ORIGINAL ARTICLE

Pharmacists as Care Providers for Stroke Patients: A Systematic Review*

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ABSTRACT: ***Background:*** Pharmacists have become an integral member of the multidisciplinary team providing clinical patient care in various healthcare settings. Although evidence supporting their role in the care of patients with other disease states is well-established, minimal literature has been published evaluating pharmacist interventions in stroke patients. The purpose of this systematic review is to summarize the evidence evaluating the impact of pharmacist interventions on stroke patient outcomes. ***Methods***: Study abstracts and full-text articles evaluating the impact of a pharmacist intervention on outcomes in patients with an acute stroke/transient ischemic attack (TIA) or a history of an acute stroke/TIA were identified and a qualitative analysis performed. ***Results***: A total of 20 abstracts and full-text studies were included. The included studies provided evidence supporting pharmacist interventions in multiple settings, including emergency departments, inpatient, outpatient, and community pharmacy settings. In a significant proportion of the studies, pharmacist care was collaborative with other healthcare professionals. Some of the pharmacist interventions included participation in a stroke response team, assessment for thrombolytic use, medication reconciliation, participation in patient rounds, identification and resolution of drug therapy problems, risk-factor reduction, and patient education. Pharmacist involvement was associated with increased use of evidence-based therapies, medication adherence, risk-factor target achievement, and maintenance of health-related quality of life. ***Conclusions***: Available evidence suggests that a variety of pharmacist interventions can have a positive impact on stroke patient outcomes. Pharmacists should be considered an integral member of the stroke patient care team.

RÉSUMÉ: Revue systématique du rôle des pharmaciens à titre de prestataires de soins dans le cas de patients victimes d'AVC. ***Contexte***: Les pharmaciens font désormais partie intégrante des équipes multidisciplinaires procurant des soins aux patients, et ce, dans plusieurs établissements de soins de santé. Bien que des données probantes aient souligné leur rôle dans les soins apportés aux patients atteints d'un certain nombre d'états pathologiques, on recense peu d'études ayant évalué leurs interventions dans le cas de patients victimes d'AVC. L'objectif de la présente revue systématique est donc de résumer les données probantes ayant évalué l'impact des interventions de pharmaciens en ce qui regarde l'évolution de l'état de santé de patients victimes d'AVC. ***Méthodes***: Dans un premier temps, nous avons identifié des résumés d'articles ou des articles complets dont le but était d'évaluer l'impact des interventions de pharmaciens sur des patients victimes d'AVC aigus/d'accidents ischémiques transitoires (AIT) ou possédant des antécédents d'AVC aigus et d'AIT. Une fois cette étape terminée, nous avons mené une analyse qualitative. ***Résultats***: Un total de 20 résumés et articles complets a été inclus. Ces publications ont fourni des données probantes justifiant les interventions de pharmaciens dans plusieurs contextes, notamment dans le cadre de services d'urgence, au moment de périodes d'hospitalisation, à l'occasion de consultations externes ou dans des pharmacies communautaires. Dans une part importante de ces publications, on a pu observer que les pharmaciens collaboraient avec les autres professionnels de la santé dans la prestation de soins. Au nombre de leurs interventions recensées, mentionnons les suivantes : participer à des équipes d'intervention en cas d'AVC ; évaluer de possibles traitements thrombolytiques ; effectuer un bilan comparatif de médicaments ; participer aux visites auprès des patients ; identifier des problèmes liés à des traitements médicamenteux et les résoudre ensuite ; réduire les facteurs de risque et sensibiliser les patients. Cette implication des pharmaciens a été associée à une utilisation accrue de traitements fondés sur des données probantes, à une meilleure adhésion à la médication, à l'atteinte d'objectifs en matière de facteurs de risque et au maintien d'une bonne qualité de vie en lien avec la santé. ***Conclusions***: Il ressort des données disponibles qu'une foule d'interventions menées par des pharmaciens peuvent avoir un impact positif sur l'évolution de l'état de santé de patients victimes d'AVC. En cela, les pharmaciens devraient être considérés comme faisant partie intégrante des équipes devant les soigner.

