The Canadian Journal of Neurological Sciences (2025), 1–8
doi:10.1017/cjn.2025.10405

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Original Article

Predicting 1-Year Stroke Recurrence and Mortality in Stable Outpatients Following Ischemic Stroke and Transient Ischemic Attack

Alisia Southwell[1,*], Anne Marie Liddy[2,*], Anna Chu[3], Bing Yu[3], Jiming Fang[3], Susan E. Bronskill[1,3,4,8], Moira Kapral[3,7,8], Peter C. Austin[1,3,8], Lusine Abrahamyan[3,8,9] and Richard H. Swartz[1,2,3,4,5,6]

[1]Evaluative Clinical Sciences Platform, Sunnybrook Research Institute, Toronto, ON, Canada, [2]Department of Medicine (Neurology), Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [3]ICES, Toronto, ON, Canada, [4]Hurvitz Brain Sciences Program, Sunnybrook Research Institute, Toronto, ON, Canada, [5]Institute of Medical Science, University of Toronto, Toronto, ON, Canada, [6]Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, Canada, [7]Department of Medicine (General Internal Medicine), University of Toronto, Toronto, ON, Canada, [8]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada and [9]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada

ABSTRACT: ***Background:*** Patients with stroke or transient ischemic attack (TIA) are at high early risk of mortality and morbidity. Current risk prediction tools focus on patients after hospital discharge but not on those surviving to outpatient follow-up. We examined whether demographic and medical history data could predict 1-year stroke recurrence and mortality, among those discharged alive and event-free for 90 days after stroke and 1 day after TIA. ***Methods:*** Data were obtained from the Ontario Stroke Registry (13,848 stroke and 13,059 TIA patients) and linked to administrative databases. Two-thirds of each cohort were used for model derivation and one-third for validation. Multivariable regression models were used to predict stroke recurrence and all-cause mortality. ***Results:*** There were 238 (2.71%) recurrent strokes in the ischemic stroke and 298 (3.44%) in the TIA cohorts at one year. Increasing age and previous stroke/TIA were associated with an increased risk of recurrent stroke in both cohorts. A higher modified Rankin Scale and diabetes were associated with an increased risk of recurrent stroke in the stroke cohort and heart failure, smoking and discharge location in the TIA cohort. Time-dependent areas under the curve were modest, 0.59 (0.54–0.64) and 0.59 (0.55–0.64) for the stroke and TIA validation cohorts, respectively. C-statistics from derivation and validation cohorts for mortality ranged from 0.74–0.78. ***Conclusion:*** The predictive accuracy of the models was quite low after accounting for several risk factors. Additional risk factors associated with stroke recurrence for people seen in outpatient stroke clinics, and innovative approaches to individualized secondary prevention are needed.

RÉSUMÉ: Pré diction de la récidive des AVC et de la mortalité au bout d'un an chez des patients ambulatoires stables après un AVC ischémique et un accident ischémique transitoire. ***Contexte*** : Les patients ayant subi un AVC ischémique ou un accident ischémique transitoire (AIT) présentent un risque élevé de mortalité et de morbidité à court terme. Les outils actuels de prédiction des risques se concentrent sur les patients après leur sortie de l'hôpital, mais pas sur ceux qui survivent et font l'objet d'un suivi ambulatoire. Nous avons ainsi examiné si des données démographiques et les antécédents médicaux de ces patients pouvaient prédire la récidive des AVC et la mortalité au bout d'un an chez les patients ayant obtenu leur congé et ne donnant à voir aucun incident pendant 90 jours après un AVC ischémique et 1 jour après un AIT. ***Méthodes*** : Nos données ont été obtenues à partir du registre des AVC de l'Ontario (13 848 patients victimes d'un AVC ischémique et 13 059 patients victimes d'un AIT) et étaient reliées à des bases de données administratives. Les deux tiers de chaque cohorte ont été utilisés pour la dérivation de notre modèle et un tiers pour la validation. Des modèles de régression multivariables ont été utilisés pour prédire la récidive des AVC et la mortalité toutes causes confondues. ***Résultats*** : On a dénombré 238 (2,71 %) AVC récurrents dans la cohorte des AVC ischémiques et 298 (3,44 %) dans la cohorte des AIT, et ce, au bout d'un an. L'âge avancé et les antécédents d'AVC ischémiques et d'AIT étaient associés à un risque accru d'AVC récurrent au sein des deux cohortes. Un score plus élevé à l'échelle de Rankin modifié et le diabète étaient associés à un risque accru de récidive d'AVC dans la cohorte des AVC ischémiques, tandis que l'insuffisance cardiaque, le tabagisme et le lieu d'obtention de son congé de l'hôpital étaient associés à un risque accru dans la cohorte des AIT. Les aires sous la courbe ROC dépendantes du temps étaient modestes, soit respectivement 0,59 (0,54-0,64) et 0,59 (0,55-0,64) pour les cohortes de validation des AVC ischémiques et des AIT. Les statistiques de concordance des cohortes de dérivation et de validation pour la mortalité variaient entre 0,74 et 0,78. ***Conclusion*** : La précision prédictive des modèles était assez faible après avoir tenu compte de plusieurs facteurs de risque. L'identification de facteurs de risque supplémentaires associés à la récidive des AVC chez les personnes suivies dans des cliniques ambulatoires spécialisées dans les AVC, ainsi que des approches innovantes en matière de prévention secondaire individualisée, demeurent nécessaires à cet égard.

