CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Mood, Cognition and Fatigue following Stroke

Update 2019

Lanctôt KL, Swartz RH (Writing Group Chairs) on Behalf of the Canadian Stroke Best Practice Recommendations Mood, Cognition and Fatigue following Stroke Writing Group and the Canadian Stroke Best Practice and Quality Advisory Committee, in collaboration with the Canadian Stroke Consortium

Heart&Stroke Foundation
Fondation des maladies du cœur et de l'AVC

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS MOOD, COGNITION AND FATIGUE FOLLOWING STROKE SIXTH EDITION, 2019

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PART ONE: INTRODUCTION AND OVERVIEW

Introduction to the Canadian Stroke Best Practice Recommendations

The *Canadian Stroke Best Practice Recommendations* (CSBPR) are intended to provide up-to-date evidence-based guidelines for the prevention and management of stroke, and to promote optimal recovery and reintegration for people who have experienced stroke (patients, families and informal caregivers). The CSBPR are under the leadership of the Heart and Stroke Foundation of Canada. They are intended for use by all members of the interdisciplinary teams who, together, care for people who have experienced a stroke across the continuum from symptom onset to long term recovery. These best practice recommendations address issues relevant to all stroke types, including acute ischemic stroke, transient ischemic attack, intracerebral hemorrhage and subarachnoid hemorrhage.

The theme of the Sixth Edition of the CSBPR is *Partnerships and Collaborations*. This theme stresses the importance of integration and coordination across the healthcare system to ensure timely and seamless care of people who have experienced a stroke to optimize recovery and outcomes. Working with people who experience stroke, their family and caregivers, stroke experts, emergency medical services, other vascular care groups, community care providers, educators and researchers will strengthen our ability to reduce risk factor prevalence and mortality from stroke. This theme also includes consideration of people who experience stroke who may also have other multi-morbidities, as well as collaborations to support stroke care in rural and remote settings.

The goal of disseminating and implementing these recommendations is to optimize stroke care across Canada, reduce practice variations in the care of people who have experienced a stroke, and reduce the gap between current knowledge and clinical practice.

Heart & Stroke works closely with national and provincial stakeholders and partners to develop and implement a coordinated and integrated approach to stroke prevention, treatment, rehabilitation, and community reintegration in every province and territory in Canada. The CSBPR provides a common set of guiding principles for stroke care delivery, and describes the infrastructure necessary at a system level, and the clinical protocols and processes that are needed to achieve and enhance integrated, high-quality, and efficient stroke services for all Canadians. Through the innovations embodied within the stroke best practices, these guidelines contribute to health system reform in Canada and internationally.

The CSBPR are developed and presented within a continuous improvement model and are written for health system planners, funders, administrators, and healthcare professionals, all of whom have important roles in the optimization of stroke prevention and care and who are accountable for results. A strong stroke research literature base is drawn upon to guide the optimization of stroke prevention and care delivery. Several implementation tools are provided to facilitate uptake into practice and are used in combination with active professional development programs. By monitoring performance, the impact of adherence to best practices is assessed and the results are then used to direct ongoing improvement. Recent stroke quality monitoring activities have compelling results which continue to support the value of adopting evidence-based best practices in organizing and delivering stroke care in Canada.

Profile of Stroke Care in Canada:

- Every year, approximately 62,000 people with stroke and transient ischemic attack are treated in Canadian hospitals. Moreover, it is estimated that for each symptomatic stroke, there are approximately nine covert strokes that result in subtle changes in cognitive function and processes.
- Stroke and other cerebrovascular diseases are the third leading cause of death in Canada and the second leading cause of death globally. While the number of deaths from stroke is decreasing in North America and parts of Europe, it is increasing in most other countries.
- Stroke is a leading cause of adult disability, with more than 400,000 people in Canada living with the effects of stroke.
- The annual cost of stroke is approximately $3.6 billion, considering both healthcare costs and lost economic output.
- The combined Canadian healthcare system costs and out-of-pocket caregiver costs for dementia amounted to $10.4 billion in 2016. By 2031, this figure is expected to increase to $16.6 billion [i]
- The human cost of stroke is immeasurable.

[i] Public Health Agency of Canada. Mapping connections: an understanding of neurological conditions in Canada: the National Population Health Study of Neurological Conditions. Ottawa (ON): Public Health Agency of Canada; [modified 2014 Dec 09; cited July 30, 2015]. bhttp://www.phac-aspc.gc.ca/publicat/cd-mc/mc-ec/index-eng.php.

Mood, Cognition and Fatigue following Stroke Module Overview

Partnerships and Collaborations is an imperative within the areas of mood, cognition and fatigue following stroke. The occurrence of post-stroke depression and changes to cognition (vascular cognitive impairment), even if subtle, are reported to affect up to 30% to 60% of people in the first year after experiencing a stroke. Of equal concern is the large number of family members and informal caregivers who also may experience depressive symptoms in the post-stroke recovery phase, and the timing of symptoms may vary from within a few weeks to a year or more after the stroke has occurred. Experiencing any of these sequelae of stroke may make it more challenging to actively participate in rehabilitation and recovery, slow progress, and potentially lead to worse outcomes for people who have experienced a stroke, including increased mortality and lower quality of life. Each of these conditions are complex, they may have similar symptoms and it can be a challenge to sort out underlying mechanisms. In addition, people may experience more than one of these issues. In current practice, people who have experienced a stroke are not consistently screened for these conditions, and the most appropriate timing to screen lacks evidence and consensus. People who have experienced a stroke often report that their symptoms get misinterpreted, for example reporting symptoms of post-stroke fatigue may be presumed to be a symptom of depression, rather than an issue unto itself. We also now understand that these conditions are not severity-dependent; any of these conditions may appear even after a seemingly mild stroke. Understanding each of these conditions, their overlap and interplay, and current best evidence in screening, assessment, and management will lead to improved person-oriented outcomes and enable people to be more likely reach their recovery goals.

The primary underpinnings of this chapter on cognitive and mood changes after stroke require individuals with stroke, their families and healthcare team members to work together in partnership to identify risk areas, agree on goals for treatment and recovery, and implement appropriate management strategies. This theme applies across the continuum of care, and emphasizes the participation of individuals with stroke, their families and caregivers, healthcare providers, and the broader community. People experiencing any of these issues following a stroke often report they feel stigmatized, first by the stroke itself, and more so if it is accompanied by any or all these conditions.

Partnerships and Collaboration involves healthcare providers, policy makers, individuals with stroke, their families and caregivers, and the public. Together, they should ensure timely access to clinicians with expertise in treating these issues, and ongoing monitoring of the effects of treatment and goal attainment. The first steps for healthcare professionals in ***Collaboration*** for mood, cognition and fatigue are to understand the frequency of occurrence and build screening for the symptoms of depression, vascular cognitive impairment, and post-stroke fatigue into regular workflows.

Ideally, when screening is suggestive of a mood or cognition issue, people who have experienced a stroke and families should be referred to these clinical experts without delay to facilitate access to appropriate in-depth assessment and management, and to receive support and education for coping and self-management. Continuity of care and strong communication among healthcare professionals, and between members of the healthcare team and the person who experienced a stroke and their family are critical to smooth transitions between care settings and for ensuring that issues related to mood, cognition and fatigue do not fall through the cracks. Frequent ‘checking in’ and ongoing education with people post stroke and their families is important as these areas can be missed if they do not appear until later stages of recovery.

Recent reports on the quality of stroke services across Canada and within specific provinces have shown that there is inconsistent screening and monitoring of people who have experienced a stroke for post-stroke depression, fatigue and vascular cognitive functioning issues, in both urban and rural settings. Delays in comprehensive assessment and management of mood and cognition issues may result in poor outcomes and slower recovery.

Notable Changes in the 2019 Update of Mood, Cognition and Fatigue Following Stroke

The 2019 update of the CSBPR *Mood, Cognition and Fatigue following Stroke* module reinforces the growing and changing body of research evidence available to guide screening, assessment and management of these conditions following stroke. A coordinated and organized approach to screening and assessment as well as appropriate management is emphasized throughout this chapter.

In some areas, the research evidence is weaker or just starting to emerge. For these topics, the writing group was able to provide preliminary guidance based on expert opinion and current clinical practices.

Highlights of the moderate and significant updates as well as new additions to the Sixth Edition of the *Mood, Cognition and Fatigue following Stroke* module 2019 include:

- ✓ New clinical considerations have been added to each section, acknowledging emerging therapies and consensus-based practices.
- ✓ New literature incorporated which suggests that prophylactic antidepressant medication can be effective in some people who have experienced a stroke.
- ✓ New information on cognitive rehabilitation strategies for people with vascular cognitive impairment.
- ✓ Updated comparison table of assessment tools for screening for vascular cognitive impairment.
- ✓ Updated information on management of post-stroke fatigue.

Guideline Development Methodology

The CSBPR present high-quality, evidence-based stroke care guidelines in a standardized framework to support healthcare professionals across all disciplines. Implementation of these recommendations is expected to reduce practice variations and close the gaps between evidence and practice.

The recommendations are targeted to health professionals throughout the health system who care for those affected by stroke. Health system policy makers, planners, funders, senior managers, and administrators who are responsible for the coordination and delivery of stroke services within a province or region will also find this document relevant and applicable to their work.

The methodology for updating the recommendations includes twelve distinct steps to ensure a thorough and rigorous process. These include the following (details available online):

1. Establish expert interprofessional writing group for module, as well as stroke survivors and/or caregivers (Appendix One);
2. Systematic search, appraisal and update of research literature up to February 2019;
3. Systematic search and appraisal of external reference guideline recommendations;
4. Update of evidence summary tables;
5. Writing group review and revision of existing recommendations and development of new recommendations as required;
6. Submission of proposed chapter update to the Canadian Stroke Best Practices Advisory Committee;
7. Internal review of proposed chapter update. Feedback to writing group, completion of edits;
8. External review, and final edits based on feedback. (List of external reviewers included in Appendix One);
9. Update of educational materials and implementation resources;
10. Final approvals, endorsement and translation of chapter;
11. Public release and dissemination of final chapter update;
12. Continue with ongoing review and update process.

The detailed methodology and explanations for each of these steps in the development and dissemination of the *CSBPR* is available in the *Canadian Stroke Best Practice Recommendations Overview and Methodology* manual available on the Canadian stroke best practices website at https://www.strokebestpractices.ca/recommendations/overview-methods-and-knowledge-exchange

Conflicts of Interest: All potential participants in the recommendation development and review process are required to sign confidentiality agreements and to declare all actual and potential conflicts of interest in writing. Any conflicts of interest that are declared are reviewed by the Chairs of the Best Practices Advisory Committee and appropriate Heart and Stroke staff members for their potential impact. Potential members of any writing group who have conflicts that are considered to be significant are not selected for advisory or writing group. Participants who have conflicts for one particular topic area are identified at the beginning of discussions for that topic, and if it is the chair, then another non-conflicted participant assumes the chair role for that discussion to ensure balanced discussions. Declarations of Conflict of interest for writing group members can be found in Appendix One.

