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Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017

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Abstract

The 2017 update of The Canadian Stroke Best Practice Recommendations for the Secondary Prevention of Stroke is a collection of current evidence-based recommendations intended for use by clinicians across a wide range of settings. The goal is to provide guidance for the prevention of ischemic stroke recurrence through the identification and management of modifiable vascular risk factors. Recommendations include those related to diagnostic testing, diet and lifestyle, smoking, hypertension, hyperlipidemia, diabetes, antiplatelet and anticoagulant therapies, carotid artery disease, atrial fibrillation, and other cardiac conditions. Notable changes in this sixth edition include the development of core elements for delivering secondary stroke prevention services, the addition of a section on cervical artery dissection, new recommendations regarding the management of patent foramen ovale, and the removal of the recommendations on management of sleep apnea. The Canadian Stroke Best Practice Recommendations include a range of supporting materials such as implementation resources to facilitate the adoption of evidence to practice, and related performance measures to enable monitoring of uptake and effectiveness of the recommendations. The guidelines further emphasize the need for a systems approach to stroke care, involving an interprofessional team, with access to specialists regardless of patient location, and the need to overcome geographic barriers to ensure equity in access within a universal health care system.

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Introduction

In Canada, stroke is the leading cause of adult neurological disability, with over 400,000 Canadians living with its effects, and it ranks as the third leading cause of death.[1] Stroke costs the Canadian economy more than $3.6 billion a year in physician services, hospital costs, lost wages, and decreased productivity.[2] The impact of stroke can be seen even among persons who have sustained seemingly minor strokes or transient ischemic attacks (TIA). Canadian data indicate that even individuals free of post-stroke complications in the short term are at increased risk for cardiovascular events over the long term.[3] Therefore, the opportunity to reduce the risk of recurrent strokes through aggressive vascular risk factor reduction efforts represent a significant opportunity to lower the total stroke burden. The Canadian Stroke Best Practice Recommendations have been developed to provide up-to-date evidence-based guidelines for the prevention and management of stroke, to promote optimal recovery and reintegration for people who have experienced stroke (patients, families, and informal caregivers). The target audience for this set of guidelines encompasses all health care professionals involved in the care of people with stroke across the continuum, and for those at increased risk of stroke. The goals of developing these recommendations and disseminating and promoting their implementation are to reduce practice variations in the care of stroke patients across geographic regions, reduce the gap between current knowledge and clinical practice, and to improve patient outcomes.

The 2017 update of the Canadian Stroke Best Practice Recommendations Secondary Prevention guidelines includes a summary of current evidence-based recommendations appropriate for use by health care professionals across all disciplines who provide care to patients following an ischemic stroke or transient ischemic attack. The focus of these recommendations is on the recurrent stroke risk reduction in patients who have experienced a stroke or transient ischemic attack. In some cases, this module may also guide health care providers for individuals at risk of a first stroke based on current health status and the presence of one or more vascular risk factors. However, only selected recommendations related to primary prevention are included.

Changes to secondary prevention of stroke recommendations in this update

The evidence for the topics addressed in this sixth edition has evolved in many areas. This module includes the development of a new set of core elements for delivering prevention services, which can be used to review, expand, and improve current stroke prevention services, regardless of setting.[4] With advances in imaging, the triage categories for estimating risk of recurrent stroke have been refined (Section 1). A new section has been added to address antithrombotic management in people with cervicocephalic artery dissection (Section 8). With the recent completion of the REDUCE[5] and CLOSE[6] trials, and long-term follow-up from the RESPECT trial,[7] the recommendations for people with patent foramen ovale have been updated (Section 9).

Sleep apnea is a recognized risk factor for stroke, and a condition that appears in some patients both before and following a stroke. However, the results from the recent SAVE trial[8] demonstrated that although treatment with continuous positive airway pressure (CPAP) for moderate-to-severe sleep apnea in patients with a history of coronary and cerebrovascular disease was associated with benefits, including reduced daytime sleepiness and improved health-related quality of life, the risks of recurrent stroke or major cardiovascular events were not reduced significantly. Accordingly, we have removed our previous recommendations for universal screening and treatment in stroke patients. Screening and treatment for sleep apnea should be performed as part of routine primary care based on the presence or absence of symptoms, as is currently done for patients without stroke.

Guideline development methodology

The *Canadian Stroke Best Practice Recommendations* development and update process follows a rigorous framework adapted from the Practice Guideline Evaluation and Adaptation Cycle.[9,10] These recommendations are an update to the previously published fifth edition, using the same methodology that has been reported previously[11,12] and are available on our website at www.strokebestpractices.ca. An interprofessional group of experts was convened to participate in reviewing, drafting, and revising all recommendation statements. Members with extensive experience in the

topic area were selected as were those who are considered leaders and experts in their field, having been involved in research on the topics addressed in this module. Persons with experience in the review and appraisal of research evidence and individuals (or family members of individuals) who had experienced a stroke were also included either as group members or external reviewers in the development process. The interprofessional writing group and external reviewers include stroke neurologists, nurses, family physicians, emergency department clinicians, epidemiologists, pharmacists, care coordinators, and health system planners. These experts work in a wide range of health care settings. This interprofessional approach ensured that the perspectives and nuances of all relevant health disciplines and care settings were considered in the development of the recommendations, and mitigated the risk of potential or real conflicts of interest from individual members.

A comprehensive systematic literature search was conducted to identify research evidence on the identification and management of persons following minor stroke or transient ischemic attack. The literature for this module was updated to September 2017. The writing group extensively reviewed and discussed the results and consensus was reached on the recommendation revisions, updated additions and deletions from the previous version. For a more detailed description of the methodology on development and dissemination please refer to the *Canadian Stroke Best Practice Recommendations* overview and methodology documentation available on the Canadian stroke best practices website at http://www.strokebestpractices.ca/wp-content/uploads/2017/08/CSBPR2017_Overview_Methodology_ENG.pdf.[13]

All recommendations are assigned a level of evidence ranging from A to C, according to the criteria defined in Table 1.[13,14] When developing and including "C-Level" recommendations, consensus was obtained within the writing group and validated through the internal and external review process. This level of evidence is used cautiously, and only when there is a lack of stronger evidence for topics considered important system drivers for stroke care. In some sections, additional information was identified as important to include, even though it did not meet the evidence criteria for a "recommendation". This information has been included as "clinical considerations" intended to provide additional guidance or clarity in the absence of evidence.[13] An additional category for Clinical Considerations has been added for the sixth edition. Included in this section are expert opinion statements in response to reasonable requests from a range of health care professionals who seek guidance and direction from the experts on specific clinical issues faced on a regular basis in the absence of any evidence on that topic.

Canadian Stroke Best Practice Recommendations: Secondary Prevention Guidelines, Update 2017

The following sections provide detailed updated recommendations associated with secondary prevention of stroke assessment and management practices, and do, on occasion address issues related to primary stroke prevention, although the focus of these recommendations is not primary prevention. Also, these recommendations pertain to patients with transient ischemic attack or ischemic stroke who are not immediate

Table 1. Summary of criteria for levels of evidence reported in the *Canadian Stroke Best Practice Recommendations* (update 2017).[14]

Level of evidence	Criteria
A	Evidence from a meta-analysis of randomized controlled trials or consistent findings from two or more randomized controlled trials. Desirable effects clearly outweigh undesirable effects or undesirable effects clearly outweigh desirable effects.
B	Evidence from a single randomized controlled trial or consistent findings from two or more well-designed nonrandomized and/or noncontrolled trials, and large observational studies. Desirable effects outweigh or are closely balanced with undesirable effects or undesirable effects outweigh or are closely balanced with desirable effects.
C	Writing group consensus and/or supported by limited research evidence. Desirable effects outweigh or are closely balanced with undesirable effects or undesirable effects outweigh or are closely balanced with desirable effects, as determined by writing group consensus. Recommendations assigned a Level-C evidence may be key system drivers supporting other recommendations, and some may be expert opinion based on common, new or emerging evidence or practice patterns.
Clinical consideration	Reasonable practical advice provided by consensus of the writing group on specific clinical issues that are common and/or controversial and lack research evidence to guide practice.

candidates for hyperacute thrombolysis treatment with intravenous alteplase (tPA) or endovascular thrombectomy. Management of patients with suspected acute stroke that warrant hyperacute evaluation to determine eligibility for thrombolysis/endovascular thrombectomy, are addressed in other Canadian Stroke Best Practice modules.[12,15]

Secondary stroke prevention is an individually based clinical approach aimed at reducing the risk of recurrent stroke and other vascular events in individuals who have already experienced a stroke or transient ischemic attack.[1,2] Secondary prevention recommendations in this document are directed to those risk factors most relevant to stroke, including lifestyle (diet, sodium intake, exercise, weight, smoking, and alcohol intake), hypertension, dyslipidemia, previous stroke or transient ischemic attack, atrial fibrillation, and carotid stenosis. Secondary prevention recommendations can be addressed in a variety of settings—acute care, stroke prevention clinics, and community-based care settings. They pertain to patients initially seen in primary care, those who are treated in an emergency department and then discharged, and those who are hospitalized because of stroke or transient ischemic attack. Each section of these recommendations is supported by detailed evidence tables and a summary of the evidence, a rationale for the importance of the topic, system implications to facilitate timely and efficient implementation, key quality indicators for measuring performance and resources to support implementation and uptake for health care professionals and for patients. These are available at www.strokebestpractices.ca.