Keywords: Ischemic stroke; mortality; outpatient clinic; predictive model; recurrent stroke

(Received 1 April 2025; final revisions submitted 7 July 2025; date of acceptance 13 August 2025)

Corresponding author: Richard H. Swartz; Email: rick.swartz@sunnybrook.ca
*Alisia Southwell and Anne Marie Liddy Authors contributed equally to this work.

Cite this article: Southwell A, Liddy AM, Chu A, Yu B, Fang J, Bronskill SE, Kapral M, Austin PC, Abrahamyan L, and Swartz RH. Predicting 1-Year Stroke Recurrence and Mortality in Stable Outpatients Following Ischemic Stroke and Transient Ischemic Attack. *The Canadian Journal of Neurological Sciences*, https://doi.org/10.1017/cjn.2025.10405

Highlights

- Existing recurrent stroke risk prediction models do not target the population that survives to outpatient follow-up.
- We developed and validated risk prediction models for patients attending stroke prevention clinics, but the predictive accuracy of the models was modest.
- Additional risk factors and innovative approaches to individualized secondary prevention are needed.

Introduction

Over the past 15 years, there has been considerable effort to reduce short-term morbidity and mortality after stroke and to reduce stroke recurrence after transient ischemic attack (TIA). For those with TIA, the emphasis on the first 90 days began in earnest in 2004 when studies showed high 30- and 90-day stroke recurrence rates.[1,2] With changes in process, expedited assessments and treatment, rates of recurrent stroke after TIA dropped significantly.[2] Similarly, organized systems of care,[3,4] and expanded eligibility for thrombolysis [5] and endovascular thrombectomy,[6,7] have helped to reduce mortality and improve 90-day outcomes after ischemic stroke. Given these changes, there are more people living with the effects of stroke than ever before.

Most of these advances have focused on the early, highest-risk period after stroke or TIA. However, the long-term risk of stroke recurrence remains high. Even when people survive the high-risk 90-day period after stroke and TIA without adverse events, they are still at over seven times the risk of having another stroke in the next 1-year and five times the risk after 3- and 5-years compared to matched controls.[8] Globally, the 10-year risk of stroke recurrence after TIA or minor stroke is 20%.[9]

It is well recognized that the more vascular risk factors are controlled, the lower the recurrence risk.[10,11] Yet, almost no stroke survivors achieve targets on all risk factors, and many have recurrent strokes despite good risk control.[11] It remains unclear how much of the long-term recurrence or mortality risks for people seen in outpatient stroke clinic settings can be attributable to identifiable factors. To date, many clinical prediction models exist for in-hospital,[12] 7-day,[13] 30-day[14,15] and 3-month outcomes[16] for stroke/TIA patients. In a systematic review of 66 prediction models for survival and functional outcome in ischemic stroke patients, outcome periods ranged from seven days to ten years, with most models examining outcomes in the first three months.[17] However, people seen in stroke prevention clinics are those who survive the initial high-risk period and typically have sufficient residual function to attend outpatient clinics. Few of the abovementioned prediction models account for this survival bias. Given the limited resources for specialty stroke prevention services, aging global population and increasing survival of people after stroke,[18] there is a need to better predict longer-term stroke recurrence and mortality for the stroke prevention clinic population.

The primary objective of this study was to determine whether demographic, medical history and stroke event data reflecting the episode of care for the index stroke, and available in an outpatient setting, could be used to create a prediction model for 1-year stroke recurrence after accounting for the competing risk of death. Specifically, we aimed to identify factors associated with 1-year outcomes among patients who survive and are event-free 90 days after stroke, and one day after TIA discharge, from acute care, to mimic when these patients would typically be seen in a secondary prevention clinic. These timings reflect national practice and guidelines for stroke management.[19]

Methods

Study cohort

Our cohort was obtained from the Ontario Stroke Registry (OSR) held at ICES (formerly known as the Institute for Clinical Evaluative Sciences). The OSR was a province-wide registry developed for monitoring and reporting on the quality of stroke care that included a population-based sample of patients with stroke and TIA who were seen at any of the province's 150 acute care institutions until 2013.[20] Stroke was determined by clinical presentation, confirmed by brain imaging and obtained through chart reviews performed by trained abstractors with clinical expertise.

We included all patients aged 18 or older who were discharged alive between April 1, 2002 and March 31, 2013 after hospitalization or emergency room visit with a diagnosis of ischemic stroke or TIA. We limited our cohort to Ontario residents who were in hospital for under 90 days and were not discharged to a long-term or palliative care facility (Figure 1). Patients with missing information on rurality index, income and modified Rankin scale (mRS) were excluded as based on our prior experience patients with missing information in these factors have higher rates of missingness in other variables in administrative datasets. Next, we selected the patients who had a recorded referral to a secondary prevention clinic at discharge resulting in a sample of 26,907 patients (13,848 with ischemic stroke and 13,059 with TIA). Finally, to capture patients who survived long enough to attend an outpatient clinic, we conducted a landmark analysis, excluding TIA patients who had died or had a recurrent stroke within one day ($n = 63$) and ischemic stroke patients who had died or had a recurrent stroke within 90 days of discharge ($n = 703$). The landmark date (1 and 90 days after hospital discharge) was used as the new index date (time zero) for the risk prediction models.