Assigning Evidence Levels: The writing group was provided with comprehensive evidence tables that include summaries of all high-quality evidence identified through the literature searches. The writing group discusses and debates the value of the evidence and through consensus develops a final set of proposed

recommendations. Through their discussions, additional research may be identified and added to the evidence tables if consensus on the value of the research is achieved. All recommendations are assigned a level of evidence ranging from A to C, according to the criteria defined in Table 1. When developing and including "C-Level" recommendations, consensus is obtained among the writing group and validated through the internal and external review process. This level of evidence is used cautiously, and only when there is a lack of stronger evidence for topics considered important system drivers for stroke care (e.g., transport using ambulance services or some screening practices). An additional category for Clinical Considerations has been added for the Sixth Edition. Included in this section are expert opinion statements in response to reasonable requests from a range of healthcare professionals who seek guidance and direction from the experts on specific clinical issues faced on a regular basis in the absence of any evidence on that topic.

Note: all references for recommendations and statements presented in this module can be found in the evidence tables and reference lists provided online for this module at www.strokebestpractcies.ca.

Table 1: Summary of Criteria for Levels of Evidence Reported in the *Canadian Stroke Best Practice Recommendations* (Sixth Edition)

Level of Evidence	Criteria*
A	Evidence from a meta-analysis of randomized controlled trials or consistent findings from two or more randomized controlled trials. Desirable effects clearly outweigh undesirable effects or vice versa.
B	Evidence from a single randomized controlled trial or consistent findings from two or more well-designed non-randomized and/or non-controlled trials, and large observational studies. Meta-analysis of non-randomized and/or observational studies. Desirable effects outweigh or are closely balanced with undesirable effects or vice versa.
C	Writing group consensus on topics supported by limited research evidence. Desirable effects outweigh or are closely balanced with undesirable effects or vice versa, as determined by writing group consensus.
Clinical Consideration	Reasonable practical advice provided by consensus of the writing group on specific clinical issues that are common and/or controversial and lack research evidence to guide practice.

* (adapted from Guyatt et al. 2008) [12]

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Citing the Mood, Cognition and Fatigue following Stroke Module Update 2019 (Sixth Edition):

Lanctôt KL, Swartz RH, on behalf of the Mood, Cognition and Fatigue following Stroke Writing Group. *Mood, Cognition and Fatigue following Stroke Module 2019.* In Lindsay MP, Mountain A, Gubitz G, Dowlatshahi D, Casaubon L, and Smith EE (Editors), on behalf of the Canadian Stroke Best Practices and Quality Advisory Committee. *Canadian Stroke Best Practice Recommendations Sixth Edition,* 2019; Toronto, Ontario Canada: Heart and Stroke Foundation.

The recommendations included in this module are also published in the International Journal of Stroke:

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Comments

We invite comments, suggestions, and inquiries on the development and application of the CSBPR.

Please forward comments to the Stroke Team at Heart and Stroke: strokebestpractices@heartandstroke.ca.

PART TWO: CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS MOOD, COGNITION AND FATIGUE FOLLOWING STROKE

Section One: Post-Stroke Depression (Sixth Edition, 2019)

1. Post-Stroke Depression Update 2019

Definitions and Descriptions:

Depression following stroke: *Within this module, we consider depression following stroke.* The DSM5 category that applies is *mood disorders due to another medical condition such as stroke with depressive features, major depressive-like episode, or mixed-mood features*. It is often associated with large vessel infarction. (DSM-5 293.83; Robinson and Jorge, AJP, Volume 173, Issue 3, March 01, 2016 **, PP. 221-231).**

- A patient who is a candidate for this diagnosis would present with depressed mood or loss of interest or pleasure along with four other symptoms of depression (e.g., weight loss, insomnia, psychomotor agitation, fatigue, feelings of worthlessness, diminished concentration, suicidal ideation) lasting two or more weeks.
- Several mechanisms, including biological, behavioural, and social factors, are involved in its pathogenesis.
- Symptoms usually occur within the first three months after stroke (early onset depression following stroke); however, may occur at any time (late onset depression following stroke). Symptoms resemble those of depression triggered by other causes, although there are some differences - people who have experienced a stroke with depression following stroke experience more sleep disturbances, vegetative symptoms, and social withdrawal.

Vascular depression is a newer concept incorporating a broader range of depressive disorders. Vascular depression is related to small-vessel ischemia and people experiencing vascular depression may have white matter disease seen on brain imaging. Vascular depression also includes post-stroke depression as a sub-category. People who have experienced a stroke with vascular depression have later age of onset, greater cognitive impairment, less family and personal history of depression, and greater physical impairment than geriatric persons with nonvascular depression. They have been found to have different responses to treatment and different prognoses. In addition, persons with vascular depression with executive dysfunction and/or persons who show progression of white matter hyperintensities over time have a poor response to treatment with antidepressants and a more chronic and relapsing clinical course (Taylor WD, Steffens DC, MacFall JR, et al: White matter hyperintensity progression and late-life depression outcomes. Arch Gen Psychiatry 2003; 60:1090–1096).

Apathy is most commonly defined as a multidimensional syndrome of diminished goal-directed behavior, emotion, and cognition (Sachdev 2017; Chen 2018). People present with loss of motivation, concern, interest, and emotional response, resulting in a loss of initiative, decreased interaction with their environment, and a reduced interest in social life. It can negatively impact recovery post-stroke. Apathy can occur as an independent syndrome, although it may also occur as a symptom of depression or dementia (Marin,1991; Starkstein 2008). Apathy has been reported to occur in 29 – 40% of people who have experienced a stroke (van Dalen 2013).

Anxiety following stroke is characterized by feelings of tension, extreme apprehension and worry, and physical manifestations, such as increased blood pressure. Anxiety disorders occur when symptoms become excessive or chronic. In the post-stroke literature, anxiety has been defined both by consideration of the presence and severity of symptoms using validated

screening and assessment scales (such as the Hospital Anxiety and Depression Scale), or by defining syndromes using diagnostic criteria (e.g., panic disorders, general anxiety disorder, social phobia).

1.0 All people who have experienced a stroke should be considered at risk for post-stroke depression, which can occur at any stage of recovery [Evidence Level A].

i. People who have experienced a stroke and families should be given information and education about the potential impact of stroke on their mood [Evidence Level C].

ii. People who have experienced a stroke and families should be provided with the opportunity to talk about the impact of stroke on their lives at all stages of care [Evidence level C]. *Refer to the CSBPR Transitions of Care Module for further information on Patient and Family Education, and Community Follow-up.*

1.1 Screening for Post-Stroke Depression

i. All people who have experienced a stroke should be screened for post-stroke depression if deemed medically appropriate, given the high prevalence of post-stroke depression and the evidence for treating symptomatic depression post stroke [Evidence Level B]. *Note: 'Medically appropriate' excludes people who have experienced a stroke who are unresponsive or who have deficits that interfere with screening for mood disorders. Any pre-stroke mental health or cognitive diagnoses should be taken into consideration during the screening process.*

ii. Screening should be undertaken by trained professionals using a validated screening tool to maximize detection of depression [Evidence Level B]. *Refer to Appendix Two, Table 1A for a summary of suggested validated screening tools.*

iii. Stroke assessments should include evaluation of risk factors for depression, particularly a history of depression [Evidence Level C]. *Refer to note below for list of risk factors.*

iv. For people who experience some degree of communication challenge or deficits following stroke, appropriate strategies that do not rely on verbal communication should be implemented for screening of possible post-stroke depression to ensure adequate screening and assessment and access to appropriate treatment [Evidence Level C]. *Refer to the CSBPR Stroke Rehabilitation Module for further information on communication deficits.*

Note: Common risk factors associated with post-stroke depression include increasing stroke severity, functional dependence, presence of cognitive impairment, and history of previous depression. Increased functional dependence (e.g. requiring help with activities of daily living) and having a history of pre-stroke depression may be the two most salient risk factors for the development of post-stroke depression. Communication deficits and social isolation may also be considered as possible risk factors for depression. Refer to CSBPR Transitions of Care Module for information on depression in family and informal caregivers of people with stroke.

1.2 Assessment for Post-Stroke Depression

i. People who have experienced a stroke whose screening indicates a high risk for depression should be assessed in a timely manner by a healthcare professional with expertise in diagnosis, management and follow-up of depression [Evidence Level C].

Clinical Considerations 1.2: Timing of Screening for Post-Stroke Depression (New in 2019)

i. Screening for post-stroke depression may take place at various stages throughout the continuum of stroke care, especially at transition points, as time of onset for post-stroke depression can vary and include:
   a. At transfer from an inpatient acute setting to an inpatient rehabilitation setting;
   b. From an inpatient rehabilitation setting before return to the community;
   c. During secondary prevention clinic visits;
   d. Following discharge to the community, during follow-up appointments with consulting specialists, and during periodic health assessments with primary care practitioners.

ii. Screening for depressive symptoms could be considered during the initial acute care stay, if deemed medically appropriate, particularly if evidence of depression or mood changes is noted or if risk factors for depression are present, as outlined in section 1.1, iii.

iii. Repeated screening may be required since the ideal timing for screening for post-stroke depression is unclear.

1.3 Non-Pharmacological Management of Post-Stroke Depression

i. It is reasonable to consider either cognitive-behavioural therapy or interpersonal therapy as one of the first line treatments for depressive symptoms post stroke [Evidence Level B], as a monotherapy.

ii. Treatment for post-stroke depression may include psychotherapy as an adjunct in combination with antidepressants [Evidence Level A], as appropriate to the person who has experienced a stroke's health state and other deficits (e.g., communication and other cognitive deficits).

Clinical Considerations 1.3

i. Other approaches to adjunctive treatment of post-stroke depression are emerging, with research in very early stages. These include music, mindfulness, and motivational interviewing. These therapies could be considered on an individual basis at the discretion of the treating healthcare professional in consultation with the person with stroke and their family if appropriate.

ii. Other therapies including deep breathing, meditation, visualization, physical exercise, repetitive transcranial magnetic stimulation, or, for severe refractory depression, electro-convulsive therapy or deep brain stimulation. These have all been suggested in the literature but lack sufficient evidence for routine use and require more research.

1.4 Pharmacotherapy for Post-Stroke Depression

i. People who have experienced a stroke with mild depressive symptoms or those diagnosed with minor depression may initially be managed by "watchful waiting" * (Evidence Level B]. *See note below for definition of watchful waiting.*
   a. Pharmacological treatment should be considered and started if the depression is persistent or worsens and interferes with clinical goals [Evidence Level B].

ii. People diagnosed with a depressive disorder following stroke should be considered for a trial of antidepressant medication [Evidence Level A].

iii. No one drug or drug class has been found to be superior for post-stroke depression treatment. Side effect profiles, however, suggest that some selective serotonin reuptake inhibitors may be favoured in this patient population [Evidence Level A].

a. Choice of an antidepressant medication will depend upon symptoms of depression, potential known side effects of the medication, particularly in the child or older adult, drug interactions with other current medications and underlying disease conditions. *Refer to Appendix Two, Table 1C for a summary of the efficacy and safety of pharmacologic agents for the treatment of post-stroke depression.*

iv. Response to treatment should be monitored regularly by a health professional. Monitoring should include evaluation of any changes in the severity of depression, review of potential side effects, and update of ongoing management plans [Evidence Level C].

v. If a good response is achieved, treatment should be continued for a minimum of six to 12 months. [Evidence Level C].

