Canadian Stroke Best Practices™

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management

7th Edition, Update 2022 & EVT Interim Update 2025

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on behalf of the Canadian Stroke Best Practice Recommendations Advisory Committee, in collaboration with the Canadian Stroke Consortium.

Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025 :

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Acute Stroke Management, 7th Edition Update 2022

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INTRODUCTION AND OVERVIEW

Introduction to the Canadian Stroke Best Practice Recommendations

The Canadian Stroke Best Practice Recommendations (CSBPR) provide up-to-date, evidence-based guidelines for the prevention and management of stroke, to promote optimal recovery and reintegration for people with stroke and support their families and informal caregivers. The CSBPR are under the leadership of the Heart and Stroke Foundation of Canada (HSF).

The theme of the 7th Edition of the CSBPR is **building connections to optimize individual outcomes**. People with stroke often present to the healthcare system with multiple pre-existing comorbid conditions – some of which may have contributed to their stroke, some of which may be consequences of it, and some of which may be unrelated. Nelson et al. (2016) found that approximately 80% of people who survive a stroke have on average five other conditions and a range of psychosocial issues. The interactions among complex comorbid conditions must be considered to ensure treatment and ongoing care planning is personalized and person centred.

In addition, in light of the strong evidence of the intrinsic connections between the heart and brain, management of people with stroke should take heart health and its possible association with vascular cognitive impairment into consideration. The healthcare system is often designed in siloes, with planning and organization for different conditions being done separately rather than being integrated across conditions, even related vascular conditions. As people move through different settings and phases of care after a stroke, they often report feeling anxious and overwhelmed. Providing individualized care and ensuring connections are made within the community have a significant impact on patients' short- and long-term outcomes.

The 7th Edition of the CSBPR takes a broad, wholistic focus and takes into consideration issues of multimorbidity and increasing complexity of people with stroke. This is particularly relevant for this module on ***acute stroke management***, as people with acute stroke often present with several other comorbidities that may have contributed to their stroke. In many cases, these comorbidities may have been first detected at the time of their stroke (e.g., hypertension, carotid stenosis, patent foramen ovale). People with both stroke and multimorbid conditions are more complex, require a coordinated interdisciplinary approach to care and recovery, and are at risk of worse outcomes.

In this edition, a more purposeful review of sex and gender representation in the seminal clinical trials upon which the recommendations are based was undertaken. This was done to determine the extent to which available evidence includes both male and female subjects, in sufficient proportions to be able to detect outcomes and generalize to a broader population. These findings are presented in the evidence summary sections and integrated into the actual recommendations where appropriate. Finally, the accompanying performance measures were expanded to include system indicators, clinical indicators, and new patient reported outcome measures, to support the wholistic focus.

The goal of disseminating and implementing these recommendations is to optimize evidence-based stroke care across Canada, reduce practice variations in the care of patients with stroke, and narrow the gap between current knowledge and clinical practice.

These recommendations have been developed in collaboration with the Canadian Stroke Consortium. We work closely with the Canadian Cardiovascular Society, Thrombosis Canada, and Hypertension Canada to ensure alignment of recommendations across guidelines where possible and appropriate.

The CSBPR Acute Stroke Management 2022 7th Edition ***supersedes*** *all recommendations contained in the CSBPR Acute Stroke Management 2018 6th Edition.*

NEW 2025: *Emerging evidence has led to an interim review of the existing 2022 Canadian Stroke Best Practice Recommendations (CSBPR) for Acute Stroke Management, 7th edition, recommendations for endovascular treatment of acute ischemic stroke (section 5.4). The updated 2025 recommendations in section 5.4 supersede the endovascular thrombectomy recommendations included in the 2022 publication of the CSBPR acute stroke management module. These changes include: updating section 5.4 and removal of boxes: 4B,4C, 5C.*

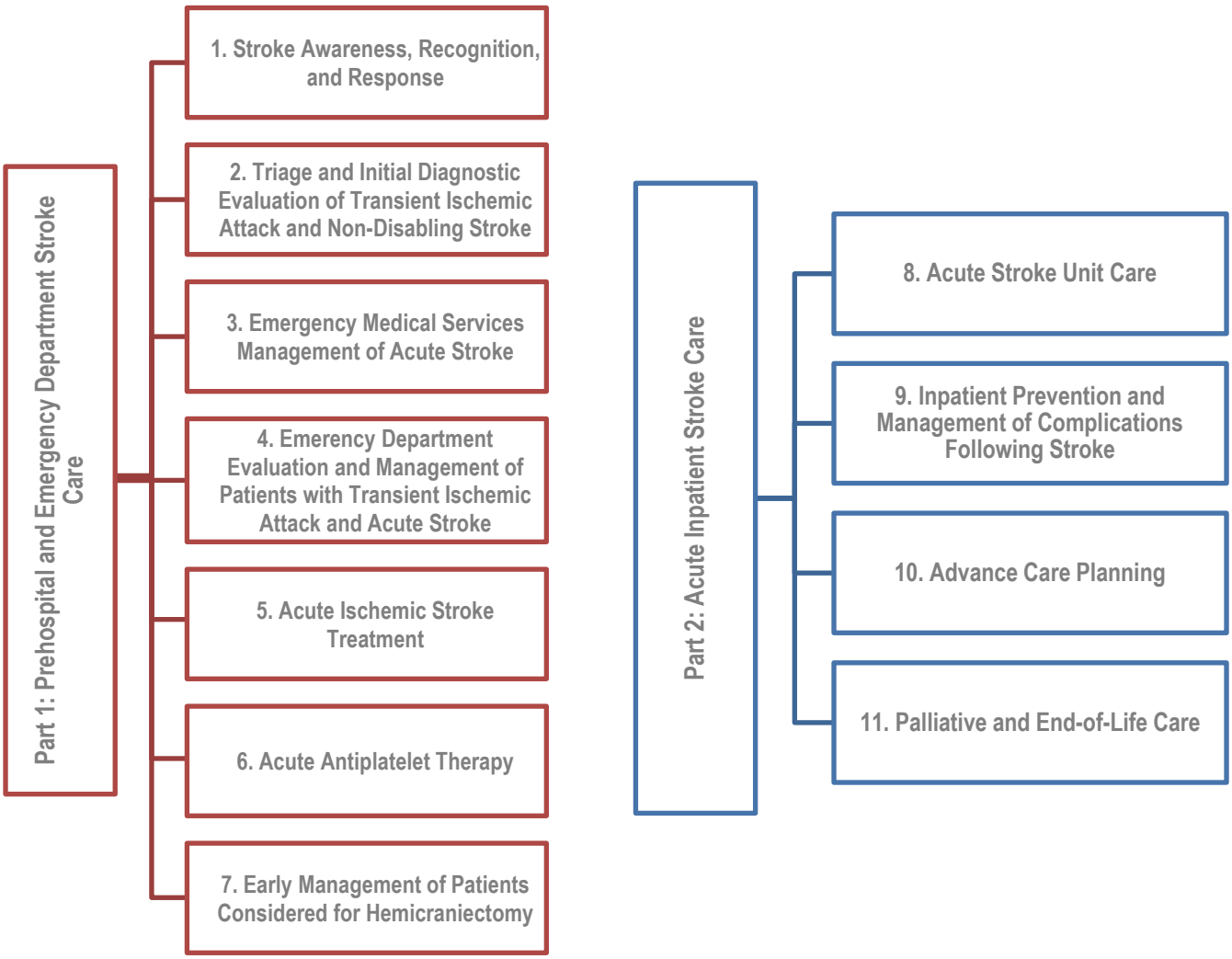
Disclaimer: The Canadian Stroke Best Practice Recommendations (CSBPR) are designed to support implementation of best practices in stroke care across Canada. Healthcare systems, health organizations and professional organizations, as well as legislation and standards, vary provincially. The CSBPR provide guidance on a national level; they do not, on the whole, account for provincial variations in legislation or standards. The CSBPR are not intended to supersede any provincial or local law or organizational or professional standard. In considering and implementing the CSBPR, users are encouraged to consult and follow all appropriate legislation or standards.

Scope of the Acute Stroke Management Module

The CSBPR **Acute Stroke Management** module provides guidance to healthcare providers caring for people who present to the healthcare system with current or very recent symptoms of acute stroke or transient ischemic attack (TIA). This module also addresses the issue of public and healthcare providers' recognition of the signs of stroke and immediate actions that should be taken, including contacting emergency medical services (EMS), arriving at a stroke-enabled emergency department, and launching local healthcare institution code stroke protocols.

This module is presented in two parts. Part 1 addresses prehospital and emergency management of acute stroke, while Part 2 addresses acute inpatient stroke care (*refer to Figure 1*).

Figure 1 CSBPR Acute Stroke Management Module Topics



- Sections 1 to 7 in the Acute Stroke Management module address **prehospital and emergency department stroke care.** This encompasses all direct care, investigations, interventions, service delivery, and interactions from first contact with the healthcare system after the onset of an acute stroke or TIA (usually by contacting EMS or presenting at a healthcare facility) through to discharge from an emergency department to another healthcare facility (usually with a higher or lower level of stroke care), an acute inpatient care unit, or the community. Sections 1 to 4 apply to all potential patients with stroke arriving at hospital; sections 5 and 6 are specific to people experiencing an acute ischemic stroke; and section 7 applies to all confirmed stroke and TIA patients.
- Sections 8 to 11 address **acute inpatient stroke care.** This encompasses all direct care, investigations, interventions, service delivery, and interactions from the time a person with stroke is admitted to an acute care hospital.

Criteria for Stroke Centres Providing Acute Ischemic Stroke Treatment

Within the Canadian Stroke Best Practices *Optimal Acute Stroke Services Framework,* all hospitals in Canada have been assessed based on their capacity to provide guideline-directed stroke care. Each acute care hospital in Canada has been classified as belonging to one of five stroke service levels (*refer to Figure 2*).

- Level 1 and 2 hospitals do not provide emergent acute stroke services. Level 3, 4, and 5 hospitals have increasing levels of coordinated stroke care services, including on-site CT imaging and acute thrombolysis.
- Level 3 hospitals are primary stroke centres that provide intravenous thrombolysis, with or without virtual telestroke support, but they do not have acute stroke units.
- Level 4 hospitals are primary or district or advanced stroke centres that offer on-site intravenous thrombolysis and have acute inpatient stroke units. Neurosurgical services are available at some Level 4 centres.
- Level 5 hospitals are comprehensive stroke centres that provide advanced stroke care including endovascular interventions, and neurosurgical and advanced interventional radiology services.

Level 4 and 5 centres accept transfers from less resourced centres to provide advanced treatment and access to rehabilitation.

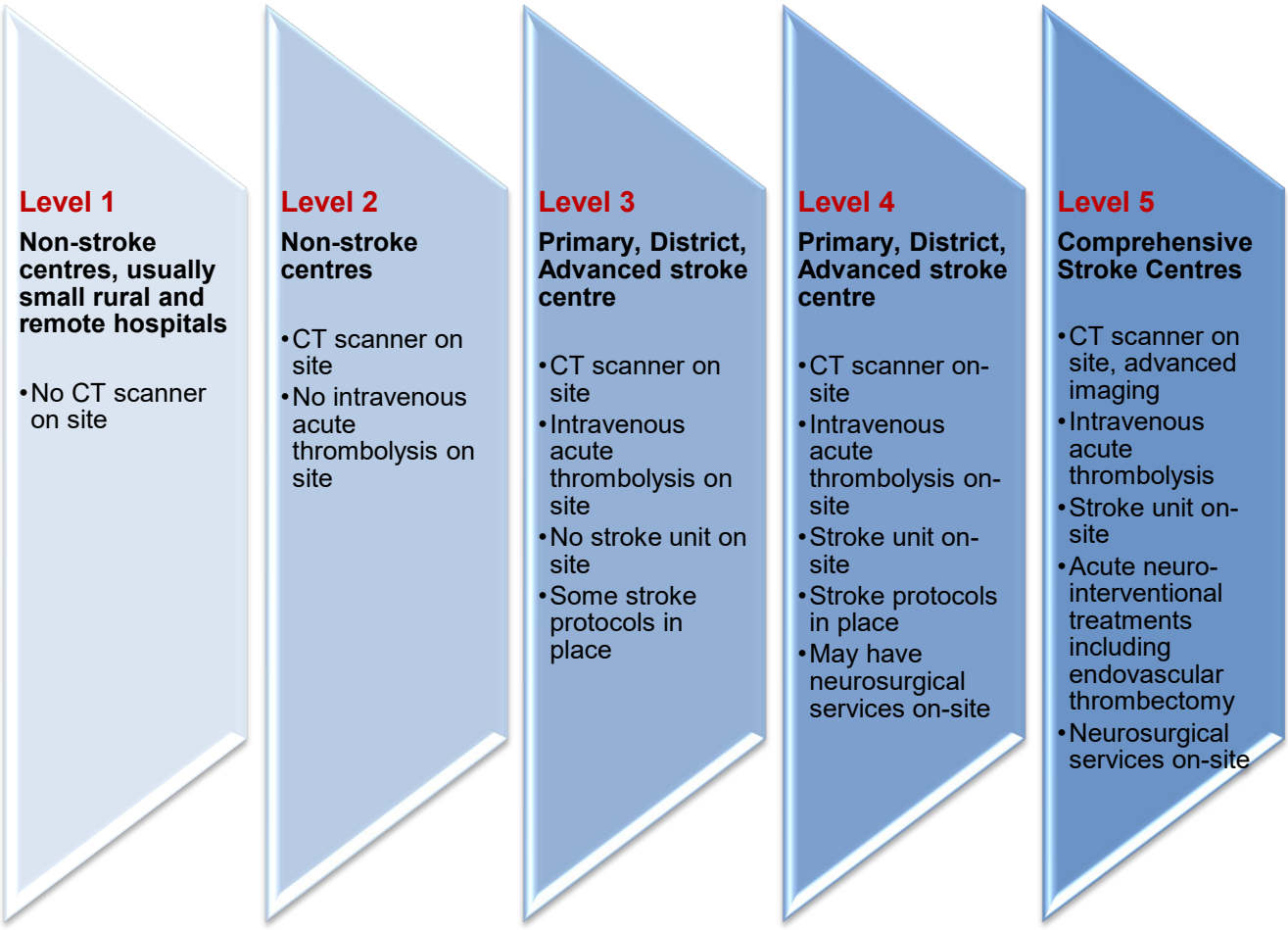
Level 5 comprehensive stroke centres must meet the following criteria to provide endovascular thrombectomy (EVT):

1. A designated stroke team that includes physicians with stroke expertise (e.g., 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 (i.e., physical therapists, occupational therapists, speech-language pathologists), dieticians, pharmacists, and social workers.
2. On-site neurointerventional expertise with 24-hour access, seven days a week.
3. On-site neurosurgery support and neurocritical care services.
4. On-site stroke imaging with 24-hour access to a scanner and rapid interpretation of images, seven days a week, including a computed tomography (CT) scanner (i.e., third-generation or higher helical scanner) with programming for CT angiography (CTA). Multiphase or dynamic CTA or CT perfusion (CTP) imaging can also be used if available on-site. Magnetic resonance imaging, angiography, or perfusion (MRI, MRA, MRP) may be considered if available on site and will not delay acute stroke treatments.
5. Capability to administer intravenous thrombolysis.
6. On-site designated acute or comprehensive stroke unit, which is a specialized, geographically

defined hospital unit dedicated to the management of patients with stroke, staffed by an experienced interdisciplinary stroke team, and providing a complex package of evidence-based care (e.g., protocols, care pathways) for acute stroke management, early rehabilitation, and education to people with stroke in hospital.

Figure 2 Acute Stroke Service Capability

Service levels determined through an Acute Stroke Resource and Services Inventory conducted and validated by Heart & Stroke in 2018.



Definitions

Acute stroke: An episode of symptomatic neurological dysfunction caused by focal brain, retinal or spinal cord ischemia or hemorrhage with evidence of acute infarction or hemorrhage on imaging (MR, CT, retinal photomicrographs), and regardless of symptomatic duration.

Ischemic stroke: An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal cell death attributable to ischemia (blockage of an artery or vein), based on pathological, imaging, or other objective (clinical) evidence of cerebral, spinal cord, or retinal focal ischemic injury or until other etiologies have been excluded. Traditional definitions suggested that symptoms of stroke must last >

24 hours, but time-based definitions are now often reconsidered based on more advanced neuroimaging.

Transient ischemic attack (TIA, sometimes referred to as a "mini-stroke"): A clinical diagnosis that refers to a brief episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, with clinical symptoms, and without imaging evidence of infarction (Easton, 2009; Sacco et al., 2013). TIA and minor acute ischemic stroke fall along a continuum. TIA symptoms fully resolve within 24 hours and usually within one hour. If any symptoms persist beyond 24 hours, this is considered a stroke, although this continuum cannot be differentiated by symptom duration alone. A TIA is significant as it can be a warning of a future stroke event. Patients and healthcare professionals should respond to an acute TIA as a medical emergency.

Minor non-disabling ischemic stroke (sometimes referred to as mild or non-disabling stroke): A brain, spinal, or retinal infarct that is typically small and associated with a mild severity of clinical deficits or disability. It may not require hospitalization. Practically speaking, deficits that if unchanged, would not impair the patient's ability to perform their ADLS, work and/or walk independently (based on PRISMS trial, 2018).

Note: For practical purposes, assessment, diagnosis, and management of individuals presenting with symptoms of TIA or minor ischemic stroke should follow similar processes as those throughout this module. Differentiating between TIA and minor stroke is less relevant and condition management should be informed by clinical history, presentation, and diagnostic imaging. Evidence shows that at least 20% of individuals presenting with TIA will experience a subsequent and more involved stroke, highlighting the need for aggressive secondary prevention for this group (OSVASC, NEJM, 2016).

Cerebral venous thrombosis (CVT): Thrombosis of the veins in the brain, either the dural venous sinuses or the more upstream cortical or deep veins. CVT may be present with neurological deficits due to venous congestion (sometimes called venous infarction) or due to hemorrhage. In the mildest circumstance CVT will present with headache only and sometimes with retinal edema (papilledema) and associated visual changes. CVT is an uncommon cerebrovascular disorder, accounting for <1% of all stroke syndromes.

Cryptogenic stroke: Cryptogenic stroke is defined as a brain infarction not clearly attributable to a definite cardioembolism, large artery atherosclerosis, small artery disease, or other identifiable cause despite extensive investigation. This group accounts for 25 to 40% of all strokes (Saver, 2016; Yaghi et al., 2017).

Embolic stroke of undetermined source (ESUS): A subset of cryptogenic strokes that represent approximately 9 to 25% of ischemic strokes, that meet the following criteria (Tsivgoulis et al., 2019; Ntaios, JACC 2020):

- Acute brain infarct visualized on neuroimaging; not a subcortical lacune <1.5 cm.
- Absence of proximal atherosclerotic arterial stenosis >50%
- No atrial fibrillation or other major-risk cardioembolic source
- No other likely cause of stroke (e.g., dissection, arteritis, cancer)

Mobile stroke unit: A mobile stroke unit has both the medical expertise and imaging technology to evaluate and treat patients with suspected stroke rapidly and accurately. The most important benefit of the mobile stroke unit is rapid diagnosis of the stroke type, allowing hemorrhage to be ruled out and treatment with intravenous thrombolysis to be started quickly if appropriate. Generally, these patients are referred to a hospital with CT imaging and a stroke (or telestroke) program (Shuaib & Jeerakathil, CMAJ, 2016).

Timeframes:

- **Prehospital and emergency department stroke care:** The key interventions needed for the assessment, diagnosis, stabilization, and treatment in the first hours after stroke onset. This includes all prehospital and initial emergency care for TIA, ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and acute cerebral venous thrombosis. This stage involves rapid triaging of patients based on time of symptom onset, stroke acuity, and brain

imaging. Treatments may include acute intravenous thrombolysis or acute endovascular interventions for ischemic stroke, emergency neurosurgical procedures, and same-day TIA diagnostic and risk stratification evaluation.

The principal aim of this phase of care is to diagnose the stroke type, and to coordinate and execute an individualized treatment plan as quickly as possible.

Prehospital and emergency department care is time-sensitive by nature: minutes for disabling stroke and hours for TIA. In addition, specific interventions are associated with their own individual treatment windows. Generally, this "hyperacute" time-sensitive window refers to care offered in the first 24 hours after an acute stroke (ischemic and hemorrhagic) or TIA.

- **Acute stroke care:** The key interventions involved in the assessment, treatment or management, and early recovery in the first days to weeks after stroke onset. This encompasses all of the initial diagnostic procedures undertaken to identify the nature and mechanism of the stroke, interdisciplinary care to prevent complications and promote early recovery, institution of an individualized secondary prevention plan, and engagement with the person with stroke and their family to assess and plan for transition to the next level of care, which includes a comprehensive assessment of the person's rehabilitation needs. New models of acute ambulatory care such as rapid assessment TIA and minor stroke clinics or day-units are also starting to emerge.

  The principal aims of this phase of care are to identify the nature and mechanism of stroke, prevent further stroke complications, promote early recovery, and, in the case of the most severe strokes, provide palliation and end-of-life care.

  Generally, "acute care" refers to the first days to weeks of inpatient treatment. The person with stroke then transitions from acute care to inpatient or community-based rehabilitation; home, with or without support services; continuing care; or palliative care. This acute phase of care is usually considered to have ended either at the time of discharge from the acute stroke unit or 30 days after hospital admission.

Hemorrhagic stroke: A stroke caused by the rupture of a blood vessel within the brain tissue, subarachnoid space or intraventricular space.

Intracranial hemorrhage includes bleeding within the cranial vault and encompasses intraventricular, intraparenchymal, subarachnoid, subdural and epidural hemorrhage.

Spontaneous, nontraumatic intracerebral hemorrhage is bleeding within the brain parenchyma without obvious systemic, neoplastic, traumatic, or macrovascular etiology. This stroke subtype accounts for about 10-15% of all strokes and a disproportionately higher number of stroke related deaths. ICH are often categorized according to their location within the brain: lobar, deep, cerebellar, and brainstem.

Hemorrhagic infarct: Hemorrhagic infarct is defined as a hemorrhagic transformation into an area of arterial ischemic infarction or venous thrombosis associated tissue congestion.

Notable Updates to the Acute Stroke Management Module, 7th Edition, 2022

With each update of the *Canadian Stroke Best Practice* modules, the most current evidence on the included topics is reviewed by the writing group members and internal and external reviewers. Recommendations from the previous edition may be continued unchanged, modified to reflect updated evidence (either wording or evidence levels), or removed. New recommendations may be added to address emerging evidence and practice changes.

The following are the most notable areas that have been added or significantly revised in this 7th edition

of the CSBPR *Acute Stroke Management* module.

- **Sex and gender considerations**: Specific attention has been given to potential differences in care and outcomes of acute stroke based on sex and gender. We are mindful that sex (a collection of biological attributes) and gender (a psycho-social construct related to our identity), may affect stroke care and outcomes differently; however, it is recognized that gender is not binary and that the literature, until recent years, used the terms gender and sex interchangeably in publications, and there are few current studies that differentiate between sex and gender. The terms “men” and “women” are used throughout the guideline to refer to people of male and female sex, with an appreciation that the gender constructs may have additional impacts and that this is an area requiring further research and reporting requirements.
- **Evidence rating scale:** Changed from the previous scale of A, B, C to the scale applied within the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology.
- **Imaging:** All recommendations related to imaging in the early phase of acute stroke have been consolidated into Section 4.
- **Addition of tenecteplase**: Based on new clinical trial evidence released in 2022, new recommendations for the use of tenecteplase (TNK) as an alternative to alteplase for acute intravenous thrombolysis has been added to Section 5.
- **Symptomatic intracranial hemorrhage** (sICH): New recommendations have been included in Section 5 on management of sICH following administration of intravenous thrombolysis.
- **Pre- and post- endovascular thrombectomy care**: New clinical practice guidance has been included in Section 5, Box 5D on the care of people undergoing EVT, pre and post procedure.
- **Combined intravenous thrombolysis and EVT**: A new clinical consideration has been added to Section 5 to address recent trials regarding combined therapy versus EVT alone, reflecting the current uncertainty in the evidence.
- **Dual antiplatelet therapy**: New recommendations have been added to Section 6 regarding the use of dual antiplatelet therapy (DAPT) in people who have experienced an acute ischemic stroke. These new recommendations are aligned with recommendations in the CSBPR *Secondary Prevention of Stroke* module, 2020.
- **Medical Assistance in Dying (MAiD)**: New statements have been added to Section 11 regarding discussions about MAiD with appropriate patients and family members.
- **Virtual care**: New and updated recommendations for virtual stroke care in the emergency department and inpatient care have been added to Sections 4, 5, and 9 to reflect the sustainable integration of this modality into daily care for people with stroke.
- **Mobile stroke units**: A clinical consideration has been added to Section 3 on the use of mobile stroke units.

NEW FOR 2025

Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025

- Recommendations have been updated to address emerging evidence related to posterior circulation stroke, stroke with large core, and stroke with medium vessel occlusion (MeVO). *These changes include: updating section 5.4 and removal of boxes: 4B,4C, 5C.*

Guideline Development Methodology

The CSBPR present high-quality, evidence-based stroke care guidelines in a standardized framework. As healthcare providers across all disciplines implement these recommendations, it is expected that practice variations will be reduced and gaps between evidence and practice will start to close, leading to improved outcomes for people with stroke.

The methodology used to develop this module followed a thorough and rigorous process. *Refer to CSBPR Overview of Methodology for additional detail.*

1. Establish an expert interprofessional writing group representing relevant disciplines across the continuum of care and a range of settings and striving for balance regarding gender and diversity. *Refer to Appendix 1 for a list of writing group members and affiliations.*
2. Consult with the acute stroke management Community Consultation and Review Panels, comprising people with stroke, informal caregivers, and family members.
3. Select clinical questions to address in the module using the population/problem, intervention or exposure, comparison, and outcome (PICO) format, where appropriate and applicable.
4. Conduct a systematic search and appraisal of research literature to January 2022, and update evidence summary. Refer to the assigning evidence levels section of this module for more information on the GRADE approach.
5. Conduct a systematic search and appraisal of external reference guideline recommendations.
6. Writing group and community consultation panels review and revise existing recommendations, develop new recommendations, address clinical questions, and adhere to the elements of the Agree 2 criteria where appropriate (Agree Trust). This includes rating the quality of evidence and the strength of the recommendations.
7. Review of the proposed module by the Canadian Stroke Best Practices Advisory Committee, and incorporation of edits as required.
8. Review of the proposed module by external leading experts in Canada and internationally, and incorporation of edits as required.
9. Update educational materials and implementation resources.
10. Obtain final approval and endorsement and undertake French translation.
11. Disseminate through publication and public release knowledge translation activities.
12. Continue with ongoing review and update process.

More detail for each of these steps is available in the CSBPR *Overview, Methods and Knowledge Translation* manual on the Canadian Stroke Best Practices website.

NEW for 2025: Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025

Interim analyses are undertaken when new evidence emerges for a topic covered within the module that has a direct impact on current practice and warrants an immediate shift in the recommendations ahead of the prescheduled full module update.

For the interim analysis, the chairs and expert advisors of the acute stroke management scientific writing group were convened, and a structured literature review was conducted (to April 2025). The evidence was synthesized, and draft recommendations were developed. These underwent review by a broader set of collaborators and final wording was confirmed through consensus.

For more information related to the Rapid Review process used for Interim update, please see the CSBPR *Overview, Methods and Knowledge Translation* manual on the Canadian Stroke Best Practices website.

Assigning evidence levels

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology and terminology has been applied throughout these guidelines. With GRADE, each recommendation was assessed for:

1. The **strength of the guidance** (strong or conditional), based on the balance of desirable and undesirable consequences, quality of evidence, values and preferences of those affected, and resource use.
    - A strong recommendation is one for which the guideline panel is confident that the desirable effects of an intervention outweigh its undesirable effects.
    - A conditional recommendation is one for which the guideline panel finds that the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists.

    and
2. The **quality of the evidence** (high, moderate, low) upon which the recommendations are formulated: risk of bias, directness of evidence, consistency and precision of results, risk of publication bias, magnitude of the effect, dose-response gradient, and influence of residual plausible confounding (Schünemann et al., 2013).

The writing group was provided with comprehensive evidence tables that included summaries of high-quality evidence identified through the structured literature searches. The group discussed and debated the quality of the evidence and through consensus developed a final set of proposed recommendations. Each recommendation was assigned a rating as to the strength of the recommendation and the quality of the evidence. Where appropriate and feasible, full GRADE review and analysis using relevant GRADE tables has been conducted (GRADE Handbook)

Clinical considerations

The CSBPR uses the additional category of clinical considerations, consisting of expert opinion statements. These are included when it is determined that guidance related to common clinical issues would be helpful, but the topic lacked sufficient evidence to form an actual recommendation.

Conflicts of Interest

All potential participants in the recommendation development and review process are required to complete confidentiality agreements and declare all actual and potential conflicts of interest prior to participation. Declared conflicts of interest are reviewed by the co-chairs of the CSBPR Advisory Committee and Heart & Stroke staff to assess the potential impact. Those with significant conflicts with respect to the module topic are not selected for writing group or reviewer roles.

Participants who have conflicts for a particular topic area are identified at the beginning of discussions for that topic and are recused from voting. If a co-chair is in conflict, they are recused from their responsibilities for that discussion and another non-conflicted participant assumes the role for that discussion and vote. Heart & Stroke senior staff members participate in all writing group discussions and intervene if they perceive an untoward bias by a writing group member.

Conflict of interest declarations for the Acute Stroke Management module writing group members can be found in Appendix 1.

Acknowledgements

Heart & Stroke gratefully acknowledges the Acute Stroke Management writing group leaders and members, all of whom have volunteered their time and expertise to the update of these recommendations. Members of the Canadian Stroke Consortium were involved in all aspects of the development of these recommendations. The recommendations underwent external review by: Philip A Barber, Treena Bilous, Renee Denise Cashin, Luciana Catanese, Seemant Chaturvedi, Michael Chow, Adam A. Dmytriw, Ian Drennan, Claire Dyason, Barb Field, Romayne Gallagher Peter A. Gooderham,

M. Shazam Hussain, Ebru Kaya, Katie Lin, Gordon McDonald, Stefan Pagliuso, Trudy Robertson, Julie Savoie, Joanna Schaafsma, Brenda Semenko, Ravinder Jeet Singh, Sean William Taylor, Aleksander Tkatch, Jenny P. Tsai, Gregory Brett Walker and Hope Weisenberg. We thank the Canadian Stroke Best Practices and Quality Advisory Committee members: Eric E. Smith (Co-Chair), Anita Mountain (Co-Chair), Aline Bourgoin, Gord Gubitz, Dar Dowlatshahi, Dylan Blacquiere, Margie Burns, Louise Clement, Thalia Field, Farrell Leibovitch, Christine Papoushek, Jeffrey Habert, Joyce Fung, Michael D Hill, Eddy Lang, Pascale Lavoie, Beth Linkewich, Colleen O'Connell, Jai Shankar, Debbie Timpson, Theodore Wein, and Katie White. The performance measures were reviewed and updated by the Heart & Stroke health systems quality council including Amy Yu (Chair), Michael Hill, Aravind Ganesh, Sacha Arsenault, Christine Hawkes, Jessalyn Holodinsky, Raed Joundi, Laura Gioia, Noreen Kamal, Shannon MacDonald, Katharine Mckeen, Kathryn Yearwood, Leigh Botly, and Laura Holder.

We acknowledge and thank Norine Foley and the evidence analysis team at workHORSE; Shelley Sharp and Trish Helm-Neima for the review of Acute Stroke Management Performance Measures; Adrian Salonga for writing group participation and contributions, Laurie Charest of Heart & Stroke for her coordination of the CSBPR teams and processes; and Francine Forget Marin and the Heart & Stroke internal teams who contributed to the development and publication of these recommendations (Translation, Communications, Knowledge Translation, Engagement, Health Policy, and Digital Solutions).

Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025

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Community Consultation and Review Panel

Heart & Stroke is especially grateful to the members of the Community Consultation and Review Panel who reviewed this module and shared their personal experiences and insights on what made or could have made their journey easier. CCRP members included: Ashley Voth, Sarah Blanchard-Eng, Allan Morrison, Patricia Pollock, Heather Purvis, Donna Sharman, Andy Sharman, and Louise Nichol.

Funding

The development of the CSBPR is funded by Heart & Stroke. No funds for the development of these recommendations come from commercial interests, including pharmaceutical and device companies. Writing group members and external reviewers are volunteers who do not receive any remuneration for their participation. All participants complete a conflict of interest declaration prior to participating.

Citing the Acute Stroke Management Module 7th Edition, Update 2022

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Schlamp, Donatella Tampieri, Brian van Adel, David Volders, Ruth Whelan, Samuel Yip, Norine Foley, Eric E. Smith, Dar Dowlatshahi, Anita Mountain, Michael D Hill, Chelsy Martin, and Michel Shamy (Co-Chair, Senior Author).

on Behalf of the Canadian Stroke Best Practice Recommendations Advisory Committee, in collaboration with the Canadian Stroke Consortium. *Canadian Stroke Best Practice Recommendations: Acute Stroke Management, 7th Edition, 2022;* Toronto, Ontario, Canada: Heart and Stroke Foundation. In M. Patrice Lindsay, Anita Mountain, Rebecca Lund, Chelsy Martin, Gord Gubitz, Amy Yu, Dar Dowlatshahi, and Eric E. Smith (Editors), on behalf of the Canadian Stroke Best Practices and Advisory Committee in collaboration with the Canadian Stroke Consortium. *Canadian Stroke Best Practice Recommendations, 7th edition, 2022*; Toronto, Ontario, Canada: Heart and Stroke Foundation of Canada.

The recommendations in this module are also published in the Canadian Journal of Neurological Sciences.

Heran, M., Lindsay, P., Gubitz, G., Yu, A., Ganesh, A., Lund, R., . . . Shamy, M. (2022). Canadian Stroke Best Practice Recommendations: Acute Stroke Management, 7th Edition Practice Guidelines Update, 2022. Canadian Journal of Neurological Sciences / Journal Canadien Des Sciences Neurologiques, 1-94. doi:10.1017/cjn.2022.344

English link: https://www.cambridge.org/core/journals/canadian-journal-of-neurological-sciences/article/abs/canadian-stroke-best-practice-recommendations-acute-stroke-management-7th-edition-practice-guidelines-update-2022/ADE40445915FC8DB1D0C72F9954386D8

French link: https://www.cambridge.org/core/journals/canadian-journal-of-neurological-sciences/article/abs/canadian-stroke-best-practice-recommendations-acute-stroke-management-7th-edition-practice-guidelines-update-2022/ADE40445915FC8DB1D0C72F9954386D8

Citing the Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025 (Section 5.4)

Manraj KS Heran (Co-Chair), David Volders, M. Patrice Lindsay (Senior Editor and co-writer), Michael D Hill, Dylan Blacquiere (Advisory Co-Chair), Gord Gubitz, Norine Foley, Rebecca Lund, Anita Mountain (Advisory Co-Chair), and Michel Shamy (Co-Chair),
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Canadian Stroke Best Practice Recommendations Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025; Toronto, Ontario, Canada: Heart and Stroke Foundation.

The recommendations in this Interim Update are also published in the Canadian Journal of Neurological Sciences:

Heran MK, Volders D, Lindsay MP, et al. Canadian Stroke Best Practice Recommendations: Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025. *Canadian Journal of Neurological Sciences / Journal Canadien des Sciences Neurologiques*. Published online 2025:1-17. doi:10.1017/cjn.2025.10444

Link: https://www.cambridge.org/core/journals/canadian-journal-of-neurological-sciences/article/abs/canadian-stroke-best-practice-recommendations-endovascular-thrombectomy-for-acute-ischemic-stroke-interim-update-2025/BDD528F39C8BC04CAE534737A270DF35

Comments

The Heart and Stroke Foundation of Canada's stroke team invites your comments, suggestions, and inquiries about the development and application of the CSBPR at strokebestpractices@heartandstroke.ca.

ACUTE STROKE MANAGEMENT RECOMMENDATIONS 2022

Part 1 Prehospital and Emergency Department Stroke Care Recommendations

Section 1 Stroke Awareness, Recognition, and Response

1. Stroke Awareness, Recognition, and Response Recommendations 2022

i. Organized and integrated stroke systems of care should be established and sustained in every health region in Canada to enable rapid emergency stroke management, including a public awareness campaign, public emergency system (such as 9-1-1), and monitoring systems that consider equity, age, sex, and gender diverse populations [Strong recommendation; Moderate quality of evidence].

ii. All members of the public and all healthcare providers should be educated that stroke is a medical emergency [Strong recommendation; Low quality of evidence].

   a. Education for the public and healthcare providers should include information that stroke can affect persons of any age including newborns, children, and adults. [Strong recommendation; Low quality of evidence].

   b. Education for the public and healthcare providers should emphasize the benefits of early emergency treatment [Strong recommendation; Moderate quality of evidence].

iii. Awareness campaigns and education for the public and healthcare providers should emphasize recognition of the signs and symptoms of stroke, including the use of an acronym such as FAST (Face, Arms, Speech, Time) to facilitate awareness of and easy recall of these signs [Strong recommendation; Moderate quality of evidence]. *Refer to Box 1A for additional information.*

   a. The public and healthcare providers should ***respond immediately*** when witnessing someone experiencing signs or symptoms of stroke by calling 9-1-1 or their local emergency number [Strong recommendation; Moderate quality of evidence], even if the signs or symptoms resolve. *Refer to Box 1B for additional information on discussions with emergency medical services (EMS) dispatch.*

   b. The public should be aware of the importance of following instructions from the EMS dispatch centre [Strong recommendation; Low quality of evidence]. *Refer to Section 3 Emergency Medical Services Management of Acute Stroke for additional information.*

Box 1A FAST Signs of Stroke

Heart & Stroke, www.heartandstroke.ca/fast

Box 1B Core Information Generally Required by Emergency Medical Services Dispatch, Paramedics, and Receiving Healthcare Facility

1. Stroke symptom onset time if witnessed, and last known well time if not witnessed
2. Total symptom duration at anticipated arrival in the emergency department
3. Presenting signs of stroke and stroke severity score, based on standardized screening tools
4. Current condition of the patient having a stroke, including previous functional status and independence level, and changes in their condition since stroke symptom onset
5. Current medications (e.g., anticoagulants) if known
6. Advance care plans, if any
7. Expected time of arrival at the receiving hospital
8. Additional health problems, if known

Refer to Section 3 Emergency Medical Services Management of Acute Stroke for additional information.

Rationale

When it comes to stroke, *time is brain!* On average, two million neurons die with every minute that elapses following symptom onset, leading to permanent damage to the brain (Saver JL. Stroke. 2006 Jan;37(1):263-6). Although stroke is a medical emergency, many people do not recognize it as such, or they attribute the signs and symptoms to a less serious health issue and delay seeking medical attention. It is critical that anyone with signs of stroke arrive at the emergency department as soon as possible, as earlier assessment and treatment may allow time for disability-limiting or life-saving interventions. People who experience a transient ischemic attack (TIA) are also considered a medical emergency and require rapid assessment and treatment; therefore, enhancing the emergency medical system response to improve public awareness of stroke signs and symptoms and need to contact EMS should be encouraged. These recommendations apply across all geographic regions in Canada, and

education should be available uniformly, with targeted approaches for diverse populations and regardless of local issues related to time to access care.

People with lived experience emphasized the importance of recognizing stroke signs and symptoms in order to get the care that is needed. They highlighted the importance of ongoing research, particularly for women and for all age groups; and how ongoing education about stroke signs and symptoms for youth and adults and healthcare providers is critical to support access to appropriate care. Stroke can happen at any age, and the public and healthcare providers need to be able to recognize all signs of stroke in anyone, regardless of age.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Government funding and support for awareness initiatives to improve the recognition and recall of the signs of stroke (e.g., FAST, which is a global best practice) and the importance of contacting 9-1-1 immediately. Awareness and education campaigns should prioritize reaching communities who are less aware of the signs of stroke and most at risk of stroke and should be informed collaboratively through community engagement activities with those audiences.
2. Enhanced collaboration among community organizations and healthcare professionals to ensure consistency in public education of the signs of stroke with a strong emphasis on the urgency of responding when the signs of stroke are recognized.
3. Training and education for EMS, emergency department and all in-hospital staff, medical and nursing students, physicians in primary and acute care as well as specialists, nurses, and allied health professionals to increase their ability to recognize potential patients with stroke and provide rapid assessment and management.
4. Comprehensive systems in place to ensure all people in Canada have access to timely and appropriate emergency medical services, including ambulatory services (e.g., outpatient services, emergency department, community health centres, nursing stations) without financial burden, and quality stroke care regardless of geographic location.
5. Enhanced monitoring and awareness of stroke among all people in Canada. Healthcare systems and provincial/territorial and federal governments should generate linked health and social surveillance population-based and regional data and use it to drive quality improvement through better understanding of the health and social issues facing people in Canada.

Performance Measures

System Indicators:

1. Proportion of people with suspected stroke or TIA transported to hospital by paramedics (core).
2. Proportion of the population who live within 4.5 and 6 hours by ground transportation of a Stroke services Level 3, 4, or 5 stroke-enabled hospital (e.g., has CT scanner on-site and ability to deliver intravenous thrombolysis).
3. Proportion of hospitals that pre-register patients or have workflows to bypass the ED.

Process Indicators:

4. Proportion of patients with stroke who contact any member of the healthcare system within 4.5, 6, and 24 hours of stroke symptom onset (core).
5. Median (and interquartile range) time lapse between stroke symptom onset and first contact with EMS, defined as time call placed to 9-1-1 or local emergency medical system dispatch.

6. Median time (hours) from stroke symptom onset to arrival at an emergency department for all suspected patients with stroke presenting to hospital.

Patient Oriented Outcomes and Experience Indicators:

7. Proportion of the population (and specific population subgroups) aware of the signs of stroke as presented in FAST/VITE (core).

Refer to Section 3 for additional performance measures related to prehospital care and transport.

Measurement Notes

a. Performance measure 6: Data may be obtained from specific public polling on the signs of stroke, by the Heart and Stroke Foundation, and other organizations.
b. Performance measures 1 to 5: Denominator is patients with stroke who are treated in hospital. Data may be obtained from the Canadian Institute for Health Information (CIHI) NACRS and DAD databases and Stroke Special Project 340 and/or from primary chart audit.
c. Performance measure 3: Emergency department triage time should always be used as the proxy time for emergency department arrival. This is available in CIHI NACRS, and a calculated value in the DAD. The three time windows reflect the treatment times in this 7th edition (2022) of the Acute Stroke Management recommendations.
d. Performance measures 3 – 5: Time of stroke symptom onset may be known if the patient was awake and conscious at the time of onset, or it may be unknown if symptoms were present on awakening. It is important to record whether the time of onset is estimated or exact. The time qualifies as exact provided that (1) the patient is competent and definitely noted the time of symptom onset or (2) the onset was observed by another person who took note of the time.
e. Performance measure 3: These data may be obtained by performing geo-spatial analysis based on location of ambulance base stations, location of hospitals with hyperacute stroke services, and road geography for a specified region.
f. Hospitals should make all effort to still report the time of patient arrival as the ED triage time in CIHI NACRS. This will help stroke directors or administrative push the hospitals to do this.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices team or Heart & Stroke. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke and https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- World Stroke Organization: http://www.world-stroke.org/
- Stroke Engine: http://strokengine.ca/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke
- Heart & Stroke: What is Stroke? https://www.heartandstroke.ca/stroke/what-is-stroke

- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-strokebest-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: A Family Guide to Pediatric Stroke: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/a-family-guide-to-pediatric-stroke-en.ashx?rev=ff206495b5a4479da4b1a1d7b54c7734
- Heart & Stroke: Stroke in Young Adults: A Resource for Patients and Families: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/stroke_young_final.ashx?rev=7338abd3dba746dc96180a057e244ce9
- Heart & Stroke: Transient Ischemic Attack: https://www.heartandstroke.ca/stroke/what-is-stroke/types-of-stroke/tia?_ga=2.260911109.98775338.1657032029-2092542146.1608572095
- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

Failure to recognize the signs of an acute stroke, by witnesses or the person experiencing the stroke, can delay the time to contact emergency services, which may in turn decrease a patient's opportunity to receive time-sensitive treatments.

The results from many cross-sectional surveys indicate that, among members of the general public, knowledge of the signs and symptoms associated with stroke remains disappointingly low. Lundelin et al. (2012) conducted telephone surveys of 11,827 adults living in Spain who had participated in the Study on Nutrition & Cardiovascular Risk, to assess their ability to identify stroke symptoms, including sudden confusion or trouble speaking; numbness of face, arm, or leg; sudden trouble seeing in one or both eyes; sudden chest pain (decoy); sudden trouble walking; dizziness or loss of balance; or severe headache. While 65.2% of the participants could correctly identify four to six symptoms of stroke, only 19% could identify all 6 symptoms correctly, and 11.4% were unable to identify a single symptom. In addition, 81.1% of participants indicated they would call an ambulance if they suspected someone was having a stroke. Persons who could identify more stroke symptoms were more likely to call for an ambulance. Mochari-Greenberger et al. (2014) surveyed 1,205 women aged ≥25 years living in the United States who had participated in the American Heart Association National Women's Tracking Survey. Participants were contacted by telephone and asked standardized questions related to stroke warning signs and actions to take in the event of stroke. Sudden weakness and/or numbness of the face or limb of one side was the most commonly cited symptom (51%). Loss of or trouble understanding speech was also frequently recognized as a symptom (44%); while headache, unexplained dizziness, and loss of vision in one eye were recognized by fewer participants (23%, 20% and 18%, respectively). One in 5 women could not name a stroke warning sign.

In a survey of 790 respondents who were friends and family members of patients at a Canadian vascular outpatient clinic waiting room, who were sampled on two occasions 5 years apart, over 80% of participants were able to identify one or more stroke risk factors (Metias et al., 2017). Trouble speaking and weakness, numbness, or paralysis were the signs identified most frequently. The results of surveys conducted by random sampling of members of the general community in Saudi Arabia (Naguib et al., 2020) and New Zealand (Krishnamurthi et al., 2020) also indicate that most people were familiar with at least one stroke risk factor and almost 80% recognized slurred speech and weakness as stroke symptoms.

When surveyed even after they had suffered a stroke, many patients remained unaware of stroke risk factors, including their own. Of 173 patients admitted to a stroke unit following a first-ever stroke, only 21% of patients could identify hypertension as a risk factor. Smoking was recognized by 26.6% and obesity by 12% of patients (Faiz et al., 2018). Of 195 patients admitted to hospital following a confirmed stroke or TIA, a high percentage could not identify their own stroke risk factors (Soomann et al., 2015). Diabetes was the most recognized risk factor at 89%, while 78% and 77% of patients were aware of atrial fibrillation and previous stroke, respectively. Sundseth et al. (2014) reported that among 287 patients admitted to hospital with a suspected stroke or TIA, 43.2% were able to name at least one stroke risk factor, while 13.9% could identify two and 1.7% knew three. Smoking and hypertension were the two most commonly cited risk factors for stroke, while 70.7% of patients knew at least one symptom of stroke. In terms of their knowledge of the signs and symptoms of stroke, 66.6% identified numbness or weakness of the face, arm, or leg; 45.6% identified confusion or trouble speaking or understanding speech; and 42.9% were able to identify both of these symptoms of stroke.

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 most recognized programs is FAST, a mnemonic standing for (F)ace drooping, (A)rm weakness, (S)peech difficulties and (T)ime to call 911. The results of several studies indicate that persons exposed to these campaigns become more aware of the signs and symptoms of stroke. Response to the FAST campaign, through television and public transit displays, which ran from 2009 intermittently though 2014 in the UK (Wolters et al., 2018) was associated with significantly increased use of EMS for major stroke (58.8% before April 1, 2009 vs. 78.9% after April 1, 2009) and first medical attention was sought more quickly (within 3 hours) after April 1, 2009 (67.6% vs. 81.3%; OR=2.08; 95% CI, 1.40-3.11). The effect of a 27-month public awareness campaign designed to increase knowledge of the Swedish translation of FAST was less successful (Nordanstig et al., 2017). From pre-campaign (survey 1) to end of the campaign (survey 8), the number of persons who had heard of FAST increased from 15% to 50%. The percentage of respondents who could recall all keywords in the mnemonic increased from 0.3% to only 2%, while those who could recall some or all of the keywords increased from 4% to 14%.