To assess outcomes, we used the Canadian Institute for Health Information Discharge Abstract Database (DAD) to capture hospital admissions for ischemic stroke, and the Ontario Registered Persons Database (RPDB) to capture deaths. The DAD includes data from the discharge abstracts of all acute care hospitals in Ontario, including admission and discharge dates and diagnoses, and the RPDB provides basic demographic information and vital statistics about anyone who has ever been eligible for Ontario's universal health insurance plan. These datasets were linked using unique encoded identifiers and analyzed at ICES.

Candidate variable selection

The OSR collected 505 variables on patients with stroke/TIA including sociodemographic characteristics, vascular risk factors, comorbidities, stroke type, severity, Charlson comorbidity index score, CHADS2 and CHA2DS2-VASc risk scores at admission, hospital care, complications and outcomes including length of stay, neurologic deficit and mRS at discharge, discharge medications and disposition.

To begin variable selection, we used clinician input to filter from the initial variables in OSR to 136 clinically relevant variables, including those with a potential relationship to stroke recurrence and excluding those with known poor coding reliability. We excluded variables that would not be potentially available to a clinician assessing a patient's risk in an outpatient clinic setting, had high missingness (>10%) or low prevalence (<3%). This selection process resulted in 18 candidate variables for univariable analysis for all models.

https://doi.org/10.1017/cjn.2025.10405

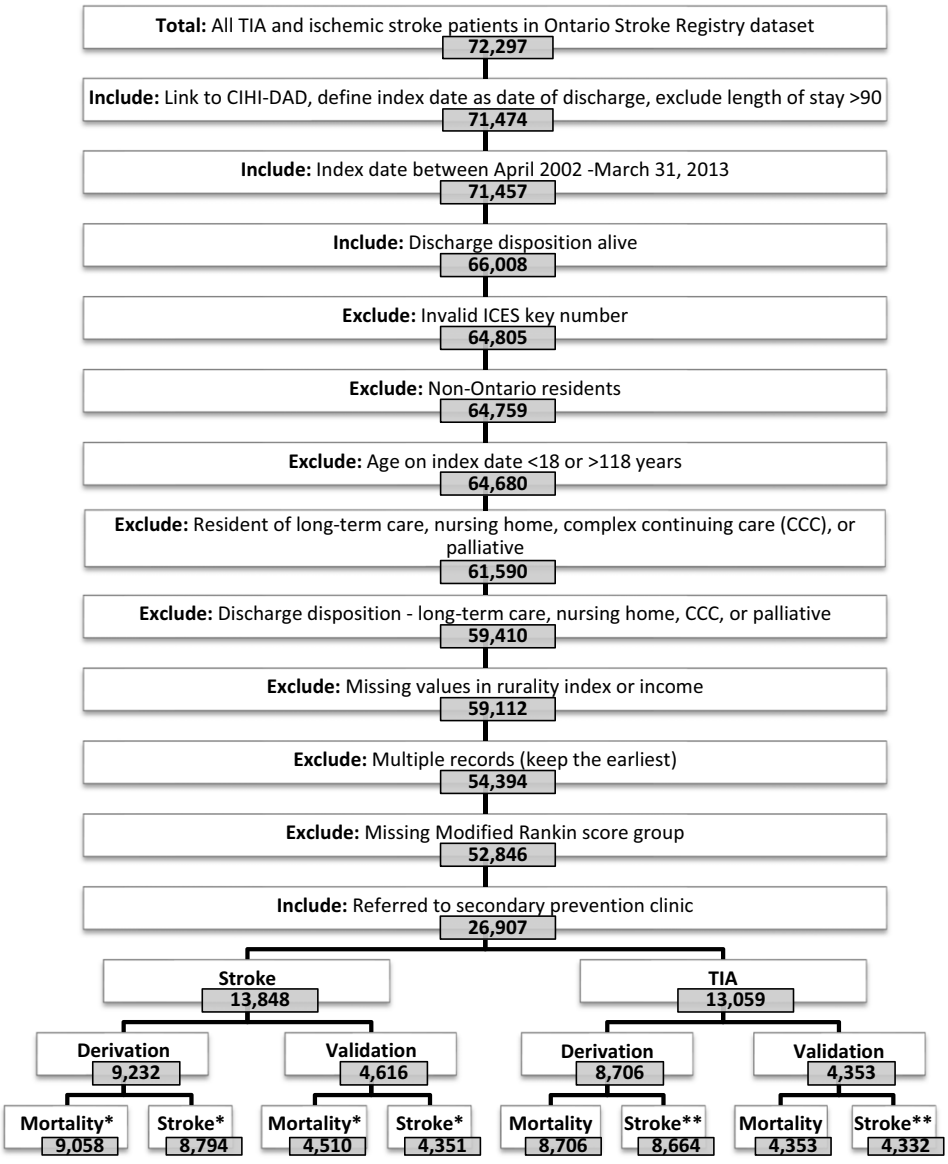

Figure 1. Flowchart of final cohort creation from OSR and CIHI-DAD datasets. *CIHI-DAD = Canadian Institute for Health Information Discharge Abstract Database.* *Excluded patients who had died/recurrent stroke within 90 days of discharge. **Excluded patients who had died/recurrent stroke within one day of discharge.