Section 1: Initial risk stratification and management of nondisabling stroke or TIA

The goal of outpatient management of transient ischemic attack and nondisabling ischemic stroke is to rapidly identify cardiovascular risk factors, which may have precipitated the initial event, and to initiate treatments to reduce the risk of recurrent events. Historically, the 90-day risk of recurrent stroke following an index transient ischemic attack has been estimated to be relatively high, between 12% and 20%,[16,17] with the greatest risk of recurrence within the first two days following initial symptom onset. However, the long-term risk of recurrent events over 5 years among persons with minor stroke or transient ischemic attack who did not experience any early complications has been recently shown to be over 5 times greater.[3] For patients with multiple risk factors, the 7-day risk of stroke following a transient ischemic attack can be as high as 36%.[18] With the recent adoption or expansion of the availability of rapid transient ischemic attack clinics, and urgent evaluation by stroke specialists, the risk of recurrent stroke has been reduced significantly. The increased use and availability of sensitive neuroimaging to identify minor events as well as increased use of antiplatelets, anticoagulants, antihypertensive agents, lipid-lowering agents, and carotid endarterectomy has been shown to significantly reduce the risk of major stroke after an initial minor event.[19] A recent study by the transient ischemic attack Registry.Org group reported updated rates that were less than half that expected from historical cohorts, which were attributed to better and faster implementation of stroke prevention strategies through rapid-access transient ischemic attack clinics. Stroke recurrences at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively.[20] Similar risk reductions were demonstrated in the Early Use of Existing Preventive Strategies for Stroke (EXPRESS) study.[21] The 90-risk of recurrent stroke among patients who were referred to a dedicated transient ischemic attack clinic was 2.1% as compared with 10.3% for patients from an earlier time period, who did not have immediate access.

1.0 Patients with stroke or transient ischemic attack who present to an ambulatory setting (such as primary care) or a hospital should undergo clinical evaluation by a healthcare professional with expertise in stroke care to determine risk for recurrent stroke and initiate appropriate investigations and management strategies.

1.1 Timing of initial assessment

Table Two summarizes the triage categories and target times for initial assessment of patients with transient ischemic attack and non-disabling ischemic stroke.

1.1.1 VERY HIGH Risk for Recurrent Stroke (Symptom onset within last 48 hours)

i. Patients who present **within 48 hours** of a suspected transient ischemic attack or non- disabling ischemic stroke with the following symptoms are **considered at highest risk** of first or recurrent stroke:
   a. transient, fluctuating or persistent unilateral weakness (face, arm and/or leg) [Evidence Level B];
   b. transient, fluctuating or persistent speech disturbance/aphasia [Evidence Level B];

c. transient, fluctuating or persistent symptoms *without motor weakness or speech disturbance* (e.g. hemibody sensory symptoms, monocular vision loss, hemifield vision loss, ± other symptoms suggestive of posterior circulation stroke such as binocular diplopia, dysarthria [Evidence Level B].

ii. Patients identified as highest risk should be ***immediately*** sent to an emergency department with capacity for advanced stroke care (such as brain imaging on site, and ideally access to acute stroke treatments) [Evidence Level C] *Refer to Section 1.2 for more information on investigations.*

iii. Urgent brain imaging (CT or MRI) and noninvasive vascular imaging (CTA or MRA from aortic arch to vertex) should be completed as soon as possible **within 24 hours** [Evidence Level B]. *Refer to Section 1.2 for more information on investigations.*

iv. An electrocardiogram should be completed without delay [Evidence Level B].

1.1.2 HIGH Risk for Recurrent Stroke (Symptom onset between 48 Hours and 2 weeks)

i. Patients who present **between 48 hours and 2 weeks** from onset of a suspected transient ischemic attack or non-disabling ischemic stroke with symptoms of transient, fluctuating or persistent unilateral weakness (face, arm and/or leg), or speech disturbance/aphasia are considered at higher risk for first or recurrent stroke [Evidence Level B].

ii. These patients should receive a comprehensive clinical evaluation and investigations by a health care professional with stroke expertise as soon as possible [Evidence Level B]**, ideally initiated within 24 hours** of first contact with the health care system [Evidence Level C]. *Refer to Section 1.2 for more information on investigations.*

1.1.3 MODERATE (INCREASED) Risk for Recurrent Stroke (Symptom onset between 48 hours and 2 weeks)

i. Patients who **present between 48 hours and 2 weeks** of a suspected transient ischemic attack or nondisabling ischemic stroke with transient, fluctuating or persistent symptoms *without unilateral motor weakness or speech disturbance* (e.g. with hemibody sensory symptoms, monocular vision loss, binocular diplopia, hemifield vision loss, or ataxia) may be considered at increased risk of recurrent stroke [Evidence Level C].

ii. These patients should receive a comprehensive clinical evaluation and investigations by a health care professional with stroke expertise as soon as possible [Evidence Level B], ideally within 2 weeks of first contact with the health care system [Evidence Level C]. *Refer to Section 1.2 for more information on investigations.*

1.1.4 LOWER Risk for Recurrent Stroke (Time lapse since symptom onset greater than 2 weeks)

i. Patients **presenting more than 2 weeks** following a suspected transient ischemic attack or nondisabling ischemic stroke, may be considered as being less urgent, and should be seen by a neurologist or stroke specialist for evaluation, ideally within one month of symptom onset [Evidence Level C]. *Refer to Section 1.2 for more information on investigations.*

1.2 Diagnostic investigations

1.2.1 Initial assessment

i. Patients presenting with suspected acute or recent transient ischemic attack or non-disabling ischemic stroke should undergo an initial assessment that includes brain imaging, noninvasive vascular imaging (including carotid imaging), 12-lead ECG, and laboratory investigations.

a. Brain imaging (CT or MRI) and noninvasive vascular imaging (CTA or MRA from aortic arch to vertex) should be completed within time frames based on triage category above. [Evidence Level B]. *Refer to Table 2.*

b. CT angiography including extracranial and intracranial vasculature from aortic arch to vertex, which can be performed at the time of initial brain CT, is recommended as an ideal way to assess both the extracranial and intracranial circulation [Evidence Level B].

c. Vascular imaging is recommended to identify significant symptomatic extracranial carotid artery stenosis for which patients should be referred for possible carotid revascularization [Evidence Level A].

d. Carotid ultrasound (for extracranial vascular imaging) and MR angiography are acceptable alternatives to CTA, and selection should be based on immediate availability, and patient characteristics [Evidence level C].

ii. The following laboratory investigations should be routinely considered for patients with transient ischemic attack or nondisabling ischemic stroke as part of the initial evaluation:

a. **Initial bloodwork**: hematology (complete blood count), electrolytes, coagulation (aPTT, INR), renal function (creatinine, e-glomerular filtration rate), random glucose or hemoglobin A1c, and troponin [Evidence Level C]. *Refer to Table 3 for full list of recommended lab tests.*

b. **Subsequent** laboratory tests may be considered during patient encounter or as an outpatient, including a lipid profile (fasting or nonfasting); and, screening for diabetes with either a fasting plasma glucose, or 2-hour plasma glucose, or glycated hemoglobin (A1C), or 75 g oral glucose tolerance test [Evidence Level C].

iii. Patients with suspected transient ischemic attack or ischemic stroke should have a 12-lead ECG to assess cardiac rhythm and identify atrial fibrillation or flutter or evidence of structural heart disease (e.g. myocardial infarction, left ventricular hypertrophy) [Evidence Level B].

iv. For patients being investigated for an acute embolic ischemic stroke or transient ischemic attack, ECG monitoring for more than 24 hours is recommended as part of the initial stroke work-up to detect paroxysmal atrial fibrillation in patients who would be potential candidates for anticoagulant therapy [Evidence Level A].

Clinical considerations

i. MRI is superior to CT scan in terms of diagnostic sensitivity for transient ischemic attack, and may provide additional information that could guide diagnosis, prognosis, and management decision-making. Decisions regarding MRI scanning should be based on MRI access, availability, and timing of appointments.

1.2.2 Additional cardiac investigations for embolic stroke of undetermined source (ESUS)

i. For patients being investigated for an acute embolic ischemic stroke or transient ischemic attack of undetermined source *whose initial short-term ECG monitoring does not reveal atrial fibrillation* but a cardioembolic mechanism is suspected, prolonged ECG monitoring for at least 2 weeks is recommended to improve detection of paroxysmal atrial fibrillation in selected patients aged $\geq$55 years who are not already receiving anticoagulant therapy but would be potential anticoagulant candidates [Evidence Level A].
ii. Echocardiography should be considered in cases where a stroke mechanism has not been identified [Evidence Level C].

1.3 Functional assessment

i. Selected patients with transient ischemic attack or ischemic stroke should be assessed for neurological impairments and functional limitations when appropriate (e.g. cognitive evaluation, screening for depression, screening of fitness to drive, need for potential rehabilitation therapy, and assistance with activities of daily living), especially for patients who are not admitted to hospital [Evidence Level B]. *Refer to Rehabilitation Module for additional information (Hebert et al 2016).*[22]
ii. Patients found to have any neurological impairments and functional limitations should be referred to the appropriate rehabilitation specialist for in-depth assessment and management [Evidence Level C].

