

Canadian Stroke Best Practice Recommendations for Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care, 6th Edition, Update 2018

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Abstract

The 2018 update of the *Canadian Stroke Best Practice Recommendations for Acute Stroke Management*, 6th edition, is a comprehensive summary of current evidence-based recommendations, appropriate for use by healthcare providers and system planners caring for persons with very recent symptoms of acute stroke or transient ischemic attack. The recommendations are intended for use by a interdisciplinary team of clinicians across a wide range of settings and highlight key elements involved in prehospital and Emergency Department care, acute treatments for ischemic stroke, and acute inpatient care. The most notable changes included in this 6th edition are the renaming of the module and its integration of the formerly separate modules on prehospital and emergency care and acute inpatient stroke care. The new module, *Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care* is now a single, comprehensive module addressing the most important aspects of acute stroke care delivery. Other notable changes include the removal of two sections related to the emergency management of intracerebral hemorrhage and subarachnoid hemorrhage. These topics are covered in a new, dedicated module, to be released later this year. The most significant recommendation updates are for neuroimaging; the extension of the time window for endovascular thrombectomy treatment out to 24 h; considerations for treating a highly selected group of people with stroke of unknown time of onset; and recommendations for dual antiplatelet therapy for a limited duration after acute minor ischemic stroke and transient ischemic attack. This module also emphasizes the need for increased public and healthcare provider's recognition of the signs of stroke and immediate actions to take; the important expanding role of paramedics and all emergency medical services personnel; arriving at a stroke-enabled Emergency Department without delay; and launching local healthcare institution code stroke protocols. Revisions have also been made to the recommendations for the triage and assessment of risk of recurrent stroke after transient ischemic attack/minor stroke and suggested urgency levels for investigations and initiation of management strategies. The goal of this updated guideline is to optimize stroke care across Canada, by reducing practice variations and reducing the gap between current knowledge and clinical practice.

Keywords

Ischemic stroke, acute stroke therapy, guidelines, neurovascular imaging, endovascular procedures, acute thrombolysis, acute stroke unit, complications, early mobilization, palliative care

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Introduction

Approximately 62,000 people with stroke and transient ischemic attack (TIA) are treated in Canadian hospitals each year, of which 53,000 are admitted to acute care.¹ In Canadian hospitals, one patient is treated every 9 min for a stroke or a TIA.¹ Stroke is a leading cause of adult disability; over 400,000 people in Canada are living with its effects.² That number is expected to double in the next 20 years.² Stroke is the third leading cause of death³ and costs the Canadian economy more than \$3.6 billion a year in physician services, hospital costs, lost wages, and decreased productivity.⁴ Hypertension, physical inactivity, unhealthy diets, and our aging population of baby boomers are all significant factors affecting stroke rates in Canada.³

The 2018 update of the *Canadian Stroke Best Practice Recommendations for Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care Practice Guidelines* includes a comprehensive summary of current evidence-based recommendations appropriate for use by healthcare professionals across all disciplines that provide care to patients following an acute stroke or TIA

within the population of Canada. These guidelines address the first hours and days after stroke occurs, starting with the onset of stroke signs and symptoms through to discharge from the Emergency Department (ED) or acute inpatient care.

The recently published trials showing that endovascular thrombectomy (EVT) is an effective treatment for acute ischemic stroke, including for some patients arriving 16–24 h after last known to be well, have prompted a broader review of emergency systems of care for acute stroke. Increasing timely access to EVT will require an expanded role for paramedics, to ensure that patients with large vessel occlusion are triaged to thrombectomy-capable hospitals, and an expanded role for advanced imaging for patient selection for later arriving patients. This 2018 guideline update provides additional recommendations in these areas.

What's new in 2018?

The most notable change in the 6th edition of this module is the combining of two previously separate modules, Hyperacute Stroke Care and Acute Inpatient Stroke Care into a single, comprehensive

module. The second notable change in this combined module, *Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care* is that all recommendations pertaining to hemorrhagic stroke (intracerebral hemorrhage and subarachnoid hemorrhage [SAH]) after *the point of diagnosis* have been removed. A new module within the Canadian Stroke Best Practices series focusing on *hemorrhagic stroke* is in development for release later in 2018. The 6th edition also includes revisions to the recommendations that reflect new evidence available since the previous release of these recommendations^{5,6} for the triage and assessment of risk of recurrent stroke after TIA or nondisabling stroke and suggested urgency levels for investigations and initiation of management strategies (Section 2); updates to management of blood pressure in the first hours following stroke (Section 4); updates, clarification, and consolidation into a single section of initial imaging recommendations in the ED (Section 4); new clinical considerations for treatment of people with stroke of unknown onset time (Section 5.1); updates to EVT recommendations and time windows based on recent evidence from the DWI or CTP Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo (DAWN)⁷ and the Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke (DEFUSE-3)⁸ trial (Section 5.5); revisions to the aspirin recommendations based on additional evidence from the Platelet-Oriented Inhibition in New TIA & Minor Ischemic Stroke (POINT) Trial⁹ (Section 6); revisions to recommendations for care of patients experiencing stroke while already in hospital for other causes (Section 8); updates to early mobilization recommendations (Section 9) based on additional analysis from the A Very Early Rehabilitation Trial (AVERT);¹⁰ and revisions to advanced care planning, palliative and end-of-life care recommendations (Sections 10 and 11, respectively).

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.^{11,12} The methodology has been used in previously published updates^{13,14} and can be found on our Canadian Stroke Best Practices website at www.strokebestpractices.ca.¹⁵ An interdisciplinary 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 interdisciplinary writing group and external reviewers include stroke neurologists, ED physicians, interventional radiologists, neurosurgeons, nurses, paramedics, family physicians, hospitalists, rehabilitation therapists, epidemiologists, care coordinators, and health system planners. These experts work in a wide range of healthcare settings. This interdisciplinary 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. These guidelines were developed in collaboration with the Canadian Stroke Consortium and the Canadian Association of Emergency Physicians as well as consultation with the Paramedic Chiefs of Canada and the Paramedic Association of Canada. This interprofessional collaboration among these groups was aimed at encouragement of wide-spread adoption of these recommendations and to further drive systems change for more consistent and efficient care of acute stroke patients from the onset of stroke.

A comprehensive systematic literature search was conducted to identify research evidence on the identification and management of persons following acute stroke or TIA. The literature for this module was updated to May 2018. The writing group was provided with comprehensive evidence tables that included summaries of all high-quality evidence identified through the literature searches (evidence tables are available at www.strokebestpractices.ca). Systematic reviews, meta-analyses, randomized controlled trials, and observational studies were included, where available. The writing group discussed and debated the value of the evidence and, through consensus, developed a set of proposed recommendations. Through their discussions, additional research may have been identified and included in the evidence tables if consensus on the value of the research was achieved.

All recommendations are assigned a level of evidence ranging from A (systematic reviews, meta-analyses, multiple homogenous randomized controlled trials), B (single randomized controlled trials, quasi-experimental design with large samples and power), to C (weak evidence, expert opinion achieved by consensus). 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.

After completion of the draft update to the recommendations, the module underwent an internal review by the Canadian Stroke Best Practices Advisory Committee and an external review by Canadian and international experts who were not involved in any aspects of the guideline development. These recommendations were also reviewed by members of the Canadian Stroke Consortium, the Canadian Association of Emergency Physicians, the Paramedic Chiefs of Canada, and the Paramedic Association of Canada. All feedback was reviewed and addressed by the writing group members and the advisory committee to ensure a balanced approach to addressing suggested edits.

All recommendations are accompanied by additional supporting information, including a rationale for inclusion of the topics, system implications to ensure the structural elements and resources are available to achieve recommended levels of care, performance measures to monitor care delivery and patient outcomes as well as implementation resources and a summary of the evidence on which the recommendations were based. Brief summaries of current research evidence are provided at the beginning of each section below. More detailed evidence summaries and links to all evidence tables, and additional knowledge translation information for the recommendations included in this publication can be found at www.strokebestpractices.ca/acute-stroke-management.

Part I: Canadian Stroke Best Practice Recommendations for Prehospital and Emergency Department Stroke Care, 6th edition, update 2018

The first minutes and hours from the onset of stroke signs and symptoms are critical and strongly linked to patient outcomes. Rapid assessment, diagnosis, and decision-making could have a significant impact on mortality and long-term recovery and quality of life. Recommendations pertaining to pre-hospital and ED stroke care involve topics related to all direct care, including investigations, interventions, service delivery, and interactions from first contact with the healthcare system after the onset of stroke symptoms through to discharge from an ED to

another healthcare facility (usually with a higher or lower level of stroke care available), to an acute inpatient care unit, or to return to the community. They include topics related to stroke recognition and response, assessment, triage and management of TIA, and mild nondisabling stroke; initial triage and management by emergency medical services (EMS), ED rapid assessment and diagnosis, acute stroke treatments including intravenous thrombolysis with alteplase and EVT, acute antiplatelet therapy, and the early management of patients considered for hemicraniectomy.

Section I: Stroke awareness, recognition, and response

Many people do not recognize the signs and symptoms of a stroke, or they will attribute them to a less serious health issue and may fail to seek immediate medical attention. In Canada, 40% of people who responded in a recent public poll conducted by the Heart and Stroke Foundation did not know any of the FAST (Face, Arms, Speech, and Time) signs of stroke.¹⁶ Failure of recognition on the part of either those witnessing a stroke or the person experiencing a stroke can initiate a series of delays, beginning with the lag in contacting EMS, and may ultimately decrease a patient's opportunity to receive time-sensitive treatments. The most commonly identified symptoms of stroke among members of the general public are unilateral weakness and slurred speech.^{17–19}

The number of public health campaigns designed to increase the recognition of the signs and symptoms of stroke has increased over the past decade. One of the best recognized programs in the healthcare community is FAST. Exposure to these campaigns has proven to be effective, resulting in increased awareness of the signs and symptoms of stroke²⁰ and an increase in the number of persons who indicated they would call 9-1-1 in response to witnessing specific stroke symptoms.²¹ Mass media campaigns have also been shown to be associated with increases in the use of thrombolytic agents following acute stroke. Advani et al.²² reported that the average number of patients treated with tissue plasminogen activator (t-PA) in a month increased by 54.7%, and the average number of patients treated in the ED increased significantly from 37.3% to 72.8% (an increase of 95.7%, $p < 0.001$) in the 6-month period following the introduction of a mass media intervention that featured the FAST mnemonic, compared to the preceding 12-month period. In the same study, which also included a telephone survey of 1400 members of the public, the number of people who could name any stroke symptom increased from 66% to 75%.

Section I: Recommendations for stroke awareness, recognition, and response

- i. All members of the public and all healthcare providers should be educated that stroke is a medical emergency [Evidence Level C].
- ii. Public and healthcare provider education should focus on recognizing the signs and symptoms of stroke and actions to take when experiencing or witnessing the signs of stroke [Evidence Level C].
- iii. Public awareness campaigns and education should include use of the FAST (Face, Arms, Speech, and Time) acronym to facilitate memory and recognition of these signs [Evidence Level B].
- iv. Public and healthcare provider education should emphasize the need to *respond immediately* by calling 9-1-1 or their local emergency number [Evidence Level B], even if symptoms resolve.
 - a. The public should be prepared to provide relevant information and answer questions from the dispatcher, paramedics, and others [Evidence Level C]. *Refer to Box 1 below.*
 - b. The public should be aware of the importance of following instructions of the emergency medical system dispatch center [Evidence Level C].
- v. Public and healthcare providers education should include information that stroke can affect persons of any age including newborns, children, and all adults. Education should also emphasize the benefits of early emergency treatment [Evidence Level B].

For recommendations on EMS and Prehospital Care, refer to Section 3.

Box 1: Core information required by dispatch, paramedics, and receiving healthcare facility

- Where permitted, limited identifiers such as name, date of birth and/or health card number be provided in order to expedite the registration process.
- Location of patient
- Signs of stroke apparent and visible in patient—including face, arm, speech involvement
- Signs of stroke onset time if witnessed, and last seen well time if not witnessed
- Current condition of the patient having a stroke, and changes in their condition since the stroke symptoms started
- Current medications, if known
- Additional health problems, if known
- Collect phone number of witness to verify information
- Advanced care directives if available

Section 2: Outpatient management of TIA and nondisabling stroke

Ideally, people experiencing any of the signs of an acute stroke should immediately call 9-1-1 or local emergency services number and go to an ED. Unfortunately, this is not always the case; the reality is that some people experiencing signs of acute stroke may present to an outpatient setting such as a primary care physician or family health team office, community clinic, or urgent care center. People experiencing signs of stroke require rapid assessment, diagnosis, and determination of risk for a recurrent stroke. Patients determined to have TIA, or subacute, nondisabling ischemic strokes who are not candidates for hyperacute treatment with intravenous alteplase or EVT still require timely assessment and management, which can be provided in an outpatient setting. The goal of outpatient management of TIA and nondisabling ischemic stroke is to rapidly identify vascular 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 has been estimated to be relatively high, between 12% and 20%,^{23,24} with the greatest risk of recurrence within the first two days following initial symptom onset. The risk of recurrent stroke at two and seven days following a TIA was estimated to be 3.1% and 5.2%, respectively, with lower estimates associated with specialized care.²⁵ Among patients with multiple risk factors, the seven-day risk of stroke following a TIA can be as high as 36%.²⁶ With the recent adoption or expansion of the availability of rapid TIA 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. A recent study by the TIARegistry.Org group reported updated recurrence rates that were less than half that expected from historical cohorts. This decline was attributed to better and faster access to stroke prevention strategies through rapid-access TIA clinics. Stroke recurrences at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%,

and 5.1%, respectively.²⁷ Similar risk reductions were demonstrated in the Early Use of Existing Preventive Strategies for Stroke (EXPRESS) study.²⁸ The 90-day risk of recurrent stroke among patients who were referred to a dedicated TIA clinic was 2.1% compared with 10.3% for patients with non-immediate access.