Statistical analysis

Model creation

The ischemic stroke and TIA cohorts were randomly divided into a derivation cohort (2/3 of the sample; n = 9,232 for ischemic stroke, 8,706 for TIA) and a validation cohort (1/3 of sample; n = 4,616 for stroke; 4,353 for TIA). Characteristics of the derivation and validation cohorts were reported prior to model development using means for age and proportions for categorical variables and compared using standardized mean differences, with values of <0.10 indicating negligible differences between the two cohorts.

Our primary and secondary outcomes were stroke recurrence and all-cause mortality one year after their respective landmark periods. For univariate analysis, we examined the association between each candidate predictor and recurrent stroke outcome using a Fine-Gray subdistribution hazard (sdHR) model to account for the competing risk of death. For univariate analysis to predict risk of death at one year, we used a univariate Cox proportional hazards model. For age, as a continuous variable, we tested linearity of association with outcomes using cubic spline analyses with five knots at percentiles 5, 25, 50, 75 and 95. We performed multivariable regression analyses with backward selection using a p-value of <0.10 for variable inclusion in the first model. Age, as a continuous variable, and sex were chosen a priori for inclusion; and other variables with a p-value <0.10 were included in the final models.

Model evaluation

Multicollinearity was assessed by evaluating condition indices, and no instances of high correlations (condition index >10) between variables in the initial and final models were found. Model discrimination was evaluated using time-dependent area under the curve (AUC) for the competing risk stroke models and c-statistic for the mortality models. We assessed the performance of each model in the validation cohorts, applying the risk coefficients from the derivation models and determining the c-statistic or time-dependent AUC. We also constructed calibration plots to compare the outcome rates by decile of predicted risk versus observed risk in the validation cohorts.

https://doi.org/10.1017/cjn.2025.10405

Table 1. Baseline characteristics of the derivation and validation cohorts: candidate predictor variables

	Ischemic stroke cohort		TIA cohort	
Candidate predictor variables	**Derivation cohort (n = 9,232)**	**Validation cohort (n = 4,616)**	**Derivation cohort (n = 8,706)**	**Validation cohort (n = 4,353)**
Age at discharge (mean ± SD)	69 ± 14	68 ± 14	70 ± 13	70 ± 13
Sex (Female)	3,983 (43%)	2,011 (44%)	4,302 (49%)	2,114 (49%)
Modified Rankin (0–2)	3,072 (33%)	1,513(33%)	8,392 (96%)	4,205 (97%)
History of:				
Asthma/COPD	986 (11%)	514 (11%)	852 (10%)	405 (9%)
Atrial fibrillation	1,226 (13%)	640 (14%)	887 (10%)	442 (10%)
CAD*	2,009 (22%)	960 (21%)	1,775 (20%)	885 (20%)
Cancer	622 (7%)	330 (7%)	488 (6%)	249 (6%)
Dementia**	315 (3%)	168 (4%)	308 (4%)	150 (3%)
Diabetes	2,313 (25%)	1,190 (26%)	1,912 (22%)	883 (20%)
Hyperlipidemia	3,954 (43%)	1,934 (42%)	3,673 (42%)	1,805 (42%)
Hypertension	6,315 (68%)	3,100 (67%)	5,547 (64%)	2,721 (63%)
Peripheral vascular disease	461 (5%)	225 (5%)	321 (4%)	152 (4%)
HF/Pulmonary edema	511 (6%)	267 (6%)	316 (4%)	176 (4%)
Hemodialysis or renal disease	281 (3%)	116 (3%)	230 (3%)	101 (2%)
Smoking (in past 6 months)	1,964 (21%)	1,075 (23%)	1,241 (14%)	602 (14%)
Stroke/TIA	2,175 (24%)	1,058 (23%)	2,502 (29%)	1,212 (28%)
Valvular heart disease	405 (4%)	176 (4%)	330 (4%)	130 (3%)
Discharge location				
Acute other	375 (4%)	196 (4%)	150 (2%)	96 (2%)
Inpatient rehab	2,281 (25%)	1,167 (25%)	56 (1%)	21 (1%)
Home/Retirement home	6,576 (71%)	3,253 (75%)	8,500 (97%)	4,236 (97%)

Data presented as n (%) unless otherwise indicated. Standardized differences were<0.10 for comparisons of all variables between derivation and validation cohorts (data not shown). *Includes myocardial infarction, angina, percutaneous coronary intervention or coronary artery bypass grafting. **Includes Alzheimer's disease, chronic confusion or senility. CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; HF = heart failure; TIA = transient ischemic attack; SD = standard deviation.

All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. We followed the TRIPOD guideline[21] for reporting our study (Supplemental Table S1).

Results

A full summary of baseline characteristics of the derivation and validation cohorts is available in Table 1. Univariate analyses between each candidate predictor and outcome variable in derivation cohorts are reported in Supplemental Tables S2 and S3.

Among patients with an ischemic stroke (mean age 69 years; 43% female), 238 (2.7%) had a recurrent stroke within one year of landmark period. Of the 18 candidate variables, seven entered the final model. Age, prior stroke/TIA, mRS 3–5 and diabetes were associated with an increased risk of recurrent stroke. Comorbid hypertension predicted a reduction in risk of recurrent stroke. The time-dependent AUC was 0.62 (0.59–0.66) in the derivation cohort and 0.59 (0.54–0.64) in the validation cohort (Table 2, Figure 2A).