Note: Examples of a 'good response' may be indicated by positive changes in thoughts and self-perceptions (e.g., hopelessness, worthlessness, guilt), emotional symptoms (e.g., sadness, tearfulness), neurovegetative symptoms (e.g., sleep, appetite), and improved motivation to carry out daily activities.

a. If the person's mood has not improved 2-4 weeks after initiating treatment, assess patient compliance with medication regime. If compliant, then consider increasing the dosage, adding an additional medication, or changing to another antidepressant [Evidence Level B].

b. Following the initial course of treatment, maintenance therapy could be considered on an individual basis (consider previous history and risk factors for recurrence of depression). [Evidence Level C].

c. If a decision is made to discontinue an antidepressant, it should be tapered over one to two months [Evidence level C].

vi. Following initial treatment for post-stroke depression, people who have experienced a stroke should continue to be monitored for relapse or recurrence of depression [Evidence Level C].

vii. Pseudobulbar Affect: In cases of severe, persistent or troublesome tearfulness, emotional incontinence or lability, a trial of antidepressant medication should be considered [Evidence Level A].

a. Side effect profiles suggest that some selective serotonin reuptake inhibitors may be preferred over others for this population. There is no evidence for non-pharmacologic interventions for this condition. *Refer to Appendix Two, Table 1C for a summary of suggested pharmacotherapy agents for the treatment of post-stroke depression.*

Note: Watchful waiting is defined as a period when the person who experienced a stroke displays mild depressive symptoms is monitored closely without additional therapeutic interventions to determine whether the mild depressive symptoms will improve. The timeframe for watchful waiting varies in the literature, typically between 2-4 weeks. It is often described as including suggestions for self-help strategies and participation in physical exercise.

Clinical Considerations

i. The involvement and feedback of people who have experienced a stroke, their family and caregivers is an important component of ongoing monitoring for post-stroke mood changes and conditions.

ii. Counselling and education should include information about potential relapse or recurrence of symptoms, signs to be aware of, the importance of adherence with prescribed medication regime, and contacting their primary care physician or mental health expert should those signs reappear.

1.5 Prophylactic Treatment for Post-Stroke Depression

i. While prophylactic pharmacotherapy has been shown to prevent post-stroke depressive symptoms [Evidence Level A], their impact on function is less clear. At this time routine use of prophylactic antidepressants for ALL people who have experienced a stroke is not recommended as the risk–benefit ratio has not been clearly established [Evidence Level B].

ii. Further research is required to define *at risk* people who have experienced a stroke, choice of antidepressant agents, optimal timing and duration of intervention.

iii. Problem-solving therapy (i.e., cognitive-behaviour therapy) has been shown to have efficacy for prophylactic treatment for post-stroke depression [Evidence-Level B].

1.6 Other Mood States

i. Screening for anxiety may be considered in people who have experienced a stroke as increased prevalence has been demonstrated following stroke [Evidence Level B].

   a. A validated screening tool should be used to detect presence of anxiety [Evidence Level B].

   b. People who have had a stroke with resulting communication limitations should be screened for anxiety using appropriate methods validated for aphasic people who have experienced a stroke [Evidence Level B].

ii. Anxiety frequently co-exists with depression following stroke or may appear in people who have experienced a stroke who are not clinically depressed. For people who have experienced a stroke with marked anxiety with or without clinical depression, it is reasonable to offer pharmacotherapy [Evidence level C].

   a. Although evidence is limited in people who have experienced a stroke, psychotherapy may be considered as an adjunct to pharmacotherapy [Evidence Level C].

iii. Problem-solving therapy (i.e., cognitive behaviour therapy) has been shown to have efficacy for anxiety post-stroke [Evidence Level B].

iv. Apathy frequently co-exists with depression following stroke or may appear in people who have experienced a stroke who and not clinically depressed. For people who have experienced a stroke with marked apathy, with or without clinical depression, it is reasonable to offer nonpharmacological intervention such as exercise or music therapy [Evidence Level C]. Psychostimulants have been trialed, but evidence remains limited [Evidence Level C].

1.7 Ongoing Monitoring, Support and Education

i. People who have experienced a stroke and families should continue to be given information and education about the potential impact of stroke on mood [Evidence level C].

ii. People who have experienced a stroke and families should be provided with the opportunity to talk about the impact of stroke on their lives at all stages of care. *Refer to the CSBPR Transitions of Care Module for further information on Patient and Family Education, and Community Follow-up.*

Rationale

Approximately one-third of all individuals who experience stroke will exhibit symptoms of depression at some time following the stroke event (acute, sub-acute and at long-term follow-up). A substantially increased prevalence of depression following stroke has been reported in up to 24% of people who have experienced a stroke (24% vs 8% compared to general population). Many studies report the highest incidence of post-stroke depression may present within the first three to six months following stroke, and other studies with longer follow-up have reported new onset of post-

stroke depression emerging up to two years after index stroke. In one study, post-stroke depression also was reported in 48% of 71 young people who have experienced a stroke after at least one year of follow-up. Post-stroke depression may prove to be persistent for as many as one-half of the individuals identified as depressed soon after stroke. Severity of functional limitations, stroke severity, cognitive impairment, age of stroke onset, and a previous history of depression have all been identified as important risk factors for the development of post-stroke depression.

Post-stroke depression is associated with poorer functional recovery, increased risk for dependence, poorer cognitive function and reduction in social participation. In addition, the presence of post-stroke depression has been associated with increased risk for mortality. Appropriate identification, diagnosis and treatment of post-stroke depression have been associated with improved outcomes.

Families and caregivers of people who have experienced a stroke are also at risk for depression, with the reported incidence as high as 30% to 60% of caregivers experiencing depressive symptoms.

Anxiety and apathy have been reported in 20-30% of people who have experienced stroke, either alone or in combination with a diagnosis of post-stroke depression.

System Implications

The findings of this review lead to several implications for the healthcare system as follows:

1. Education for primary care practitioners and healthcare providers across the continuum of stroke care on recognition, assessment, and management of post-stroke depression.
2. Screening tools should be available that are sensitive to unique circumstances, such as people who have experienced a stroke with communication or cognitive deficits and tools that may be culturally appropriate.
3. Timely access to appropriate mental health specialists as needed who are able to diagnose and evaluate severity of depression and provide guidance for ongoing management.
4. Timely access to and availability of specialized therapies to manage post-stroke depression, including counseling and psychotherapy as required.
5. The development and implementation of an equitable and universal pharmacare program, implemented in partnership with the provinces, designed to improve access to cost-effective medicines for all people in Canada regardless of geography, age, or ability to pay. This program should include a robust common formulary for which the public payer is the first payer.
6. Mechanisms to ensure good communication and information flow between the range of specialists and programs beyond the core stroke care providers to meet the varied needs of individuals post stroke (e.g., mental health specialists, cognitive specialists, geriatric programs).
7. Process for ongoing monitoring of any person who experienced a stroke with positive screening for depression during screening and assessment process.
8. Education and support for caregivers of people who have had a stroke.
9. Processes should be in place to provide education and ensure that the caregivers' emotional needs are monitored and addressed, ideally through involvement of the primary health care team.
10. Optimization of strategies to prevent the recurrence of stroke.

Performance Measures

1. **Proportion of people with acute stroke with documentation indicating initial screening for post-stroke depression was performed (either informally or using a formal screening tool) in the acute care, rehabilitation, long-term care and community settings (e.g., homecare) setting. (Core Indicator)**

2. Proportion of people with acute stroke referred for additional assessment or intervention for a suspected diagnosis of depression.
3. Proportion of people who have experienced a stroke diagnosed with post-stroke depression who are treated with antidepressants and/or psychotherapy at appropriate time points following the initial stroke event, such as at 30, 60, and 90 days, six months, and one year.

Measurement Notes

- Recommendations for screening and assessment of post-stroke depression and corresponding performance measures apply across the continuum of stroke care and should be considered in the acute, early rehabilitation, and longer-term recovery in the community, and apply across all healthcare settings.
- When monitoring these performance measures, it is important to record when and in what context (continuum of care) the measurements were conducted, as well as the specific tools used for measurement.
- Data for measurement may be found through primary chart audit. Data quality will be dependent on the quality of documentation by healthcare professionals.
- For people who have experienced a stroke referred to psychiatry, information may be available through provincial physician billing databases; some privacy regulations may limit access to certain data.
- For persons over 65 years old, information on medication prescriptions may be available through provincial and territorial senior drug benefit plan databases.
- For performance measure 3, the intent is to increase the number of people with post-stroke depression who are adequately treated and reduce the number of people who have experienced a stroke with depression who are untreated (depressive disorder + no antidepressant medication) and undertreated (depressive symptoms + antidepressant medication + ongoing symptoms). This should be considered in the measurement and analysis plan.

Implementation Resources and Knowledge Transfer Tools

Health Care Provider Information

- Table 1A: Selected Validated Screening and Assessment Tools for Post-Stroke Depression (Appendix Two)
- Table 1B: Selected Validated Screening and Assessment Tools for Post-Stroke Anxiety (Appendix Two)
- Table 1C: Summary Table for Selected Pharmacotherapy for Post-Stroke Depression (Appendix Two)
- Evidence-based Review of Post-Stroke Depression (EBRSR) http://www.ebrsr.com/evidence-review/18-post-stroke-depression
- Stroke Engine, Mood/Depression section https://www.strokengine.ca/en/assess_domain/assess-mood-depression/
- NHS Stroke Recovery: https://www.nhs.uk/conditions/stroke/recovery/
- APA Diagnostic and Statistical Manual of Mental Disorders (DSM) http://www.psychiatry.org/practice/dsm

Information for People who have Experienced a Stroke, their Families and Caregivers

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

- Post-Stroke Checklist: https://www.strokebestpractices.ca/-/media/1-stroke-best-practices/resources/patient-resources/002-17_csbp_post_stroke_checklist_85x11_en_v1.ashx
- Your Stroke Journey: A Guide for People Living with Stroke https://www.heartandstroke.ca/-/media/pdf-files/canada/your-stroke-journey/en-your-stroke-journey-v20.ashx
- Recovery and Relationships:

  https://www.heartandstroke.ca/stroke/recovery-and-support/relationships
- Depression, Energy, Thinking and Perception

  https://www.heartandstroke.ca/stroke/recovery-and-support/emotions
- Recognizing and dealing with depression: http://www.heartandstroke.ca/heart/recovery-and-support/emotions-and-feelings/depression
- The Heart & Stroke Living with Stroke™ program: https://www.heartandstroke.ca/stroke/recovery-and-support/living-with-stroke
- Canadian Partnership for Stroke Recovery - Life after Stroke: http://www.lifeafterstroke.ca
- Support for family members and caregivers:

  https://www.heartandstroke.ca/stroke/recovery-and-support/family-care-partners-need-care-too
- Recognizing and Handling Stress:

  https://www.heartandstroke.ca/heart/recovery-and-support/emotions-and-feelings/stress

Summary of the Evidence Update 2019

Post-stroke depression (PSD) is a common consequence of stroke, although reported estimates may be unreliable given possible under-reporting of unusual mood, and the variability in the methods used to assess and define cases of depression within the literature. In a systematic review of 61 prospective, observational studies of post-stroke depression conducted in hospital-, rehabilitation-, and population-based settings, Hackett & Pickles (2014) estimated that approximately one-third of all individuals who experience stroke exhibited depressive symptoms at some point following the event (i.e., at acute, sub-acute or long-term follow-up). The overall pooled frequency estimate of PSD was 31% (95% CI 28% to 35%). Salinas et al. (2017) reported that of 1,424 postmenopausal women included in the Women's Health Initiative who experienced a first-ever stroke, new-onset PSD occurred in 21.4% of participants, at an average of 16 months post stroke. Jorgensen et al. (2016) reported the incidence of persons developing depression was significantly higher compared with those of the general population matched for age and sex. During a two-year observation period, the incidence of depression was 25.4% vs. 7.8% (adj HR=4.09, 95% CI 4.00-4.18). In the prospective *Depression Predictors after Ischemic Stroke* study *(DEPRESS),* Guiraud et al. (2016) reported that among 251 patients with new onset stroke, the incidence of depression was 19% at two months and 24.3% at six months. Risk factors for the development of PSD include increasing age, living alone, high levels of comorbidity, a history of depression, female gender, physical disability (mRS score >2 at discharge), increased initial stroke severity, cognitive impairment and prior history of stroke. (Guiraud et al. 2016, Jorgensen et al. 2016, Kutlubaev & Hackett 2014, Ayerbe et al. 2013b).