Keywords: Pharmacist interventions, pharmacist, multidisciplinary team, stroke

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INTRODUCTION

Stroke is associated with significant morbidity and mortality. In Canada, approximately 46,500 people are hospitalized for stroke each year. It is the third leading cause of death, a significant cause of long-term disability, and exacts a significant cost to the economy. In 2012, the estimated cost of stroke in Canada was $3.6 billion.[1] Interventions that reduce the risk of stroke and improve outcomes in stroke patients are certainly of great importance.

The pharmacist has become an integral member of the multidisciplinary team providing clinical patient care in various healthcare settings. A meta-analysis evaluated the effects of pharmacist interventions in outpatient, inpatient, and emergency department settings. There was improvement in control of modifiable risk factors (blood pressure, cholesterol, hemoglobin A_{1C} [HbA_{1C}], and blood glucose) and reduced hospitalizations and mortality. Safety

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outcomes included a reduction in adverse drug events and medication errors.[2] It is reasonable to infer that pharmacist interventions may benefit patients with cerebrovascular disease. However, minimal literature has been published evaluating the role of the pharmacist in caring for this population. The objective of the present systematic review was to summarize the available evidence evaluating the impact of pharmacist interventions on outcomes in stroke patients.

Methods

Literature Search

A systematic search was performed using the following databases: Embase (1974 to March of 2015), International Pharmaceutical Abstracts (1970 to January of 2014), Medline (1948 to March of 2015), and Medline In-Process & Other Non-Indexed Citations (1948 to March of 2015). Disease-related search and MeSH terms included: transient ischemic attack, stroke, cerebral infarction, cerebrovascular accident, brain ischemia, ischemic stroke, cerebral hemorrhage, hemorrhagic stroke, and intracranial hemorrhage. Provider-related terms included: pharmacist, pharmacy student, and pharmacy resident. No limits were applied.

Study Selection

Studies were identified and duplicates removed. One author (JB) independently screened all of the titles and abstracts, identifying relevant articles for potential inclusion. Two authors (JB and MP) independently reviewed all the remaining abstracts and full-text articles (if available) for eligibility. Discrepancies were resolved by reviewer discussion. If consensus could not be reached, two of the authors (TM and KGP) were consulted. To be eligible, the abstracts/articles had to contain an intervention by a pharmacist, pharmacy resident, or pharmacy student, and the study population had to comprise patients with an acute stroke or TIA or a history of stroke or TIA. Studies where a portion of the population had an acute stroke or TIA or a history of a stroke or TIA were included if the results pertaining to that population were reported separately. Studies were excluded if: they were not written in English; when the pharmacist intervention was inconsistent, not clearly defined, or limited to drug distribution; if the article was a review, case report, or descriptive study; or where no objective outcomes were reported. Studies in which the main intervention was anticoagulation management were also excluded, as this area of pharmacy practice is well-established in previous literature.

Data Extraction

Two authors (JB and MP) independently performed data extraction using a standardized data collection form. The following data were collected from each abstract or full-text article: (1) study characteristics (including study design, sample size, duration of follow-up); (2) patient care setting (including location and patient population); and (3) characteristics of provided care (including collaboration, degree of patient interaction, mode of patient interaction, hours of service, type of intervention, and provision of follow-up). All study outcomes were recorded.

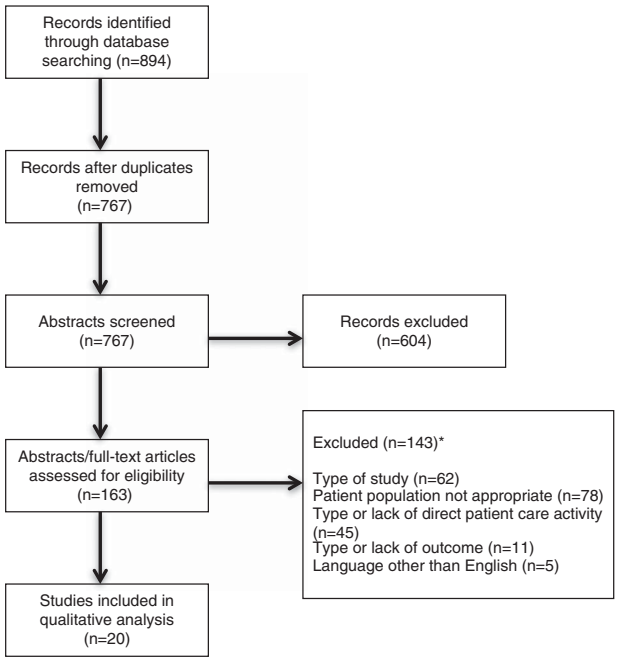

Figure 1: *Study flow diagram. *More than one reason of exclusion could be selected for each study.*

Data Analysis

A qualitative analysis was performed. The results are presented in a descriptive manner. A risk-of-bias assessment was not completed because of a lack of randomized trials and the limited number of full-text articles.