Among patients with a TIA (mean age 70.0 years; 49% female), 298 recurrent strokes were observed within one year (3.44%). Nine of the 18 candidate variables entered the final model. Age, hypertension, prior stroke/TIA, CHF or pulmonary edema, smoking and discharge location (acute other) were all associated with an increased risk of recurrent stroke. Cancer and valvular heart disease were associated with a decreased risk of recurrent stroke. The time-dependent AUC was 0.67 (0.65–0.70) in the derivation cohort and 0.59 (0.55–0.64) in the validation cohort (Table 3, Figure 2B).

Models for mortality in both the TIA and stroke cohorts had greater discrimination (Supplemental Table S4). The C-statistics of both the derivation and validation models ranged from 0.74–0.78 in the stroke and TIA cohorts (Supplemental Table S5; Figures 2C and 2D).

Discussion

Most outcome prediction models for stroke/TIA were developed to identify outcomes after discharge; however, these models may not apply to the population of people seen in stroke prevention clinics. One-third of people discharged alive will pass away, be institutionalized, have a recurrent stroke or MI within 1 day of discharge for TIA or 90 days of stroke.[8] Thus, most predictive models are weighted to outcomes that occur before clinic visits, limiting utility in an outpatient clinical setting. By imposing a

https://doi.org/10.1017/cjn.2025.10405

Table 2. Predictors of recurrent stroke among ischemic stroke patients in the final model, derivation cohort

Predictor variables	***n* = 8,794**	
Number (%) of outcomes	238 (2.71%)	
	sdHR (95% CI)	***P*-value**
Age	1.02 (1.01–1.03)	< 0.01
Sex (Female)	1.04 (0.81–1.35)	0.74
Modified Rankin (3–5)	1.33 (1.02–1.73)	0.04
History of:		
Atrial Fibrillation	1.34 (0.96–1.86)	0.09
Diabetes	1.34 (1.00–1.79)	0.048
Hypertension	0.74 (0.55–0.99)	0.04
Stroke/TIA	1.52 (1.14–2.01)	< 0.01
Time–dependent AUC (derivation cohort)	0.62 (0.59–0.66)	
Time-dependent AUC (validation cohort)	0.59 (0.55–0.64)	

AUC = area under the curve; CI = confidence interval; sdHR = subdistribution hazard ratio; TIA = transient ischemic attack.

landmark period – including only those who survived to typical stroke prevention clinic visit windows without events – the current study sought to provide better models to guide clinicians in stroke clinics on identifying the highest-risk individuals.

In the stroke cohort, the model predicting stroke recurrence had relatively few variables: age, sex, mRS, atrial fibrillation, diabetes, hypertension and previous history of stroke/TIA. Although most of these predictors have been included in previous models, it is interesting to note that some predictors do not appear consistently. For instance, age has been found to be unrelated or being of low importance in predicting the risk of recurrent stroke in a number of previous studies, but was important in our models.[22,23] In the TIA cohort, age, prior history of stroke/TIA, CHF, smoking, cancer, hypertension, valvular heart disease and discharge to another facility other than rehabilitation were predictors of recurrent stroke, and similarly some of these variables do feature as significant predictors in other studies exploring the risk of stroke after TIA but not consistently.[24–26]

The association between hypertension and the decreased risk of recurrent strokes in the ischemic stroke cohort may be unexpected, but information on the relationship between hypertension and recurrent stroke in the literature is contradictory.[27] It is possible that there is greater adherence to hypertension treatment when the diagnosis is a stroke rather than a TIA. This is reflected in our TIA cohort findings, where hypertension was positively associated with a risk of stroke one year post TIA. Unfortunately, data concerning the effectiveness of treatment for known hypertension or treatment adherence were not available for this analysis.

The negative association between stroke outcome and history of cancer in the TIA cohort is contrary to the literature which reports an increased risk of recurrent stroke in patients with cancer.[28–30] However, prior studies suggest that this increased stroke risk may be associated with more recent cancer diagnoses (i.e., within the first 6–12 months)[31] and our dataset only specifies "history of cancer" without information on diagnosis dates or cancer type. Though the exact associations between cancer and stroke recurrence require further investigation, our results reinforce the complexity of this relationship.[32] The unexpected protective effect of the baseline cancer and valvular heart disease on the risk of recurrent stroke in the TIA cohort might also be explained by unmeasured confounding.

The unreliability of sex as a significant predictor variable was expected given the competing evidence for and against its impact on stroke recurrence and mortality.[33,34] We did not find sex as a predictor of stroke recurrence or mortality. There is some evidence that women have poorer medical management at presentation, which may act as an additional confounder in the relationship between sex and stroke recurrence and/or mortality.[34] In the TIA cohort, there were no sex effects for the stroke recurrence model. However, women had a reduced mortality risk compared to men. Women presenting with TIA are more likely to have atypical symptoms and less likely to have diffusion-weighted MR imaging changes showing a minor stroke,[35] so women may be at a lower recurrence risk.

We conducted a targeted search of past prediction models but found no model that predicted stroke recurrence or death among stroke or TIA patients treated in stroke prevention clinics or surviving the early high-risk periods. Published c-statistics from models of in-hospital or discharged cohorts have similar performance characteristics as our models, with modest predictive accuracy, which limits clinical utility (Supplemental Table S6). Historically, clinical prediction models have had more success in predicting death as opposed to stroke recurrence.[17,26,36] Those findings were consistent with our results, with models for all-cause mortality in the stroke and TIA cohorts having the greater c-statistics than the models for stroke recurrence.