Section 2: Recommendations for outpatient assessment and management of stroke and transient ischemic attack

2.0 Patients with stroke and TIA 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. (Please refer to online Appendix 1 for summary of Stroke Risk Levels and Actions)

2.1 Timing of initial assessment

2.1.1 VERY HIGH risk for recurrent stroke (symptom onset within last 48 h)

- i. Patients who present *within 48 h* of a suspected TIA or nondisabling 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 *language/speech disturbance* [Evidence Level B];
 - c. fluctuating or persistent symptoms *without motor weakness or language/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, dysphagia, ataxia) [Evidence Level B].
- ii. Patients identified as highest risk should be **immediately** sent to an ED 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 2.2 for more information on investigations.
- iii. Urgent brain imaging (computed tomography (CT) or magnetic resonance imaging (MRI)) and non-invasive vascular imaging (CT angiography (CTA) or MR angiography (MRA) from aortic arch to vertex) should be completed as soon as possible **within 24 h** [Evidence Level B]. Refer to Section 2.2 for more information on investigations.
- iv. An electrocardiogram (ECG) should be completed without delay [Evidence Level B].

2.1.2 HIGH risk for recurrent stroke (symptom onset between 48 h and two weeks)

- i. Patients who present **between 48 h and two weeks** from onset of a suspected TIA or nondisabling ischemic stroke with symptoms of transient, fluctuating or persistent unilateral weakness (face, arm, and/or leg), or language/speech disturbance 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 healthcare professional with stroke expertise as soon as possible [Evidence Level B], **ideally initiated within 24 h** of first contact with the healthcare system [Evidence Level C]. Refer to Section 2.2 for more information on investigations.

2.1.3 MODERATE (INCREASED) risk for recurrent stroke (symptom onset between 48 h and two weeks)

- i. Patients who **present between 48 h and two weeks** of a suspected TIA or nondisabling ischemic stroke with transient, fluctuating or persistent symptoms *without unilateral motor weakness or language/speech disturbance* (e.g., with hemibody sensory symptoms, monocular vision loss, binocular diplopia, hemifield vision loss, dysarthria, dysphagia, or ataxia) may be considered at increased risk of first or recurrent stroke [Evidence Level C].
- ii. These patients should receive a comprehensive clinical evaluation and investigations by a healthcare professional with stroke expertise as soon as possible [Evidence Level B], **ideally within two weeks** of first contact with the healthcare system [Evidence Level C]. Refer to Section 2.2 for more information on investigations.

2.1.4 LOWER risk for recurrent stroke (time lapse since symptom onset greater than two weeks)

- i. Patients **presenting more than two weeks** following a suspected TIA 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 2.2 for more information on investigations.

2.2 Diagnostic investigations

2.2.1 Initial assessment

- i. Patients presenting with suspected acute or recent TIA or nondisabling ischemic stroke should undergo an initial assessment that includes brain imaging, non-invasive vascular imaging (including carotid imaging), and 12-lead ECG and laboratory investigations.
 - a. Brain imaging (CT or MRI) and non-invasive vascular imaging (CTA or MRA from aortic arch to vertex) should be completed as appropriate and within time frames based on triage category and severity described in Section 2.1 [Evidence Level B]. Refer to *online Appendix 1 for additional information, and Section 4 for detailed recommendations on neuroimaging.*
 - b. CTA 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]. *Note: Some facilities may not have CTA readily available and vascular imaging will need to be based on available resources and equipment.*
 - 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 TIA 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 and troponin [Evidence Level C]. Refer to *online Appendix 1 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 non-fasting); and screening for diabetes with either a glycated hemoglobin (HbA1c) or 75 g oral glucose tolerance test [Evidence Level C].
- iii. Patients with suspected TIA 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 TIA, ECG monitoring for more than 24 h 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 small strokes 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.

2.2.2 Additional investigations for embolic stroke of undetermined source (ESUS)

- i. For patients being investigated for an acute embolic ischemic stroke or TIA 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 two weeks is recommended to improve detection of paroxysmal atrial fibrillation in selected patients aged ≥ 55 years who are not already receiving anticoagulant therapy but would be potential anticoagulant candidates [Evidence Level A]. Refer to *CSBPR Secondary Prevention of Stroke Module for additional guidance in management of patients with stroke and atrial fibrillation.*
- ii. Echocardiography could be considered in cases where a stroke mechanism has not been identified [Evidence Level C].

For recommendations on immediate clinical management with antiplatelet therapy, refer to Section 6 in this module.

2.3 Functional assessment

- i. Patients with TIA or ischemic stroke should be assessed for neurological impairments and functional limitations (e.g., cognitive evaluation, screening for depression, screening of fitness to drive, need for potential rehabilitation therapy, and assistance with activities of daily living) [Evidence Level B]. Refer to *Rehabilitation Module Recommendations 5.1 and 5.6 for additional information.*
- 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 3: Emergency Medical Services management of acute stroke patients

The role of paramedics in acute stroke care is expanding and they are essential members of all well-functioning stroke systems of care. These recommendations cover management of potential stroke patients between the time of first contact with the local Emergency Medical System to transfer of care to the hospital as well as care of suspected or confirmed stroke patients who are being transferred between healthcare facilities by paramedics. They are directed to paramedics and those individuals who support Emergency Medical Systems, including communications officers and dispatchers. It also applies to other first responders such as emergency medical responders and other paramedics who have been trained to screen for stroke and manage potential stroke patients during transfer. The most notable update in these recommendations is the addition of a two-step stroke screening to be performed by paramedics on scene. The first step includes standard screening for signs of stroke using an instrument such as FAST or the Cincinnati Prehospital Stroke Scale.²⁹ A second, subsequent screen is now recommended if the first screen is positive to assess stroke severity and identify severe stroke patients who may be potential candidates for mechanical thrombectomy. Several validated scales are currently available, such as the Field Assessment Stroke Triage for Emergency Destination (FAST-ED),³⁰ Stroke vision, aphasia, neglect (VAN),³¹ and the Los Angeles Motor Scale (LAMS),³² among others.

Patients arriving to hospital using EMS following a stroke experience fewer delays in receiving appropriate diagnostic tests (e.g., brain imaging) and are more likely to receive intravenous thrombolysis and mechanical thrombectomy, if eligible. Transport by EMS is also safer and enables patients to be triaged to appropriate hospitals that provide specialized stroke services. Approximately 63% of all patients who seek acute

care for stroke in Canada arrive at the ED by ambulance^{1,33}; Patients are also more likely to receive timely transportation and care when prenotification systems, including the use of trained EMS dispatchers, are adopted. Hospital prenotification typically involves informing ED physicians and other relevant personnel (blood and EKG technicians, radiologists, and pharmacologists) of the arrival of a potential stroke patient. The results from several studies indicate that a significantly higher proportion of patients are treated with thrombolytic agents after EMS dispatchers completed training aimed at improving their ability to detect suspected stroke patients.^{34,35} Watkins et al.³⁶ reported that the percentage of stroke patients correctly dispatched as suspected stroke increased significantly (63% to 80%, $p < 0.01$) after EMS dispatchers completed training. Process times associated with thrombolysis treatment may also be shortened for patients arriving to hospitals by EMS with prenotification protocols. In a study that included 27,566 patients who were identified as suspected stroke patients by dispatchers, the mean times associated with transportation, including time to scene, time at scene, time from scene to destination, and total transportation time were all significantly reduced, compared to persons whose final diagnosis was stroke, but who were not identified by dispatchers.³⁵ Berglund et al.³⁴ reported that patients in the Hyper Acute STroke Alarm (HASTA) Study assigned an upgraded priority level by dispatching personnel experienced fewer delays along the chain of stroke care from symptom onset to arrival at a stroke unit and were more likely to be treated with t-PA compared with patients who had been assigned to a standard-priority level by the emergency medical communications center. Patients classified as Priority Level 1 received thrombolysis more often than those classified as priority Level 2 (24% vs. 10%, $p < 0.001$) and a greater number arrived at the stroke unit within 3 h of symptom onset (61% vs. 46%, $p = 0.008$).

Section 3: Recommendations for Emergency Medical Services Management management of acute stroke patients

3.0 Out-of-hospital patient management should be optimized to meet the needs of suspected acute stroke patients, including recognition, management, and rapid transport, usually done concurrently [Evidence Level C].

3.1 Access to Emergency Medical Services (EMS)

- i. Immediate contact with emergency medical systems (e.g., 911) by people experiencing the signs of stroke, a witness or other members of the public is strongly recommended [Evidence Level B]. Refer to Section 1 for additional information on signs of stroke.
- ii. **EMS communications center:** All regions should implement a dispatch process through the EMS communications center to recognize the probable stroke signs (such as FAST—Face, Arms, Speech, and Time), potential stroke diagnosis, and need for priority response to the scene and transport to a hospital capable of providing acute services for the rapid diagnosis and time-sensitive treatment of stroke (such as neuroimaging and acute thrombolysis) [Evidence Level C].

- iii. After dispatching the ambulance, it is recommended that emergency medical system communications center personnel provide pre-arrival instructions to the person reporting the stroke (such as unlock door, move pets, determine stroke symptom onset time, determine current medications) in order to expedite and optimize prehospital care [Evidence Level C]. *Note: If the person experiencing the signs of stroke is the one to contact EMS, they may not be able to comply with these requests.*

3.2 Paramedic on-scene management

Note: On-scene goal is to “recognize and mobilize”—it is of the utmost importance to proceed rapidly and safely to transport suspected stroke patients, as on-scene management for stroke patients is limited.

- i. EMS personnel should use validated acute stroke out-of-hospital diagnostic screening tools as part of on-scene assessment [Evidence Level B]. [New for 2018]
 - a. Patients should be screened for **signs of stroke** using a validated stroke assessment tool that includes the components of FAST (Face, Arm, Speech, and Time) [Evidence Level B].
 - b. Patients who demonstrate any FAST signs should then undergo a second screen using a tool validated to assess **stroke severity**, which may be considered in decisions for transportation destination [Evidence Level B]. [New for 2018] *Note: The purpose of this second screen is to look for possible EVT candidates, such as people exhibiting signs of cortical dysfunction (aphasia, visual changes, and neglect).*
- ii. It is recommended that EMS personnel obtain information from the patient, family members, or other witnesses about the suspected stroke event (presenting symptoms, time of onset or time of symptom recognition or time last known well, and sequence of events), comorbid conditions, current medications (especially anticoagulants), and any formal or informal advance directives that may influence care by EMS and in the ED [Evidence Level C].
- iii. On-scene time with suspected stroke patients should be as short as possible; ideally a median time of 20 minutes or less* for patients who present within the 4.5-h treatment time window [Evidence level C]. (*Target median of 20 min based on median EMS on-scene time data from across provinces contained in HSF Stroke Report 2015).
- iv. Initial assessment provided by paramedic’s on-scene should include capillary blood glucose measurement [Evidence Level B].
- v. Prior to transport, it is recommended that paramedics on-scene provide instructions to the patients’ family, including recommending that the family/decision-maker accompany the patient to hospital or be accessible by phone for decision-making, as well as confirming time last known well, and providing required information about existing health conditions, current medications, and other information as needed [Evidence Level C].

3.3 Transport of suspected stroke patients

- i. Direct transport protocols must be in place to facilitate the transfer of suspected acute stroke patients who are potentially eligible for thrombolytic and/or EVT to the most appropriate acute care hospital capable of providing services for the diagnosis and treatment of acute stroke [Evidence Level C].
- ii. It is recommended that direct transport protocol criteria be based on:
 - a. an EMS system set up to categorize patients exhibiting signs and symptoms of an acute stroke as a high priority for evaluation, response, and transport [Evidence Level C];
 - b. the medical stability of the patient [Evidence Level B];
 - c. the presenting signs and symptoms of stroke [Evidence Level B];
 - d. the probability that the patient is acutely treatable with either intravenous alteplase and/or EVT [Evidence Level B];
 - e. patients are eligible for medical thrombolysis (intravenous alteplase) within 4.5 h of known or presumed symptom onset [Evidence Level B];
 - f. some patients may be eligible for endovascular treatment when highly selected by neurovascular imaging up to 24 h from known or presumed symptom onset. Transport time and receiving hospital projected treatment time must be considered when making transport and triage decisions [Evidence Level B];
 - g. the ED ability to provide acute stroke services within a target 90th percentile for door-to-needle (i.e., arrival to treatment) time of 60 min (upper limit) and a target median door-to-needle time of 30 min or less [Evidence Level B];
 - h. other acute care needs of the patient [Evidence Level B].

- iii. Patients with suspected stroke should be triaged by EMS personnel as Canadian Triage Acuity Scale (CTAS) Level 2 in most cases and as a CTAS Level 1 for patients with compromised airway, breathing or cardiovascular function [Evidence Level B].
 - a. For pediatric stroke cases, patients with suspected stroke should be triaged by EMS personnel as Pediatric Canadian Triage Acuity Scale (P-CTAS) Level 2 in most cases, and as a P-CTAS Level 1 for patients presenting with severe symptoms or compromised airway, breathing, or cardiovascular function [Evidence Level C].
- iv. **Prenotification:** While en route to the receiving hospital with acute stroke services, paramedics should notify the ED of the incoming suspected acute stroke patient, providing sufficient details such that a “Code Stroke” can be activated at that time [Evidence Level B].
 - a. Information required includes time of stroke onset or time of symptom recognition or time when last known well (as accurate as possible), total symptom duration at anticipated arrival in the ED, presenting signs and symptoms of stroke, Glasgow Coma Scale (GCS) score, CTAS triage score (or P-CTAS), patient age, current use of antithrombotic drugs, and expected time of arrival at the receiving hospital. *Refer to Box 3 for details of information required during prenotification.*
- v. Patients who are considered ineligible for thrombolytic therapy or EVT should still be transported urgently (either directly or indirectly) to the closest hospital capable of providing services for the diagnosis and treatment of stroke (ED, access to neurovascular imaging, stroke unit, and stroke expertise on site or through Telestroke modalities) [Evidence Level C].

3.4 Hospital arrival and EMS handover to Emergency Department (ED) Staff

- i. Transfer of care from paramedics to receiving hospital personnel should occur with minimal delay; patients with suspected hyperacute stroke who are potentially eligible for thrombolytic therapy or EVT should receive the highest priority in the ED triage queue [Evidence Level B]. *Refer to Section 4.1 for more information.*
- ii. Paramedics should provide the receiving hospital with the following information on hospital arrival: time of stroke onset or time of symptom recognition or time when last known well (as accurate as possible), total symptom duration at arrival in the ED, GCS score, CTAS triage score (or P-CTAS), patient age, comorbidities, current medications including antithrombotic drugs and medication allergies, and vital signs (including capillary glucose) [Evidence Level C].
 - a. Paramedics should ensure all information noted above is documented on the patient’s emergency medical system record and provided to the receiving hospital during prenotification and upon arrival to the hospital [Evidence Level B].