Results

A total of 894 articles were identified from the literature search, 20 of which were included in this systematic review (Figure 1). A total of 10 were published as full text and the remainder only as abstracts. The included studies consisted of four randomized controlled trials, one nonrandomized controlled trial, nine prospective observational studies, and six retrospective observational studies. Seven of the studies included patient-important outcomes such as patient satisfaction, adherence to or independence with medication, health-related quality of life (HRQoL), and readmission rates. The remainder (13) looked at such surrogate outcomes as number of drug therapy problems, changes in blood pressure or lipid panels, or medication prescription rates. The most common direct patient care activity implemented was medication counseling. While nine additional studies were included initially, they were removed after further discussion, as the intervention provided by the pharmacist within the team was unclear.[3-11] The characteristics of the included studies are outlined in Table 1.

Emergency Department

One abstract (Brandon et al.[12]) described pharmacist participation with stroke patients in the emergency department (ED). It demonstrated that addition of a pharmacist to the stroke pager team, as well as participation in assessment, dose verification, and

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Table 1: Characteristics of included studies

Study population First author, year of publication Study design	Number of patients	Direct patient care activity	Outcome(s) measured
Emergency department			
Acute stroke patients who are candidates for thrombolysis[12] Brandon, 2013 Prospective observational	Unknown	Stroke response team Thrombolytic dose calculation/verification Thrombolytic preparation Thrombolytic assessment Patient/family medication education	Decision-to-needle time
Inpatient			
Acute TIA/stroke patients taking at least two medications during hospital stay and at discharge[13*] Hohmann, 2012 Prospective observational	156	Drug-related problems identification and resolution Medication history and/or reconciliation Monitoring of drug therapy Patient assessment Recommendations	Percentage of patients who experienced a drug-related problem (DRP) Percentage of pharmacist interventions accepted by the physicians
Acute stroke patients admitted to a stroke unit[14] Hohmann, 2010 Prospective observational	250	DRP identification and resolution	DRPs identified Percentage of DRPs resolved by pharmacist
Ischemic stroke patients[15*] Khalil, 2014 Retrospective observational	124	Medication history and reconciliation Medication management review	Percentage of patients discharged on ■ lipid lowering therapy ■ antihypertensives ■ antithrombotics
Patients admitted to the stroke unit[16] Barnett, 2013 Prospective observational	93	Medication counseling Telephone referral to community pharmacy Referral letter for community medication follow up given to patient	Postdischarge use of outpatient medication adherence service
Acute stroke/TIA patients[17*] Hedegaard, 2014 Randomized controlled trial	203	Focused medication review Motivational interview approached consultation Three follow-up telephone calls over 6 months	Medication possession ratio of antiplatelets, anticoagulants, and statins 1 year after hospitalization
Acute TIA/stroke patients taking at least two medications during hospital stay and at discharge[18*] Hohmann, 2013 Prospective observational	310	Communication with HCP Medication history and/or reconciliation	Medication adherence to entire regimen at 3 months Medication adherence to antithrombotics at 3 months Medication adherence to statins at 3 months
Acute stroke patients[19] Tsai, 2012 Retrospective observational	648	Participation in stroke team Recommendations	Thrombolytic administration Early antithrombotic use Discharge antithrombotic use Antithrombotic use for atrial fibrillation Lipid-lowering therapy use
Stroke patients admitted to a rehabilitation hospital[20] Sreenivasan, 2012 Retrospective observational	116[†]	Patient education	Evaluation of educational sessions
Acute stroke patients[21] Scott, 1989 Prospective observational	Unknown	Patient education	Independence with medications
Outpatient			
Patients with a previous TIA/stroke attending a stroke prevention clinic[22*] Lindblad, 2008 Retrospective observational	153[‡]	Care plan development Communication with HCP DRP identification and resolution Medication history and/or reconciliation Monitoring of drug therapy Patient assessment Patient education Recommendations Risk-factor reduction	Targeted outcomes per intervention Physician acceptance of pharmacist suggestions
Outpatients with recent minor ischemic stroke or transient ischemic attack[23*] McAlister, 2014 Randomized controlled trial	279	Monthly clinic follow up visits x 6 months Provided lifestyle advice Monitored blood pressure and LDL level Initiated or titrated antihypertensive and/or lipid-lowering therapy	Proportion of participants who attained optimal blood pressure and fasting LDL
Stroke outpatients who had visited clinics at a hospital regularly for more than 12 months[24*] Chiu, 2008 Randomized controlled trial	160	Risk-factor reduction Patient education	Change in blood pressure, lipid profile, and fasting blood glucose Proportion of patients with satisfactory management of blood pressure, dyslipidemia, and diabetes