Bray et al. (2013) surveyed 12,439 people ≥40 years of age from the general population in Australia and reported that from 2004 to 2010, there had been a significant increase in the number of respondents who were aware of the national multimedia stroke awareness campaigns (31% vs 50%), which included FAST. There was also an increase in the number or participants who were able to name one or more warning signs of stroke (69% vs 81%), two or more (43% vs 63%), and three or more (19% vs 32%). Respondents who could identify two or more warning signs were significantly more likely to be aware of the campaign (OR= 1.88, 95% CI 1.74 to 2.04). Bray et al. (2015) also reported increases in the monthly volumes of ambulance dispatches for stroke associated with 12 National Stroke Foundation multimedia regional public awareness campaigns that ran from 2004 to 2014. The increases ranged from 1.0% to 9.9%. In 2006, there was a decrease of 2.2% in call volumes.

Jurkowski et al. (2010) also reported that following a public awareness campaign to increase awareness of FAST, respondents who were exposed to a three-phase multimedia campaign over a seven-month period were more likely to be aware of the campaign and its primary message to call 9-1-1. The percentage of respondents who reported they would call 9-1-1 in response to specific stroke symptoms increased from 9% to 12% for specific symptoms identified in oneself and 4% to 12% for specific symptoms, from pre-to post campaign, compared to those who had not been exposed to the campaign.

Mass media campaigns have also been shown to be associated with increases in the use of thrombolytic agents following acute stroke. Advani et al. (2016) reported the average number of

patients treated with t-PA increased significantly from 7.3 to 11.3 patients per month (an increase of 54.7%, p=0.02) during the period from the 12 months preceding the mass media intervention, featuring the FAST mnemonic, to the 6 months after. The average number of patients treated in the emergency department increased significantly from 37.3 to 72.8 patients per month (an increase of 95.7%, p<0.001) during the same period. Although the mean number of patients treated with t-PA dropped to 9.5 per month after the first 6 months of the campaign, it was still significantly higher than the preceding 12 months. In a telephone survey of 1,400 participants, the number of people who could name any stroke symptom increased from 66% to 75%. Of those who could name a symptom, 52% recognized facial droop, 42% named speech difficulties, and 42% named arm weakness.

Sex and Gender Considerations

Women have been reported to have better knowledge of stroke symptoms and stroke risk factors and learn more from public stroke awareness campaigns (Stroebele et al. 2011). Marx et al. (2010) reported that prior to a mass media campaign designed to improve stroke recognition and response, significantly more women than men could correctly answer the question “where does stroke happen in the body?” and knew the stroke emergency call number to call. Following the intervention, while the number of men and women who could answer the two questions correctly increased, although the percentage change from pre to post intervention was higher for women. There were increases in the mean number of stroke warning signs that could be named before and after the intervention (women: 5.4 to 6.2; men: 5.1 to 5.9). Following a public health campaign conducted in Ontario, significantly more women could identify ≥2 stroke warning signs (Hodgson et al. 2007).

Reference List and Evidence Tables

Evidence Table and Reference List 1: Stroke Awareness, Recognition and Response

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 2 Triage and Initial Diagnostic Evaluation of Transient Ischemic Attack and Non-Disabling Stroke

2. Triage and Initial Diagnostic Evaluation of Transient Ischemic Attack and Non-Disabling Stroke Recommendations 2022

Notes

- *Section 2 recommendations pertain to the initial management of patients with a suspected acute transient ischemic attack (TIA) or acute ischemic stroke **who are not candidates** for acute thrombolysis or endovascular intervention. For patients with suspected acute stroke that warrant hyperacute assessment to determine eligibility for intravenous thrombolysis and endovascular thrombectomy (EVT), refer to the current CSBPR Acute Stroke Management treatment recommendations, Sections 4 and 5.*
- *Some people experiencing acute stroke signs or symptoms may present to an outpatient setting such as a primary care physician or family health team office, community clinic, or urgent care centre. Processes should be in place to transport to emergency departments when indicated.*
- *The timing of symptom onset in patients who present to any healthcare facility with a suspected acute stroke or TIA should be carefully assessed.*
- *Individuals experiencing signs or symptoms of acute stroke require rapid assessment, diagnosis, and determination of risk for a recurrent stroke. Patients diagnosed with TIA or minor ischemic stroke who are not candidates for acute stroke treatment with intravenous thrombolysis or endovascular intervention may be prioritized for secondary prevention of stroke assessment and management.*
- *Ischemic stroke is a heterogenous condition with many different subtypes and causes, and it is beyond the scope of this guideline to address all of them. Section 2 focuses on the diagnostic studies that are relevant to the identification of common conditions (e.g., atherosclerosis, atrial fibrillation) or uncommon conditions requiring immediate treatment (e.g., bacterial endocarditis).*
- *Patients who present with onset of symptoms within 4.5 hours, regardless of whether the symptoms have resolved or not, should be sent for emergent assessment. Refer to Sections 3 and Section 4 for additional information.*
- *Patients with onset of symptoms within 4.5 to 48 hours, regardless of whether the symptoms have resolved or not, should be referred for urgent assessment. Refer to Section 2.0 and 2.1 for additional information.*

2.0

i. Patients with acute stroke or TIA who present to an outpatient setting (such as primary care) or to a hospital should undergo clinical evaluation by a healthcare professional with stroke expertise to determine the patient's risk for recurrent stroke and initiate appropriate and timely investigations and management strategies [Strong recommendation; Moderate quality of evidence].

ii. Shared decision-making should take into account patient values, preferences, health goals, medical complexity, social determinants of health, health literacy and health needs [Strong recommendation; Low quality of evidence].

2.1 HIGH Risk for Recurrent Stroke (Symptom Onset Within Last 48 Hours)

i. Individuals presenting within 48 hours of symptoms consistent with a new acute stroke or TIA (especially transient focal motor or speech symptoms, or persistent stroke symptoms) are ***at the highest risk for recurrent stroke*** and should be immediately sent to an emergency department (refer to Clinical Consideration 2.1.3) with a capacity for stroke care, which

includes on-site brain imaging and ideally access to acute stroke treatments [Strong recommendation; Moderate quality of evidence].

ii. Urgent brain imaging (computerized tomography [CT] or magnetic resonance imaging [MRI]) with concurrent neurovascular imaging (e.g., CT angiography [CTA] or MR angiography [MRA]) should be completed as soon as possible and before discharge from the emergency department [Strong recommendation; Moderate quality of evidence].

iii. Patients presenting after 48 hours from the onset of an acute stroke or TIA should receive a comprehensive clinical evaluation and investigations as soon as possible by a healthcare professional with stroke expertise [Strong recommendation; Low quality of evidence]. *Refer to Section 2.2 for more information on investigations.*

Section 2.1 Clinical Considerations

1. Referral to a healthcare professional with stroke expertise should be considered for patients with a suspected uncommon cause of stroke, including for young patients with stroke (e.g., <45 years of age)[a]; family history of young-onset stroke; suspected cerebral vasculitis or other intracranial arteriopathy/vasculopathy; or suspected hereditary or acquired thrombophilia.
2. Patients with symptoms of vertebrobasilar ischemia may present with fluctuating brainstem/cerebellar type symptoms (e.g., diplopia, dysarthria, dysphagia, non-positional vertigo, ataxia; rarely as isolated symptoms) over a longer time course (i.e., >48 hours) and can be mistaken for stroke mimics; however, these patients also require urgent assessment, neurovascular imaging, and management as these types of strokes can have a high morbidity. Consultation with a healthcare professional with stroke expertise is strongly encouraged.
3. **Setting**: In some regions, urgent/rapid TIA clinics are available that have rapid access to diagnostic services and specialist assessment and management. These clinics may be considered an appropriate referral option for patients with TIA and minor stroke.

2.2 Brain and Vascular Imaging

i. Brain imaging (CT or MRI) and non-invasive vascular imaging (CTA or MRA) from aortic arch to vertex should be completed as soon as possible following acute disabling or non-disabling stroke, or TIA [Strong recommendation; Moderate quality of evidence].

   a. CTA of the head and neck from aortic arch to vertex, performed at the time of initial brain CT is recommended as an ideal way to assess both extracranial and intracranial circulation [Strong recommendation; Moderate quality of evidence]. *Note: Some facilities may not have CTA readily available and so the timing and type of vascular imaging will need to be based on available resources and local practice protocols.*

   b. Neurovascular imaging is recommended to identify patients with significant symptomatic extracranial carotid artery stenosis (i.e., 50-99% stenosis), which should trigger an urgent referral for potential carotid revascularization [Strong recommendation; High quality of evidence].

   c. CTA is the first-line vascular imaging test for stroke or TIA patients. If CTA is not possible, MRA and carotid ultrasound for extracranial vascular imaging are reasonable alternatives as first-line tests for assessment of carotid vessels, and selection should be based on availability and patient characteristics [*Conditional recommendation*; Low quality of evidence].

[a] Kapoor et al, CJNS 2020

Section 2.2 Clinical Considerations

1. MRI brain scanning is superior to head CT in terms of diagnostic sensitivity for identifying small ischemic lesions in patients presenting clinically with a TIA or minor stroke and can provide additional information to guide decisions about diagnosis, prognosis, and treatment. Decisions about MRI scanning should be based on MRI access, availability, and timing of appointments. For maximal diagnostic yield, MRI should be completed as soon as possible after the symptomatic event, ideally within 7 days of symptom onset so that diffusion-weighted imaging can identify any potential restricted diffusion changes representing infarct. MRI is particularly useful in lower-risk patients with transient symptoms where the presence of ischemia would change their management.

2. Common scenarios where urgent brain MRI can be valuable include:
    a. Normal CT head despite symptoms persisting >24 hours. If diffusion-weighted imaging MRI is negative, cerebral ischemia is unlikely.
    b. Normal CT head where there is suspected brainstem or cerebellar ischemia (CT head is relatively insensitive for detecting strokes in the posterior fossa due to bone artifact).
    c. Focal transient symptoms that are clinically atypical for ischemia.

2.3 Blood Work

i. The following laboratory investigations should be routinely considered for patients with a TIA or minor ischemic stroke as part of the initial evaluation:
    a. **Initial blood work**: Hematology (complete blood count), electrolytes, coagulation (aPTT, INR), renal function (creatinine, estimated glomerular filtration rate), random glucose, ALT [Strong recommendation; Low quality of evidence]. *Refer to Table 2A for full list of recommended laboratory tests.*
    b. **Additional laboratory tests** may be completed during the patient encounter or as an outpatient, including a lipid profile (fasting or non-fasting); and screening for diabetes with either a glycated hemoglobin (HbA1c), fasting glucose or 75g oral glucose tolerance test [Strong recommendation; Low quality of evidence]. *Refer to Diabetes Canada Guidelines for additional information related to glucose testing.*
    c. **(NEW FOR 2022) Giant Cell Arteritis:** If giant cell arteritis is suspected (e.g., retinal ischemia or headache), ESR or CRP should be measured [Strong recommendation; Low quality of evidence].

ii. **(NEW FOR 2022)** Extensive thrombophilia testing for hereditary hypercoagulable disorders is not recommended for routine investigation of a patient with arterial ischemic stroke and should be limited to selected situations [Strong recommendation; Low quality of evidence].
    a. If a hypercoagulable state is suspected, consultation with a healthcare professional with hematology or thrombosis expertise should be considered [Strong recommendation; Low quality of evidence].

2.4 Cardiac Studies

2.4A Detection of Atrial Fibrillation

i. Patients with suspected ischemic stroke or TIA should have a 12-lead electrocardiogram (ECG) to assess for atrial fibrillation, concurrent myocardial infarction, or structural heart disease (e.g., left ventricular hypertrophy) as potential causes or risk factors of stroke [Strong recommendation; Moderate quality of evidence].

ii. For patients being investigated for an acute embolic ischemic stroke or TIA, ECG monitoring for 24 hours or more 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 [Strong recommendation; High quality of evidence].

iii. For patients being investigated for an 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, continuous ECG monitoring for at least 2 weeks is recommended to improve detection of paroxysmal atrial fibrillation in selected patients aged ≥55 years who are not already receiving anticoagulant therapy but who would be potential candidates for anticoagulant therapy [Strong recommendation; High quality of evidence]. *Refer to CSBPR Secondary Prevention of Stroke module Section 7 for additional guidance in management of patients with stroke and atrial fibrillation. Refer to the current Canadian Cardiovascular Society recommendations on atrial fibrillation.*

2.4B Echocardiography

iv. Routine echocardiography is not required for all patients with stroke [Strong recommendation; Low quality of evidence].

v. Echocardiography should be considered for patients with an embolic ischemic stroke or TIA of undetermined source or when a cardioembolic etiology or paradoxical embolism is suspected [Strong recommendation; Moderate quality of evidence].

vi. For patients ≤60 years who are being investigated for an embolic ischemic stroke or TIA of undetermined source, echocardiography with saline bubble study is recommended for detection of a patent foramen ovale (PFO) if it may change patient management (i.e., in patients who would be potential candidates for PFO closure or anticoagulant therapy if a PFO were detected) [Strong recommendation; Moderate quality of evidence].

a. Contrast-enhanced (agitated saline) transesophageal echocardiography or transcranial Doppler has greater sensitivity than transthoracic echocardiography for detection of right-to-left cardiac and extra-cardiac shunts and should be conducted when available [Strong recommendation; Moderate quality of evidence].

2.5 Functional Assessment

i. Patients with stroke should be assessed for neurological impairments and functional limitations (e.g., cognitive evaluation, screening for depression, screening for dysphagia, screening for aphasia, screening for fitness to drive, need for rehabilitation therapy, assistance with activities of daily living, functional mobility) [Strong recommendation; Moderate quality of evidence]. *Refer to Rehabilitation and Recovery Following Stroke module for additional information.*

ii. Patients with stroke found to have neurological impairments that could impact daily functioning should be referred to the appropriate rehabilitation specialist for in-depth assessment and management [Strong recommendation; Moderate quality of evidence].

2.6 (NEW FOR 2022) Virtual Care for Secondary Stroke Prevention

i. Secondary stroke prevention services should establish information technology infrastructure and protocols to increase and ensure access to virtual care delivery for patients who do not require in-person visits. Emphasis should be placed on considerations for those individuals who do not require in person visits such as, for patients living in rural and remote settings who do not have local access to healthcare professionals with stroke expertise [Strong recommendation; Low quality of evidence]. *Refer to CSBPR Virtual Stroke Care Implementation Toolkit for additional information.*

ii. Clinicians should follow established/validated criteria to determine the best form of visit for each patient at each encounter (i.e., virtual or in person) based on the purpose, goals, digital literacy, and availability for each visit [Strong recommendation; Low quality of evidence]. *Refer to Heart & Stroke Virtual Care Decision Framework for additional information and criteria.*

Section 2.6 Clinical Considerations

1. Consulting sites and individual clinicians should have triage protocols and local intake criteria to ensure patients referred to their services are seen in a timely manner, especially high-risk patients described in Section 2.1.
2. The use of virtual care for stroke prevention should include decision tools to identify patients who require in-person visits and those who can reasonably be managed through virtual care, and a scheduling mechanism for virtual visits that support a collaborative team approach to care where appropriate and feasible. *Refer to Heart & Stroke Virtual Care Decision Framework for additional guidance and criteria.*
3. A contingency plan should be established to quickly see patients in person should the need arise following a virtual care encounter. *Refer to CSBPR Virtual Stroke Care Implementation Toolkit for additional information.*
4. Virtual care-enabled evaluations of patients for secondary stroke prevention should be modeled on the topics defined in the post-stroke checklist and core elements of stroke prevention care. *Refer to CSBPR Post Stroke Checklist for additional information*
5. Validated approaches to virtual neurological exams should be followed.
6. Processes should be in place to book follow-up tests, referrals, and other consultations after a virtual care visit.
7. Processes to ensure appropriate documentation and communication to other team members who may be involved in remote care should be in place.
8. Patients and their families should be encouraged to acquire home blood pressure monitors where appropriate and education or reliable resources on proper use should be provided. Mechanisms should be in place for follow-up and management of blood pressure for patients using home blood pressure devices, by either primary care providers or a stroke prevention service.
9. For timely investigations, the use of prolonged cardiac monitors, if available, that can be sent to patient's homes, self-applied, and returned by mail, should be considered.

Rationale

The goal of outpatient management in the early period following discharge from the hospital or other healthcare setting is rapid assessment and management to reduce the risk of a recurrent, possibly more serious, stroke.

TIAs or minor strokes are unstable conditions that warn of a high risk of recurrent stroke, other vascular events, or death. The risk of recurrent stroke after a TIA has been reported to be 4.7% within 90 days (Shahjouei et al., 2021; JAMA Neurol. 2021;78(1):77-87), with the risk being "front-loaded": 3.8% of recurrent strokes occur in the two days following initial symptom onset. These percentages are an improvement from the 20% estimate reported previously and reinforce the importance and benefits of timely, aggressive management. The seven-day risk of stroke following a TIA can be as high as 36% in patients with multiple risk factors. Timely initiation of secondary prevention medical therapy and carotid revascularization has been shown to significantly reduce the risk of major stroke after an initial TIA or non-disabling stroke. A study by the TIARegistry.org group reported that the estimates of stroke at days 2, 7, 30, 90, and 365 from 2009 to 2011 were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively. These estimates were almost half of those compared with historical cohorts and were attributed to the widespread establishment of TIA clinics, providing faster access to secondary stroke prevention treatments (Amarenco et al., N Engl J Med 2016;374:1533-42). In Canada, a decreased trend in stroke

recurrence over 12 years, from 2003 to 2015, has been reported (Wang R et al., Can J Neurol Sci. 2021;48(3):335-343), a trend which is also attributed to improvements in early care.

There is growing implementation of virtual care modalities across healthcare, and they are particularly impactful for stroke care. Cost and time of travel can be a barrier to rural and remote residents trying to access distant specialty services, and often they decline referrals or fail to attend appointments due to travel time, cost, and adverse weather conditions, especially in winter.

People with lived experience and their families expressed the importance of early access to assessment and diagnosis to prevent a recurrent event. They emphasized the need to receive timely education about signs and symptoms of stroke, and clear explanations about the risk for recurrent stroke and the relevance of the time frames for those who are at different risk levels for recurrence events. The wait time from an initial TIA to further investigations can be stressful and patients would like this to be considered in management planning. People with lived experience also expressed concerns about potential biases for women seeking treatment and experiencing missed or delayed diagnosis, especially when they present with a TIA or with fluctuating symptoms, emphasizing the need for individualized assessment and management.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Well-established and accessible stroke prevention clinics or broader vascular prevention programs appropriately funded and available in all communities through traditional or technological/virtual means, and referral pathways and promotion of programs for healthcare practitioners to increase timely access.
2. Education for the public and healthcare providers (primary care, emergency services, acute care, specialty care) about the urgent need for assessment and management of TIA or non-disabling ischemic stroke, to reduce the risk of recurrent, potentially more serious events.
3. Availability of services and systems to refer patients and families to access services that support ongoing education about prevention and management of risk factors, along with additional resources and supports such as lists of self-management programs and education materials that are easily accessible and updated regularly.
4. Education and training for healthcare professionals who work in primary, secondary, and tertiary care settings, to enable the management of patients with transient ischemic attack or non-disabling ischemic stroke in a timely manner. Education should also include content about the heart-brain connection and need to approach care holistically, considering all vascular risk factors.
5. Processes, protocols, and infrastructure in place to enable rapid access to diagnostic tests and expertise for patients with TIA or minor stroke in community healthcare settings and acute healthcare facilities.
6. Universal access to necessary stroke prevention medicines like anti-hypertensives for management and secondary prevention. Provincial and national systems should develop an equitable pharmaceutical strategy to improve access to cost effective medicine for all people in Canada, regardless of geography or ability to pay.
7. Mechanisms to monitor, assess, and improve uptake, adherence to, and quality of stroke prevention programs to ensure patients can access effective services. Consideration should be given to community and individual barriers as well as motivators and enablers.

Virtual Care

1. Mitigation of challenges to virtual care delivery, including how health professions are regulated to deliver virtual care and cross-border barriers (interprovincial and cross-provincial/territorial).
2. Virtual care service models within stroke systems of care that improve the accessibility of secondary prevention services for patients in rural and remote locations, and for patients who have difficulty attending in-person appointments. Governments and organizations should consider ways to ensure that barriers to access and use are addressed and mitigated.
3. Mitigation of barriers to access, equity, and use of virtual care.
4. Data collection and quality improvement mechanisms to monitor efficiency, effectiveness, and quality of virtual care encounters.

Performance Measures

System Indicators:

1. Proportion of acute stroke and TIA patients who are discharged alive from an emergency department or an inpatient stay and then readmitted to hospital for any cause within 7 days and/or 14 days of index acute stroke discharge (core).

Process Indicators

2. Proportion of patients with TIA or non-disabling stroke who are investigated and discharged from the emergency department who are referred to organized secondary stroke prevention services at discharge (KQI).
3. Time from first encounter with medical care (primary care or emergency department) to assessment by a stroke expert (in clinic or other setting).
4. Time from first encounter with medical care to brain imaging (CT/MRI); and vascular imaging (Doppler of cervical arteries, CT or MRA).
5. Proportion of patients with motor and speech TIAs or minor stroke who have CT head and CTA (or other vascular imaging) completed within 24 hours of presentation.

Patient-oriented Outcome and Experience Indicators:

6. Proportion of people discharged with a minor stroke or TIA who are readmitted within 30 days (or 90 days) with a recurrent stroke or TIA.

Measurement Notes

a. Data access and quality with respect to timing of first encounter and referral dates and times.
b. Primary care data from physician billing. This should rely on International Classification of Diseases (ICD) codes and not on physician descriptions of diagnoses, as these may be less accurate.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices team or Heart & Stroke. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practice Recommendations Prehospital and Emergency Department Module Table 2A: Recommended Laboratory Investigations for Patients with Acute Stroke or Transient Ischemic Attack
- Canadian Stroke Best Practice Recommendations Acute Stroke Management Module Appendix 3: Table 3A of Standardized Acute Prehospital Stroke Screening Tools; Table 3B Additional Tools and Table 3C Prehospital Stroke Screening Scales to Identify Large Vessel Occlusion (LVO)
- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke 2020 CPR & EEC Guidelines: https://cpr.heartandstroke.ca/s/article/Guidelines?language=en_US&_ga=2.82009246.98775338.1657032029-2092542146.1608572095
- Heart & Stroke: Canadian Neurological Scale Training: https://www.youtube.com/watch?v=9fD8BEmuB8U
- Heart & Stroke: Virtual Stroke Care Implementation Toolkit: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/csbpr-virtual-stroke-toolkit-final
- Stroke Engine: Canadian Neurological Scale: https://strokengine.ca/en/assessments/canadian-neurological-scale-cns/
- Canadian Cardiovascular Society: Atrial Fibrillation Guidelines: https://ccs.ca/guidelines-and-position-statement-library/
- Thrombosis Canada: Clinical Guidelines: https://thrombosiscanada.ca/clinicalguides/
- Diabetes Canada: Clinical Practice Guidelines: http://guidelines.diabetes.ca/
- American College of Chest Physicians (ACCP) Pulmonary Vascular Guidelines: https://www.chestnet.org/Guidelines/Pulmonary-Vascular
- American College of Chest Physicians (ACCP) Anticoagulation Guidelines: https://www.chestnet.org/guidelines-and-topic-collections
- Virtual neurological exam examples:
    - Hussona MA, Maher M, Chan D, et al. The virtual neurologic exam: Instructional videos and guidance for the COVID-19 era. Can J Neurol Sci. 2020;47;598–603. DOI:10.1017/cjn.2020.96
    - American Academy of Neurology: https://www.aan.com/practice/telehealth#Education
- CorHealth: Secondary Stroke Prevention Resources: https://www.corhealthontario.ca/resources-for-healthcare-planners-&-providers/stroke-general/piwp/secondary-prevention/resources
- CorHealth: ED Assessment and Triage: https://www.corhealthontario.ca/resources-for-healthcare-planners-&-providers/evt/section2-ed-assessment-&-triage
- Canadian Association of Radiologists guidelines: https://car.ca/patient-care/practice-guidelines/
- Depression, Obstructive Sleep Apnea and Cognitive Impairment – DOC Screening Tool: http://www.docscreen.ca/about.html

- Recommendations of the 5th Canadian Consensus Conference on the diagnosis and treatment of dementia: https://alz-journals.onlinelibrary.wiley.com/doi/full/10.1002/alz.12105

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke
- Heart & Stroke: What is Stroke? https://www.heartandstroke.ca/stroke/what-is-stroke
- Heart & Stroke: Atrial Fibrillation: http://www.heartandstroke.ca/heart/conditions/atrial-fibrillation
- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-strokebest-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Are You at Risk for Heart Disease and Stroke?: http://www.heartandstroke.ca/-/media/pdf-files/iavc/health-information-catalogue/en-are-you-atrisk.ashx?la=en&hash=91D622380B55E55ADB31E7ECE37C9F51BCD26D9
- Heart & Stroke Canadian Resuscitation and First Aid Guidelines: https://cpr.heartandstroke.ca/s/?language=en_US&_ga=2.145584188.98775338.1657032029-2092542146.1608572095
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Virtual Healthcare Checklist: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbp-infographic-virtual-healthcare-checklist
- Heart & Stroke: Secondary Prevention Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7-infographic-secondaryprevention-final
- Heart & Stroke: Rehabilitation and Recovery Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/rehabilitation-nov2019/csbp-infographic-rehabilitation
- Heart & Stroke: Transitions and Community Participation Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/transition-of-care-nov2019/csbp-infographic-transitions-and-participation
- Heart & Stroke: Online and Peer Support: https://www.heartandstroke.ca/heart-disease/recovery-and-support/the-power-of-community
- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

The risk of recurrent ischemic stroke is heightened, especially in the early days following stroke or TIA. In a systematic review and meta-analysis including the results from 68 studies, Shahjouei et al. (2021) reported the frequency of recurrent events was 2.4% within 2 days, 3.8% within 7 days, 4.1% within 30 days, and 4.7% within 90 days. Rapid clinical assessment by stroke specialists and subsequent investigations to differentiate between TIA and minor stroke from other potential causes are essential

to ensure secondary prevention strategies can be implemented as soon as possible.

Urgent TIA clinics provide such a model of care. The TIARegistry.org project is a prospective registry designed to follow patients presenting with TIA or minor stroke over a five-year period. Patients were included if the event had occurred within the previous 7 days. The preliminary one-year results, which included 4,583 patients recruited from 61 sites in 21 countries from 2009 to 2011, indicated that 78.4% of patients were seen by a stroke specialist within 24 hours of the event (Amarenco et al., 2016). Most patients received key urgent investigations before discharge and appropriate treatments were initiated. For example, 5% of patients received a new diagnosis of atrial fibrillation, of which 66.8% received anticoagulant therapy before discharge. Carotid stenosis of ≥50% was found in 15.5% of patients, of which 26.9% underwent carotid revascularization before discharge. The one-year estimate of risk of the primary outcome, a composite of death from cardiovascular causes, nonfatal stroke and nonfatal acute coronary syndrome, was 6.2% (95% CI 5.5-7.0%). Estimates of the stroke rate at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively. These estimates were much lower than those compared with historical cohorts and were attributed to the widespread establishment of TIA clinics. Rothwell et al. (2007) reported that patients who had immediate access to a TIA clinic (EXPRESS) had a significantly reduced risk of recurrent stroke (2.1% vs.10.3%, p=0.0001), compared with an historical cohort who did not have immediate access to the same care. Patients with immediate access also received their prescriptions sooner (median of 1 vs. 20 days). Lavallée et al. (2007) reported the 90-day risk of stroke for all patients seen at their TIA-SOS clinic was lower than that predicted by their $ABCD^2$ score (1.24% vs. 5.96%).

Laboratory investigations and assessment of physiological variables as part of a patient's initial evaluation provides important information for patient management. A small case control study found that maintenance of normal physiological variables within the first 3 days of stroke has a beneficial effect on outcomes post stroke (Langhorne et al., 2000). Blood biomarkers have been shown to correlate with cerebral lesion size and stroke severity (Kisialiou et al., 2012). Ferrari et al. (2010) found that hypertension, diabetes, possible etiology, acute infection, and cardiac abnormalities were all independent predictors of deterioration following TIA or minor stroke, and recommended immediate diagnostic testing for their identification. Together, these findings suggest a complete evaluation of patients presenting with suspected stroke or TIA is beneficial for predicting risk of recurrent stroke and guiding patient management.

Atrial fibrillation (AF) is a common arrhythmia which is associated with an increased risk of ischemic stroke. Following minor stroke or TIA, detecting AF in patients with no previous history is important, particularly in those with a cryptogenic stroke or embolic stroke of unknown source. Once identified, AF can be effectively managed, typically with a switch from an antiplatelet to an anticoagulant. However, AF is under-diagnosed because it is frequently paroxysmal and asymptomatic, and patients do not routinely undergo prolonged screening. AF can be detected using a variety of methods including a12-lead ECG, Holter monitoring, event recorders, and implantable devices. Prolonged ECG monitoring using wearable or insertable devices has been shown to be effective for improving the detection of paroxysmal AF (numbers needed to screen range from 8 – 14) in persons with recent stroke with longer monitoring durations, ranging from 7 days to 1 year associated with an increased probability of AF detection (Bernstein et al., 2021; Haeusler et al., 2021; Wachter et al., 2017; Higgins et al., 2013). At 12 months, newly diagnosed AF was identified significantly more frequently in patients who received additional Holter-ECG recording for up to 7 days in hospital, compared with those who received usual care (5·8% vs. 4·0%; HR=1·4, 95% CI 1·0–2·0) (Haeusler et al., 2021). In the FIND-AF trial, Wachter et al. (2016) reported that at both 6 and 12 months, detection of AF was significantly higher in the prolonged Holter ECG monitoring group (10 days) compared with the standard care group, which received an average of 73 hours of inpatient telemetry plus an average of 24 hours of Holter monitoring

(13.5% vs. 4.5% and 13.5% vs. 6.1%, respectively). The associated numbers needed to screen were 11 and 13. There were no significant differences between groups in stroke recurrence (2.5 vs. 4.5%, p=0.28) or death (3.0 vs. 4.5%, p=0.45).

It has been estimated that 5% of all people >65 years of age in Canada have evidence of vascular cognitive impairment. The reported prevalence tends to be higher in those individuals who have experienced a stroke, with up to 29% developing vascular cognitive impairment over the five years following stroke (Pendlebury et al., 2015). Therefore, patients should be screened at the time of presentation using validated instruments such as the Montreal Cognitive Assessment test (MoCA) or the Mini-Mental State Exam (MMSE).

When in-hospital or in-clinic visits are not possible, some prevention interventions can be provided through virtual means, such as telephone or computer-mediated communication. Virtual care interventions have been shown to be effective for cardiovascular risk factor reduction. Monthly phone calls with a health advisor resulted in significantly lower systolic and diastolic blood pressures, and was also associated with significant improvements in diet, physical activity, drug adherence, and satisfaction with access to care, compared with usual care (Salisbury et al., 2016). Mobile health interventions were associated with a significantly reduced HgbA1$_C$ compared with the control condition, and significantly increased the odds of smoking cessation at 6 months (Liu et al. 2017). Digital health interventions including telemedicine, web-based strategies, email, mobile applications, text messaging, and monitoring sensors significantly reduced the risk of cardiovascular events (RR=0.61, 95% CI, 0.46–0.80, p<0.001) (Widmer et al., 2015).

Sex and Gender Considerations

In terms of risk factors, the prevalence of hypertension and atrial fibrillation tend to be higher in women, while diabetes and smoking tend to be lower. Women specific factors such as the use of oral combined contraceptives, gestational hypertension, pre-term delivery and hormone replacement therapy, among others can also increase the risk of ischemic stroke (Cordonnier et al. 2017). Women are more likely to be diagnosed as stroke mimics, less likely to be diagnosed with stroke, and less likely to have a full work-up to establish stroke etiology, compared with men (Kapral & Bushnell 2021). As for investigations for cardiac abnormalities, in two trials, FIND-AF (Wachter et al. 2016) and CRYSTAL-AF (Sanna et al. 2014), examining the potential benefit of prolonged cardiac monitoring for the detection of previously unknown atrial fibrillation, no interactions were found with respect to sex and treatment group.

Reference List and Evidence Tables

Evidence Table and Reference List 2: Triage and Initial Diagnostic Evaluation of Transient Ischemic Attack and Non-Disabling Stroke

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

TABLE 2A Recommended Laboratory Investigations for Patients with Acute Stroke or Transient Ischemic Attack

Recommended Laboratory Investigations for Patients with Stroke and Transient Ischemic Attack		
*Note: This list presents the recommended **initial** laboratory tests for patients with stroke and TIA. Patient presentation, clinical judgment, and local stroke protocols should be considered in selecting appropriate laboratory investigations and the timing of completion.*		
Complete blood count (CBC)	International Normalized Ratio (INR)	Partial thromboplastin time (PTT)
Electrolytes	Creatinine and glomerular filtration rate (eGFR)	Liver enzymes (e.g., AST, ALT)
Random glucose or hemoglobin A1c	**Fasting** plasma glucose, or 2-hour plasma glucose, or glycated hemoglobin (A1c), or 75 g oral glucose tolerance test	Lipid profile (Fasting optional and decision should be based on individual patient factors)

Additional Laboratory Investigations for Consideration in Specific Circumstances			
*Note: All patients are individuals, and some may require additional investigations to fully understand their clinical situation. The investigations noted below may not be indicated for many patients with stroke and should be considered in **selected** patients with stroke based on clinical presentation and medical history.*			
Calcium, Magnesium, Phosphate	If female <50 years of age, consider pregnancy test	Blood cultures if infection suspected (per individual institutional protocol)	
ESR	CRP	Troponin, where indicated	
Blood and/or urine drug screen	HIV and syphilis serology, where indicated		
Arterial hypercoagulability screen: For consideration in selected patients *only if clinically indicated* *Consultation with a specialist in thrombosis to evaluate for hypercoagulable state is recommended.*			
Anticardiolipin antibodies, Beta-2-glycoprotein	Lupus anticoagulant	Sickle cell screen	Serum homocysteine and vitamin B12
Venous hypercoagulability screen: For consideration in selected patients *only if clinically indicated (e.g., a young person with a PFO)* *Consultation with a specialist in thrombosis to evaluate for hypercoagulable state is recommended.*			
Protein S	Protein C	Factor V Leiden	
Prothrombin gene mutation	Antithrombin III		
Special considerations especially in young adults and children with stroke in absence of identified etiology *(Note: There is not strong evidence for the investigations listed below, and they should be considered only in selected patients with stroke based on clinical presentation and medical history.)* ***Consultation with a hematologist or neurologist is recommended.***			
Lumbar puncture for CSF analysis (cell count and differential, protein, glucose, bacterial and viral studies; possibly cytology/flow cytometry if CNS lymphoma is a consideration)	Brain biopsy (if vasculitis of the central nervous system or angiocentric lymphoma is a consideration)		
Advanced neuroimaging (i.e., diagnostic catheter cerebral angiography and or MRI vessel wall imaging)	Further genetic tests – CADASIL, Fabry's, MELAS		

Section 3 Emergency Medical Services Management of Acute Stroke

3. Emergency Medical Services Management of Acute Stroke Recommendations 2022

Notes:

- *The recommendations in Section 3 cover the management of potential patients with stroke from the time of first contact with the local emergency medical services (EMS) to transfer of care to the hospital and transfer between healthcare facilities by EMS.*
- *These recommendations are **directed to EMS personnel and those individuals who support EMS**, including communications officers and dispatchers. They also apply to other first responders such as emergency medical responders and primary care paramedics who have been trained to screen for stroke and manage potential patients with stroke during transfer. These recommendations are intended to be **translated into practice by the entire breadth of out-of-hospital healthcare providers** within the defined scope of practice of each.*

Context and Definitions

Approximately two-thirds of all patients who seek acute care for stroke arrive at the emergency department by ambulance. Local variations should be taken into consideration for prehospital time (e.g., remote locations with poor road access).

The three timelines below have been established to describe EMS in Canada for patients with stroke who may be eligible for acute ischemic stroke therapy, including intravenous thrombolysis and endovascular thrombectomy (EVT). ***The probability of disability-free survival decreases as the time from symptom onset to treatment increases. Therefore, all phases of patient care should aim for the shortest possible process and treatment times.***

Prehospital phase (**Timeline 1):** Starts with symptom onset and ends with hospital arrival and includes on-scene management and transport time. Patients with ischemic stroke who can arrive at hospital within a **4.5 hour** time window from witnessed stroke symptom onset or last known well and be treated as soon as possible may be eligible to receive medical treatment with intravenous thrombolysis; thrombolysis may be offered alone or in combination with endovascular intervention (e.g., thrombectomy, other endovascular procedures such as stenting) which has a **6-hour** time window for most patients. Highly selected patients may be eligible for EVT **up to 24 hours** from stroke symptom onset or last known well. *Refer to Section 4 Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke for more information.*

Emergency department phase (**Timeline 2):** Starts with hospital arrival and ends with disposition time from the emergency department. People with stroke may transition from the emergency department to various settings: admission (ideally to a stroke unit) for inpatient care, transfer to another healthcare facility, or discharge to the community (usually place of residence). *Refer to Section 4 Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke for more information.*

Interhospital transfer time (Timeline 3): Applies to patients with stroke who require ***transfer from one hospital to another*** to receive more advanced stroke care. The delay for patients who first arrive at an emergency department that has limited acute stroke services and who then requires transfer can be an important factor in determining outcomes. The recommendations in this section suggest that this time be as short as possible, and EMS plays a key role in timing and the transfer process.

Recommendations

3.0 Out-of-hospital patient management should be organized to achieve the rapid assessment and treatment of patients with suspected stroke, including rapid recognition of potential stroke symptoms, EMS mobilization, and transport to an acute care hospital with acute stroke management capability [Strong recommendation; Moderate quality of evidence].

3.1 Access to Emergency Medical Services

i. A person experiencing the signs or symptoms of stroke, or any witness, should immediately contact EMS by calling 9-1-1 or the local emergency number [Strong recommendation; Moderate quality of evidence]. *Refer to Section 1 for additional information.*

ii. EMS communications centre: All regions in Canada should implement a dispatch process through their EMS communications centres to rapidly recognize signs or symptoms of stroke (e.g., FAST: Face, Arms, Speech, Time), prioritize response to the scene, and transport the patient to a hospital capable of providing acute services for rapid diagnosis and time-sensitive treatment of stroke (such as neuroimaging, and acute thrombolysis) [Strong recommendation; Low quality of evidence].

iii. After dispatching the ambulance, it is recommended that EMS communications centre personnel provide pre-arrival instructions to the person reporting the stroke (e.g., unlock door, move pets, determine stroke symptom onset time, determine current medications), in order to expedite, optimize, and improve safety for prehospital care [*Conditional recommendation*; Low quality of evidence]. *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: The on-scene goal is to **recognize and mobilize.** It is of the utmost importance to rapidly and safely transport suspected patients with stroke, as on-scene management for patients with stroke is limited.*

i. To minimize time to acute treatment for thrombolysis or EVT, EMS personnel should use a validated acute stroke out-of-hospital diagnostic screening tool that includes the components of FAST [Strong recommendation; Moderate quality of evidence].

   a. To optimize access to EVT, patients who demonstrate FAST signs of stroke should then undergo a valid secondary screen to assess stroke severity, which may be used to identify candidates for *direct transport to an EVT capable centre where possible* [Strong recommendation; Moderate quality of evidence]. *Note: The purpose of the second screen is to look for possible EVT candidates, such as people exhibiting signs of cortical dysfunction (e.g., aphasia, visual changes, neglect).*

   b. Screening for potential stroke and likelihood of large vessel occlusion (LVO) should be done early in the on-scene assessment. If the stroke screen is positive, all on-scene actions from that point should be focused on moving to the ambulance and beginning transport [Strong recommendation; Moderate quality of evidence].

Refer to Appendix 3, Canadian Stroke Best Practices Table 3a of Standardized Acute Prehospital Stroke Screening Tools; Table 3b Additional Tools and Table 3c Prehospital Stroke Screening Scales to Identify Large Vessel Occlusion (LVO).

ii. Treatments that are not immediately required could be undertaken while the patient is enroute to the hospital or after hospital arrival [Strong recommendation, Low quality of evidence].

iii. EMS personnel should obtain information from the patient, family members or other witnesses about the suspected stroke event, including presenting symptoms, time of onset or time of symptom recognition and time last known well, sequence of events, co-morbid conditions, current medications (especially anticoagulants), and any formal or informal advance directives

that may influence care by EMS and in the emergency department [Strong recommendation; Moderate quality of evidence]. *Refer to Box 3A for additional information.*

iv. On-scene time with any patient with suspected stroke should be as short as possible; ideally a median time of <20 minutes [Strong recommendation; Low quality of evidence].

v. Initial assessment provided by paramedics should include capillary blood glucose measurement [Strong recommendation; Moderate quality of evidence].

   a. Ideally capillary blood glucose measurement should be done on-scene to inform transport decisions [*Conditional recommendation*; Low quality of evidence].

vi. Prior to transport, on-scene EMS personnel should provide instructions to the patients' family, including recommending that the family member or other decision-maker accompany the patient to hospital or be accessible by phone for decision-making; confirming time last known well; and providing information about existing health conditions, current medications, and other information as needed [Strong recommendation; Low quality of evidence].

3.3 Transport of Patients with Suspected Stroke

i. Direct transport protocols should be in place to facilitate the transfer of patients with suspected acute stroke 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 [Strong recommendation; Moderate quality of evidence].

ii. Direct transport protocols should take into account the medical stability of the patient, last known well time, severity of the stroke, and any regional factors [Strong recommendation; Moderate quality of evidence]. *Refer to Box 3B for additional information.*

iii. Patients with suspected stroke should be triaged by EMS 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 [Strong recommendation; Moderate quality of evidence].

iv. **Pre-notification**: While enroute to the receiving hospital that provides acute stroke services, EMS should notify the emergency department of the incoming suspected acute stroke patient and provide sufficient details such that a "Code Stroke" can be activated at that time [Strong recommendation; Moderate quality of evidence]. *Refer to Box 3A for additional information.*

v. Patients with suspected stroke who are considered ineligible for intravenous thrombolytic therapy or EVT (e.g., they are outside the time window) should still be transported immediately to the closest hospital capable of providing acute stroke diagnosis and management services, where assessment and determination can be made for transport to a higher level of care as appropriate [Strong recommendation; High quality of evidence].

3.4 Hospital Arrival and Emergency Medical Services Handover to Emergency Department Staff

i. Transfer of care from paramedics to receiving hospital personnel should occur with minimal delay and patients with suspected acute stroke who are potentially eligible for thrombolytic therapy or EVT should receive highest priority in the emergency department triage queue [Strong recommendation; Moderate quality of evidence]. *Refer to Section 4.1 for more information.*

ii. At hospital arrival, paramedics should provide the receiving hospital with verbal and written information related to the patient's stroke onset time, last known well time, presenting symptoms, and medications, to facilitate rapid assessment and decision-making [Strong recommendation; Low quality of evidence]. *Refer to Box 3A for more information.*

Section 3 Clinical Considerations

1. The standard window for intravenous thrombolysis is 4.5 hours and the standard time window for EVT is 6 hours. However, patients may be considered eligible beyond these windows based on clinical factors and neuroimaging findings.
2. Direct transport in many regions may take one of two potential pathways based on local or regional considerations:
    a. Patients who may be eligible for intravenous thrombolysis may be directed to the closest centre, which may be a primary/advanced stroke centre or comprehensive stroke centre.
    b. Patients who are likely candidates for EVT may be directed to (1) an EVT-enabled comprehensive stroke centre OR (2) a primary centre to rapidly receive intravenous thrombolysis and then be considered for transport to an EVT-enabled comprehensive stroke centre.
3. On-scene time is an important variable that EMS professionals can control and needs to be monitored closely. Time lost due to inefficient on-scene care cannot be made up during subsequent transport to hospital, regardless of the use of lights and sirens.
4. Patients should be transported by the method that allows the shortest transport time. In the event that a ground EMS response may cause significant delay in the patient transport, air transport should be considered where available.
5. Pre-notification contact with the receiving emergency department should be initiated as soon as possible; where possible, the paramedics and receiving emergency department physician or stroke team member should communicate while enroute.
6. For EVT-eligible patients, processes and or algorithms should be put in place that will easily enable a discussion to arrange for the patient to be transferred to the EVT-enabled comprehensive stroke centre in a timely manner. A three-way conference call among the referring clinician (paramedic or emergency department physician at a primary/advanced stroke centre), the receiving physician at the EVT-enabled centre, and the ambulance service involved in patient transport should support decision-making regarding direct to EVT centre or closer centre for initial imaging and assessment.
7. **Mobile Stroke Units**: The Canadian Stroke Best Practices writing group is currently unable to make a recommendation about mobile stroke units as published data on their use in the context of Canadian geography and health system organization are lacking. The group encourages further research into mobile stroke units in Canada as high-quality studies from other jurisdictions suggest that the use of these specialized units is associated with a reduced time to thrombolysis, an increased proportion of patients receiving thrombolysis, and better functional outcomes at 90 days.

Box 3A Core Information That May Be Required by Dispatch, Emergency Medical Services, and Receiving Healthcare Facility

1. Where permitted, patient name, date of birth, and health card number *Note: In general, this confidential personal health information is not allowed to be transmitted by radio; however, some provinces have received a waiver and had this restriction lifted for emergency cases such as stroke*.
2. Location of patient
3. Stroke symptom onset time if witnessed, and last known well time if not witnessed
4. Total symptom duration at anticipated arrival in the emergency department
5. Presenting signs of stroke and stroke severity score, based on standardized screening tools
6. Current condition of the patient having a stroke, including medical stability, previous functional status and independence level, and changes in their condition since stroke symptom onset

7. Current medications (e.g., anticoagulants) if known, and time taken
8. Advance care plans, if any
9. Expected time of arrival at the receiving hospital, including in scene time
10. Additional health problems, if known

Box 3B Considerations in EMS Transport Decisions

The following elements should be considered when making transport decisions for patients with suspected acute stroke:

1. An EMS system should be set up to triage patients exhibiting signs and symptoms of an acute stroke as a high priority for evaluation, response, and transport.
2. The patient's presenting signs and symptoms.
3. Anticipated transport time, including bypass time.
4. The probability that the patient is acutely treatable with either intravenous thrombolysis and/or EVT:
    a. Patients are eligible for intravenous thrombolysis within 4.5-hours of known or presumed symptom onset or last known well
    b. Some patients may be eligible for endovascular thrombectomy when highly selected by neurovascular imaging up to 24 hours from known or presumed symptom onset or last known well. Transport time and receiving hospital projected treatment time must be considered when making transport and triage decisions.
5. The emergency department's ability to provide acute intravenous thrombolysis within a target 90th percentile for door-to-needle (i.e., arrival to treatment) time of ≤60 minutes (upper limit) and a target ***median*** door-to-needle time of ≤30 minutes.
6. Other acute care needs of the patient, including stabilization or advanced airway control that is beyond the capabilities of the responding EMS personnel.
7. **(NEW for 2022)** A system of rapid transport should be available to facilitate the movement of patients from one emergency department to another when time-sensitive stroke-specific care cannot be provided in the emergency department where the patient is first assessed.

Rationale

Acute stroke is a medical emergency and optimizing out-of-hospital (prehospital) care improves patient outcomes. EMS plays a critical role in prehospital assessment and management of patients with suspected stroke. Acute interventions such as thrombolytic therapy and EVT are time sensitive; therefore, strategies to reduce delays such as re-directing ambulances to stroke centres and prenotification by EMS staff can help identify patients with more severe strokes who may be eligible for such treatments.

Intravenous thrombolytic therapy should be administered within a 4.5-hour treatment window, while EVT is best performed within 6 hours from stroke onset. In selected patients, EVT can be used in combination with intravenous thrombolysis (given within 4.5 hours of symptom onset), with numbers needed to treat reported as low as 3 – 4. EVT is also beneficial as a sole treatment for those persons who are ineligible for intravenous thrombolysis. In addition, a small group of patients may still benefit from EVT up to 24 hours from symptom onset when selected by neurovascular imaging in the context of a coordinated stroke system that includes access to experts in stroke and neurointerventional care.