Section 2: Lifestyle behaviors and risk factor management

A healthy lifestyle, which includes a healthy balanced diet, exercise, weight control, reduction and avoidance of alcohol and tobacco, reduces the risk of an initial stroke and the risk of a subsequent stroke for patients with a prior history of stroke. Data from the Global Burden of Disease Study 2013[23] were used to estimate the population-attributable fraction (PAF) of stroke-related disability-adjusted life-years (DALYs) associated with 17 potentially modifiable risk factors. While global estimates were provided, data from separate countries were also reported. Stroke burden among Canadians was attributed to a variety of modifiable risk

Note: These recommendations are applicable to stroke of ischemic and hemorrhagic origin unless otherwise stated.

2.0 Risk factor assessment

i. Persons at risk of stroke and patients who have had a stroke should be assessed for vascular disease risk factors, lifestyle management issues (diet, sodium intake, exercise, weight, alcohol intake, smoking), as well as use of oral contraceptives or hormone replacement therapy [Evidence Level B].
ii. Persons at risk of stroke should receive individualized information and counseling about possible strategies to modify their lifestyle and risk factors [Evidence Level B].
iii. Referrals to appropriate specialists should be made where required [Evidence Level B].
    a. The specialists may provide more comprehensive assessments and structured programs to manage specific risk factors [Evidence Level B].

2.1 Healthy balanced diet

i. Counsel and educate individuals with transient ischemic attack or stroke to eat a healthy balanced diet that includes:
    a. a variety of natural and whole foods at each meal [Evidence Level B].
    b. fewer highly processed foods which include highly refined foods, confectionaries, sugary drinks, and processed meats [Evidence Level B].
    c. a diet high in vegetables and fruit; encourage patients to choose fresh or frozen unsweetened fruit, or fruit canned in water without added/free sugars or artificial/noncaloric sweeteners; fresh or frozen vegetables without added sauce, or canned vegetables with no added salt [Evidence Level B].

d. lean meats, whole grains and protein from plant sources which are low in saturated and trans fats, low in cholesterol (<200 mg daily for patients at increased vascular risk) and low in sodium [Evidence Level B].

ii. Counsel and educate individuals with transient ischemic attack or stroke to follow a Mediterranean-type diet, which is high in vegetables, fruit, whole grains, fish, nuts and olive oil and low in red meat [Evidence Level B].

iii. Counsel and educate individuals with transient ischemic attack or stroke to have a total intake of free sugars that does not exceed 10% of total daily calorie (energy) intake [Evidence Level B]

Note: While sugar is a problematic part of our diet, sugar in liquid beverage form is of particular concern. Sugary drinks that may include soft drinks, juice, vitamin waters and sports drinks are considered energy-dense, nutrient poor beverages because of their high caloric levels and minimal nutritional value. Heart & Stroke Position Statement on Sugary Drinks 2016.[26]

2.2 Sodium intake

i. Counsel and educate individuals with transient ischemic attack or stroke to have a daily sodium intake from all sources to no more than 2000 mg per day [Evidence Level A].

2.3 Exercise

i. Counsel and educate individuals with transient ischemic attack or stroke to reduce sedentary behaviors and to work towards increased activity goals as tolerated throughout their stroke recovery [Evidence Level B].

ii. Counsel and educate individuals with transient ischemic attack or stroke to participate in dynamic exercise of moderate intensity (such as brisk walking, jogging, swimming, cycling) 4 to 7 days per week, to accumulate at least 150 minutes in episodes of 10 minutes or more, in addition to routine activities of daily living[27] [Evidence Level B].

iii. Most people who have had a stroke or transient ischemic attack should be encouraged to start a regular exercise program [Evidence Level C].

a. Supervision by a health care professional (such as a physiotherapist) at exercise initiation should be considered in individuals with stroke at risk of falls or injury, or in individuals with other comorbid disease (such as cardiac disease), which may place them at higher risk of medical complications [Evidence Level C].

2.4 Weight

i. Counsel and educate individuals with transient ischemic attack or stroke to achieve a body mass index (BMI) of 18.5 to 24.9 kg/m^2; or a waist circumference of <88 centimeters for women and <102 centimeters for men* [Evidence Level B]. *(*Note: these numbers are reflective of current research based mostly on Caucasian patients. Refer to Reference list for waist circumference values for other ethnic groups.)*

ii. Counsel and educate individuals with transient ischemic attack or stroke who are overweight to set healthy weight loss goals and develop individualized plans to achieve goals [Evidence Level B].

a. Referral to dietitian should be considered [Evidence Level B].

2.5 Alcohol consumption

i. Counsel and educate individuals with transient ischemic attack or stroke to avoid heavy alcohol use as excessive alcohol intake increases the risk of ischemic stroke and intracranial hemorrhage [Evidence Level B].

ii. Counsel and educate individuals with transient ischemic attack or stroke to follow Canada's Low-Risk Alcohol Drinking Guidelines (2011):[28] for women, no more than 10 drinks per week, with no more than 2 drinks per day most days and no more than 3 drinks on any single occasion; for men, no more than 15 drinks per week, with no more than 3 drinks per day most days and no more than 4 drinks on any single occasion [Evidence Level C].

Note: One standard drink is considered to be 13.6 g or 17.2 mL of ethanol, or approximately 44 mL of 80 proof (40%) spirits, 355 mL of 5% beer or 148 mL of 12% wine.

2.6 Oral contraceptives and hormone replacement therapy

i. Estrogen-containing oral contraceptives or hormone replacement therapy should be discouraged or discontinued in female patients with transient ischemic attack or ischemic stroke [Evidence Level B]. Management alternatives should be considered in these patients [Evidence Level C].

2.7 Recreational drug use

i. Individuals with stroke and known recreational drug use that may increase the risk of stroke (such as cocaine, amphetamines) should be counseled to discontinue use if not prescribed for medical indications [Evidence Level C]; and should be provided with appropriate support and referrals to services and resources for drug addiction and rehabilitation [Evidence Level B].

2.8 Smoking cessation

Note: The term "Smoking" in these recommendations refers to tobacco and other inhaled substances.

i. In all health care settings along the stroke continuum (inpatient, ambulatory, and community), patient smoking status should be identified, assessed and documented [Evidence Level A].
ii. Provide unambiguous, nonjudgmental, and patient-specific advice regarding the importance of cessation to all smokers [Evidence Level B] and others who reside with the patient.
iii. Offer assistance with the initiation of a smoking cessation attempt – either directly or through referral to appropriate resources [Evidence Level A].
iv. People who are not ready to quit should be offered a motivational intervention to help enhance their readiness to quit [Evidence Level B]. *Refer to implementation resources at www.strokebestpractices.ca for a summary of motivational interviewing tools.*
v. A combination of pharmacological therapy and behavioral therapy should be considered in all smoking cessation programs and interventions [Evidence Level A].
vi. The three classes of pharmacological agents that should be considered as first-line therapy for smoking cessation are nicotine replacement therapy, varenicline, and bupropion [Evidence Level A].
    a. The choice of appropriate pharmacotherapy should take into account the patient's medical stability, clinical needs, other medical factors, and patient preferences [Evidence Level C]. *Refer to summary table on Pharmacotherapy for Smoking Cessation Treatment at www.strokebestpractcies.ca.*
vii. For stroke patients in hospital who are current smokers, protocols should be in place to manage nicotine withdrawal during hospitalization [Evidence Level B].
viii. Interdisciplinary team members should counsel patients, family members, and caregivers about the harmful effects of exposure to environmental (second-hand) smoke [Evidence Level B].

2.9 Adherence to individual prevention plans

i. At each stroke prevention visit with health care team members, assess patients for adherence to individualized secondary prevention plans (pharmacotherapy and lifestyle changes) [Evidence Level C].

Note: Adherence topics include medication compliance; diet management, rehabilitation therapy and/or exercise participation, and other areas specific to each patient.

factors, including 20% for diets low in fruits and vegetables, 13% for diets high in sodium, 11% for low levels of physical activity, 28% for a body mass index greater than 23.0, and 13% for tobacco use. These results are consistent with other reports. The recent INTERSTROKE 2 study[24] reported that among 10 risk factors, the odds of all stroke were 2.5 times higher among persons with a self-reported history of hypertension, 2 times higher among heavy alcohol consumers and over 1.5 times higher for tobacco smokers. The associated population attributable risk estimates were 34%, 5.8%, and 12%, respectively. Since rates of recurrent stroke and other vascular disorders are known to be significantly elevated during the first four years after hospitalization for first stroke,[25] and potentially modifiable risk factors represent approximately 90% of the population-attributable risk for stroke,[24] secondary prevention measures represent an important opportunity to reduce the risk of future stroke.

Section 3: Blood pressure and stroke prevention

Elevated blood pressure is the single most important risk factor for stroke, and is also regarded as the most important modifiable risk factor. Numerous population-based studies have found that elevated blood pressure is a significant risk factor for first and recurrent stroke. Systolic hypertension is estimated to account for about 64% of the stroke burden, globally, while In Canada, the contribution is lower, estimated at about 45%.[23] Results from the INTERSTROKE 2

Note: These recommendations are applicable to transient ischemic attack and stroke of ischemic and hemorrhagic origin unless otherwise stated.

3.0 Hypertension is the single most important modifiable risk factor for stroke. Blood pressure should be assessed and managed in all persons at risk for stroke [Evidence Level A].