Due to limitations of data availability, current models include stroke and TIA populations between 2002 and 2013 in Ontario and do not capture any potential changes in population characteristics, patient management strategies and outcomes that might have occurred thereafter, and, hence, may differ meaningfully from contemporary practice. In addition, study data did not include information on race and ethnicity, post-discharge changes in adherence to medications, rehabilitation care, lifestyle modifications and other cardiovascular health metrics such as control of blood pressure, blood glucose and total cholesterol, which could be available in outpatient settings and could improve the predictive ability of the models. Lastly, our aim was to predict outcomes

https://doi.org/10.1017/cjn.2025.10405

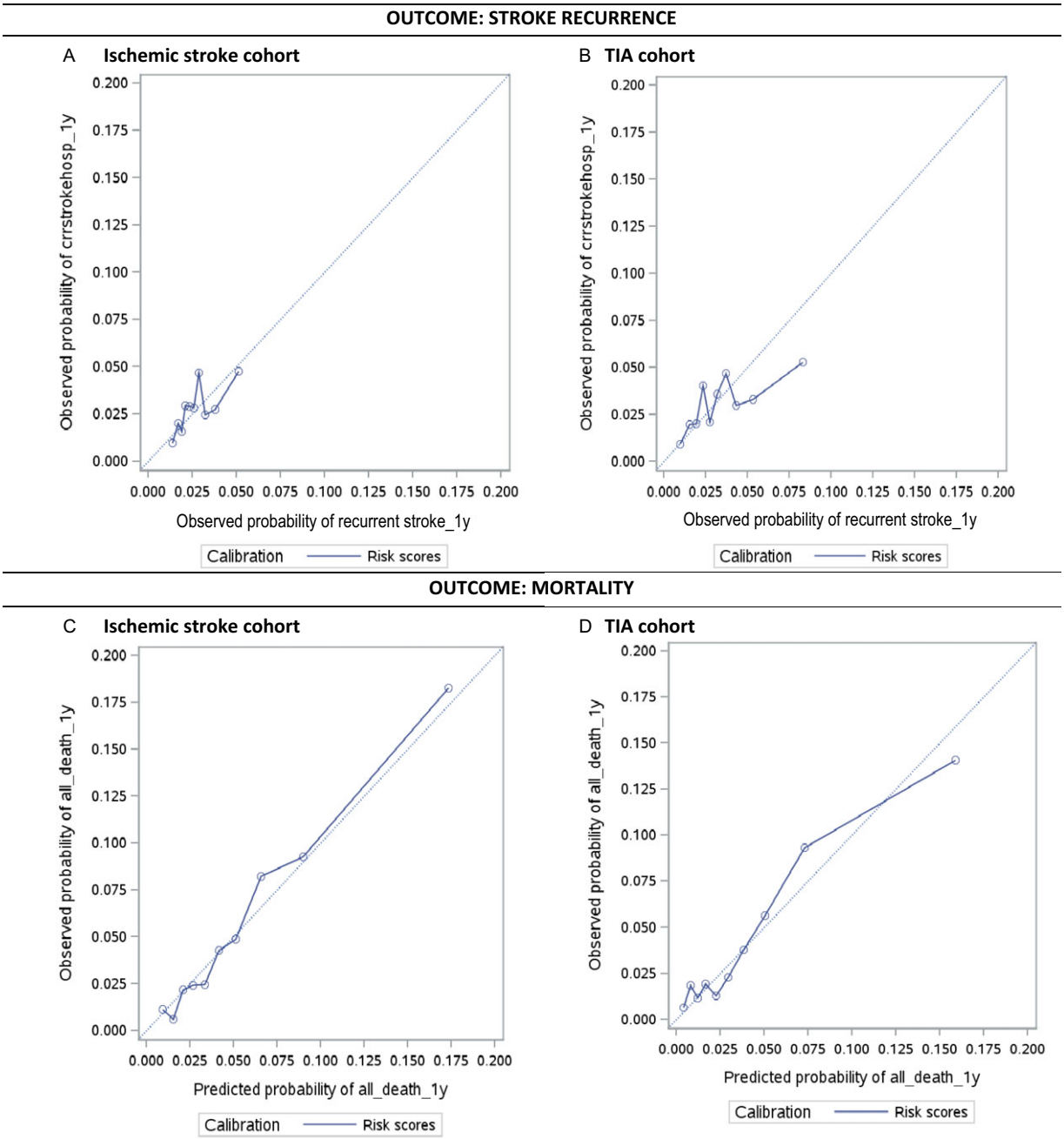

Figure 2. Calibration figures for risk prediction models in validation cohorts.

among patients who were referred to a secondary prevention clinic after TIA/stroke. While the results are not intended to be generalizable to those who were not referred it is noteworthy to mention that it has previously been shown that, in comparison with people referred to stroke prevention clinics, those who are not referred tend to be older, more likely to have dementia, live in a long-term care or in a rural residence, more often treated for the index event in a hospital without an on-site SPC and have a higher risk of 1-year mortality, but no difference in risk for recurrent stroke or TIA.[37] We also could not assess if the patient, in fact, attended the clinic after the referral and the factors potentially affecting referral decisions or access.