People with lived experience stressed the importance of quick EMS arrival, as well as transport to the appropriate hospital to receive care. They emphasized the importance of calling 911 (or the local

emergency number) when stroke signs are present, and not driving yourself or a loved one to the hospital.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. EMS personnel training in stroke recognition (signs and symptoms including FAST mnemonic), rapid assessment (including severity), management and transport requirements in the prehospital phase of care for the geographic region being serviced.
2. Ongoing paramedic education on the use of validated prehospital stroke screening protocols and tools and the ability to incorporate such protocols and tools into all prehospital assessments of patients with suspected stroke. (The CSBPR include assessment tools and educational materials, developed in collaboration with EMS leaders, for implementation across Canada.)
3. Ambulance services in all parts of Canada with direct transport protocols and agreements for bypass or redirect between EMS providers and regional health authorities and/or receiving hospitals.
4. EMS able to provide coordinated seamless transport (land, water, and air) and care for patients with acute stroke.
5. Communication systems such as virtual stroke care (telestroke) to support timely access to specialized stroke service consultations.
6. Protocols and agreements to support the transfer of patients with disabling stroke to hospitals that provide advanced acute stroke treatments including EVT, regardless of geographic location.
7. In each region that has adult and pediatric acute stroke services, development of criteria and processes regarding whether to transport of children with suspected stroke to pediatric or adult stroke centres. The criteria should be based on symptoms and age and agreed upon by the adult and pediatric centres, and EMS.
8. Development of processes and pathways for EMS to support decision-making regarding transportation models for patients with suspected stroke (e.g., directly to comprehensive stroke centres that have EVT services or initial imaging and care at primary stroke centres).

Performance Measures

System indicators:

1. Proportion of patients with stroke (or suspected stroke) arriving in the emergency department who were transported by EMS.

Process indicators:

2. Time from initial call received by emergency dispatch centre to EMS arrival on scene.
3. Time from EMS arrival on scene to arrival at the receiving emergency department (ideally at a stroke-enabled hospital capable of providing intravenous thrombolysis).
4. Time from initial call received by emergency dispatch centre to patient arrival at an emergency department that provides stroke services.
5. Proportion of acute patients with stroke transported by EMS to a stroke-enabled hospital (i.e., designated acute stroke treatment centre) as first hospital destination. Performance target is ≥90%.
6. Percent of EMS transports of patients with suspected stroke which the receiving hospital received notification enroute (pre-notification) of an incoming acute stroke patient.

7. Proportion of EMS calls where out-of-hospital time is <3.5 hours from stroke symptom onset or time last known well to arrival at the emergency department. Performance target is ≥75%.

Patient-oriented outcome and experience indicators:

8. Proportion of potential patients with stroke transported by EMS who received a final diagnosis of stroke or transient ischemic attack in the emergency department or at hospital discharge.
9. Proportion of respondents with a stroke diagnosis who report experiencing culturally safe and appropriate care.

Measurement Notes

a. Emergency department records and administrative databases track patients with stroke who arrive by ambulance (land, air, or water) as a standard data element.
b. An appropriate/acceptable "over-triage" rate should be <15% (i.e., false positive stroke determinations). (Indicator 9).
c. Refer to the *Quality of Stroke Care in Canada Key Quality Indicators and Stroke Case Definitions 7th Edition* for additional measures related to hospital bypass and pre-notification.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices team or Heart & Stroke. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practice Recommendations Acute Stroke Management Module Appendix 3: Table 3a of Standardized Acute Prehospital Stroke Screening Tools; Table 3b Additional Tools and Table 3c Prehospital Stroke Screening Scales to Identify Large Vessel Occlusion (LVO)
- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke
- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Canadian Triage Acuity Scale for Adults (CTAS) and Pediatric Scale (P-CTAS): http://caep.ca/resources/ctas#intro
- Stroke Engine: http://strokengine.ca/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-strokebest-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke
- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947

- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

Patients arriving to hospital using EMS following a stroke experience fewer delays in receiving appropriate diagnostic tests such as brain imaging, and are more likely to receive revascularization treatments, if eligible. For example, the odds of a patient receiving treatment with intravenous thrombolysis following transport to hospital by EMS increased by 52% in a cohort of 2,600 patients with a final diagnosis of ischemic stroke (Nielsen et al., 2020). Additionally, hospital pre-notification by EMS staff can significantly decrease the door-to-physician, door-to-CT scan times, and door-to-needle time (Abboud et al., 2016; Hsieh et al., 2016; Kim et al., 2016; McKinney et al., 2013; Lin et al., 2012) and increase the proportion of patients who receive intravenous thrombolysis (Nielsen et al., 2020).

In a US study based on registry data (Patel et al., 2011), of 13,894 patients who whose discharge diagnosis was stroke, patients arriving by EMS with hospital prenotification were more likely to have brain imaging completed within 25 minutes (RR= 3.0, 95% CI 2.1-4.1) and to have the results interpreted within 45 minutes (RR= 2.7, 95% CI 2.3-3.3), compared to arriving by private transport. Patients eligible for t-PA were also more likely to receive brain imaging if arriving by EMS with pre-notification (RR=1.5, 95% CI 1.1-1.9). In contrast to these findings, a cluster randomized trial (PASTA, Price et al., 2020) randomized paramedics to the PASTA pathway, which included structured prehospital information collection, prompted pre-notification, structured handover of information in hospital, and assistance with simple tasks during the initial hospital assessment or to standard care reflecting national guidelines. During the study period, 1,214 patients with confirmed stroke, last known to be well within the previous four hours, were attended to by 597 paramedics. Among patients with ischemic stroke, there was no significant difference between groups in the proportion of patients who received thrombolysis (49.7% [PASTA] vs. 52.6% [standard care], adjusted OR=0.84, 95% CI 0.60-1.17). Paramedics in the PASTA group took an average of 13.4 minutes longer to clear a care episode.

To rule in stroke as a potential cause for the patient's symptoms, EMS personnel should first use a validated acute stroke out-of-hospital diagnostic screening tool, such as FAST. The accuracy of such scales was assessed in a recent Cochrane review. Zhelev et al. (2019) evaluated the test accuracy of several stroke recognition scales (e.g., Recognition of Stroke in the Emergency Room [ROSIER], Los Angeles Prehospital Stroke Scale [LAPSS], Ontario Prehospital Stroke Screening Tool [OPSST], Medic Prehospital Assessment for Code Stroke [MedPACS], and PreHospital Ambulance Stroke Test [PreHAST]) intended for use in a prehospital (n=17) or emergency room (n=6) setting, using data from 23 primary studies. The scales assessed in a prehospital setting in these studies included the CPSS (n=9), LAPSS (n=5), FAST (n=3), and MASS (n=3). Due to high unexplained between-study heterogeneity, and the high risk of bias in most of the studies assessing the CPSS scale, the results were not pooled. Within the 11 individual studies, sensitivity ranged from 0.44 to 0.95 and specificity from 0.21 to 0.79. For LAPSS, summary statistics were pooled. Sensitivity was 0.83 (95% CI 0.75 to 0.89) and summary specificity was 0.93 (95% CI 0.88 to 0.96). For FAST and MASS, within individual studies, sensitivity ranged from 0.64 to 0.97 and 0.74 to 0.90, respectively; specificity ranged from 0.13 to 0.92 and 0.67 to 0.86, respectively.

Endovascular revascularization techniques are now more widely available, several on-scene screening tools to identify patients with suspected LVO, designed for use by EMS technicians, have emerged. Most of these scales were derived from 3 to 6 components of the National Institutes of Health Stroke scale. Examples of these scales include Face, Arm, Speech, Time—Vision Aphasia Neglect (FAST VAN, Wasyliw et al., 2022), Field Assessment of Critical Stroke by Emergency Services for Acute Delivery ($FACE_2AD$, Okuno et al., 2020), Field Assessment Stroke Triage for Emergency Destination (FAST-ED,

Lima et al., 2016), Vision, Aphasia, and Neglect (VAN, Taleb et al., 2016), the Prehospital Acute Stroke Severity Scale (PASS, Hastrup et al., 2016), Cincinnati Prehospital Stroke Severity Scale (CPSSS, Katz et al., 2015), and The Los Angeles Motor Scale (LAMS, Nazliel et al., 2008). The sensitivities and specificities associated with these scales range from 61% to 100% and 40% to 92%, respectively. Scales were developed using data from patients with both (later confirmed) ischemic stroke and suspected stroke. Unfortunately, the performance of these scales is not ideal. Smith et al. (2018) included the results from 36 studies evaluating the accuracy of LVO prediction scales in patients with suspected stroke or presumed acute ischemic stroke in prehospital or emergency department settings. The authors concluded that no scale had both high sensitivity and specificity to determine the presence vs. absence of LVO, and that in clinical practice that the probability of LVO given a negative test could still be ≥10%.

Direct transport by EMS to a hospital that has on-site expertise in the provision of recalculation procedures increases the chance that eligible patients will receive these treatments. In the RACECAT trial (De la Ossa et al., 2022), 1,401 patients with suspected acute LVO identified by EMS in the field were randomized to transport to 6 thrombectomy-capable centres or 22 local stroke centres. Prenotification criteria for the EMS coordination centre were established to provide high sensitivity in identifying potential candidates. Compared with patients first transported to local stroke centres, patients with confirmed ischemic stroke or TIA directly transported to thrombectomy-capable centres were less likely to receive treatment with intravenous thrombolysis (47.5% vs. 60.4%, OR= 0.59, 95% CI, 0.45-0.76) but were more likely to receive thrombectomy (48.8% vs. 39.4%, OR=1.46, 95% CI 1.13-1.89). A systematic review (Mohamed et al., 2021) included the results from 19 studies examining a mothership model with a drip and ship model. Compared with patients with suspected LVO who were transported directly to a thrombectomy-capable hospital, those who were transported to the closest hospital, received intravenous thrombolysis, and were then transferred to a thrombectomy capable hospital had lower odds of a good functional outcome (mRS 0-2) at 90 days (OR=0.74, 95% CI 0.65-0.84). Similar findings were reported in another systematic review (Ismail et al., 2019), which included the results of 8 studies. Patients who underwent thrombectomy after direct transport to a comprehensive stroke centre were more likely to have a better outcome at 90 days.

The use of mobile stroke units (MSUs), which are ambulances equipped with specialized equipment such as on-site laboratories and CT scanners and staffed with additional personnel with stroke expertise, are now appearing in some large, urban cities. A recent systematic review (Turc et al., 2022) included the results of 14 controlled studies. Studies compared MSU deployment with usual care for prehospital management of acute ischemic stroke, within a 6-hour window of symptom onset. In adjusted analysis, the pooled odds of the primary outcome (mRS score of 0-2 at 90 days) were significantly higher in the MSU group (OR=1.64, 95% CI 1.27-2.13). The odds of treatment with intravenous thrombolysis were significantly higher in the MSU group (unadjusted OR= 1.83, 95% CI 1.58-2.12), as were the odds of treatment with intravenous thrombolysis within 60 minutes (unadjusted OR= 7.71, 95% CI 4.17-14.25). The results from two large trials (n=1,500) of MSUs were published in 2021. In the BEST-MSU trial (Grotta et al., 2021), MSU use was associated with a significantly increased number of t-PA eligible patients receiving the treatment, reduced time to t-PA administration, and a significantly higher utility-weighted mRS (UW-mRS) score at 90 days (the primary outcome) compared with weeks when the MSU was not deployed. Similar trends were reported in the B_PROUD Study (Ebinger et al., 2021) whereby significantly more patients in the MSU group received treatment with t-PA compared with conventional EMS, and t-PA process times were significantly shorter. Median time from dispatch to imaging was 45 vs. 60 minutes ($p<0.001$), and the median time from dispatch to t-PA was 50 vs. 70 minutes ($p<0.001$). The distribution of mRS scores also favoured the MSU group (adj common OR=0.71, 95% CI 0.58 to 0.86).

Sex & Gender Considerations

While the results from some studies indicate that women tend to utilize EMS more than men, the finding

is not consistent, and reasons for the potential differences are unclear (Bushnell et al. 2018). In a retrospective study including 463,310 adult patients (Kapoor et al. 2020), ambulance utilization and time to hospital presentation across sex and age groups were examined. Older women (≥45 years) were more likely to arrive by ambulance compared with older men (68.4% vs. 63.9%; $p < 0.001$). There were no sex differences between younger men vs. women. Older women with ischemic stroke were significantly more likely to arrive by ambulance. Older women arrived at hospital sooner than older men (6.6 vs. 6.9 hours, $p < 0.0001$), while younger women arrived significantly later than younger men (9.2 vs. 7.5 hours, $p = 0.004$). Using data from 47,209 participants of the Austrian Stroke Registry, women were less likely to arrive at hospital via private transport (age-adjusted OR= 0.94, 95% CI 0.89–0.99) (Gattringer et al. 2014). Women may also experience greater prehospital delays and longer door-to-imaging times (Pacheco et al. 2021).

Reference List and Evidence Tables

Evidence Table and Reference List 3: Emergency Medical Services Management of Acute Stroke

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 4 Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke

4. Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke Recommendations 2022

4.1 Initial Emergency Department Evaluation

i. All patients presenting to an emergency department with suspected acute stroke should be immediately assessed and undergo investigations without delay to establish a diagnosis and determine eligibility for thrombolysis and/or endovascular thrombectomy (EVT) [Strong recommendation; High quality of evidence].

   a. Patients with suspected acute stroke should have a rapid initial evaluation for airway, breathing, and circulation [Strong recommendation; High quality of evidence].

   b. Patients with suspected stroke should be triaged as Canadian Triage Acuity Scale (CTAS) Level 2 in most cases and as CTAS Level 1 for patients with compromised airway, breathing, or cardiovascular function [Strong recommendation; Low quality of evidence].

ii. Patients with suspected acute stroke should have a ***rapid neurological examination*** to determine focal neurological deficits using a validated scale such as FAST (Face, Arm, Speech, Time) [Strong recommendation; Moderate quality of evidence]; and to assess for stroke severity using a validated screen [Strong recommendation; High quality of evidence].

   a. A standardized stroke scale such as the National Institutes of Health Stroke Scale (NIHSS) should be included in the initial assessment [Strong recommendation; High quality of evidence].

   b. Initial assessment should include consideration of time of stroke symptom onset, stroke mimics, development of a plan for further management, and establishment of goals for care [Strong recommendation; Low quality of evidence] *Refer to Section 2 Triage and Initial Diagnostic Evaluation of Transient Ischemic Attack and Non-Disabling Stroke for additional information.*

iii. Patients with suspected acute stroke should undergo an assessment of heart rate and rhythm, blood pressure, temperature, oxygen saturation, point-of-care glucose, and presence of seizure activity [Strong recommendation; High quality of evidence].

   a. **(NEW FOR 2022)** Use or non-use of anticoagulants, including the timing of the last dose taken, should be sought and recorded [Strong recommendation; Moderate quality of evidence].

iv. Acute blood work should be conducted as part of the initial evaluation [Strong recommendation; Moderate quality of evidence].

   a. Initial blood work should include electrolytes, random glucose, complete blood count (CBC), coagulation status (INR, aPTT), and creatinine [Strong recommendation; High quality of evidence]. *Refer to Table 2A for additional information on recommended laboratory investigations for acute stroke and TIA.*

      *Note: Initial blood work tests **should not delay imaging or treatment decisions and treatment initiation** for intravenous thrombolysis and EVT.*

v. **Seizure assessment:** Seizure in the presence of suspected acute stroke is not a contraindication for reperfusion and could be treated using appropriate short-acting medications (e.g., lorazepam IV) if the seizures are not self-limited [Strong recommendation; High quality of evidence]. *Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke for additional information.*

Note: If initial brain imaging reveals a hemorrhagic stroke, refer to CSBPR Management of Intracerebral Hemorrhage module for additional information.

4.2 Neurovascular (Brain and Vascular) Imaging

i. All patients with suspected acute stroke should undergo brain and vascular imaging computerized tomography (CT) or magnetic resonance imaging (MRI) [Strong recommendation; High quality of evidence].

   a. Vascular imaging should be preformed from arch-to-vertex and include the extra- and intra-cranial circulation to determine eligibility for acute treatment [Strong recommendation; High quality of evidence]. *Refer to target timelines in the Performance Measures section below.*

   Note: Primary stroke centres should make all efforts to perform combined CT and CTA on patient arrival. The CT and CTA should be done at same time and not in separate visits to the imaging suite. Stroke centres that cannot do CTA should have pre-planned arrangements for rapid transfer of appropriate patients. They should complete non-contrast CT (NCCT) and offer intravenous thrombolysis as appropriate and then rapidly transfer the patient to a comprehensive stroke centre for more advanced imaging and consideration for EVT. (Refer to IV thrombolysis Section 5 for additional information).

ii. All patients with suspected acute ischemic stroke who arrive at hospital **within 6 hours** who are potentially eligible for intravenous thrombolysis and/or EVT should undergo ***immediate non-contrast CT (NCCT)*** **combined with CT angiography (CTA) of the head and neck,** performed and interpreted without delay [Strong recommendation; High quality of evidence]. *Refer to eligibility criteria in Boxes 4A, 5A, 5B, and section 5.4. Note: Box 4B and 5C have been removed and replaced with content in section 5.4 for the Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025.*

iii. All patients with suspected ischemic stroke due to large vessel occlusion (LVO) **arriving 6 to 24 hours** after stroke symptom onset (including stroke on awakening or with unknown onset time) and who are potentially eligible for late window EVT should undergo immediate brain imaging with NCCT with CTA and CT perfusion (CTP); or magnetic resonance imaging (MRI) with MR angiography (MRA) and MR perfusion (MRP) [Strong recommendation; High quality of evidence]; or CT with multiphase CTA [Strong recommendation; Moderate quality of evidence]. *Refer to Section 4.1 for criteria regarding screening with use of validated screening tools. Note: Box 4C has been removed and replaced with 5.4 for the Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025.*

iv. A validated triage tool, such as ASPECTS, should be used to rapidly identify patients who may be eligible for EVT and who may require transfer to a different facility for EVT [Strong recommendation; Moderate quality of evidence].

v. Advanced CT imaging such as CT perfusion (CTP) or multiphase CTA to assess pial collateral vessels is strongly encouraged as part of initial imaging to aid patient selection for EVT [Strong recommendation; Moderate quality of evidence]. However, advanced imaging must not substantially delay decision-making and treatment with intravenous thrombolysis or EVT. *Refer to Boxes 4A, 5A, 5B and section 5.4 for additional information. Note: Box 4B, 4C and 5C have been removed and replaced with content in section 5.4 for the Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025.*

   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 judgement of the treating physician.

   Note: In most Canadian centres 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.

Refer to Section 5 Acute Ischemic Stroke Treatment for information on administration of intravenous thrombolysis and EVT.

Section 4.2 Clinical Considerations

1. MRI as a first line for imaging can be challenging to obtain urgently in an emergency department setting. Obtaining an MRI scan should not delay decision-making regarding intravenous thrombolysis and EVT eligibility.
2. Patients with a known allergy to contrast dye or with existing renal failure should not be excluded from consideration for EVT.

4.3 Acute Blood Pressure Management

i. **Patients with ischemic stroke eligible for thrombolytic therapy**: Blood pressure should be lowered and sustained below 185/110 while initiating and during IV thrombolysis therapy, and for the next 24 hours for ischemic stroke patients who are eligible for thrombolytic therapy [Strong recommendation; Low quality of evidence].

ii. **Patients with ischemic stroke not eligible for thrombolytic therapy**: Patients with moderate blood pressure elevation (up to 220 mmHg systolic) should not be routinely treated if they are not eligible for thrombolytic therapy [*Conditional recommendation*; Low quality of evidence].

   a. Patients with extreme blood pressure elevation (e.g., systolic BP >220 or diastolic BP >120 mmHg) should be considered for blood pressure lowering therapy if they are not eligible for thrombolytic therapy [*Conditional recommendation*; Low quality of evidence].

iii. Rapid or excessive lowering of blood pressure should be avoided as this might exacerbate existing ischemia or might induce ischemia, particularly in the setting of intracranial or extracranial arterial occlusion [*Conditional recommendation;* Low quality of evidence].

   a. Reducing the blood pressure by approximately 15% and not >25% over the first 24 hours, with further gradual reduction thereafter to targets for long-term secondary stroke prevention, may be considered [*Conditional recommendation*; Low quality of evidence].

Note: Refer to CSBPR Management of Intracerebral Hemorrhage module for information on blood pressure management of hemorrhagic stroke.

Section 4.3 Clinical Considerations

1. The choice of agents to manage blood pressure should be based on current Hypertension Canada blood pressure treatment guidelines. *Refer to www.hypertension.ca.*

4.4 Cardiovascular Investigations

i. Patients with acute ischemic stroke or TIA 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) [Strong recommendation; Moderate quality of evidence].

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 [Strong recommendation; Moderate quality of evidence].

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 CSBPR Secondary Prevention of Stroke module, Section 7 for additional information.

Refer to CSBPR Secondary Prevention of Stroke module for additional information on echocardiography and rhythm monitoring.

4.5 Blood Glucose Abnormalities

i. All patients with suspected acute stroke should have their blood glucose concentration checked on arrival to the emergency department (*or review glucose provided by EMS for any immediate management required)* [Strong recommendation; Moderate quality of evidence]. *Refer to Table 2A Recommended Laboratory Investigations for Patients with Acute Stroke or Transient Ischemic Attack for additional information. Refer to Section 3 Emergency Medical Services Management of Acute Stroke for additional information on EMS management.*

ii. Hypoglycemia should be corrected immediately using local protocols [Strong recommendation; High quality of evidence].

iii. Although no optimal glucose target has been identified in the acute stage, it may be reasonable to treat hyperglycemia (glucose >20 um/l) as per local protocols as this has been associated with increased risk of hemorrhagic transformation when treating with intravenous thrombolysis [*Conditional recommendation*; Low quality of evidence].

4.6 Additional Management Considerations in the Emergency Department

i. **Chest X-ray:** A routine chest x-ray is not required for acute stroke; chest x-ray should be considered if there is concern for acute cardio-pulmonary disease [Strong recommendation; Low quality of evidence]; otherwise, this should not delay the CT scan and decisions regarding reperfusion [Strong Recommendation; Moderate Quality of evidence].

ii. **Swallowing assessment**: All patients with acute stroke or TIA should have a swallowing screen completed as soon as possible as part of initial assessment by a practitioner trained to use a validated swallowing screening tool; however, screening should not delay decision-making regarding eligibility for reperfusion treatments [Strong recommendation; High quality of evidence].

   a. Ideally swallowing screens should be done within 24 hours of hospital arrival, including for patients that receive acute stroke treatments such as intravenous thrombolysis and EVT [Strong recommendation; Moderate quality of evidence].

   b. Patients should remain NPO (*nil per os* [no oral intake]) until a swallowing screen is completed, for patient safety [Strong recommendation; High quality of evidence].

   c. Oral medications should not be administered until a swallowing screen using a validated tool has been completed and found to be normal [Strong recommendation; Moderate quality of evidence]; 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 [Strong recommendation; Low quality of evidence].

   e. Patients found to have abnormal swallowing ability on screening should remain NPO and be referred to a healthcare professional with expertise in this area for further swallowing assessment [Strong recommendation; Moderate quality of evidence].

   Note: *Swallow assessments are particularly important for patients discharged to the community directly from the emergency department or repatriated to a lower level of care.*

Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke, and CSBPR Rehabilitation and Recovery following Stroke module, Section 7 for additional information on screening for swallowing ability and dysphagia management.

iii. **Urethral catheters:** The use of indwelling urethral catheters should generally be avoided due to the risk of urinary tract infections [Strong recommendation; Moderate quality of evidence]. *Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke for additional information.*

a. Insertion of an indwelling urethral catheter should be considered for patients undergoing EVT when necessary, but this should not delay beginning the procedure. The need to retain the catheter should be reconsidered after the end of the EVT procedure, and the use of the catheter should be discontinued as soon as the patient is able to resume voiding on their own [*Conditional recommendation*; Low quality of evidence].

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 [Strong recommendation; Moderate quality of evidence].

c. If used, indwelling catheters should be reassessed daily and removed as soon as possible [Strong recommendation; High quality of evidence].

d. Fluid status and urinary retention should be included as part of routine monitoring of vital sign assessments [Strong recommendation; Moderate quality of evidence].

iv. **Temperature:** Temperature should be routinely monitored and treated per local protocols [Strong recommendation; Moderate quality of evidence]. *Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke for additional information.*

v. **Oxygen:** Supplemental oxygen is not required for patients with normal oxygen saturation levels [Strong recommendation; Moderate quality of evidence].

4.7 Virtual Acute Stroke Care (Telestroke)

Note: The recommendations in Section 4.7 are mainly aimed at Level 3, 4, and 5 stroke centres (based on CSBPR categories; refer to Figure 2, Acute Stroke Service Capability). Patients with suspected acute stroke presenting to a Level 1 or 2 hospital that does not have acute stroke capability should be immediately transferred to the closest Level 3, 4, or 5 stroke centre per local bypass protocols and agreements.

i. Virtual acute stroke care delivery modalities should be integrated into stroke care planning and service delivery to ensure equitable access to care across geographic regions in Canada [Strong recommendation; Moderate quality of evidence].

4.7.1 Organization of Virtual Healthcare Services for Acute Stroke Management

i. Virtual acute stroke care networks should be in place and readily available when stroke expertise is not available on-site, to allow access to consultations with stroke experts for acute stroke assessment, diagnosis, and treatment, including acute thrombolytic therapy and decision-making for EVT [Strong recommendation; Moderate quality of evidence].

ii. Consulting and referring sites should have standardized protocols and processes in place to ensure access to stroke experts through virtual healthcare modalities, available 24 hours a day, seven days a week to provide equitable access to time-driven advanced stroke care across Canada [Strong recommendation; Moderate quality of evidence].

iii. The consultant should be a physician with specialized training in acute stroke management and must have timely access to diagnostic-quality neurovascular (e.g., brain CT, CTA) images during the virtual acute stroke consultation [Strong recommendation; High quality of evidence].

Refer to CSBPR Virtual Stroke Care Implementation Toolkit for additional information.

Note: The decision to use acute stroke therapies in emergency management requires imaging to rule out hemorrhage. Refer to Sections 4, 5, and 6 in this document for additional information on imaging and revascularization.

iv. Real-time two-way audiovisual communication should be in place to enable remote clinical assessment of the patient by the consulting stroke expert [Strong recommendation; Moderate quality of evidence].

   a. Virtual acute stroke modalities including video-conferencing and teleradiology systems may be considered to support screening and decision-making regarding candidacy for thrombolysis and/or EVT in appropriate cases and to facilitate transfer to endovascular-enabled stroke centres [Strong recommendation; Moderate quality of evidence].

   b. The benefits of telephone consultation without video are not well-established and every attempt should be made to connect via a video link [Conditional recommendation; Low quality of evidence].

v. All laboratory and diagnostic results required by the consultant should be made readily available during the virtual acute stroke care consultation [Strong recommendation; Moderate quality of evidence].

vi. Referring physicians should follow an established protocol or algorithm that describes the critical steps and inclusion/exclusion criteria for thrombolysis and/or recanalization therapies, which are agreed to by both the referring and consulting sites [Strong recommendation; High quality of evidence]. *Refer to Section 3 Emergency Medical Services Management of Acute Stroke for additional information.*

vii. Referring physicians and nursing staff who may be involved in virtual acute stroke consultations should ideally be trained in administration of the NIHSS, so they can assist the telestroke consultant efficiently and competently during the remote video neurological examination [Strong recommendation; Moderate quality of evidence].

viii. The most responsible physician remains the attending physician at the referring site. Decision-making is a consensus process that is achieved in consultation with the attending medical staff at the referring site, the patient and family, and the consulting physician with stroke expertise [Strong recommendation; Low quality of evidence].

ix. A consulting physician with stroke expertise should remain accessible as they may be required to provide ongoing guidance to the referring site following initial consultation [Strong recommendation; Low quality of evidence].

x. Protocols should be in place that define patient transfer criteria to a more advanced stroke care facility when clinically indicated (e.g., for endovascular [if available], neurosurgical intervention) [Strong recommendation; Low quality of evidence].

   a. The virtual acute stroke care system should identify the stroke centres that are able to provide endovascular and neurosurgical care [Strong recommendation; Low quality of evidence].

   b. For patients who are deemed eligible for endovascular treatment or neurosurgical interventions, protocols should be in place to define the process for patient transfer [Strong recommendation; Moderate quality of evidence]. *Refer to Section 6 Acute Antithrombotic Therapy for additional information.*

xi. The use of standardized documentation should be considered for both the referring site and the consulting site, in accordance with hospital processes, jurisdictional legislation, and regulatory bodies [Strong recommendation; Low quality of evidence]. This may include:

   a. A consultation note provided by the consulting physician to the referring site at the end

of the consultation, to be included in the patient medical record [Strong recommendation; Low quality of evidence].

b. A discharge summary sent by the referring site to the consulting virtual acute stroke physician to provide feedback about the patient's outcome [Strong recommendation; Low quality of evidence].

c. For patients who are transferred to another hospital (e.g., "drip and ship"), a discharge summary from the receiving hospital to the referring physician and the virtual acute stroke physician [Strong recommendation; Low quality of evidence].

xii. Processes should be in place to ensure timely and effective transfer of up-to-date, relevant information in the patient medical record (e.g., patient progress, treatment plans, plans for ongoing follow-up, discharge recommendations) from the consulting healthcare provider to the referring site, in accordance with clinical care processes, organizational requirements, jurisdictional legislation, and regulatory requirements [Strong recommendation; Low quality of evidence]. *Refer to CSBPR Transitions and Community Participation Following Stroke Section 3.3 for additional information.*

xiii. Data related to the virtual acute stroke consultation and outcome should ideally be collected by the virtual acute stroke program for continuing quality improvement [Strong recommendation; Low quality of evidence].

4.7.2 Staff Training and Ongoing Education

i. Consulting physicians and other healthcare professionals involved in virtual acute stroke consults should have expertise and experience in managing patients with stroke [Strong recommendation; Low quality of evidence].

ii. It is recommended that virtual acute stroke care providers attain and maintain the necessary competencies required in provide safe, competent virtual care and to create a satisfactory telehealth encounter for both the patient and the healthcare provider [Strong recommendation; Low quality of evidence].

iii. Referring and consulting service providers should be trained to use the virtual acute stroke system and should understand their roles and responsibilities for the technical and clinical aspects of an acute virtual stroke care consultation [Strong recommendation; Low quality of evidence].

iv. Virtual stroke care training should include physicians, nurses, therapists, and any support staff (e,g., members of technology department) who may be involved in any virtual acute stroke consultation or therapy appointment [Strong recommendation; Low quality of evidence].

v. Ongoing virtual acute stroke training and education with a regular update cycle is useful to ensure competency of providers [Strong recommendation; Low quality of evidence]. *Refer to CSBPR Virtual Stroke Care Implementation Toolkit for additional information and resources for staff training.*

vi. Continuing education in online and face-to-face formats is useful to ensure remote-based practitioners have access to ongoing education [Strong recommendation; Low quality of evidence].

Section 4.7 Clinical Considerations

1. Mock acute stroke patient scenarios and practice cases may be helpful, especially for acute/emergent virtual stroke care at new sites, and where the ongoing volume of cases is low.

2. Routine checks of acute virtual stroke care equipment (both video-conferencing and imaging systems such as PACS) should be done to ensure the equipment will function properly in an emergency. This may be done as part of routine checks on other emergency equipment such as crash carts. Some systems may have a back-up system or alarms for malfunctioning

equipment.

3. Where electronic health records are available, health information sharing regulations that comply with provincial and federal privacy legislation should be developed, to allow an individual patient's record to be shared with referring and consulting facilities.
4. Efforts should be made to design telestroke technology, so it is easy to use and operate, to facilitate adoption of the technology and decrease the time needed to meet educational requirements.

Box 4A Exclusion Criteria for IV Thrombolysis Selection Imaging: CT Findings

1. Signs of hemorrhagic stroke on CT.
2. CT showing early signs of extensive loss of grey/white matter differentiation and/or low attenuation changes in the affected territory such that the majority of the territory has already infarcted. For the middle cerebral artery (MCA) territory, this would correspond with an ASPECTS of <6.

Refer to Section 5 Acute Ischemic Stroke Treatment for additional intravenous thrombolysis clinical inclusion and exclusion criteria.

Rationale

Patients with suspected stroke often have significant comorbidities which may complicate management of stroke. In addition, factors that may explain the cause of the stroke or predict later complications (e.g., space-occupying infarction or bleeding, or recurrent stroke), will have an impact on treatment decisions; therefore, an efficient and focused assessment is required to understand the needs of each patient. Given that up to 20% of clinicians may disagree on the clinical diagnosis of stroke (versus non stroke), one of the most important initial assessments is brain imaging. Since it is impossible to differentiate a lesion's etiology, which may be ischemic or hemorrhagic in nature, by clinical examination alone, a CT scan or MRI is essential to identify patients who may be eligible for time-sensitive treatments. Other essential initial investigations include vascular imaging, monitoring of vital signs, blood work, cardiovascular investigations, dysphagia screens, and seizure assessment.

Initial management of elevated blood pressure in acute patients with stroke remains controversial due to the lack of evidence to clearly guide practice. At the same time, this is an area where clinicians often seek guidance from stroke specialists. Blood pressure recommendations emphasize caution and diligence in monitoring and treating extremely high blood pressure in the first hours after stroke onset.

People with lived experience discussed the value of healthcare providers providing information about the scan process. They discussed how being in hospital can be frightening, and that a CT or MRI may be new for the individual and so support, validation of feelings, and information can help the person get through this experience.

People with lived experience also talked about the value of having someone present to help explain to the person with stroke and their family or informal caregivers what is occurring during the acute phase, from an intervention and experiential perspective. They shared that fears, stress, and anxiety can affect their ability to understand information in the moment and can make it harder to ask the right questions. Having someone to provide this type of support and navigation would be helpful. People with lived experience also identified that mental health support is an important part of care, starting right in the emergency department.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Local protocols to ensure all patients with stroke have rapid access to CT with CTA of the extracranial and intracranial vessels completed at the same time as the initial brain imaging.
2. Protocols for “code stroke” activation of the stroke team and diagnostic services prompted by receiving pre-notification by paramedics of an incoming suspected stroke patient.
3. Protocols to prioritize suspected patients with stroke in triage queues at emergency departments and diagnostic suites to ensure timely access to diagnostic service, thrombolysis and EVT (where applicable), and priority transport to the nearest acute treatment capable centre.
4. Agreements to ensure patients initially managed in rural hospitals without neurovascular imaging capability have timely access to CTA with imaging of the extracranial and intracranial vessels at partnering hospitals.
5. Protocols and standing orders to guide initial blood work and other clinical investigations.
6. Local protocols, especially in rural and remote locations, for rapid access to clinicians experienced in interpretation of diagnostic imaging, including access through telemedicine technology.
7. Repatriation protocols in place to enable the patient to be transferred back to the originating hospital after acute treatments when appropriate.
8. Availability of physicians and other healthcare professionals with stroke expertise across provinces and regions, including provincial and regional recruitment and retention strategies to increase accessibility of acute stroke services for all Canadians.

Performance Measures

System indicators

1. Proportion of people with acute stroke who are pronounced dead by EMS or in the emergency department.

Process indicators

2. Median time from patient with suspected stroke’s arrival to hospital to first non-contrast CT head or brain MRI imaging scan.
3. Median time from patient with suspected stroke’s arrival to hospital to first CTA or MRA of extracranial and intracranial vessels.
4. Proportion of patients with stroke who receive a CT or MRI scan in <15 minutes from hospital arrival. Applies to patients arriving <6 hours from last known well time, and without contraindications to thrombolysis.
5. Proportion of all patients with stroke who receive a brain CT/CTA within 12 hours of hospital arrival. (*Note, Accreditation Canada indicator states on ‘same day of arrival’)*
6. Proportion of patients with carotid territory stroke syndrome who have carotid imaging in the ED or outpatient carotid imaging.
7. Proportion of people with acute stroke who receive a virtual care consult to a stroke expert at another site.
8. Virtual stroke care: Time to initiation of virtual acute stroke consult from:
    a. stroke symptom onset (last time patient was known to be normal)

b. arrival in emergency department
c. completion of the CT scan

9. Proportion of patients managed with Telestroke where the Telestroke consultant's note is found in the patient's chart.
10. Proportion of patients with acute stroke screening in the emergency department or inpatient unit for dysphagia within 12 hours of arrival to hospital.

Patient-oriented outcome and experience indicators

In development.

Measurement Notes

a. Emergency department activities are addressed in Section 4. Include the diagnostic evaluation, consideration of treatment options, and initiation of treatment which should be completed in <60 minutes. The goal is a target 90th percentile for door-to-needle time of 60 minutes (upper limit); and a target ***median*** door-to-needle time of 30 minutes or less [Kamal et al., CJNS 2015]. *Note: The goal is to transfer admitted patients with stroke within four hours of arrival where possible; however, many hospitals operate at full capacity and patients may have to remain in the emergency department after they are admitted to inpatient care while waiting for an inpatient bed.*
b. Data may be obtained from laboratory reports or patient chart.
c. CT and CTA imaging time should be based on time of first slice by the scanner. Specify in the results which type of scan (CT or CTA, separately or combined) was measured and reported.
d. Stratify analysis for patients who arrive within 3.5 hours of stroke symptom onset and those who arrive within 4.5, 6, and 24 hours from stroke symptom onset.
e. Performance measure 1: Applies to patients who may be candidates for acute thrombolysis (i.e., who arrive at hospital within 4.5 hours of stroke symptom onset) and to patients who may be eligible for other time-sensitive interventions.
f. Time interval measurements for CT and MRI should be calculated from the time the patient enters the emergency department until the time noted on the actual brain imaging scan.
g. For outpatient carotid imaging, a notation should appear in the discharge summary, or in nursing notes, with an indication that the test has actually been requested or requisitioned prior to the patient leaving the hospital.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practices Acute Stroke Management Module Appendix 3, Table 4: Screening and Assessment Tools for Acute Stroke Severity
- Canadian Stroke Best Practices Acute Stroke Management Section 2, Table 2A: Recommended Laboratory Investigations for Acute Stroke and Transient Ischemic Attack
- Heart & Stroke: Virtual Stroke Care Implementation Toolkit: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/csbpr-virtual-stroke-toolkit-final

- Canadian Cardiovascular Society Atrial Fibrillation Guidelines: https://ccs.ca/guidelines-and-position-statement-library/
- American College of Chest Physicians (CHEST) Pulmonary Vascular Guidelines and Expert Panel Reports: https
- Canadian Association of Radiologists guidelines: http://www.car.ca/en/standardsguidelines.aspx
- Hypertension Canada Guidelines: www.hypertension.ca
- Stroke Engine: http://strokengine.ca/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Signs of Stroke: http://www.heartandstroke.ca/stroke/signs-of-stroke
- Heart & Stroke: FAST Signs of Stroke: https://www.heartandstroke.ca/stroke/signs-of-stroke/fast-signs-of-stroke-are-there-other-signs
- Heart & Stroke: What is Stroke? https://www.heartandstroke.ca/stroke/what-is-stroke
- Heart & Stroke: Atrial Fibrillation: https://www.heartandstroke.ca/heart-disease/conditions/atrial-fibrillation
- Heart & Stroke: Virtual Healthcare Checklist: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbp-infographic-virtual-healthcare-checklist
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

Initial Assessment

Standard assessments for patients with suspected acute stroke presenting to the emergency department include a neurological examination, monitoring of vital signs, blood work, imaging and cardiovascular investigations, dysphagia screens, and seizure assessment. It is also important to identify patients with stroke “mimics,” to avoid unnecessary and expensive investigations and inappropriate long-term prevention treatments. Patients presenting with stroke symptoms may ultimately be diagnosed with other conditions such as migraine headache, vertigo, metabolic disturbances, brain tumours, presyncope/syncope, or anxiety (Karliński et al., 2015). To assess stroke severity, the NIHSS is used most widely, is known to have good validity and reliability, and correlates well with stroke outcome. It has also been suggested as the best scale to identify patients with potential LVO who may be eligible for mechanical thrombectomy (Smith et al., 2018).

Neurovascular Imaging

Immediate access to brain and vascular imaging is required for all patients arriving to hospital with suspected stroke or TIA. A NCCT scan is considered the imaging standard and the most cost-effective method to be used initially to identify acute ischemic stroke and rule out intracranial hemorrhage (Wardlaw et al., (2004). While MRI with diffusion-weighted sequences (DWI) may be more sensitive in detecting early changes associated with ischemia, especially in patients with small infarcts, it may not be immediately available. Using the results from 8 studies, Brazzelli et al. (2009) reported that the

sensitivity of MRI was higher compared with CT (99% vs. 33%). Both imaging modalities had good specificity (92% and 100%). If an MRI is available and performed in place of CT, enhanced imaging in the form of DWI, GRE, and FLAIR is indicated. Brunser et al. (2013) included 842 patients admitted to the emergency department with a suspected ischemic stroke. Diffusion-weighted imaging (DWI) examinations were performed for all patients. For patients with a final diagnosis of stroke, the sensitivity of DWI in detecting ischemic stroke was 90% (95% CI 87.9 to 92.6), and specificity was 97% (95% CI 91.8 to 99.0).

Early detection of hemorrhage is essential since the presence of blood in the brain or subarachnoid space is the main contraindication for the administration of antithrombotics, intravenous thrombolytic therapy, and mechanical thrombectomy. Early imaging is particularly important for patients who may be potential candidates for thrombolytic therapy, since there is a narrow therapeutic window for its administration. While an NCCT may be sufficient for patients presenting within 4.5 hours of symptom onset who may be eligible for treatment with intravenous thrombolysis, those presenting with an unknow time of symptom onset require advanced imaging using either penumbral imaging, or MRI with DWI-FLAIR mismatch. In the WAKE-UP trial (Thomalla et al., 2018), MRI with DWI-FLAIR mismatch was used as the primary imaging modality (although MRP data were also used in a subgroup of patients), while the imaging criteria in the EXTEND trial (Ma et al., 2019) required either CTP or perfusion-diffusion MRI to identify potentially eligible patients. In both trials, patients who received treatment with t-PA had better 90-day functional outcome compared to those who received placebo. While CTP imaging has been shown to be more accurate than NCCT, with similar accuracy to CTA in detecting acute ischemic stroke (Shen et al., 2017), its availability is limited, with increased radiation and contrast doses and has the potential for causing treatment delays. The use of CTP for acute patients with stroke should be reserved for centres with well-established protocols and experience in interpreting the results, or the use of quantitative CTP using RAPID software.

Early trials of mechanical thrombectomy, including patients who were last known well within the previous 6 hours, required CTA or MRA diagnosis of LVO as an inclusion criterion (REVASCAT, Jovin et al., 2015; SWIFT PRIME, Saver et al., 2015; ESCAPE, Goyal et al., 2015). In the EXTEND-IA trial, (Campbell et al., 2015), inclusion required a 20% mismatch between core infarct and ischemic penumbra identified using CTP. In trials where the treatment window was extended to 6 to 24 hours since last known well, the imaging criteria were more advanced. The criteria for the DAWN trial (Nogueira et al., 2018) included clinical imaging mismatch defined using both core infarct size and NIHSS score on MR-DWI or CTP-rCBF maps, while DEFUSE-3 (Albers et al., 2018) used target mismatch profile on CTP or MRI (ischemic core volume <70 ml, mismatch ratio ≥1.8 and mismatch volume 15 ml).

Acute Blood Pressure Management

For patients eligible for treatment with intravenous thrombolysis, reductions in blood pressure may be indicated when elevations are extreme (e.g., systolic blood pressure [SBP] ≥220 mm Hg or diastolic blood pressure [DBP] ≥120 mm Hg); however, trials including patients with these levels of extreme hypertension have not been published. In the blood pressure arm of the ENCHANTED Trial, Anderson et al. (2019) included 2,227 patients ≥18 years who were eligible to receive t-PA within 4.5 hours of stroke onset, with a SBP ≤150 mmHg and who were able to begin intensive treatment for hypertension within 6 hours. Patients were randomized to an intensive SBP lowering group, with target SBP of 130–140 mmHg achieved within 60 minutes of randomization, which was to be maintained for ≥72 hours, or hospital discharge, or death; or to guideline-recommended BP lowering group with target SBP < 180 mmHg, after commencement of thrombolysis treatment. Although mean SBP over 24 hours was significantly lower in the intensive group (144·3 vs. 149·8 mm Hg), the percentage of patients who

experienced death or disability at 90 days did not differ significantly between groups (46·5% vs. 48·0%, adj OR=0·94, 95% CI 0·78–1·14, p=0·55). Significantly fewer patients in the intensive groups had an ICH (14.8% vs. 18.7%, OR= 0·75, 0·60–0·94).

Yuan et al. (2020) recruited 483 patients with acute severe stroke (excluding those who received intravenous thrombolysis or mechanical thrombectomy), and elevated blood pressure in the Controlling Hypertension After Severe Cerebrovascular Event (CHASE) Trial. Patients were randomized to receive an individualized blood pressure lowering group (with 10–15% reduction in SBP from admission level, achieved within 2 hours and sustained for 1 week) or standard blood pressure lowering group (with a target SBP of <200 mm Hg in acute ischemic stroke group, sustained for 1 week). During the first 24 hours, the mean SBP was 144.0 mm Hg in the individualized treatment group and 148.2 mm Hg in the standard treatment group. The odds of a poor outcome (mRS 3-5 or all-cause death, at 90 days) were not reduced significantly in the individualized group (71.1% vs. 73.4%, with adjustment for age, sex, and baseline Glasgow Coma Scale score: OR=0.89, 95% CI 0.47 to 1.19; p=0.222); however, individualized blood pressure lowering treatment had a significant effect on reducing the neurological deficits at hospital discharge as evaluated by NIHSS (β estimate=0.13; 95%CI -0.2 to -0.03; p= 0.009).

Cardiovascular Investigations

An ECG) should be performed immediately to identify arrhythmias for all patients with stroke and TIA presenting to the emergency department. Atrial fibrillation (AF) is commonly diagnosed post-stroke and is of particular concern due to its role in forming emboli. Sposato et al. (2015) included the results from 11 studies in which cardiac monitoring was initiated in the emergency department. An estimated 7.7% of patients without a history of AF were newly diagnosed.

Glucose Management

Baseline hyperglycemia has been identified as independent predictor of poor stroke outcome and may be a marker of increased stroke severity. The presence of hyperglycemia may be of particular concern among patients without a history of premorbid diabetes. Using patient data from the ECASS II trial, Yong & Kaste (2008) examined the association between stroke outcomes and four patterns of serum glucose over the initial 24-hour period post stroke. Among 161 patients with pre-morbid diabetes, the odds of poor outcome were not increased significantly for patients with persistent hyperglycemia, or among patients with hyperglycemia at 24 hours, compared with patients with persistent normoglycemia. However, among 587 non-diabetics, patients with persistent hyperglycemia experienced significantly worse outcomes compared to those with persistent normoglycemia. The odds of a good functional outcome at 30 days, minimal disability at 90 days, or neurological improvement over 7 days were significantly reduced compared with patients with persistent normoglycemia, while the odds of 90-day mortality and parenchymal hemorrhage were increased significantly. Since initial hyperglycemia has been associated with poor stroke outcome, several trials have evaluated the potential benefit of tight blood glucose control early following stroke, with null results. In the Stroke Hyperglycemia Insulin Network Effort (SHINE) trial, 1,151 patients ≥18 years with hyperglycemia following acute ischemic stroke were recruited (Johnston et al., 2019). Patients were randomized to receive intensive or standard glucose-lowering treatment during hospital stay. Patients in the intensive treatment group received a continuous intravenous insulin infusion as needed to maintain a blood glucose concentration of 4.44-7.22 mmol/L. Patients in the standard treatment group received insulin on a sliding scale to maintain a blood glucose concentration of 4.44-9.93 mmol/L. The trial was halted prematurely due to futility. While mean blood glucose level was significantly lower in the intensive group during treatment (6.6 vs. 9.9 mmol/L), there was no significant increase in the odds of a favourable outcome at 90 days (20.5% of patients in the intensive groups had a favourable outcome at

90 days vs. 21.6% in the standard group [adj RR=0.97, 95% CI 0.87 to 1.08, p=0.55]). A significantly higher percentage of patients in the intensive group experienced severe hypoglycemia (2.2% vs. 0%, p<0.01). Similar findings were reported in the GIST-UK trial (Gray et al., 2007) in which 899 patients were randomized to receive variable-dose-insulin glucose potassium insulin (GKI) to maintain blood glucose concentration between 4-7mmol/L or saline (control) as a continuous intravenous infusion for 24 hours. For patients in the control group, if capillary glucose >17 mmol/L, insulin therapy could be started at the discretion of the treating physician. Treatment with GKI was not associated with a significant reduction in 90-day mortality (OR= 1.14; 95% CI 0.86 to 1.51; p=0.37) or the avoidance of severe disability (OR= 0.96; 95% CI 0.70 to 1.32). Rescue dextrose was given to 15.7% of GKI-treated patients for asymptomatic prolonged hypoglycemia. The trial was stopped prematurely due to slow enrollment.