3.1 Blood pressure assessment

i. All persons at risk of stroke should have their blood pressure measured routinely, no less than once annually and more frequently based on individual clinical circumstances [Evidence Level C].
ii. Proper standardized techniques should be followed for initial and subsequent blood pressure measurement including office, home, and community testing [Evidence Level B] as outlined by the Hypertension Canada Guidelines.
iii. Patients found to have elevated blood pressure (systolic greater than 130 mmHg and/or diastolic greater than 85 mmHg) should undergo thorough assessment for the diagnosis of hypertension [Evidence Level C].
    a. A specific follow-up visit may be scheduled and completed for the assessment and diagnosis of hypertension following an initial elevated blood pressure measurement [Evidence Level C].
    b. During a specific visit for assessment of hypertension consider including three blood pressure measurements conducted in accordance with the current Hypertension Canada Guidelines [Evidence Level C].
iv. Patients with refractory hypertension should have comprehensive investigations for secondary causes of hypertension [Evidence Level B].
v. Patients with hypertension or at risk for hypertension (in pre-hypertension state or other risk factors) should receive aggressive risk factor modification, lifestyle counseling and lifestyle modification interventions [Evidence Level B]. *Refer to recommendations in Section 2 on Lifestyle Management for additional information.*

3.2 Blood pressure management

i. For patients **who have had a stroke or transient ischemic attack**, blood pressure lowering treatment is recommended to achieve a target of consistently lower than 140/90 mm Hg [Evidence Level B].
    a. For patients **who have had a small subcortical stroke,** blood pressure lowering treatment to achieve a systolic target of consistently lower than 130 mm Hg is reasonable [Evidence Level B] (New for 2017).
ii. **In patients with diabetes**, blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke to attain systolic blood pressure targets consistently lower than 130 mm Hg [Evidence Level C] and diastolic blood pressure targets consistently lower than 80 mm Hg [Evidence Level A].
iii. **In patients with nondiabetic chronic kidney disease and stroke**, blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke to attain a blood pressure consistently lower than 140/90 mm Hg [Evidence Level C].
iv. Randomized controlled trials have not defined the optimal time to initiate blood pressure lowering therapy after stroke or transient ischemic attack. Blood pressure lowering treatment should be initiated or modified before discharge from hospital [Evidence Level B]. *Refer to Hyperacute Module Recommendations Section 3.3 for blood pressure management during the acute phase of stroke (0–72 hours) (Casaubon et al 2016).*[15]
v. Patients who are not started on hypertensive therapy in acute care should have arrangements made for follow-up with primary care or stroke prevention service for ongoing evaluation and management [Evidence Level C*]. Note: Blood pressure management is the responsibility of all health care team members, and initially stroke patients require frequent monitoring (e.g. monthly) until they achieve target blood pressure levels and optimal therapy has been established.*
vi. For children, blood pressure lowering should be targeted to below the 95th percentile on normative value tables for age, height, and gender [Evidence Level B].[32]

Clinical considerations

i. Children who have had a stroke, and their families, should be counseled to avoid hypotensive situations where they might drop their cerebral perfusion pressure and risk ischemia, such as dehydration especially with vomiting/diarrhea.

study suggested the odds of experiencing any stroke were 2.56 times higher among persons with self-reported hypertension and 3.7 times higher for hemorrhagic stroke.[24] The odds were even higher when the criteria for hypertension also included measured blood pressure in excess of 140/90 mm Hg. Using data from 1.25 million people, included in the CALIBER database Rapsomanki et al.[29] estimated the lifetime risk of ischemic stroke (from age of 30 years) in persons with hypertension to be 7.6% compared with 6.5% without hypertension, corresponding to loss of life of approximately a half a year due to ischemic stroke.

While the optimal target blood pressure to prevent a first or recurrent stroke has not been formally established, the current treatment recommendation is to attain a blood pressure of consistently lower than 140/90 mm Hg for people who have had a cerebrovascular event. There is a wealth of evidence from large clinical trials and meta-analyses that have been published over the past 30 years indicating that stroke risk is significantly reduced among at-risk persons when blood pressure is reduced and maintained within recommended levels, using a variety of antihypertensive agents, alone, or in combination with other agents. Using the results from 147 randomized controlled trials (RCTs), Law et al.[30] reported that a blood pressure treatment resulting in a reduction of 10 mm Hg systolic and 5 mm Hg diastolic was

Table 2. Summary of HSF recurrent stroke risk levels and initial management (based on CSBPR Secondary Prevention of Stroke, Section 1: Initial Risk Stratification and Management)

Risk For Recurrent Stroke	Time from Stroke Symptom Onset to Healthcare Presentation	Presenting Symptoms	When Patients Should be Seen by Healthcare Professional	Where Patients Should be Seen	Tests to be Done on Initial Assessment
Very HIGH RISK	Within 48 hours	- Transient, fluctuating or persistent unilateral weakness (face, arm and/or leg) - Transient, fluctuating or persistent speech disturbance/aphasia. - Fluctuating or persistent symptoms **without motor weakness or speech disturbance** (e.g. hemibody sensory symptoms, monocular visual loss, hemifield visual loss, ± other symptoms suggestive of posterior circulation stroke such as diplopia, dysarthria, and/or ataxia).	Immediately	Emergency Department [ideally ED with brain imaging onsite and access to alteplase (tPA)]	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
HIGH RISK	Between 48 hours and 2 weeks	- Transient, fluctuating or persistent unilateral weakness (face, arm, and/or leg), or speech disturbance/aphasia	As soon as possible, ideally within 24 hours	Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
Moderate (INCREASED) RISK	Between 48 hours and 2 weeks	- Fluctuating or persistent symptoms ***without motor weakness*** or speech disturbance (e.g., hemibody sensory symptoms, monocular vision loss, binocular diplopia, hemifield vision loss, or ataxia)	As soon as possible, ideally within 2 weeks	Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
LOWER RISK	More than 2 weeks	- Any typical or atypical symptoms of stroke or transient ischemic attack	Ideally within 1 month	Ambulatory Clinic with access to Neurologist or Stroke Specialist, Nurse Practitioner	As appropriate based on assessment by health care team

Canadian Stroke Best Practice Recommendations

Table 3. Recommended laboratory investigations for patients with acute stroke or transient ischemic attack

Table 3a. Initial recommended laboratory investigations for patients with stroke and transient ischemic attack			
Complete Blood Count (CBC)	International Normalized Ratio (INR)	Partial Thromboplastin Time (PTT)	Random Glucose or Hemoglobin A1C
Electrolytes	Creatinine/eGFR	ALT	Troponin
Follow-up Blood work: to be completed as soon as possible after initial bloodwork once patient has fasted for an appropriate amount of time.		Either a fasting plasma glucose, or 2 hour plasma glucose, or glycated hemoglobin (A1C), or 75 g oral glucose tolerance test	Lipid profile (Fasting optional and decision should be based on individual patient factors)

Note: This list presents the recommended initial laboratory tests for patients with stroke and transient ischemic attack. Patient presentation, clinical judgment, and local stroke protocols should be considered in selecting appropriate laboratory investigations and the timing of completion.

Table 3b. Additional Laboratory Investigations for Consideration in Specific Circumstances			
Optional laboratory investigations			
Calcium, Magnesium, Phosphate		If female less than 50 years of age, consider pregnancy test	Blood cultures x 3 (per individual institutional protocol)
Blood and/or urine drug screen		HIV, syphilis serology	
Coagulopathy Screen – For consideration in selected patients *only if clinically indicated* *Recommend consultation with a specialist in thrombosis to evaluate for hypercoagulable state*			
Anticardiolipin (Antiphospholipid) antibody	Lupus anticoagulant	Sickle cell screen	Homocysteine (fasting serum level)
Special considerations especially in young adults and children with stroke in the absence of identified etiology *(Note there is no strong evidence base for these investigations, and they should be considered only in selected stroke patients based on clinical presentation and medical history*			
Consider LP for CSF analysis (cell count and differential, protein, glucose, bacterial and viral cultures; possibly cytology/flow cytometry if CNS lymphoma is a consideration)		Brain biopsy (if vasculitis of the central nervous system or angiocentric lymphoma is a consideration)	
Catheter cerebral angiography		Further genetic tests – CADASIL, Fabry's, MELAS	

Note: All patients are individual and some may require additional investigations to fully understand their clinical situation. The investigations noted above may not be indicated in many stroke patients and should be considered in selected stroke patients based on clinical presentation and medical history.

associated with a 41% reduced risk of stroke. The results from a Cochrane review[31] suggested that among persons 60 years of age or greater, with moderate to severe hypertension treated primarily with first-line thiazide diuretic therapy for an average of 4.5 years, there was a significantly reduced risk of all-cause mortality, and lower total cardiovascular morbidity and mortality.

Section 4: Lipid management

Given the well-documented causal relationship between dyslipidemia and the development of atherosclerosis, its appropriate management is important for both primary and secondary prevention of stroke. Current strategies emphasize the need to balance lifestyle factors modifications through behaviors change with pharmacological intervention, as required. Those who have already had an ischemic stroke or transient ischemic attack will benefit from treatment with a statin. While the superiority of the long-term use of a statin agent relative to a placebo for primary stroke prevention has been well-established in numerous large RCTs, there are fewer trials that have examined the additional benefit from higher (versus lower) statin doses. Results from the treating to new targets (TNT) trial[33] suggest that aggressive reduction of low-density lipoprotein (LDL) cholesterol, achieved through higher doses of a statin, are associated with greater benefit than more modest reductions. In this trial, the LDL cholesterol levels of participants with clinically evident coronary heart disease and baseline LDL-chol of <3.4 mmol/L, who received 80 mg atorvastatin for approximately 5 years were reduced from 2.6 to 2.0 mmol/L. The risk of fatal or nonfatal stroke or transient ischemic attack was subsequently reduced by 23% compared with person taking a 10-mg dose. The Cholesterol Treatment Trialists,[34] meta-analysis including the results of 14 statin trials showed a dose-dependent relative reduction in cardiovascular disease with LDL cholesterol lowering. Every 1.0 mmol/L reduction in LDL cholesterol was associated with a corresponding 20% to 25% reduction in cardiovascular disease mortality and non-fatal myocardial infarction. The risk of any stroke was reduced by 15% with statin therapy. Results from the recent FOURIER trial[35] highlight the benefit of more aggressive treatment, using additional agents when necessary, for patients with clinically evident atherosclerotic cardiovascular disease.

