subgroup > 65 years.

^ Lipid-lowering therapies included statins, ezetimibe, or fibrates

#Antihypertensive medications included angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, diuretics, or alpha blockers

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