Additional Management Considerations

Chest x-ray: Saber et al. (2016) reviewed data from 615 patients included in the Interventional Management of Stroke III (IMS-III) trial who had a chest radiograph. Patients with a chest radiograph that was completed before intravenous thrombolysis treatment had a significantly longer mean door-to-needle times than those who had x-rays completed after thrombolysis treatment (75.8 vs. 58.3 minutes, p=0.0001). Chest radiograph before thrombolysis was an independent predictor of door-to-needle time ≥60 minutes (OR=2.78, 95% CI 1.97–3.92).

Swallowing assessment: In the T^3 trial (Middleton et al., 2019) evaluating the benefit of nursing protocols aimed at prompt identification and treatment of patients with fever, hyperglycemia, and dysphagia, over 85% of patients in both the intervention and control group remained NPO until screened. Over 80% received a swallow screen or assessment within 24 hours of emergency department admission.

Urethral catheters: Data from 11,093 patients with acute stroke included in the HeadPoST trial, which examined the effect of head position (flat vs. elevated) on stroke outcome, were used to evaluate the use of indwelling urinary catheter (IUC). Ouyang et al. (2020) compared the outcomes of the 12% of patients who received an IUC with the remainder who did not. Those with an IUC had a greater likelihood of a poor outcome (76.6% vs. 34.7%; p < 0.0001). IUC was an independent predictor of a poor outcome (OR=1.40, 95% CI 1.13–1.74). Those with IUC had a greater likelihood of a UTI (1.5% vs. 0.6%; p= 0.0002), although IUC was not an independent predictor of UTI after multiple adjustment (OR=1.13, 95% CI: 0.59–2.18).

Supplemental oxygen: Roffe et al. (2017) recruited 8,003 adults with acute stroke within 24 hours of hospital admission, with no clear indications for or contraindications to oxygen treatment. Participants were randomized 1:1:1 to receive continuous oxygen for 72 hours, nocturnal oxygen (21:00 to 07:00 hours) for 3 nights, or control (oxygen only if clinically indicated). Oxygen was given via nasal tubes at 3 L/min if baseline oxygen saturation was 93% or less and at 2 L/min if oxygen saturation was >93%. Oxygen supplementation did not significantly improve functional outcome at 90 days. There were no significant differences between groups (2 oxygen groups combined vs. control and continuous oxygen vs. nocturnal oxygen) for any of the 7- or 90-day outcomes (neurological improvement, mortality, or disability).

Virtual Acute Care

Telestroke can be used to increase access to thrombolytic treatment at facilities that lack 24 hour, 7 day a week on-site stroke expertise, using two-way audiovisual equipment to carry out a detailed stroke examination, combined with a system to reliably transmit CT scan results. The safety, feasibility,

and efficacy of the "spoke and hub" model, which connects a tertiary stroke centre to one or more distant primary care centres, has been established in many studies conducted in Europe and North America (LaMonte et al., 2003; Wiborg et al., 2003; Schwamm et al., 2004; Audebert et al., 2005; Waite et al., 2006; Vaishnav et al., 2008; Legris et al., 2016). In some of these studies, although minor technical difficulties were reported, the number of patients treated with t-PA increased at the stroke sites where telestroke systems were implemented and the symptom onset-to-treatment time decreased. The outcomes for 153,272 patients treated at hospitals with and without telestroke capacity following admission for acute ischemic stroke in the United States were compared (Wilcock et al., 2021). The frequency of reperfusion therapies received was significantly higher at telestroke hospitals (6.8% vs 6.0%; difference, 0.78 percentage points; 95% CI 0.54-1.03, p < .001). The risks of receiving thrombolysis and thrombectomy were both significantly higher at telestroke hospitals (RR=1.12, 95% CI 1.08 to 1.17 and RR=1.42, 95% CI 1.25 to 1.62, respectively). Both 7- and 30-day mortality was significantly lower in the telestroke hospitals (7-day: 6.03% vs. 6.33%; RR=0.95, 95% CI 0.92 to 0.99, 30-day:13.1% vs 13.6%; RR=0.96, 95% CI 0.94 to 0.99). In Ontario, Porter et al. (2018) conducted an audit to determine whether the safety outcomes of 214 patients treated using the Ontario Telestroke Program with intravenous thrombolysis over a two-year period were compared with those of 1,885 patients treated at regional stroke centres, district stroke centres, and non-designated centres. The administration of t-PA using telestroke was not associated with an increased risk of death within 7 or 90 days (adjusted HR=1.29, 95% 0.68- 2.44 and adjusted HR=1.01, 95% CI 0.67-1.50, respectively), nor was its use associated with an increased risk symptomatic intracerebral hemorrhage (ICH) or poor outcome (adjusted HR=0.71, (95% 0.29-1.71 and adjusted HR=0.75, 95% CI 0.46-1.23, respectively). The results from a systematic review also indicate the outcomes of patients treated with t-PA through telemedicine vs. traditional in-hospital care are similar. Zhai et al. (2015) conducted a systematic review & meta-analysis including the results of 8 studies that compared the outcomes of patients treated with t-PA through telemedicine vs. traditional in-hospital care. Telestroke systems were not associated with increased odds of symptomatic ICH (OR=1.08, 95% CI 0.47-2.5, p=0.85) or mortality (OR=0.95, 95% CI 0.82-1.11, p=0.51.

The outcomes and indicators associated with telestroke services provided by videoconferencing and telephone only appear similar. In the Stroke Team Remote Evaluation using a Digital Observation Camera (Stroke DOC) trial, Meyer et al. (2008) randomized 222 patients to receive telestroke using real-time, two-way audio/video or telephone consultations, to assess the patient's candidacy for t-PA treatment. Consultations were provided by staff at a single hub institution to patients located at 4 remote sites. The number of patients treated with t-PA was similar between groups (28% vs. 23%). Mean times from stroke onset to t-PA were 157 and 143 minutes in the telemedicine and telephone groups respectively (p=0.137). There were no differences between groups (telemedicine vs. telephone) in the occurrence of ICH (7% vs. 8%, p=1.00), good outcome at 90 days, defined as a mRS score of 0-1 (30% vs. 32%, p=1.00), or 90-day mortality after adjustment for baseline NIHSS score (OR=3.4, 95% CI 0.6-19, p=0.168). However, correct treatment decisions were made more often using videoconferencing (98% vs. 82%, p=0.0009). In a follow-up study (Meyer et al., 2012), which assessed six- and twelve-month outcomes, there were no differences between groups in mortality or the proportion experiencing a good outcome at either assessment point.

Sex & Gender Considerations

Based on the results of studies presented in the accompanying evidence tables, examinations of sex differences were largely absent, with two exceptions. Sex was not found to be a significant effect modifier on the primary outcome in the treatment of hypertension in the ENCHANTED trial (Anderson et al. 2019). Sex was also not found to be a significant effect modifier for the outcomes of either reperfusion treatment or 30-day mortality in a study comparing telestroke-enabled hospitals with those

without telestroke capacity (Wilcock et al. 2021).

Reference List and Evidence Tables

Evidence Table and Reference List 4: Emergency Department Evaluation and Management of Patients with TIA and Acute Stroke

Evidence Table and Reference List 4B: Emergency Department Evaluation and Management of Patients with TIA and Acute Stroke – Neurovascular Imaging

Evidence Table and Reference List 4C: Emergency Department Evaluation and Management of Patients with TIA and Acute Stroke - Virtual Care

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 5 Acute Ischemic Stroke Treatment

*Note: Treatment benefits from revascularization decrease over time, and 1.9 million brain cells die every minute following stroke onset (Saver, 2006); therefore, all patients with stroke **should be treated as quickly as possible** to maximize the potential for the best outcomes. The new extended time windows should not be interpreted to mean that time to treatment should be slowed in any way.*

Acute stroke treatment is shifting from a time-based to a tissue-based paradigm as emerging evidence suggests that the speed of stroke progression differs between individuals and beneficial treatment may be offered beyond standard time windows. Using time as the sole criterion to select patients for thrombolysis and endovascular thrombectomy (EVT) may lead to missed opportunities for treatment. Nevertheless, "time is brain" remains a reality, and delays in stroke diagnosis and treatment are associated with worse outcomes" (Desai and Smith, Cardiovascular Disease and Stroke, 2013).

5. Acute Ischemic Stroke Treatment Recommendations 2022

5.1 Patient Selection for Acute Ischemic Stroke Treatments

i. **Within 6 hours of stroke symptom onset:** 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 virtual acute stroke care/telestroke consultation) to determine their eligibility for both intravenous thrombolysis and/or interventional treatment with EVT within a 6-hour window from stroke symptom onset or last known well time) [Strong recommendation; High quality of evidence].

   a. When it is unclear if a patient should be treated with IV thrombolysis, urgent consultation with a stroke specialist on-site or through virtual stroke services is recommended [Strong recommendation; Low quality of evidence]

   b. If there is uncertainty about interpretation of CT imaging, urgent consultation with a radiologist either on-site or through virtual telestroke services is recommended [Strong recommendation; Low quality of evidence].

ii. **Beyond 6 hours of stroke symptom onset or last known well:** All patients with disabling acute ischemic stroke who are between 6 and 24 hours of stroke symptom onset or last known well should be rapidly screened to determine eligibility for urgent advanced neurovascular imaging and acute stroke treatments [Strong recommendation; Moderate quality of evidence]. *Refer to Box 5A for a summary of treatment time windows.*

Section 5.1 Clinical Considerations

1. Intravenous thrombolysis beyond 4.5 hours may be considered, in consultation with a physician with stroke expertise and based on advanced imaging.
2. If a large vessel occlusion (LVO) is present, consideration for thrombolysis beyond 4.5 hours from the time the patient was last known well should not delay decisions regarding EVT.

5.2 (REVISED FOR 2022) Intravenous Thrombolysis Administration

i. All eligible patients with disabling ischemic stroke, who can receive intravenous thrombolysis with either alteplase or tenecteplase within 4.5 hours of stroke symptom onset time or last known well time should be offered intravenous thrombolysis [Strong recommendation; High quality of evidence]

Refer to Section 4.2 and Box 4A for detailed recommendations on neuroimaging. Refer to Box 5A for time windows, and Box 5B for inclusion and exclusion criteria for intravenous thrombolysis eligibility. Refer to Section 5.1 Clinical Considerations for information about

patients who arrive beyond the 4.5-hour time window.

ii. All eligible patients should receive intravenous thrombolysis ***as soon as possible*** after hospital arrival [Strong recommendation; High quality of evidence]~~,~~ with a target median door-to-needle time of <= 30 minutes and a door-to-needle time of <= 60 minutes in at least 90% of treated patients [Strong recommendation; Moderate quality of evidence]

   a. Treatment should be initiated as soon as possible after patient arrival and CT scan completion [Strong recommendation; High quality of evidence].

   b. Every effort should be made to ensure door-to-needle times are routinely monitored and improved [Strong recommendation; Moderate quality of evidence].

iii. **Alteplase dose:** If using alteplase, the dose of 0.9 mg/kg to a maximum of 90 mg total dose should be administered, 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 minutes [Strong recommendation; High quality of evidence].

iv. **(NEW FOR 2022) Tenecteplase** may be considered as an alternative to alteplase within 4.5 hours of acute stroke symptom onset [Strong recommendation; Moderate quality of evidence].

   a. **Tenecteplase dose**: If administering Tenecteplase, the dose of 0.25 mg/kg up to a maximum of 25 mg should be administered, given as a single bolus over 5 seconds [Strong recommendation; Moderate quality of evidence].

Caution: The dosing of alteplase and tenecteplase for stroke is NOT the same as the dose protocols for administration of these medications for myocardial infarction or massive pulmonary embolism.

v. Individuals receiving IV thrombolysis should be closely monitored for the first 24 hours for complications from IV thrombolysis administration:

   a. For patients with sudden deterioration during or following administration of IV thrombolysis, an emergent CT scan should be done [Strong recommendation; Moderate quality of evidence].

   b. For patients with orolingual angio-edema:

      1. IV thrombolysis should be discontinued if still infusing at the first signs of angioedema [Strong recommendation; Moderate quality of evidence].

      2. The following medications are recommended: antihistamines (H1 blocker [e.g., diphenhydramine], H2 blocker [e.g., famotidine]). Consider glucocorticoids inhaled racemic epinephrine as part of standard airway management [Strong recommendation; Low quality of evidence].

For patients with symptomatic ICH following IV thrombolysis refer to section 5.6.

   c. **Systemic hemorrhage**: For patients with spontaneous systemic hemorrhage at a non-compressible site (e.g., gastrointestinal hemorrhage, oral hemorrhage), IV thrombolysis should be discontinued, consideration should be given to lowering blood pressure, and hemostatic management should be considered [Strong recommendation; Low quality of evidence].

      1. Consultation with appropriate specialists should be undertaken to aid in achieving hemostasis [Strong recommendation; Low quality of evidence].

Section 5.2 Clinical Considerations

1. **Consent:** Intravenous thrombolysis and EVT are considered the standard of care for acute stroke treatment. Routine procedures for emergency consent apply.

2. **Intravenous thrombolytic administration for patients on DOACs**: Intravenous

thrombolytics should ***not*** routinely be administered to patients on DOACs who present with acute ischemic stroke. In comprehensive stroke centres 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 thrombosis specialists, patients, and their families.

a. The benefits and risks of providing intravenous thrombolysis to a patient who is being treated with the combination of antiplatelet and low-dose DOAC (i.e., COMPASS trial protocol) are unclear. Treatment may be considered in consultation with a stroke expert.

b. Anticoagulation is not a contraindication for EVT, and the decision to treat should be based on individual patient factors and assessment of benefit and risk.

c. Patients who present with stroke who are taking a DOAC may be considered for rapid reversal if otherwise eligible for IV thrombolysis and if a reversal agent is readily available. Consultation with an expert in stroke care in strongly advised for these cases.

3. The use of epinephrine in angioedema or refractory hypotension should be reserved for life-threatening emergencies due to increased risk of hypertension post-medication administration.

4. There are some situations where 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 along with the clinical judgment of the treating physician and discussion with the patient or substitute decision-makers.

   a. For example, this may apply to pediatric patients with 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 additional information.*

5. **(NEW FOR 2022)** Evidence for the use of intravenous thrombolysis and EVT is derived from randomized trials that enrolled patients who were functionally independent at baseline. The use of intravenous thrombolysis and/or EVT in patients who are ***not functionally independent*** may be considered, based on careful review of risks and benefits for the patient. The patient's goals of care should be discussed in consultation with a physician with stroke expertise, and/or a neurointerventionalist, and the patient and/or family and/or substitute decision-makers.

6. **(NEW FOR 2022) Hypertension with symptomatic ICH**: In patients with symptomatic ICH who are hypertensive (>185/110 mm HG), blood pressure should be lowered, however, the specific target and duration of therapy are unknown at this time.

5.3 Stroke While Already in Hospital

i. **Patients already admitted to hospital*** who present with a sudden onset of new stroke symptoms should be rapidly evaluated without delay for eligibility for acute stroke treatment and provided with access to appropriate acute stroke treatments (including IV thrombolysis and EVT) [Strong recommendation; Moderate quality of evidence].

Note: When an inpatient has a stroke while in hospital, all other sections of the CSBP modules apply to these patients for assessment, diagnosis, management, and recovery.

**"Admitted to hospital" is defined as any person admitted to an emergency department, inpatient unit, or outpatient clinic or rehabilitation service in a hospital setting.*

5.4 Endovascular Thrombectomy for Acute Ischemic Stroke, Interim Update 2025

Emerging evidence has led to an interim review of the existing 2022 Canadian Stroke Best Practice Recommendations (CSBPR) for Acute Stroke Management, 7th edition, recommendations for endovascular treatment of acute ischemic stroke (section 5.4). The updated 2025 recommendations in section 5.4 supersede the endovascular thrombectomy recommendations included in the 2022

publication of the CSBPR acute stroke management module. These changes include: updating section 5.4 and removal of boxes: 4B,4C, 5C.

5.4.1. Endovascular Thrombectomy Selection Criteria and Management

i. Endovascular Thrombectomy (EVT) should be offered within a coordinated system of care including coordination among emergency medical services, access to rapid neurovascular (brain and vascular) imaging, the emergency department, the stroke team and radiology, local experts in neuro intervention, anesthesia, and access to a stroke unit for ongoing management [Strong recommendation; High quality of evidence].

ii. EVT is indicated in patients based on imaging selection, most commonly performed with non-contrast CT head and CT angiography (including extracranial and intracranial arteries) [Strong recommendation; High quality of evidence].

iii. EVT may be indicated in patients who have received intravenous thrombolysis, as well as those who are not eligible for intravenous thrombolysis [Strong recommendation; High quality of evidence].

iv. Intravenous thrombolysis should be provided to all eligible patients, including those patients who are also eligible for EVT [Strong recommendation; High quality of evidence].

   a. For patients who are also eligible for intravenous thrombolysis, this should be initiated while simultaneously preparing the angiography suite for EVT [Strong recommendation; High quality of evidence]. Treatment with either intravenous thrombolysis or EVT should not be delayed for any reason.

   b. For patients undergoing EVT following or concurrently with the administration of intravenous thrombolysis, there should not be a delay in proceeding to EVT to determine clinical effectiveness of thrombolysis [Strong recommendation; High quality of evidence].

v. Endovascular Thrombectomy should be offered to all patients meeting 4 eligibility criteria: patient, symptom, occlusion, and brain tissue criteria [Strong Recommendation; High Quality Evidence].

   a. Patient criteria:

      1. Age greater than 18

         AND

      2. Baseline independent function

   b. Symptom criteria:

      1. Disabling acute ischemic stroke (e.g., NIHSS > 5)

         AND

      2. Last known well within 24 hours.

   c. Occlusion criteria:

      1. Relevant intracranial occlusion of a large vessel of the anterior circulation (e.g., intracranial ICA, MCA-M1) OR relevant occlusion of the basilar artery

AND

2. The occlusion is technically accessible in the opinion of the treating neurointerventionalist.

d. Brain parenchyma criteria:

1. Assessment of the estimated volume of infarcted tissue as seen on imaging, using CT and CT Angiography-based assessment of collaterals, or CT and CT Perfusion, or MRI. In the anterior circulation, a 'small core' is usually consistent with an ASPECTS score of 6 or greater and a 'moderate core' is usually consistent with an ASPECT score of 3-5.

vi. Decisions about endovascular thrombectomy should be undertaken in a team approach involving a physician with stroke expertise and a neurointerventionalist, on the basis of shared decision-making with the individual with stroke, and their family/substitute decision maker [Strong recommendation, Moderate quality evidence].

5.4.1 Clinical Considerations

1. When a patient who is eligible for *both* intravenous thrombolysis and EVT presents **directly to an EVT-capable hospital**, a decision *not* to administer intravenous thrombolysis and proceed straight to EVT must balance both the patient-related and operational factors in play at that moment, for that patient. The overarching focus is to improve patient outcomes while safely reducing door-to-needle and door-to-puncture times. The main driver for an excellent outcome remains "time is brain."
2. Plain CT, CTA with assessment of collaterals, and/or Perfusion imaging may all be used to assess the volume of core infarct in patients eligible for thrombectomy. In patients who are beyond 6 hours from last known well, CTA collaterals or perfusion imaging should be used to identify the candidates most likely to benefit.
3. Outcomes after endovascular thrombectomy for acute ischemic stroke can be difficult to predict. However, the greatest likelihood of excellent functional outcome (mRS 0-1) is seen in patients with baseline functional independence, who are treated early after symptom onset, and who have a small amount of infarcted core on parenchymal imaging.
4. Patient age, comorbidities, baseline functional status, frailty, and the degree of ischemic damage (core – e.g. ASPECTS 6-10 vs. ASPECTS 3-5) are clinically relevant variables that all contribute to determining prognosis. All of these variables should be taken into account when considering EVT in patients who do not meet guideline-based criteria.
5. Patients with a moderate to large core of infarcted tissue in the anterior circulation who are otherwise eligible for EVT may do better with EVT than with medical management alone, though determining candidacy for EVT must clearly take into account all relevant variables including age, comorbidities, functional status, and frailty. In cases where prognosis is poor, as determined by the degree of established infarction/core based on imaging findings, treatment may not be indicated.
6. At present, data from randomized clinical trials do not support the uniform use of EVT in patients with medium-vessel occlusions (M2, A2 or P2). Patients with these occlusions in

these locations who are otherwise eligible may be considered for EVT after consultation between a physician with stroke expertise and the neurointerventionalist.

7. Evidence for the use of intra-arterial thrombolysis in conjunction with EVT is continuing to be explored. More data is required before making a recommendation regarding IA thrombolysis.

Note: Clinical consideration 1 is controversial. It will be updated as additional evidence becomes available. In the meantime, clinicians involved in acute stroke care should focus on improving patient outcomes while safely reducing door-to-needle and door-to-puncture times. The main driver for excellent outcomes remains "time is brain.".

5.4.2 Sedation for Endovascular Interventions

i. For endovascular interventions, procedural sedation is generally preferred over intubation and general anesthesia for most patients undergoing EVT [Strong recommendation; Moderate quality of evidence]

ii. General anesthesia is appropriate if medically indicated (e.g., for airway compromise, respiratory distress, depressed level of consciousness, severe agitation, or other indication potentially impairing the technical ability to perform the procedure, as determined by the treating physician). General anesthesia may also be considered when technical complexity is anticipated during the stroke intervention. In such cases, excessive and prolonged hypotension and time delays should be avoided [Strong recommendation; Moderate quality of evidence].

iii. A process should be in place at EVT enabled centres to activate notification of Anesthesiology without delay when deemed necessary for patients who meet criteria for EVT [Strong recommendation; Moderate quality of evidence].

5.5 Seizure Management

i. Seizure in the presence of suspected acute stroke is not a contraindication for revascularization and could be treated using appropriate short-acting medications (e.g., lorazepam IV) if the seizures are not self-limited [Conditional recommendation; Low quality of evidence].

5.6 (NEW FOR 2022) Emergency Management of Thrombolysis-Associated Hemorrhage

Note: Section 5.6 applies to patients experiencing a cerebral or systemic hemorrhage following administration of intravenous thrombolysis. Refer to CSBPR guidelines on Management of Intracerebral Hemorrhage for additional information.

5.6.1 Intracranial Hemorrhage

i. Intracranial hemorrhage should be considered if there is a change in neurological symptoms or signs, especially a reduction in level of consciousness, or a spike in blood pressure with persisting blood pressure elevation, or new or worsened headache [Strong recommendation; Moderate quality of evidence].

ii. An immediate non-contrast CT head should be done to assess for intracranial hemorrhage [Strong recommendation; Moderate quality of evidence].

iii. The patient should be accompanied to the CT by a member of the stroke team and the results reviewed immediately. If there is no intracranial hemorrhage, CTA should be urgently

considered to identify intracranial occlusion and the need for urgent EVT should be considered [Strong recommendation; Moderate quality of evidence].

iv. If intracranial hemorrhage is identified, the intravenous thrombolysis infusion should be discontinued immediately if it is still running [Strong recommendation; Moderate quality of evidence].

v. If intracranial hemorrhage is identified, blood work, including a complete blood count (CBC) and INR (PT), as well as type and cross, should be drawn [Strong recommendation; Moderate quality of evidence], with STAT results requested [Strong recommendation; Low quality of evidence].

vi. The following agents may be considered, as they have shown potential benefit and limited harm: cryoprecipitate, human fibrinogen concentrate fresh frozen plasma, tranexamic acid. Use of these medications should be considered on an individual, case-by-case basis [Conditional recommendation; Low quality of evidence].

vii. The following treatment options should probably be avoided as they have ***not*** shown benefit and have shown potential for harm: prothrombin complex concentrates, platelet transfusions, factor VIIa [Conditional recommendation; Low quality of evidence].

5.6.2 Extracranial (Systemic) Hemorrhage Management

Note: For systemic hemorrhage, follow local protocol for management guidance.

i. A diagnosis of systemic bleeding should be considered when the following are present or suspected [Strong recommendation; Moderate quality of evidence]:

   a. Visible bleeding at a compressible site

   b. Reduction in blood pressure, localized pain, diaphoresis, or other signs of hypovolemic shock.

ii. If systemic bleeding is identified, blood work including a CBC, INR (PT), and fibrinogen, should be drawn [Strong recommendation; Moderate quality of evidence], with STAT results requested [Strong recommendation; Low quality of evidence].

iii. If systemic bleeding is identified, the intravenous thrombolysis infusion should be discontinued immediately if it is still running [Strong recommendation; Moderate quality of evidence].

iv. If there is visible bleeding (e.g., at the IV site, abrasion, epistaxis), compression should be applied, and the application of ice considered [Strong recommendation; Moderate quality of evidence].

v. Patient should be transfused as required and according to local protocols [Strong recommendation; Low quality of evidence].

Section 5.6 Clinical Considerations

1. Hypertension with symptomatic ICH: In patients with secondary ICH who are hypertensive (>185/110 mm HG), blood pressure should be lowered, however, the specific target and duration of therapy are unknown at this time**.**

Box 5A Time Windows for Reperfusion in Acute Ischemic Stroke

Available treatments	Time from stroke onset or last known well	Population	Notes and criteria
Screening for stroke signs and symptoms	Within 24 hours	All patients showing signs of acute disabling stroke	
Intravenous thrombolysis	0 to 4.5 hours	All patients showing signs of acute disabling stroke	Based on CT/CTA
	4.5 to 6 hours	Select patients showing signs of acute disabling stroke	Requires advanced imaging for tissue-based decision-making
	6 to 9 hours	Select patients - in discussion with a stroke expert	Requires advanced imaging for tissue-based decision-making
Endovascular thrombectomy	0 to 6 hours	All patients showing signs of acute disabling stroke with LVO	Based on CT/CTA
	6 to 24 hours	All persons showing signs of acute disabling stroke with LVO	Requires advanced imaging for tissue-based decision-making

Box 5B Criteria for Intravenous Thrombolysis Treatment

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

While these criteria are designed to guide clinical decision-making, the decision to use thrombolysis should be based on the clinical judgment of the treating physician. The relative benefits of thrombolysis versus potential risks or contraindications should be weighed on an individual basis.

Inclusion Criteria

Patients should be considered eligible for intravenous thrombolysis and/or EVT if they fulfill the following clinical criteria:

- Diagnosed with an acute ischemic stroke.
- The stroke is disabling (i.e., significantly impacting function), usually defined as National Institutes of Health Stroke Scale (NIHSS)>4.
- The risks and benefits of thrombolysis are within the patient's goals of care and take into consideration their functional status prior to stroke.
- Life expectancy of 3 months or more.
- Age ≥18 years. (Refer to pediatric guidelines for treatment <18 years of age).
    - For adolescents, a decision to administer intravenous thrombolysis should be based on clinical judgment; presenting symptoms; patient age; and, if possible, consultation

with a pediatric stroke specialist.

- Time from last known well (onset of stroke symptoms) is <4.5 hours before thrombolysis administration. **For patients >4.5 hours refer to Section 5.1 for additional information.*

Absolute Exclusion Criteria

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

Relative Exclusion Criteria (requiring clinical judgement based upon the specific situation. Consult Stroke Specialist at Comprehensive Stroke Centre if there are any questions or concerns about these criteria).

Historical

- History of intracranial hemorrhage.
- Stroke or serious head or spinal trauma in the preceding 3 months.
- Major surgery (e.g., 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 7 days.

Clinical

- 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 <180/105 cannot be both achieved and maintained.
- Currently prescribed and taking a direct non-vitamin K oral anticoagulant. *Refer to Section 5.2 Clinical Considerations for additional information.*

CT or MRI Findings

- CT showing early signs of extensive infarction (e.g., >1/3 of middle cerebral artery [MCA] territory, or ASPECTS score <6).

Laboratory

- Blood glucose concentration <2.7 mmol/L or >22.2 mmol/L.
- Elevated activated partial-thromboplastin time.
- International Normalized Ratio >1.7.
- Platelet count <100,000 per cubic millimetre.

Box 5D (NEW FOR 2022) Pre- and Post-Management of Patients Undergoing Endovascular Thrombectomy

Note: The following information is provided as general management considerations for patients with stroke undergoing EVT. All EVT-enabled sites should follow local post-procedural protocols and assessment algorithms for neuro vitals, puncture site and extremity perfusion assessments, and patient mobilization restrictions.

5D.1 General Management Before and During Endovascular Thrombectomy

1. **Team Communication**: Maintain ongoing open communication between the stroke physician and the interventionalist for treatment decision-making; and before, during and after the EVT procedure.
2. **Airway:** Adequate airway control and oxygenation should be ensured, with a goal of maintaining oxygen saturation at >92%.
3. **Intubation:** Intubation may be necessary for patients with reduced oxygenation, those who are vomiting, or those who require significant sedation to remain calm for the procedure.
4. **Anesthesia:** Some EVT providers may be comfortable administering their own procedural sedation for EVT. Consultation with anesthesiology may be considered for patients who are anticipated to have airway difficulties or marked difficulties cooperating with the procedure.
5. **Contrast allergy:** A contrast allergy is not an absolute contraindication to EVT. If the patient has a known or suspected contrast allergy:
    a. Pre-treat with:
        1. H1 antagonist 50 mg IV diphenhydramine
        2. Steroid 40 mg IV methylprednisolone or 200mg IV hydrocortisone
        3. H2 blockers: ranitidine 50mg IV or famotidine 20mg IV;
    b. Consider:
        1. Supplemental oxygen
        2. Epinephrine
        3. Intubation (if severe laryngeal edema)
6. **Cardiac monitoring:** Blood pressure should be maintained according to targets for patients who receive thrombolysis; however, aggressive blood pressure lowering should be avoided, especially before reperfusion is achieved. Patients should be monitored for arrhythmias.
7. **Temperature regulation:** The goal is to aim for euthermia. There is no known benefit to hypothermia.
8. **Hyperglycemia:** The goal is to aim for normoglycemia. Hyperglycemia is associated with harm in acute ischemic stroke.
9. **Catheter:** Insertion of a foley catheter could be considered only if necessary to reduce patient distress and movement during the procedure and should not delay reperfusion.

5D.2 General Management After Endovascular Thrombectomy

1. The patient should remain supine for the first 2 to 6 hours, with the head of the bed at no more than30 degrees.
2. The puncture site (groin or wrist) should be closed by manual compression, sandbag, or other device.

3. The puncture site should be assessed for swelling or hematoma Q15 minutes for the first hour, then Q30 minutes for the next hour, then Q1 hourly for the next 1 to 5 hours depending whether a vascular closure device was used and on the access location.
4. Pulses at the puncture site and distal to it should be assessed along with vital signs as per local protocols.
5. Puncture site hematoma should be suspected if there is local bleeding, groin swelling, bruising, pain or unexplained reduction in hemoglobin or hematocrit.
6. If puncture site hematoma is suspected, on-call physician should be called, and prolonged manual compression applied. A stat CBC should be obtained and repeated Q4 to 6 hours.
7. If puncture site hematoma persists despite manual compression, a CT angiogram, or ultrasound if CT not available, should be obtained to assess for pseudoaneurysm or other abnormality, and consultation with vascular surgery for thrombin injection or other intervention should be considered.
8. Retroperitoneal hemorrhage should be suspected if the patient has back pain, flank bruising (Grey Turner sign), abdominal distention with periumbilical ecchymosis (Cullen sign), hypotension and tachycardia, or unexplained anemia. This is most often seen in the first 24 hours.
9. If retroperitoneal hemorrhage is suspected, a three-phase CT of the abdomen should be obtained as soon as possible, and fluid resuscitation, blood transfusion or surgical consultation should be considered.
10. If there is neurologic deterioration, stat CT and CTA should be obtained, to assess for hemorrhagic conversion, reperfusion injury, extracranial occlusion, or intracranial occlusion.
11. If extracranial occlusion is detected, particularly after stenting, urgent endovascular intervention should be considered, in consultation with a stroke specialist and interventional radiology specialist.
12. If intracranial reocclusion is detected, urgent EVT should be considered, in consultation with a stroke specialist and interventional radiology specialist.
13. Creatinine should be obtained and assessment for contrast-induced nephropathy conducted.
14. If contrast-induced nephropathy is identified, local protocols should be followed and consultation with nephrology considered.
15. The ideal blood pressure target after EVT is unknown. Blood pressure targets should be individualized based on clinical factors, such as the degree of recanalization achieved, whether there was an intraprocedural complication, whether intravenous thrombolysis was given, and the patient's baseline blood pressure. *Refer to Section 4 Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke for additional information on managing blood pressure in acute stroke.*

Rationale

Meta-analyses of randomized controlled trials (RCTs) of intravenous alteplase for acute ischemic stroke have shown the treatment can reduce the risk of disability and death, despite a small risk of serious bleeding. The widest time window for alteplase administration after stroke onset remains imprecisely defined, but currently available data show clear evidence of benefit when given up to 4.5 hours after the onset of symptoms. There remains a strong inverse relationship between treatment delay and clinical outcome; therefore, eligible patients should be treated as soon as possible.

Endovascular therapy (EVT) has been demonstrated to reduce disability and reduce mortality following acute ischemic stroke. Initially, EVT was limited to individuals with anterior circulation large vessel occlusion (LVO), small infarct core (ASPECTS ≥6), moderately disabling strokes and treatment within a narrow time window (typically up to 6 hours from symptom onset). The number needed to treat to

reduce disability by at least one point on mRS at 90 days for one patient has been reported to be as low as 2.6 (3). (Goyal et al. 2016) More recently the use of EVT has been expanded to include patients with late onset stroke, mild stroke, infarcts in the posterior circulation and large core infarcts (ASPECTs 2-5), enabling more patients to benefit from this life-saving therapy.

People with lived experience expressed the importance of having conversations with loved ones before health changes occur. Without these conversations, it can be difficult to know what the person would want. Some individuals shared that those conversations, even around desire to be involved in trials and/or experimental treatments, can be helpful to have in advance of changes in health status. Similarly, people with lived experience stated the importance of sharing personal values and preferences with the healthcare team, to help with treatment decisions.

(Note: DAWN trial criteria: To obtain mRS of 0-2 at 90 days (49% vs. 13%=NNT of 2.8); HERMES 2016 meta-analysis to obtain mRS score of 0-2 at 90 days (46% vs. 26.5%=NNT of 5.1).

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Local protocols should prioritize patients with stroke for immediate access to appropriate diagnostics such as CT imaging and neurovascular imaging with CTA. This should include patients with known times of stroke symptom onset (or time last known well), and patients who are discovered with stroke symptoms on wakening.
2. Coordinated and integrated systems of care involving all relevant personnel in the prehospital and emergency care of patients with stroke, including paramedics, emergency department staff, stroke teams, radiologists and neurointerventionists. Protocols should be in place in partnership with EMS agencies and treating hospitals, and between hospitals within stroke systems to ensure rapid transport to centres providing advanced stroke services within treatment time windows.
3. Consideration should be given to northern, rural, remote, and Indigenous residents to ensure immediate access to appropriate diagnostics and treatment is not delayed.
4. **(NEW FOR 2022)** Health system leaders should work with hospitals to coordinate plans for launching tenecteplase and consider group purchase opportunities. Health Canada should undertake rapid review and approval for use of tenecteplase in acute stroke.
5. Health regions and stroke systems should examine and determine the possible resource impact of the EVT time window extension (up to 24 hours in highly selected cases). Demand for imaging will increase especially at comprehensive stroke and EVT-enabled centres. Staffing, service hours and capacity should be considered to ensure efficiency and effectiveness of services.
6. System planners and patient flow specialists should plan for significant challenges associated with diversion of potential EVT candidates to EVT-enabled centres. This will affect emergency departments, radiology departments, and acute inpatient units where occupancy rates are often stretched (over 100% in many hospitals).
7. Stroke neurology and neurointerventional expertise should be regionalized, with a system in place across regions for rapid access to physicians experienced in acute thrombolysis and endovascular therapies, including through telemedicine. This includes protocols for contacting physicians with stroke expertise for administration of intravenous thrombolysis, as well as transport to higher levels of stroke care, as needed, for emergent treatments.

8. Health regions and academic institutions should build capacity for trained neurointerventionists to ensure sufficient availability to meet regional and provincial EVT healthcare needs.
9. Urgent acute protocols should be put in place and well-communicated to all healthcare practitioners within the hospital regarding management of in-hospital patients with stroke, ensuring access to CT imaging of the brain, and CTA of the extracranial and intracranial vessels as soon as possible after stroke symptom onset.
10. Access to specialized acute stroke units where staff are experienced in managing patients who have received intravenous thrombolysis or EVT should be available to all patients.
11. Endovascular interventional programs are in evolution across Canada; decisions around appropriate site, transfer and bypass protocols, and timelines will be determined at the provincial or regional level. Decisions about when those services are fully operational, and who should be transferred by paramedics to those facilities should be made at the provincial or regional level and communicated to all relevant stakeholders.
12. Access to helical CT scanners with appropriate programming for CTA (multiphase or dynamic CTA) and CTP sequences, and appropriate post-processing software optimized for the production of high-quality imaging.
13. Monitor access, outcomes, and key processes of care that support timeliness of intervention.
14. Ensuring ongoing capacity of EVT-capable hospitals as EVT volumes grow (i.e., ensure appropriate accountabilities for all providers accessing or providing services, ensure funding keeps pace, and ensure ability to ensure safe and timely care is maintained).

Performance Measures

System Indicators:

1. Proportion of patients in rural or remote communities who receive intravenous thrombolysis through the use of telestroke technology, as a proportion of all patients with ischemic stroke in that community and as a proportion of all telestroke consults for ischemic stroke.

Process indicators:

2. Overall proportion of all patients with ischemic stroke who receive treatment with intravenous thrombolysis (core).
3. Median time (in minutes) from patient arrival in the emergency department to administration of intravenous thrombolysis.
4. Proportion of patients with ischemic stroke who receive treatment with intravenous thrombolysis within 3.0 and 4.5 hours of symptom onset.
5. Proportion of all thrombolyzed patients with stroke who receive thrombolysis within 30 minutes of hospital arrival (core).
6. Proportion of all patients with ischemic stroke who receive treatment with EVT (core).
7. Median time from hospital arrival to arterial puncture, and from CT scan (first slice of the non-contrast CT) to arterial puncture for patients undergoing EVT.
8. Median time from hospital arrival to first reperfusion for patients undergoing EVT. Time of first reperfusion is defined as the first angiographic image showing partial or complete reperfusion of the affected arterial territory. (CIHI Stroke Special Project for EVT440 indicator. Refer to Measurement Note ii below.)
9. Proportion of patients with stroke who receive BOTH intravenous thrombolysis and EVT.
10. For patients with stroke that occurs while in hospital for other medical reasons (in-hospital strokes), median time from last known well to brain imaging.

11. For patients with stroke while in hospital for other medical reasons (in-hospital strokes), median time from last known well to acute thrombolysis or EVT (arterial puncture).
12. Final reperfusion status for patients undergoing endovascular reperfusion therapy, quantified using the modified Thrombolysis in Cerebral Infarction (mTICI) system. (CIHI Stroke Special Project for EVT440 indicator. Refer to Measurement Note ii below.)
13. Proportion of patients with symptomatic subarachnoid or intracerebral hemorrhage following intravenous thrombolysis or EVT (defined as any PH1, PH2, RIH, SAH, or IVH associated with a four-point or more worsening on the NIHSS within 24 hours).
14. Virtual stroke care: Proportion of people with acute stroke who receive a virtual care consult with a stroke expert at another site who receive acute thrombolysis as a result.
15. Virtual stroke care: Proportion of stroke patients managed with Telestroke who received tPA, who had a symptomatic secondary intracerebral hemorrhage, systemic hemorrhage, died in hospital, and were discharged to long-term care vs. home or to rehabilitation.

Patient-oriented outcome and experience indicators:

16. Level of functional impairment following acute stroke - ability to perform activities of daily living independently.
17. Modified Rankin Scale (mRS) score of all patients with stroke who receive intravenous thrombolysis or EVT at 30 days and at 90 days following hospital discharge.
18. Proportion of patients with symptomatic subarachnoid or intracerebral hemorrhage following EVT (defined as any PH1, PH2, RIH, SAH, or IVH associated with a four-point or more worsening on the NIHSS within 24 hours).
19. In-hospital mortality rates (overall and 30-day) for patients with ischemic stroke, stratified by those who receive intravenous thrombolysis or EVT and those who do not.

Measurement Notes

a. Refer to the *Quality of Stroke Care in Canada Key Quality Indicators and Stroke Case Definitions 7th Edition* for calculations, process timelines, and outcome measures for intravenous thrombolysis and EVT.

b. The **denominator** for treatment indicators is the number of people discharged from the emergency department (CIHI NACRS) or inpatient care (CIHI DAD) with a diagnosis of ischemic stroke – see data dictionary for relevant ICD10 codes.

c. The Canadian Institute of Health Information has a stroke quality of care special project (#440) as part of the Discharge Abstract Database extraction that enables data collection on six performance measures for EVT. Referred to in performance measures 7 and 10 above as CIHI Stroke Special Project for EVT440.

d. Data may be obtained from patient charts, through chart audit, registry or review.

e. Time interval measurements should be taken from the time the patient is triaged at the hospital (according to emergency department standards of care, triage should come before registration. Triage time should always be used to standardize) until the time of intravenous thrombolysis administration noted in the patient chart (nursing notes, emergency department record, or medication record).

f. For performance measures related to time intervals: Calculate all percentiles and examine 50th and 90th percentiles and inter-quartile range.

g. When recording if intravenous thrombolysis is given, include times for both the administration of the bolus (both alteplase and TNK), and the time when the infusion is started (alteplase), as there are often delays between bolus and infusion which may decrease alteplase efficacy. The route of administration should also be recorded, as there are different times to administration benchmarks for intravenous and endovascular routes.

h. For EVT, treatment time should be time of first arterial puncture.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practice Recommendations Acute Stroke Management Module Appendix 3, Table 4: Screening and Assessment Tools for Acute Stroke Severity
- Canadian Stroke Best Practices Management of Acute Stroke during Pregnancy Consensus Statement
- Refer to Box 5A for Criteria for Stroke Centres Providing Acute Ischemic Stroke Treatment
- Refer to Box 5B for Inclusion and Exclusion Criteria for Intravenous Thrombolysis Eligibility
- Heart & Stroke: Virtual Stroke Care Implementation Toolkit: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/csbpr-virtual-stroke-toolkit-final
- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls
- American College of Chest Physicians (ACCP) Anticoagulation Guidelines: http://www.chestnet.org/Guidelines-and-Resources
- ASPECTS: http://aspectsinstroke.com/
- Stroke Engine: http://strokengine.ca/
- Heart & Stroke: Acute Ischemic Stroke Intravenous Thrombolysis Protocol Checklist
- Heart & Stroke: 2022 Acute Stroke Management Key Quality Indicators

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-strokebest-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls

  Stroke Engine: http://strokengine.ca/

Summary of the Evidence

The weight of evidence from many large, international trials over a time frame of 20 years clearly indicate that treatment with intravenous alteplase reduces the risk of death or disability following ischemic stroke, at 3 to 6 months post-treatment. The NINDS trial (1995) was one of the earliest, large trials conducted in the USA. Patients were randomized to receive alteplase or placebo within three hours of symptom onset. At 3 months, significantly more patients in the t-PA group had experienced a good outcome (using any one of the study's four metrics), with no difference in 90-day mortality between groups. In contrast, patients who received alteplase within 3 to 5 hours in the ATLANTIS trial (1999) were no more likely to have a good neurological or functional outcome at 90 days than patients in the placebo group.

In the first ECASS trial (1995) 620 patients received alteplase or placebo within 6 hours of the stroke event. Using intention-to-treat analysis and including the data from 109 patients with major protocol violations, the authors did not report a significant benefit of treatment. The median Barthel Index and modified Rankin scores at 90 days did not differ between groups. In an analysis restricted to patients in the target population, there were differences favouring patients in the alteplase group. In the ECASS II trial (1998), there was again no significant difference on any of the primary outcomes. The percentages of patients with a good outcome at day 90 (mRS<2) treated with alteplase and placebo were 40.3% vs. 36.6% respectively, absolute difference=3.7%, p=0.277. In subgroup analysis of patients treated <3 hours and 3 to 6 hours, there were no between-group differences on any of the outcomes. The authors suggested that the reason for the null result may have been that the study was underpowered, since it was powered to detect a 10% difference in the primary outcome, but the observed difference between groups in previous trials was only 8.3%. Finally, in the ECASS III trial (2008) 821 patients were randomized within 3 and 4.5 hours of symptom onset. In this trial, a higher percentage of patients in the alteplase group experienced a favourable outcome, defined as mRS scores <2 (52.4% vs. 45.2%, adjusted OR=1.34, 95% CI 1.02 to 1.76, p=0.04). A higher percentage of patients in the alteplase group also had NIHSS scores of 0 or 1, (50.2% vs. 43.2%, adjusted OR=1.33, 95% CI 1.01 to 1.75, p=0.04). Secondary outcomes of the ECASS III trial were reported by Bluhmki et al. (2009). At 90 days, there were no between-group differences in the percentages of patients with mRS score of 0-2 (59% vs. 53%, p=0.097) or BI score ≥85 (60% vs. 56%, p=0.249, but a significantly greater percentage of patients had improved NIHSS scores of ≥8 points (58% vs. 51%, p=0.031). In all of the trials described above there was an increased risk of symptomatic intracerebral hemorrhage (ICH) associated with treatment with alteplase and in some cases, increased short-term mortality; however, there were no differences between treatment and placebo groups in 90-day mortality.

The Third International Stroke Trial (IST-3, 2012) is the largest (n=3,035) and most recent trial of alteplase, in which patients were randomized to receive a standard dose of alteplase (0.9 mg/kg) or placebo. Investigators aimed to assess the risks and benefits of treatment among a broader group of patients, and determine if particular subgroups of patients might benefit preferentially from treatment. In this trial, 95% of patients did not meet the strict licensing criteria, due to advanced age or time to treatment. Unlike all previous large trials, which excluded them, IST-3 included patients >80 years of age. In fact, the majority of patients (53%) were >80 years of age. Approximately one-third of all patients were treated within 0-3 hours, 3.0-4.5 hours, and 4.5-6.0 hours of onset of symptoms. Overall, there was an increase in the risk of death within 7 days in patients who had received alteplase, although there was no difference in 6-month mortality in both crude and adjusted analyses. There was no significant difference in the percentage of patients who were treated with alteplase who were alive and independent (defined as an Oxford Handicap Score of 0-1) at 6 months (37% vs. 35%, adjusted OR=1.13, 95% CI 0.95 to 1.35, p=0.181, although a secondary ordinal analysis suggested a significant,

favourable shift in the distribution of OHS scores at 6 months. Significantly improved odds of a good outcome at 6 months were associated with the subgroups of older patients (≥80 years), higher NIHSS scores, higher baseline probability of good outcome and treatment within 3 hours. Fatal or non-fatal symptomatic intracranial hemorrhage within 7 days occurred more frequently in patients in the t-PA group (7% vs. 1%, adjusted OR=6.94, 95% CI 4.07 to 11.8, p<0.0001). The 3-year risk of mortality (2016) was similar between groups (47% vs. 47%, 95% CI 3.6%, 95% CI -0.8 to 8.1); however, patients who received rt-PA had a significantly lower risk of death between 8 days and 3 years (41% vs. 47%; HR= 0.78, 95% CI 0·68–0·90, p=0·007).