Clinical considerations: [New for 2018]

1. Direct transport in many regions involves two considerations: (1) patients who may be eligible for intravenous alteplase may be directed to the closest center (primary/advanced stroke center or comprehensive stroke center) and, (2) patients who are determined to be a likely candidate for EVT may proceed directly to an EVT-enabled comprehensive stroke center OR to the primary center first to rapidly receive intravenous alteplase, and then be considered for transport to the EVT-enabled comprehensive stroke center.
2. Screening for potential stroke and likelihood of large vessel occlusion should be done early in the on-scene assessment. If the stroke screen is positive, all actions on-scene from that point should be directed at moving to the ambulance and beginning transport. All treatments not immediately required (IVs, etc.) *could* be undertaken while the patient is en route to the hospital or after hospital arrival. Scene time (location of patient at time of stroke) is an important variable that EMS professionals can control and needs to be monitored very closely. Time lost due to inefficient scene care cannot be made up during subsequent transport to hospital, regardless of the use of lights and sirens.
3. Prenotification contact with the receiving ED should be as soon as possible; where possible, the paramedics and receiving ED physician or stroke team member should speak en route.
4. The term “eligible” for acute stroke therapies is usually defined within regional jurisdictions. Generally, it refers acute stroke patients within the 4.5-h time window for medical thrombolytic therapy; however, local definitions should be clarified during implementation of these recommendations.
5. For EVT, the strongest evidence for benefit exists for treatment received within 6 h of stroke symptom onset (with or without concurrent medical thrombolytic therapy). However, randomized trial evidence exists to show that highly selected patients may be considered for EVT based upon neurovascular imaging within a 24-h window from symptom onset.
6. In some stroke centers, the alteplase treatment time window may extend beyond 4.5 h under the directive of a research or local protocols. These factors should be taken into consideration during transport and agreements should be in place between the provincial/regional EMS system and the receiving hospitals.
7. In regions with a specialized pediatric hospital, every attempt should be made to transport children with signs of stroke to that specialized pediatric hospital.

Box 3A: Core information required by dispatch, paramedics, and receiving healthcare facility

- Where permitted, name, date of birth, and health card number of patient. *Note: In general, this confidential personal health information is not allowed to be transmitted by radio; however, some provinces have been able to receive a waiver and the restriction lifted for emergency cases such as stroke.*
- Location of patient
- Stroke symptom onset time if witnessed, and last seen well time if not witnessed
- Presenting signs of stroke and stroke severity score, based on standardized screening tools
- Current condition of the patient having a stroke, including previous functional status/independence and changes in their condition since the stroke symptoms started
- Current medications if known (such as anticoagulants)
- Advanced care directives if any
- Additional health problems, if known

Section 4: ED evaluation and management of acute stroke and TIA

Patients require immediate evaluation when presenting to the ED with suspected stroke or TIA. Systems of care must be in place to ensure highly coordinated rapid assessment and access to imaging. In this update, recommendations for urgent imaging have been clarified, expanded, and consolidated all in this section. For those patients presenting with TIA, their risk for imminent stroke (i.e., within one week) can be evaluated, and investigations/treatment initiated to prevent a future stroke (refer to Section 2 for more information). Standard assessments for patients with suspected acute stroke include a neurological examination, immediate neurovascular imaging, monitoring of vital signs, blood work, cardiovascular investigations, and dysphagia screens. Immediate access to brain and vascular imaging is required for all patients arriving to hospital with suspected stroke or TIA. A non-contrast CT (NCCT) scan or MRI should be used as first line initially to identify the presence of stroke and stroke type—ischemic or of hemorrhagic origins. Although MRI has been shown to be more sensitive in detection of the early changes associated with ischemia, especially in patients with small infarcts,³⁷ timely access to the technology is not widely available in Canada, in particular in the context of an acute stroke. In MRI-equipped centers, patients with suspected stroke may not get immediate access to this technology, which could lead to delays in treatment decisions. Combined multimodal vascular imaging with angiography, and in highly selected cases perfusion scans, with CT or MRI has the potential to identify patients with an ischemic penumbra and potentially

viable brain tissue who may be appropriate for acute reperfusion therapies. Perfusion scans can be especially useful in selecting patients eligible for endovascular therapy in the 6–24 h window whereas in the 0–6 h time-frame, most cases can be selected with the use of CT and CTA alone. For all potential stroke patients, once adequate breathing and circulation have been secured, neuro-imaging must be the highest priority on arrival to hospital. Blood work and other assessments such as an electrocardiograph can be done after imaging in most cases.

The initial management of elevated blood pressure in acute stroke patients remains controversial, given the lack of evidence to clearly guide practice. In ischemic stroke, high initial blood pressure has been associated with cerebral edema or hemorrhagic transformation, but rapid reduction of blood pressure, regardless of the degree of hypertension, may also be harmful. Aggressive efforts to lower blood pressure may decrease perfusion pressure, which may worsen ischemia.³⁸ Since optimal blood pressure targets are not yet known, the current, consensus-based recommendation for patients who are not candidates for thrombolytic therapy is to lower blood pressure only when systolic pressure exceeds 220 mm Hg or when diastolic pressure exceeds 120 mm Hg. For patients who are candidates for thrombolytic therapy, since elevated blood pressure (systolic blood pressure (SBP) ≥ 185 mm Hg or diastolic blood pressure (DBP) ≥ 110 mm Hg) is a contraindication to the use of thrombolytics, blood pressure must be reduced to avoid hemorrhagic complications. Results from the blood pressure-lowering arm of the ENCHANTED trial, when released, will provide additional information to guide patient management.³⁹

Section 4: Recommendations for Emergency Department evaluation

- i. All patients presenting to an ED with suspected acute stroke or TIA must have an immediate clinical evaluation and investigations to establish a diagnosis, rule out stroke mimics, determine eligibility for intravenous thrombolytic therapy and EVT treatment and develop a plan for further management, including goals for care [Evidence Level A].

Note: If initial brain imaging reveals a hemorrhagic stroke, then refer to new CSBPR for Hemorrhagic Stroke for guidance on further investigations, acute treatments, and ongoing management. (for release Fall 2018)

4.1 Initial ED evaluation

- i. Patients with suspected acute stroke should have a rapid initial evaluation for airway, breathing, and circulation [Evidence Level A].
- ii. A neurological examination should be conducted to determine focal neurological deficits and assess stroke severity [Evidence Level A].
 - A standardized stroke scale should be used (such as the National Institutes of Health Stroke Scale (NIHSS)) [Evidence Level C].
- iii. Assessment in the acute phase should include heart rate and rhythm, blood pressure, temperature, oxygen saturation, hydration status, and presence of seizure activity [Evidence Level B].
- iv. Acute blood work should be conducted as part of the initial evaluation [Evidence Level B]. Initial blood work should include electrolytes, random glucose, complete blood count, coagulation status (INR, aPTT), and creatinine. Refer to Appendix 1 online for Recommended Laboratory Investigations for Acute Stroke and TIA for additional information.
 - Note these tests should not delay imaging or treatment decisions and treatment initiation for intravenous thrombolysis and EVT.
- v. **Seizure assessment:** New onset seizures at the time of an acute stroke, occurring either immediately before or within 24 h of the stroke onset, should be treated using appropriate short-acting medications (e.g., lorazepam IV) if they are not self-limited [Evidence Level C].
 - a. A single, self-limiting seizure occurring at the onset, or within 24 h after an acute stroke (considered an “immediate” post-stroke seizure) should not be treated with long-term anticonvulsant medications [Evidence Level C].
 - b. Patients that have an immediate post-stroke seizure should be monitored for recurrent seizure activity during routine monitoring of vital signs and neurological status. Recurrent seizures in patients with ischemic stroke should be treated as per treatment recommendations for seizures in other neurological conditions [Evidence Level C].
 - c. Seizures are a common presentation with stroke in neonates and children. Consider enhanced or prolonged electroencephalogram (EEG) in at-risk populations such as neonates, children with stroke and adults with otherwise unexplained reduced level of consciousness [Evidence Level C].
 - d. Prophylactic use of anticonvulsant medications in patients with acute stroke is not recommended [Evidence Level C]. There is no evidence to support the prophylactic use of anticonvulsant medications in patients with acute stroke and there is some evidence to suggest possible harm with negative effects on neural recovery.

4.2 Neurovascular (brain and vascular) imaging

- i. All patients with suspected acute stroke should undergo brain imaging with NCCT or MRI [Evidence Level A].
- ii. All patients with suspected acute ischemic stroke who arrive **within 4.5 h** and are potentially eligible for intravenous thrombolysis (refer to criteria in Box 4A) should undergo **immediate** brain imaging with non-contrast CT (NCCT) without delay to **determine eligibility for thrombolysis** [Evidence Level A].
- iii. All patients with suspected acute ischemic stroke who arrive **within 6 h** and are potentially eligible for EVT (refer to criteria in Box 4B and Section 5) should undergo **immediate** brain imaging **non-contrast CT and CT angiography (CTA)** without delay, from arch-to-vertex including the extra- and intra-cranial circulation, to identify large vessel occlusions **eligible for endovascular thrombectomy** [Evidence Level A].

Note: Primary stroke centers that cannot do CTA should have pre-planned arrangements for rapid transfer of appropriate patients. They should complete NCCT and offer intravenous alteplase as appropriate and then rapidly transfer the patient to a CSC for more advanced imaging and consideration for EVT.

- a. A validated triage tool (such as ASPECTS) should be used to rapidly identify patients who may be eligible for EVT treatment and may require transfer to a different facility for EVT [Evidence Level B]. [New for 2018]
- b. Advanced CT imaging such as CT perfusion (CTP) or multiphase or dynamic CTA (to assess pial collateral vessels) can be considered as part of initial imaging to aid patient selection [Evidence Level B]. However, this must not substantially delay decision and treatment with intravenous thrombolysis with alteplase or EVT treatment. Refer to Box 4C. Refer to Section 5 for additional criteria for EVT.

Note: If there are signs of hemorrhage on initial CT images, there is no need to proceed to CTP imaging as part of initial imaging and CTA should be completed based on the clinical judgment of the treating physician.

- iv. All patients with suspected ischemic stroke who arrive at **6–24 h** after stroke onset (late presentation and stroke on awakening with unknown onset time) and are potentially eligible for late window EVT treatment (*Refer to Box 4D and Section 5*) should undergo **immediate** brain imaging with NCCT with CTA and CTP, or MRI with MRA and MRP [Evidence Level B]. *Note: In most Canadian centers, a CT approach may be more practical and more readily available than an MR approach. Choice of imaging modality should be based on most immediate availability and local resources.*

4.3 Acute blood pressure management

- i. The ideal level of blood pressure target to achieve and sustain in the hyperacute phase is unknown at this time. Pharmacological agents and routes of administration should be chosen to avoid precipitous falls in blood pressure [Evidence Level C].
- ii. **Ischemic stroke patients eligible for thrombolytic therapy:** Very high blood pressure (greater than 185/110 mm Hg) should be treated concurrently with thrombolysis to reduce the risk of hemorrhagic transformation [Evidence Level B]. Blood pressure should be lowered and sustained below 185/110 prior to alteplase therapy and to below 180/105 mmHg for the next 24 h after alteplase administration [Evidence Level C].
- iii. **Ischemic stroke patients not eligible for thrombolytic therapy:** Treatment of hypertension in the setting of acute ischemic stroke or TIA should not be routinely treated [Evidence Level C].
- iv. Extreme blood pressure elevation (e.g., SBP > 220 mm Hg or DBP > 120 mmHg) should be treated to reduce the blood pressure by approximately 15%, and not more than 25%, over the first 24 h with further gradual reduction thereafter to targets for long-term secondary stroke prevention [Evidence Level C].
- v. Avoid rapid or excessive lowering of blood pressure because this might exacerbate existing ischemia or might induce ischemia, particularly in the setting of intracranial or extracranial arterial occlusion [Evidence Level C].
- vi. Choice of agents for managing blood pressure should be based on current Hypertension Canada Blood Pressure treatment guidelines (www.hypertension.ca).

Note: For guidance on blood pressure management of hemorrhagic stroke, refer to Canadian Stroke Best Practices Management Intracerebral Hemorrhagic Stroke Module. [New recommendations, expected release Fall 2018]

4.4 Cardiovascular investigations

- i. Patients with suspected TIA 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. Unless a patient is hemodynamically unstable, ECG should not delay assessment for intravenous thrombolysis and EVT and can be deferred until after a decision regarding acute treatment is made [Evidence Level C].
Note: For patients being investigated for an acute embolic ischemic stroke or TIA of undetermined source whose initial short-term ECG monitoring does not reveal atrial fibrillation but a cardioembolic mechanism is suspected, refer to Canadian Stroke Best Practices Secondary Prevention of Stroke Module, Section 7 on Management of Atrial Fibrillation in Stroke for additional information.
- iii. Echocardiography (2D or TEE) may be considered in patients where a cardiac cause of stroke is suspected, including in young adults and children who present with stroke, and when infectious endocarditis is suspected [Evidence Level C].

4.5 Blood glucose abnormalities

- i. All patients with suspected acute stroke should have their blood glucose concentration checked upon arrival to the ED. (*Note: For patients arriving by EMS, the capillary glucose measured by EMS should be reviewed by the ED team for any immediate management required.*) [Evidence Level B]. *Refer to Appendix 1 online for Recommended Laboratory Investigations for Patients with Acute Stroke or TIA for further details. Refer Section 3 of this module for further details regarding EMS management.*
- ii. Hypoglycemia should be corrected immediately [Evidence Level B].

- iii. Although no optimal glucose target has been identified, it is reasonable to treat hyperglycemia which has been associated with hemorrhagic transformation when treating with IV alteplase thrombolysis [Evidence Level C].