Previous prediction models have emphasized early stroke recurrence within the highest-risk period in the first 90 days post stroke or TIA,[24,25] unlike in the present study, where the emphasis is on patients who survived the first 90 days post ischemic stroke, or one day post TIA, without a recurrent stroke. Thus, the small number of predictor variables in the final models, the unexpected findings (e.g., hypertension and cancer), and low c-statistics in both cohorts reflect a broader theme in the stroke literature: after the early high-risk period, the risk of longer-term ischemic stroke recurrence is difficult to predict.[27] Yet, this risk is 7-fold higher than age-matched controls at one year and remains five times higher even five years after an event.[8] The current prediction models underscored the critical gaps that exist in our understanding of risk factors for stroke recurrence. Without knowledge of additional factors that increase the risk of recurrent stroke, the ability to mitigate this risk is limited. Measures of target attainment

https://doi.org/10.1017/cjn.2025.10405

Table 3. Predictors of recurrent stroke among TIA patients in the final model, derivation cohort

Predictor variables	***n* = 8,664**	
Number (%) of outcomes	298 (3.44%)	
	sdHR (95% CI)	***P*-value**
Age	1.03 (1.02–1.04)	< 0.0001
Sex (Female)	0.90 (0.72–1.13)	0.38
Discharge Location (Acute Other)	2.06 (1.19–3.57)	< 0.01
Discharge Location (Inpatient Rehab)	0.38 (0.05–2.82)	0.34
History of:		
Cancer	0.46 (0.24–0.89)	0.02
Hypertension	1.51 (1.15–2.00)	< 0.01
HF/Pulmonary Edema	1.84 (1.19–2.85)	< 0.01
Smoking (in past 6 months)	1.41 (1.01–1.98)	0.04
Stroke/TIA	1.64 (1.30–2.08)	< 0.0001
Valvular Heart Disease	0.42 (0.19–0.94)	0.04
Time-dependent AUC (derivation cohort)	0.67 (0.65–0.70)	
Time-dependent AUC (validation validation)	0.59 (0.55–0.64)	

AUC = area under the curve; CI = confidence interval; HF = heart failure; sdHR = subdistribution hazard ratio, TIA = transient ischemic attack.

and adherence to risk reduction targets may help to fill this gap, and novel, modifiable risk factors may be needed to identify new targets. The laudable advancements in the acute treatment of stroke in recent years bring with them an increasing challenge: keeping those who have survived stroke and TIA, often with relatively little or no disability, free of recurrent stroke in the long term. Work to achieve and sustain long-term vascular risk reduction, identify novel predictors of risk, and innovative approaches to long-term individualized management are needed for improved secondary stroke prevention.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2025.10405.

Acknowledgments. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). This document used data adapted from the Statistics Canada Postal CodeOM Conversion File, which is based on data licensed from Canada Post Corporation, and/or data adapted from the Ontario Ministry of Health Postal Code Conversion File, which contains data copied under license from ©Canada Post Corporation and Statistics Canada. Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information. The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Author contributions. SA and LAM: conception, interpretation, drafting and final approval; CA, YB and FJ: analysis, interpretation, drafting and final approval; BSE, KMK and AL: interpretation, drafting and final approval; APC: analysis and interpretation, drafting and final approval; SRH: conception, acquisition, analysis, interpretation, drafting and final approval. All authors reviewed and edited the manuscript and approved its final version.

Funding statement. This study was supported by CIHR (Grant Ref No. 137038) and HSF (Project No. 000392). RHS receives salary support from an Ontario Clinician Scientist (Phase II) Award from the HSF Canada. In-kind support from the Ontario Brain Institute. Dr Moira Kapral holds the Lillian Love Chair in Women's Health, University Health Network/University of Toronto.

Competing interests. RHS reports stock ownership of Follow MD, and has contributed to an advisory board for Roche. All other authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Gladstone DJ, Kapral MK, Fang J, Laupacis A, Tu JV. Management and outcomes of transient ischemic attacks in Ontario. *CMAJ*. 2004;170:1099–1104.
2. Lioutas VA, Ivan CS, Himali JJ, et al. Incidence of transient ischemic attack and association with long-term risk of stroke. *JAMA*. 2021;325:373–381.
3. Ganesh A, Lindsay P, Fang J, et al. Integrated systems of stroke care and reduction in 30-day mortality: a retrospective analysis. *Neurology*. 2016;86:898–904.
4. Kapral MK, Fang J, Silver FL, et al. Effect of a provincial system of stroke care delivery on stroke care and outcomes. *CMAJ*. 2013;185:E483–E491.
5. Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-guided thrombolysis for stroke with unknown time of onset. *N Engl J Med*. 2018;379:611–622.
6. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731.
7. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 Hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378:11–21.
8. Edwards JD, Kapral MK, Fang J, Swartz RH. Long-term morbidity and mortality in patients without early complications after stroke or transient ischemic attack. *CMAJ*. 2017;189:E954–E961.
9. Writing Committee for the PERSIST Collaborators; Khan F, Yogendrakumar V, et al. Long-term risk of stroke after transient ischemic attack or minor stroke: a systematic review and meta-analysis. *JAMA*. 2025;333(17):1508–1519.
10. Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, Sacco RL. Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study. *Circulation*. 2012;125:2975–2984.
11. Lin MP, Ovbiagele B, Markovic D, Towfighi A. Life's simple 7' and long-term mortality after stroke. *J Am Heart Assoc*. 2015;4(11):e001470.