The best time to screen formally for the possible presence of PSD is not certain. Although incident rates decline over time and there is a general trend toward improvement in depressive symptomatology during the first-year post stroke, PSD may prove to be persistent for a longer

duration for a significant proportion of individuals. Screening for depression should be considered during the acute inpatient stay, at the point of transition to, or during inpatient rehabilitation, upon discharge to the community and during periodic health assessments. Swartz et al. (2017) describes the feasibility of using the 2-item version of the Patient Health Questionnaire during routine clinical practice using 1,500 outpatients attending a stroke prevention clinic. All patients were able to complete the screen, 89% of whom did so in less than 5 minutes. Karamchandani et al. (2015) reported that 70% of patients were eligible for depression screening prior to hospital discharge or transfer to another service. The remaining patients were not eligible due to aphasia, other medical condition, hospice/comfort measures, or prolonged intubation.

The diagnostic accuracies of several post-stroke depression screening and assessment tools have been examined. Meader et al. (2014) included the results of 24 studies and evaluated the performance of 18 previously-validated scales. The three best performing scales for the identification of any depression included Center of Epidemiological Studies-Depression Scale (CES-D) with a sensitivity and specificity of 75% and 85%, the Hamilton Depression Rating Scale (HDRS, sensitivity 84%, specificity 83%) and the 9-item version of the Patient Health Questionnaire (PHQ-9, sensitivity 86%, specificity 79%). The best two performing scales for the identification of major depression were HDRS and the PHQ-9. In a Canadian study (Prisnie et al. 2016) including 122 outpatients attending a stroke prevention clinic, the diagnostic accuracies of the PHQ-9 and PHQ-2 were evaluated. Using a cut-point of 13, the sensitivity and specificity of the PHQ-9 was 81.8% and 97.1%, and 75.0% and 96.3%, for PHQ-2, using a cut point of three.

Once possible depression has been detected via formal screening using a validated screening tool and the diagnosis confirmed by an experienced healthcare professional, treatments may be initiated. Pharmacotherapy with antidepressants has been associated with a reduction of depressive symptomatology. Xu et al. (2016) included the results from 11 RCTs of patients with a clinical diagnosis of post-stroke depression. Treatment with an antidepressant was associated with a significant reduction in depression scores (SMD=-0.96, 95% CI -1.41 to -0.51, $p<0.0001$), and better response to treatment (RR=1.36, 95% CI 1.01-1.83, p=0.04). A Cochrane review authored by Hackett et al. (2008), also reported the odds of remission of depression (i.e. a reduction of ≥50% in depression scale scores) were significantly higher with pharmacotherapy. Most of the agents evaluated in these reviews were selective serotonin reuptake inhibitors and tricyclic antidepressants. A systematic review by Chen et al. (2006) identified a relationship between duration and benefit of treatment. Analysis of studies with treatment durations of one and two weeks revealed no significant treatment effects; however, when treatment lasted for three weeks or more, the effects were greater. Many adverse events were associated with the use of pharmacotherapy in these studies. Antidepressants have also been shown to improve functional recovery and reduce dependency in a person post stroke, both with, and without post-stroke depression (Mead et al. 2012, Chollet et al. 2011). The use of antidepressants has also been associated with reductions in emotional lability (Hackett et al. 2010), a common consequence of stroke. Pooling the results from 3 trials, the odds of improvement (i.e., reduction) in tearfulness were significantly increased in the treatment group (OR=9.35, 95% CI 4.26 – 20.54).

Non-pharmacological approaches to the treatment of post-stroke depression include different forms of psychotherapy, physical activity, non-invasive brain stimulation, and acupuncture. Psychotherapy (including problem solving therapy, cognitive behavioural therapy and motivational interviewing), has not been shown to be an effective treatment for depression in person recovering from stroke when used in isolation (Hackett et al. 2008), however, these same techniques may be effective when used in combination with pharmacotherapy (Mitchell et al. 2009). Behavioral therapy was shown to be effective for the treatment of post-stroke depression in persons with aphasia (Thomas et al. 2012).

Acupuncture was shown to be superior to pharmacotherapy in the treatment of post-stroke depression. In a meta-analysis including the results of 15 RCTs of persons with post-stroke depression (Zhang et al. 2012), treatment with acupuncture was associated with improved odds of recovery/remission compared with pharmacotherapy (OR=1.48, 95% CI 1.10-1.97). Non-invasive brain stimulation using either repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) has been shown to improve symptoms of depression. Significant reductions in Hamilton Rating Scale for Depression (HAD-D) scores were reported following two to eight weeks of rTMS therapy, compared with sham treatment in a meta-analysis including the results from 22 RCTs (Shen et al. 2017). At the end of treatment, the mean reduction in HAM-D scores was significantly greater for the rTMS group (MD=-6.09, 95% CI -7.74 to -4.45, p<0.0001). The ability of persons to perform ADLs was also significantly greater in the rTMS group (SMD=1.20; 95% CI 0.68-1.72, p<0.001). Treatment with 12, 30-minute sessions of tDCS (2 mA) in persons with post-stroke depression, treated an average of 15 months post stroke has also been associated with significant reductions in HAD-D scores (Valiengo et al. 2017). Physical activity has been associated with a small, but significant reduction in depression scores in a meta-analysis authored by Eng & Reime (2014) including the results from 13 RCTs (SMD=−0.13, 95% CI −0.26 to −0.01, p=0.03).

Prevention of Post-Stroke Depression

Given the high prevalence of post-stroke depression and the negative consequences associated with it, there has been increasing attention paid to strategies for its prevention. Pharmacologic prophylaxis, using many of the same agents, used for treatment, has been most commonly evaluated. In a pooled analysis based on 776 observations from 12 RCTs, Salter et al. (2012) reported the odds of developing post-stroke depression were reduced significantly with the use of prophylactic pharmacotherapy (OR=0.34, 95% 0.22-0.53, p<0.001). Similar effects have been reported in other systematic reviews (Yi et al. 2010, Chen et al. 2007). Non-pharmacological approaches have also been evaluated for the prevention of post-stroke depression. A Cochrane review (Hackett et al. 2008) included four trials that evaluated psychotherapeutic interventions, including problem-solving therapy (PST), home-based therapy and motivational interviewing. The odds of developing depression were significantly lower for participants in the active intervention groups (OR= 0.64, 95% CI 0.42 to 0.98, p=0.04), while psychological interventions were associated with a significant improvement in General Health Questionnaire (GHQ)-28 scores from baseline to end of treatment (MD= -1.37, 95% CI -2.33, -0.40, p=0.006). In a trial that included pharmacological and non-pharmacological study arms with long-term follow-up, Robinson et al. (2008) randomized 176 patients without depression to receive escitalopram, problem-solving or placebo, which was provided for 12 months. At one year, in the per-protocol analysis, adjusted for previous history of mood disorders, patients assigned to the placebo condition were significantly more likely to develop depression compared with those receiving either therapy with escitalopram (adj. HR= 4.5, 95% CI 2.4-8.2, p<0.001) or problem-solving therapy (adj. HR=2.2, 95% CI 1.4-3.5, p<0.001). In a follow-up study, Mikami et al. (2011) reported that when escitalopram was discontinued at the end of the study period, persons were more likely to develop major depression and had increased Hamilton Depression Rating Scale HDRS scores during the next six months, compared with those given placebo or PST. Finally, after a mean duration of eight years of follow-up, Robinson et al. (2017) reported that participants who received PST were significantly less likely to have died, compared with the combined group of escitalopram + placebo. Increasing age and the development of depression were found to be significant predictors or mortality.

Treatment of Anxiety Following Stroke

People with depression may also have a comorbid generalized anxiety disorder (GAD). Anxiety following stroke occurs in 20-25% of patients and is more common in women (Campbell et al. 2013).

Despite the prevalence of post-stroke anxiety, very few studies have included evaluation of the effectiveness of potential treatments. A Cochrane review (Knapp et al. 2017) identified only three RCTs examining pharmacotherapy (paroxetine, buspirone) and a self-help autogenic relaxation CD). While the results from individual trials were positive, the results could not be pooled. The authors concluded there was insufficient evidence to guide treatment. Non-pharmacological approaches to the treatment of anxiety that have been reported to reduce anxiety symptoms include a self-help program (Golding et al. 2016 a,b), multidisciplinary in-home visits from rehabilitation therapists (Ryan et al. 2006) and acupuncture (Ping & Songhai 2008).

Post-Stroke Depression and Mood Evidence Tables and Reference List

- Evidence Table 1A Post stroke Depression Screening and Assessment
- Evidence Table 1B Non-pharmacological Interventions
- Evidence Table 1C Pharmacotherapy and Combined Treatment

Section Two: Vascular Cognitive Impairment (Sixth Edition, 2019)

2. Vascular Cognitive Impairment (Update 2019)

In 2024, a new stand-alone module was released on Vascular Cognitive Impairment as part of the 7th edition update of the CSBPR. The new 7th edition VCI CSBPR module is available here on the CSBPR website, as well as published in the journal Alzheimer's & Dementia.

Section Three: Post-Stroke Fatigue (Sixth Edition, 2019)

3. Post-Stroke Fatigue 2019

Definitions and Descriptions:

Post-Stroke Fatigue: Fatigue following stroke is a multidimensional motor-perceptive, emotional and cognitive experience characterized by a feeling of early exhaustion with weariness, lack of energy and aversion to effort that develops during physical or mental activity and is usually not ameliorated by rest. Fatigue can be classified as either objective or subjective. Objective fatigue is defined as the observable and measurable decrement in performance occurring with the repetition of a physical or mental task, while subjective fatigue is a feeling of early exhaustion, weariness and aversion to effort (Acciarresi et al, 2014; Staub 2001, Annoni 2008, Lerdal 2009, Eskes 2011).