Although it is known that the optimal timing of administration of intravenous alteplase is <3 hours, debate continues as to the safety and efficacy of treatment provided between 3 and 6 hours post stroke. The results from a few studies suggest that treatment is still beneficial if provided beyond the three-hour window. The Safe Implementation of Treatment in Stroke-International Stroke Thrombolysis Registry (SITS-ISTR) includes patients who were treated with intravenous alteplase under strict licensing criteria and also those who were thought to be good candidates based on clinical/imaging assessment of the treating facility. Wahlgren et al. (2008) used data from a cohort of patients collected from 2002–2007 to compare the outcomes of patients who had been treated with alteplase within 3 hours of symptom onset (n=11,865) and those treated within 3 to 4.5 hours (n=644). The primary focus of this analysis was to assess treatment safety beyond the three-hour treatment window. Patients in the <3-hour group had significantly lower initial median NIHSS scores (11 vs. 12, p<0.0001). There were no significant between-group differences on any of the outcomes (symptomatic ICH within 24-36 hours, mortality within 3 months, or percentage of patients who were independent at 3 months); however, there was a trend towards increased number of patients treated from 3 to 4.5 hours who died (12.7% vs. 12.2%, adjusted OR=1.15, 95% CI 1.00-1.33, p=0.053) and who experienced symptomatic ICH (2.2% vs. 1.6%, adjusted OR=1.32, 95% CI 1.00-1.75, p=0.052). Additional analysis from the SITS-ISTR cohort was conducted to further explore the timing of alteplase treatment (Ahmed et al. 2010). In this study, patients treated within 3 hours (n=21,566) and 3 to 4.5 hours (n=2,376) of symptom onset between 2007 and 2010, were again compared. Significantly more patients treated from 3-4.5 hours experienced a symptomatic ICH (2.2% vs.1.7%, adjusted OR=1.44, 95% CI 1.05-1.97, p=0.02), and were dead at 3 months (12.0% vs. 12.3%, adjusted OR=1.26, 95% CI 1.07-1.49, p=0.005). Significantly fewer patients treated from 3-4.5 hours were independent at 3 months: (57.5% vs. 60.3%, adjusted OR=0.84, 95% CI 0.75-0.95, p=0.005).

Emberson et al. (2014) used data from 6,756 patients from 9 major t-PA trials (NINDs a/b, ECASS I/II, III, ATLANTIS a/b, EPITHET, IST-3) to examine the effect of timing of administration more closely. Earlier treatment was associated with the increased odds of a good outcome, defined as an (mRS score of 0-1 (≤3.0 h: OR=1.75, 95% CI 1.35-2.27 vs. >3 to ≤4.5 h: OR=1.26, 95% CI 1.05-1051 vs. >4.5 h: OR=1.15, 95% CI 0.95-1.40). Framed slightly differently, when patient-level data from the same 9 major randomized controlled trials (RCTs) were recently pooled, Lees et al. (2016) reported that for each patient treated within 3 hours, significantly more would have a better outcome (122/1,000, 95% CI 16-171), whereas for each patient treated >4.5 hours, only 20/1,000 (95% CI -31-75, p=0.45) would have a better outcome. Wardlaw et al. (2013), including the results from 12 RCTs (7,012 patients), concluded that for every 1,000 patients treated up to 6 hours following stroke, 42 more patients were alive and independent (mRS<2) at the end of follow-up, despite an increase in early ICH and mortality. The authors also suggested that patients who did not meet strict licensing criteria due to age and timing of treatment (i.e., patients from the IST-3) trial were just as likely to benefit; however, early treatment, within 3 hours of stroke onset, was more effective.

Results from several recent trials indicate that thrombolysis with t-PA can be used for patients outside of the previously established therapeutic window. In the Extending the Time for Thrombolysis in

Emergency Neurological Deficits (EXTEND) trial (Ma et al., 2019), 225 patients with an ischemic stroke were included, where symptom onset was estimated to be 4.5 to ≤9 hours previously. Recruitment was suspended after the results of the WAKE-UP trial became available. The primary outcome (mRS 0-1 at 90 days) occurred in 35.4% of the patients in the alteplase group and 29.5% in the control (placebo) group. After adjustment for age and baseline severity, the likelihood of the primary outcome significantly increased in the alteplase group (RR=1.44, 95% CI 1.01–2.06), as did the proportion of patients who attained a mRS score of 0-2 at 90 days (49.6% vs. 42.9%; adjusted RR=1.36, 95% CI, 1.06 to 1.76); however there was no significant difference between groups in functional improvement at 90 days (i.e., shift in mRS scores; RR=1.55, 95% CI 0.96 to 2.49). The results from the Efficacy and Safety of MRI-based Thrombolysis in Wake-up Stroke (WAKE-Up) trial (Thomalla et al., 2018) also suggest 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 were not eligible for treatment with mechanical thrombectomy and were selected based on a pattern of DWI-FLAIR-mismatch. A significantly higher proportion of patients in the alteplase group had a favourable 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 type 2 parenchymal hemorrhage was significantly higher compared with placebo (4% vs. 0.4%, adj OR=10.46, 95% CI 1.32 to 82.77, p=0.03).

The standard treatment dose of rt-PA is established to be 0.9 mg/kg, with a maximum dose of 90 mg. The non-inferiority of a lower dose (0.6 mg/kg) was recently examined in the Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) trial (Anderson et al., 2016). The primary outcome (death or disability at 90 days) occurred in 53.2% of low-dose patients and 51.1% in standard-dose patients (OR=1.09, 95% CI 0.95-1.25, p for non-inferiority=0.51), which exceeded the upper boundary set for non-inferiority of 1.14. The risks of death within 90 days or serious adverse events did not differ significantly between groups (low dose vs. standard dose: 8.5% vs. 10.3%; OR=0.80, 95% CI 0.63-1.01, p=0.07 and 25.1% vs. 27.3%; OR=0.89, 95% CI 0.76-1.04, p=0.16, respectively), although the risk of symptomatic ICH was significantly higher in patients that received the standard dose of rt-PA.

Earlier treatment with thrombolytic agents is associated with better stroke outcomes. Using data from 61,426 Medicare patients aged ≥65 years admitted to Get With The Guidelines (GWTG)–stroke participating hospitals between January 1, 2006, and December 31, 2016, Man et al. (2020) found that among patients treated with intravenous alteplase, all-cause mortality was significantly higher in those that with door-to-needle times (DTN) of <45 minutes (vs. ≥45 minutes) and <60 minutes (vs. ≥60 minutes). The authors estimated that every 15-minute increase in DTN time was associated with a 4% increase in all-cause mortality within 90 minutes after hospital arrival, but not after 90 minutes, and a 2% increase in all-cause readmission. Analyzing data from the alteplase arm of seven major trials, the HEREMES Collaborators (Goyal et al., 2019) reported the common odds of a better outcome were decreased by each 60-minute delay in onset-to- treatment time (OTT) (OR=0.80, 95% CI 0.68–0.95). The odds of an excellent outcome (mRS 0-1) were also decreased by each 60-minute delay in OTT (OR=0.76, 95% CI 0.58–0.99).

Strategies to improve guideline adherence have been shown to help improve thrombolysis uptake and shorten thrombolysis process times. In Canada, following the initiation of an Improvement Collaborative intervention during 2016–2017, the number of patients receiving thrombolysis increased from 9.35% in the pre-period to 15.73% in the post-period, the median DTN time was reduced significantly from 70 to 39 minutes, and a significantly higher number of patients were discharged home in the post-period (46.5% to 59.5%) (Kamal et al., 2020). Using data from 71,169 patients admitted to 1,030 GWTG-participating hospitals, the outcomes and process times of patients admitted before and after the initiation of a quality improvement initiative (Target:Stroke) were examined (Fonarow et al., 2014).

During that time the median DTN were reduced significantly from pre- to post- intervention (77 vs. 67 minutes, p<0.001), the percentage of patients treated within 60 minutes of stroke onset increased significantly from 26.5% to 41.3%, and in-hospital mortality decreased significantly from 9.93% to 8.25%. The percentage of patients discharged home also increased significantly from 37.6% to 42.7%.

The results from several studies indicate that tenecteplase, which has some pharmacokinetic advantages over alteplase, may be non-inferior to alteplase. Several clinical trials are ongoing and the results are not yet available. In these trials tenecteplase was compared with either alteplase (ATTEST2 NCT0281440) or placebo, or best medical management (TIMELESS NCT03785678, TWIST NCT03181360, and TEMPO-2 NCT02398656). Among completed trials comparing tenecteplase with alteplase, all were used as a potential bridging treatment prior to thrombectomy. The Alteplase Compared to Tenecteplase in Patients with Acute Ischemic Stroke (AcT) Trial (Mennon et al., 2022) was the first trial to report that tenecteplase is non-inferior to alteplase for 90-day functional outcomes. In this trial, 1,600 patients recruited from 22 centres who were eligible for treatment with alteplase (+/- thrombectomy) were randomized to receive intravenous tenecteplase (0.25mg/kg, maximum 25m) or 0.9 mg/kg alteplase. At a median of 97 days 36.9% of patients in the tenecteplase group achieved the primary outcome (mRS score of 0-1) vs.34.8% in the alteplase group (unadjusted difference=2.1%, 95% CI -2.6% to 6.9%; adjusted RR=1·1, 95% CI 1·0 to 1·2), meeting the non-inferiority threshold, (the lower bound 95% CI of which was set at >-5%). There was no significant difference between groups in mortality at 90 days (15.3% vs. 15.4%), or in the proportion with symptomatic ICH at 24 hours (3.4% vs. 3.2%). In contrast to these findings, the NOR-TEST 2 (Kvistad et al., 2022) was halted early due to safety concerns, which included an increased risk of intracranial hemorrhage and mortality; however, the dose in the tenecteplase group was higher (0.4 mg/kg) than is currently recommended (0.25 mg/kg). In the EXTEND-IA TNK (Campbell et al., 2018), which compared 0.25mg/kg tenecteplase vs. 0.9 mg/kg alteplase, at initial angiographic assessment, a significantly higher number of patients in the tenecteplase group achieved substantial reperfusion (22% vs. 10%, p=0.02 for superiority), although the percentage of patients who were functionally independent at 90 days or who had achieved an excellent outcome, did not differ between groups.

The evidence base for the safety and effectiveness of the use of thrombolysis during pregnancy and the puerperium is derived from a series of case reports. The results from a total of 15 previous cases (10 intravenous and 5 intra-arterial), in addition to the presentation of their own case were summarized by Tversky et al. (2016). The neurological outcomes of these women were described as similar to non-pregnant patients who met the eligibility criteria. Most of the women who experienced significant recovery went on to deliver healthy babies. The evidence in terms of thrombolytic treatment for patients <18 years comes primarily from the International Pediatric Stroke Study (IPSS), an observational study (n=687) in which the outcomes of 15 children, aged 2 months to 18 years, who received thrombolytic therapy (9 with intravenous Alteplase, 6 with intra-arterial alteplase). Overall, at the time of hospital discharge, 7 patients were reported having no or mild neurological deficits, 2 had died, and the remainder had moderate or severe neurological deficits. The Thrombolysis in Pediatric Stroke (TIPS) study (Amlie-Lefond et al., 2009) is currently recruiting subjects for a five-year, prospective cohort, open-label, dose-finding trial of the safety and feasibility of intravenous and intra-arterial t-PA to treat acute childhood stroke (within 4.5 hours of symptoms). The TIPS investigators are aiming to include 48 subjects.

Sex and Gender Considerations

Possible interactions (treatment group x sex) were not analyzed in the initial reports of early trials of alteplase including NINDS (1995), ATLANTIS (1995), or ECASS (1995, 1998, 2008). The IST-III examined this relationship and reported there were no significant interactions based on sex, as did the

authors of the ENCHANTED trial (2016) that examined low vs. standard dose alteplase. In more recent trials of late window treatment, including WAKE-UP (2018) and EXTEND (2019), the results of subgroup analyses based on sex were not conducted or reported. In the RCTs of tenecteplase including NOR-TEST 2 (2022), EXTEND-IA TNK (2018), and NOR-TEST (2017), the effect of treatment based on sex was not reported in subgroup analyses in the initial publications. Subgroup analysis for interactions based on sex for the AcT trial (2022) were conducted and no interactions were found.

Endovascular Thrombectomy

Over the past decade, the use of endovascular thrombectomy (EVT) for acute ischemic stroke has evolved, particularly in terms of patient selection criteria. Initially, EVT was limited to individuals with anterior circulation large vessel occlusion (LVO), small infarct core (ASPECTS ≥6), and treatment within a narrow time window (typically up to 6 hours from symptom onset). Compared with best medical management, the efficacy of EVT was established in landmark trials such as MR CLEAN, (Berkhemer et al. 2015) ESCAPE,(Goyal et al. 2015) and SWIFT PRIME. (Saver et al. 2015) Subsequent studies, including DAWN (Nogueira et al. 2018) and DEFUSE 3, (Albers et al. 2018) expanded eligibility to patients presenting up to 24 hours since last known well, provided there was a mismatch between clinical deficit and infarct core identified through advanced imaging. More recently, trials such as SELECT-2, (Albers et al. 2018) ANGEL-ASPECT, (Huo et al. 2023) and TENSION (Bendszus et al. 2023) have further broadened inclusion criteria by demonstrating the benefit of EVT in patients with large infarct cores (e.g., ASPECTS 3–5 or core volumes up to 100–150 mL). Treatment with EVT has been explored for the treatment of posterior artery infarctions (ATTENTION,(Hu et al. 2025) BAOCHE (Jovin et al. 2022) and BASICS (Langezaal et al. 2021)) and for medium and distal occlusions (ESCAPE-MeVO, (Goyal et al. 2025) DISTAL,(Psychogios et al. 2025) and DISCOUNT [NCT05030142]).

Several recent trials evaluated EVT in patients with medium-to-large core infarcts (ASPECTs 2-5) or high infarct core volumes. Traditionally these patients were considered poor candidates for reperfusion therapies. LASTE, (Costalat et al. 2024) TENSION, (Bendszus et al. 2023) ANGEL-ASPECT, (Huo et al. 2023) and SELECT-2, (Sarraj et al. 2023) trials all enrolled patients with anterior circulation LVO and low ASPECTS scores or large infarct volumes. LASTE included 333 patients with ASPECTS 0–5 (if less than 80 years old) identified on non-contrast CT, randomized within 6.5 hours of symptom onset. TENSION enrolled 253 patients with ASPECTS 3–5, on baseline computed tomography (CT) or diffusion-weighted imaging – magnetic resonance imaging (DWI-MRI) and occlusion defined by computed tomography angiography (CTA) or magnetic resonance angiography (MRA), treated within 12 hours. SELECT-2 (Sarraj et al. 2023) included 352 patients with ASPECTS 3–5 or infarct core measuring 50-100 mL using CT perfusion or diffusion-weighted MRI, with a treatment window of up to 24 hours. ANGEL-ASPECTS (Huo et al. 2023) included 456 patients with either an ASPECTS of 3–5 (regardless of core volume) or an ASPECTS of 0–2 with an infarct core volume of 70–100 mL, assessed within 24 hours of symptom onset. Additionally, patients with ASPECTS > 5 were included only if they had a core volume between 70–100 mL and presented between 6 and 24 hours after onset. All four of the trials were stopped early due to demonstrated efficacy of EVT at interim analysis, whereby EVT was associated with significantly improved functional outcomes (favourable shift in the distribution of mRS scores) at 90 days compared to best medical management alone. The benefit was consistent across subgroups, including those with ASPECTS as low as 3 and large core volumes. While symptomatic intracranial hemorrhage (sICH) occurred more frequently in the EVT group, overall mortality was either unchanged or reduced. The results were similar in RESCUE-Japan LIMIT, (Yoshimura et al. 2022) although the benefit was not as pronounced. The TESLA trial,(Yoo et al. 2024)

included 300 patients with ASPECTS 2–5 up to 24 hours from last known well. The mean average utility weighted mRS score at 90 days was not significantly different between the groups, nor was the percentage of patients with an mRS score of 0-2 at 90 days significantly higher in the EVT group (14.5% vs. 8.9%, RR=1.64, 95% CI 0.86-3.12); however, the percentage of patients with an mRS score of 0-3 at 90 days was significantly higher in the EVT group. Across all trials, the majority of patients (61%-69%) were dead or severely disabled at 90 days, despite EVT.

The use of EVT for medium vessel occlusions (MeVOs), including occlusions in the M2/M3 segments of the middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA) is a new area of interest. While EVT is well established for anterior LVOs, its role in MeVOs remains under investigation. In the ESCAPE-MeVO trial, (Goyal et al. 2025) EVT in addition to best medical management was not associated with benefit compared with best medical management only, in 530 patients with occlusions located in the M2 segment of the proximal MCA (23.3%), M2 segment of the distal MCA (20.3%) and the M3 segment of MCA (41.4%). The median mRS score at 90 days was 2 in both groups. The likelihood of the primary outcome (mRS 0-1 at 90 days) was not significantly higher in the EVT group (adjusted common RR=0.95, 95% CI 0.79 to 1.15), nor was the likelihood of an mRS score of 0 -2 at 90 days (adjusted RR=0.92, 95% CI 0.80 to 1.05). Ninety-day mortality was significantly higher in the EVT group (13.3% vs. 8.4%, HR=1.82, 95% CI 1.06 to 3.12). The incidence of serious adverse events was higher in the EVT group (33.9% [in 87 patients]) than in the usual-care group (25.7% [in 70 patients]). In the DISTAL trial, (Psychogios et al. 2025) which included 543 patients with an isolated occlusion of medium or distal vessels (M2 [44.0%], M3 [26.9%], M1 [13.4%], P2 [13.4%], and P1 [5.5%] segments), there was no significant difference between groups in the distribution of mRS scores at 90 days (median mRS score was 2 vs. 2; common OR=0.90; 95% CI 0.67 to 1.22). Preliminary results from the DISCOUNT trial (NCT05030142), which was terminated early following the first interim analysis also suggests potential harm associated with EVT treatment. The primary outcome (mRS 0-2 at 90 days) occurred in 45/75 patient (60%) in the EVT group vs. 59/77 (77%) in the usual care group (adjusted OR=0.42, 95% CI 0.2-0.88). Additionally, sICH occurred in 12% of the patients in the EVT group vs. 6% in the usual care group.

Intra-arterial thrombolysis administered following EVT may help to dissolve residual thrombus in distal vessels, potentially improving microvascular reperfusion and functional outcomes, without significantly increasing the risk of sICH. However, in the POST-UK(Liu et al. 2025) and POST-TNK (Huang et al. 2025) trials, patients with anterior circulation LVO infarcts, who achieved near complete or complete reperfusion following EVT and who received intra-arterial thrombolysis post procedure, with either tenecteplase or urokinase, did not have a higher likelihood of achieving an mRS score of 0-1 at 90 days compared with patients who did not receive thrombolysis, nor did thrombolysis reduce the risk of 90-day mortality. In contrast, ppreliminary results presented at the International Stroke Conference in 2025, from the PEARL trial (NCT05856851) indicated that patients with anterior circulation LVO infarcts who achieved near complete or complete reperfusion (expanded Thrombolysis in Cerebral Infarction score of 3 or 2b50) following EVT, and received thrombolysis with either tenecteplase or alteplase post EVT had higher likelihood of having an mRS score of 0-1 at 90 days (44.8% vs 30.2%; RR=1.45, 95% CI 1.08-1.96), with no increased risk of sICH within 36 hours or 48 hours. Intra-arterial thrombolysis post EVT did not increase the likelihood of freedom from disability at 90 days in patients with posterior circulation strokes in the ATTENION-IA trial.(Hu et al. 2025)

For large artery occlusions in the posterior circulation, 4 RCTs have compared EVT with best medical management only, with conflicting results. In the ATTENTION trial (Tao et al. 2022) which included 342 patients, recruited <12 hours from onset with NIHSS ≥10, a significantly higher percentage of patients

in the EVT group achieved an mRS score of 0-3 compared with those in the medical management group (46.0% vs. 22.8%; adjusted RR= 2.06, 95% CI 1.46 to 2.91, NNT=4). Ninety-day mortality was also lower (36.7% vs. 55.3%: adj RR= 0.7,95% CI 0.5 to 0.8, NNT=5.4). A benefit of EVT was also demonstrated in the BAOCHE trial, (Jovin et al. 2022) which included 217 patients enrolled within 6–24 hours after symptom onset and NIHSS ≥6. In contrast, Liu et al. (Liu et al. 2020) included 131 adult patients presenting within 8 hours of vertebrobasilar occlusion to 28 centres in China in the BEST trial. The trial was terminated early due to excessive crossovers and low enrollment. In the intention-to-treat analysis, the percentage of patients with a favourable outcome (mRS 0-3) at 90 days was not significantly higher in the intervention group (42% vs. 32%; adjusted [age and baseline NIHSS] OR=1.74, 95% CI 0.81–3.74, p=0.23), nor was the percentage of patients who were functionally independent; however, in both the per protocol and as treated analyses, the percentage of patients with a favourable outcome was significantly higher in the EVT group. There was no significant difference between groups in 90-day mortality or in sICH. The BASICS trial recruited 300 patients with basilar artery occlusion. (Langezaal et al. 2021) Intravenous alteplase was used in close to 80% of patients in both the EVT and control groups. The percentage of patients in the EVT group who experienced a favourable (mRS 0-3) or excellent (mRS 0-2) outcome at 90 days was not significantly higher in the EVT group. The results of these two RCTs and three observational studies were pooled in a systematic review by Katsanos et al. (Katsanos et al. 2021) With low certainty of evidence, there was no significant difference found between the groups for the primary outcome of mRS score 0–3 at 90 days (RR= 0.97, 95% CI: 0.64-1.47). There were no significant differences between groups for the proportion of patients with mRS scores of 0-2 at 3 months, all-cause mortality or functional outcome (ordinal shift analysis of mRS scores), with significant heterogeneity. The risk of sICH was significantly higher in the EVT group (RR=5.42, 95% CI 2.74-10.71).

To date, 6 RCTs have been published comparing direct EVT with intravenous alteplase prior to EVT for LVO infarcts (i.e., bridging), with conflicting results. The most recent trials, DIRECT SAFE (Mitchell et al. 2022) and SWIFT DIRECT (Fischer et al. 2022) both reported that EVT alone was not shown to be non inferior to EVT plus thrombolysis. For the primary outcome of mRS score of 0-2 at 90 days, the adjusted differences in proportions between groups were −7.3% (95% CI −16.6 to 2.1, p=0·12) in the SWIFT-DIRECT trial and −5.1% (95% CI −16 to 5.9, p=0.19) in the DIRECT SAFE trial, which crossed the lower boundaries of the two-sided 95% confidence interval set for non-inferiority at 12% and 10%, respectively. Two previously published trials, the SKIP trial (Suzuki et al. 2021) and MR CLEAN–NO IV trial, (LeCouffe et al. 2021) also did not demonstrate the non-inferiority of EVT alone. In the MR CLEAN–NO IV trial, the adjusted common odds ratio (OR) for shift in mRS score at 90 days was 0.84 (95% CI 0.62 to 1.15), which showed neither superiority nor noninferiority of EVT alone. In the SKIP trial, (Suzuki et al. 2021) mechanical thrombectomy alone was not associated with a favorable shift in the distribution of the mRS score at 90 days (OR=0.97, 1-sided 97.5% CI 0.60 to ∞; noninferiority p =0.27, which crossed the 0.74 threshold). In contrast, DIRECT-MT (Yang et al. 2020) and DEVT (Zi et al. 2021) reported that EVT alone was non-inferior to alteplase followed by EVT. In the DEVT trial, 54.3% of patients in the EVT group achieved functional independence vs. 46.6% in the bridging group (difference= 7.7%; 1-sided 97.5% CI −5.1% to ∞; p = .003 for noninferiority, threshold for non-inferiority was -10%). Finally, EVT alone was noninferior to bridging in an ordinal shift analysis of mRS scores at 90 days (adjusted common OR=1.07; 95% CI 0.81 to 1.40; p=0.04 for noninferiority) in the DIRECT-MT trial. (Yang et al. 2020) In a systematic review and patient-level meta-analysis including the results from all 6 RCTs described above, (Majoie et al. 2023) non-inferiority of EVT alone was not established. For an average patient, the estimated difference in probability of reaching functional independence (mRS 0-2) at 90 days when omitting intravenous thrombolysis was –2.5% (95% CI –6.5% to 1.0%). Thrombolysis prior to EVT using tenecteplase has also been evaluated. In the BRIDGE-TNK trial, (Qiu

et al. 2025) the likelihood of achieving an mRS score of 0-2 at 90 days was significantly higher in patients who received tenecteplase (0.25 mg/kg) prior to EVT compared with those who did not (52.9% vs. 44.1%; adjusted RR=1.18, 95% CI 1.01–1.39).

Sedation

There have been a limited number of RCTs specifically comparing the use of general anesthesia versus conscious sedation for EVT procedure. The results are conflicting. Results from the AMETIS trial, (Chabanne et al. 2023) indicated that conscious sedation increased the probability of a good outcome (mRS 0-2) at 90 days by 29%, while 10.9% of the conscious sedation patients converted to general anesthesia. Previous single-centre trials including GOLIATH, (Simonsen et al. 2018) AnStroke Trial, (Löwhagen Hendén et al. 2017) and SIESTA (Schönenberger et al. 2016) trials, reported that general anesthesia was associated with better outcome (mRS 0-2) at 90 days. The conversion from conscious sedation to general anesthesia in these trials occurred in 6.3%, 14.3% and 15.5% of patients. Preliminary results from the SEdation Versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (SEGA, NCT03263117), also suggest that general anaesthesia was associated with a significantly higher likelihood of functional independence measured by mRS at 90 days (OR=1.22).

A systematic review (Campbell et al. 2021) including the results of 3 RCTs (GOLIATH, AnStroke and SIESTA) in addition to data from a pilot study of 40 patients, (Sun et al. 2020) found the odds of successful recanalization and good functional outcome were significantly higher in the general anesthesia group (OR=2.14, 95% CI 1.26-3.62, p=0.005 and OR=1.71, 95% CI: 1.13-2.59; P=0.01, respectively), with no significant differences between groups in the risk of mortality or intracerebral hemorrhage. A Cochrane review (Tosello et al. 2022) included the results from 7 RCTs and reported on both short and long-term outcomes. In the short-term, general anesthesia was not associated with better early neurological recovery or stroke related mortality, but was associated with a decreased risk of adverse events and greater likelihood of artery revascularisation. The likelihood of having a good functional outcome (mRS ≤2) at 90 days was not significantly higher in the general anesthesia group.

The outcomes of patients who received general anesthesia or conscious sedation has also been examined within the landmark EVT trials. Using the results from 7 RCTs including MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT, PISTE and THRACE, Campbell et al. (Campbell et al. 2018) performed a patient-level meta-analysis comparing the outcomes of patients randomized to the EVT groups who had received general anesthesia or non-general anesthesia. The odds of improved outcome using non-general anesthesia were significantly higher in ordinal analysis of mRS scores. The authors estimated for every 100 patients treated under general anesthesia (compared with non-general anesthesia), 18 patients would have worse functional outcome, including 10 who would not achieve functional independence. There was no increased risk of 90-day mortality associated with general anesthesia.

Sex and Gender Considerations

In a patient-level meta-analysis using data from 5 RCTs, conducted by the HERMES Collaborators, (Goyal et al. 2016) there were no significant treatment effects of EVT based on pre-specified subgroups including age, sex, NIHSS, site of intracranial occlusion, intravenous alteplase received or ineligible, ASPECTS, time from onset to randomization, or the presence of tandem cervical carotid occlusion. The same finding was reported in another Hermes Collaboration, using data from 7 RCTs, (Chalos et al. 2019) which was confined to an examination of sex differences. No evidence of

heterogeneity of treatment effect based on sex was detected in prespecified subgroups in the DEFUSE 3 trial, (Albers et al. 2018) DAWN trial, (Nogueira et al. 2018) ESCAPE, (Goyal et al. 2015) or THRACE(Bracard et al. 2016) trials, where subgroup analysis was performed. In the two, most recent trials examining EVT with bridging therapy, (DIRECT SAFE, (Mitchell et al. 2022) and SWIFT DIRECT (Fischer et al. 2022)), differences in sexes between treatment groups were examined in prespecified subgroup analyses; none were found. Sex differences were examined specifically in 3,422 patients included in the IRETAs database who had undergone EVT treatment since 2011.(Casetta et al. 2022) The outcomes of women vs. men were compared in the original cohort (1,621 men and 1,801 women) and in a propensity-matched cohort of 1,150 men and women. In both the whole cohort and matched-pair cohort, the odds of functional independence at 90 days given EVT treatment were significantly higher in women (OR= 1.19, 95% CI 1.02–1.38 and OR=1.25, 95% CI 1.04-1.51, respectively). Time metrics (e.g., onset to groin puncture) were similar for men and women. Kobeissi et al.(Kobeissi et al. 2023) included 10 studies (10,209 patients) treated with EVT. There was no significant difference between the sexes in the odds of achieving the primary outcome (mRS 0-2 at 90 days: OR= 1.16, 95% CI 0.87-1.56), nor were there any differences between groups on any of the secondary outcomes (mRS 0-1, sICH, thrombolysis in cerebral infarction (TICI) score of 2b-3, and mortality).

Note: The CSBPR Acute Stroke Management writing group and the National Advisory Committee strongly endorse all of the recommendations in Section 5, based on available research evidence, clinical expertise, and international consensus. A recent technology assessment report provided a focused assessment of some of these data and suggested there is "substantial uncertainty" regarding the effectiveness of alteplase; however, this technology report did not synthesize all the available evidence and their conclusions differ from most other international guideline organizations as well as the CSBPR writing group. Refer to evidence table (CADTH, 2022).

Reference List and Evidence Tables

Evidence Table and Reference List 5: Acute Ischemic Stroke Treatment – Thrombolytic Therapy

Evidence Table and Reference List 5B: Acute Ischemic Stroke Treatment – Endovascular Therapy, 2025

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 6 Acute Antithrombotic Therapy

6. Acute Antithrombotic Therapy Recommendations 2022

6.1 Acute antithrombotic therapy *for patients not receiving intravenous thrombolysis*

i. All patients with acute ischemic stroke or transient ischemic attack (TIA) who are not already on an antiplatelet agent should be treated with at least 160 mg of acetylsalicylic acid (ASA) immediately as a one-time loading dose after brain imaging has excluded intracranial hemorrhage [Strong recommendation; High quality of evidence].

   a. For patients with delayed swallow screen or potential dysphagia, ASA (81 mg daily) or clopidogrel (75 mg daily) may be administered by enteral tube or ASA (325 mg daily) by rectal suppository [Strong recommendation; Moderate quality of evidence]. *Note: ASA and clopidogrel should only be administered orally once dysphagia screening has been performed and indicates an absence of potential dysphagia.*

ii. For endovascular thrombectomy (EVT) patients who did not receive intravenous thrombolysis and with no other contraindications, administration of an antiplatelet agent should not be delayed [Strong recommendation; Moderate quality of evidence].

iii. For patients with stroke who are discharged directly from the emergency department to the community, antiplatelet therapy should be started prior to discharge [Strong recommendation; Moderate quality of evidence].

6.1.1 Acute antithrombotic therapy *for patients receiving IV thrombolysis*

i. For patients receiving intravenous thrombolysis therapy, antiplatelet therapy should be avoided within the first 24 hours; antiplatelet therapy could then be initiated after brain imaging has excluded secondary hemorrhage [Strong recommendation; Moderate quality of evidence].
Refer to Secondary Prevention of Stroke module Sections 6 and 7 for additional information on antithrombotic therapy and anticoagulation for people with atrial fibrillation beyond the acute period.

6.2 Short-Term Dual Antiplatelet Therapy for Secondary Stroke Prevention

i. For patients with an acute high-risk TIA or minor ischemic stroke of non-cardioembolic origin (National Institutes of Health Stroke Scale [NIHSS] 0-3), who are not at high bleeding risk, dual antiplatelet therapy (DAPT) is recommended [Strong recommendation; High quality of evidence].

ii. Suggested regimens include at least:

   a. ASA 162 mg loading dose followed by ASA 81 mg daily plus clopidogrel 300-600 mg loading dose followed by clopidogrel 75 mg daily, for 21 days [Strong recommendation; High quality of evidence]

      OR

   b. ASA 162 mg load dose followed by ASA 81 mg daily plus ticagrelor 180 mg loading dose followed by ticagrelor 90 mg BID for 30 days [Strong recommendation; Moderate quality of evidence]

Note: The choice of the antiplatelet agent to add to ASA (i.e., clopidogrel or ticagrelor) should be based on individual patient and clinical factors, including the risk of moderate to severe hemorrhage described in the clinical trials.

iii. Use of dual antiplatelet therapy for longer than prescribed, as per 6.2ii/a and 6.2ii/b, following a TIA or minor stroke is ***not recommended*** unless there is a specific indication (e.g., arterial stent; symptomatic intracranial artery stenosis), due to an increased risk of bleeding [Strong recommendation; Moderate quality of evidence].

a. Patients should be counselled that their dual antiplatelet regimen should be followed by single antiplatelet therapy with either ASA or clopidogrel indefinitely [Strong recommendation; High quality of evidence].

iv. Patients not meeting criteria for dual antiplatelet therapy should be initiated on a single antiplatelet agent within 24 hours of symptom onset. Suggested regimens include either:

a. ASA 162 mg loading dose followed by 81 mg daily [Strong recommendation; High quality of evidence]

OR

b. Clopidogrel 300 to 600 mg loading dose followed by 75 mg daily [Strong recommendation; High quality of evidence].

6.3 Anticoagulation for Stroke Prevention

i. Patients with TIA who are found to have atrial fibrillation should receive oral anticoagulation instead of antiplatelet therapy [Strong recommendation; High quality of evidence] as soon as possible, and ideally within 24 hours of symptom onset [Strong recommendation; Moderate quality of evidence].

ii. Patients with stroke who are found to have atrial fibrillation should receive oral anticoagulation instead of antiplatelet therapy [Strong recommendation; High quality of evidence], with timing of initiation at the discretion of the physician based on patient-specific factors including size of infarct [Strong recommendation; Moderate quality of evidence].

Section 6 Clinical Considerations

1. Patients who are at a very high risk for 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 surgeon or interventionalist to determine the appropriate timing and selection of antiplatelet agent(s).
2. For patients on dual antiplatelet therapy, gastrointestinal protection may be considered for those at higher risk of gastrointestinal bleeding.
3. For patients with acute stroke or TIA and non-valvular atrial fibrillation, anticoagulation should be initiated; however, there is a lack of randomized evidence to guide specific timing. According to expert consensus, a general approach to the target timing of initiation of DOAC therapy post-stroke is as follows:
    a. For patients with a brief TIA and no visible infarct or hemorrhage on imaging, anticoagulation may be started within the first 24 hours post-TIA.
    b. For patients with a minor clinical stroke/small non-hemorrhagic infarct on imaging, anticoagulation may be started 3 days post-stroke.
    c. For patients with a moderate clinical stroke/moderate-sized infarct on imaging (without hemorrhage on CT), anticoagulation may be started 6 to 7 days post-stroke.
    d. For patients with a severe clinical stroke/large-sized infarct on imaging (without hemorrhage on CT), anticoagulation may be started 12 to 14 days post-stroke.
    e. Antiplatelet therapy may be used prior to initiating anticoagulation.

    Refer to CSBPR Secondary Prevention of Stroke module sections 6 and 7 for additional information on management of atrial fibrillation and choice of therapeutic agents.
4. For patients who experience a stroke while receiving one antiplatelet agent, stroke etiology should be reassessed and addressed, and all other vascular risk factors aggressively managed. Continuing the current antiplatelet agent or switching to a different agent are

reasonable options. At the time of writing, evidence is lacking to make more specific recommendations.

5. **(NEW FOR 2022)** Platelet function assays and pharmacogenetic testing may indicate antiplatelet activity and patients with potential clopidogrel resistance; however, the clinical implications for stroke prevention treatment are unclear at the time of writing and publication.

Rationale

Acetylsalicylic acid (ASA) initiated within the first day following stroke and continued for the next several weeks reduces the risk of early recurrent ischemic stroke and early death. For every 1,000 patients treated with aspirin following stroke, seven recurrent ischemic strokes could be avoided, corresponding to a number needed to treat of 140 (Sandercock et al., 2014; Cochrane Database Syst Rev. 2014; 2014(3):CD000029). Long-term aspirin therapy reduces the risk of ischemic stroke, myocardial infarction, and vascular death. A short course of dual antiplatelet with clopidogrel or ticagrelor can also significantly reduce the risk of recurrent stroke or death with the first month following stroke, with number need to treat of 92 (THALES trial JAMA Neurol. 2020 ;78(2):1–9). In clinical trials of alteplase, antithrombotic drugs (including aspirin) were avoided until after the 24-hour post-thrombolysis scan had excluded intracranial hemorrhage.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Development and dissemination of protocols and standing order sets to guide initial management of ischemic stroke and TIA patients.
2. Optimization of comprehensive strategies at the local, regional and provincial levels to prevent the recurrence of stroke.
3. Stroke prevention awareness and education about secondary prevention for all healthcare providers who manage patients with stroke during the acute phase and after discharge from acute care, including content regarding the heart-brain connection and the importance of integrated care that addresses vascular risk factors in a coordinated manner.
4. For patients taking warfarin, access to a dedicated anticoagulant management clinic is associated with better patient outcomes compared to routine medical care post discharge.
5. Universal and equitable access to cost-effective medicines for all people in Canada, regardless of ability to pay or geography, through private and/or public drug coverage plans which can help manage atrial fibrillation.

Performance Measures

System Indicators:

In development.

Process Indicators:

1. Proportion of ischemic stroke or TIA patients who receive acute antiplatelet therapy within the first 48 hours following symptom onset.
2. Proportion of patients with ischemic stroke or transient ischemic attack prescribed antiplatelet therapy on discharge from acute care.

Patient-oriented outcome and experience indicators:

3. Proportion of people discharged with a minor stroke or TIA who are readmitted within 30 days (or 90 days) with a recurrent stroke or TIA.

Measurement Notes

a. Time interval measurements should be taken from the time the patient is triaged at the hospital until the time the first dose is administered.

b. These indicators now expands to include other antiplatelet medications, such as clopidogrel or ASA combined with extended-release dipyridamole. In cases where another agent is used instead of aspirin in the first 48 hours, this should be noted in the local indicator definition.

c. Possible data sources include history and physical, physician's admission notes, nurses' admission notes, medication record.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Canadian Cardiovascular Society Antiplatelet Therapy Guidelines: https://ccs.ca/guideline-resources/
- Thrombosis Canada Clinical Guides: http://thrombosiscanada.ca/?page_id=18
- CHEST Antithrombotic Guidelines: https://journal.chestnet.org/GuidelineAntithrombotic
- Canadian Cardiovascular Society Antiplatelet Therapy Guidelines: https://ccs.ca/guidelines-and-position-statement-library
- Canadian Cardiovascular Society Guideline Resource: https://ccs.ca/guideline-resources/
- CLOT PLUS (CLOT+) is a continuously updated repository of current best evidence from research to support evidence-based clinical decisions: https://plus.mcmaster.ca/ClotPlus

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Antiplatelets: https://www.heartandstroke.ca/heart-disease/treatments/medications/antiplatelet-medications

- Heart & Stroke: Online and Peer Support: https://www.heartandstroke.ca/heart-disease/recovery-and-support/the-power-of-community
- Thrombosis Canada: Patient and Family Information: https://thrombosiscanada.ca/resourcepage/patient-family-information/
- Thrombosis Interest Group of Canada, Medical Information for Patients Taking Antiplatelets: http://www.tigc.org/getattachment/ddd6fce2-ebc9-4ac5-b0ea-fae1b2fb5131/medical-information-for-patients-taking-antiplatel.aspx

Summary of the Evidence

Early antiplatelet therapy provided acutely following ischemic stroke is known to reduce the risk of recurrent ischemic stroke. ASA is arguably the most commonly used agent. Results from two of the largest trials of ASA indicate that treatment can reduce the risk of death and recurrent stroke.

In the Chinese Acute Stroke Trial (CAST, Chen et al., 1997), 21,106 patients with acute stroke onset within the previous 48 hours were randomized to receive 160 mg/day of aspirin or placebo for four weeks during hospitalization. There were significantly fewer deaths among patients in the aspirin group (3.3% vs. 3.9%, absolute benefit 5.4/1,000) and fewer recurrent ischemic strokes (1.6% vs. 2.1%, absolute benefit of 4.7/1,000). Aspirin therapy was associated with an excess of 2.7/1,000 transfused or fatal extracranial bleeds during the treatment period (0.8% vs. 0.6%, p=0.02). In the aspirin arm of the factorial IST (1997) 9,720 patients with a suspected acute ischemic stroke with onset of <48 hours were randomized to receive 300 mg/day of aspirin and a similar number avoided aspirin for 14 days. The median time to randomization was 19 hours, while 20% of patients were randomized within 6 hours of symptom onset. Fourteen-day mortality was non-significantly lower in the aspirin group (9.0% vs. 9.4%). Recurrent ischemic stroke was significantly lower in the aspirin arm (2.8% vs. 3.9%, number needed to treat [NNT] 91), with no significant difference between groups in the frequency of symptomatic intracerebral hemorrhage (0.9% vs. 0.8%). In a recent Cochrane review (Minhas et al. 2022), in which the results of CAST and IST contributed 96% of the data, the odds of the primary outcome (death or dependence at follow-up) were significantly lower in the antiplatelet group (OR=0.95, 95% CI 0.90-0.99), with 13 fewer events/1,000 patients treated, and a number needed to benefit of 79. The odds of recurrent ischemic stroke were also significantly lower without any significantly increased risk of intracerebral hemorrhage.

The results of a retrospective study suggest that an initial loading dose of at least 160 mg ASA is required for therapeutic benefit. Su et al. (2016) examined the outcomes of patients with acute stroke who had received high-dose aspirin (160-325 mg) vs. low-dose aspirin (<160 mg), as a loading dose in the emergency department. Propensity matching (3:1) was used to balance baseline differences between groups. The mean loading doses of aspirin in the groups were high-dose: 211.4 mg and 100.0 mg, respectively. After propensity matching and further adjustment for age and other potential confounders, the odds of a favourable outcome (mRS 0-1) at hospital discharge were increased significantly for patients in the high-dose group (OR=1.54, 95% CI 1.23-1.93). High-dose aspirin was associated with a 20% increased risk of minor bleeding events, but not major bleeding events, with an increase of 10%.

Short-term DAPT with either clopidogrel or ticagrelor is effective in reducing the risk of recurrent ischemic stroke in selected patients. Johnston et al. (2018) enrolled 4,881 patients with recent (within previous 12 hours) minor stroke or TIA from centres located mainly in the United States in the Platelet-Oriented Inhibition in New TIA & Minor Ischemic Stroke (POINT) Trial. Patients were randomized to receive 81 mg aspirin plus 75 mg clopidogrel (following a loading dose of 600 mg) vs. aspirin plus

placebo for 90 days. At the end of the trial, significantly fewer patients in the clopidogrel–aspirin group had experienced a new vascular event (5% vs. 6.5%, HR=0.75, 95% CI 0.59–0.95), or ischemic stroke (4.6% vs. 6.3%; HR=0.72, 95% CI 0.56–0.92, p= 0.01); however, 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 1,000 patients treated with clopidogrel plus aspirin for 90 days, 15 ischemic strokes would be prevented but five major hemorrhages would result. The greatest protection from treatment was seen in the first 21 days during which the risk of a major ischemic event was significantly lower in the clopidogrel–aspirin group (HR=0.65, 95% CI 0.50–0.85, p=0.0015), but not from 22 to 90 days (HR=1.38, 95% CI 0.81–2.35, p=0.24) (Johnston et al., 2019). Although the antiplatelet regimen in the Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE, Wang et al., 2013) trial was slightly different than the POINT trial, as patients in the DAPT group received an aspirin placebo for days 22 to 90, and the dose was 75 mg daily, the results were similar, whereby significantly fewer patients in the clopidogrel plus aspirin group experienced a stroke within 90 days (8.2% vs. 11.7%, HR=0.68, 95% CI 0.0.57-0.81, p<0.001). The composite outcome of myocardial infarction, stroke, or vascular death stroke was also reduced significantly in the dual antiplatelet group (8.4% vs. 11.9%, HR=0.69, 95% CI 0.58- 0.82, p<0.001), with no significant increased risk of any bleeding events between groups (2.3% vs. 1.6%, p=0.09). The Acute STroke or Transient IscHaemic Attack Treated with TicAgreLor and ASA for PrEvention of Stroke and Death (THALES) trial (Johnston et al., 2020) included 11,0161 patients from 450 sites globally, with minor acute ischemic stroke (NIHSS score of ≤5) or high-risk TIA ($ABCD^2$ score of ≥6) or symptomatic intracranial or extracranial arterial stenosis. Patients were randomized to receive 90 mg ticagrelor twice a day plus 75-100 aspirin mg/day vs. 75-100 mg aspirin daily, within five days of stroke onset, for 30 days. The risk of the primary event (recurrent stroke or death within 30 days) was significantly lower in the ticagrelor–aspirin group (5.5% vs. 6.6%, HR=0.83, 95% CI 0.71-0.96, NNT=92), as was the risk of recurrent stroke (5.0% vs. 6.3%, HR=0.79, 95% CI 0.63-0.94). The risks of severe bleeding and intracranial hemorrhage or fatal bleeding were significantly higher in the ticagrelor–aspirin group (0.5% vs. 0.1%, HR=3.99, 95% CI 1.74–9.14, and 0.4% vs. 0.1%, HR=3.66, 95% CI 1.48–9.02, respectively).

A systematic review, including the results of four trials of DAPT with either clopidogrel (POINT, CHANCE and FASTER [Kennedy et al,. 2007]) or ticagrelor (THALES) found that DAPT significantly reduced the risk of stroke recurrence (RR=0.74, 95% CI 0.67–0.82, absolute risk difference=2%, NNT=50), while increasing the risk of major bleeding compared with aspirin (RR=2.54, 95% CI 1.65 to 3.92, absolute risk difference= 0.4%, NNH=250). Both of these findings were associated with high certainty of evidence (Pomero et al., 2022). The risk of disabling stroke (mRS>2) was also reduced significantly with DAPT (RR=0.84, 95% CI 0.75 to 0.95). In a meta-analysis which pooled the results of the patient-level data from the POINT and CHANCE trials, Pan et al. (2019), reported that the risks of ischemic stroke and disabling or fatal stroke were reduced by 31% in the DAPT group, with no significant increases in major hemorrhage or hemorrhagic stroke. The risk of a major ischemic event associated with DAPT was reduced significantly with treatment provided during days 0 to 21, with the effect being most pronounced during days 1 to 10. There was no significant reduction in events associated with DAPT use from days 22 to 90.

For those who are unable to tolerate DAPT, monotherapy with either ASA or clopidogrel is indicated. In the CAPRIE trial (Gent et al., 1996), 19,185 patients who had experienced an ischemic stroke thought to be of atherothrombotic origin, or myocardial infarction, or had peripheral artery disease, were randomized to receive 75 mg of clopidogrel or 325 mg aspirin daily for one to three years. The mean time from stroke onset to randomization was 53 days. After a mean duration of follow-up of 1.9 years, the risk of the primary outcome (ischemic stroke, myocardial infarction, or vascular death) was significantly lower in the clopidogrel group (event rate/year 5.32% vs. 5.83%, absolute risk reduction=0.51%; relative risk reduction=8.7%, 95% CI 0.3%-16.5%, p=0.043). There were no major

differences between groups on any of the bleeding outcomes.

Sex & Gender Considerations

Sex as a potential effect modifier was examined in the analysis of the primary outcome in all of the major trials of DAPT used to inform the current guideline recommendations including POINT, CHANCE, and THALES. In all trials, no differences in outcomes between men vs. women were found in the comparison of the DAPT and monotherapy groups. In the early trials of ASA monotherapy (CAST 1997 and IST 1997), the effect of sex on outcome was not examined in subgroup analysis.