4.6 Additional Management Considerations in the Emergency Department

- i. **Chest x-ray:** A chest x-ray should be completed when the patient has evidence of acute heart disease or pulmonary disease [Evidence Level B]. Unless a patient is hemodynamically unstable, chest x-ray can be deferred until after a decision regarding acute treatment and it should not delay assessment for thrombolysis and EVT.
- ii. **Swallowing assessment:** Patient swallowing screen should be completed as early as possible by a practitioner trained to use a validated swallowing screening tool as part of initial assessment, **but should not delay decision-making regarding eligibility for acute stroke treatments** [Evidence Level A]. Refer to Section 9, and Stroke Rehabilitation Module, Section 7, for additional information on screening for swallowing ability and dysphagia management.
 - a. Ideally swallow screening should be done within 24 h of hospital arrival, including patients that receive acute stroke treatments (intravenous alteplase and EVT) [Evidence Level C].
 - b. Patients should remain NPO (nil per os—no oral intake) until swallowing screen completed for patient safety [Evidence Level B];
 - c. Oral medications should not be administered until swallowing screen using a validated tool has been completed and found normal [Evidence Level B]; alternate routes such as intravenous and rectal administration should be considered while a patient is NPO;
 - d. A patient's clinical status can change in the first hours following a stroke or TIA; therefore, patients should be closely monitored for changes in swallowing ability following initial screening [Evidence level C];
 - e. Patients found to have abnormal swallowing ability on screening should be referred to a healthcare professional with expertise in swallowing assessments for an in-depth swallowing assessment [Evidence Level B].
- iii. **Urethral catheters:** The use of chronic indwelling urethral catheters should generally be avoided due to the risk of urinary tract infections [Evidence Level A]. Refer to Section 9 for additional information.
 - a. Insertion of an indwelling urethral catheter could be considered for patients undergoing EVT but should not delay achieving reperfusion. The need for retaining the catheter should be reconsidered after the end of the EVT procedure, and it should be discontinued as soon as the patient can be expected to resume voiding on their own [Evidence Level C].
 - b. Insertion of an indwelling urethral catheter is not routinely needed prior to intravenous thrombolysis, unless the patient is acutely retaining urine and is unable to void. If inserted for patient-specific reasons, it should not delay acute treatment [Evidence Level C].
 - c. If used, indwelling catheters should be assessed daily and removed as soon as possible [Evidence Level A].
 - d. Fluid status and urinary retention should be assessed as part of vital sign assessments [Evidence Level C].
 - e. Excellent pericare and infection prevention strategies should be implemented to minimize risk of infections [Evidence Level C].
- iv. **Temperature:** Temperature should be routinely monitored and treated if above 37.5°C [Evidence Level B]. Refer to Section 9.3 for additional information.
- v. **Oxygen:** Supplemental oxygen is not required for patients with normal oxygen saturation levels [Evidence Level C].

Clinical considerations: [New for 2018]

- 1. There is no evidence to support the practice of routine reversal of anticoagulation, either during non-thrombolytic conservative care or in order to give alteplase in patients presenting with acute ischemic stroke who are on warfarin or direct oral anticoagulants (DOACs). EVT may be considered despite anticoagulation if patients are otherwise eligible.

Box 4A: Alteplase selection imaging exclusion criteria: CT findings

- 1. CT showing early signs of extensive infarction.
- 2. Signs of hemorrhagic stroke on CT imaging.

Refer to Section 5 for additional intravenous alteplase clinical inclusion and exclusion criteria.

Box 4B: Endovascular selection imaging criteria for patients arriving within 6 h of stroke onset

1. A small-to-moderate ischemic core (which may be estimated as an ASPECT score of 6 or higher).
 - For patients with a large ischemic core, such as with an ASPECT score less than 6, the decision to treat should be based on the potential benefits and risks of the treatment, made by a physician with stroke expertise in consultation with the neuro-interventionalist, and patient and/or family/substitute decision-makers.
2. Intracranial artery occlusion in the anterior circulation, including proximal large vessel occlusions in the distal internal carotid artery or middle cerebral artery (MCA) and immediate branches.
3. For patients with basilar artery occlusions, the decision to treat with EVT should be based on the potential benefits and risks of the therapy, made by a physician with stroke expertise in consultation with the neuro-interventionist, and the patient and/or decision-makers. *Note: There are ongoing randomized trials in this area and this issue will be reviewed once the results become available.*

Refer to Section 5 for additional EVT clinical inclusion and exclusion criteria.

Box 4C: Advanced CT imaging criteria for EVT Selection

1. Sites using CTP imaging should utilize software that provides reproducible objective measurements of ischemic core and penumbra.
2. An occluded proximal intracranial artery (carotid artery, M1 segment of the MCA, or proximal M2 divisions) of the anterior circulation, which is a target lesion amenable to EVT. The location of occlusion is defined by an arterial phase CTA from ascending aorta to the vertex of the head. Inclusion of the aortic structures allows planning and assessment of the technical feasibility of an endovascular approach to the occluded intracranial artery.
3. There is evidence to suggest that moderate-to-good pial collateral filling (as defined by CTA) or evidence of CTP mismatch predict a better response to EVT.
4. Stroke imaging on-site with 24-h access, seven days a week, including a CT scanner (i.e., third-generation or higher helical scanner) with programming for CTA; multiphase or dynamic CTA or CTP imaging can also be used if available on-site.

Note: ASPECTS score is one tool to estimate core: A small-to-moderate ischemic core can be defined by an ASPECTS score of 6 or higher on NCCT or areas of low cerebral blood volume (CBV) or cerebral blood flow (CBF) maps on CTP imaging.

Box 4D: Endovascular selection imaging criteria for patients arriving later than 6 h of stroke onset

1. Sites using CTP imaging should utilize software that provides reproducible objective measurements of ischemic core and penumbra.
2. An occluded proximal intracranial artery (carotid artery, M1 segment of the MCA, or proximal M2 divisions) of the anterior circulation, which is a target lesion amenable to EVT. The location of occlusion is defined by an arterial phase CTA from ascending aorta to the vertex of the head. Inclusion of the aortic structures allows planning and assessment of the technical feasibility of an endovascular approach to the occluded intracranial artery.
3. Imaging and clinical evidence of small core and large area at risk, defined in the trials as either:
 - a. NIHSS ≥ 10 and either 0–21 ml core infarct (≥ 80 years old) or 0–31 ml core infarct (< 80 years old), or NIHSS ≥ 20 and 3 l to < 5 l ml core infarct and < 80 years old (DAWN trial criteria).⁷
 - OR
 - b. Ischemic core volume is < 70 ml, mismatch ratio is ≥ 1.8 and mismatch volume* is ≥ 15 ml (DEFUSE3 trial criteria).⁸

Section 5: Acute ischemic stroke treatment

The weight of evidence from many large, international randomized controlled trials over the previous 20+ years clearly indicate that treatment with intravenous alteplase, administered within 3–4.5 h of symptom onset improves stroke outcome, reducing the risks of death and or disability substantially.⁴⁰ The focus of more recent lines of enquiry have been directed at the potential non-inferiority of lower doses of alteplase (e.g., 0.6 vs. 0.9 mg/kg),⁴¹ different thrombolytic agents (e.g.,

tenecteplase),⁴² issues related to the treatment window,^{43,44} the use of anticoagulant reversal agents,^{45,45} and the use of specialized imaging to identify additional, potentially eligible candidates for thrombolysis beyond the 4.5-h time window. The results from the Efficacy and Safety of MRI-based Thrombolysis in Wake-up Stroke (WAKE-UP) trial⁴⁶ demonstrated that highly selected patients with mild-to-moderate ischemic strokes and an unknown time of symptom onset, treated with alteplase, may also benefit from treatment. Patients in this trial who had unknown time of stroke onset, were

outside the 4.5-h time window, and were not eligible for treatment with mechanical thrombectomy, were selected based on a pattern of DWI-FLAIR mismatch. A significantly higher proportion of patients in the alteplase group had a favorable clinical outcome (mRS 0–1) at 90 days (53.3% vs. 41.8%, adj OR = 1.61, 95% CI 1.06–2.36, $p = 0.02$), although the risk of parenchymal hemorrhage type 2 was significantly higher compared with placebo (4% vs. 0.4%, adj OR = 10.46, 95% CI 1.32–82.77, $p = 0.03$), with notably wide confidence intervals. The lack of confidence on safety endpoints was in part related to early termination of the trial, with 503 of the intended 800 randomized, due to slow enrollment and lack of funds.

Recent attention has been focused on mechanical revascularization with specialized devices. To date, many major RCTs have been completed for which results have been published, whereby endovascular therapies were compared with best medical management.^{47–51} Several trials are still ongoing or have yet to report their findings. The results from most of these trials indicate that rapid endovascular treatment using second-generation devices is a safe and effective treatment for patients with anterior circulation ischemic strokes with a proximal occlusion, when performed within 6 h of symptom onset, with more limited data in the 6- to –12-h treatment window. The estimated number of patients needed-to-treat with mechanical thrombectomy to achieve a modified Rankin Scale score of 0–2, 90 days post procedure, ranged from 4⁴⁹ to 8⁴⁷ among these trials. The recent results from both the DEFUSE-3 and DAWN trials^{7,8} suggest that the treatment window for mechanical thrombectomy may

be wider than previously understood for highly selected patients. Patients in the DAWN trial⁷ were eligible for treatment up to 24 h after last known well, while patients in the DEFUSE-3⁸ trial were eligible for up to 16 h. In both trials, a significantly higher proportion of patients had achieved recanalization at 24 h and were independent at 90 days compared with treatment with best medical management (49% vs. 13%⁷ and 44.6% vs. 16.7%⁸). In both trials, there was no significant difference between groups in the proportion of patients with symptomatic intracerebral hemorrhage at 24 h.

Recent evidence from the EXTEND-IA TNK trial,⁵² which included a small number of patients with ischemic stroke with arterial occlusion, suggested that intravenous tenecteplase (TNK) was superior to alteplase with respect to arterial recanalization when given prior to mechanical thrombectomy. While a significantly higher percentage of patients in the tenecteplase group achieved the primary outcome (substantial reperfusion, defined as $\geq 50\%$ of the involved territory or the absence of retrievable thrombus at initial angiographic assessment: 22% vs. 10%), the percentage of patients who were functionally independent or who had achieved an excellent outcome at 90 days did not differ between groups; neither did the percentage of patients who experienced early neurological improvement. It was not powered to demonstrate an effect on clinical outcomes. Further evidence from ongoing trials (TASTE (ACTRN12613000243718), TEMPO-2 (NCT02398656), TWIST (NCT03181360), and ATTEST—2 (NCT02814409)) is required before changes to clinical practice can be recommended.

Section 5: Recommendations for the acute ischemic stroke treatment

Box 5A: Criteria for stroke centers providing acute ischemic stroke treatment

Within the Canadian Stroke Best Practices Optimal Stroke Services Framework, all hospitals in Canada have been identified as comprehensive, advanced/primary, general non-stroke acute care hospitals, or basic healthcare facilities (generally small rural and remote sites). Comprehensive and advanced/primary stroke centers are those that have coordinated stroke care services, including CT imaging and alteplase administration available on-site.

Some comprehensive stroke centers and a select group of advanced/primary stroke centers will be able to provide EVT (with mechanical embolectomy) for acute ischemic stroke. To provide EVT, centers must meet the following criteria:

- A designated stroke team which includes physicians with stroke expertise (stroke neurologist or other physicians with advanced stroke training); stroke nurses and advanced practice nurses (and/or nurse practitioners); neurosurgeons; (neuro)-radiologists, Emergency Physicians; critical care physicians; rehabilitation therapists (physical therapists, occupational therapists, speech-language pathologists, and dietitians), pharmacists, and social workers.
- Neurointerventional expertise on-site with available 24-h access, seven days a week.
- On-site neurosurgery support and neurocritical care services.
- Stroke imaging on-site with 24-h access, seven days a week, including a CT scanner (i.e., third-generation or higher helical scanner) with programming for CTA. Multiphase or dynamic CTA or CTP imaging can also be used if available on-site. MR imaging (MRI, MRA, and MRP) may be considered if available on site and will not delay acute stroke treatments.
- Capability to administer intravenous alteplase.
- Designated stroke unit on-site—a geographically defined hospital unit dedicated to the care of stroke patients, with protocols in place that follow current evidence-based stroke best practice recommendations for acute stroke management and early access to rehabilitation assessment and therapy.

5.1 Patient selection for acute ischemic stroke treatments

Note: Treatment benefits from revascularization decreases over time as an estimated 1.9 million brain cells die every minute following stroke onset (Saver J. *Stroke* 2006;37:263–266); therefore, all patients with stroke **should be treated as fast as possible** to maximize potential for the best outcomes, and the new extended time windows should not be interpreted to mean that time to treatment can be slowed down in any way.

- i. All patients with *disabling* acute ischemic stroke within 24 h of stroke symptom onset or last known well should be rapidly screened clinically and with neurovascular imaging [Evidence Level B].
- ii. All patients with *disabling* acute ischemic stroke who can be treated within the indicated time windows must be screened *without delay* by a physician with stroke expertise (either on-site or by telemedicine/teletroke consultation) to determine their eligibility for both intravenous alteplase (**within 4.5 h** from stroke symptom onset) and/or interventional treatment with EVT (within a 6-h window from stroke symptom onset). [Evidence Level A].
- iii. Patients meeting criteria in 5.1 (i) (**within 6 h**) should immediately undergo neurovascular imaging with NCCT and including CTA then considered for treatment on the basis of imaging [Evidence Level A].
- iv. There are randomized controlled trials which indicate that **highly selected** patients with disabling stroke symptoms may benefit from EVT **up to 24 h** from the time they were last known well, including patients with stroke on awakening, and patients should be considered for eligibility within the extended time window on a case-by-case basis [Evidence Level A]. Note: These patients were selected using CTP or diffusion-weighted criteria (as defined in Box 5C below). [new for 2018]
- v. Highly selected patients being considered for EVT beyond 6 h will require additional advanced neurovascular imaging [Evidence Level A]. Refer to Box 4D for additional Imaging Selection Criteria.