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Table 1. *Continued*

Study population First author, year of publication Study design	Number of patients	Direct patient care activity	Outcome(s) measured
Patients with a history of stroke[25] Nguyen, 2011 Randomized controlled trial	30	Care plan development Communication with HCP Patient education Patient assessment Recommendations Risk-factor reduction	Patient adherence to all medications (according to pharmacy refill records) Patient adherence to antithrombotics (according to pharmacy refill records) Patient achievement of blood pressure goals Patient achievement of LDL goals Patient achievement of blood glucose control goals
Patients attending a stroke bridge clinic[26] Hooker, 2012 Retrospective observational	Unknown	Care plan development Communication with HCP Medication history and/or reconciliation Patient education Risk-factor reduction	Readmission rates
Newly diagnosed stroke/TIA patients following hospital admission[27] Bruner, 2012 Prospective observational	72	DRP identification and resolution Patient education	Average pharmacist interventions per patient 30-day readmission rates
Stroke patients with a need for medication education[28] Lee, 2004 Prospective observational	22	Patient education	Change in accuracy of patient knowledge
Community pharmacy			
Patients with a TIA/ischemic stroke with Barthel index >30 at time of discharge, now living at home[29*] Hohmann, 2009 Nonrandomized controlled trial	255	Communication with HCP Patient education Patient assessment Recommendations Risk-factor reduction	Change in health-related quality of life Use of appropriate secondary prevention with antithrombotics Patient satisfaction
Patients with a history of stroke with a prescription for ticlopidine[30*] Fincham, 2000 Prospective observational	659	Monitoring of drug therapy Patient education	Number of days off from refill date
Long-term care			
Patients admitted to LTC[31*] Horning, 2007 Retrospective observational	104[§]	Recommendations	Adherence to clinical practice guidelines

DRP = drug-related problem; HCP = healthcare provider; LDL = low-density lipoprotein; LTC = long-term care, TIA = transient ischemic attack.
[*]Full-text article. [†] Number of evaluations. [‡] Number of patient encounters. [§] Number of stroke patients.

patient education, resulted in a reduction of decision-to-needle thrombolytic administration times.

Inpatient Setting

Nine studies involved a pharmacist practicing in an inpatient setting.[13-21] Hohmann et al.[13] demonstrated that a pharmacist completing medication reconciliation and participating in stroke team rounds resulted in identification of drug therapy problems in 68% of the patients, with an average of 1.8 problems per patient. In an another abstract by Hohmann et al.,[14] the stroke unit pharmacist identified an average of 1.9 drug therapy problems per patient and resolved over 95% of the problems identified. Khalil et al.[15] found that 83% of stroke inpatients who received a medication management review by a pharmacist were on antihypertensive agents, compared to 59% of patients not reviewed by a pharmacist ($p = 0.005$); 92% were on antithrombotic agents, in contrast to 77% of patients not reviewed by a pharmacist ($p = 0.025$); while the difference in percentage of patients who were on lipid-lowering agents between the two groups was not significant. Barnett et al.[16] found that telephone referral from the hospital to a community pharmacist increased the proportion of patients receiving follow-up within 4 weeks of discharge from 1.5 to 32%. Two studies evaluated the impact of pharmacist intervention on medication adherence postdischarge. Hedegaard et al.[17] randomized TIA and stroke patients to a multifaceted intervention by a pharmacist compared to usual care (no pharmacist) and demonstrated no significant difference in adherence to or persistence with secondary stroke prevention medications. Conversely, Hohmann et al.[18] found that a letter communicating medication changes sent from an inpatient pharmacist to a patient's primary care provider at hospital discharge after a stroke or TIA increased medication adherence from 83 to 91% at 3 months postdischarge ($p = 0.01$) when compared to the control group, who had medication lists included in the discharge letter by the neurologist, as before. Tsai et al.[19] suggested that recommendations by clinical pharmacists improved stroke guideline performance indicators. Sreenivasan[20] found that patient satisfaction with stroke educational sessions improved when an interdisciplinary team including pharmacists presented the program. Scott et al.[21] reported that a self-medication program that included pharmacist medication teaching resulted in 78.1% of stroke patients achieving independence with their medications.