Characteristics of post-stroke fatigue may include: overwhelming tiredness and lack of energy to perform daily activities; abnormal need for naps, rest, or extended sleep; more easily tired by daily activities than pre-stroke; unpredictable feelings of fatigue without apparent reason.

3.0 Post-stroke fatigue is a common condition and can be experienced following a stroke at any point during the recovery process. Post-stroke fatigue is often under-recognized; thus, healthcare professionals should anticipate the possibility of post-stroke fatigue and prepare people who have experienced a stroke and families to mitigate fatigue through assessment, education, and interventions throughout the stroke-recovery continuum [Evidence Level B].

Note: Post-stroke fatigue does not appear to be correlated to the severity of stroke. People who experience very mild stroke may still experience post-stroke fatigue.

3.1 Screening and Assessment

i. Prior to discharge from acute care or inpatient rehabilitation, people who have experienced a stroke, their families and informal caregivers, should be provided with basic information regarding the potential experience of post-stroke fatigue [Evidence Level C].

ii. Following return to the community, people who have experienced a stroke should be periodically screened for post-stroke fatigue during follow-up healthcare visits (e.g., primary care, home care, and outpatient prevention or rehabilitation clinics) [Evidence Level C]. *Refer to Appendix Table 3A for a summary of suggested screening tools.*

iii. People who experience post-stroke fatigue should be screened for common and treatable post-stroke co-morbidities and for medications that are associated with and/or exacerbate fatigue [Evidence Level B].

a. These may include: signs of depression or other mood-related conditions; sleep disorders or factors that decrease quality of sleep (e.g. sleep apnea, pain); other common post-stroke medical conditions and medications that increase fatigue, e.g. systemic infection such as urinary tract infections, dehydration, sedating drugs, hypothyroidism.

3.2 Management of Post-Stroke Fatigue

i. People who have experienced a stroke should be cared for by healthcare professionals who are knowledgeable in the symptoms of fatigue and its management [Evidence Level C].

ii. There is limited evidence suggesting that pharmacological treatment for post-stroke fatigue with modafinil may be considered in some people who have experienced a stroke [Evidence Level C]. More research is required to fully understand the benefits of this treatment.

iii. There is currently insufficient evidence to recommend antidepressant treatment for post-stroke fatigue [Evidence Level B].

iv. Psychotherapy (cognitive behavioural therapy) may be considered as an adjunct treatment for post-stroke fatigue [Evidence Level B].

v. Mindfulness based stress reduction may be considered as an adjunct treatment for post-stroke fatigue [Evidence Level B].

vi. Counselling on graduated exercise schedules with increasing physical demands appropriate to tolerance level to improve deconditioning and physical tolerance is recommended [Evidence Level C].

vii. Counselling on energy conservation strategies that consider optimizing daily function in high priority activities is recommended (e.g. daily routines and modified tasks that anticipate energy needs and provide a balance of activity/rest) [Evidence Level C]. *Refer to Box 3 for detailed examples of energy conservation strategies.*

viii. Counselling on the establishment of good sleep hygiene behaviours is recommended [Evidence Level B]

ix. Provide education to people who have experienced a stroke, their families and informal caregivers, on daily time management and planning a balance of activities with rest periods [Evidence Level C].

x. Encourage people who have experienced a stroke and are experiencing post-stroke fatigue to communicate energy status and rest needs to healthcare providers, family members, caregivers, employers and social groups [Evidence Level C].

Box 3: Examples of Specific Energy Conservation Strategies

The following list includes energy conservation strategies described across a broad literature base. These are provided as helpful information and guidance in counseling people who have experienced a stroke; they should not be regarded as evidence-based recommendations.

- Structuring the day to include a balance of activity and scheduled periods of rest; anticipating energy requirements for each task and for completion of high priority activities;
- Keeping an agenda of daily activities, planning higher energy activities immediately following a period of rest, planning activities a day in advance, anticipating energy requirements for each task, prioritizing tasks and energy requirements;
- Organizing the physical environment to minimize efforts to move around, reduce stair climbing, and have ready access to the most frequently used items;
- Sitting rather than standing when possible when doing chores (such as washing dishes or ironing);
- Teaching people who have experienced a stroke to use appropriate body mechanics, posture and sitting positions and locations (i.e. rest in bed, rather than in a chair);
- Establishing good sleep hygiene patterns, and avoiding sedating drugs and excessive alcohol;
- Using energy saving equipment and technology to reduce physical efforts (e.g., electric can opener, online shopping);
- Engaging in enjoyable vocational and leisure activities that are planned ahead to ensure the person with stroke is well rested prior to activities;

- Delegating activities that are low priority or can be done by someone else, such as family members;
- Developing a plan for healthy diet or proper nutrition to help with energy levels.

Rationale

Post-stroke fatigue is generally under-diagnosed and not routinely assessed in people who have experienced a stroke. However, symptoms of fatigue are often reported by people who have experienced a stroke in both the acute and chronic stages of recovery following a stroke. Prevalence rates of post-stroke fatigue (PSF) are substantial, varying between 38 and 73%. Additionally, these rates have not shown marked decline after the post-acute stage to even years following the injury. It can occur in any person who has experienced a stroke and has not been found to be dependently related to size, location or severity of stroke. It is commonly associated with low mood and sleep disturbances but can arise in their absence. However, it has been shown to negatively impact a person's ability to actively participate in rehabilitation, which has been associated with poorer long-term outcomes. Therefore, recommendations are included here to raise awareness of the frequency of post-stroke fatigue, the physical and emotional impact of PSF on people who have experienced a stroke and the negative impact on recovery and outcomes.

System Implications

1. Protocols for the inclusion of post-stroke fatigue in screening and assessments at all transition points and stages of care following a stroke.
2. Resources and mechanisms to plan and deliver community-based services which consider the needs of the survivor and family/caregiver and are focused on energy conservation (e.g., access to assistive devices, transportation, and counseling).
3. Models of care that include technology such as telemedicine, regular telephone follow-up and web-based support to reduce excess visits to healthcare providers that consume energy.
4. Education and increased awareness about post-stroke fatigue and management strategies for people who have experienced a stroke, caregivers, employers and health care professionals.

Performance Measures

1. The number and proportion of people who have experienced a stroke who report symptoms of post-stroke fatigue, measured at each transition point as a proportion of all people who have experienced a stroke.
2. The proportion of people who have experienced a stroke who return to the emergency department or are readmitted to hospital for failure to cope or other fatigue-related reasons.

Measurement Notes

- Standardized and validated measures of post-stroke fatigue have not been published for this population. Many validated scales for fatigue as a condition may be applicable and are reasonable choices at this time.

Implementation Resources and Knowledge Transfer Tools

Health Care Provider Information

- Table 3A: Summary of Selected Assessment Tools for Post-Stroke Fatigue (Appendix Two)
- Multidimensional Inventory: http://www.cas.usf.edu/~jacobsen/HANDOUT.FSI&MFSI.pdf
- Fatigue severity scale: https://www.healthywomen.org/sites/default/files/FatigueSeverityScale.pdf
- Stroke Engine, Fatigue Section https://www.strokengine.ca/en/intervention/fatigue/

Information for People who have Experienced a Stroke, their Families and Caregivers

- Stroke Engine, https://www.strokengine.ca/en/
- Taking Charge of Your Stroke Recovery: A survivor's guide to the Canadian Stroke Best Practice Recommendations": http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.5056519/k.C841/Stroke__A_Patients_Guide_to_Canadian_Best_Practice_Recommendations_for_Stroke_Care.htm
- Fatigue After Stroke: https://www.stroke.org.uk/resources/fatigue-after-stroke
- Fatigue http://www.stroke.org.uk/about/fatigue
- Fatigue http://www.stroke.org/site/PageServer?pagename=fatigue
- Let's Talk About Feeling Tired After Stroke: https://www.strokeassociation.org/-/media/stroke-files/stroke-resource-center/recovery/patient-focused/spost_feelingtired_2015.pdf?la=en&hash=80418AF3E2275E109177C932EAE7CCD82F42FA05
- Activity Journal: http://www.cdc.gov/healthyweight/pdf/physical_activity_diary_cdc.pdf

Summary of the Evidence Update 2019

Post-stroke fatigue (PSF) is known to occur commonly, is associated with mood disorders and pain, and negatively impacts recovery. Persons experiencing PSF report common experiences including having less capacity and energy, an abnormal tiredness and an overwhelming need for long-lasting sleep, being easily fatigued, fatigue for which there was no obvious cause or explanation and increased stress sensitivity (Eilertsen et al. 2013).

The incidence of PSF is difficult to estimate given that many patients report symptoms of pre-stroke fatigue (Lerdal et al. 2011). Estimates of incidence/prevalence also vary depending on when fatigue is assessed in the recovery process and which tool is used for assessment. At the time of admission to inpatient rehabilitation, fatigue was present in 51.5% of patients (Schepers et al. (2006) and at the point of discharge, in 58.3% of patients (Van Eijsden et al. 2012). Schepers et al. (2006) reported that fatigue was present in 64.1% and 69.5%, respectively at six months and one year. Overall, fatigue was present in 37.7% of patients and absent in 17.4%, at all assessment points. Of the patients reporting fatigue at one year, 29.3% were also depressed. Van der Port et al. (2007) reported that the percentages of patients considered fatigued at six, 12 and 36 months were 68%, 74% and 58%, respectively, in 223 acute stroke patients followed prospectively. In all these studies, the presence of fatigue was identified based on a score of ≥4 on the Fatigue Severity Scale. Parks et al. (2012) reported that of 228 participants who were surveyed 12 months post stroke, 37% reported symptoms of fatigue at least once during the previous month. Among those reported fatigue, 59.5% stated that fatigue was one of the worst or the worst symptom they experienced. Two years following stroke, of 5,189 patients who were alive and included in the Riks-Stroke national stroke registry, and who responded to a postal survey, 10% and 29.2% of respondents reported "always" or "often" being tired (Glader et al. 2002). In perhaps the largest systematic review of its kind, Cumming et al. (2016) included the results of 49 studies and estimated the prevalence of PSF at any point following stroke. Using the results from 22 studies that used the Fatigue Severity Scale and a cut-off level of ≥4 or >4, the prevalence of post-stroke fatigue was 50%, 95% CI 43–57%.

The clinical course of PSF is unclear; therefore, it's even unknown if PSF increases or decreases over time. Snaphaan et al. (2011) reported that the prevalence of fatigue was 35% at two months post-stroke and 33% at 18 months. 26% of patients reported fatigue at both assessment points, while 9% reported fatigue at baseline but not at follow-up, and 8% reported no fatigue at baseline but did at follow-up. In a systematic review (Duncan et al. 2012), which included the results of nine studies, the percentage of patients reporting fatigue increased from assessment time one to time two in seven studies, while it had decreased between assessment points in two studies. In contrast, Cumming et al. (2016) reported the estimates of fatigue were relatively stable across time (within three months of stroke 55%, 95% CI 25–85%; one to six months 46%, 95% CI 31–62%; and greater than six months

53%, 95% CI 48–58%). Independent predictors of fatigue that have been identified include depression, low levels of physical functioning, and pre-stroke fatigue (Lerdal et al. 2011). Both increasing (Snaphaan et al. 2011) and decreasing age (Parks et al. 2012), have been reported as predictors of PSF, as have female (Schepers et al. 2006) and male sex (Gladder et al. 2002).