Clinical considerations:

- i. One recent multicenter randomized double-blind placebo controlled trial compared alteplase to placebo for ischemic stroke patients with unknown time of onset, using MRI selection criteria (DWI-FLAIR mismatch). It included ischemic stroke patients who were not candidates for EVT and who would otherwise have met the criteria for acute intravenous alteplase administration⁴⁶ (refer to Box 5B for alteplase criteria)
 - This trial demonstrates a clinical benefit of intravenous alteplase administered more than 4.5 h from the time the patient was last known well in patients where onset time is unknown (no upper time limit defined).
 - If intravenous alteplase is considered **after 4.5 h**, a consultation with a physician with stroke expertise should be obtained. Selection of patients for intravenous alteplase in patients presenting *after 4.5 h* on the basis of CT, CTA, and CTP remains unproven at this time.
 - MRI scanning can be challenging to obtain urgently in an ED setting. This must be considered in decision-making and not delay decisions regarding EVT eligibility.

5.2 Imaging criteria

Refer to Section 4.2 for detailed recommendations and Boxes 4A, 4B, 4C, and 4D for selection criteria for neuroimaging.

- i. Patients should be considered for revascularization treatment when there is no evidence of extensive early infarct changes [Evidence Level B], in consultation with physicians with stroke expertise. Note: One possible tool to assess infarct change is the ASPECT score: www.aspectsinstroke.com
 - a. Timely access to CT or MR perfusion scanning can also be used to demonstrate a perfusion mismatch and to determine the extent of the ischemic core [Evidence Level A], especially in patients beyond 6 h from last known well, including patients with stroke on awakening.
- ii. For EVT, patients should have a proximal occlusion in the anterior circulation [Evidence Level A]. Refer to Box 5C for EVT inclusion and exclusion criteria.

5.3 Intravenous thrombolysis with alteplase

- i. All eligible patients with disabling ischemic stroke should be offered intravenous alteplase [Evidence Level A]. Eligible patients are those who can receive intravenous alteplase within 4.5 h of the onset of stroke symptoms [Evidence Level A]. Refer to

Section 4.2 and Boxes 4A–4D for detailed recommendations on neuroimaging; Refer to Box 5B for inclusion and exclusion criteria for intravenous alteplase eligibility.

- a. When it is unclear whether or not a patient should be treated with alteplase, urgently consult with a stroke specialist within the institution or through telestroke services [Evidence Level C].
 - b. If there is uncertainty regarding CT imaging interpretation, consult a radiologist in your institution [Evidence Level C].
- ii. All eligible patients should receive intravenous alteplase *as soon as possible* after hospital arrival [Evidence Level A], with a target door-to-needle time of less than 60 min in 90% of treated patients, and a median door-to-needle time of 30 min [Evidence Level B].
- a. Treatment should be initiated as soon as possible after patient arrival and CT scan [Evidence Level B]; every effort should be made to ensure door-to-needle times are routinely monitored and improved [Evidence Level C].
 - b. Alteplase should be administered using a dose of 0.9 mg/kg to a maximum of 90 mg total dose, with 10% (0.09 mg/kg) given as an intravenous bolus over one minute and the remaining 90% (0.81 mg/kg) given as an intravenous infusion over 60 min [Evidence Level A].
- Caution: The dosing of alteplase for stroke is not the same as the dosing protocol for administration of alteplase for myocardial infarction.*
- iii. **Hospital inpatients** that present with a sudden onset of new stroke symptoms should be rapidly evaluated by a specialist team and provided with access to appropriate acute stroke treatments (including thrombolysis and EVT) [Evidence Level B]. *Note: Once stroke occurs to an existing inpatient, all other sections of the Canadian Stroke Best Practice modules apply to these patients for assessment, diagnosis, management, and recovery.*
- iv. Management of complications from alteplase administration:
- a. For patients with angioedema, a staged response using antihistamines, glucocorticoids, and standard airway management should be used as per local protocol [Evidence Level C].
 - b. There is insufficient evidence to support the routine use of cryoprecipitate, fresh frozen plasma, prothrombin complex concentrates, tranexamic acid, factor VIIa, or platelet transfusions for alteplase-associated bleeding [Evidence Level C]. Use of these medications should be decided on an individual case basis.

Clinical considerations for alteplase administration [new for 2018]

1. Consent—Intravenous thrombolysis and endovascular therapy are considered the standard of care for acute stroke treatment. Routine procedures for emergency consent apply.
2. Intravenous alteplase is considered the standard of care and is currently the only approved thrombolytic agent for acute ischemic stroke treatment. There are other drugs being investigated; however, at this time are not approved for use in stroke patients.
3. Alteplase administration for patients on DOACs: alteplase should **not** routinely be administered to patients on DOACs presenting with acute ischemic stroke. EVT may be considered in these cases for eligible patients, and decisions should be based on individual patient factors and assessment of benefit and risk.
 - a. In comprehensive stroke centers with access to specialized tests of DOAC levels and reversal agents, thrombolysis could be considered, and decisions should be based on individual patient characteristics, in consultation with hematology specialists, patients, and their families.
4. There remain situations in which clinical trial data to support the use of intravenous thrombolytic therapy is more limited. In these situations, urgent consultation with a stroke expert is recommended alongside the clinical judgment of the treating physician and discussion with the patient or substitute decision-maker.
 - a. This may apply to pediatric stroke (newborn to age 18 years) and pregnant women who experience an acute ischemic stroke. Refer to Canadian Stroke Best Practices Management of Acute Stroke during Pregnancy Consensus Statement for further information

5.4 Acute Endovascular Thrombectomy Treatment (EVT)

Refer to Section 4.2 and Boxes 4B, 4C, and 4D for detailed recommendations on neuroimaging-based selection criteria.

- i. EVT should be offered within a coordinated system of care including agreements with EMS, access to rapid neurovascular (brain and vascular) imaging, coordination between EMS, the ED, the stroke team and radiology, local expertise in neurointervention, and access to a stroke unit for ongoing management [Evidence Level A].
- ii. EVT is indicated in patients based upon imaging selection with NCCT head and CTA (including extracranial and intracranial arteries) [Evidence Level A]. Refer to Box 5C for Inclusion Criteria for EVT.

- iii. EVT is indicated in patients who have received intravenous alteplase and those who are not eligible for intravenous alteplase [Evidence Level A].
- iv. Patients eligible for intravenous alteplase as well as EVT should also be treated with intravenous alteplase, which can be initiated while simultaneously preparing the angiography suite for EVT [Evidence Level A].
- v. Eligible patients who can be treated with EVT *within 6 h* of symptom onset (i.e., arterial access **within 6 h** of onset) should receive EVT [Evidence Level A]. Refer to Box 4B for Imaging Inclusion Criteria for EVT.
- vi. **Highly selected patients** with large vessel occlusion who can be treated with EVT *within 24 h* of symptom onset (i.e., arterial access **within 24 h** of onset) and those patients with stroke discovered on awakening should receive EVT [Evidence Level A]. Refer to Box 4C for Imaging Inclusion Criteria for EVT beyond 6 h from onset.
- vii. For large artery occlusions in the posterior circulation (e.g., basilar artery occlusion), the decision to treat with EVT should be based on the potential benefits and risks of the treatment for the individual patient, and made by a physician with stroke expertise in consultation with the patient and/or substitute decision-makers. [Evidence Level C]. Note: Randomized trials are currently ongoing and guidance will be reviewed when trial results are available.
- viii. **Sedation:** For endovascular procedures, procedural sedation is generally preferred over general anesthesia and intubation in most patients when necessary [Evidence Level B].
 - a. General anesthesia and intubation is appropriate if medically indicated (e.g., for airway compromise, respiratory distress, depressed level of consciousness, severe agitation, or any other indication determined by the treating physician) and in such cases, excessive and prolonged hypotension and time delays should be avoided [Evidence Level B].

Clinical Considerations for EVT [new for 2018]

1. For patients transferred to an EVT-enabled hospital, in order to ensure patient remains a candidate for EVT, consider doing repeat NCCT immediately on arrival if most recent CT was completed more than 60 min prior to arrival at the EVT-enabled site.
2. Device selection should be at the discretion of the interventionalists based on clinical and technical factors during the procedure.
3. For patients undergoing EVT following administration of alteplase, there should not be a delay in proceeding to EVT to determine clinical effectiveness of alteplase.

Box 5B: Criteria for acute thrombolytic therapy with intravenous alteplase

Refer to Section 4.2 and Box 4A for detailed recommendations on neuroimaging-based selection criteria

These criteria are designed to guide clinical decision-making; however, the decision to use alteplase in these situations should be based on the clinical judgment of the treating physician. The relative benefits of alteplase therapy versus any potential risks or contraindications should be weighed on an individual basis.

IV alteplase treatment inclusion criteria

- Diagnosis of ischemic stroke causing disabling neurologic deficit in a patient who is 18 years of age or older.
 - For adolescents, decision to administer alteplase should be based on clinical judgment, presenting symptoms, and patient age; and, if possible, consultation with a pediatric stroke specialist.
- Time from last known well (onset of stroke symptoms) less than 4.5 h before alteplase administration.
 - * For patients beyond 4.5 hours refer to Section 5.1 Clinical considerations for more information.

Absolute exclusion criteria

- Any source of active hemorrhage or any condition that could increase the risk of major hemorrhage after alteplase administration.
- Any hemorrhage on brain imaging.

Relative exclusion criteria (requiring clinical judgment based upon the specific situation)

Historical

- History of intracranial hemorrhage.

- Stroke or serious head or spinal trauma in the preceding three months.
- Major surgery, such as cardiac, thoracic, abdominal, or orthopedic in the preceding 14 days. Risk varies according to the procedure.
- Arterial puncture at a non-compressible site in the previous seven days.

Clinical

- Symptoms suggestive of SAH.
- Stroke symptoms due to another non-ischemic acute neurological condition such as seizure with post-ictal Todd's paralysis or focal neurological signs due to severe hypo- or hyperglycemia.
- Hypertension refractory to aggressive hyperacute antihypertensive treatment such that target blood pressure less than 180/105 cannot be achieved or maintained. Blood pressure should be treated rapidly and aggressively in order to minimize delays to thrombolysis.
- Patient currently prescribed and taking a direct non-vitamin K oral anticoagulant (DOAC). Refer to Section 5.2 clinical considerations for additional information.

CT or MRI Findings

- CT showing early signs of extensive infarction

Laboratory

- Blood glucose concentration below 2.7 mmol/L or above 22.2 mmol/L.
- Elevated activated partial-thromboplastin time.
- International normalized ratio greater than 1.7.
- Platelet count below 100,000 per cubic millimeter.

Box 5C: Inclusion criteria for EVT

Refer to Section 4.2 and Boxes 4B, 4C, and 4D for detailed recommendations on neuroimaging-based selection criteria

1. If intravenous alteplase is given in conjunction with EVT, refer to Box 5B for additional inclusion criteria.
2. **Age:** Patients under 18 years of age. There is no current evidence for use of EVT in pediatric populations and the decision to treat should be based on the potential benefits and risks of the therapy, made by a physician with Pediatric stroke expertise in consultation with the patient and/or family/substitute decision-makers.
3. **Premorbid condition criteria:** In general, functionally independent and life expectancy greater than three months.
4. **Imaging:**
 - a. A small-to-moderate ischemic core (such as with ASPECTS score of 6 or higher).
 - For patients with large ischemic core, such as with ASPECTS score less than 6, the decision to treat should be based on the potential benefits and risks of the treatment, made by a physician with stroke expertise in consultation with the neuro-interventionalist, and patient and/or family/substitute decision-makers.
 - b. Intracranial artery occlusion in the anterior circulation, including proximal large vessel occlusions in the distal ICA or MCA and immediate branches.
 - c. For patients with basilar artery occlusions, the decision to treat with EVT should be based on the potential benefits and risks of the therapy, made by a physician with stroke expertise in consultation with the neuro-interventionist, and the patient and/or decision-makers.
5. **Time to treatment:** The decision to proceed with EVT should be shared between the physician with clinical stroke expertise and the neuro-interventionalist, who will make use of the available imaging information as is indicated. Details regarding imaging parameters commonly used in the literature are included in Box 4B – 4D.
 - a. Specifically:
 - i. Patients should have immediate neurovascular imaging (see above) to determine eligibility. Patients can be considered for imaging within a 24-h window from stroke onset or last known well.
 - ii. For patients presenting less than 6 h from onset of stroke symptoms or last known well to initiation of treatment (i.e., arterial puncture), all patients who meet eligibility criteria should be treated.
 - iii. For patients presenting between 6 and 24 h from last seen well, highly selected patients may be treated if they meet clinical and imaging criteria, and based on local protocols and available expertise in EVT.

Section 6: Acute antiplatelet therapy

Early aspirin therapy reduces the risk of early recurrent ischemic stroke.^{53,54} Results of a Cochrane review,⁵⁵ using data primarily from two large trials indicated that aspirin at doses of 160 and 300 mg, initiated within 48 h of stroke onset, was associated with a significant reduction in the odds of recurrent ischemic/unknown stroke (OR=0.77, 95% CI 0.69–0.87, $p < 0.0001$) and death or functional dependence (OR=0.95, 95% CI 0.91–0.99, $p = 0.01$). For every 1000 people treated with aspirin, 13 fewer people were dead or dependent, 9 fewer were dead, and 7 fewer experienced a recurrent stroke. The results from a patient-level meta-analysis by Rothwell et al.⁵⁶ using three RCTs suggested that the greatest reduction in early stroke recurrence was associated with aspirin monotherapy given to patients presenting with mild and moderately disabling stroke. Aspirin therapy was not associated with a significant reduction in stroke recurrence among those with a severe stroke.