4.0 Patients who have had an ischemic stroke or transient ischemic attack should have their serum lipid levels assessed and aggressively managed [Evidence level A].

4.1 Lipid assessment

i. Lipid levels, including total cholesterol, total triglycerides, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol, should be measured on all patients presenting with stroke or transient ischemic attack [Evidence Level B].

4.2 Lipid management

i. Patients with ischemic stroke or transient ischemic attack should be managed with aggressive therapeutic lifestyle changes to lower lipid levels, including dietary modification, as part of a comprehensive approach to lower risk of first or recurrent stroke unless contra-indicated [Evidence Level B]. *Refer to Prevention of Stroke Module, Section 2 for Lifestyle Management recommendations*.
ii. A statin should be prescribed for secondary prevention in patients who have had an ischemic stroke or transient ischemic attack in order to achieve a target LDL cholesterol consistently less than 2.0 mmol/L or >50% reduction of LDL cholesterol, from baseline [Evidence Level B].[36]
   a. For individuals with stroke and acute coronary syndrome or established coronary disease, treatment to more aggressive targets (LDL-C <1.8 mmol/L or >50% reduction) should be considered [Evidence Level A].
iii. Adults with diabetes and ischemic stroke are at high risk of further vascular events and should also be treated with a statin to achieve a LDL cholesterol ≤2.0 mmol/L [Evidence Level B].
iv. Statin therapy is not indicated for prevention of intracerebral hemorrhage [Evidence Level B].

Section 5: Diabetes and stroke

In persons with diabetes, the risk of stroke, particularly ischemic stroke, is increased. The independent contribution of diabetes is difficult to determine, since many other risk factors for stroke, including hypertension, dyslipidemia, and atrial fibrillation, are more frequent in persons with diabetes. In addition to the traditional risk factors, those specifically associated with metabolic syndrome (insulin resistance, central obesity, impaired glucose tolerance and hyperinsulinemia), which are

common in diabetes, also contribute to the increased risk.

Consequently, in persons with diabetes, stroke outcomes are worse, and are associated with increased mortality, more residual neurologic and functional disability and longer hospital stays. Although tighter glycemic control along with other risk factor reduction strategies, including hypertension and hyperlipidemia, can collectively help to reduce stroke risk, aggressive glycemic control may not confer greater protection. In the glucose-lowering arm of the ACCORD Study,[37] the benefit of intensive therapy to reduce glycated hemoglobin (HbA1c) levels to reduce cardiovascular events in patients with type 2 diabetes who had either established cardiovascular disease or additional cardiovascular risk factors, was assessed. Patients with a median HbA1c level of 8.1% were randomly assigned to receive intensive therapy (targeting an HbA1c level <6.0%) or standard therapy (targeting a level from 7.0% to 7.9%). The trial was stopped early due to mortality trends suggesting an increased risk of death from any cause associated with intensive therapy. By 4 months, although mean HbA1c values had fallen to 6.7% in the intensive group compared with 7.5% in the control group, there was no reduction in the risk of nonfatal MI, nonfatal stroke or death from cardiovascular causes, associated with intensive glucose lowering. Patients in the intensive group required medical assistance for hypoglycemia more frequently and a greater proportion gained >10 kg. Results from the Veterans Affairs Diabetes Trial[38] also examined intensive glucose control in persons with poorly-controlled diabetes. While HbA1c values were significantly lower in the intensive glucose control group, after a median

5.0 Patients with diabetes who have had an ischemic stroke or transient ischemic attack should have their diabetes assessed and optimally managed [Evidence level A].

5.1 Diabetes screening and assessment

i. 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 inpatient or outpatient setting [Evidence Level C; Diabetes Canada 2016].
ii. For patients with diabetes and either ischemic stroke or transient ischemic attack, glycated hemoglobin (A1C) should be measured as part of a comprehensive stroke assessment [Evidence Level B].

Refer to Section 3 for information on blood pressure management in an individual with stroke and diabetes; refer to Prevention of Stroke Section 4 for information on lipid management in an individual with stroke and diabetes.

5.2 Diabetes management

i. Glycemic targets should be individualized; however, lowering A1C values to ≤7% in both type 1 and type 2 diabetes and stroke or transient ischemic attack, provides strong benefits for the prevention of microvascular complications [Evidence Level A].
ii. To achieve a target of A1C ≤7.0%, most patients with type 1 or type 2 diabetes should aim for a fasting plasma glucose or preprandial plasma glucose target of 4.0 to 7.0 mmol/L [Evidence Level B].
iii. The 2-hour postprandial plasma glucose target is 5.0 to 10.0 mmol/L [Evidence Level B]. If A1C targets cannot be achieved with a postprandial target of 5.0 to 10.0 mmol/L, further postprandial blood glucose lowering, to 5.0 to 8.0 mmol/L, should be considered [Evidence Level C].

Note: For recommendations on the use of SGLT2 inhibitors, please refer to the current Diabetes Canada guidelines at www.diabetes.ca.

Clinical considerations (New for 2017)

i. The results from a recent trial, *Pioglitazone after Ischemic Stroke or Transient Ischemic Attack*[41] suggested that while there is a benefit of pioglitazone for stroke prevention in patients with positive insulin resistance, it is offset by the increased risk of fractures and bladder cancer. The decision to use this agent could be considered based on the specific risk profile for each patient.
ii. More intensive glucose control (A1C ≤6.5%), may be considered in patients with a shorter duration of diabetes, no evidence of significant cardiovascular disease and longer life expectancy, provided this does not result in a significant increase in hypoglycemia (Diabetes Canada 2016).

duration of follow-up 5.9 years, there were no significant differences between groups on any of the primary or secondary outcomes, including the risk of stroke or transient ischemic attack. A meta-analysis including the results from six trials reported no significant reduction in the risk of all-cause mortality, stroke or cardiovascular mortality associated with intensive glycemic treatment; however, there was a significant 14% reduction in nonfatal myocardial infarction.[39]

For patients with established cardiovascular disease whose blood glucose levels are not well controlled using standard therapy, the addition of a sodium glucose co-transpoter-2 inhibitor may reduce the risk of further events. In a trial using the SGLT-2 inhibitor, empagliflozin, after a median duration of follow-up of 3.1 years, the risks of cardiovascular mortality and all-cause mortality were reduced by 38% and 32%, respectively.[40]

Section 6: Antiplatelet therapy for individuals with ischemic stroke or transient ischemic attack

Antiplatelet agents, including acetylsalicylic acid (ASA), clopidogrel, and the combination of ASA and extended-release dipyridamole have been shown to reduce the risk of recurrent stroke. Using data from secondary prevention trials, the 2009 Antithrombotic Trialists' Collaborative (ATTC) meta-analysis, reported that the use of aspirin was associated with a 19% reduction in the risk of future ischemic stroke and a 23% reduction in stroke of unknown cause, without a significantly increased risk of hemorrhagic stroke.[42] The combination of clopidogrel plus aspirin has been associated with a 21% reduction in the risk of stroke and a 15% reduction in the risk of major vascular events, compared with aspirin alone; however, the risks of major bleeding and intracranial hemorrhage

Note: These recommendations are applicable to ischemic stroke and transient ischemic attack.

6.1 All patients with ischemic stroke or transient ischemic attack should be prescribed antiplatelet therapy for secondary prevention of recurrent stroke unless there is an indication for anticoagulation [Evidence Level A].

i. Acetylsalicylic acid (80–325 mg daily), combined acetylsalicylic acid (25 mg) and extended-release dipyridamole (25 mg/200 mg twice daily), or clopidogrel (75 mg daily) are all appropriate options and selection should depend on the clinical circumstances [Evidence Level A].
   a. Short-term concurrent use of acetylsalicylic acid and clopidogrel (up to 21 days) has not shown an increased risk of bleeding and may be protective following minor stroke or transient ischemic attack [Evidence Level B].
   b. Longer-term use of acetylsalicylic acid and clopidogrel is not recommended for secondary stroke prevention, unless there is an alternate indication (e.g. coronary drug-eluting stent requiring dual antiplatelet therapy), due to an increased risk of bleeding and mortality [Evidence Level A]. *This combination of efficacy is currently being investigated in the POINT trial (www.Clinicaltrials.gov; Identifier NCT00991029).*

6.2 Pediatric stroke considerations

i. In children with stroke the usual maintenance dosage of acetylsalicylic acid is 3 to 5 mg/kg per day for the prevention of recurrent stroke [Evidence Level B]. The usual maximum dose in adolescents is 81 mg/day.
   a. There is no evidence available on the optimal duration of therapy; this should be based on individual clinical circumstances.
ii. The evidence for clopidogrel use in children is sparse at this time. Clopidogrel may be considered as an alternative for adolescents at a dose of 1 mg/kg/day up to a maximum of 75 mg/day especially in the context of ASA allergy. Younger children may have higher anti-platelet effects of clopidogrel, and the suggested doses should be considered within the range of 0.2–0.5 mg/kg/day [Evidence Level C].