A few controlled studies have been conducted comparing fatigue in persons recovering from stroke with persons from the general population and in cases of transient ischemic attack. When compared with 1,069 persons of similar ages selected from the general population, the fatigue scores of 165 patients with acute stroke were significantly higher after adjusting for age, sex and living arrangements. Of the five subscale components of the Multidimensional Fatigue Inventory (MFI-20), stroke patients had significantly higher general and physical fatigue scores and also higher reduced activity scores at three months (Christensen et al. 2008). Winward et al. (2009) compared 73 subjects with minor stroke and 76 subjects with transient ischemic attack who were participants in the Oxford Vascular study. At six months, a higher proportion of participants with stroke reported significant fatigue, assessed using the Chalder Fatigue Scale (56% vs. 29%, p=0.008). A higher proportion of subjects with stroke, who had initial NIHSS scores of 0 reported significant fatigue compared with transient ischemic attack with initial NIHSS scores of 0 (57% vs. 29%, p=0.015). Subjects who felt they had not made a full recovery were more likely to be fatigued compared to those who felt they had (72% vs. 23%, p<0.0001).

There are few treatments for post-stroke fatigue that have been evaluated. A Cochrane review (Wu et al. 2015) included the results from 12 RCTs, four evaluating four pharmacological and four evaluating non-pharmacological approaches. In the remaining four trials, PSF was not the primary target of investigation, but fatigue was reported as an outcome. Using the results from seven trials (five pharmacological, two no-pharmacological), treatment was associated with a significant reduction in fatigue scores (WMD= -1.07, 95% CI -1.93, -0.21, p=0.014).

Pharmacological agents that have been evaluated in the treatment of PSF include selective serotonin reuptake inhibitors (fluoxetine) and modafinil. In the Modafinil in Debilitating Fatigue After Stroke (MIDAS) trial, 36 participants with PSF received 200 mg modafinil or placebo for six weeks (Bivard et al. 2017). Active treatment was associated with a significantly greater decrease in mean total Multidimensional Fatigue Inventory (MFI)-20 scores (MD= −7.38, 95% CI −21.76 to −2.99; *P*<0.001), mean FSS scores (MD= -6.31, 95% CI -10.7 to -1.9, p=0.048) and a significantly greater increase in total mean Stroke-Specific Quality of Life scores (MD=11.8, 95% CI 2.3 to 21.3, p=0.015). Poulsen et al. (2015) randomized 41 persons with PSF to receive 400 mg modafinil for 90 days. The results were ambiguous. At 90 days, there was no significant difference between groups in the median MFI-20 GF score (11 modafinil vs placebo 14, p=0.32), or in the median score of other MFI domains (physical fatigue, reduced activity, reduced motivation); however, median FSS and FSS-7 were significantly lower at 90 days for patients in the modafinil group (36 vs. 49.5, p=0.02 and 22 vs. 37.5, p=0.042). Fluoxetine was examined in a trial including 83 participants with post-stroke emotional disturbances, an average of 14 months after stroke onset, were randomized to receive 20 mg/day of fluoxetine (n=40) or placebo, (n=43) for three months (Choi-Kwon et al. 2007). At the end of treatment, there were no significant differences in the number of patients with PSF. At six months, 34 patients (85%) in the fluoxetine group reported PSF compared with 40 (93%) in the control group. However, at three months, fewer patients in the fluoxetine group reported excessive/inappropriate crying (n=16, 40% vs. n=27, 62.8%, p=0.038), and at six months fewer patients in the fluoxetine group were identified with depression (n=5, 12.5% vs. n=13, 30.2%, p=0.05).

Among trials evaluating non-pharmacological treatments for PSF, two reported significant improvements in symptoms. Zedlitz et al. (2013) randomized 83 participants with severe fatigue >4 months post stroke to participate in a 12-week program consisting of group cognitive treatment (control condition) or group cognitive treatment combined with graded activity training (COGRAT). Cognitive treatment consisted of cognitive behavioural therapy and compensatory strategy teaching. Those in the COGRAT group also received 24 sessions, each two hours in duration of graded activity training, including treadmill walking, strength training, and homework assignments. Participants who received COGRAT were significantly more likely to experience clinically relevant improvement in fatigue severity (57.9% vs. 24.4%, p=0.002). Johansson et al. (2012) randomized 29 patients, of whom 18 were recovering from stroke (11 from traumatic brain injury) with mental fatigue to participate in an eight-week program of Mindfulness–Based Stress Reduction (MBSR), which included yoga, body scan, and

sitting meditation, or to a wait list control group. Compared with those in the wait list control group, participants who received the MBSR program immediately reported a significantly greater decrease in Mental Fatigue Scale scores. Non-pharmacological interventions that have been evaluated for the treatment of PSF and found not to be effective include the use of continuous positive airway pressure (Brown et al. 2011), a fatigue management education program (Clarke et al. 2012) and a six-month chronic disease self-management program (Lorig et al. 2001).

Post-Stroke Fatigue Evidence Tables and Reference List

APPENDIX ONE

Canadian Stroke Best Practice Recommendations
Mood, Cognition and Fatigue following Stroke
Writing Group 2019

NAME	PROFESSIONAL ROLE	LOCATION	DECLARED CONFLICTS OF INTEREST
Lanctôt, Krista L. Ph.D	Writing Group Co-Chair; Senior Scientist, Sunnybrook Research Institute and Heart and Stroke Foundation Centre for Stroke Recovery; Professor of Psychiatry and Pharmacology/Toxicology, University of Toronto	Ontario	**Potential conflict:** Lundbeck - consulting fees, funded research **Potential conflict:** Merk - consulting fees **Potential conflict:** Otsuka - consulting fees **Potential conflict:** AbbVie - funded research **Potential conflict:** Novartis - funded research
Swartz, Richard MD PhD FRCPC	Stroke Neurologist; Medical Director North East GTA Regional Stroke Program; Director, University of Toronto Stroke Program; Assistant Professor, Department of Medicine (Neurology), University of Toronto	Ontario	**Potential Conflict:** DOC Screen. Nature of Relationship: I have published on screening methods for Depression, Obstructive sleep apnea and Cognitive impairment (the DOC screen) in Stroke clinic populations. The screen is offered online without charge - there is no financial conflict, but there is potential for academic credit or appearance of Professional conflit.
Sahlas, Demetrios J MSc, MD, FRCP(C), DABPN	Stroke Neurologist **,** MG DeGroote Professor in Stroke Management, Associate Professor, Division of Neurology, Department of Medicine, Faculty of Health Sciences, McMaster University; Director, Neurology Residency Training Program; Central South Regional Stroke Centre, Hamilton General Hospital, Hamilton Health Sciences	Ontario	No conflicts to declare
Austin, Melissa MSc (OT)	Occupational Therapist, Clinical Resource Occupational Therapist for Neurology/Spine Populations, Clinical Instructor, Dept of Occupational Science and Occupational Therapy,	British Columbia	No conflicts to declare

NAME	PROFESSIONAL ROLE	LOCATION	DECLARED CONFLICTS OF INTEREST
	Faculty of Medicine, University of BC		
Ball, Kristyn BMR PT	Physiotherapist, Clinical Advisor – Physiotherapy; Acute Neurosurgery & Medicine, Health Sciences Centre	Manitoba	No conflicts to declare
Blake, Treena PhD	Psychologist, Neuropsychologist, Acquired Brain Injury Program, GF Strong Rehabilitation Centre, Vancouver	British Columbia	No conflicts to declare
Herrmann, Nathan MD, FRCPC	Geriatric Psychiatrist; Head, Division of Geriatric Psychiatry, Sunnybrook Health Sciences Centre, Professor, Faculty of Medicine, University of Toronto	Ontario	No conflicts to declare
Hogan, David MD, FACP, FRCPC	Geriatrician, Professor and Brenda Strafford Centre on Aging Academic Leader, University of Calgary	Alberta	No conflicts to declare
Khan, Aisha BScOT	Occupational Therapist, CSSS Cavendish - Richardson Hospital and Montreal University Health center, Royal Victoria Hospital	Quebec	No conflicts to declare
King, Andrea BA, BScR, MA, CTRS	Recreation Therapist, Neurosciences Program, Halifax Infirmary, Nova Scotia Health Authority	Nova Scotia	No conflicts to declare
Leonard, Carol PhD	Speech Language Pathologist, Associate Professor, Audiology and Speech-Language Pathology Program, University of Ottawa	Ontario	No conflicts to declare
Longman, Stewart PhD	Rehabilitation Psychologist, Clinical Neuropsychologist, Calgary Stroke Program, Alberta Health Services	Alberta	No conflicts to declare
Shoniker, Tricia BScOT, M.OT	Occupational Therapist, Parkwood Institute, London, Ontario	Ontario	No conflicts to declare
Taylor, Trudy RN BN	Nurse Clinician Nurse Clinician Carewest Dr. Vernon Fanning 2E Neuro-Rehab	Calgary	No conflicts to declare

NAME	PROFESSIONAL ROLE	LOCATION	DECLARED CONFLICTS OF INTEREST
Teed, Moira MSc, MSW, RSW	Social Worker The Ottawa Hospital	Ontario	No conflicts to declare

Canadian Stroke Best Practice Recommendations
Mood, Cognition and Fatigue following Stroke
External Reviewers 2019

EXTERNAL REVIEWER	PROFESSIONAL ROLE	LOCATION	DECLARED CONFLICTS OF INTEREST
Biessels, Geert Jan	PhD Professor of Neurology, Chair on Cerebrovascular Disease and Cognition, Department of Neurology, Brain Center Rudolf Magnus, *University Medical Center Utrecht*	Netherlands	No conflicts to declare
Bocti, Christian	MD, FRCPC Professeur agrégé, Neurologie Faculté de médecine et des sciences de la santé Université de Sherbrooke; Service de Neurologie, Clinique de Mémoire et Centre de recherche sur le vieillissement, *Centre hospitalier universitaire de Sherbrooke*	Quebec	**Potential conflict:** IMEKA (Investor)
Eskes, Gail A.	Ph.D. Professor, Department of Psychiatry and Psychology & Neuroscience, *Dalhousie University*; Cross-appointments in Department of Medicine (Neurology), *Dalhousie University*; Department of Physiology & Pharmacology, *University of Calgary*	Nova Scotia	**Potential conflict:***:* NovaResp (profit) (consultant re sleep apnea machine R&D) **Potential conflict:***:* NovaResp (paid consultant) **Potential conflict:***:* HSF (grant in aid) **Potential conflict:***:* HSF (Best practices working group) Organization: Dalhousie
Greer, Lee-Anne	Ph.D., C. Psych. Psychologist, *Queen Elizabeth Hospital + PEI Organized Stroke Program*	Prince Edward Island	No conflicts to declare