Dual therapy using clopidogrel plus aspirin has also been evaluated for the prevention of recurrent stroke following minor events. In CHANCE,⁵⁷ significantly fewer patients in the clopidogrel (75 mg/day) + aspirin (75 mg/day) group experienced a stroke within 90 days, compared with patients in the aspirin only

group (8.2% vs. 11.7%, HR = 0.68, 95% CI 0.57–0.81, $p < 0.001$). Although the CHANCE trial suggested a benefit of short-term dual therapy, since the study was performed exclusively in China, the generalizability of the results in a North American population was questioned. This potential limitation appears unsubstantiated based on the recent results of the POINT trial⁹ where the majority of the 4881 patients recruited were from centers in the United States. Eligibility criteria for POINT were similar to that of the CHANCE trial,⁵⁷ although the intervention differed somewhat (dual antiplatelet for 90 vs. 21 days, and loading doses of 600 vs 300 mg in the POINT and CHANCE trials, respectively). Patients in POINT⁹ were randomized to receive 81 mg aspirin + 75 mg clopidogrel or aspirin + placebo for 90 days. The risk of ischemic stroke was significantly lower in the clopidogrel plus aspirin group (4.6% vs. 6.3%; HR = 0.72, 95% CI 0.56–0.92, $p = 0.01$), although the risk of major hemorrhage was significantly increased (0.9% vs. 0.4%, HR = 2.32, 95% CI 1.10–4.87, $p = 0.02$). The authors estimated that for every 1000 patients treated with clopidogrel plus aspirin for 90 days, 15 ischemic strokes would be prevented but 5 major hemorrhages would result. For these reasons, we have limited the new recommendation for dual antiplatelet therapy to 21–30 days only.

Section 6: Recommendations for acute antiplatelet therapy

- i. All acute stroke patients not already on an antiplatelet agent and not receiving alteplase therapy should be given at least 160 mg of acetylsalicylic acid (ASA) immediately as a one-time loading dose after brain imaging has excluded intracranial hemorrhage and after dysphagia screening has been performed and passed. [Evidence Level A].
 - a. ASA (81–325 mg daily) should then be continued indefinitely or until an alternative antithrombotic regime is started [Evidence Level A]. Refer to *Canadian Stroke Best Practice Recommendations Prevention of Stroke Module Sections 6 and 7 for additional information on antithrombotic therapy*
- ii. In very high-risk TIA patients (refer to Box 6A below and Section 2.1 for the determination of very high-risk patients or per POINT trial criteria of ABCD² score >4) or minor stroke of noncardioembolic origin (NIHSS 0-3), a combination of clopidogrel and ASA should be given for a duration of 21–30 days followed by antiplatelet monotherapy (such as ASA or clopidogrel alone) [Evidence Level A]. A minimal loading dose of 300 mg Clopidogrel (based on dose in CHANCE) up to 600 mg (based on dose used in POINT) and 160 mg of ASA should be given at the start of treatment [Evidence Level A].^{9,57}
 - a. Dual antiplatelet therapy should be started as soon as possible after brain imaging, within 24 h of symptom onset, and ideally within 12 h.
 - b. Dual antiplatelet therapy should be started prior to discharge from the ED.
 - c. Patients should be counseled that dual antiplatelet therapy with aspirin and clopidogrel should continue for only 21–30 days. Patients should resume monotherapy after the completion of dual therapy and continue monotherapy indefinitely.
- iii. In patients treated with tissue plasminogen activator (alteplase), initiation of antiplatelet agents should be delayed until after the 24-h post-thrombolysis scan has excluded intracranial hemorrhage [Evidence Level B].
- iv. In dysphagic patients, ASA (80 mg daily) and clopidogrel (75 mg daily) may be given by enteral tube or ASA by rectal suppository (325 mg daily) [Evidence Level A].
- v. In pediatric patients, initial treatment with anticoagulation (heparin) or aspirin at established pediatric dosing should be considered and continued until cervical artery dissection and intracardiac thrombus is excluded. If neither is present, switch to acute aspirin therapy at dose of 1–5 mg/kg [Evidence Level B].

Refer to Canadian Stroke Best Practice Recommendations Secondary Prevention of Stroke Module Sections 6 and 7 for additional information on use of antithrombotic agents beyond the acute period

Clinical considerations:

1. Patients with very high-risk TIA or minor ischemic stroke caused by high-grade carotid stenosis who are candidates for urgent carotid endarterectomy or carotid stenting, should be reviewed with the interventionalist or surgeon to determine the appropriate timing and selection of antiplatelet agent(s). In some circumstances it may be appropriate to use aspirin monotherapy rather than dual antiplatelet therapy if carotid endarterectomy is planned urgently, to reduce perioperative bleeding risk.
2. For patients on dual antiplatelet therapy, GI protection may be considered in patients at higher risk of GI bleeding [In POINT (90-day study) extracranial bleeding events were 0.9% in the dual antiplatelet therapy group and 0.4% in the monotherapy group; in CHANCE (21-day study) extracranial bleeding events were 0.3% in the dual antiplatelet therapy group and 0.3% in the monotherapy group.]

Box 6A: VERY HIGH risk for recurrent stroke (symptom onset within last 48 h):

Patients who present **within 48 h** of a suspected TIA or nondisabling ischemic stroke with the following symptoms are **considered at highest risk** of first or recurrent stroke: transient, fluctuating or persistent unilateral weakness (face, arm and/or leg); transient, fluctuating or persistent *language/speech disturbance*; and/or *fluctuating or persistent symptoms without motor weakness or language/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, dysphagia, ataxia).

For additional risk stratification, refer to Section 2 of this module.

Section 7: Early management of patients considered for hemicraniectomy

Patients with malignant MCA stroke have higher mortality related to cerebral edema, increased intracranial pressure, and subsequent cerebral herniation. Decompressive hemicraniectomy may be a surgical option for those experiencing a large volume MCA stroke. The benefit of decompressive hemicraniectomy early following MCA infarction has been established in persons under the age of 60 years, based on the results of three major randomized controlled trials (Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY 1),⁵⁸ the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial (HAMLET),⁵⁹ and decompressive craniectomy in malignant MCA infarcts trial (DECIMAL)⁶⁰). In all trials, surgery was associated with a significant reduction in the risk of mortality up to one-year follow-up. The results of these trials when pooled in a Cochrane review⁶¹ indicated that hemicraniectomy was associated with a significantly reduced risk of death at the end of follow-up (OR = 0.19, 95% CI

0.09–0.37) and in the risk of death or severe disability (mRS > 4) at 12 months (OR = 0.26, 95% CI 0.13–0.51). A more recent systematic review, which included the results from seven trials,⁶² documented that the odds of a favorable outcome (mRS 0–3) and survival at 6–12 months were significantly increased for patients in the hemicraniectomy group with odds ratios of 2.04 (95% CI 1.03–4.02, $p=0.04$) and 5.56 (95% CI 3.40–9.08, $p<0.001$), respectively. The benefit of surgery in older patients is less certain. While the surgery may be lifesaving, it can result in survival with moderate or severe disability. In the DESTINY II trial,⁶³ a significantly higher proportion of patients in the surgical group were alive and living without severe disability at six months (38% vs. 18%, OR = 2.91, 95% CI 1.06–7.49, $p=0.04$). However, no patients in either the surgical or medical care groups had overall good outcomes (mRS score of 0–2) at 6 or 12 months and most of the survivors required assistance with most bodily needs. Discussions with patients and or substitute decision-makers should include information about likely outcomes, and potential for survival with significant disabilities that may add increased burden to families.

Section 7: Recommendations for the early management of patients considered for hemicraniectomy

- 7.0 Hemicraniectomy should be considered in patients in the early stages of extensive (malignant) MCA territory ischemic stroke as a life-saving measure for patients willing to accept a significant risk of living with a degree of disability that may leave them dependent on others for their activities of daily living [Evidence Level A for patients age 18–60 years; Evidence Level B for patients 60–80 years].

7.1 Patient selection

- i. Patients who meet the following criteria alone or in combination should be considered for hemicraniectomy [Evidence Level A]:
 - a. Patients over the age of 18;
 - b. Children under 18 years with progressive extensive (malignant) MCA syndrome [Evidence Level C];
 - c. Malignant MCA infarct with evidence of significant edema and mass effect;
 - d. Infarction size greater than 50% MCA territory on visual inspection, or an ischemic lesion volume greater than 150 cm³;
- ii. Posterior fossa decompression can be considered in selected patients with significant cerebellar stroke with evidence of mass effect and/or hydrocephalus [Evidence Level C].
- iii. If a potential patient's location is initially outside a comprehensive stroke center, the patient should have expedited transfer to a tertiary or quaternary center where advanced stroke care and neurosurgical services are available [Evidence Level C].

7.2 Initial clinical evaluation

- i. Urgent consultation with a stroke specialist for assessment and for determination to involve neurosurgery [Evidence Level C].
- ii. For patients who meet criteria for potential hemicraniectomy during initial assessment, an urgent neurosurgical consultation should be initiated in-person, by telephone, or using telemedicine (Telestroke services) [Evidence Level C].
- iii. Initiate a discussion with patient, family members, and legal decision-maker regarding a potential hemicraniectomy [Evidence Level C].
 - a. Key issues to be discussed with the patient and/or alternate decision-makers include stroke diagnosis and prognosis if untreated, the risks of surgery, the possible and likely outcomes following surgery including the odds of living with severe disability, and the patient's previously expressed wishes concerning treatment in the event of catastrophic illness and probability of living with severe handicap.
 - b. The discussion with the patient and decision-makers should state more clearly that there is a survival benefit, but an uncertain impact on quality of life and disability. Furthermore that even with treatment, a good outcome (MRS 0–2) is rare.

7.3 Patient management prior to hemicraniectomy surgery

- i. In patients selected for decompressive hemicraniectomy, proceed urgently to surgery prior to significant decline in GCS or pupillary change [Evidence Level C]. Proceeding within 48 h from stroke onset may provide benefit [Evidence Level B].
- ii. Patients should be transferred to an intensive care unit or neuro step-down unit for close and frequent monitoring of neurological status prior to surgery [Evidence Level C].
 - a. Monitoring should include assessments of level of consciousness (e.g., Canadian Neurological Scale Score (CNS)), worsening symptom severity, and blood pressure at least hourly; more frequently as the individual patient condition requires [Evidence Level C].
 - b. If changes in status occur, the stroke team and neurosurgeon should be notified immediately for re-evaluation of the patient [Evidence Level C]. Change in status may include level of drowsiness/consciousness, change in CNS score by greater than or equal to 1 point, or change in NIHSS score by greater than or equal to 4 points.
 - c. Repeat CT scans are recommended for patients when deterioration in neurological status occurs [Evidence Level C].
- iii. Patients with suspected elevation in intracranial pressure may be managed according to institutional protocols (e.g., administration of hyperosmolar therapy, head of bed elevation) [Evidence Level C].

Part 2: Canadian Stroke Best Practice Recommendations for Acute Inpatient Stroke Care, 6th edition, update 2018

This section includes recommendations related to management of acute stroke patients once diagnosis is confirmed and decisions made regarding early acute stroke treatments. It involves all direct care, investigations, interventions, service delivery, and interactions occurring during the time a person who has had a stroke is

admitted to inpatient care within an acute care hospital. The principal aims of this phase of care are to identify the nature and mechanism of stroke, prevent stroke complications, promote early recovery, and (in the case of severest strokes) provide palliation or end-of-life care. This acute phase of care is usually considered to have ended either at the time of acute stroke unit discharge or by 30 days of hospital admission. Section 8 also provides guidance for people who experience an acute stroke while already in hospital for another condition.

Section 8: Acute stroke unit care

Patients who are admitted to stroke units are more likely to survive, return home, and regain their independence compared to patients who are admitted to non-specialized units. Stroke unit care is characterized by an interdisciplinary stroke team, composed of physicians, nurses, physiotherapists, occupational therapists, speech-language pathologists, and pharmacists, among others with a special interest and expertise in stroke care, who are dedicated to the management of patients recovering from stroke. The other defining feature of a stroke unit is beds that are located within a geographically defined area and are occupied exclusively by patients with stroke.⁶⁴ The most recent update of the Stroke Unit Trialists' Collaboration⁶⁴ included 28 randomized and quasi-randomized trials

comparing stroke unit care with an alternative, less organized form of care (e.g., general medical ward). After a median one-year follow-up, stroke unit care was associated with a significant reduction in death (OR = 0.76, 95% CI 0.66–0.88, $p = 0.0001$), death or institutionalization (OR = 0.76, 95% CI 0.67–0.86, $p = 0.0001$), and death or dependency (OR = 0.80, 95% CI 0.67–0.97, $p < 0.00001$). Moreover, stroke unit care was found to be superior regardless of sex, age, or stroke severity. In Canada, access to stroke unit care varies by region. Within our large comprehensive stroke centers, over 70% of stroke patients are admitted to stroke units. For patients cared for in primary stroke centers, just over half of all acute ischemic stroke patients spend any time on an acute stroke unit.¹ Systems improvement to increase the number of patients cared for on a stroke unit is an imperative.

Section 8: Recommendations for acute stroke unit care

8.1 Patients admitted to hospital with an acute stroke or TIA should be treated on an inpatient stroke unit [Evidence Level A] as soon as possible; ideally within 24 h of hospital arrival [Evidence Level C].

- i. Patients should be admitted to a stroke unit which is a specialized, geographically defined hospital unit dedicated to the management of stroke patients [Evidence Level A].
 - a. For facilities without a dedicated stroke unit, the facility must strive to focus care on the priority elements identified for comprehensive stroke care delivery (including clustering patients, interdisciplinary team, access to early rehabilitation, stroke care protocols, case rounds, patient education). Refer Box 8A for Optimal Inpatient Stroke Care criteria.
- ii. The core interdisciplinary team on the stroke unit should consist of healthcare professionals with stroke expertise including physicians, nurses, occupational therapists, physiotherapists, speech-language pathologists, social workers, and clinical nutritionists (dietitians) [Evidence Level A].
 - a. All stroke teams should include hospital pharmacists to promote patient safety, medication reconciliation, provide education to the team and patients/family regarding medication(s) (especially side effects, adverse effects, interactions), discussions regarding adherence, and discharge planning (such as special needs for patients, e.g., individual dosing packages) [Evidence Level B].
 - b. Additional members of the interdisciplinary team may include discharge planners or case managers, (neuro) psychologists, palliative care specialists, recreation and vocational therapists, spiritual care providers, peer supporters, and stroke recovery group liaisons [Evidence Level B].
- iii. The interdisciplinary team should assess patients within 48 h of admission to hospital and formulate a management plan [Evidence Level B].
 - a. Clinicians should use standardized, valid assessment tools to evaluate the patient's stroke-related impairments and functional status [Evidence Level B].
 - b. Assessment components should include dysphagia, mood and cognition, mobility, functional assessment, temperature, nutrition, bowel and bladder function, skin breakdown, discharge planning, prevention therapies, venous thromboembolism prophylaxis [Evidence Level B]. Refer to Section 9 of this module for further information.
 - c. Alongside the initial and ongoing clinical assessments regarding functional status, a formal and individualized assessment to determine the type of ongoing post-acute rehabilitation services required should occur as soon as the status of the patient has stabilized, and within the first 72 h post-stroke, using a standardized protocol (including tools such as the alpha-FIM) [Evidence Level B]. Refer to Canadian Stroke Best Practice Recommendations Stroke Rehabilitation Module Section 3 for further information.
- iv. Any child admitted to hospital with stroke should be managed in a center with pediatric stroke expertise when available; if there is no access to specialized pediatric services, children with stroke should be managed using standardized pediatric stroke protocols [Evidence Level B].