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Outpatient Setting

Seven studies reported outcomes associated with pharmacist interventions in outpatient settings.[22-28] Lindblad et al.[22] found that a pharmacist in a stroke prevention clinic was able to make an average of 2.8 interventions per patient encounter. McAlister et al.[23] compared pharmacist-led and nurse-led case management of stroke patients in a randomized controlled trial. The control group received monthly follow-up from a nurse, who provided lifestyle advice, measured blood pressure and lipid levels, and faxed the results to their primary care physician. Patients in the intervention group were managed by a pharmacist with prescribing authority, and they received the same follow-up as the control group, as well as initiation/titration of antihypertensives and/or lipid-lowering therapy. After 6 months, 43% of patients managed by a pharmacist met both systolic blood pressure and low-density lipoprotein (LDL) goals, and 31% of patients managed by a nurse met both goals (number needed to treat = 8, $p = 0.03$). In another randomized controlled trial, Chiu et al.[24] evaluated the effect of monthly pharmacist education compared with usual care on modifiable risk factors. In the pharmacist intervention group, there was no significant difference in blood glucose control at the end of the study, but 83% of patients had adequately controlled blood pressure (compared to 40% at baseline, $p \leq 0.001$) and 40% of patients had adequately controlled lipids (compared to 13% at baseline, $p = 0.01$). In contrast, the control group had nonsignificant differences in all three endpoints. Similarly, Nguyen et al.[25] recruited patients from a stroke prevention clinic and randomized them to pharmacist intervention or usual care. The pharmacist intervention group received telephone follow-up at 3 and 6 months to evaluate medication adherence, provide education, and reassess stroke prevention goals. Patients in the pharmacist intervention group were more likely to achieve blood pressure, cholesterol, and blood glucose goals at 6 months than those in the control group, and these improvements were maintained at 1 year. Hooker et al.[26] evaluated the impact of a stroke bridge clinic involving a pharmacist, nurse practitioner, and nurse navigator on hospital readmission rates. Patients visited the clinic a week after discharge for education on risk factors and stroke prevention, medication reconciliation, and individualized treatment plans. Hospital readmission rates decreased from 14.5 to 2.2%. Similarly, Bruner et al.[27] reviewed pharmacist participation in stroke clinics, addressing drug therapy problems and providing medication education, noting that the clinics had a positive effect on 30-day hospital readmission rates. Lee et al.[28] found a non-statistically-significant improvement in patients' knowledge of their current drug therapy after pharmacist medication counseling.

Community Pharmacy

There were two studies[29,30] conducted in a community pharmacy setting. Hohmann et al.[29] evaluated the impact of pharmaceutical care on the HRQoL of patients with a TIA or stroke who were discharged home. The pharmacist provided medication reviews and education, and resolved drug therapy problems. HRQoL was assessed using a scale validated in stroke patients. In the pharmacist intervention group, HRQoL remained stable, with only one of the HRQoL scales significantly decreased from baseline; in contrast, the control group had decreases in seven of eight scales. Fincham et al.[30] found that community pharmacist intervention reduced the average number of days patients were late for ticlopidine prescription pickup from 11 to 2.

Long-Term Care

Only one study was performed in a long-term care setting. Horning et al.[31] found that the difference in stroke guideline adherence between patients receiving active pharmacist disease state management consultation services compared to traditional pharmacist drug review was not statistically significant ($p = 0.096$).