Clinical considerations (New for 2017)

i. At the present time, there is not enough evidence to guide management if a patient has a stroke while on a specific antiplatelet agent. In all cases of recurrent stroke while on antiplatelet therapy, all other vascular risk factors and stroke etiology should be reassessed and aggressively managed.
ii. Expert opinion suggests that if a patient experiences a stroke while on ASA, it may be reasonable to consider switching to clopidogrel; if a patient experiences a stroke while on clopidogrel it may be reasonable to consider switching to combined acetylsalicylic acid (25 mg) and extended-release dipyridamole (200 mg).

Refer to Section 7 on Stroke and Atrial Fibrillation for additional recommendations on anticoagulant therapy.

were significantly increased.[43] A stratified analysis from the same study suggested that a significant increase in the risk of intracranial hemorrhage was only associated with long-term dual antiplatelet use. In contrast, the dual use of dipyridamole plus aspirin, was not associated with a significantly decreased risk of stroke recurrence compared with aspirin alone in a meta-analysis including the results of ESP-2, ESPRIT, and EARLY.[44]

Section 7: Anticoagulation for individuals with stroke and atrial fibrillation

Atrial fibrillation (AF), a common arrhythmia, is a significant risk factor for stroke. Detecting AF following a stroke or transient ischemic attack is important since, once identified, it can be effectively treated. Since most patients do not undergo prolonged screening, AF is often undetected and hence, the condition is generally under-diagnosed. The results from several RCTs have demonstrated that prolonged post-stroke ECG monitoring using wearable or insertable devices is effective for improving the detection of paroxysmal AF, with numbers needed to screen ranging from 8 to 14.[45–47] Longer monitoring durations have been associated with an increased probability of AF detection. In terms of treatment, new classes of drugs, such as direct thrombin inhibitors (e.g. dabigatran) and Factor Xa inhibitors (apixaban, edoxaban and rivaroxaban) have demonstrated benefits over previous standard therapy with warfarin. These direct-acting oral anticoagulants (DOACs) have been shown to be as effective, or superior to warfarin to reduce the risk of stroke or systemic embolism, with fewer side-effects.[48,49] In addition to the recommendations below, practical guidance documents for DOAC therapy are available.[46,50]

7.1 Detection of Atrial Fibrillation

i. Patients with suspected transient ischemic attack or ischemic stroke should have a 12-lead ECG to assess cardiac rhythm and identify atrial fibrillation or flutter or evidence of structural heart disease (e.g. myocardial infarction, left ventricular hypertrophy) [Evidence Level B].
ii. For patients being investigated for an acute embolic ischemic stroke or transient ischemic attack, ECG monitoring at least 24 hours is recommended as part of the initial stroke work-up to detect paroxysmal atrial fibrillation in patients who would be potential candidates for anticoagulant therapy [Evidence Level A].
iii. For patients being investigated for an acute embolic ischemic stroke or transient ischemic attack of undetermined source whose initial short-term ECG monitoring does not reveal atrial fibrillation but a cardioembolic mechanism is suspected, prolonged ECG monitoring for at least 2 weeks is recommended to improve detection of paroxysmal atrial fibrillation in selected patients are not already receiving anticoagulant therapy but would be potential anticoagulant candidates [Evidence Level A].

7.2 Prevention of recurrent stroke in patients with nonvalvular atrial fibrillation

i. Patients with transient ischemic attack or ischemic stroke *and* nonvalvular atrial fibrillation should receive oral anticoagulation [Evidence Level A].
   a. In most patients requiring anticoagulants for atrial fibrillation, direct non-vitamin K oral anticoagulants (DOAC) such as apixaban, dabigatran, edoxaban, or rivaroxaban should be prescribed in preference over warfarin [Evidence Level A].
   b. For patients already receiving warfarin with good International Normalized Ratio (INR) control (range 2.0–3.0, with TTR >70%), continuing warfarin is a reasonable anticoagulation option [Evidence Level B].
   c. When selecting choice of oral anticoagulants, patient specific criteria should be considered [Evidence level C]. *Refer to summary table for Selection of Anticoagulant Agents for Management of Atrial Fibrillation after stroke or transient ischemic attack, available at www.strokebestpractices.ca.*
ii. For patients with acute ischemic stroke and atrial fibrillation, routine use of bridging with heparin is not recommended [Evidence Level B].
   a. Bridging with antiplatelet therapy is suggested until the patient is anticoagulated [Evidence Level C]. *Refer to Section 6 on Antiplatelet Therapy for Ischemic Stroke and Transient Ischemic Attack for additional recommendations on antithrombotic therapy.*
iii. For patients with ischemic stroke or transient ischemic attack and atrial fibrillation who are unable to take oral anticoagulant therapy (DOAC or warfarin), aspirin alone is recommended [Evidence Level A] (New for 2017).
   a. The addition of clopidogrel to aspirin therapy, compared with aspirin therapy alone, may be reasonable and decisions should be individualized based on patient bleeding risk [Evidence Level B].
iv. For patients with a mechanical heart valve, warfarin is recommended for stroke prevention with careful INR monitoring; nonvitamin K oral anticoagulants are contraindicated [Evidence Level B].
v. For patients in whom long-term anticoagulant therapy is contraindicated, a left atrial appendage closure procedure may be considered [Evidence Level B].

Clinical considerations (new for 2017)

i. The optimal timing to start anticoagulant therapy after stroke has not been defined by clinical trial evidence, and should be based on individual benefit/risk assessment taking into account the clinical circumstances, infarct size, imaging appearances, age, comorbidities, and estimated stroke recurrence risk.
ii. According to expert consensus, a general approach to the target timing of initiation of DOAC therapy post stroke may include: 1 day post-event or same day after a TIA, 3 days post stroke after a mild stroke, 6 days post stroke after a moderate stroke, and 12–14 days post stroke after a severe stroke.[51]

7.3 Enhancing anticoagulant therapy effectiveness in practice and minimizing bleeding complications

i. Medication adherence should be continually assessed and reinforced for patients on all oral anticoagulants at each follow-up visit [Evidence Level B].
   a. For patients with atrial fibrillation taking warfarin, careful dosing and consistent international normalized ratio monitoring is recommended to minimize adverse events; warfarin efficacy is dependent on maintaining therapeutic INR control (INR range 2.0–3.0; if the presence of mechanical valve range is 2.5–3.5), and declines significantly when the international normalized ratio falls below 2.0 [Evidence Level A].
   b. Patients who are prescribed a DOAC should be reassessed at intervals and educated regarding the short half-life of this class of drugs, the importance of daily medication adherence and the dangers of missed doses or prolonged interruptions of therapy [Evidence Level B].
ii. For patients prescribed apixaban, dabigatran, edoxaban, or rivaroxaban, creatinine clearance should be routinely monitored at least once annually, and when there is a change in health status [Evidence Level C]. *Refer to summary table for Selection of Anticoagulant Agents for Management of Atrial Fibrillation after stroke or transient ischemic attack at www.strokebestpractices.ca.*
   a. Dose adjustments or a change in selected agent may be required based on changes in renal function if detected.
   b. More frequent monitoring of renal function (every 6 months or more frequently) may be considered for patients with moderate or severe renal impairment or a dehydrating illness for medication adjustment if required [Evidence Level C].
iii. Concomitant antiplatelet therapy with oral anticoagulant therapy is not routinely recommended in patients with atrial fibrillation due to increased bleeding risk unless there is a specific additional medical indication [Evidence Level B].

Section 8: Management of extracranial carotid disease and intracranial atherosclerosis

Carotid endarterectomy (CEA) has been shown to prevent stroke recurrence in patients who have sustained a minor stroke or transient ischemic attack with ipsilateral high-grade carotid stenosis. Pooling the results from three major trails, the risk of any stroke or operative death at 5 years in patients with severe stenosis (70–99%) was significantly reduced among those in the CEA group (RR = 0.53, 95% CI 0.42–0.67, $p < 0.0001$, NNT = 6) compared with best medical management, with an associated absolute risk reduction of 16.0%.[52] For patients with moderate stenosis (50–69%) the risk was also reduced significantly (RR = 0.77, 95% CI 0.63–0.94, $p = 0.001$, NNT = 22), while patients with mild stenosis did not benefit from treatment.

Perioperative death or stroke incidence was 7.0%. The greatest benefit of treatment was found in men, patients aged 75 years or over, and patients randomized within two weeks after their latest ischemic event. The use of CEA for asymptomatic carotid artery disease is more controversial. For selected patients with asymptomatic carotid stenosis, CEA reduces the risk of stroke from about 2% per year to about 1% per year.[53] Significant improvements have been made in the medical management of stroke risk factors during the previous 20 years, including the use of statins, antihypertensive agents, and antiplatelets or anticoagulants. These changes have reduced the frequency in which the procedure is undertaken.