8.2 Management of stroke that occurs while patient already in hospital:

- i. Hospital in-patients who experience a new stroke while hospitalized should undergo immediate assessment by a physician with stroke expertise, undergo neurovascular imaging without delay, and be assessed for eligibility for intravenous alteplase and/or EVT [Evidence Level B]. Refer to Sections 4 and 5 for additional information.
- a. All hospitals should have protocols in place for management of acute inpatient stroke and all staff trained on these protocols, especially in units with higher risk patients [Evidence Level C].

Box 8A: Optimal acute inpatient stroke care criteria

Definition:

A stroke unit is a specialized, geographically defined hospital unit dedicated to the management of stroke patients and staffed by an experienced interdisciplinary stroke team. Refer to the resource *Taking Action Towards Optimal Stroke Care* for detailed information about stroke unit criteria.

Alternate Stroke Care Models: It is recognized that many models of acute stroke care exist across Canada. Many organizations do not have the official administrative designation as an “acute stroke unit”; however, they have most or all of the stroke unit criteria in place and should be recognized as attempting to meet optimal stroke care in the face of administrative/structural resource challenges. These models are sometimes referred to as clustered acute stroke care, or purposeful grouping of stroke patients.

Core elements of comprehensive stroke and neurovascular care

(Based on Stroke Unit Trialists Collaboration 2007)

- a. It is recognized that not all hospitals are able to deliver all of the stroke unit elements, and every hospital should be Taking Action to establish protocols and processes of care to implement as many elements as possible to achieve optimal stroke care delivery within their geographic location, hospital volumes, and resource availability (human, equipment, and funding). Refer to *Taking Action Towards Optimal Stroke Care resource kit* at www.strokebestpractices.ca
- b. Specialized care for patients with ischemic stroke, intracerebral hemorrhage, and TIA (care may be expanded in some institutions to include patients with SAH and other neurovascular conditions);
- c. Dedicated stroke team with broad expertise—including neurology, nursing, neurosurgery, physiatry, rehabilitation professionals, pharmacists, and others;
- d. Consistent clustered model where all stroke patients are cared for on the same hospital ward with dedicated stroke beds by trained and experienced staff, including rehabilitation professionals;
- e. Access to 24/7 imaging and interventional neuroradiology expertise;
- f. Emergent neurovascular surgery access;
- g. Protocols in place for hyperacute and acute stroke management, and seamless transitions between stages of care (including prehospital, ED and inpatient care);
- h. Dysphagia screening protocols in place to assess all stroke patients without prolonged time delays prior to commencing oral nutrition and oral medications;
 - i. Access to post-acute rehabilitation services, including inpatient, community-based, and/or early supported discharge therapy;
 - j. Discharge planning starting as soon as possible after admission, and anticipating discharge needs to facilitate smooth transitions;
- k. Daily/bi-weekly patient care rounds with interdisciplinary stroke team to conduct case reviews, discuss patient management issues, family concerns or needs, and discharge planning (discharge or transition to the next step in their care, timing, transition requirements);
 - l. Patient and family education that is formal, coordinated, and addresses learning needs and responds to patient and family readiness;
- m. Provision of palliative care when required, ideally by a specialized palliative care team;
- n. Ongoing professional development for all staff—stroke knowledge, evidence-based best practices, skill building, orientation of trainees;
- o. Involvement in clinical research for stroke care.

Section 9: Inpatient prevention and management of complications following stroke

Despite the best care, patients remain at high risk of medical complications, which are relatively common following stroke. They are associated with increased mortality, lengths of hospital stay, and higher cost. Therefore, appropriate investigations and management strategies should be implemented for all hospitalized patients to avoid complications and improve the odds of a good recovery. Estimates of the percentage of patients who experience at least one medical complication during hospitalization vary widely from 25%⁶⁵ to 85%.⁶⁶ Complications tend to occur more frequently in older patients, who often have multimorbidity and patients with more severe strokes. Some of the most commonly cited complications include urinary tract infections, fever, pneumonia, and deep vein thrombosis.^{67–69}

Controversy continues as to the benefit of early mobilization. Although the primary endpoint of the AVERT

trial⁷⁰ indicated early mobilization reduced the odds of a good outcome at three months (OR = 0.73, 95% CI 0.59–0.90, $p = 0.004$), a prespecified dose-response analysis suggested that shorter, more frequent mobilizations early after acute stroke were associated with improved odds of favorable outcome, while increased amount (minutes per day) of mobilization reduced the odds.¹⁰ Regardless of group assignment, increasing the frequency of out-of-bed sessions significantly improved the odds of favorable outcome by 13% (OR for each additional session = 1.13, 95% CI 1.09–1.18, $p < 0.001$) and improved the odds of walking 50 m unassisted by 66% (OR for each additional session = 1.66, 95% CI 1.53–1.80, $p < 0.001$), after controlling for age and stroke severity. At the same time, keeping time to first mobilization and frequency constant, every extra 5 min of out-of-bed activity per day reduced the odds of a favorable outcome (OR = 0.94, 95% CI 0.91–0.97, $p < 0.001$) and reduced the odds of walking unassisted for 50 m (OR = 0.85, 95% CI 0.81–0.89, $p < 0.001$).¹⁰

Section 9: Recommendations for prevention and management of complications following stroke

9.0 Appropriate *investigations and management strategies* should be implemented for all hospitalized stroke and TIA patients to optimize recovery, avoid complications, prevent stroke recurrence, and provide palliative care when required.

- i. During acute inpatient care, stroke patients should undergo appropriate investigations to determine stroke mechanism and guide stroke prevention and management decisions [Evidence Level B].
- ii. Individualized care plans should address nutrition, oral care, mobilization and incontinence, and reduce the risk of complications such as urinary tract infection, aspiration pneumonia, and venous thromboembolism [Evidence Level B].
- iii. Discharge planning should begin as a component of the initial admission assessment and continue throughout hospitalization as part of ongoing care of hospitalized acute stroke patients [Evidence Level B]. Refer to *Canadian Stroke Best Practice Recommendations Managing Stroke Transitions of Care Module Section 3* for additional information.
- iv. All patients, family members, and informal caregivers should receive timely and comprehensive information, education, and skills training by all interdisciplinary team members [Evidence Level A]. Refer to *Canadian Stroke Best Practice Recommendations Managing Stroke Transitions of Care Module Sections 1 and 2* for additional information.
- v. A past history of depression should be identified for all acute stroke inpatients [Evidence Level C]. Refer *Canadian Stroke Best Practice Recommendations Mood, Cognition and Fatigue Module Section 1* for additional information.
- vi. Patients should undergo an initial screening for vascular cognitive impairment when indicated [Evidence Level B]. Refer *Canadian Stroke Best Practice Recommendations Mood, Cognition and Fatigue Module Section 2* for additional information.

9.1 Cardiovascular investigations

- i. For patients being investigated for an acute embolic ischemic stroke or TIA 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 two weeks is recommended to improve detection of paroxysmal atrial fibrillation in selected patients aged ≥ 55 years who are not already receiving anticoagulant therapy but would be potential anticoagulant candidates [Evidence Level A]. Refer to *CSBPR Secondary Prevention of Stroke Module* for additional guidance in management of patients with stroke and atrial fibrillation.
- ii. Echocardiography, either 2D or transesophageal, should be considered for patients with suspected embolic stroke and normal neurovascular imaging [Evidence Level B] as well as no contraindications for anticoagulant therapy. This is particularly relevant for younger adults with stroke or TIA and unknown etiology.

- iii. Children with stroke should undergo a comprehensive cardiac evaluation including echocardiography as well as detailed rhythm monitoring if clinically indicated [Evidence Level B].

9.2 Venous thromboembolism prophylaxis

- i. All stroke patients should be assessed for their risk of developing venous thromboembolism (deep vein thrombosis and pulmonary embolism). **Patients at high risk include those who are unable to move one or both lower limbs; those who are unable to mobilize independently; a previous history of venous thromboembolism; dehydration; and comorbidities such as cancer.**
 - ii. Patients at high risk of venous thromboembolism should be started on thigh-high intermittent pneumatic compression devices (IPC) or pharmacological venous thromboembolism prophylaxis immediately if there is no contraindication (e.g., systemic or intracranial hemorrhage) [Evidence Level A]. At present, there is no direct evidence to suggest the superiority of one approach over the other.
 - a. If IPC is selected, it should be applied as soon as possible and within the first 24 h after admission. IPC should be discontinued when the patient becomes independently mobile, at discharge from hospital, if the patient develops any adverse effects, or by 30 days (whichever comes first) [Evidence Level B].
 - 1) For patients wearing IPC devices, skin integrity should be assessed daily [Evidence Level B].
 - 2) Consultation with a wound care specialist is recommended if skin breakdown begins during IPC therapy [Evidence Level C].
 - 3) If IPC is considered after the first 24 h of admission, venous leg Doppler studies should be considered [Evidence Level C].
 - b. Low-molecular-weight heparin (i.e., enoxaparin) should be considered for patients with acute ischemic stroke at high risk of venous thromboembolism; or *unfractionated* heparin for patients with renal failure [Evidence Level A].
 - c. For stroke patients admitted to hospital and remaining immobile for longer than 30 days, the use of ongoing venous thromboembolism prophylaxis (e.g., with pharmacological venous thromboembolism prophylaxis) is recommended [Evidence Level C].
 - ii. The use of anti-embolism stockings alone for post-stroke venous thromboembolism prophylaxis is not recommended [Evidence Level A].
 - iii. Early mobilization and adequate hydration should be encouraged for all acute stroke patients to help prevent venous thromboembolism [Evidence Level C].

9.3 Temperature Management

- i. Temperature should be monitored as part of vital sign assessments; ideally, every 4 h for the first 48 h, and then as per ward routine or based on clinical judgment [Evidence Level C].
- ii. For temperature $>37.5^{\circ}\text{C}$, increase frequency of monitoring, initiate temperature-reducing care measures, investigate possible infection such as pneumonia or urinary tract infection [Evidence Level C], and initiate antipyretic and antimicrobial therapy as required [Evidence Level B].

9.4 Mobilization (revised for 2018)

Mobilization is defined as "the process of getting a patient to move in the bed, sit up, stand, and eventually walk."

- i. All patients admitted to hospital with acute stroke should have an initial assessment, conducted by rehabilitation professionals, as soon as possible after admission [Evidence Level A].
- ii. Initial screening and assessment should be commenced within 48 h of admission by rehabilitation professionals in direct contact with the patient [Evidence Level C]. *Refer to Canadian Stroke Best Practice Recommendations Stroke Rehabilitation Module for additional recommendations on mobilization following an acute stroke.*
- iii. Rehabilitation therapy should begin as early as possible once the patient is determined to be medically able to participate in active rehabilitation [Evidence Level A].
- iv. Frequent, *brief*, out-of-bed activity involving active sitting, standing, and walking, beginning within 24 h of stroke onset is recommended if there are no contraindications [Evidence Level B]. More intense early sessions are not of more benefit. Clinical judgment should be used.

Note: Contraindications to early mobilization include, but are not restricted to, patients who have had an arterial puncture for an interventional procedure, unstable medical conditions, low oxygen saturation, and/or lower limb fracture or injury.

9.5 Seizure management

- i. New-onset seizures in admitted patients with acute stroke should be treated using appropriate short-acting medications (e.g., lorazepam IV) if they are not self-limiting [Evidence Level C].
 - a. A single, self-limiting seizure occurring at the onset, or within 24 h after an ischemic stroke (considered an “immediate” post-stroke seizure) should not be treated with long-term anticonvulsant medications [Evidence Level C].
 - b. Patients that have an immediate post-stroke seizure should be monitored for recurrent seizure activity during routine monitoring of vital signs and neurological status. Recurrent seizures in patients with ischemic stroke should be treated as per treatment recommendations for seizures in other neurological conditions [Evidence Level C].
- ii. Seizures are a common presentation with stroke in neonates and children. Consider enhanced or increased seizure/electroencephalogram monitoring in at-risk populations such as neonates, children with stroke, and adults with otherwise unexplained reduced level of consciousness [Evidence Level B].
 - a. Other investigations may include EEG and tests to rule out other precipitating factors of seizures (e.g., infections) and may be warranted in acute stroke patients with seizures based on patient factors and clinical judgment [Evidence Level C].
 - b. Prophylactic use of anticonvulsant medications in patients with ischemic stroke is not recommended [Evidence Level B] and there is some evidence to suggest possible harm with negative effects on neurological recovery [Evidence Level B].

9.6 Nutrition and dysphagia

- i. Interdisciplinary team members should be trained to complete initial swallowing screening for all stroke patients to ensure patients are screened in a timely manner [Evidence Level C].
- ii. The swallowing, nutritional and hydration status of stroke patients should be screened as early as possible, ideally on the day of admission, using validated screening tools [Evidence Level B].
- iii. Abnormal results from the initial or ongoing swallowing screens should prompt referral to a speech-language pathologist, occupational therapist, and/or dietitian for more detailed assessment and management of swallowing, nutritional, and hydration status [Evidence Level C]. An individualized management plan should be developed to address therapy for dysphagia, nutrition needs, and specialized nutrition plans [Evidence Level C].
- iv. Stroke patients with suspected nutritional concerns, hydration deficits, dysphagia, or other comorbidities that may affect nutrition (such as diabetes) should be referred to a dietitian for recommendations:
 - a. to meet nutrient and fluid needs orally while supporting alterations in food texture and fluid consistency recommended by a speech-language pathologist or other trained professional [Evidence Level B];
 - b. for enteral nutrition support (nasogastric tube feeding) in patients who cannot safely swallow or meet their nutrient and fluid needs orally. The decision to proceed with tube feeding should be made as early as possible after admission, usually within the first three days of admission in collaboration with the patient, family (or substitute decision-maker), and interdisciplinary team [Evidence Level B]. Refer to *Canadian Stroke Best Practice Recommendations Stroke Rehabilitation Module Section 7* for additional information on dysphagia screening, assessment and management.