Discussion

Stroke patients interact with healthcare providers at many points throughout the course of their disease management. Diagnosis is often made in the ED, patients are admitted to acute-care hospitals, and, following discharge, stroke outpatient clinics assist patients with transition to the community and with chronic disease management. In the community, stroke patients seek medication and health-related advice from their primary care providers and may also require care in a long-term care facility. Our systematic review provides evidence that stroke patients benefit from pharmacist interventions in multiple care settings.

The available full-text studies suggest that pharmacists can positively impact stroke patient care in inpatient and outpatient settings with increased use of evidence-based therapies, medication adherence, risk-factor target achievement, and maintenance of HRQoL. The best available evidence demonstrates improvement in surrogate endpoints, and the cumulative evidence is positive for both surrogate and patient important outcomes. While providing fewer details, the reviewed abstracts largely support these studies and previously published literature supporting the value of pharmacists in several of these settings.

The acute treatment of stroke involves emergent administration of thrombolytic agents to reduce the risk of disability and death.[32] Current guidelines recommend thrombolytic therapy within 4.5 hours of symptom onset, with a door-to-needle goal time of 60 minutes.[33,34] In the ED, a pharmacist's assessment of patient eligibility and appropriateness of thrombolytic orders decreases time to administration, increases thrombolytic administration within the goal time, and improves order accuracy. Previous studies have shown that pharmacists in the ED add value through identification of medication errors, optimization of drug therapy, improvement of medication utilization, and increasing adherence to evidence-based practices.[35-38] Our systematic review provides further evidence in support of pharmacists working within the ED, with an emphasis on the subset of patients with suspected or confirmed stroke.

Organized inpatient (stroke unit) care is described as "focusing of care for stroke patients in hospital under a multidisciplinary team who specialize in stroke management."[39] When compared to care provided on a general ward, stroke unit care is associated with reductions in mortality, requirement for institutionalized care, and dependency. Pharmacists use their drug-focused therapeutic knowledge and medication management expertise to make valuable contributions to inpatient stroke care teams. A systematic review by Kaboli et al.[40] discussed the benefits provided by clinical inpatient pharmacists, including less adverse drug events, increased accuracy of medication and allergy information, shorter lengths of stay, and reductions in hospital costs. Our systematic

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review further suggests that stroke patients may also benefit from having pharmacists integrated into inpatient stroke care in order to perform these evidence-based activities.

The period of time following hospital discharge can be difficult for the patients and their family members. Previous studies[41-43] have demonstrated that pharmacist interventions in the outpatient setting are associated with significant improvements in management of modifiable risk factors, including reductions in HbA_{1C}, blood pressure, and lipid levels. Our review found that outpatient pharmacists provide patient education and risk-factor modification, which results in reduced readmission and stroke recurrence rates. In conjunction with previous literature, the results from this systematic review provide support for pharmacists in the care of stroke patients in the outpatient setting.

Despite the available evidence, there remains a significant gap between research and practice in the care of stroke patients. Until recently, national stroke guidelines in North America[44] did not include pharmacists on the list of recommended members of a stroke team. Interventions should be made in an effort to close this gap and ensure that pharmacists are active members of stroke teams in all settings.

Limitations of the Study

This review has limitations that warrant discussion. The quality and consistency of the research literature supporting integration of pharmacists into the stroke setting are limited. A search for unpublished literature was not performed. Studies with negative results may not be published, and this could lead to publication bias and an overestimation of the benefit of pharmacists in stroke care. Another limitation is that 50% of the studies included have not been published in full-text version, and abstracts provide limited information.

Conclusions

Pharmacists provide care to stroke patients in multiple settings. Supporting existing literature in other patient types, our review suggests that pharmacists improve the use of evidence-based therapies, reduce stroke risk through control of modifiable risk factors, and improve patient adherence in stroke-specific populations as well. Pharmacists should be considered an integral provider in the care of stroke patients.

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Statement of Authorship

All four authors meet the criteria set out by the International Committee of Medical Journal Editors—namely, having had substantial contributions to the conception, design, analysis, and interpretation of the work; drafting and revising the paper; final approval of the attached version; and agreement to be accountable for all aspects of the work.

Disclosures

Jade E. Basaraba, Michelle Picard, Kirsten George-Phillips, and Tania Mysak hereby declare that they have no conflicts of interest to disclose.

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