External Reviewer	Professional Role	Location	Declared Conflicts of Interest
Liu-Ambrose, Teresa	PhD, PT Professor and Canada Research Chair (Tier 2), Department of Physical Therapy, Faculty of Medicine, *University of British Columbia, Vancouver Coastal Health Research Institute*	British Columbia	**Potential conflict:** Hong Kong Polytech University (Invited Speaker) **Potential conflict:** CIHR; Jack Brown and Family Alzheimer Research Foundation (Peer-reviewed grants; Donor funds) **Potential conflict:** UBC Start Up Company on Brain Wellness (provides expertise on exercise prescription.)
Mandzia, Jennifer	MD, PhD, FRCPC Assistant Professor, Department of Clinical Neurosciences, *Western University*;	Ontario	**Potential conflict:** Member of an advisory board or equivalent with a commercial organization*:* attended Bayer ad board
Martineau, Isabelle	Stroke Nurse Specialist, *Champlain Regional Stroke Network*	Ontario	**Potential conflict:** Recipient of Nursing Catalyst Research Award at The Ottawa Hospital (Employee of The Ottawa Hospital)
McMillan, Taylor	BSW, RSW Social Worker Clinical Social Worker, Community Stroke Care Service, Winnipeg Regional Health Authority	Manitoba	No conflicts to declare
Patel, Ronak	C. Psych. Clinical Neuropsychologist and Assistant Professor, Max Rady College of Medicine, Rady Faculty of Health Sciences, *University of Manitoba*	Manitoba	No conflicts to declare
Quraishi, Fatima	OT Reg. (Ont), BSc., EMBA (c) Regional Education Coordinator, North & East GTA Stroke Network, *Sunnybrook Health Sciences;* Status Only Appointment, Department of Occupational Science and Occupational Therapy, Faculty of Medicine,	Ontario	No conflicts to declare

External Reviewer	Professional Role	Location	Declared Conflicts of Interest
	University of Toronto		
Subramanian, Sandeep	PhD, BPTh Assistant Professor, Department of Physical Therapy, School of Health Professions, *UT Health San Antonio, TX, USA* Center of Biomedical Neurosciences, UT Health San Antonio, San Antonio, TX USA and University Hospital-University Health System, San Antonio TX USA	United States	**Potential conflict:** UT Health San Antonio (salary); **Potential conflict:** Center for Biomedical Neurosciences, UT Health San Antonio (pilot funding)
Troyer, Angela	PhD, C. Psych Program Director and Professional Practice Chief, *Baycrest Health Sciences*; Assistant Professor, Psychology, *University of Toronto*	Ontario	No conflicts to declare
Verhey, Frans	MD, PhD Professor, Neuropsychiatry and Old Age Psychiatry, *University of Maastricht*	Netherlands	No conflicts to declare

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APPENDIX TWO

Table 1A: Selected Validated Screening and Assessment Tools for Post-Stroke Depression

This table provides a summary of the psychometric properties of a selected set of screening and assessment tools that have been validated for use with stroke patients, or frequently reported in the stroke literature. This list is not exhaustive, rather it highlights the more commonly used and validated tools. It is recommended that these tools be considered as first line options for all stroke services. (Table completed by Katherine Salter, PhD candidate with thesis research in Post-Stroke Depression).

Notes:

- It should be emphasized that a score indicating depression on a screening tool is not equivalent to a diagnosis of depression. Rather, a positive score indicates the need for further follow-up and assessment
- A more detailed review of these screening tools may be obtained via the ebrsr.com, strokengine.com or in Salter et al. (2007).

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
Recommended First Line Tools						
Geriatric Depression Scale (GDS) http://web.stanford.edu/~yesavage/GDS.html	30	Self-report Yes/No responses	0-30	**Reliability**: Though thoroughly evaluated in populations of elderly individuals, relatively little has been done specific to individuals with stroke. Agrell and Dehlin (1989) reported high internal consistency (α=0.90) as did Sivrioglu et al. (2009) (α=0.88). **Concurrent Validity**: Agrell and Dehlin (1989) reported good correlations between GDS scores and scores on self-report and observational depression assessment scales. **Discriminative Validity**: Sivrioglu et al. (2009) demonstrated significant differences in GDS scores between groups of depressed vs. non-depressed participants (p<0.001).	Normal = 0 – 10, scores ≥11 indicate presence of depression; 11-20 = mild depression, 21-30 = moderate to severe depression (McDowell et al. 1996)	Many studies have examined the relative sensitivity and specificity of the GDS – most have reported sensitivity and specificity values > 80% (Stiles and McGarrahan (1998). Within the stroke population, Johnson et al. (1995) using a cut-off of 10/11, Johnson et al. (1995) reported sensitivity = 85%, specificity = 66% and a misclassification rate of 29%. More recently, using DSM-IV-TR as the criterion for diagnosis, Sivrioglu et al. (2009) reported sensitivity = 69% & specificity = 75% for using a cutoff point of 10/11, and sensitivity = 66% and specificity = 79% for a cut off of 11/12.
Hospital Anxiety and Depression Scale (HADS) http://www.strokengine.ca/assess/hads/	14 (2 x 7-item sub-scales)	Self-report Multiple choice response options graded on a 4 pt scale	0-42 (0-21 for each subscale)	**Reliability**: Visser et al (1995) reported test retest reliability (0.87); reported internal consistency reliability for the depression portion of the HADS has been >0.70 (Johnston et al. 2000, Aben et al. 2002); most	Scale authors recommended either 8/9 (high sensitivity) or 10/11 (high specificity) be used to identify	Aben et al. (2002) reported sensitivity of 72.5% and specificity of 78.9% for the HADS-D, using a cut-off score of ≥7. For the total scale, using a cut-off of ≥11, sensitivity and specificity were 86.8% and 69.9% respectively.

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
				recently Sagen et al (2009) reported α=0.83. **Construct validity**: Reported satisfactory on confirmatory factor analysis (Johnston et al. 2000). **Discriminative validity**: HADS-D and HADS-A scores obtained by stroke patients differed significantly from controls (p<0.001) (Visser et al. 1995).	the presence of depression using the depression subscale of the HADS (Zigmond and Snaith 1983). Alternate cut-off points have been evaluated for the post stroke population.	Johnson et al. (1995) used a cut-off of 4/5 for the HADS-D and demonstrated a sensitivity of 93% and specificity of 44% while O-Rourke et al. (1998) reported sensitivity of 80% and specificity of 79% using the same cut-off point as Aben et al. More recently, Sagen et al. (2009) reported sensitivity and specificity for the HADS-total (relative to the DSM-IV) of 90% and 83% (cut off ≥11), 79% and 85% (cut off ≥12) respectively. For the HADS-D, sensitivity = 79% and specificity = 82% (cut off ≥5). AUC for HADS-D was 0.87 (95% CI 0.78-0.96) and for HADS-total 0.91 (95% CI 0.85-0.97) (Sagen et al. 2009)
Patient Health Questionnaire -9 (PHQ-9) http://strokengine.ca/assess/module_phq9_intro-en.html http://www.phqscreeners.com/	9	Multiple choice response options, 4pt scale	0-27	**Reliability**: Inter-rater reliability = 0.98, test re-test = 0.75 and internal consistency = 0.79 (de Man-van Ginkel et al. 2012). **Concurrent validity**: PHQ-9 was significantly correlated with GDS-15 scores (r=0.8, p<0.01) (de Man-van Ginkel et al. 2012).	Scores ≥10 (sensitivity=80%, specificity=78%) for identification of PSD 6-8 weeks post stroke (deMan van Ginkel et al. 2012)	A single study evaluated the sensitivity and specificity of the PHQ-9 for both major depression and any depression against a structured clinical interview in a subgroup of outpatients with stroke who endorsed either 2 or more symptoms on the PHQ-9 or either of the PHQ-2 items at study baseline (Williams et al. 2005). The authors reported sensitivity of 91% and specificity of 89% for major depression as well as sensitivity of 78% and specificity of 96% for any depression associated with a cut-off score ≥10. These numbers may, however, have been influenced by the pre-screening (using items from the PHQ-9) and formal assessment of selected individuals only. De Man-vanGinkel et al. (2012) also reported the results of a validation study that evaluated the PHQ-9 against the results of a composite international diagnostic interview for the DSM-IV conducted with 164 individuals with stroke (outpatients approximately 6-8 weeks post stroke). Similar to Williams et al., the authors reported that the accuracy of the PHQ-9 was best using a cutoff of ≥10 with a sensitivity of 80% and specificity of 78%. Using the PHQ-9 in patients pre-screened

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
						with the PHQ-2 increased the accuracy of identification (sensitivity = 87%) (de man-van Ginkel et al. 2012).
Additional Tools for Consideration						
Beck Depression Inventory (BDI-II) http://strokengine.ca/assess/module_bdi_intro-en.html http://www.pearsonassessments.com/HAIWEB/Cultures/en-us/Productdetail.htm?Pid=015-8018-370	21	Self-report Multiple-choice response set graded for severity	0-63	**Reliability**: Aben et al. (2002) confirmed high internal consistency reliability of the BDI in a population of individuals with stroke. Outside of the stroke population estimates of internal consistency tend to exceed 0.80 (Beck et al. 1988) **Predictive validity**: BDI scores are predictive of functional recovery and need for institutional care following stroke (Kotila et al. 1999, Desrosiers et al. 2002).	Threshold for presence of depression = 10; 10 – 18 = mild depression, 19 – 29 = moderate depression, 30 – 63 = severe depression (Beck et al. 1988)	ROC analysis completed by Lincoln et al. (2003) suggests that the accepted cut-off point indicative of presence of depression might be too low – recommends 15/16 to optimize sensitivity; however, specificity is reduced relative to the DSM-III-R. Aben et al. (2002) reported the standard cut-off points to be acceptable for used for individuals with stroke.
Center for Epidemiological Studies Depression Scale (CES-D) http://cesd-r.com/	20	Self-report 4-pt scale	0-60	**Reliability**: Internal consistency reliability has been reported ranging from 0.64-0.86 (Agrell & Dehlin 1989, Toedter et al. 1995). Reported item-to-total correlations ranged from 0.39-0.75 (Shinar et al. 1986). **Concurrent validity**: Results of the CES-D used to assess individuals with stroke have correlated significantly with results of other standardized self-report and observational depression assessment tools (Agrell and Dehlin 1989, Shinar et al. 1986, Parikh et al. 1988)	Presence of depression = ≥16 (Radloff et al. 1977)	Using the suggested cut-off score, Shinar et al. 1986 and Parikh et al. 1988 reported sensitivity of 73% and 86%, and specificity of 100% and 90% respectively (relative to the DSM-III-R)
Depression, Obstructive sleep apnea and Cognitive impairment (DOC) Screen http://www.docscreen.ca/	16	Self-report	20	**Feasibility:** 89% of patients completed the screen in 5 minutes or less (mean 4.2 minutes; 9% CI: 4.1 to 4.3 mins). (Swartz et al. 2017) Time to complete was significantly higher in patients with stroke compared to those with TIA. **Validity:** The DOC showed excellent diagnostic characteristics for the Patient Health Questionnaire-2 (PHQ-2), STOP, and Montreal Cognitive Assessment (MoCA) components. (Swartz et al. 2017)	**Doc-Mood:** Score 0 indicated low-risk for depression. Scores ≥4 indicated high-risk of depression; **Doc-obstructive sleep apnea (OSA):** Score 0 indicated low-risk for OSA; scores 1 to 3 indicated intermediate risk	**Sensitivity and specificity** Doc-Mood: Sensitivity 92%; and specificity: 99% Doc-Apnea: Sensitivity: 91%; specificity: 93% Doc-Cog: Sensitivity 96%; specificity 91% For DOC-Mood, 29% of those scoring in the intermediate-risk were impaired according to the SCID-D; therefore, clinicians may want to use caution for patients scoring at intermediate-risk depression by applying more detailed screening tools or pairing with additional clinical questions. (Swartz et al. 2017)