Reference List and Evidence Tables

Evidence Table and Reference List 6: Acute Antithrombotic Therapy

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 7 Early Management of Patients Considered for Hemicraniectomy

7. Early Management of Patients Considered for Hemicraniectomy Recommendations 2022

7.1 Patient Selection

i. For patients aged 18 – 60 years old, hemicraniectomy should be considered as a life-saving measure for patients in the early stages of extensive (malignant) middle cerebral artery (MCA) territory ischemic stroke (defined as infarction size >50% MCA territory on visual inspection, or an ischemic lesion volume >150 cm^3 and concomitant clinical features) if patients or their substitute decision-makers are 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. years [Strong recommendation; High quality of evidence].

   a. Hemicraniectomy could also be considered for patients aged 60 – 80 years [Conditional recommendation; Moderate quality of evidence].

ii. Posterior fossa decompression should be considered early in patients with significant cerebellar stroke with evidence of mass effect and/or hydrocephalus [Strong recommendation; Low quality of evidence].

iii. Patients at risk for malignant edema should have a consultation with a stroke specialist and neurosurgeon [Strong recommendation; Low quality of evidence].

   a. If these services are not available on-site, patients should be considered for expedited transfer to a centre where advanced stroke care and neurosurgical services are available [Strong recommendation; Low quality of evidence].

7.2 Initial Clinical Evaluation

i. Urgent decisions regarding decompressive craniectomy should be undertaken based on discussions with patient, family members, and substitute decision-maker regarding a potential decompressive craniectomy [Strong recommendation; Low quality of evidence].

   a. Patients with severe stroke due to large vessel occlusions may be at higher risk of developing malignant edema. In these patients, early discussions should be considered [Conditional recommendation; Low quality of evidence].

   b. Key issues to be discussed with the patient, family members, and substitute 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 [Strong recommendation; Low quality of evidence].

7.3 Considerations Prior to Hemicraniectomy Surgery

i. Patients at risk of malignant edema should be monitored in an intensive care unit or neuro step-down unit [Strong recommendation; Low quality of evidence].

   a. Monitoring should include assessments of level of consciousness (e.g., Glasgow Coma Scale, Canadian Neurological Scale Score (CNS)), worsening symptom severity, and blood pressure at least hourly or more frequently if the patient's condition requires it [Strong recommendation; Low quality of evidence].

   b. If changes in status occur, the stroke team and neurosurgeon should be notified immediately for re-evaluation of the patient [Strong recommendation; Low quality of evidence]. Changes in status include level of drowsiness/consciousness, change in CNS score by ≥1 point, or change in National Institutes of Health Stroke Scale (NIHSS) score by ≥4 points [Strong recommendation; Low quality of evidence].

ii. In patients selected for decompressive craniectomy, surgery should be performed within 48 hours from stroke onset, and ideally before clinical deterioration occurs [Strong recommendation; Moderate quality of evidence].

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) [Conditional recommendation; Low quality of evidence].

Section 7 Clinical Considerations:

1. Global disability and quality of life outcomes are similar regardless of whether the hemicraniectomy was for right or left sided MCA infarction.
2. Whereas age alone is not a reason to forego hemicraniectomy, the DESTINY II trail reported that for 0% of patients over 60 years had mild or no disability (mRS of 0 – 2), and only 7% could function independently (mRS 0-3) after hemicraniectomy surgery.

Rationale

The morbidity and mortality of patients with malignant hemispheric strokes is higher than other stroke subgroups. In selected cases, hemicraniectomy may significantly reduce mortality, with numbers needed to treat as low as 2 (Reinink H et al., JAMA Neurol 2021;78(2):208-216), and increase the probability of a reasonable outcome (mRS ≤3).

Consideration for hemicraniectomy must be individualized, with careful clinical consideration of patient selection. Decisions regarding hemicraniectomy involve several members of the interdisciplinary stroke team, including neurology, neurosurgery, intensive care, and nursing, through a collaborative and coordinated system of care.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Timely access to diagnostic services such as neuroimaging, with protocols for prioritizing potential patients with stroke.
2. Timely access to specialized stroke care (i.e., a neuro-intensive care unit) and neurosurgical specialists for consultation and patient management, including rapid referral process if neurosurgical services are not available within the initial treating hospital.
3. Access to organized stroke care, ideally stroke units with a critical mass of trained staff and an interdisciplinary stroke team.
4. Education for emergency department and hospital staff on the characteristics and urgency for management of patients with severe stroke.

Performance Measures

System Indicators:

1. Risk-adjusted mortality rates for patients with stroke who undergo craniectomy (in-hospital, 30-day, and one year). (Also PROM)

Process Indicators:

2. Time from arrival to hospital to start of hemicraniectomy procedure.
3. Percentage of hemicraniectomy patients who experience intraoperative complications.

Patient-oriented outcome and experience indicators:

4. Distribution of functional ability measured by standardized functional outcome tools at time of discharge from hospital and over time in the community (e.g., 90 days, 1 year).
5. Quality of life rating for people who have undergone craniectomy following an acute stroke, using validated quality of life measures.

Measurement Notes

a. Mortality rates should be risk-adjusted for age, sex, stroke severity, and comorbidities.
b. Time interval measurements should start from symptom onset of known or from triage time in the emergency department as appropriate.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practice Recommendations Acute Stroke Management Module Appendix 3, Table 4: Screening and Assessment Tools for Acute Stroke Severity
- Canadian Stroke Best Practices Table 2A: Recommended Laboratory Investigations for Acute Stroke and Transient Ischemic Attack

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947

Summary of the Evidence

The benefit of decompressive hemicraniectomy compared with standard medical treatment, early following malignant MCA infarction in patients <60 years has been evaluated in three major RCTs, all of which had comparable inclusion criteria and primary outcome measures (DESTINY 1, HAMLET, and DECIMAL). In the first DESTINY trial (Juttler et al., 2007), which randomized 32 patients to receive either surgical plus medical treatment or conservative medical treatment only, there was a trend toward more favourable outcome (mRS 0-3) among patients in the surgical arm at 6 months (47% vs. 27%, (p=0.23; OR=2.44, 95% CI 0.55 to 10.83). Thirty-day survival was significantly higher among patients in the surgical arm (88% vs. 47%, OR=6.4, 95% CI 1.35 to 29.2). In the HAMLET trial (Hofmeijer et al., 2009), while there were no differences between groups in the proportion of patients who had experienced either a good (mRS 0-1) or poor (mRS 4-6) outcome at 1 year, surgery was associated with a 38% absolute risk reduction (95% CI 15 to 60, p=0.002) in one-year mortality. Patients who received decompressive hemicraniectomy had significantly lower mean physical summary scores on the SF-36 Quality of Life scale, compared with those treated with medical care

only (29 vs. 36; mean difference = −8, 95% CI -14 to -1, p = 0.02). No significant differences were found between the two treatment groups with respect to the mental summary score of the SF-36 score, mood, or the proportion of patients or carers dissatisfied with treatment. At 3 years follow-up (Geurts et al., 2013), a significantly lower percentage of patients in the surgical group had died (26% vs. 63%, p=0.002) In the DECIMAL trial (Vahedi et al. 2007b), while there was no difference in the number of patients with mRS scores of 0-3 between groups at 6 months, a significantly higher proportion of surgical patients had mRS scores of 0-4 and there was also a survival advantage among patients in the surgical arm. The results from all three trials were pooled in a Cochrane review (Cruz-Flores et al., 2012), which reported that decompressive hemicraniectomy was associated with a significantly reduced risk of death at the end of follow-up (OR = 0.19, 95% CI 0.09 to 0.37) and the risk of death or severe disability (mRS > 4) at 12 months (OR = 0.26, 95% CI 0.13 to 0.51). Surgery was also associated with a non-significant trend towards increased survival with severe disability (mRS of 4 or 5; OR = 2.45, 95% CI 0.92 to 6.55). No significant between group differences were found for the combined outcome of death or moderate disability (mRS 4-6) at the end of follow-up (OR = 0.56, 95% CI 0.27 to 1.15). In a more recent systematic review, which included the results from 7 trials, including DESTINY, DESTINY II, DECIMAL and HAMLET (Reinink et al., 2021), similar findings were reported. The odds of a favourable outcome (mRS 0-3) at one year were significantly higher in the surgical group (adjusted OR=2.95, 95% CI 1.55-5.60) and the odds of death of death at one year were significantly lower (adjusted OR=0.16; 95% CI, 0.10-0.24).

The upper age limit for decompressive hemicraniectomy in malignant MCA infarct has been a focus of debate, given that the evidence is conflicting. Using data from 276 patients obtained from 17 case series, McKenna et al. (2012) reported that patients ≥60 years of age who underwent surgery had a higher mortality rate and poorer outcome compared with younger patients. In the DECIMAL trial's surgical group, younger age correlated with better outcomes at 6 months (r = 0.64, p < 0.01) (Vahedi et al., 2007b). A retrospective study investigating decompressive hemicraniectomy in older adults compared the outcomes of individuals aged between 61 and 70 years and those >70 years of age (Inamasu et al., 2013). The mortality rate was significantly higher among those in the older cohort (60% vs. 0%, p = 0.01). However, there is also evidence suggesting that older patients also benefit from surgery. Zhao et al. (2012) randomized 47 patients aged 18 to 80 years, 29 of whom were >60 years. Decompressive hemicraniectomy within 48 hours of stroke onset was associated with a significant overall reduction in mortality at both 6 (12.5% vs. 60.9 %, p = 0.001) and 12-month follow-up (16.7% vs. 69.6 %, p < 0.001). In the subgroup of older patients, 61% fewer patients in the surgical arm had an unfavourable outcome (mRS 5–6) at 6 months (31.2% vs. 92.3%) with similar results reported at one year. Authors from the HAMLET trial reported that there was a trend towards greater benefit of surgery in patients between the ages of 51 and 60 compared with patients ≤50 years of age (Hofmeijer et al., 2009). In the DESTINY II trial (Juttler et al., 2014), 112 patients ≥61 years admitted with unilateral MCA infarction were randomized to receive conservative treatment or early surgical intervention. A significantly higher proportion of patients in the surgical group were alive and living without severe disability ($\mathrm{mRS}\ 0-4$) at 6 months (38% vs.18%, OR=2.91, 95% CI 1.06-7.49, p=0.04). Although no patients in either the surgical or medical care groups had good outcome (mRS score of 0-2) at 6 or 12 months, a significantly higher percentage of patients in the surgical group had mRS scores of 3-4 (38% vs. 16%) and a significantly lower percentage had mRS scores of 5-6 (62% vs. 84%).

Timing of surgical intervention is also an important consideration when deciding whether to perform decompressive hemicraniectomy. In the HAMLET trial there was a significant reduction in both mortality and poor outcome when patients were randomized to surgery within 48 hours of stroke onset, with no significant benefit when patients received surgery within 96 hours (Hofmeijer et al., 2009). However, in a pooled analysis using the subgroup results from the DECIMAL, DESTNY I and

HAMLET trials examining the outcomes of patients treated within 24 hours vs. >24 hours following stroke onset, no differences in outcome were reported (Vahedi et al., 2007a). Taken together, these findings suggest that the appropriate time interval to perform decompressive hemicraniectomy may be within 48 hours; however, further research is needed to determine if earlier treatment (e.g., within 24 hours) is associated with better outcomes.

Sex and Gender Considerations

The mean percentage of men enrolled in the trials reviewed was ≥50%, ranging from 50% (DESTINY 2) to 72% (Zhao et al., 2012), except in the DESTINY and DECIMAL trials, where men represented 47% of participants. Sex was not explored as a potential effect modifier in any of the hemicraniectomy trials.

Reference List and Evidence Tables

Evidence Table and Reference List 7: Early Management of Patients Considered for Hemicraniectomy

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Part 2 Acute Inpatient Stroke Care Recommendations

Section 8 Acute Stroke Unit Care

8. Acute Stroke Unit Care Recommendations 2022

8.1 Patients admitted to hospital with an acute stroke or transient ischemic attack (TIA) should be treated on an inpatient stroke unit [Strong recommendation; High quality of evidence] as soon as possible; ideally within 24 hours of hospital arrival [Strong recommendation; Low quality of evidence].

i. All efforts should be made to admit patients to an acute stroke unit, which is a specialized, geographically defined hospital unit dedicated to the management of patients with stroke [Strong recommendation; High quality of evidence].

a. Facilities without a dedicated stroke unit must strive to focus care on the priority elements for comprehensive stroke care delivery, including clustering patients, having an interdisciplinary team, providing access to early rehabilitation, using stroke care protocols, conducting case rounds, and providing patient education [Strong recommendation; Moderate quality of evidence].

Note: Stroke unit care is the gold standard for care following acute stroke. Alternate models may be discussed with system planners and should only be considered if it is not possible to create or access a stroke unit. Refer to Box 8A Optimal Acute Inpatient Stroke Care for additional information.

ii. The core interdisciplinary stroke team should consist of healthcare professionals with stroke expertise including physicians, nurses, occupational therapists, physiotherapists, speech-language pathologists, social workers, dietitians, patients, and family members [Strong recommendation; High quality of evidence], who are ideally available seven days a week [Strong recommendation; Low quality of evidence].

a. All interdisciplinary stroke teams should include hospital pharmacists to promote patient safety; conduct medication reconciliation; provide education to the team and patients and families about medications and their side effects, adverse effects, and interactions; promote adherence; and participate in discharge planning which could include addressing special needs for patients, such as individual dosing packages [Strong recommendation; Moderate quality of evidence].

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 [Strong recommendation; Moderate quality of evidence].

c. The patient and family should be included as part of the core team [Strong recommendation; Low quality of evidence].

d. All professional members of the interdisciplinary stroke team should have specialized training in stroke care and recovery [Strong recommendation; Moderate quality of evidence].

iii. The interdisciplinary stroke team should assess all patients as soon as possible after admission to hospital, and ideally within 48 hours, and formulate a management plan [Strong recommendation; High quality of evidence].

iv. Assessments of impairment, functional activity limitations, role participation restrictions, and environmental factors should be conducted using standardized, valid assessment tools [Strong recommendation; Moderate quality of evidence].

a. Patients should be assessed for areas such as dysphagia, mood and cognition, mobility, functional assessment, temperature, nutrition, bowel and bladder function,

skin breakdown, vision, apraxia, neglect, and perception [Strong recommendation; Moderate quality of evidence]. *Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke for additional information.*

b. Patients should have a formal and individualized assessment to determine the type of ongoing post-acute rehabilitation services they require as soon as their status has stabilized, and within the first 72 hours post-stroke, using a standardized protocol [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Rehabilitation and Recovery Following Stroke module Section 3 for additional information.*

c. Tools should be adapted for use with patients who have communication differences or limitations as required [Strong recommendation; Moderate quality of evidence].

v. Discharge planning discussions, prevention therapies, and venous thromboembolism prophylaxis should be initiated soon after arrival on the acute stroke unit [Strong recommendation; Moderate quality of evidence]. *Refer to Section 9 Inpatient Prevention and Management of Complications Following Stroke for additional information.*

8.2 Management of Stroke Occurring While Patient is Already in Hospital

i. Patients who experience onset of signs and symptoms of a new acute stroke while already in hospital should have an immediate assessment by a physician with stroke expertise, undergo neurovascular imaging without delay, and be assessed for eligibility for intravenous thrombolytics and/or endovascular thrombectomy [Strong recommendation; Moderate quality of evidence]. *Refer to Section 4 Emergency Department Evaluation and Management of Patients with TIA and Acute Stroke, and Section 5 Acute Ischemic Stroke Treatment, for additional information.*

ii. All hospitals should have protocols to manage acute inpatient stroke, and all staff should be familiar with these protocols, especially in units with higher risk patients [Strong recommendation; Moderate quality of evidence].

8.3 Virtual Inpatient Stroke Care

i. Virtual stroke care modalities should be considered to support optimal in-hospital stroke care when patients cannot be transferred to an acute stroke unit (i.e., virtual stroke unit care) including support for medical decision-making and rehabilitation treatment [Conditional recommendation; Low quality of evidence]. *Refer to the CSBPR Virtual Stroke Care Implementation Toolkit for additional information.*

ii. Virtual care technology should be available to provide education to admitted patients and to staff working with patients, and to allow patients to access programs available at other locations if not available on-site, when safe to do so [Conditional recommendation; Low quality of evidence].

Box 8A Optimal Acute Inpatient Stroke Care

Definitions

Acute stroke unit: A specialized, geographically defined hospital unit dedicated to the management of patients with stroke, staffed by an experienced interdisciplinary stroke team, and providing a complex package of evidence-based care (e.g., protocols, care pathways) for acute stroke management, early rehabilitation, and education to patients with stroke in hospital.

Rehabilitation stroke unit: A specialized, geographically defined hospital rehabilitation unit dedicated to the management and recovery of people following stroke. These units accept patients for intensive rehabilitation provided by an interdisciplinary team, once patients are medically stable, usually within five to seven days after an acute stroke event. *Refer to CSBPR Rehabilitation and*

Recovery Following Stroke, Section 2 for additional information.

Comprehensive stroke unit: A comprehensive stroke unit is a specialized, geographically defined hospital unit that combines acute stroke care and stroke rehabilitation. It accepts patients with acute stroke and also provides them with rehabilitation services all in one place, usually for up to several weeks. Both the rehabilitation unit model and the comprehensive unit model offer prolonged periods of rehabilitation (Langhorne, 2020).

Alternate stroke care delivery models: Many models of acute stroke care exist across Canada. Although many organizations do not have an official administrative designation as an acute stroke centre, they meet most or all of the stroke unit criteria listed as core elements below, and should be recognized as attempting to provide optimal, evidence-based stroke care despite administrative and structural resource challenges. These models are sometimes referred to as clustered acute stroke care, or purposeful grouping of patients with stroke.

Core Elements of Comprehensive Stroke and Neurovascular Care

(Adapted from the Stroke Unit Trialists Collaboration, 2020)

Efforts should be made to provide all the elements of stroke unit care or have processes in place to transfer patients to the closest acute or comprehensive stroke unit to meet their care needs.

a. **Ensures the person with stroke and their family and informal caregivers are at the centre of all stroke care planning and delivery**.
b. Has processes and mechanisms to prioritize access to stroke unit beds for patients with acute stroke within 24 hours of hospital arrival or in-hospital stroke (when medically appropriate, in consultation with other care team members).
c. Accepts patients with acute stroke for comprehensive stroke management within hours of the patient's arrival at hospital.
d. Has established protocols and processes of care in place to implement as many elements as possible to achieve optimal stroke care delivery within the geographic location, hospital volumes and resource availability (human, equipment, funding).
e. Provides advanced diagnostic capability, specialized care, and close monitoring for patients with ischemic stroke, intracerebral hemorrhage, and TIA. Care may be expanded in some institutions to include patients with subarachnoid hemorrhage and other neurovascular conditions.
f. Includes a dedicated interdisciplinary stroke team with broad range of expertise, including neurology, nursing, neurosurgery, physiatry, rehabilitation professionals, pharmacists, and others (on-site or rapid access off-site).
g. Has access to 24/7 imaging and interventional neuroradiology expertise.
h. Has access to emergent neurovascular surgery.
i. Has protocols for emergent and acute stroke management in place, and for seamless transitions between stages of care, including prehospital, emergency department, and inpatient care.
j. Has dysphagia screening protocols to assess all patients with stroke without prolonged time delays prior to commencing oral nutrition and oral medications.
k. Has access to post-acute rehabilitation services, including inpatient, outpatient, community-based, and/or early supported discharge therapy.
l. Initiates transition/discharge planning as soon as possible after admission, and anticipates discharge needs to facilitate smooth transitions.

m. Holds daily or bi-weekly patient care rounds with the interdisciplinary stroke team to conduct case reviews and discuss patient management issues, family concerns or needs, and discharge planning (e.g., discharge or transition to the next step in the patient's care, timing, transition requirements).

n. Provides patient and family education that is formal, coordinated, and addresses learning needs and responds to patient and family readiness.

o. Provides palliative and end-of-life care when required and ideally by health professionals with specialized expertise in a palliative approach to care.

p. Ensures ongoing professional development for all staff on stroke knowledge, evidence-based best practices, skill building, and orientation of trainees.

q. Participates in clinical research for stroke care.

r. Routinely collects process and patient-oriented outcome data on all patients with stroke, and regularly reviews data to inform quality improvement and address gaps in service delivery.

Rationale

Stroke unit care is characterized by a coordinated interdisciplinary team comprising physicians, nurses, physiotherapists, occupational therapists, speech- language pathologists, and pharmacists, among others. They have a special interest and expertise in stroke care and are dedicated to the management of patients recovering from stroke. Staff on these units tend to have greater expertise, better nursing care is provided, and patients are mobilized sooner. As a result, patients treated on stroke units experience fewer complications and receive rehabilitation therapies earlier. Typically, patients have better outcomes compared with those treated on less specialized units. Stroke unit care is associated with reductions in the likelihood of death, death and disability, and death or the need for institutionalization by approximately 25%. For every 100 participants receiving care on a stroke unit, there would be 2 extra people who survived, 6 more living at home, and 6 more living independently (SUTC, Cochrane Database of Systematic Reviews 2020, Issue 4. Art. No.: CD000197).

People with lived experience expressed the value of including family and other caregivers as early as possible in helping the person with stroke through their recovery process. They provided examples such as having a list or cheat sheet of activities that families and caregivers can complete with the person with stroke, as a way to provide support.

People with lived experience valued the ability to be aware of and track the stroke patient's progress while the patient was on the acute stroke unit. They discussed that at times, patients may not realize the progress they've made, particularly when spending more time in bed and potentially losing track of days. They shared instances where family members, informal caregivers, and healthcare providers provided this type of support by using videos, notes, and voice memos to document and communicate the patient's progress.

People with lived experience also discussed their experience transitioning from acute care to another setting. They valued being a part of the conversation and receiving explanations about transition planning out of acute care and understanding their transition date plan. Recognizing that transitions can look very different depending on the person's circumstances, people with lived experience stressed the importance of having healthcare providers explain available services to support their recovery, regardless of transition destination, as well as the importance of receiving education and preparation about the transition plan, including next steps such as rehabilitation, stroke prevention clinic, and activities that can be done while wait for rehabilitation. While people with lived experience emphasized the value in having someone in the role of a stroke patient navigator and/or care

coordinator, to support the patient and their family throughout their journey, they recognized that this is not always available.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Organized systems of stroke care including stroke units with a critical mass of trained staff (interdisciplinary team). Availability of Health Human Resources to appropriately staff stroke units and provide recommended best practice service (e.g., 7 days/week) and promote optimal outcomes.
2. Protocols and mechanisms to enable the rapid transfer of patients with stroke from the emergency department to a specialized stroke unit as soon as possible after arrival in hospital, ideally within the first six hours.
3. Comprehensive and advanced stroke care centres with leadership roles within their geographic regions, to ensure specialized stroke care access is available to patients who may first appear at general healthcare facilities (usually remote or rural centres) and facilities with basic stroke services only.
4. Telestroke service infrastructure and utilization optimized to ensure access to specialized stroke care across the continuum to meet individual needs (including access to rehabilitation and stroke specialists) including the needs of northern, rural, and remote residents in Canada.
5. Information on geographic location of stroke units, rehabilitation, and home care services, and other specialized stroke care models available to community service providers, to facilitate navigation to appropriate resources and to strengthen relationships between each sector along the stroke continuum of care.
6. Efforts to facilitate building and maintaining of stroke expertise among staff to provide appropriate and evidence-based best practice care to patients with stroke. The interprofessional healthcare team members should have stroke-specific knowledge, skills, and expertise, and access regular education to maintain competency.

Performance Measures

System Indicators:

1. Proportion of designated stroke unit beds that are filled with patients with stroke (weekly average). (Core)
2. Percentage increase in virtual stroke care coverage to remote communities to support organized stroke care across the continuum.

Process Indicators:

3. Number of patients with stroke who are admitted to hospital and treated on a specialized stroke unit at any time during their inpatient hospital stay for an acute stroke event (numerator) as a percentage of total number of patients with stroke admitted to hospital.
4. Proportion of patients admitted to the stroke unit who arrive in the stroke unit within 24 hours of emergency department arrival.
5. Proportion of patients admitted to the stroke unit who have a rehabilitation assessment within 48 hours of admission.
6. Proportion of patients with stroke discharged to their home or previous place of residence following an inpatient admission for stroke.

7. Proportion of patients with stroke discharged to inpatient rehabilitation following an inpatient admission for stroke.
8. Proportion of total time in hospital for an acute stroke event that is spent on an acute stroke unit.
9. Length of stay for patients with stroke admitted to hospital.

Patient-oriented outcome and experience indicators:

10. Proportion of patients with stroke who die in hospital within 7 days and within 30 days of hospital admission for an index stroke (reported by stroke type).
11. Functional outcome scores at 30 and 90 days following acute hospital discharge, using validated tools, for patients with stroke treated on an acute stroke unit compared to those not treated on an acute stroke unit.

Refer to Canadian Stroke Quality and Performance Measurement Manual for detailed indicator definitions and calculation formulas. www.strokebestpractices.ca.

Measurement Notes

a. Calculate for all cases, and then stratify by type of stroke where appropriate.
b. Definition of stroke unit varies among institutions. Where stroke units do not meet the criteria defined in the Section 8 recommendations; then a hierarchy of other stroke care models could be considered: (a) dedicated stroke unit; (b) designated area within a general nursing unit or neuro-unit where patients with stroke are clustered; (c) mobile stroke team care; or (d) managed on a general nursing unit by staff using stroke guidelines and protocols.
c. Institutions collecting these data must note their operational definition of “stroke unit” to ensure standardization and validity when data is reported across institutions.
d. Performance measure 6: Start time for assessing stroke unit admission within 24 hours should be emergency department triage time.
e. Patient and family experience surveys should be in place to monitor care quality during inpatient stroke admissions.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Canadian Stroke Best Practices Table 2A: Recommended Laboratory Investigations for Acute Stroke and Transient Ischemic Attack
- Canadian Stroke Best Practices Recommendations Acute Stroke Management Module Appendix 3, Table 4: Screening and Assessment Tools for Acute Stroke Severity
- Box 8A: Optimal Acute Inpatient Stroke Care
- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-strokebest-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1

- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls
- Heart & Stroke: Virtual Stroke Care Implementation Toolkit: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/csbpr-virtual-stroke-toolkit-final
- Stroke Engine: http://strokengine.ca/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Enabling Self-management Following Stroke: A Checklist for Patients, Families and Caregivers: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr-enabling-self-management-following-stroke-checklist-jan2021-final
- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls
- Heart & Stroke: Virtual Healthcare Checklist: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbp-infographic-virtual-healthcare-checklist
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Secondary Prevention Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7-infographic-secondaryprevention-final
- Heart & Stroke: Rehabilitation and Recovery Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/rehabilitation-nov2019/csbp-infographic-rehabilitation
- Heart & Stroke: Transitions and Community Participation Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/transition-of-care-nov2019/csbp-infographic-transitions-and-participation
- Heart & Stroke: Online and Peer Support: https://www.heartandstroke.ca/heart-disease/recovery-and-support/the-power-of-community
- Canadian Partnership for Stroke Recovery, Video Resources: https://canadianstroke.ca/tools-videos/
- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

It is well-established that patients who receive stroke unit care are more likely to survive, return home, and regain independence compared to patients who receive less organized forms of care. Stroke unit care is characterized by an experienced interprofessional stroke team, including physicians, nurses, physiotherapists, occupational therapists, speech therapists, among others, who are dedicated to the

management of patients with stroke, often located within a geographically defined space. Other features of stroke units include staff members who have an interest in stroke, routine team meetings, continuing education/training, and involvement of caregivers in the rehabilitation process (Langhorne et al., 2020). In an updated Cochrane Review (2020), the Stroke Unit Trialists' Collaboration identified 29 randomized and quasi-randomized trials (5,902 participants) comparing stroke unit care with alternative, less organized care (e.g., an acute medical ward). Compared to less organized forms of care, stroke unit care was associated with a significant reduction in the odds of death (OR= 0.76, 95% CI 0.66 to 0.88), a poor outcome (OR=0.77, 95% CI 0.69 to 0.87), and death or dependency (OR= 0.75, 95% CI 0.66 to 0.85) at a median follow-up of one year. Based on the results from a small number of trials, the authors also reported that the benefits of stroke unit care are maintained for periods up to 5- and 10-years post-stroke. Moreover, subgroup analyses demonstrated benefits of stroke unit care regardless of sex, age, or stroke severity. Saposnik et al. (2011) investigated the differential impact of stroke unit care on four subtypes of ischemic stroke (cardioembolic, large artery disease, small vessel disease, or other) and reported that stroke unit care was associated with reduced 30-day mortality across all subtypes.

To determine if the benefits of stroke unit care demonstrated in clinical trials can be replicated in routine clinical practice, Seenan et al. (2007) conducted a systematic review of 25 observational studies (n=42,236) comparing stroke unit care to non-stroke unit care. Stroke unit care was associated with a reduction in the risk of death (OR=0.79, 95% CI 0.73 to 0.86, p<0.001) and of death or poor outcome (OR=0.87, 95% CI=0.80 to 0.95; p=0.002) within 1 year of stroke. Similar findings were reported for the outcome of death at one year in a secondary analysis limited to multi-centred trials (OR=0.82, 95% CI 0.77 to 0.87, p<0.001).

In-hospital Stroke

Estimates of persons who experience a stroke while already hospitalized for other conditions range from 4% to 17% (as cited by Cumbler et al., 2014). Many of these patients have pre-existing stroke risk including hypertension, diabetes, cardiac diseases, and dyslipidemia. These in-hospital strokes often occur following cardiac and orthopedic procedures, usually within 7 days of surgery. There is evidence to suggest that, compared with persons who suffer a stroke in the community, patients who experience an in-hospital stroke have more severe strokes, worse outcomes, and do not receive care in as timely a fashion (Kimura et al., 2006; Farooq et al., 2006). Comparing the outcomes of over 250,000 patients who experienced a stroke with in-hospital (3.0%) or out-of-hospital onset, Akbik et al. (2020) reported patients with in-hospital stroke were significantly less likely to be treated with intravenous thrombolysis within 60 minutes of onset (adjusted OR=0.45, 95% CI, 0.42-0.48), were 22% less likely to be independent ambulators at discharge, and had an increased likelihood of in-hospital mortality or discharge to hospice (adjusted OR= 1.39; 95% CI, 1.29-1.50). Similar treatment delays and outcomes were reported for patients treated for in-hospital stroke with EVT.

Sex and Gender Considerations

In none of the major trials of stroke unit care was sex considered as a potential effect modifier. However, in a systematic review (Carcel et al. 2019) including data from 5 acute randomized controlled trials examining sex differences on stroke outcomes, among the findings was that women were more likely to be admitted a stroke unit (OR=1.17, 95% CI 1.01–1.34), compared with men.

Reference List and Evidence Tables

Evidence Table and Reference List 8: Acute Stroke Unit Care

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 9 Inpatient Prevention and Management of Complications Following Stroke

9. Inpatient Prevention and Management of Complications Recommendations 2022

9.0 Evidence-based investigations and management strategies should be implemented for all hospitalized stroke and transient ischemic attack (TIA) patients to optimize recovery, avoid complications, prevent stroke recurrence, and provide palliative care when required [Strong recommendation; Moderate quality of evidence].

i. During acute inpatient care, patients with stroke should undergo appropriate investigations to determine stroke mechanism and guide stroke prevention and management decisions [Strong recommendation; Moderate quality of evidence].

ii. Patients should be evaluated and treatment plans initiated for secondary prevention of vascular risk factors, including hypertension, diabetes, dyslipidemia and smoking cessation [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Secondary Prevention of Stroke module for additional information.*

iii. Individualized care plans should address nutrition, oral care, mobilization, and incontinence, and reduce the risk of complications such as urinary tract infection (UTI), aspiration pneumonia, and venous thromboembolism [Strong recommendation; Moderate quality of evidence].

iv. Transition planning should begin as a component of the initial admission assessment and continue throughout hospitalization as part of ongoing care of patients with acute stroke [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Transitions and Community Participation Following Stroke module Section 3 for additional information.*

v. All patients, family members, and informal caregivers should receive timely and comprehensive information, education, and skills training about stroke from interdisciplinary team members [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Transitions and Community Participation Following Stroke module Sections 1 and 2 for additional information.*

vi. Patients should undergo an initial screening for depression, including screening for a history of depression [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Mood, Cognition and Fatigue Section 1 for additional information.*

vii. Stroke assessments should include evaluation of risk factors for depression, particularly a history of depression [Strong recommendation; Low quality of evidence].

viii. Patients should undergo an initial screening for vascular cognitive impairment when indicated [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Mood, Cognition and Fatigue Section 2 for additional information.*

9.1 Cardiovascular Investigations

i. Patients with suspected ischemic stroke or TIA should have a 12-lead electrocardiogram (ECG) to assess for atrial fibrillation, concurrent myocardial infarction, or structural heart disease (e.g., left ventricular hypertrophy) as potential causes of or risk factors for stroke [Strong recommendation; Moderate quality of evidence].

ii. For patients being investigated for an acute embolic ischemic stroke or TIA, ECG monitoring for 24 hours or more 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 [Strong recommendation; High quality of evidence].

iii. 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 2 weeks is

recommended, as soon as practically possible, to improve detection of paroxysmal atrial fibrillation in selected patients ≥55 years who are not already receiving anticoagulant therapy but would be potential anticoagulant candidates [Strong recommendation; High quality of evidence]. *Refer to CSBPR Secondary Prevention of Stroke module for additional information.*

iv. Routine echocardiography is not recommended for all patients with stroke. Echocardiography should be considered for patients with an embolic ischemic stroke or TIA of undetermined source, or when a cardioembolic etiology or paradoxical embolism is suspected [Strong recommendation; Moderate quality of evidence].

v. For patients ≤60 years who are being investigated for an embolic ischemic stroke or TIA of undetermined source, echocardiography with saline bubble study is recommended for detection of a patent foramen ovale (PFO) if it may change patient management (i.e., in patients who would be potential candidates for PFO closure or anticoagulant therapy if a PFO were detected) [Strong recommendation; Moderate quality of evidence].

   a. Contrast-enhanced (agitated saline) transesophageal echocardiography or transcranial Doppler has greater sensitivity than transthoracic echocardiography for detection of right-to-left cardiac and extra-cardiac shunts and should be conducted when available [Strong recommendation; Moderate quality of evidence].

9.2 Venous Thromboembolism Prophylaxis

i. All patients with stroke should be assessed for their risk of developing venous thromboembolism (deep vein thrombosis [DVT] and pulmonary embolism [PE]). ***Patients at high risk*** include those who are unable to move one or both lower limbs; those who are unable to mobilize independently; those with a previous history of venous thromboembolism, those who are dehydrated; and those with comorbidities such as active or suspected malignancy [Strong recommendation; Moderate quality of evidence].

ii. Patients at high risk of venous thromboembolism should be started on thigh-high intermittent pneumatic compression (IPC) devices or pharmacological venous thromboembolism prophylaxis (e.g., low molecular weight heparin [LMWH] or unfractionated heparin [UFH]) beginning on day of admission if there is no contraindication (e.g., systemic or intracranial hemorrhage) [Strong recommendation; High quality of evidence]. At present, there is no direct evidence to suggest the superiority of one approach over the other.

   a. Intermittent pneumatic compression devices should be discontinued when the patient becomes independently mobile, at discharge from hospital, if the patient develops adverse effects, or by 30 days, whichever comes first [Strong recommendation; Moderate quality of evidence].

iii. Graduated compression stockings are not recommended for deep vein thrombosis prevention [Strong recommendation; High quality of evidence].

iv. For patients with stroke admitted to hospital and who are immobile for >30 days, the use of ongoing venous thromboembolism prophylaxis (e.g., with pharmacological venous thromboembolism prophylaxis) is recommended [Strong recommendation; Low quality of evidence].

v. If intermittent pneumatic compression is considered after the first 24 hours of admission, venous leg Doppler studies should be considered [Strong recommendation; Low quality of evidence].

Section 9.2 Clinical Consideration:

1. Use of LMWH or UFH should be weighed against the potential risk for intracerebral hemorrhage for each individual patient.

9.3 Temperature Management

i. Temperature should be monitored as part of vital sign assessments; ideally every 4 hours for the first 48 hours, and then as per ward routine or based on clinical judgment [Strong recommendation; Moderate quality of evidence].

ii. For temperature >37.5 Celsius, frequency of monitoring should be increased, temperature-reducing measures should be initiated, causes of possible infection such as pneumonia or UTI should be investigated, and antipyretic and antimicrobial therapy should be initiated as required [Strong recommendation; Moderate quality of evidence].

9.4 Mobilization

***Definition**: Mobilization is 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 and using a standardized tool [Strong recommendation; Moderate quality of evidence].

ii. Initial screening and assessment should be commenced as early as possible, and ideally within 48 hours of admission by rehabilitation professionals who are in direct contact with the patient [Strong recommendation; Moderate quality of evidence]. *Refer to the CSBPR Rehabilitation and Recovery Following Stroke 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 [Strong recommendation; High quality of evidence].

iv. Early prolonged mobilization of patients within ***the first 24 - 48 hours after*** a stroke, especially a severe stroke, is not recommended [Strong recommendation; High quality of evidence].

v. Earlier mobilization may be reasonable for some patients with acute stroke (e.g., people with milder strokes or TIA) but caution is advised and clinical judgement should be used [Conditional recommendation; Low quality of evidence].

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

Refer to CSBPR Rehabilitation and Recovery Following Stroke module for additional recommendations on mobilization following an acute stroke.

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 the seizures are not self-limiting [Strong recommendation; Moderate quality of evidence].

   a. Patients who have an immediate post-stroke seizure should be monitored for recurrent seizure activity [Strong recommendation; Low quality of evidence].

   b. Recurrent seizures in patients with ischemic stroke should be treated as per local treatment recommendations for seizures in other neurological conditions [Strong recommendation; Moderate quality of evidence].

ii. A single, self-limiting seizure occurring at the onset or within 24 hours after an ischemic stroke is considered an "immediate" post-stroke seizure and does not require long-term anticonvulsant medications [Conditional recommendation; Low quality of evidence].

iii. Prophylactic use of anticonvulsant medications in patients with ischemic stroke is not recommended [Strong recommendation; Moderate quality of evidence]

iv. Continuous or repeat electroencephalogram monitoring in patients with a stroke and unexplained reduced level of consciousness should be considered [Conditional recommendation; Moderate quality of evidence].

9.6 Nutrition and Dysphagia

i. Patients should be screened for swallowing impairment before any oral intake, including medications, food, and liquid, by an appropriately trained professional using a valid screening tool [Strong recommendation; Moderate quality of evidence]. Refer to Appendix 3: Table 5 Canadian Stroke Best Practices: Selection of Validated Swallowing Screening Tools

ii. The swallowing, nutritional and hydration status of patients with stroke should be screened as early as possible, ideally on the day of admission, using validated screening tools [Strong recommendation; Moderate quality of evidence].

iii. Abnormal results from the initial or ongoing swallowing screens should trigger a prompt referral to a speech-language pathologist, occupational therapist, dietitian, and/or other trained dysphagia clinicians for more detailed assessment and management of swallowing, feeding, nutritional, and hydration status [Strong recommendation; Moderate quality of evidence].

   a. An individualized management plan should be developed to address therapy for dysphagia, dietary needs, and specialized nutrition plans [Strong recommendation; Moderate quality of evidence].

iv. For patients who cannot safely swallow or meet their nutrient and fluid needs orally, enteral nutrition (e.g., nasogastric tube feeding) should be considered in consultation with the patient, family, or substitute decision-maker, and the interdisciplinary team as early as possible after admission, usually within the first three days of admission [Strong recommendation; Moderate quality of evidence]. *Refer to CSBPR Rehabilitation and Recovery Following Stroke module section 7 for additional information on dysphagia screening, assessment, and management.*

   a. Nasogastric feeding tubes should be replaced by gastric-jejunum tube (GJ-tube) if the patient requires a prolonged period of enteral feeding [Strong recommendation; Moderate quality of evidence]

9.7 Continence

i. Indwelling catheters should be used cautiously due to the risk of UTIs [Strong recommendation; High quality of evidence].

   a. If used, indwelling catheters should be assessed daily and removed as soon as possible [Strong recommendation; High quality of evidence].

   b. Peri care and infection prevention strategies should be implemented to minimize risk of infection [Strong recommendation; Moderate quality of evidence]. *Refer to Section 4.6(iii) for additional information.*

ii. Patients with stroke should be screened for urinary incontinence and retention, with or without overflow; fecal incontinence; and constipation [Strong recommendation; Moderate quality of evidence].

iii. The use of a portable ultrasound machine is recommended as the preferred non-invasive method to assess post-void residual [Conditional recommendation; Low quality of evidence].

iv. Patients with stroke with urinary incontinence should be assessed by trained personnel using a structured functional assessment to determine cause and develop an individualized management plan [Strong recommendation; Moderate quality of evidence].

v. Patients with stroke with urinary incontinence should have a bladder-training program implemented [Conditional recommendation; Low quality of evidence].

   a. The bladder training program should include timed and prompted toileting on a consistent schedule [Conditional recommendation; Moderate quality of evidence].

   b. Appropriate intermittent catheterization schedules should be established based on amount of post-void residual [Conditional recommendation; Moderate quality of evidence].

vi. Patients with stroke with persistent constipation or bowel incontinence should have a bowel management program implemented [Strong recommendation; Moderate quality of evidence].

9.8 Oral Care

i. At or soon after admission, patients with stroke should have an oral/dental assessment, including screening for signs of dental disease, level of oral care, and appliances [Strong recommendation; Low quality of evidence].

ii. For patients with stroke wearing a full or partial denture it should be determined if they have the neuromotor skills to safely wear and use the appliance(s) [Strong recommendation; Low quality of evidence].

iii. For patients where there are concerns about oral hygiene and/or appliances, a referral to a dentist for consultation and management should be made as soon as possible [Strong recommendation; Moderate quality of evidence].

iv. Patients with stroke should receive oral care consistent with the Canadian Dental Association recommendations, and the oral care should address areas such as frequency of oral care (ideally after meals and before bedtime); types of oral care products (toothpaste, floss, mouthwash); and management for patients with dysphagia [Strong recommendation; Moderate quality of evidence].

Rationale

Medical complications are common following acute stroke and are associated with prolonged lengths of stay and increased costs compared to other causes of hospitalization in Canada. Patients with acute stroke are at risk for complications such as venous thromboembolism, pyrexia, and seizures, among others during the early phase of recovery. The priorities for inpatient care are management of stroke sequelae to optimize recovery, prevention of post-stroke complications that may interfere with recovery, and prevention of stroke recurrence.

People with lived experience valued the person-centred care approach and found it helpful to know *why* something was happening. They described that at times it can feel as though things are being done *to* you and shared that having an explanation of what was happening helped them feel more engaged and part of the team. They also emphasized the importance of healthcare providers repeating information as needed for the patient and their family and/or caregivers. Fear and stress from having recently gone through the shock of having a stroke can make it more difficult to absorb information, and so repeating the information can help the person process and understand. They suggested that a one-page handout of “what’s important over the next few days” might be a helpful tool for people with stroke and their families while in acute care. This document could explain what is important in the early days and why; this would also help them absorb and remember the information, and help ensure consistent information is shared by all of the healthcare providers involved in the patient’s care.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Standardized evidence-based protocols instituted for optimal inpatient care of all patients with acute stroke, regardless of where they are treated in the healthcare facility (stroke unit or other ward), and across the regional stroke system of care.
2. Ongoing professional development and educational opportunities for all healthcare professionals who care for patients with acute stroke.
3. Referral systems to ensure rapid access to specialty care such as dentistry and hematology.

Performance Measures

System Indicators:

1. Median length of stay, stratified by stroke type, during acute phase of care for all patients with stroke admitted to hospital (core).
2. Proportion of patients with stroke who experience prolonged length of stay beyond expected length of stay as a result of experiencing one or more complications.

Process Indicators:

3. Median length of stay, stratified by stroke type and complication type, during acute phase of care for all patients with stroke admitted to hospital who experience one or more complications during hospitalization (core).

Patient-oriented outcome and experience indicators:

4. Proportion of patients admitted to hospital with a diagnosis of acute stroke who experience one or more complications during hospitalization (e.g., deep venous thrombosis, pulmonary embolus, secondary cerebral hemorrhage, gastrointestinal bleeding, pressure ulcers, UTI, pneumonia, seizures, or convulsions) during inpatient stay.
5. Quality of life rating at 30 and 90 days for people who experience complications during acute inpatient admission following acute stroke, using a validated tool.

Measurement Notes

Note, refer to the Quality of Stroke Care in Canada Key Quality Indicators and Stroke Case Definitions 7th Edition document for more detailed information. www.strokebestpractices.ca

a. Risk adjustment to account for other comorbidities, age, and sex.
b. Length of stay analysis should be stratified by presence or absence of in-hospital complications to look for the impact of a complication on length of stay.
c. Patient and family experience surveys should be in place to monitor care quality during inpatient stroke admissions.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their

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- Heart & Stroke: Virtual Stroke Care Implementation Toolkit: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/csbpr-virtual-stroke-toolkit-final
- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls
- RNAO Guidelines for Oral Health: https://rnao.ca/bpg/guidelines/oral-health-supporting-adults-who-require-assistance-second-edition
- RNAO Continence Care Resources: http://rnao.ca/bpg/guidelines/resources/continence-care-education-selflearning-package
- RNAO Guidelines for Falls Prevention in the Older Adult: http://rnao.ca/bpg/guidelines/prevention-falls-and-fall-injuries
- Canadian Continence algorithms: http://www.canadiancontinence.ca/EN/urinary-incontinence-charts.php
- Canadian Cardiovascular Society Atrial Fibrillation Guidelines: https://ccs.ca/guidelines-and-position-statement-library/
- American College of Chest Physicians (ACCP) Guidelines for Pulmonary Vascular Guidelines and Expert Panel Reports: http://www.chestnet.org/Guidelines-and-Resources/CHEST-Guideline-Topic-Areas/Pulmonary-Vascular
- Canadian Association of Radiologists Guidelines: https://car.ca/patient-care/practice-guidelines/
- Stroke Engine: http://strokengine.ca/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: Virtual Healthcare Checklist: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbp-infographic-virtual-healthcare-checklist

- Heart & Stroke: Secondary Prevention Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7-infographic-secondaryprevention-final
- Heart & Stroke: Rehabilitation and Recovery Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/rehabilitation-nov2019/csbp-infographic-rehabilitation
- Heart & Stroke: Transitions and Community Participation Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/transition-of-care-nov2019/csbp-infographic-transitions-and-participation
- Heart & Stroke: Living with Physical Changes: http://www.heartandstroke.ca/stroke/recovery-and-support/physical-changes
- Heart & Stroke: Taking Action for Optimal Community and Long-Term Stroke Care (TACLS) A Resource for Healthcare Providers: https://www.strokebestpractices.ca/resources/professional-resources/tacls
- Heart & Stroke: Online and Peer Support: https://www.heartandstroke.ca/heart-disease/recovery-and-support/the-power-of-community
- Canadian Continence Foundation patient resources: http://www.canadiancontinence.ca/EN/health-care-professionals.php
- Stroke Engine: http://strokengine.ca/

Summary of the Evidence

Medical complications are relatively common following stroke and are associated with increased lengths of stay and higher cost. Appropriate investigations and management strategies should be implemented for all hospitalized patients to avoid complications, prevent stroke recurrence, 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% (Ingeman et al., 2011) to 85% (Langhorne et al., 2000). Some of the most commonly cited complications include UTIs, fever, pneumonia, and DVT (Otite et al., 2017; Indredavik et al., 2008; Roth et al., 2001).