9.7 Continence

- i. The use of indwelling catheters should be used cautiously due to the risk of urinary tract infection [Evidence Level A]. If used, indwelling catheters should be assessed daily and removed as soon as possible [Evidence Level A]. Excellent pericare and infection prevention strategies should be implemented to minimize risk of infections [Evidence Level B]. Refer to *Section 4.6(iii)* for additional information.
- ii. All stroke patients should be screened for urinary incontinence and retention (with or without overflow), fecal incontinence, and constipation [Evidence Level C].
- iii. The use of a portable ultrasound machine is recommended as the preferred noninvasive painless method for assessing post-void residual [Evidence Level C].
- iv. Stroke patients with urinary incontinence should be assessed by trained personnel using a structured functional assessment to determine cause and develop an individualized management plan [Evidence Level B].

- v. A bladder training program should be implemented in patients who are incontinent of urine [Evidence Level C], including timed and prompted toileting on a consistent schedule [Evidence Level B].
- vi. Appropriate intermittent catheterization schedules should be established based on amount of post-void residual [Evidence Level B].
- vii. A bowel management program should be implemented for stroke patients with persistent constipation or bowel incontinence [Evidence Level A].

9.8 Oral Care

- i. Upon or soon after admission, all stroke patients should have an oral/dental assessment, including screening for signs of dental disease, level of oral care, and appliances [Evidence Level C].
- ii. For patients wearing a full or partial denture it should be determined if they have the neuromotor skills to safely wear and use the appliance(s) [Evidence Level C].
- iii. An appropriate oral care protocol should be used for every patient with stroke, including those who use dentures [Evidence Level C]. The oral care protocol should be consistent with the Canadian Dental Association recommendations [Evidence Level B] and should address areas such as frequency of oral care (ideally after meals and before bedtime); types of oral care products (toothpaste, floss, and mouthwash); and management for patients with dysphagia.
- vi. If concerns with implementing an oral care protocol are identified, consider consulting a dentist, occupational therapist, speech-language pathologist, and/or a dental hygienist [Evidence Level C].
- v. If concerns are identified with oral health and/or appliances, patients should be referred to a dentist for consultation and management as soon as possible [Evidence Level C].

Section 10: Advance care planning

Advance care planning (ACP) is a process through which a patient, in consultation with healthcare providers and family members make decisions regarding their health care, should they become incapable of participating in decision-making. Ideally, this process takes place before stroke or other life-threatening illness occurs, to help mitigate the anxiety associated with the uncertainty of

stroke prognosis and recovery, and the many complex decisions that may need to be made. Elements of advance care planning include the patients' prognosis, treatment options, goals of care, and the identification and documentation of end-of-life wishes. Research suggests that less than 50% of adults have had these conversations with family members and that ACP discussions more frequently occur when patients and families are faced with a serious or life-threatening illness.⁷¹

Section 10: Recommendations for advanced care planning following stroke

- 10.0** Patients surviving a stroke, as well as their families and informal caregivers, should be approached by the stroke healthcare team to participate in advance care planning [Evidence Level C]. Refer to *Advanced Care Planning definitions at www.strokebestpractices.ca*
- i. The primary goal of advance care planning conversations is to prepare patients and substitute decision-makers for providing consent in future situations (for example, in light of recent significant illness such as stroke) [Evidence Level B].
 - a. Advance care planning may include identifying a substitute decision-maker (proxy, agent, or Power of Attorney) and discussion of the patient's personal values and wishes which they can apply in future if the need arises to make medical decisions or provide consent on behalf of the patient [Evidence Level B].
 - b. Advance care planning discussions should be documented and reassessed regularly with the active care team and substitute decision-maker [Evidence Level C].
 - ii. The advance care planning conversation should be revisited periodically, such as when there is a change in the patient's health status [Evidence Level B].
 - iii. The interdisciplinary team should have the appropriate communication skills and knowledge to address the physical, spiritual, cultural, psychological, ethical, and social needs of stroke patients, their families, and informal caregivers [Evidence Level C].

- a. Respectful discussion of patient's values and wishes should be balanced with information regarding medically appropriate treatment related to ongoing stroke management and future medical care [Evidence Level C].
- iv. Capacity-related provincial legislation should be reviewed and appropriate substitute decision-makers should be identified if a survivor is deemed incapable of making specific decisions re: their personal health care and/or discharge-related finances [Evidence Level C].

Section 11: Palliative and end-of-life care

Palliative care is a comprehensive approach to end of life care that aims to control pain, provide comfort, improve quality of life, and effectively manage patients' and their families' psychosocial needs. Decisions to withhold or withdraw life-prolonging treatments after stroke affect a substantial proportion of patients who have experienced a severe stroke; therefore, palliative care is an important

component of stroke care. The most commonly identified stroke-associated palliative needs of patients identified included pain, respiratory secretions, dyspnea, agitation, and psychological distress.⁷² Given the multifaceted nature of stroke care, the core elements of palliative care should be in routine practice across the various providers of a stroke team (e.g., neurologist, nurses, and therapists) and across multiple settings (ED, acute rehabilitation unit, and nursing homes).

Definitions:

Palliative care is an approach that focuses on comfort and quality of life for those affected by life-limiting illness, such as large hemispheric strokes, and severe hemorrhagic stroke. It aims to prevent and relieve physical, social, psychological, or spiritual suffering of stroke patients, their families and informal caregivers. Palliative care can complement life-prolonging or disease-modifying therapies post-stroke and need not be reserved for those whose death is imminent.

A palliative approach to care refers to palliative care that is provided by non-palliative care specialists, i.e., the basic symptom management and basic psychosocial care that all clinicians provide to patients and their families.

End-of-life care is part of the palliative approach and is the management and treatment of dying patients as well as their families and informal caregivers. The end-of-life period often involves a period of change (e.g., worsening functional status) rather than an acute event.

Goals of care for palliative care: In the event of a potentially poor prognosis, the medical team may initiate a "goals of care" discussion with the individual and/or their substitute decision-maker. This conversation would have the objective of establishing consensus on a direction of care and would incorporate the individual's previous wishes/advanced care planning as well as their current status and needs. Some potential topics of discussion may be: preferred location of palliation, the cessation of certain medical interventions, comfort care options, and preferences in the event of immanent death (e.g., resuscitation). The intent is to then have a written communication for the healthcare team to assist in the provision of individualized palliative care in a timely manner. Health status can change over time and this written plan should be reviewed in conjunction with shifts in status or changes in the care team. The goals of care can be amended or revised at any time by the individual and/or substitute decision-maker.

Section 11: Recommendations for palliative and end-of-life care

- 11.0 A palliative care approach should be applied when there has been a catastrophic stroke or a stroke in the setting of significant pre-existing comorbidity, to optimize care for these patients, their families, and informal caregivers [Evidence Level B].
 - i. The interdisciplinary stroke team should have discussions with the patient and decision-makers regarding the patient's current state and likely progression of the effects of the stroke, and come to agreement on the general direction of care—whether care will focus on comfort or focus on life prolongation and functional improvement [Evidence Level B].
 - ii. Based on decisions regarding the direction of care (i), the interdisciplinary stroke team should communicate with patients, decision-makers, families, and informal caregivers on an ongoing basis, and provide information and counseling regarding

- diagnosis, prognosis and what can be expected regarding progression of stroke impact, and management, based on direction of care (see recommendation i) [Evidence Level C].
- iii. Content to be discussed with patients, families, and informal caregivers may include:
 - a. the appropriateness of life-sustaining measures including mechanical ventilation, enteral/intravenous feeding, and intravenous fluids [Evidence Level B];
 - b. reassessment of all medications, and recommendations for cessation of medications no longer necessary when the goals of care shift to comfort measures only (e.g., antiplatelets, anticoagulants, statins, hypoglycemics) [Evidence Level C];
 - c. cessation of routine vital sign checks, bloodwork, and diagnostic tests [Evidence Level C];
 - d. oral care [Evidence Level C];
 - e. assessment and management of pain [Evidence Level B];
 - f. assessment and management of delirium [Evidence Level C];
 - g. assessment and management of respiratory distress and secretions [Evidence Level B];
 - h. assessment and management of incontinence, nausea, vomiting, constipation, and skin and wound care [Evidence Level C].
 - i. assessment and management of seizures [Evidence Level C];
 - j. assessment and management of anxiety and depression [Evidence Level C]. Refer to Canadian Stroke Best Practice Recommendations *Mood, Cognition and Fatigue Module* Section I for additional information [Evidence Level C];
 - k. Preferred location of palliative care (e.g., Home, Hospice another supportive living environment) [Evidence Level C];
 - l. Preferred person to be notified upon time of death [Evidence Level C].
 - iv. The interdisciplinary stroke team should have the appropriate communication skills and knowledge to address the physical, spiritual, cultural, psychological, and social needs of patients, families, and informal caregivers who are receiving end-of-life care. There should be regular communication with the patient, family, and informal caregivers to ensure that these needs are being met [Evidence Level C].
 - v. Advance care planning discussions should be documented and reassessed regularly with the active care team and substitute decision-maker [Evidence Level C].
 - vi. Patients, families, informal caregivers, and the healthcare team should have access to palliative care specialists, particularly for consultation regarding patients with difficult-to-control symptoms, complex or conflicted end-of-life decision-making, or complex psychosocial family issues [Evidence Level C].
 - vii. Formalized palliative care processes and a team experienced in providing end-of-life care for stroke patients (especially nursing staff) should be considered to introduce and monitor standards of care provided to patients at the end of life [Evidence Level B].
 - viii. Organ donation should be discussed with families and caregivers as appropriate [Evidence Level C].
 - ix. Supportive counseling, funeral supports, and bereavement resources should also be provided to families and caregivers, post patient death [Evidence Level C].

Discussion

The 2018 update of the Canadian Stroke Best Practice Acute Stroke Management Recommendations provide a common set of guiding principles for important aspects of acute stroke management. The Heart and Stroke Foundation of Canada has undertaken an extensive review of all current literature for the management of people experiencing a stroke from stroke symptom onset to discharge from acute care services with EDs and inpatient care (available at www.strokebestpractices.ca). Acute stroke care has advanced significantly in the past five years with the emergence of EVT as an established evidenced-based therapy. Given the strength of the evidence for this procedure, stroke

programs globally have been obliged to review and update their existing processes and protocols to accommodate the increased demand for service. These changes will improve the assessment and management of all acute stroke patients, even those not receiving acute thrombolytic treatment or endovascular procedures. Changes to stroke systems of care must involve representatives of all stakeholders, not just stroke neurology. The update of these recommendations involved a close collaboration between the Heart & Stroke Foundation of Canada, our stroke best practice advisory committees, the Canadian Stroke Consortium, the Canadian Association of Emergency Physicians, the Paramedic Chiefs of Canada, the Paramedics Association of Canada, and consultation with people

who have personally experienced an acute stroke as well as their family and informal caregivers. This collaboration brings strength and consistency to stroke care coordination and delivery which leads to increased efficiencies and better outcomes.

Challenges and controversies have been encountered as a result of recent advances in stroke care. With the clear benefits of EVT demonstrated, the question as to which patients are the best candidates for the procedure persists and issues of supply and demand as well as overall impact within a publicly funded healthcare system have arisen. The extended time window of up to 24 h, for highly selected patients, will increase demand for the procedure, resulting in an increased number of patients who will require advanced neuroimaging, including CTA and CTP (or MRA and MRP). However, not all primary stroke centers can perform such investigations due to older generation CT scanners, a lack of trained personnel, or funding for out-of-hours on-call staffing. Consequently, hospitals capable of advanced imaging may not be able to manage the increased volumes of patients who may be diverted or transferred to them. ED personnel are also concerned about increased demand. There have been debates related to the issue of whether all stroke patients should be transported directly to comprehensive stroke centers versus stopping at the closest primary stroke center for imaging and initiation of intravenous thrombolysis for eligible patients before determining appropriateness of transferring to an endovascular enabled hospital.^{73–75} In order to answer these questions, valid data are required. As stroke systems evolve, it is imperative that data collection systems are built that facilitate close monitoring of treatment access, process times, and patient outcomes. Additional indicators to be considered include home time in the first 90 days, functional outcomes at 90 days,⁷⁶ and patient-reported outcomes such as quality of life⁷⁷ and caregiver burden.^{78,79}

These recommendations are intended to drive systems change and quality improvement for acute stroke care. The recommendations continue to be a work in progress and are regularly updated every two to three years to integrate newly released data to help maximize patient outcomes from this disabling disease.

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Author Contributions

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Declaration of Conflicts of Interest

JM Boulanger is a speaker for Bayer and Pfizer; G Gubitz is a speaker for Bayer, Boehringer Ingelheim, and BMS Pfizer; C O'Kelly is a course instructor for Medtronic; D Blacquiere is a speaker for Bayer; LK Casaubon is a speaker and advisory committee member for Bayer and Covidien Canada, an independent neurological assessor for Medtronic, and a site principal investigator for NoNO; M Kelly is a speaker for Penumbra, and a proctor for Medtronic; K Butcher is a speaker for Bayer, Boehringer Ingelheim, and BMS Pfizer, and had received research funding from Bayer and Boehringer Ingelheim. *The following authors do not have any conflicts of interest to declare with respect to this manuscript:* Lindsay MP, Stotts G, Smith EE, Foley N, Bhogal S, Boyle K, Braun L, Goddard T, Heran MKS, Kanya-Forster N, Lang E, Lavoie P, McClelland M, Pageau P, Pettersen J, Purvis H, Shamy M, Tampieri D, vanAdel B, Verbeek R, Ferguson D, Hegedus Y, Jacquin GJ, Linkewich B, Lum C, Mann B, Milot G, Newcommon N, Poirier P, Simpkin W, Snieder E, Kamal N, Trivedi A, Whelan R, and Smitko E.


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