12. Smith EE, Shobha N, Dai D, et al. Risk score for in-hospital ischemic stroke mortality derived and validated within the get with the guidelines-stroke program. *Circulation*. 2010;122:1496–1504.
13. Ay H, Arsava EM, Johnston SC, et al. Clinical- and imaging-based prediction of stroke risk after transient ischemic attack: the CIP model. *Stroke*. 2009;40:181–186.
14. ODonnell MJ, Fang J, D'Uva C, et al. The PLAN score: a bedside prediction rule for death and severe disability following acute ischemic stroke. *Arch Intern Med*. 2012;172:1548–1556.
15. Wang Y, Lim LL, Levi C, Heller RF, Fischer J. A prognostic index for 30-day mortality after stroke. *J Clin Epidemiol*. 2001;54:766–773.
16. Weimar C, Konig IR, Kraywinkel K, Ziegler A, Diener HC, German Stroke Study Collaboration. Age and National Institutes of Health Stroke Scale Score within 6 hours after onset are accurate predictors of outcome after cerebral ischemia: development and external validation of prognostic models. *Stroke*. 2004;35:158–162.
17. Fahey M, Crayton E, Wolfe C, Douiri A. Clinical prediction models for mortality and functional outcome following ischemic stroke: a systematic review and meta-analysis. *PLoS One*. 2018;13:e0185402.
18. Heart & Stroke Foundation of Canada. 2019 Report on heart, stroke and vascular cognitive impairment. Accessed 19 December 2024. https://www.heartandstroke.ca/articles/report-2019.
19. Gladstone DJ, Lindsay MP, Douketis J, et al. Canadian stroke best practice recommendations: secondary prevention of stroke update 2020. *Can J Neurol Sci*. 2022;49:315–337.
20. Kapral MK, Silver FL, Richards JA, et al. *Registry of the Canadian Stroke Network. Progress Report 2001–2005*. Toronto: Institute for Clinical Evaluative Sciences, 2005.
21. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *Ann Intern Med*. 2015;162:55–63.
22. Elhefnawy ME, Sheikh Ghadzi SM, Albitar O, et al. Predictive model of recurrent ischemic stroke: model development from real-world data. *Front Neurol*. 2023;14:1118711.
23. Elneihoum AM, Goransson M, Falke P, Janzon L. Three-year survival and recurrence after stroke in Malmo, Sweden: an analysis of stroke registry data. *Stroke*. 1998;29:2114–2117.
24. Lemmens R, Smet S, Thijs VN. Clinical scores for predicting recurrence after transient ischemic attack or stroke: how good are they? *Stroke*. 2013;44:1198–1203.
25. Gupta HV, Farrell AM, Mittal MK. Transient ischemic attacks: predictability of future ischemic stroke or transient ischemic attack events. *Ther Clin Risk Manag*. 2014;10:27–35.
26. Purroy F, Jimenez Caballero PE, Gorospe A, et al. Prediction of early stroke recurrence in transient ischemic attack patients from the PROMAPA study: a comparison of prognostic risk scores. *Cerebrovasc Dis*. 2012;33:182–189.
27. Rundek T, Sacco RL. Prognosis after *Stroke*. In: Grotta JC, Albers G, Broderick JP, et al. *Stroke*. 6th ed. Elsevier, 2016:234–252.
28. Lau KK, Wong YK, Teo KC, et al. Stroke patients with a past history of cancer are at increased risk of recurrent stroke and cardiovascular mortality. *PLoS One*. 2014;9:e88283.
29. Navi BB, Reiner AS, Kamel H, et al. Risk of arterial thromboembolism in patients with cancer. *J Am Coll Cardiol*. 2017;70:926–938.
30. Navi BB, Iadecola C. Ischemic stroke in cancer patients: a review of an underappreciated pathology. *Ann Neurol*. 2018;83:873–883.
31. Wei YC, Chen KF, Wu CL, et al. Stroke rate increases around the time of cancer diagnosis. *Front Neurol*. 2019;10:579.
32. Dardiotis E, Aloizou AM, Markoula S, et al. Cancer-associated stroke: pathophysiology, detection and management (Review). *Int J Oncol*. 2019;54:779–796.
33. Phan HT, Blizzard CL, Reeves MJ, et al. Sex differences in long-term mortality after stroke in the INSTRUCT (INternational STRoke oUtComes sTudy): a meta-analysis of individual participant data. *Circ Cardiovasc Qual Outcomes*. 2017;10(2):e003436.
34. Rexrode KM, Madsen TE, Yu AYX, Carcel C, Lichtman JH, Miller EC. The impact of sex and gender on stroke. *Circ Res*. 2022;130:512–528.
35. Coutts SB, Moreau F, Asdaghi N, et al. Rate and prognosis of brain ischemia in patients with lower-risk transient or persistent minor neurologic events. *JAMA Neurol*. 2019;76:1439–1445.
36. Saposnik G, Kapral MK, Liu Y, et al. IScore: a risk score to predict death early after hospitalization for an acute ischemic stroke. *Circulation*. 2011;123:739–749.
37. Kapral MK, Hall R, Fang J, et al. Association between hospitalization and care after transient ischemic attack or minor stroke. *Neurology*. 2016;86:1582–1589.