Cardiovascular Investigations

Detecting atrial fibrillation (AF) after a stroke or TIA is important since it is a major risk factor for subsequent stroke and, once identified, can be effectively treated. However, AF is under-diagnosed because it is frequently paroxysmal and asymptomatic. Additionally, although many abnormalities can be detected within the first few days of monitoring, prolonged screening may be required to detect others. In the Systematic MONitoring for Detection of Atrial Fibrillation in patients with acute Ischaemic Stroke (MonDAFIS) Trial, Haeusler et al. (2021) randomized 3,465 patients with no history of AF, admitted to 38 stroke units with an acute stroke or TIA to receive usual diagnostic procedures for AF detection, which included a baseline 12-lead ECG on admission and at least 24 hours of ECG monitoring (control group) or additional Holter-ECG recording for up to 7 days in hospital (intervention group). At 12 months, there was no significant difference between groups in the number of patients on oral anticoagulants (13.7% vs. 11.8%, OR=1·2, 95% CI 0·9–1·5), although AF was newly detected in significantly more patients in hospital in the intervention group (5.8% vs. 4.0%, HR=1·4, 95% CI 1·0–2·0). The Finding Atrial Fibrillation in Stroke – Evaluation of Enhanced and Prolonged Holter Monitoring FIND-AF trial, (Wachter et al,. 2017) recruited 398 patients, admitted with acute ischemic stroke, within 7 days of symptom onset, in sinus rhythm at admission, and without a history of AF. Patients were randomized to receive prolonged Holter ECG monitoring for 10 days, starting in the first week post-

stroke, and repeated at 3 and 6 months or standard care (an average of 73 hours of inpatient telemetry plus an average of 24 hours of Holter monitoring). At both 6 and 12 months, detection of AF was significantly higher in the prolonged monitoring group (13.5% vs. 4.5% and 13.5% vs. 6.1%, respectively). The associated numbers needed to screen were 11 and 13. There were no significant differences between groups in stroke recurrence (2.5 vs. 4.5%, p=0.28) or death (3.0 vs. 4.5%, p=0.45). A systematic review (Kishore et al., 2014) including the results from 32 studies (5,038 patients) of patients with acute ischemic stroke or TIA who had undergone invasive or non-invasive cardiac monitoring for a minimum of 12 hours following the event. The different types of cardiac monitoring evaluated included inpatient cardiac monitoring; 24, 48, 72 hour, and 7-day Holter; external loop recorder; invasive cardiac monitoring; and mobile cardiac outpatient telemonitoring. The overall detection rate of AF was 11.5% (95% CI 8.9%-14.3%) and was higher in selected (pre-screened or cryptogenic) patients (13.4%, 95% CI 9.0%-18.4%) compared with unselected patients (6.2%, 95% CI 4.4%-8.3%). The detection rate of AF in cryptogenic stroke was 15.9% (95% CI 10.9%-21.6%).

The use of transesophageal echocardiography (TEE) has been shown to be more sensitive compared with transthoracic echocardiography (TTE) for detecting cardiac abnormalities following ischemic stroke or TIA, although it is costlier and less acceptable to patients. Common TEE findings following stroke have included atheromatosis, PFO, and atrial septal aneurysm (Marino et al., 2016; Katsanos et al,. 2015). Marino et al. (2016) reported that 42.6% of 263 patients admitted following an acute ischemic stroke had a TEE finding which could explain the etiology of stroke/TIA. De Bruijn et al. (2006) included 231 patients with recent stroke (all types) or TIA whose stroke etiology remained in question following initial ECG, ultrasound assessments, and blood tests. All patients had a TEE followed by a TTE and the identification of major and minor cardiac sources of embolism were compared between the two diagnostic tools. A potential cardiac source of embolism was detected in 55% of the patients. Significantly more abnormalities were identified using TEE. A cardiac source was detected in 39% of patients where TEE was positive and the TTE negative. A major cardiac risk factor was detected based on TEE in 16% of patients. The detection of possible cardiac sources of embolism was statistically significantly greater using TEE compared to TTE in both patients aged ≤45 years and >45 years.

Venous Thromboembolism Prophylaxis

The use of LMWHs has been shown to be more effective for the prevention of venous thromboembolism compared with UFH), and is associated with a lower risk of serious bleeding events. A Cochrane review (Sandercock et al., 2017) included the results from 9 randomized controlled trials (RCTs) (n= 3,137) of patients with acute ischemic stroke who were randomized within 14 days of stroke onset to receive LMWHs or heparinoids, or UFH for an average of 10 to 12 days. The odds of DVT occurrence during the treatment period were significantly lower in the LMWH/heparinoid group (OR=0.55, 95% CI 0.44 -0.70, p<0.0001). There was no difference between groups in mortality during the treatment period or follow-up, nor in the odds of any ICH/hemorrhagic transformation during treatment (OR= 0.75, 95% CI 0.46- 1.23, p=0.25). The authors cautioned that the event rates for serious events (pulmonary embolus, death, and serious bleeding) were too low to provide reliable estimates of the risk and benefits.

The use of external compression stockings/devices has been investigated in a series of 3 large, related RCTs: the Clots in Legs Or sTockings after Stroke (CLOTS) trials. In CLOTS 1 (Dennis et al., 2009), 2,518 patients, admitted to hospital within 1 week of acute ischemic stroke or ICH and who were immobile, were randomized to either routine care plus thigh-length graded compression stockings (GCS) or to routine care plus avoidance of GCS. Patients wore the garments day and night until the patient became mobile, was discharged, or there were concerns with skin breakdown. At 30 days there

was no significant difference between groups in the incidence of proximal DVT (GCS 10.0% vs. avoid GCS 10.5%). GCS use was associated with a non-significant absolute reduction in risk of 0.5% (95% CI -1.9% to 2.9%). The incidence of any DVT or PE was non-significantly lower in the GCS group (17.0% vs. 18.4%, OR=0.91, 95% CI 0.74-1.11), but the frequency of skin ulcers or breakdown were significant higher in the GCS group (5.1% vs. 1.3%, OR=4.18, 95% CI 2.40-7.27). The inclusion criteria for the CLOTS 2 trial (The CLOTS Trials Collaboration, 2010) were similar to those of CLOTS 1. In this trial, 3,114 patients were randomized to wear thigh-length stockings or below-knee stockings while they were in the hospital, in addition to routine care, which could have included early mobilization, hydration, and/or the use of anticoagulants/antiplatelets. At 30 days, there was a significant reduction in the incidence of proximal DVT associated with thigh-length GCS (6.3% vs. 8.8%, adj OR=0.69, 95% CI 0.53-0.91, p=0.008). The incidence of asymptomatic DVT was also lower in the thigh-length GCS group (3.2% vs. 4.8%, adj OR=0.64, 95% CI 0.44-0.93, p=0.02). The use of thigh-length GCS was associated with an increased risk of skin breakdown (9.0% vs. 6.9%, OR=1.33, 95% CI 1.031.73, p=0.03). Finally, in CLOTS 3 (Dennis et al., 2013) 2,876 patients were randomized to wear a thigh-length IPC)device or to no IPC at all times except for washing and therapy, for a minimum of 30 days. The mean duration of IPC use was 12.5 days and 100% adherence to treatment was achieved in only 31% in the IPC group. The incidence of proximal DVT within 30 days was significantly lower for patients in the IPC group (8.5% vs. 12.1%, OR=0.65, 95% CI 0.51-0.84, p=0.001, ARR=3.6%, 95% CI 1.4%-5.8%). There were no significant differences between groups for the outcomes of: death at 30 days (10.8% vs. 13.1%, p=0.057), symptomatic proximal DVT (2.7% vs. 3.4%, p=0.269), or PE (2.0% vs. 2.4%, p=0.453). The incidence of any DVT (symptomatic, asymptomatic, proximal or calf) was significantly lower for the IPC group (16.2% vs. 21.1%, OR=0.72, 95% CI 0.60-0.87, p=0.001). Skin breakdown was more common in the IPC group (3.1% vs. 1.4%, OR=2.23, 95% CI 1.31-3.81, p=0.002). At 6 months, the incidence of any DVT remained significantly lower in the IPC group (16.7% vs. 21.7%, OR=0.72, 95% CI 0.60-0.87, p=0.001). The incidence of any DVT, death, or PE also remained significantly lower for the IPC group (36.6% vs. 43.5%, OR=0.74, 95% CI 0.63-0.86, p<0.0001).

Temperature Management

Elevated body temperature in the early post-stroke period has been associated with worse clinical outcomes. A meta-analysis conducted by Prasad & Krishnan (2010), including the results from six studies demonstrated that fever within the first 24 hours of ischemic stroke onset was associated with twice the risk of short-term mortality (OR= 2.20, 95% CI 1.59–3.03). Fever may result from a secondary infection, such as pneumonia, or may have occurred as a cause of stroke (e.g. infective endocarditis). While interventions to reduce temperature may improve the viability of brain tissue and/or prevent other medical complications post stroke, efforts to reduce fever, through a wide range of modalities including pharmacological agents (e.g., paracetamol) and physical interventions (e.g., cooling blankets and helmets and endovascular treatments) have not been convincingly shown to be effective in reducing or avoiding poorer outcomes. The largest trial examining the use of pharmacological agents for the reduction of fever was Paracetamol (Acetaminophen) In Stroke (PAIS) trial (den Hertog et al., 2009). In this trial, 1,400 patients were randomized to receive one gram of paracetamol, 6 times daily for 3 days or placebo within 12 hours of symptom onset. While treatment with paracetamol did significantly lower body temperature by a mean of 0.26°C, it was not associated with improvement beyond expectation (adjusted OR=1.20, 95% CI 0.96-1.50), nor did it increase the odds of a favourable outcome. Treatment with paracetamol was associated with a decrease in 14-day mortality (OR=0.60, 95% CI 0.36-0.90), but there was no difference at 3 months (OR=0.90, 95% CI 0.68-1.18). The PAIS 2 trial (De Ridder et al., 2017) was terminated after enrolling 26 of 1,500 planned patients. In this trial, high-dose (2 grams) or placebo was given for 3 days to patients with a temperature of ≥36.5° C. There was no

significant difference between groups in the shift in mRS scores at 90 days associated with paracetamol (common adj OR=1.15, 95% CI 0.74-1.79).
In a Cochrane review, den Hertog et al. (2009) included the results from 8 RCTs, 5 of which examined pharmacological agents (paracetamol, n=3, metamizole n=1, ibuprofen placebo n=1) versus placebo. Pharmacological treatment significantly reduced temperature at 24 hours following treatment (mean difference of -0.21° C 95% CI -0.28, -0.15, p<0.0001), but was not associated with a reduction in the odds of death or dependency at 1 to 3 months (OR= 0.92, 95% CI 0.59- 1.42, p=0.69).

Mobilization

Early mobilization post-stroke is intended to reduce the risk of medical complications including DVT, pressure sores, and respiratory infections. The potential benefits of early mobilization have been examined in several RCTs, with ambiguous results. Recently, a Cochrane review (Langhorne et al., 2018) included the results from 9 RCTs (n= 2,958) of participants who had sustained an acute stroke and could be mobilized within 48 hours. Trials included the AVERT trials (Bernhardt et al., 2008, 2015), AKEMIS (Sundseth, 2012), SEVEL (Herisson et al., 2016) and VERITAS (Langhorne et al., 2010). The median delay to starting mobilization after stroke onset was 12.7 hours shorter in the early mobilization group (18.5 vs. 33.3 hours). There were no significant differences in the odds of death or poor outcome at 3 months between groups (51% vs. 49%; OR= 1.08, 95% CI 0.92 to 1.26, p = 0.36), or the odds of death (7% vs. 8.5%; OR=1.27, 95% CI 0.95 to 1.70; p = 0.11). These results were supported by medium quality of evidence. The mean Barthel Index (20-point scale) was significantly higher in the early mobilization group (mean difference of 1.94, 95% CI 0.75 to 3.13, p = 0.001) at a median follow-up of 3 months. The mean length of hospital stay was 1.44 days shorter in the early mobilization group. Additional analysis of the AVERT 3 trial (Bernhardt et al., 2016) indicate that after controlling for age and stroke severity, regardless of group assignment, keeping time to first mobilization and frequency constant, every extra 5 minutes of out-of-bed activity per day reduced the odds of a favourable outcome by 6%, while increasing the frequency of each out-of-bed session improved the odds of favourable outcome by 13%, In 2021, Bernhardt et al. reported that by day 14, the risk of mortality was significantly higher in the very early mobilization group (OR=1.76, 95% CI 1.06-2.92).

Seizure Management

The incidence of post-stroke seizure ranges from 5%-15%, depending on stroke etiology, severity, and location (Gilad, 2012). Hemorrhagic events and cortical lesions are associated with the highest risk of both first and recurrent seizure (Gilad et al. ,2013). Evidence on the effectiveness of pharmacological treatment for post- stroke seizures is limited. A recent Cochrane review (Chang et al., 2022) sought studies including patients of any age recovering from ischemic stroke or intracerebral hemorrhage that evaluated antiepileptic drugs compared with a placebo or no drug for the primary and secondary prevention of post stroke seizures. Two publications were included. Gilad et al. (2011) randomized 72 patients to receive 800 mg/day valproic acid or placebo daily for one month. In the second trial, based on data presented in an abstract (Tujil et al., 2021), 784 patients were randomized to receive 10 mg diazepam or placebo, which was given within 12 hours after stroke onset, followed by oral 10 mg tablets twice daily for 3 days. The use of antiepileptic drugs was not associated with a significant reduction in the risk of primary seizure prevention at the end of follow-up, the durations of which were 3 months and 1 year (RR= 0.65, 95% CI 0.34 to 1.26). The certainty of the associated evidence was low to moderate.

Nutrition and Dysphagia

A standardized program for screening, diagnosis, and treatment of dysphagia following acute stroke

has been shown to reduce the incidence of pneumonia and feeding tube dependency. Bedside screening may include components related to a patient's level of consciousness, an evaluation of the patient's oral motor function and oral sensation, as well as the presence of a cough. It may also include trials of fluid. Coughing during and up to 1 minute following test completion and/or "wet" or hoarse voice are suggestive of an abnormal swallow. A recent Cochrane review (Boaden et al. 2021), evaluated the test characteristics of 37 dysphagia screening tests. Tests evaluated water only, water + other consistencies and water swallow test combined with an instrumental assessment. Among these three categories, the best performing screening tests were the Toronto Bedside Swallowing Screening Test (water only), the Gugging Swallowing Screen (water + other consistencies) and the Bedside Aspiration test (combined water + an instrumental assessment). The sensitivity of all tests was 100% with specificities of 64%, 69% and 71%.

Silent aspiration may occur in patients who do not cough or complain of any problems with swallowing or have no wet-sounding voice, highlighting the importance of dysphagia screen for all patients as soon as possible following stroke. A prospective study (Ouyang et al., 2020) of 11,093 patients with acute stroke included in the HeadPoST trial examined the association between dysphagia screening and assessment, and outcome. In 362 (3.3%) patients who developed pneumonia, compared to patients who passed a dysphagia screen, screen-fail patients had a significantly higher risk of pneumonia (1.5% vs. 10.0%; adj OR= 3.00, 95% CI 2.19–4.10) and poor outcome at 90 days (68.1% vs. 30.8%, adj OR= 1.66, 95% CI 1.41–2.95). Using United Kingdom registry data, Bray et al. (2017) reported a higher risk of stroke-associated pneumonia with increasing times to dysphagia screening and assessment. The overall incidence of stroke-associated pneumonia was 8.7% (13.8% for patients who were not screened, 8.0% for patients who were screened, and 14.7% for patients who received a comprehensive assessment).

Dietary modifications, including altered texture of solids and fluids and the use of restorative swallowing therapy, and compensatory techniques, are the most commonly used treatments for the management of dysphagia in patients who are still safe to continue oral intake. Unfortunately, there is little direct evidence of their benefit. Carnaby et al. (2006) randomized 306 patients with dysphagia admitted to hospital within 7 days of acute stroke, to receive usual care, standard low-intensity intervention (composed of environmental modifications, safe swallowing advice, and appropriate dietary modifications), or standard high-intensity intervention and dietary prescription (daily direct swallowing exercises, dietary modification), for up to 1 month. When the results from the high-intensity and low-intensity groups were combined and compared with the usual care group, patients in the active therapy group regained functional swallow sooner and had a lower risk of chest infections at 6 months.

For patients who cannot obtain nutrient and fluid needs orally, enteral nutrition may be required. The decision to use enteral support should be made within the first 7 days post-stroke. The largest trial that addresses both the issues of timing of initiation of enteral feeding and the choice of feeding tube was the FOOD trial (Dennis et al., 2005), which included 1,210 patients admitted within 7 days of stroke from 47 hospitals in 11 countries. In one arm of the trial, patients were randomized to receive either a percutaneous endoscopic gastrostomy or nasogastric feeding tube within 3 days of enrollment into the study. Percutaneous endoscopic gastrostomy feeding was associated with an absolute increase in risk of death of 1.0% (–10.0 to 11.9, p=0.9) and an increased risk of death or poor outcome of 7.8% (0.0 to 15.5, p=0.05) at 6 months. In the second part of the trial patients were randomized to receive feeds as early as possible or to avoid feeding for 7 days. Early tube feeding was associated with non-significant absolute reductions in the risk of death or poor outcome (1.2%, 95% CI -4.2 to 6.6, p=0.7) and death (15.8%, 95% CI -0.8 to 12.5, p=0.09) at 6 months.

Incontinence

To avoid the onset of UTIs, the use of indwelling catheters is largely discouraged in clinical settings and is typically limited to patients with incontinence that cannot be managed any other way. If used, the catheter should be changed or removed as soon as possible. Ersoz et al. (2007) reported that among 110 patients consecutively admitted for rehabilitation following stroke, 30 developed a symptomatic UTI during hospitalization. UTIs occurred more frequently in patients with indwelling catheters, compared with patients who could void spontaneously (7/14 vs. 23/96, p=0.041) and in patients with residual urine volumes of >50 mL (41.2% vs. 19.5%, p=0.039). Several infection prevention strategies that have been identified to prevent or delay the onset of catheter-associated UTIs include inserting the catheter using aseptic technique, correctly positioning the drainage tube and the collection bag, maintaining uncompromising closed drainage, achieving spontaneous voiding, and administering intermittent catheterizations. The effectiveness of bladder-training programs, which typically include timed/prompted voiding, bathroom training, pelvic floor exercises, and/or drug therapy, has been evaluated in a small number of studies. In one study, 42 patients admitted to a single acute stroke unit were each was prescribed an individualized bladder program consisting of bladder scanning, intermittent catheterizations/ post-void residual regimen, non-invasive voiding strategies (e.g., pelvic muscle exercises) and/or drug therapy. The regimen was continued until the post-void urine residual was below 100 ml for three consecutive days (Chan et al., 1997). Eighty-four percent of all patients achieved urinary continence within the first month of stroke. Among this group, all females became continent, while 23% of the male patients did not. In a Cochrane review, Eustice et al. (2000) included the results of 9 RCTs (n= 674), examining the potential benefit of prompted voiding (vs. no prompted voiding) provided for 10 days to 13 weeks. Prompted voiding was associated with a reduction in the number of incontinent episodes in 24 hours (MD= -0.92, 95% CI -1.32 to -0.53, p<0.0001). Thomas et al. (2014) conducted a cluster feasibility trial, Identifying Continence Options after Stroke (ICONS). Compared with usual care, the systematic voiding program was not associated with significantly increased odds of being continent at 6 or 12 weeks.

Oral Care

Physical weakness following stroke may prevent patients from independently completing their activities of daily living, including oral care. Poor oral care, combined with potential side effects of medication (e.g., dry mouth, oral ulcers, stomatitis), may contribute to a greater amount of bacteria in the mouth, leading to the development of pneumonia. Patients have also reported lower oral health-related quality of life as a result of poor or inadequate dental care following stroke (Schimmel et al., 2011). Therefore, on admission to hospital, all patients should have an oral/dental assessment to examine mastication, tooth wear, oral disease, and use of appliances following stroke. However, few studies have examined interventions to improve oral hygiene in patients following stroke. A Cochrane review conducted by Brady et al. (2006) included the results of three RCTs (n=470) that included patients receiving some form of assisted oral healthcare in a healthcare facility following stroke. Treatments evaluated included oral healthcare plus timed tooth brushing, healthcare education, and selective decontamination of digestive tract using an antimicrobial gel applied to the mucous membranes of the mouth several times per day. Due to the small number of studies and variability in treatments, pooled analyses were not possible. The use of decontamination gel was associated with a reduction in the incidence of pneumonia (OR=0.20, CI 95% 0.05 to 0.84). A single education session was not associated with a reduction in dental plaque tooth coverage, the presence of gingivitis, or denture-induced stomatitis at 1 or 6 months following training, but was associated with a significant reduction in denture plaque at both assessment points and higher knowledge scores among care providers.

Sex and Gender Considerations

Medical Complications
Otite et al. (2017) reported sex differences in the frequencies of various post stoke complications. Urinary tract infections, the most common complication, was reported in 19.8% of women compared with 9.9% in men. Acute renal failure was more commonly reported in men (10.6% vs. 5.9% in women). Overall, the risks of other complications including pneumonia, DVT and pulmonary embolism were approximately 30% greater in men. Older age and female sex were identified as risk factors for urinary tract infection in a systematic review of acute post-stroke infections (Westendorp et al. 2011).

Cardiovascular Investigations
In the FIND-AF trial (Wachter et al. 2017), in which patients were randomized to receive prolonged Holter ECG monitoring (10-days) and repeated at 3 and 6 months or standard care (minimum of 24 hours of cardiac monitoring), there were no interactions in subgroup analyses based on age, sex, baseline NIHSS, CHADS-2 score, symptoms at admission and imaging (lacunar vs. non-lacunar). Sex was not examined as a potential effect modifier in the MonDAFIS trial (Haeusler et al. 2021).

Venous Thromboembolism Prophylaxis
In the Cochrane review of (Sandercock et al. 2017) comparing LMWH with UFH, no subgroup analyses (including sex) were conducted. Sex was not a variable examined in prespecified subgroup analyses in the CLOTS trials (2009, 2010, 2013).

Temperature Management
Sex was not among the variables included in prespecified analysis of the PAIS 2 trial (De Ridder et al. 2017). However, in a systematic review (Carcel et al. 2019) including data from 5 acute randomized controlled trials examining sex differences on stroke outcomes, was the finding that women were less likely to be treated for fever (OR=0.82, 95% CI 0.70-0.95).

Mobilization
In the Cochrane review (Langhorne et al. 2018) comparing early mobilization with usual care, no subgroup analyses based on sex, were conducted. No subgroup analyses were conducted in any of the primary trials included in the review.

Seizure Management
The frequency of post-stroke seizures in the literature review was low. No subgroup analyses based on sex were conducted in trials examining the effectiveness of oral antiepileptic agents.

Nutrition and Dysphagia
The incidence of dysphagia post stroke and potential differences in treatment effectiveness in men versus women was not examined in any of the literature reviewed. No subgroup analyses based on sex were conducted in any of the trials of enteral feeding.

Incontinence
The effectiveness of behavioral interventions for the treatment of urinary incontinence, based on sex, was not examined in the literature reviewed.

Oral Care
The effectiveness of oral care protocols to promote oral hygiene, based on sex, was not examined in subgroup analyses in any of the literature reviewed.

Reference List and Evidence Tables

Evidence Table and Reference List 9: Inpatient Prevention and Management of Complications Following Stroke

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 10 Advance Care Planning

10. Advance Care Planning Recommendations 2022

Definitions

Advance Care Planning is a process of reflection and communication. It is a time for individuals to reflect on their values and wishes, and to communicate their preferences about future healthcare decisions if they were unable to speak for themselves. (Adapted from: https://www.advancecareplanning.ca/)

Goals of Care are the clinical and personal goals for a patent's episode of care that are determined through a shared decision-making process. They reflect a shared understanding between patients, family, caregivers, other support people and the clinical team. (Adapted from: https://www.safetyandquality.gov.au/our-work/comprehensive-care/essential-elements-comprehensive-care/essential-element-2-identifying-goals-care)

Advance Care Planning

i. Persons with stroke, as well as their families and informal caregivers, should be approached by the interdisciplinary stroke team to participate in advance care planning (ACP) [Strong recommendation; Low quality of evidence].

i. Respectful advance care planning should be integrated as part of a comprehensive care plan, taking into consideration values and preferences with information regarding the patient's illness, understanding, prognosis, medically appropriate treatments and future medical care [Strong recommendation; Low quality of evidence].

ii. Advance care planning may include identifying a substitute decision-maker (proxy, agent, or power of attorney), and discussing the patient's personal values and preferences to be applied in future if the need arises to make healthcare decisions or provide consent on behalf of the patient [Strong recommendation; Moderate quality of evidence].

   a. Advance care planning discussions should be documented and reassessed regularly with the active care team and substitute decision-maker, especially when there is a change in the patient's health status [Strong recommendation; Low quality of evidence].

Section 10 Clinical Considerations

1. The interdisciplinary stroke care team should have the appropriate communication skills and knowledge to respectfully address the physical, spiritual, cultural, psychological, ethical, and social needs of the person with stroke and their family and informal caregivers.
2. Ensure advance care planning discussions are individualized and culturally sensitive.
3. Processes should be established to support, patients, family and healthcare staff who are experiencing conflicts over advanced care decisions being made by the patient or substitute decision maker. Referrals can be made to social work, palliative care, spiritual care, and ethics.

Rationale

Advance care planning is a process through which a patient, in consultation with healthcare providers and family members, states their preferences about future healthcare decisions if the patient become incapable of participating in decision-making regarding their healthcare needs. Elements to consider in ACP include the patients' prognosis, treatment options, goals of care, and the identification and documentation of end-of-life wishes. Advance care planning is an important educational aspect of any patient encounter when a serious or chronic condition is involved and where the risk of a recurrent event is higher, such as with stroke.

People with lived experience stressed the importance of advance care planning among family members and loved ones and discussed how the concept may not be well-known. They talked about the difficulty that family members may experience when making healthcare decisions for someone else, especially if those discussions did not take place when the person was competent and able to participate. People with lived experienced explained that although these types of conversations may be new or challenging, they ultimately allow the person to have some control and allow their voice to be heard. These conversations can also support family members when they are faced with stressful decisions about the person's health. People with lived experience also emphasized the importance of having advance care planning conversations throughout their lives, and to be aware that one conversation may not be enough as people's wants and wishes can change over time.

People with lived experience expressed that normalizing the process of developing an advance care plan would be helpful, and they see this lack as a gap. They also discussed the value of having a resource to guide these discussions, especially for those who haven't considered advance care planning previously.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Protocols for advance care planning to elicit patient and family goals for care preferences and ensuring these are documented and communicated to decision-makers and healthcare team members.
2. Information on advance care planning and links to local stroke support organizations and their services for staff to share with patients and families.
3. Communication and skills training for physicians, nurses, and allied health professionals that addresses supporting patients and their families through advance care planning and dealing with potential conflicts over a patient's wishes and decisions.

Performance Measures

System Indicators:

In development.

Process indicators:

1. Proportion of patients with stroke who have been approached to participate in advance care planning and/or who have a documented conversation with a healthcare provider.
2. Proportion of patients with stroke who identify a substitute decision-maker.

3. Proportion of patients with stroke who complete a personal or advance care plan and have it documented on their chart.

Patient-oriented outcome and experience indicators:

4. Proportion of patients with stroke with advance care plans whose actual care was consistent with the care defined in their plan.

Measurement Notes

a. Documentation for the advance care plan measures may appear in consult notes, nursing notes, social work notes, or physician notes.

b. A copy of the advance care plan should ideally be included in the patient's chart.

c. Data quality may be an issue with some of these performance measures. Improved documentation should be promoted among healthcare professionals.

d. Patient and family experience surveys should be used to monitor care quality which includes end-of life experiences.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Advance Care Planning in Canada: http://www.advancecareplanning.ca/
- Canadian Virtual Hospice: My Grief Learning Modules: https://mygrief.ca/
- Canadian Virtual Hospice: The Learning Hub: https://www.virtualhospice.ca/learninghub
- Canadian Hospice Palliative Care Association Resource: https://www.chpca.ca/knowledge/resources/
- Canadian Virtual Hospice: Decisions: https://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/Topics/Topics/Decisions.aspx
- Canadian Virtual Hospice: My Grief Learning Modules: https://mygrief.ca/
- Canadian Virtual Hospice: The Learning Hub: https://www.virtualhospice.ca/learninghub

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Canadian Virtual Hospice: My Grief Learning Modules: https://mygrief.ca/

- Canadian Virtual Hospice: The Learning Hub: https://www.virtualhospice.ca/learninghub
- Advance Care Planning in Canada: http://www.advancecareplanning.ca/
- Canadian Hospice Palliative Care Association Resources: https://www.chpca.ca/knowledge/resources/
- Canadian Virtual Hospice: Decisions: https://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/Topics/Topics/Decisions.aspx

Summary of the Evidence

Elements to consider in advance care planning (ACP) include the patients' prognosis, treatment options, goals of care, and the identification and documentation of end-of-life wishes. In a recent survey, Johnson et al. (2019) surveyed 219 patients attending an outpatient stroke clinic a median of 5 months following a stroke. Patients completed the Planning After Stroke Survival survey, designed to explore the prevalence, experiences, and influencing factors around goals-of-care and ACP conversations. Seventy-three percent of patients reported having previously discussed ACP with a physician, while 58% were interested in having additional ACP conversations with their stroke doctor. Green et al. (2014) used participant observation and semi-structured interviews to gather information from 14 patients recruited from an acute stroke unit, 2 rehabilitation units, and 4 healthcare professionals, that was related to the communication processes regrading advance care planning (ACP). Four key themes emerged related to why participants engaged or did not engage in the ACP process: 1) lack of perceived urgency by participants, many of whom felt the physician and/or family members would make decisions in accordance with their wishes; 2) a lack of initiation by healthcare professionals to discuss issues around ACP; 3) healthcare professionals being hesitant about initiating discussions related to ACP, and uncertain as to the best timing for such discussions. There was also a lack of awareness on the part of healthcare professionals as to what ACP is, or thinking it was outside their scope of practice. Finally, 4) confusing ACP with advance directives, designation of care, and living wills.

Although no stroke-specific studies have been published that examine the effectiveness of ACP, several exist that include patients with mixed diagnoses. Results from a small number of studies suggest that interventions aimed at increasing ACP have been successful in significantly increasing the likelihood that end-of-life wishes are known and respected. In a study of 309 patients admitted to internal medicine, cardiology, or respiratory medicine, Detering et al. (2010) randomized patients to receive usual care or formal advance care planning from a trained facilitator. The intervention was based on the Respecting Patient Choices model, which involves reflection on goals, values, and beliefs; documentation of future healthcare wishes; and appointment of a surrogate decision-maker. Of those who died, end-of life wishes were significantly more likely to be known and respected for participants in the intervention group compared with those in the control group (86% vs. 30%, $p<0.01$). Following the death of a loved one, family members of those in the intervention group reported significantly less anxiety and depression and more satisfaction with the quality of their relative's death, compared to control group family members. Kirchhoff et al. (2012) randomized 313 patients with congestive heart failure or end-stage renal disease who were expected to experience serious complication or death within 2 years, as well as their surrogate decision-makers, to receive a patient-centred advance care planning intervention or usual care. The intervention was composed of a 60- to 90-minute interview with a trained facilitator to discuss disease-specific end-of-life care issues and options and documentation of treatment preferences. There were 110 patients who died within the study period, of which 26% required a surrogate decision-maker at the end-of-life. Only 1 patient in the intervention group and 3 in the control group received end-of-life care that was contrary to their

wishes for reasons other than medical futility. With respect to resuscitation preferences, non-significantly fewer patients in the intervention group received care that was contrary to their wishes (1/62 vs. 6/48).

Sex and Gender Considerations

An online opinion survey of 1,523 randomly selected Canadians in the general population, sponsored by Canadian Researchers at the End-of-Life Network (CARENET), examined knowledge and attitudes towards ACP (Teixeira et al. 2015). Six sociodemographic and economic variables examined, of which sex was one. Models were developed to explore independent predictors of several outcomes including: 1) has heard of ACP, 2) discussed ACP with family/friends, 3) discussed ACP with healthcare provider, 4) has a written ACP plan, 5) has a designated decision maker and 6) an aggregate ACP outcome. While recognition of the term ACP was generally low, there were some significant sex differences in responses based on statistical models. Women were 58% more likely to discuss ACP with their friends. In the aggregate model of ACP knowledge, female sex was also a significant predictor. Other independent predictors were older age and higher income.

Reference List and Evidence Tables

Evidence Table and Reference List 10: Advance Care Planning

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

Section 11 Palliative and End-of-Life Care

11. Palliative and End-of-Life Care Recommendations 2022

Definitions

Palliative care *is an approach that aims to reduce suffering and improve the quality of life for people who are living with life-limiting illness through the provision of pain and symptom management; psychological, social, emotional, spiritual, and practical support; and support for caregivers during the illness and after the death of the person they are caring for. Palliative care provides comprehensive care throughout a person's illness trajectory and is not solely limited to end of life care.* (Adapted from: https://www.canada.ca/en/health-canada/services/health-care-system/reports-publications/palliative-care/framework-palliative-care-canada.html#p1.1/).

In a palliative approach to care, *the health care team identifies patients early on who would benefit from a palliative approach and initiates appropriate discussions and care management. Healthcare providers (e.g., primary care providers, nurses, stroke neurologist, palliative care specialists) are central to facilitate care to all patients throughout the many transitions. Specialist palliative care teams provide care in an advisory-consultant-educational-coaching role and shared care with primary care clinicians and specialist stroke teams. (Adapted from* ***Staffing a Specialist Palliative Care Service, a Team-Based Approach: Expert Consensus White Paper, J Pal Med 2019).***

End-of-life care: *Part of the palliative approach that involves the management and treatment of dying patients, and support for their families and informal caregivers.*

Goals of care for palliative care: *In the event of a treatment decision needing to be made, the medical team may initiate a "goals of care" discussion with the patient and/or their substitute decision-maker. This conversation should establish or clarify the patient's advance care wishes (see Section 10) in the context of their prognosis. Potential topics of discussion may include preferred location of palliation, the cessation of certain medical interventions, and comfort care options and preferences (e.g., resuscitation) in the event of immanent death. The intent is to have a written communication plan for the healthcare team help the team provide individualized palliative care in a timely manner. The person with stroke's health status can change over time and the written plan should be reviewed in conjunction with such changes in status or changes in the healthcare team. The goals of care plan can be amended or revised at any time by the individual and/or substitute decision-maker.*

Medical Assistance in Dying (MAiD): *A procedure in which a patient receives medications to intentionally and safely end their life. Canadian federal law defines very specific criteria for MAiD eligibility. Each province and territory have established procedures for patients and clinicians to assess information about MAiD, as well as detailed MAiD assessment and provision protocols. Some people who have experienced a stroke may be eligible for MAiD. Clinicians providing post-stroke care should be aware of this and understand what to do if they are asked about MAiD.*

Palliative and End-of-Life Care

i. A palliative approach should be used when there has been a catastrophic stroke or a stroke in the setting of significant pre-existing comorbidity, to optimize care for the patients, and their family members and informal caregivers [Strong recommendation; Low quality of evidence].

ii. The interdisciplinary stroke team should have discussions with the patient and decision-makers regarding the patient's goals of care that includes consideration of the patient's diagnosis, prognosis, values, wishes, and whether care should focus on comfort or on prolonging life [Strong recommendation; Low quality of evidence].

a. There should be regular communication with the patient, family, and informal caregivers to ensure their goals and needs are being met [Strong recommendation; Low quality of evidence].

b. Palliative and end-of-life discussions should be ongoing and take into account reflect any changes in diagnosis or prognosis [Strong recommendation; Low quality of evidence].

c. Topics to be discussed with patients, families, and informal caregivers may include the appropriateness of life-sustaining measures, including mechanical ventilation, enteral/intravenous feeding, and intravenous fluids, and the purpose of all medications, including those for symptom management [Strong recommendation; Low quality of evidence].

iii. Palliative care discussions should be documented and reassessed regularly with the healthcare team and substitute decision-maker [Strong recommendation; Low quality of evidence].

iv. Patients, families, informal caregivers, and the healthcare team should have access to palliative care specialists, particularly for consultation about patients with difficult-to-control symptoms, complex or conflicted end-of-life decision-making, or complex psycho-social family issues [Strong recommendation; Low quality of evidence].

v. Decisions to initiate, withdraw, or forgo life-prolonging treatments after stroke, including artificial nutrition and hydration, should be made in discussion with the patient, family, and informal caregivers as appropriate, taking into account the best interests of the person, and including whenever possible their prior expressed wishes, either in an advanced care plan or through discussions [Strong recommendation; Low quality of evidence].

vi. Each member of the healthcare team should understand their roles and responsibilities as defined by their respective provincial or territorial college or professional organization regarding discussions about medical assistance in dying (MAiD) [Strong recommendation; Low quality of evidence].

vii. Organ and tissue donation should be discussed with families and informal caregivers as appropriate [Strong recommendation; Low quality of evidence].

viii. Supportive counselling, funeral support, and bereavement resources should be provided to families and informal caregivers after the patient's death [Strong recommendation; Low quality of evidence].

Section 11 Clinical Considerations

1. The interdisciplinary stroke team should have the appropriate communication skills and knowledge to respectfully address the physical, spiritual, cultural, psychological, ethical and social needs of the person with stroke, their family and informal caregivers who are involved in the patient's end-of-life care.
2. For patients with stroke at the end of life, the following areas may be considered where appropriate (note, other areas may be relevant as well for each individual):
    a. Need for formal palliative care consultation
    b. Cessation of routine vital sign checks, blood work, and diagnostic tests
    c. Oral care
    d. Eye care
    e. Pain
    f. Delirium
    g. Respiratory distress and upper airway secretions

h. Nausea and vomiting, incontinence and constipation,
i. Skin and wound care
j. Seizures
k. Anxiety and depression. *Refer to CSBPR Mood, Cognition and Fatigue module Section 1 for additional information.*
l. Interdisciplinary support for patients, families, and caregivers during dying process
m. Preferred location of palliative care (e.g., home, hospice, another supportive living environment)
n. Preferred person to be notified of patient's death

Rationale

Palliative care is a comprehensive approach to care that aims to control pain, provide comfort, improve quality of life, and effectively manage patients' and their families' psychosocial needs. It is an important component of stroke care given that a high proportion of patients with stroke will die during their initial hospitalization. Recognizing and addressing the needs of the person with a life-limiting stroke or who is close to death after a stroke can enhance the quality of the time left and improve the satisfaction of the patient, family, caregivers, and the healthcare team.

People with lived experience recognized that palliative and end-of-life discussion can be very challenging. They suggested it would be helpful if one person from the healthcare team could be designated to ensure appropriate conversations are held with the appropriate parties about palliative and end-of-life care needs. They stated that sometimes people need "permission" to know it's okay to bring up the topic with family, friends, and loved ones, or with a healthcare provider, and having someone initiate the conversation in a supportive environment can be helpful. They expressed that palliative and end-of-life care wishes should be brought up and discussed before they are required, to help give the person some control and let them express what they want and need for this time in their life.

System Implications

To ensure people experiencing a stroke receive timely stroke assessments, interventions and management, interdisciplinary teams need to have the infrastructure and resources required. These may include the following components established at a systems level.

1. Formalized palliative care processes and standards need to be established, including a team experienced in providing end-of-life care for patients with stroke, with the ability to monitor of quality of palliative care delivery.
2. Established referral process to specialist palliative care services, either within the same organization or through telehealth technology in rural and remote locations.
    - These services should be able to address the needs of patients and families, including physical, spiritual, cultural, psychological, and social needs.
3. Communication and skills training for physicians, nurses, and allied health professionals that addresses supporting patients and their families through poor prognoses, and dealing with potential conflicts over patient wishes and decisions (e.g., consultation with ethics experts).
4. Protocols for advance care planning and palliative care to elicit patient and family goals for care preferences, and for ensuring care preferences are documented and communicated to decision-makers and healthcare team members.
5. Palliative care protocols that are integrated into ongoing care delivery.

6. Information on palliative care and linkages to local stroke support organizations and their services for staff to share with patients and families.

Performance Measures

System Indicators:

In development.

Process Indicators:

1. Proportion of patients with stroke who had a referral to specialist palliative care services during inpatient care.
2. Proportion of patient who are dying following a stroke whose symptoms are routinely being assessed and monitored, and care plans adjusted as status changes.
3. Proportion of dying patients with stroke who were who are cared for under a palliative care approach.
4. Proportion of patients with stroke who die in the location specified in their palliative care plan.

Patient-oriented outcome and experience indicators:

5. Family and caregiver ratings on the palliative care experience following the death in hospital of a patient with stroke.

Measurement Notes

a. Documentation for palliative and end-of-life measures may appear in consult notes, nursing notes, social work notes, or physician notes. Just the presence of an order for palliative consultation should not be accepted as adequate documentation.

b. Data quality may be an issue with some of these performance measures. Improved documentation should be promoted among healthcare professionals.

c. Patient and family experience surveys should be in place to monitor care quality with end-of life situations.

Implementation Resources and Knowledge Transfer Tools

Resources and tools listed below that are external to Heart & Stroke and the Canadian Stroke Best Practice Recommendations may be useful resources for stroke care. However, their inclusion is not an actual or implied endorsement by the Canadian Stroke Best Practices writing group. The reader is encouraged to review these resources and tools critically and implement them into practice at their discretion.

Healthcare provider information

- Palliative Care Education for All Care Providers: http://pallium.ca/
- Burton and Payne Palliative Care Pathway: http://www.biomedcentral.com/1472-684X/11/22
- Bernacki RE, Block SD. Serious Illness Communications Checklist. Virtual Mentor. 2013;15(12):1045–9. https://www.researchgate.net/profile/Rachelle_Bernacki/publication/259316398_Serious_Illness_Communications_Checklist/links/54463d190cf2f14fb80f2c96/Serious-Illness-Communications-Checklist.pdf

- Registered Nurses Association of Ontario Guidelines for End-of-Life Care: https://rnao.ca/bpg/guidelines/endoflife-care-during-last-days-and-hours
- Canadian Virtual Hospice: Decisions: https://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/Topics/Topics/Decisions.aspx
- Canadian Virtual Hospice: My Grief Learning Modules: https://mygrief.ca/
- Canadian Virtual Hospice: The Learning Hub: https://www.virtualhospice.ca/learninghub
- Canadian Hospice Palliative Care Association Resource: https://www.chpca.ca/knowledge/resources/

Information for people with lived experience of stroke, including family, friends and caregivers

- Heart & Stroke: Your Stroke Journey: https://www.heartandstroke.ca/-/media/1-stroke%20best-practices/resources/patient-resources/en-your-stroke-journey-v21
- Heart & Stroke: Post-Stroke Checklist: https://www.heartandstroke.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1
- Heart & Stroke: Acute Stroke Management Infographic: https://heartstrokeprod.azureedge.net/-/media/1-stroke-best-practices/resources/patient-resources/csbpr7_infographic_acutestrokemanagement_en_final.ashx?rev=3477e77c1e4f4069bb0c6a440b541947
- Heart & Stroke: End of Life Care and Palliative Care: https://www.heartandstroke.ca/stroke/recovery-and-support/end-of-life-and-palliative-care
- Canadian Hospice Palliative Care Association Resource: https://www.chpca.ca/knowledge/resources/
- Canadian Virtual Hospice: Decisions: https://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/Topics/Topics/Decisions.aspx
- Canadian Virtual Hospice: My Grief Learning Modules: https://mygrief.ca/
- Canadian Virtual Hospice: The Learning Hub: https://www.virtualhospice.ca/learninghub

Summary of the Evidence

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. It is an important component of stroke care given that a high proportion of patients with stroke will die during their initial hospitalization.

The palliative care needs of 191 acute patients with stroke were evaluated using the Sheffield Profile for Assessment and Referral to Care (SPARC), a screening tool developed to be used in advanced illness, regardless of diagnosis. SPARC included domains related to physical, psychological, religious and spiritual, independence and activity, and family and social issues (Burton et al., 2011). Patient dependence, defined as a Barthel Index score of <15, and increasing age were found to be independent predictors of palliative care need. Holloway et al. (2010) compared the reasons for palliative consults for patients following stroke to other conditions including cancer, congestive heart failure, chronic obstructive pulmonary disease, and dementia. Of the total stroke admissions during the three-year study period, 101 (6.5%) were referred for a palliative care consult. Patients with stroke had the lowest (worst) mean Palliative Performance Scale scores compared with all other conditions.

Compared to patients with other conditions, patients with stroke who received a palliative care consult were more often referred for end-of-life issues and more likely to die in hospital. Patients who had suffered a stroke were more likely to be unconscious during the assessment and more frequently lacked the capacity to make or participate in their own medical care decisions. When compared by stroke sub type, patients who had suffered an ischemic stroke were the least likely to be referred for palliative care (3.2%) while those with a subarachnoid hemorrhage were referred most often (15.0%). The relatives of patients who had died from a stroke were interviewed approximately 6 weeks later and questioned about their perceptions of the quality of dying they received in the hospital (Reinink et al., 2021). While the participants were generally satisfied with the quality of care received, there were a few areas of concern that were related to feeding, inability to say goodbye to loved ones, and not retaining a sense of dignity. Eriksson et al. (2016) used data from 1,626 patients included in a national quality register for end-of-life care who had died of stroke in a hospital or nursing home and compared care during the last week of life with 1,626 patients in the same register who died of cancer, matched for place of death, age, and sex. The odds of experiencing dyspnea, anxiety, and severe pain were significantly lower for patients with stroke; however, family members of patients with stroke were less likely to be offered bereavement follow-up. Patients were also less likely to be informed about transition to end-of-life care.

Palliative care pathways have been developed to ensure that patients receive the most appropriate care possible in the last days of their lives. However, there is an absence of high-quality of evidence to suggest that the pathways are effective. In a Cochrane Review, Chan et al. (2016) sought studies that examined the use of an end-of-life care pathway compared with usual care for the dying. A single cluster RCT was identified (n=16 hospital wards), comparing an Italian version of the Liverpool Care Pathway (LCP-I), a continuous quality improvement program of end-of-life care vs. usual care. In this trial, 232 family members of 308 patients who died from cancer were interviewed. Outcomes were assessed during face-to-face interviews of family members 2 to 4 months after the patient's death. Only 34% of the participants were cared for in accordance with the care pathway as planned. The odds of adequate pain control and control of nausea or vomiting were not significantly higher in the LCP-I group. In terms of specific interventions designed to address many common palliative care issues including dysarthria, anxiety, depression, urinary and fecal incontinence, vomiting, delirium, and pressure ulcers, Cowey et al. (2021) concluded there was insufficient evidence to guide their use, following a review of 77 primary studies including patients with stroke requiring palliative care.

Several studies have examined the characteristics of patients who are transferred to palliative care units. San Luis et al. (2013) included data retrieved from chart review of 236 patients admitted to hospital with a confirmed diagnosis of stroke; 97 of these patients were transitioned to palliative care. These patients were more likely to be older, have atrial fibrillation, have more severe dysphagia on the first swallowing evaluation, have suffered a left middle cerebral artery stroke, have higher initial stroke severity, have received t-PA, and be admitted on a weekday. Gott et al. (2013) reported that the diagnosis of stroke was a strong predictor of transfer to palliative care among a mixed diagnosis group of 514 patients with palliative care needs (OR=8.0, 95% CI 2.5-25.9, p=0.001).

Decisions to withhold or withdraw life-prolonging treatments after stroke affect a substantial proportion of patients who have experienced a severe stroke. Alonso et al. (2016) reviewed the charts of 117 patients with ischemic or hemorrhagic stroke who died during hospitalization, to identify those with do-not-resuscitate-orders (DNRO) and therapy goal modifications with transition to symptom control. Factors that contributed to the decision to limit life-sustaining therapies were sought. A DNRO was made in 101 (86.3%) patients, usually within 48 hours of admission, and 40 patients were transferred to palliative care after a mean of five days. Thirty-eight patients were not able to communicate at the time of decision-making. Following transfer, monitoring of vital parameters (95%)

and diagnostic procedures (90%) were discontinued. Antibiotic therapy (86%), nutrition (98%), and oral medication (88%) were never ordered or withdrawn. Low-dose heparin was withdrawn in 23% of cases. All patients were maintained on intravenous fluids until death. Disturbance of consciousness at presentation, dysphagia on day 1, and large supratentorial strokes were independent predictors of decisions to withdrawing or withholding further treatment. Patients died an average of 2.6 days following therapy restrictions.