Carotid-artery angioplasty with stenting (CAS) has emerged as an alternative to carotid endarterectomy in patients at high risk for complications for endarterectomy such as contralateral occlusion or severe coronary artery disease. The percutaneous approach also avoids the risks of general anesthesia and the local complications of neck hematoma, infection, cervical strain, and cranial nerve damage associated with endarterectomy and requires a shorter recovery period. In the SAMPRISS trial, aggressive medical management was found to be superior to intracranial stenting for patients with 70% to 99% stenosis of a major intracranial artery. Within 30 days of the procedure, the probability of the primary endpoint, stroke or death occurring, was significantly higher in the percutaneous transluminal angioplasty and stenting group (14.7% vs. 5.8%, $p = 0.0016$).[54]

Cephalocervical artery dissection, while relatively rare, is a common etiology of stroke in persons less than 45 years. To prevent recurrent events, treatment for three months with an antiplatelet or anticoagulant is recommended. Results from the CADISS trial[55]

Note: These recommendations are applicable to ischemic stroke and transient ischemic attack.

8.1 Symptomatic Carotid Stenosis

i. Patients with recent transient ischemic attack or non-disabling stroke and ipsilateral **50 to 99** percent symptomatic carotid stenosis should have an evaluation by a clinician with stroke expertise and selected patients should be offered carotid endarterectomy (revascularization) as soon as possible [Evidence Level B].
ii. Carotid stenosis should ideally be measured by CTA to guide surgical decision-making [Evidence Level C].
iii. In individuals with nondisabling stroke or transient ischemic attack and **70–99%** symptomatic carotid stenosis, carotid endarterectomy should be performed [Evidence Level A], on an urgent basis.
    a. Ideally carotid endarterectomy should be performed within the first days following nondisabling stroke or transient ischemic attack [Evidence Level B] and within 14 days of ischemic event onset for patients who are not clinically stable in the first few days [Evidence Level A].
iv. Carotid endarterectomy should be performed by a surgeon/center that routinely audits their performance results, especially perioperative stroke and death rates. The randomized trials upon which these recommendations are based (benefits accrued for patients undergoing surgery within six months of symptoms) involved combined perioperative stroke and death rates of 6–7% [Evidence Level A].
v. Carotid endarterectomy is generally more appropriate than carotid stenting for patients over age 70 years who are otherwise fit for surgery as current evidence indicates stenting carries a higher peri-procedural risk of stroke and death in older patients. [Evidence Level A].
vi. Carotid stenting may be considered for patients who are not operative candidates for technical, anatomic, or medical reasons [Evidence Level A].
    a. Carotid stenting should be performed by an interventionist/center with expertise that routinely audits their performance results, especially perioperative stroke and death rates. The randomized trial upon which these recommendations are based involved combined peri-procedural stroke and death rates of 5% [Evidence Level B].

8.2 Asymptomatic and remotely symptomatic carotid stenosis

i. Patients with symptoms of transient ischemic attack and nondisabling stroke who are found to have an asymptomatic carotid stenosis should be evaluated by a physician with expertise in stroke management [Evidence Level C].
ii. Stroke patients with asymptomatic carotid stenosis should receive aggressive medical management of risk factors as defined throughout the Secondary Prevention of Stroke Module (for example, blood pressure, cholesterol, antiplatelet therapy lifestyle changes) [Evidence Level B].
iii. Carotid endarterectomy may be considered for selected patients with 60% to 99% carotid stenosis who are asymptomatic or were remotely symptomatic (i.e. greater than six months) [Evidence Level A].
    a. Patients should be evaluated to determine eligibility for carotid endarterectomy, such as a life expectancy of more than five years, and an acceptable risk of surgical complications [Evidence Level A].
    b. In carefully selected patients, carotid endarterectomy should be performed by a surgeon who routinely audits their performance results and demonstrates a less than 3% risk of peri-operative morbidity and mortality [Evidence Level A].
iv. Carotid stenting may be considered in patients with 60–99% carotid stenosis who are not operative candidates for technical, anatomic, or medical reasons provided there is a less than 3% risk of peri-procedural morbidity and mortality [Evidence Level A].

8.3 Intracranial stenosis

i. Intracranial stenting is not recommended for the treatment of recently symptomatic intracranial 70% to 99% stenosis [Evidence Level B].
ii. Based on the SAMMPRIS trial,[54] the medical management arm included dual antiplatelet therapy with ASA 325 mg and Clopidogrel 75 mg started within 30 days of stroke or transient ischemic attack and treated for up to 90 days [Evidence Level B], and should be considered for each patient on an individual basis. In addition, there should be aggressive management of all vascular risk factors including blood pressure, lipids, diabetes mellitus, and other at-risk lifestyle patterns [Evidence Level A].
iii. In patients who have been managed with maximal medical therapy in the presence of intracranial stenosis and experience a recurrent stroke, there is lack of clear evidence to guide further management decisions; intracranial angioplasty (with or without stenting) may be reasonable in carefully selected patients [Evidence Level C].

8.4 Cervicocephalic artery dissection (new for 2017)

i. A diagnosis of carotid or vertebral dissection can be established by CTA, MRA, or DSA [Evidence Level C].

Note: CTA or MRA are the preferred noninvasive diagnostic imaging tests for patients with a suspected cervicocephalic artery dissection, as neck ultrasound does not fully visualize the vertebral arteries and can miss distal or carotid dissection originating above the angle of the jaw.

ii. Antithrombotic therapy for stroke prevention is recommended for individuals with a diagnosis of an extracranial carotid or vertebral artery dissection [Evidence Level B].
   a. There is uncertainty about the comparative efficacy of antiplatelet therapy vs. anticoagulation with heparin/warfarin; either treatment is considered reasonable and decision should be based on individual risk/benefit analysis [Evidence Level B].
   b. There is a lack of evidence regarding the optimal duration of antithrombotic therapy and the role of repeat vascular imaging in decision-making. Decisions may be based on individual clinical factors [Evidence Level C].

   Note: There is insufficient evidence at this time to make a recommendation regarding the use of DOACs in patients with arterial dissections.

iii. There is a lack of evidence regarding the use of anticoagulation in intracranial arterial dissection. Decisions may be based on individual clinical factors [Evidence Level C].

indicate that use of either agent is equally effective. In both groups, the frequency of stroke was low (2.4% for antiplatelets and 0.81% for anticoagulants), with no deaths in either group.

Section 9: Other cardiac issues in individuals with stroke

For many years, the role of percutaneous closure of a patent foramen ovale (PFO) for secondary stroke prevention was controversial for several reasons. While PFOs are known to be common in the general population (25%),[56] they are often incidental rather than pathogenic, and the results from previous RCTs were inconclusive.[57–59] In 2017, the publication of two new RCTs[5,6] and long-term follow-up of an earlier one,[7] demonstrated that among carefully- selected patients, PFO closure was superior to medical therapy for prevention of stroke recurrence.

The CLOSE trial[60] enrolled patients aged 16–60 years (mean age approximately 43 years) with a recent stroke and no identifiable cause other than a PFO, following detailed etiological work- up by a neurologist. The PFO had to be associated with either an atrial septal aneurysm (excursion >10 mm) or a large interatrial shunt (>30 microbubbles in the left atrium within three cardiac cycles after opacification of the right atrium). Mean follow-up was 5.3 ± 2.0 years. The stroke rate was 0 in the PFO-closure group vs. 6.0% in the antiplatelet-only group (mostly aspirin) (HR 0.03; 95% CI 0–0.26; $p < 0.001$; NNT = 20 to prevent 1 stroke in 5 years; 95% CI: 17–25). The rate of procedural complications was 5.9%, mostly consisting of atrial fibrillation (4.6% in the closure group vs. 0.9% in the antiplatelet group); most cases of atrial fibrillation were transient and did not recur during follow-up. The REDUCE trial[5] enrolled patients aged 18–59 years (mean age 45.2 years) with a PFO with a right-to-left shunt (spontaneous or during Valsalva maneuver), of whom 81% had moderate (6–25 microbubbles) or large (>25 microbubbles) interatrial shunts. Median follow-up was 3.2 years. The rate of ischemic stroke was 1.4% in the closure group vs. 5.4% in the antiplatelet-only group (HR 0.23; 95% CI 0.09–0.62; $p = 0.002$; NNT = 28 to prevent 1 stroke in 2 years). Serious device-related adverse events occurred in 1.4%, and 6.6% developed atrial fibrillation post-procedure (vs. 0.4% in the antiplatelet-only group); most cases of atrial fibrillation in the closure group were transient. The RESPECT trial has reported its extended follow-up results.[7] This trial enrolled patients aged 18–60 years (mean age 45.9 years) with a cryptogenic stroke and PFO. During a median follow-up of 5.9 years, the rate of recurrent ischemic stroke was 3.6% in the PFO closure group vs. 5.8% in the medical therapy group (antiplatelet therapy or warfarin) (HR 0.55; 95% CI 0.31–0.999; $p = 0.046$; NNT = 42 to prevent 1 stroke in 5 years). In subgroup analysis, the benefit of closure appeared to be driven by those with an atrial septal aneurysm or a "substantial" shunt size (grade 3).

In light of these new trial data, in addition to pooled analyses of earlier trials,[61,62] there is now sufficient evidence to recommend PFO closure for very carefully-selected patients aged 60 years or younger with an unexplained embolic stroke event who are found to have a PFO and who do not require chronic anticoagulant therapy for another reason. PFO closure is not recommended for patients with stroke or TIA who are aged >60 years, and those at any age whose PFO is most likely incidental rather than causal for the index stroke event. In such circumstances, antiplatelet therapy alone is recommended for secondary stroke prevention, unless there is a separate evidence-based indication for anticoagulant therapy. PFO closure is also not recommended for primary stroke prevention. Patient counseling and shared decision-making, taking into account patient values and preferences, are important considerations. Patients considering PFO closure need to understand the benefits and risks of the procedure and the alternatives, and accept an up-front risk of procedural complications that is relatively small but potentially serious, including atrial fibrillation.