Sex and Gender Considerations

Women are less likely to receive critical life-prolonging care than men. In a retrospective study including 137,358 adult patients hospitalized for acute stroke in Ontario from 2003-2017 (Joundi et al. 2021), compared with men, each year after 2003 was associated with 20% decreased odds of receiving ICU care, among women. The odds of receiving mechanical ventilation, a percutaneous feeding tube, and tracheostomy were all significantly lower for women, regardless of stroke type (ischemic vs. intracerebral hemorrhage). Women are also more likely to opt for comfort care measures than men (Gott et al. 2020).

Singh et al. (2017) included 395,411 patients with stroke include in the National Inpatient Sample from 2010-2012. Demographics, comorbidities, procedures, and outcomes between patients with and without a palliative care encounter (PCE) were compared. Patient characteristics that were independently associated with the use of PCE were older age, hemorrhagic stroke, white race and female sex.

Reference List and Evidence Tables

Evidence Table and Reference List 11: Palliative and End-of-Life Care

Evidence Table and Reference List: Additional Sex & Gender Considerations Reference List

APPENDIX 1: ACUTE STROKE MANAGEMENT WRITING GROUP 2022

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	University		DSMB Member: CATIS-ICAD Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Canadian Association of MAiD Assessors and Providers(CAMAP) Co-Chair - Canadian MAiD Curriculum Development Committee (funded by Health Canada)
Harris, Devin MD, MHSC.	Executive Medical Director, Quality and Patient Safety, Interior Health Clinical Professor University of B.C., Department of Emergency Medicine	Kelowna, BC	CIHR, Brain Canada - Payments made to institution Participation on a Data Safety Monitoring Board or Advisory Board - PulsePoint Randomized Controlled Trial (DSMB) Council Chair, B.C. Patient Safety and Quality Council
Kanya-Forstner, Nick BSc MD	Assistant Professor, Northern Ontario School of Medicine, Stroke Team Physician, Timmins & District Hospital	Sudbury, ON	None to declare
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Liederman, Zachary MD, MScCH, FRCPC	Hematologist, Clinician Teacher Assistant Professor University of Toronto and University Health Network, Department of Medicine	Toronto, ON	No payment has currently been received but agreement for honoraria (to personal account) for presentation at annual thrombosis Canada conference (warfarin in 2022) as well as creation of patient education pamphlet (cancer associated thrombosis) Advisory board work with SOBI regarding ITP treatment (Avatrombopag) CanVECTOR Training, Mentoring, & Early Career Development Platform (unpaid)

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Milot, Genevieve MD FRSCP	Neurosurgeon Associate Professor Laval University, surgery dept	Quebec City, QC	Participation on a Data Safety Monitoring Board or Advisory Board - Royal college of Canada council member Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Fellowship affair board
Minuk, Jeffrey MD, MSc, FRCPC	Chief, Division of Neurology, The Integrated Health and Social Services University Network for West Central Montreal Associate Professor of Neurology and Neurosurgery McGill University	Montreal, QC	McCarthy-Tetreault - Medical expertise for CMPA cases Payment for expert testimony - McCarthy-Tetreault - Written expertise only
Mountain, Anita MD, FRCPC	Medical Lead, Acquired Brain Injury Program Queen Elizabeth II Health Sciences Centre Assistant Professor	Halifax, NS	No conflicts

	Division of Physical Medicine & Rehabilitation ,Department of Medicine Dalhousie University		
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Perry, Jeffrey J. MD, MSc, CCFPEM	Professor and Vice-Chair Research, Department of Emergency Medicine, Senior Scientist, Ottawa Hospital Research Institute Professor University of Ottawa	Ottawa, ON	Mid-Career Award (paid to institution) – HSFC
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Yu, Amy Y. X. MDCM, MSc	Stroke neurologist, Sunnybrook Health Sciences Centre Assistant Professor University of Toronto, Department of Medicine	Toronto, ON	National New Investigator Award from the Heart & Stroke Foundation of Canada

ENDOVASCULAR THROMBECTOMY FOR ACUTE ISCHEMIC STROKE, INTERIM UPDATE WRITING GROUP 2025

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Dylan Blacquiere, MD, MSc, FRCPC	Medical Director, Champlain Regional Stroke Network Assistant Professor, University of Ottawa, Department of Medicine, Division of Neurology	Ottawa, ON	Payment or honoraria for support for travel/presentation from Diabetes Canada Support for attending meetings and/or travel from Diabetes Canada Participation on a data safety Advisory board, Roche Canada Board Member, Canadian Stroke Consortium
Norine Foley, MSc	WorkHORSE Consulting Group	London, ON	None to declare
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Michael D. Hill, MD, MSc, FRCPC	Medical Director for Stroke, Alberta Health Services PIN Professor, University of Calgary, Cumming School of Medicine, Department of		Grants from NoNO Inc to the University of Calgary for the ESCAPE-NA1 trial, ESCAPE-NEXT trial; Canadian Institutes for Health Research to the

	Clinical Neurosciences and Community Health Sciences		University of Calgary for the ESCAPE-NA1 trial, ESCAPE-NEXT trial; Medtronic to the University of Calgary for the ESCAPE-MeVO Study; Canadian Institutes for Health Research University of Calgary for the TEMPO-2 trial; Heart and Stroke Foundation of Canada to the University of Calgary for the TEMPO-2 trial Consulting fees from Sun Pharma and Brainsgate Inc - Paid work for adjudication of clinical trial outcomes Patents - US Patent 62/086,077 Licensed to Circle NVI US Patent 10,916,346 Licensed to Circle NVI Data Safety Monitoring Board Chair - Oncovir Hiltonel trial (end 2023) and DUMAS trial (end 2023) Data Safety Monitoring Board member ARTESIA trial (end 2023); BRAIN-AF trial (end 2023);LAAOS-4 trial (ongoing) President - Canadian Neurological Sciences Federation (not for profit) Stock - Circle Inc, Basking Biosciences - Private stock ownership
M. Patrice Lindsay RN, M.Ed., PhD, FWSO	MarcLind Health Consulting	Toronto, ON	Contracts with Canadian Neurological Sciences Federation; Health PEI; Heart and Stroke Foundation of Canada - payments to self Honorarium from CHEP Plus -

			payment to self Advisory Board Member, ICRH, voluntary
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Anita Mountain, MD, FRCPC	Medical lead Acquired Brain Injury Program, Nova Scotia Rehabilitation and Arthritis Centre Assistant Professor, Dalhousie University, Division of Physical Medicine & Rehabilitation, Department of Medicine	Halifax, NS	All support for the present manuscript, Heart and Stroke Foundation of Canada, no payments Grants or contracts from any entity - Qualified site investigator for research supported by Brain Canada, Heart and Stroke Foundation of Canada, Canadian Partnership for Stroke Recovery/CIHR/Governors of the University of Calgary. No payments to self. Support for research coordinator and research activities related to research grants from primary organization Leadership or fiduciary role as Rehabilitation co-chair for Canadian Stroke Best Practice Recommendations Advisory Committee, no payments.
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APPENDIX 2: ACUTE STROKE MANAGEMENT EXTERNAL REVIEWERS 2022

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Cashin, Renee Denise RN,BN,MN	Regional Stroke Program Manager, Eastern Health	St. John's, NFL	None to declare
Catanese, Luciana MD	Director, Neurovascular Unit, Hamilton General Hospital Physician-Lead, Hyperacute Stroke Services, Hamilton Health Sciences. Assistant Professor of Medicine (Neurology), McMaster University Medicine (Neurology), McMaster University	Hamilton, ON	Service Inc – Grant Funding Circle NV – Consulting AcT trial and TIMELESS - Site-PI
Chaturvedi, Seemant MD	System-Wide Stroke Program Director University of Maryland Medical System Professor of Neurology University of Maryland School of Medicine	Baltimore, MD USA	BrainsGate – Advisory Board
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Dmytriw, Adam A. MD, MPH, MSc	Stroke Prevention Clinic, Heart & Stoke Hospital): Interventional Neuroradiology & Endovascular Neurosurgery Harvard Medical School, Department of Radiology	Boston, MA	None to declare

Dowlatshahi, Dar MD PhD FRCP(C)	Professor, Medicine, School of Epidemiology and Public Health University of Ottawa Stroke Neurologist, Medicine, Neurology, Ottawa Hospital	Ottawa, ON	CIHR grant co-PI; no payment to my institution Astrazeneca Canada - Consulting fee for advisory board on anticoagulation reversal Castle Stroke Course - Honoraria for ICH lecture 5T conference 2022 - travel support for ESCAPE-NEXT investigator meeting Canadian Stroke Consortium - Vice Chair
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Taylor, Sean William MD MSc FRCPC	Attending Neurologist Halifax Infirmary Stroke Unit Assistant Professor & Attending staff Dalhousie University Dept medicine, Div. neurology	Halifax, NS	ESCAPE, AcT – Sub-investigator
Tkatch, Aleksander MD FRCPC	Vascular Neurology, Medical Director for Stroke, Interior Health, BC	Kelowna, BC	None to declare
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Name	Professional role	Location	Declared conflicts of interest
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Robert Fahed, MD, MSc	Interventional Neurologist Associate Professor Department of Medicine, Division of Neurology, The Ottawa Hospital	Ottawa, ON	Consultant for Medtronic, Stryker Neurovascular, Terumo Neuro, Johnson and Johnson Received payment from Medtronic, Stryker Neurovascular, Terumo Neuro, Johnson and Johnson, consultant Currently participating or have participated within the past two years in a clinical trial with ESCAPE MeVO, EASI TOC, Site co-PI
Michael Kelly, MD, PHD, FRCSC	Provincial Head of Surgery Professor University of Saskatchewan, Division of Neurosurgery	Saskatoon, SK	Shareholder of Endostream Inc., Basecamp Vascular, Custom Health, Radical Catheters Inc. Consultant with Medtronic Inc., J&J Medtec, Penumbra

			Support for attending meeting and/or travel for work from Microvention Inc., industry site visit Currently participating or have participated within the past two years in a clinical trial with University of Manitoba, Site Principle Investigator - EMMA Can
Jai Shankar, MD, DM, MSc, FRCPC	Interventional Neuroradiologist Professor University of Manitoba, Max Rady College of Medicine, Department of Radiology	Winnipeg, MB	All support for the work reported in the manuscript from Medtronic Canada, PI for EMMA Can study funded by Medtronic Canada Grant or honorarium from Medtronic Canada, PI for EMMA Can study funded by Medtronic Canada Currently participating or have participated within the past two years in a clinical trial with Medtronic Canada, PI for EMMA Can study funded by Medtronic Canada

APPENDIX 3: TABLES OF TOOLS

Table 3a: Standardized Acute Prehospital Stroke Screening Tools

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results (validity & reliability)
Cincinnati Pre-Hospital Stroke Scale (CPSS) **Kothari et al. 1999**	3 items: presence/absence of facial palsy; unilateral arm weakness; and speech impairment. Items simplified versions from the NIHSS. Abnormality demonstrated on one or more items is indicative of suspected stroke	171 patients with suspected stroke recruited through ED and inpatient neurology units. Mean age was 57.8 years, 58% male. Stroke/TIA prevalence: 49 (28.7%) Patients were assessed by 24 prehospital care providers (17 paramedics and 7 EMTs) and 2 NIH certified physicians, resulting in 860 total assessments.	Final discharge diagnosis of stroke	**Validity** Physicians: Sensitivity 1 abnormality 66%, 95% CI 49-80% 2 abnormalities 26%, 95% CI 14-43% 3 abnormalities 11%, 95% CI 3-26% Physicians: Specificity 1 abnormality 87%, 95% CI 80-92% 2 abnormalities 95%, 95% CI 90-98% 3 abnormalities 99%, 95% CI 95-100% Prehospital care workers: Sensitivity 1 abnormality 59%, 95% CI 51-67% 2 abnormalities 27%, 95% CI 21-35% 3 abnormalities 13%, 95% CI 8-20% Prehospital care workers: Specificity 1 abnormality 88%, 95% CI 86-91% 2 abnormalities 96%, 95% CI 94-97% 3 abnormalities 98%, 95% CI 96-99% The validity of this scale has been evaluated further, by both the scale developers and independent researchers. **Reliability** ICC for total scores among all prehospital workers was 0.92, 95% CI 0.89-0.93 ICC for total scores between prehospital workers and physicians was 0.92, 95% CI 0.89-0.93
Face Arm Speech Test (FAST)	3 items derived from the CPSS: facial palsy, arm weakness, speech disturbance. Assessment of speech is not dependent on the repetition	487 patients admitted by ambulance, primary care physicians and ED referrals with suspected	WHO criteria	**Validity** Sensitivity: Diagnostic sensitivity of FAST associated with paramedic use was estimated to be 79%. PPV (arrival by ambulance): 78%, 95% CI 72-84%

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results (validity & reliability)
Harbinson et al. 2003	of a stock phrase, as per CPSS, but assessed during by EMS during normal conversation with the patient. Abnormality demonstrated on one or more items is indicative of suspected stroke	stroke. Mean age was 72 years, 52% were female Stroke/TIA prevalence: 356 (73.1%). FAST was completed by paramedics over a 6-month period		The validity of this scale has been evaluated further, by independent researchers. **Reliability** Not assessed in this publication, but has been subsequently evaluated.
Los Angeles Prehospital Stroke Screen (LAPSS) **Kidwell et al. 2000 (Prospective validation study)**	6 items: 4 screening/history items (age>45 years, no history of seizures, symptom duration <24 hours, ambulation status at baseline not bedridden or wheelchair bound), blood glucose (between 60 and 400) level, a clinical assessment (of 3 items to identify obvious asymmetry: facial palsy, grip, arm strength). If the patient has positive criteria, a blood glucose level within the specified range and unilateral weakness on the clinical exam items, they are a positive screen for stroke.	206 patients (of 1,298 total runs) with neurological symptoms, who were noncomatose, with nontraumatic cause, who had a LAPSS screen conducted. Mean age was 67 years, 52% were male. Stroke/TIA prevalence: 36 (17.5%) LAPSS was completed by 18 paramedics over a 7-month period.	Hospitalized patients with final diagnosis of stroke	**Validity** Sensitivity: 91%, 95% CI 76-98% Specificity: 97%, 95% CI 93-99%) PPV: 86%, 95% CI 70-95% NPV: 98%, 95% CI 95-99% Accuracy: 96%, 95% CI 92-98% + LR: 31, 95% CI 16-147 - LR: 0.09, 95% CI 0-0.21 This validity of this scale has been evaluated further, by both the scale developers and independent researchers. **Reliability** Not assessed
Ontario Prehospital Stroke Screen (OPSS) **Chenkin et al. 2009**	At least one of the following symptoms must be present: unilateral leg/arm weakness or drift; slurred speech or muteness; unilateral facial droop), and the patient can be transported to arrive at a stroke centre within 3.5 hours of symptom onset.	325 patients transported to a stroke centre, who had been screened as positive by paramedics using the OPSS. Patients were identified through a National Stroke Registry. Mean age was 73.7 years, 47.4% were male. Stroke prevalence: 187 (58%)	Final discharge diagnosis	**Validity** Since all patients included in the sample, were screened as positive, sensitivity and specificity could not be calculated. PPV for acute stroke (1,2, or 3 positive signs): 89.5%, 95% CI 85.7-92.7% No additional validation studies have been conducted on this scale. **Reliability** Not assessed

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results (validity & reliability)
		An unknown number of EMS workers conducted OPSS over a one-year period		
Melbourne Ambulance Stroke Screen (MASS) **Bray et al. 2005**	Combination of items from CPSS and LAPSS. The presence of any physical assessment item + a response of "yes" to all history items indicates a positive screen	100 MASS assessments were conducted on patients with suspected stroke (total of 5,957 paramedic calls during the study period) Stroke/TIA prevalence: 73 (73%) 18 paramedics conducted MASS assessments over a one-year period	Final discharge diagnosis	**Validity** Sensitivity: 90%, 95% CI 81-96% Specificity: 74%, 95% CI 53-88% PPV: 90%, 95% CI 81-96% NPV: 745, 95% CI 53-88% +LR: 3.49, 95% CI 1.83-6.63 -LR: 0.13, 95% CI 0.06-0.27 Accuracy: 86% (Validity of LAPSS and CPSS was also assessed. CPSS had highest sensitivity at 95%, LAPSS had highest specificity at 85%) This validity of this scale has been evaluated further, by the scale developers. **Reliability** Not assessed
Recognition of Stroke in the Emergency Room Scale (ROSIER) **Nor et al. 2005**	7-items: 2 clinical history items (loss of consciousness, convulsive fits/syncope) and 5 neurological signs of stroke (facial palsy/weakness, arm weakness, leg weakness, speech disturbance and visual field defect). A -1 is awarded for each clinical history item present and a +1 for each neurological sign. Total scores range from -2 to +5. A score >0 is associated with possible stroke.	160 consecutive patients with suspected stroke presenting to the Emergency Department (ED) Stroke/TIA prevalence: 101 (63.1%) Assessments were conducted by ED physicians during a one-year period	Final diagnosis made by stroke consultant after review of symptoms and imaging findings	**Validity** (Prospective validation study) Sensitivity: 93%, 95% CI 89-97% Specificity: 83%, 95% CI 77-89% PPV: 90%, 95% CI 85-98% NPV: 88%, 95% CI 83-93% (Validity of LAPSS, FAST and CPSS was also assessed. CPSS had highest sensitivity at 85%, LAPSS had highest specificity at 85%). The validity of this scale has been evaluated further by independent researchers. **Reliability** Not assessed
Medic Prehospital Assessment for Code	The scale was developed by combining the strongest elements of CPSS and LAPSS and included: eligibility criteria-no prior history of	416 patients with suspected stroke, transported to one of 7 hospitals. Mean age	Final discharge diagnosis	**Validity** Sensitivity: 74.2%, 95% CI 67.2-80.2% Specificity: 732.6%, 95% CI 26.7-39.1% PPV: 47.1%, 95% CI 41.3-53.0%

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results (validity & reliability)
Stroke (MedPACS) **Studneck et al. 2013**	seizure; onset of symptoms ≤25 hours, blood glucose 60-400 mg/mL and a physical exam (facial droop, arm/leg weakness; speech difficulty; and gaze preference) The presence of any physical assessment item + a response of "yes" to at least one eligibility criterion item indicates a positive screen	was 66.8 years, 45.7% were male. Stroke prevalence: 186 (44.7%) EMS reports and stroke GWTG-S registries were reviewed over a 6-month period		NPV: 61.0, 95% CI 51.8-69.6% + LR: 1.10, 95% CI 0.973-1.24 - LR: 0.791, 95% CI 0.582-1.07 The validity of the CPSS was also assessed (SN: 79%, SP: 24%) No additional validation studies have been conducted on this scale. **Reliability** Not assessed

PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR Likelihood Ratio

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Table 3b: Additional Tools

Assessment Tool	Number and description of Items	Time to Administer	Reliability/validity	Interpretation of Scores	Sensitivity and Specificity	Training Required
Glasgow Coma Scale (GCS) **Teasdale & Jennett 1974**[1]	15 items in 3 categories: motor response (6 items), verbal response (5 items), and eye opening (4 items). Points are awarded for the best response in each category. Categories are summed to provide a total score.	Approximately 1 minute.	**Interobserver reliability**: Scale authors reported low rates of disagreement, but noted variations in motor responses based on stimulus used [2]. Reported agreements ranged 0.48 (verbal) to 0.72 (eye opening)[3] and from 0.39 – 0.79.[4] Percentage agreements have been reported as 90% overall, and as ranging from 83.8% (eye opening, right) to 98.7% (best motor response – left).[5] In addition, similar rates of between observer agreement have been reported in groups of experienced nurses (98.6% - 100%), newly graduated nurses (94.3%-96.2%) and student nurses (77.3% - 100%).[6] **Construct Validity**: In review of GCS, evidence supports association between extent of brain damage and depth of coma as assessed on GCS. GCS scores significantly associated with length of coma ($p<0.0001$). [7] **Predictive Validity**:	GCS scores range from 3 – 15, where 3 represents total unresponsiveness and 15 represents alert and fully responsive. Scores may be divided into categories by severity: 13-15 = mild; 9-12 = moderate and ≤8 represents severe injury. [21]	Not reported	Yes.

Assessment Tool	Number and description of Items	Time to Administer	Reliability/validity	Interpretation of Scores	Sensitivity and Specificity	Training Required
			GCS score is a significant predictor of death following stroke [8, 9] or traumatic brain injury (modified by age and mechanism of injury)[10], though eye-opening may be less strongly associated than either the motor or verbal score components.[11] GCS scores are also predictive of survival (AUC=0.89), though eye-opening may not add to predictive accuracy.[12] GCS scores have been demonstrated to be predictive of Glasgow Outcome scores at 6 months to 1 year post injury [7, 13-16], Disability Rating Scale scores at discharge [17] and at 6 months[18], FIM scores at discharge[17, 19] and employment status at one year.[20]			

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Table 3c Prehospital Stroke Screening Scales to Identify Large Vessel Occlusions (LVO)

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
Wasyliw et al. 2022 **Face, Arm, Speech, Time-Vision Aphasia Neglect (FAST VAN)**	3 components 1. Vision: Is there a gaze preference to either side (usually away from the hemiparesis)? 2. Aphasia: Ask the patient to name simple objects (ie: watch, pen). 3. Neglect: With eyes closed, touch each arm independently and ask which side is being touched. Then touch both simultaneously. If neglect is present the patient will only report one side being touched, almost always neglecting the left side. Any single positive response was considered to be positive for LVO.	1,080 consecutive acute stroke patients attended to by EMS personnel between April 2017 and Jan 2021.	CTA	Of 440 patients who were FAST-VAN +ve, 236 (53.6%) had LVO. Of 640 patients who were FAST-VAN -ve, 40 (6.25%) had LVO. Sensitivity was 86%; specificity was 75%. Overall accuracy was 77%. Among the 240 false positives (+ve FAST VAN, no LVO), 69 patients were stroke with no LVO, 47 were ICH, 30 had delirium/encephalopathy, 23 had seizures, 14 had TIA, and 21 had other conditions
Okuno et al. 2020 **Field Assessment of Critical Stroke by Emergency Services for Acute Delivery ($FACE_2AD$)**	6 items 1. Facial palsy (0-1) 2. Arm palsy (0-1) 3. Consciousness impairment (0-1) 4. Eye deviation (0 or 2) 5. Atrial fibrillation (0-1) 6. Diastolic blood pressure ≤ 85 mmHg (0-1) Total possible score: 7	1157 patients were included in the derivation cohort. They were patients taken to hospital by EMS because of suspected stroke or consciousness disturbance in the first 24 hours of symptom onset, from 2012 and 2015. 502 patients were included in the validation cohort, using same criteria. Patients were recruited from 4 hospitals during a 5-month period. All the items except eye	MRA, CTA, digital subtraction angiography (DSA)	In the derivation cohort, 416 patients had ischemic stroke of which 149 (13%) patients had LVO. In the validation cohort, at a cut point of ≥3, the sensitivity and specific were 0.85 and 0.80, respectively. PPV and NPV were 0.39 and 0.97, respectively. AUC was 0.88 (95% CI 0.87–0.90). In the validation cohort, 216 patients (43%) had an ischemic stroke, of which 86 (17%) patients had an LVO. In the validation cohort, at a cut point of ≥3, the sensitivity and specific were 0.80 and 0.74, respectively. PPV and NPV were 0.39 and 0.95, respectively. AUC was 0.83 (95% CI 0.81–0.86).

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
		deviation were evaluated by EMS providers, while eye deviation was evaluated by physicians or nurses.		
Gong et al. 2020 **The Conveniently-Grasped Field Assessment Stroke Triage (CG-FAST) scale**	5 items based on NIHSS 1. Level of Consciousness questions (0-1) 2. Gaze deviation (0-1) 3. Facial palsy (0-1) 4. Arm weakness (0-1) 5. Speech changes (0-1) Total possible score: 5	1,355 patients, admitted to a single centre from 2009 to 2018 with confirmed acute ischemic stroke with symptom onset within the previous 8 hours. Median NIHSS on admission was 8 (IQR 3–15). NIHSS data was abstracted from patient records by an experienced neurologist	CTA or MRA	664 patients (49.0%) were found to have LVO At a cut-point of ≥4 Sensitivity: 61.7% Specificity: 81.0% Positive predictive value: 78.5% Negative predictive value: 69.2% AUC was 0.758 Youden Index: 0.428 At a cut-point of ≥4, the performance of the CG-FAST was better than FAST-ED≥3, 3-ISS≥3, CPSSS≥2, PASS≥2, RACE≥5, LAMS≥3, and G-FAST≥3
Vidale et al. 2019 **The Large ARtery Occlusion (LARIO) stroke scale**	5 items, based on LAMS 1. Facial palsy (0-1) 2. Arm weakness (0-1) 3. Grip strength (0-1) 4. Language (0-1) 5. Neglect (0-1) Total possible score: 5	145 patients with suspected ischemic stroke presenting to an emergency department of one hospital between April and October 2017. The scale was developed and tested on the same cohort of patients. Both a neurologist and a nurse performed all assessments.	CT/CTA	54 patients (37.2%) were found to have LVO. At a cut point of >3 on The LARIO scale: Sensitivity: 100% Specificity: 83% + LR: 0.77 - LR: 1.0 AUC: 0.951 (95% CI 0.902-0.980) Compared with other scales, NIHSS had the best performance (AUC 0.915). AUC for CPSS (0.896), LAMS (0.832) and VAN (0.884). There was excellent agreement between raters (Cohen's k: 0.963).
Gropen et al. 2018 **The Emergency Medical Stroke**	5 items, based on NIHSS 1. Eye movement (0-1) 2. Facial weakness (0-1) 3. Arm weakness (0-1) 4. Leg weakness (0-1)	1,663 consecutive adult stroke patients enrolled in the Tulane Comprehensive Stroke Center (CSC) registry from 2008 to 2013.	CTA or MRA	LVO was present in 171 patients (10.3%) A cut-point of ≥3 on EMSA had the best performance to identify LVO Sensitivity: 74.5% (95% CI 68.7-80.5)

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
Assessment (EMSA)	5. Slurred speech or aphasia (0-2) Total possible score: 6	Acute stroke cohort: Used to develop the EMSA. 218 stroke patients in 2010, based on chart review.		Specificity: 50.3% (95% CI 44.4-56.2) + LR: 1.517 (95% CI 1.356-1.659) - LR: .489 (95% CI .366-0.637) Performance of EMSA was also compared with 3I-SS, C-STAT, RACE, FAST-ED, and NIHSS (3 different cut points). An EMSA ≥ 3 had a significantly higher sensitivity for prediction of LVO compared with the other scales at their published cut-points but had lower specificity. The area under the curves for the scales were similar across scales EMSA 0.688 (95% CI .736-0.640) 3I-SS 0.647 (95% CI 0.696-0.597) C-STAT 0.646 (95% CI0.693-0.598) RACE 0.666 (95% CI 0.716-0.616) FAST-ED 0.641 (95% CI 0.690-0.591) NIHSS 0.678 (95% CI 0.723-0.633) A cut point of ≥1 on a variety of scales resulted in sensitivities and specificities (95% CI) of: EMSA 93.3% (86.9-96.7), 46.9% (38.0-56.1) 3I-SS 74.3% (65.2-81.7) 54.0% (44.8-62.9) C-STAT 36.2% (27.6-45.7), 74.3% (65.6-81.5) RACE 84.8% (76.7-90.4), 55.8% (46.6-64.6) FAST-ED 78.1% (69.3-84.9), 54.9% (45.7-63.7)
Field Assessment Stroke Triage for Emergency Destination (FAST-ED) **Lima et al. 2016**	6-items, 5 based on NIHSS 1. Facial palsy (0-1) 2. Arm weakness (0-2) 3. Speech changes (0-2) 4. Eye deviation (0-2) 5. Denial/neglect (0-2) 6. Time (documentation for decision-making) not scored Total possible score: 9	741 consecutive patients enrolled in the STOP Stroke study, who were admitted to 2 university-based hospitals with unilateral, complete occlusion of the M1 and M2 segments of the MCA or basilar artery, with onset of symptoms within 24 hours. Prevalence of LVO: 240	CTA	A cut-point of ≥4 on FAST-ED had best performance Sensitivity: 0.61 Specificity: 0.83 PPV: 0.72 NPV: 0.82 Accuracy: 0.79 AUC:0.813 Performance of FAST-ED was also compared with NIHSS, RACE and CPSS scale

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
		(33%)		
Vision, Aphasia, and Neglect (VAN) **Teleb et al. 2016**	Patients are asked to raise both arms up and hold them up for 10 s. If the patient demonstrates any level of drift, weakness or paralysis, the assessment continues. Otherwise, patient is VAN -ve and screen ends. **Items** Visual disturbances: field cut, double vision, new-onset blindness (present/absent) Aphasia: Expressive, receptive, mixed (present/absent) Neglect: Forced gaze, unable to feel both sides at same time or doesn't recognize arm, ignoring one side (present/absent) Scoring: None If weakness present + ≥1 positive finding =VAN +ve	62 acute stroke codes at a single facility Prevalence of LVO: 19 (30.6%)	CTA	Performance of VAN was also compared with NIHSS ≥6 For VAN +ve patients Sensitivity: 1.00 Specificity: 0.90 PPV: 0.74 NPV: 1.00 Accuracy: 0.92 NIHSS≥6 Sensitivity: 1.00 Specificity: 0.79 PPV: 0.58 NPV: 1.00 Accuracy: 0.84
Prehospital Acute Stroke Severity Scale (PASS) **Hastrup et al. 2016**	3 NIHSS items: 1. Incorrect month and/or age? (Level of consciousness (NIHSS item >0) 1 point 2. Gaze palsy and/or deviation (NIHSS item gaze>0) 1 point 3. Arm weakness (NIHSS item arm weakness >0) 1 point Total possible score: 3	3,127 patients included in the Danish Stroke Registry (2010-2015) who were treated with t-PA. 2/3 of sample was used for scale development and 1/3 for validation Prevalence of LVO: 35%	CTA/MRA	A cut-point of ≥2 on the PASS had the best predictive value: Using the Derivation cohort Sensitivity 0.66, 95% CI 0.62-0.66 Specificity: 0.83, 95% CI 0.81-0.85 AUC: 0.74, 95% CI 0.72-0.76 OR=9.22, 95% CI 7.5-11.40 PPV/NPV: 0.68/0.81 +LR/-LR: 3.84/0.42 The values were similar when using the validation cohort
Cincinnati Prehospital Stroke	3 NIHSS items:	Derivation cohort-624 patients with mild to severe stroke from 2	CTA	**Severe stroke** AUC: 0.89 A cut point of ≥2 had the best predictive value for

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
Severity Scale (CPSSS) **Katz et al. 2015**	1. Conjugate gaze deviation (≥1 on NIHSS item for gaze) 2 points 2. Incorrectly answers to at least 1 of 2 LOC questions (NIHSS age or current month) and does not follow at least 1 of 2 commands (close eyes, open and close hand) ≥1 NIHSS items LOC 1b and 1c. 1 point 3. Cannot hold arm (left, right or both) up for 10 seconds (≥2 NIHSS motor arm). 1 point Total possible score 4	NINDS t-PA trials. Validation cohort-650 patients from the IMS-III trial Prevalence of LVO: 34% (validation cohort)		severe stroke Using the derivation cohort Sensitivity: 89% Specificity: 73% + LR/-LR: 3.30/0.15 Using the validation cohort: Sensitivity: 92% Specificity: 51% + LR/-LR: 1.89/0.1
Pérez de la Ossa et al. 2014 **Rapid Arterial oCclusion Evaluation Scale (RACE)**	5 NIHSS items: 1. Facial palsy (absent=0, mild=1, mod/severe=2) 2. Arm motor function (normal/mild=0, moderate=1, severe=2) 3. Leg motor function (normal/mild=0, moderate=1, severe=2) 4. Head and gaze deviation (absent=0, present=1) 5. Aphasia (R hemiparesis: performs both tasks correctly=0, performs 1 task correctly=1, performs neither tasks=2); Agnosia (Left hemiparesis: patient recognizes arm/impairment=0, does not recognize arm *or* impairment=1, does not recognize arm *and* impairment=2) Total possible score 9	Derivation cohort-654 patients with acute stroke or stroke mimic for whom a stroke code had been activated by EMS or a community hospital. Validation cohort-357 patients transferred by EMS to a stroke centre Prevalence of LVO: 178 patients (27%) had a LVO in derivation cohort vs. 76 (21.3%) in the validation cohort.	Transcranial Doppler, CT or MRA	In the derivation cohort, there was a strong correlation between RACE and NIHSS (r=0.76, p<0.01) In the validation cohort, a cut point of ≥5 had the best predictive value for detecting LVO Sensitivity: 85% Specificity: 68% PPV: 42% NPV: 94% The AUC for the RACE scale was 0.82, 95% CI 0.77-0.87 for the detection of LVO
The Los	3 items:	119 patients included in	MRA/CTA, or	AUC: 0.854

Assessment Tool Author	Items/Scoring	Sample	Reference Standard	Results
Angeles Motor Scale (LAMS) **Nazliel et al. 2008**	1. Facial droop (absent=0, present=1) 2. Arm drift (absent=0, drifts down=1, falls rapidly=2) 3. Grip strength (normal=0, weak=1, no grip=2) Total possible score 5	a clinical trials registry at a stroke centre from 1996-2003, and patients included in the Get with the Guidelines Registry in 2005. Patients were included if they were last known well within 12 hours of presentation to the ED and had a final diagnosis of ischemic stroke in the anterior circulation Prevalence of LVO: 74 (62%)	catheter angiography	A cut point of ≥4 had the best predictive value for detecting LVO Sensitivity: 81% Specificity: 89% Accuracy: 85% +LR: 7.36 -LR: 0.21
3-Item Stroke Scale (3ISS) **Singer et al. 2005**	3 items: Disturbance of consciousness (no= 0, mild =1, severe= 2) Gaze and head deviation (absent= 0, incomplete gaze/head deviation=1, forced gaze/head deviation= 2) Hemiparesis (absent=0, moderate=1, severe= 2) Total possible score 6	180 patients presenting to a stroke unit in 2002 with symptoms of stroke within ≤6 hours (28 patients had ICH). Prevalence of LVO: 27 (15%)	MRI/MRA/CT	A cut point of ≥4 had the best predictive value for detecting MCA occlusions Sensitivity: 67% Specificity: 92% PPV: 74% NPV: 89% Accuracy: 86% Inter-rater reliability: Intraclass correlation co-efficient was 0.947; K for individual items were 0.77, 0.77 and 0.84

PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR Likelihood Ratio; AUC Area under curve

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Table 4 Canadian Stroke Best Practices Screening and Assessment Tools for Acute Stroke Severity

Assessment Tool	Purpose	Items and Administration	Interpretation of Scores	Availability
Neurological status/stroke severity				
Canadian Neurological Scale (CNS) **Cote et al. 1986**	Evaluate and monitor the neurological status (cognitive and motor function) of patients who are conscious (alert or drowsy) in the acute phase of stroke	Items assess mentation (level of consciousness, orientation, and speech) and motor function (face, arm, and leg). Motor function evaluations are separated into sections A1 and A2. A1 is administered if the patient is able to understand and follow instructions (5 items). A2 is administered if there are comprehension deficits (3 items). Takes approximately 5-10 minutes to administer.	Motor items are rated in terms of severity. Ratings are weighted and summed to provide a total score out of 11.5. Lower scores indicate increased stroke severity.	Free download at several sites (e.g., https://strokengine.ca/wp-content/uploads/2020/07/canadian-neurological-scale_strokecenter.pdf)
National Institutes of Health Stroke Scale (NIHSS) **Lynden et al. 1994**	Evaluate neurologic outcome and degree of recovery for stroke patients.	15 items: Impairment in level of consciousness (LOC), ability to respond to questions/ obey simple commands, papillary response, gaze deviation, hemianopsia, facial palsy, resistance to gravity (weaker limb), plantar reflexes, limb ataxia, sensory loss, visual neglect, dysarthria, and aphasia. Each item is graded on an ordinal scale from 0-3 or 0-4 where 0=no impairment. Takes approximately 6 minutes to administer	Total scale score = 0-42. Higher scores reflect greater severity. Stroke severity may be stratified as follows: >25 = very severe, 15–24 = severe, 5–14 = mild to moderately severe and 1–5 = mild	Free download at: https://www.stroke.nih.gov/documents/NIH_Stroke_Scale_508C.pdf
Glasgow Coma Scale (GCS) **Teasdale & Bennett 1974**	Describe the depth and duration of impaired consciousness or coma. Typically used following traumatic brain injury	15 items in 3 categories: motor response (6 items), verbal response (5 items), and eye opening (4 items). Points are awarded for the best response in each category. Categories are summed to provide a total score. Takes approximately 1 minute to administer.	GCS scores range from 3–15, where 3 represents total unresponsiveness and 15 represents alert and fully responsive. Scores may be divided into categories by severity: 13–15 = mild; 9–12 = moderate, and ≤8 represents severe injury.	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/glasgow_coma.pdf
Glasgow Outcome Scale (GOS) **Jennett & Bond 1975**	A global outcome scale which categorizes the outcomes of patients after traumatic brain	5 categories: 1 Death	It has become common practice in clinical trial administration to use a modified version that places the scores in reverse order (i.e., "good recovery" =	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/

Assessment Tool	Purpose	Items and Administration	Interpretation of Scores	Availability
	injury (TBI). Can also be used for long-term prediction of rehabilitation after TBI.	2 Persistent vegetative state. Patient exhibits no obvious cortical function. 3 Severe disability (conscious but disabled). Patient depends upon others for daily support due to mental or physical disability or both. 4 Moderate disability (disabled but independent). Patient is independent as far as daily life is concerned. The disabilities found include varying degrees of dysphasia, hemiparesis, or ataxia, as well as intellectual and memory deficits and personality changes. 5 Good recovery. Resumption of normal activities even though there may be minor neurological or psychological deficits.	1, "moderate disability" = 2, etc.). The Extended GOS (GOSE) provides more detailed categorization into 8 categories by subdividing the categories of severe disability, moderate disability, and good recovery into a lower and upper category. (Teasdale et al., 1988).	glasgow_outcome.pdf
Assessment of function				
Modified Rankin Scale (mRS) **van Swieten et al. 1988**	The mRS is an assessment tool for rating global outcome following stroke.	Individuals are assigned a subjective grade or rank ranging from 0 (no symptoms) to 5 (severe disability) based on level of independence with reference to pre-stroke activities rather than observation of task-based performance. Takes approximately 15 minutes to administer.	mRS scores range from 0–5 such that 0 is indicative of no symptoms, while a rank of 5 is indicative of the most severe disability (described as bedridden, incontinent, requiring constant nursing care).	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/modified_rankin.pdf
AlphaFIM ® Instrument **Stillman et al. 2009**	An assessment tool designed to assess caregiver burden during acute care.	6 items assessing motor (eating, grooming, bowel management, and toilet transfers) and cognitive (expression and memory) function, which can be reliably collected in acute care. For patients who are able to walk 150 feet or more, eating and grooming items are replaced by items evaluating walking and bed transfer.	Alpha-FIM® scores are transformed to a projected FIM® scores and an estimate of patient burden of care hours using an online proprietary algorithm	Available for purchase at: www.udsmr.org/WebModules/Alpha/Alp_About.aspx

Assessment Tool	Purpose	Items and Administration	Interpretation of Scores	Availability
		Takes approximately 5 minutes to complete.		
Barthel Index of Activities of Daily Living (BI) **Mahoney & Barthel 1965**	An assessment tool for evaluating independence in self-care activities.	The BI consists of 10 common activities of daily living (ADLs), 8 related to personal care and 2 related to mobility. Administration: Self-report (<5 minutes) or direct observation (up to 20 minutes).	The index yields a total score out of 100, with higher scores indicating greater functional independence.	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/barthel.pdf
Scales to assess severity following intracranial hemorrhage				
Hunt & Hess Classification of Subarachnoid Hemorrhage (SAH) **Hunt & Hess 1968**	Designed to gauge surgical risk and aid neurosurgeons in deciding on the appropriate time after SAH at which the neurosurgeon should operate.	The grades are based on the opinion of its authors, who judged that the most important clinical signs of SAH were: (a) the intensity of meningeal inflammatory reaction, (b) the severity of neurological deficit, (c) the level of arousal, and (d) the presence of associated disease. Individuals are assigned a subjective grade of I to V.	I – asymptomatic or mild headache II – moderate-severe headache, meningism and no weakness III – mild alteration in mental status IV – depressed LOC and/or hemiparesis V – posturing or comatose	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/hunt_hess.pdf
World Federation of Neurological Surgeons Grading Scale **Drake et al. 1988**	Designed to assess the severity of SAH and to predict outcome.	The scale combines the results of the GCS plus the presence or absence of motor deficits. GCS 15 + absence of motor deficits = Grade I GCS13-14 + absence of motor deficits = Grade 2 GCS13-14 + motor deficits present = Grade 3 GCS 7-12 + motor deficits present/absent = Grade 4 GCS 3-6 + motor deficits present/absent = Grade 5	Maximum score of 15 has the best prognosis Minimum score of 3 has the worst prognosis Scores of 8 or above have a good chance for recovery Scores of 3 to 5 are potentially fatal, especially if accompanied by fixed pupils or absent oculovestibular responses	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/WWF_scale.pdf
Fisher Grading Scale for Subarachnoid Hemorrhage (SAH) **Fisher et al. 1980**	Used to predict cerebral vasospasm after SAH.	Grade 1 - No subarachnoid blood seen on CT scan Grade 2: Diffuse or vertical layers of SAH <1 mm thick Grade 3: Diffuse clot and/or vertical layer > 1 mm thick	Risk of vasospasm Grade 1: Low (0-21%) Grade 2: Low (0-25%) Grade 3: Low to high (23% to 96%) Grade 4: Low to moderate (range 0-35%)	Free download at: http://www.strokecenter.org/wp-content/uploads/2011/08/WWF_scale.pdf

Assessment Tool	Purpose	Items and Administration	Interpretation of Scores	Availability
		Grade 4: Intracerebral or intraventricular clot with diffuse or no subarachnoid blood		
Intracerebral Hemorrhage (ICH) Score **Hemphill et al. 2001**	Used to grade ICH severity and subsequent 30-day mortality, based on age and CT findings.	Components for ICH score include: *GCS score* 3-4: 2 points 5-12: 1 point 13-15: 0 points *ICH volume* ≥30 cm^3: 1 point < 30 cm^3: 0 points *IVH (intraventricular hemorrhage)* Yes: 1 point No: 0 points *Infratentorial origin of ICH* Yes: 1 point No: 0 points *Age* Age ≥80 years: 1 point < 80 years: 0 points	ICH scores with corresponding mortality risk are as follows: 0 points: 0% 1 point: 13% 2 points: 26% 3 points: 72% 4 points: 97% 5 points: 100% 6 points: 100% (estimated)	Free calculator at: https://qxmd.com/calculate/calculator_118/ich-score

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Useful Links

1. Additional information regarding the CNS, NIHSS, mRS, and FIM is available at www.ebrsr.com and at www.strokengine.ca
2. There is a site for international users of the NIHSS scale – it may be found here: http://www.nihstrokescale.org/ It provides links to the scale in English, as well as lots of good training information – but it also provides links to the scale in quite a number of other languages as well.
3. An online calculator for many of the scales listed above: https://www.mdcalc.com/
4. The Rankin scale has its own website: http://www.rankinscale.org/
5. The FIM is also reviewed at: http://www.rehabmeasures.org/lists/rehabmeasures/dispform.aspx?id=889

Table 5 Canadian Stroke Best Practices: Selection of Validated Swallowing Screening Tools

Author/ Name of test	Components of test Details of validation study	Results of original validation study
Daniels et al. 1997[1] **"Any Two"**	Items included 6 clinical features. Dysphonia, dysarthria, abnormal volitional cough (includes water-swallowing test), abnormal gag reflex, cough after swallow, and voice change after swallow were assessed. Scoring: Presence of any 2 of the items distinguished patients with/without dysphagia. Sample: 59 acute stroke survivors were studied within 5 days of hospital admission.	Diagnostic standard: VMBS exam Prevalence of dysphagia: 74.6% The sensitivities and specificities of individual items ranged from 31%-76.9% and 61%-88%, respectively. Overall: Sensitivity: 92% Specificity: 67%
Trapl et al. 2007[4] **The Gugging Swallowing Screen (GUSS)**	Preliminary Assessment (vigilance, throat clearing, saliva swallow) Direct swallow (semisolid, liquid, solid swallow trials) Scoring: Total scores ranged from 0 (worst) - 20 (no dysphagia). A cut-off score of 14 was selected. Sample: 50 first-ever acute stroke patients with suspected dysphagia.	Diagnostic standard: Fiberoptic endoscopic evaluation using the Penetration Aspiration Scale to interpret the results. Prevalence of dysphagia: 73% First group of 19 patients using the GUSS to identify subjects at risk of aspiration: Sensitivity: 100% Specificity: 50% Second group of 30 patients Sensitivity: 100% Specificity: 69% Interrater reliability: Kappa=0.835
Martino et al. 2009[5] **The Toronto Bedside Swallowing Screening Test (TOR-BSST)**	Items included presence of dysphonia before/after water swallowing test, impaired pharyngeal sensation, and abnormal tongue movement. Scoring: pass=4/4 items; fail ≥1/4 items Sample: 311 stroke patients (103 acute, 208 rehabilitation)	Diagnostic standard: VMBS exam. Prevalence of dysphagia: 39% Sensitivity: 91% Specificity: 67% Interrater reliability (based on observations from 50 subjects) ICC =0.92 (95% CI: 0.85-0.96)
Edmiaston et al. 2009 USA[6] **Acute Stroke Dysphagia Screen**	Items included Glasgow Coma Scale score <13, presence of facial, tongue or palatal asymmetry/weakness. If no to all 3 items, then proceed to 3 oz water swallowing test. Scoring: If there is evidence of change in voice quality, cough, or	Diagnostic standard: Mann Assessment of Swallowing Ability (MASA), performed by a SPL. Prevalence of dysphagia: 29% Sensitivity (Dysphagia): 91% Specificity: 74%

Author/ Name of test	Components of test Details of validation study	Results of original validation study
	change in vocal quality 1 minute after water swallowing test = fail. Sample: 300 acute stroke patients screened by nurses within 8 to 32 hours following admission.	Sensitivity (Aspiration risk): 95% Specificity: 68% Interrater reliability: Kappa=94%
Turner-Lawrence et al. 2009[7] **Emergency Physician Dysphagia Screen**	The two-tiered bedside tool was developed by SLPs. Tier 1 items included voice quality, swallowing complaints, facial asymmetry, and aphasia. Tier 2 items included a water swallow test, with evaluation for swallowing difficulty, voice quality compromise, and pulse oximetry desaturation (≥ 2%). Patients failing tier 1 did not move forward to tier 2. Scoring: Patients who passed both tiers were considered to be low-risk. Sample: A convenience sample of 84 stroke patients (ischemic/hemorrhagic) screened by 45 ER MDs.	Diagnostic standard: formal assessment conducted by an SLP Prevalence of dysphagia: 57% Sensitivity: 96% Specificity: 56% Interrater reliability: Kappa=0.90
Antonios et al. 2010[8] **Modified Mann Assessment of Swallowing Ability (MMASA)**	12 of the 24 MASA items were retained including alertness, co-operation, respiration, expressive dysphasia, auditory comprehension, dysarthria, saliva, tongue movement, tongue strength, gag, volitional cough, and palate movement. Scoring: Maximum score is 100 (no dysphagia). A cut-off score of 94 was used to identify patients at risk of dysphagia. Sample: 150 consecutive patients with acute ischemic stroke were assessed by 2 neurologists shortly after admission to hospital.	Diagnostic standard: MASA conducted by SLP Prevalence of dysphagia: 36.2% Sensitivity: 87% & 93% Specificity: 86% & 84% Interrater reliability: Kappa=0.76
Schrock et al. 2011[9] **MetroHealth Dysphagia Screen**	5 Items included alert and able to sit upright for 10 minutes; weak, wet, or abnormal voice; drooling; slurred speech; and weak or inaudible cough. Scoring: ≥1 items answered yes=failed screen. Sample: 283 patients admitted to the Emergency department with acute stroke and screened for the presence of dysphagia by nurses	Diagnostic standard: VMBS Prevalence of dysphagia at 30 days: 32% Sensitivity: 95% Specificity: 55% Interrater reliability: Kappa=0.69

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