Note: These recommendations are applicable to ischemic stroke and transient ischemic attack.

9.1 Patent Foramen Ovale (PFO) *(Revised 2017)*

i. Patients with a recent ischemic stroke or TIA attributed to a PFO should have an evaluation by clinicians with stroke and cardiovascular expertise [Evidence Level C].
ii. For carefully-selected patients with a recent ischemic stroke or TIA attributed to a PFO, PFO device closure plus long-term antiplatelet therapy is recommended over long-term antithrombotic therapy alone **provided all** the following criteria are met [Evidence Level A]:
   a. Age 18–60 years;
   b. The diagnosis of the index stroke event is confirmed by imaging as a nonlacunar embolic ischemic stroke or a TIA with positive neuroimaging or cortical symptoms;
   c. The patient has been evaluated by a neurologist or clinician with stroke expertise, and the PFO is felt to be the most likely cause for the index stroke event following a thorough etiological evaluation to exclude alternate etiologies.
iii. For patients requiring long-term anticoagulation, the decision regarding PFO closure remains unclear, and decisions should be based on individual patient characteristics and risk versus benefit profile [Evidence C].
iv. For patients with a recent ischemic stroke or TIA attributed to a PFO who do no undergo PFO closure and are aged 60 years or younger, either antiplatelet or anticoagulant therapy is recommended for secondary stroke prevention, unless there is a separate evidence-based indication for chronic anticoagulant therapy [Evidence Level B].
v. There is insufficient evidence to make a recommendation regarding the comparative effectiveness of PFO closure vs. anticoagulant therapy.

9.2 Pediatric stroke and patent foramen ovale

i. The significance of a PFO and optimal treatment of paradoxical embolism associated with PFO in a child with ischemic stroke is not known [Evidence Level C].
ii. There is insufficient research evidence in children with ischemic stroke to support closure of patent foramen ovale [Evidence Level C].

9.3 Aortic arch atheroma

i. Aortic arch atheroma should be managed by optimizing stroke prevention recommendations included in all relevant sections of the *Secondary Prevention of Stroke Module* [Evidence Level C].
ii. In the ARCH trial, no significant difference was found in individuals treated with aspirin and clopidogrel compared to warfarin; the effectiveness of anticoagulant therapy compared with antiplatelet therapy is uncertain, and the choice should be individualized [Evidence Level B].

9.4 Heart failure, decreased ejection fraction, thrombus

i. In patients with ischemic stroke or transient ischemic attack in sinus rhythm who have left atrial or left ventricular thrombus demonstrated by echocardiography or another imaging modality, anticoagulant therapy is recommended for greater than three months [Evidence Level C].
ii. In patients with ischemic stroke or transient ischemic attack in sinus rhythm with severe left ventricular dysfunction (ejection fraction $\leq$35%) without evidence of left atrial or left ventricular thrombus, the net benefit of anticoagulant therapy compared with antiplatelet therapy is uncertain, and the choice of management strategies should be individualized [Evidence Level B].
iii. The risk of stroke, including recurrent stroke, is increased by the presence of heart failure therefore individuals with stroke or transient ischemic attack and heart failure should be managed with aggressive stroke prevention therapies [Evidence Level B].

The optimal management of patients with significant aortic arch atheroma is unclear. Typically, monotherapy with an antiplatelet agent or oral anticoagulation is used to prevent further events in patients with a prior ischemic stroke. Dual antiplatelet therapy with aspirin and clopidogrel was examined as a potential alternative to oral anticoagulation in the Aortic Arch Related Cerebral Hazard Trial (ARCH).[63] After a median of 3.4 years of follow-up, the risk of the primary outcome, a composite of cerebral infarction, myocardial infarction, peripheral embolism, vascular death, or intracranial hemorrhage was not significantly lower in the dual therapy group.

Similarly, the effectiveness of anticoagulation compared with antiplatelet therapy for stroke prevention in patients with heart failure in sinus rhythm remains unclear. In the Warfarin versus Aspirin in Reduced Cardiac Ejection Fraction (WARCEF) trial,[64] warfarin was associated with a significantly reduced risk of ischemic stroke (HR = 0.52, 95% CI 0.33–0.82, $p = 0.005$); however, the risks of major and minor hemorrhages were significantly increased. In sub group analysis, age was found to be an effect modifier,[65] whereby patients <60 years benefited from warfarin over aspirin, while for patients $\geq$60 years, the risk of the

primary outcome was similar between treatment groups. Investigators of the Warfarin and Antiplatelet Therapy in Chronic Heart Failure (WATCH) Trial compared 162 mg aspirin daily versus 75 mg clopidogrel daily versus warfarin, and found the risk of the primary outcome was similar between groups (20.7% aspirin vs. 21.6% clopidogrel vs. 19.6% warfarin).[66] While warfarin was associated with a decreased risk of nonfatal and total stroke compared with either antiplatelet agent, the risk of bleeding events was significantly higher among patients in the warfarin group.

Emerging trends in stroke prevention research

A key tenant to stroke prevention is knowing one's risk for stroke. A sizeable list of modifiable and nonmodifiable risk factors for stroke has been amassed.[67] Of these risk factors, family history, or genetic predisposition, is considered one of the most important risk factors. However, despite numerous epidemiological studies providing evidence for a genetic component to stroke,[68] the extent of this predisposition is largely unknown.[69] Moreover, genetic predisposition to stroke may act at several levels by: (1) contributing to standard risk factor that have a known genetic component such as hypertension or diabetes; (2) interacting with environmental factors; (3) contributing directly to an intermediate phenotype such as atherosclerosis; or (4) affecting latency to stroke, infarct size, or stroke outcome.[69] Clearly, the quest to identify the underlying molecular mechanisms contributing to stroke risk has been challenging at best.[70]

Recent studies examining genetic risk factors for stroke found genetic predisposition to stroke to vary based on age and stroke subtype.[68,71–73] A meta-analysis of genome-wide associations studies undertaken by the METASTROKE Collaboration confirmed that although genetic variants were detected in patients with ischemic stroke when compared to controls, all genetic variations were specific to a stroke subtype.[70] The METASTROKE Collaboration posited the implications of their findings were twofold: (1) to maximize success of genetic studies in ischemic stroke, detailed stroke subtyping is required; and (2) different genetic pathophysiological mechanisms appear to be associated with different stroke subtypes, possibly leading to pharmacotherapy having different effects in different stroke subtypes. Moving forward, detailed subtyping may be required to illustrate differing effect of pharmacological profiles in secondary stroke prevention. In addition, inherited single-gene disorders can also lead to abnormalities that predispose persons toward stroke, usually a specific sub type. For example, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) syndrome is associated with a mutation of the NOTCH3 gene, which manifests independently of traditional stroke risk factors.[74] The condition results in damage to small blood vessels, which reduces blood flow, leading to recurrent subcortical cerebral infarctions. Accordingly, stroke in younger persons should raise suspicion of the presence of one of these highly penetrant mutation, either established genes (e.g. CADASIL, Fabry) or emerging ones (e.g. COL4A2). These genetic abnormalities may be identified using next generation sequencing technology, in selected individuals.

Summary

The 2017 update of the *Canadian Stroke Best Practice Secondary Prevention of Stroke Recommendations* provides a common set of guiding principles for important aspects of secondary stroke prevention. The impact of secondary stroke prevention strategies is increased when individuals who have experienced a stroke or transient ischemic attack are able to access expert prevention care in a timely way. This requires coordinated systems to be in place in all regions to address the needs of individuals following an index event. In Canada, these systems have evolved over the past decade resulting in a growing number of stroke prevention services and protocols to increase access in many under-serviced areas. With emerging biomarkers and genetic information, the field of secondary prevention for stroke will continue to evolve. These recommendations are a work in progress and will continue to be regularly updated every 2–3 years in order to integrate newly released data in a timely way to help ensure optimal evidence-based patient care and outcomes.

Author contributions

Theodore Wein (first author) and David Gladstone (senior author) co-chaired the *Secondary Prevention* expert writing group and are lead authors contributing to all aspects of the development, evidence reviews, analysis, writing, editing and final approval of this manuscript; M. Patrice Lindsay is corresponding author, and senior editor of the Canadian Stroke Best Practice Guidelines and this manuscript, and writer of supplementary documentation. Norine Foley and Sanjit Bhogal conducted the evidence searches and completed the evidence tables and evidence summaries supporting this guideline update, and contributed to the writing and editing of this manuscript. Joseph Berlingieri, Aline Bourgoin, Brian H Buck, Jafna Cox, Dion Davidson, Jim Douketis, John Falconer, Thalia Field, Laura Gioia, Jeffrey Habert, Sharon Jaspers, Cheemun Lum, Dana McNamara Morse, Paul Pageau, Mubeen Rafay,

Amanda Rodgerson, Bill Semchuk, Ashkan Shoamanesh, and Arturo Tamayo are all members of the *Secondary Prevention of Stroke* expert writing group and contributed by reviewing, analyzing and discussing the evidence and collectively finalizing the wording of all the recommendations; Dar Dowlatshahi and Gord Gubitz are senior advisors to the writing group and contributed significantly to the methodology and recommendation development and provided review and edits to this manuscript. Mukul Sharma provided external review for the recommendations and provided extensive input to the recommendation development. Elisabeth Smitko provided coordination and meeting support to the writing group and contributed to the development of supplementary materials.

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