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
				Area Under the Curve (AUC): Doc-Mood: 0.90 Doc-Apnea: 0.80 Cog-Cognitive impairment (Cog): 0.81	for OSA; Score 4 indicated high-risk for OSA **DOC-Cog:** Score of 10 indicated low-risk of cognitive impairment; scores 6 to 9 indicated intermediate risk for cognitive impairment; scores ≤5 were classified as high-risk for cognitive impairment	Doc-Cog has a low Positive Predictive Value, suggesting that Doc-Cog is more reliable to rule our moderate-severe impairment than for ruling it in.
Tools to Consider for Aphasic Patients						
Stroke Aphasic Depression Questionnaire-10 (SADQ-10) http://strokengine.ca/assess/module_sadq_intro-en.html http://www.nottingham.ac.uk/medicine/about/rehabilitationageing/publishedassessments.aspx	10	Observer rating of observed behaviour 4-point scale	30	**Reliability**: Using carers of individuals with aphasia to complete follow-up assessments, 4-week test-retest reliability was reported to be 0.69 for the SADQ-10 (Sutcliffe and Lincoln 1998). Internal consistency has been reported as α = 0.80 (Sutcliffe and Lincoln 1998, Lincoln and Sutcliffe 2000). **Construct validity**: Results of factor analysis suggested that the SADQ-10 items may be unidimensional (Sutcliffe and Lincoln 1998) **Concurrent validity**: SADQ-10 scores have been positively associated with scores on the HADS-D, HADS-A, Wakefield Depression Inventory (Sutcliffe and Lincoln 1998), and the GDS-15 (Leeds et al. 2004), though correlations with healthcare professional ratings have varied (Lincoln and Sutcliffe 2000).	Scores ≥ 15 may represent presence of depression (Leeds et al. 2004).	Using the suggest cut-off score of ≥15, Leeds et al. (2004) reported sensitivity = 70% and specificity = 77% in a group of stroke rehabilitation inpatients. Based around cut-offs used for the HADS, Bennett et al. (2006) identified a cut-off of 17/18 on the SADQ-H (sensitivity= 100% and specificity=81%), and an optimum cut-off of 5/6 on the SADQ-H 10 (sensitivity = 100% and specificity = 78%).
Aphasia Depression Rating Scale (ADRS) http://strokengine.ca/assess/module_adrs_intro-en.html	9	Observer rating based on interview & observation	0-32	**Reliability**: Test retest reported to be 0.89 by scale authors. Interobserver reliability = 0.89 (Benaim et al. 2004). **Concurrent validity**: ADRS scores were correlated with CAS ratings and	Scores of ≥ 9 are used to indicate the presence of depression	Using the cut-off indicated as appropriate by the scale author, sensitivity of 83% and specificity of 71% were reported (relative to a psychiatric diagnosis) (Benaim et al. 2004).

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
		Rating scale varies per item		with results of HRSD (Benaim et al. 2004).	(Benaim et al. 2004).	
Tools for Consideration in Children						
Children's Depression Inventory (CDI) http://www.mhs.com/product.aspx?gr=edu&id=overview&prod=cdi2#description (The CDI 2 has been recently released but test details are not available free of charge)	27	Self-report 3 pt scale	0-54	The psychometric properties of this scale have not been investigated within a stroke-specific population.	Scores of ≥ 19 have been identified as representing the 90th percentile within a general population of children in grades 3-9 (Smucker et al. 1986).	n/a
Kidscreen 52 (Generic HRQL measure) http://www.kidscreen.org/	52	Self-report 5 pt scale	Scores for each dimension are calculated as T-values (mean=50 ; SD=10).	The psychometric properties of this scale have not been investigated within a stroke-specific population.	Higher scores indicate higher Health-Related Quality of Life and well-being.	n/a

- It should be emphasized that a score indicating depression on a screening tool is not equivalent to a diagnosis of depression. Rather, a positive score indicates the need for further follow-up and assessment
- **more detailed review of these screening tools may be obtained via the ebrsr.com, strokengine.com or in Salter et al. (2007)

Table 1B: Selected Validated Screening and Assessment Tools for Post-Stroke Anxiety

This table provides a summary of the psychometric properties of a selected set of screening and assessment tools that have been validated for use with stroke patients, or frequently reported in the stroke literature. This list is not exhaustive, rather it highlights the more commonly used and validated tools.

Assessment Tool and Link	# of Items	Response Format	Total Score	Reliability & Validity	Interpretation of Scores	Sensitivity & Specificity
Validated with stroke patients						
Hospital Anxiety and Depression Scale (HADS-A) http://www.strokengine.ca/assess/hads/	14 (2 x 7-item sub-scales)	Self-report consisting of multiple-choice response options graded on a 4 pt scale	0-42 (0-21 for each subscale)	**Reliability**: Johnston et al. (2000) reported that at 6-month post-stroke, the HADS-A and overall HADS had excellent internal consistency α=0.87 and 0.89, respectively. **Construct validity**: Reported satisfactory on confirmatory factor analysis (Johnston et al. 2000). **Discriminative validity**: HADS-D and HADS-A scores obtained by stroke patients differed significantly from controls (p<0.001) (Visser et al. 1995).	A score of 0 to 7 on either the depression or anxiety subscale is considered being in the normal range; a score of 11 or higher indicates probable presence of a mood disorder; a score of 8 to 10 being suggestive of the presence of the state, (Zigmond and Snaith 1983). Alternate cut-off points have been evaluated for the post stroke population.	Aben et al. (2002) reported that using a cut-off score of 5+, the HADS-A had a sensitivity of 88.5% (AUC=0.77) and specificity of 56.1% (AUC=0.78). For the total scale, using a cut-off of ≥11, sensitivity and specificity were 86.8% and 69.9% respectively. Johnson et al. (1995), using a cut-off of 5+ for the HADS-A, demonstrated a sensitivity of 95% and specificity of 46%. Aben et al. (2002) noted a high correlation (r=0.67, p<0.01) between the depression and anxiety subscales; a result of the frequent coincidence of symptoms of anxiety and depression in stroke patients.
Behavioural Outcomes of Anxiety (BOA)	10 items	Self-reported or carer-reported consisting of multiple choices ranging from 'not at all' to 'a lot' (Kneebone et al. 2012)	0 to 21 (each item is score can range from 0 to 3)	**Construct Validity:** The BOA questionnaire correlated well with the HADS-A (r=0.77) **Test-Retest validity**: The BOA demonstrated good to excellent test-retest reliability, ranging from 0.81 at 1-week (Linley-Adamns et al. 2014) to 0.91 (Eccles et al. 2017)	There are no acceptable cut-off scores, but the following has been proposed: 0-6 = minimal anxiety; 7-13 = mild anxiety;14-17 = moderate anxiety; 18+ = moderately severe or severe anxiety	With a cut-off score of 16/17, the BOA had a sensitivity of 0.85 (0.71, 0.94), and specificity of 0.85 (0.73, 0.92). The positive predictive value was reported as 0.38 with the negative predictive value being 0.98. (Eccles et.al. 2017) A cut-off score of 13/14 yields a sensitivity and specificity of 0.77 and 058, respectively (Linley-Adamns et al. 2014)
Geriatric Anxiety Inventory (GAI) http://gai.net.au/	20 items	Self-reported or nurse administere	Range from 0 to 20	The Cronbach's α for the GAI was 0.91 for normal elderly people and 0.93 for a psychogeriatric sample (Pachana et al. 2007)	Each item is scored 0 or 1.	For stroke patients, a cut-off for 6/7 on the GAI demonstrates a sensitivity and specificity of 0.88 and 0.84, respectively (Kneebone et al. 2016)

Assessment Tool and Link	# of Items	Response Format	Total Score	Reliability & Validity	Interpretation of Scores	Sensitivity & Specificity
		d questionnaire that consist of agree-disagree items		**Internal consistency:** GIA has shown to have good internal consistency, ranging from r=0.91 to 0.95. **Convergent validity:** The GAI correlates well with other measures including the DSM-IV GAD questionnaire (r=0.653), The Penn State Worry Questionnaire (r=0.794), and the Beck Anxiety Inventory (r=0.613) and the State-Trait Anxiety Inventory (r=0.63). **Construct validity:** Total scores of the GAI correlated well with the HADS-A (β=0.61, p<0.001) **Test-retest reliability**: The GAI demonstrated acceptable test-retest reliability, ranging from r=0.91 to 0.99 (β=0.53, <0.001) Note: Validations studies have shown the GAI has weak divergent validity from depression measures.	Suggested cut-offs for healthy population: 10/11 out of 20 for identifying likely GAD 8/9 out of 20 for identifying any anxiety disorder For stroke patients, a lower cut-off is used to identify anxiety	A cut-point of 10/11 correctly identifies 83% of patients for DSM-IV generalized anxiety disorder (GAD), with a specificity of 84% and sensitivity of 75% (AUC-0.80; 95%: 0.64-0.97)
Additional tools, which have not been validated in the stroke population						
Beck Anxiety Inventory (BAI) http://www.pearsonclinical.com/psychology/products/100000251/beck-anxiety-inventory-bai.html	21 items	Self-report or interviewer administered questionnaire consisting of multiple-choice response	0 to 63 (sum of scores for each item)	Validity and reliability estimates reported here are from the general population **Construct validity:** Demonstrates good convergence with other measures of anxiety including Hamilton Anxiety Rating Scale (r=0.51), the State-Trait Anxiety Inventory (STAI) (r=0.47-0.58) and the anxiety scale of the Symptom Checklist-90 (r=0.81) (Beck & Streer 1991) **Internal consistency:** Demonstrates high internal consistency (α rang 0.90 to 0.94). (Fydrich et al 1993; Creamer et al. 1995; Osman et al. 1993)	From the sum from all 21 items: 0-9 = normal or no anxiety; 10-18 = mild to moderate anxiety; 19-29 = moderate to severe anxiety; 30-63 = severe anxiety	There are no published reports of the sensitivity and specificity of the BAI in screening for post-stroke anxiety. The BAI is intended to be used a screening measure that discriminates anxiety from depression; and not be used a diagnostic measure itself

Assessment Tool and Link	# of Items	Response Format	Total Score	Reliability & Validity	Interpretation of Scores	Sensitivity & Specificity
				Test-retest: BIA demonstrates reasonable test-retest coefficients ranging from 0.62 at 7-week to 0.91 at 1-week intervals.		
Hamilton Anxiety Rating Scale (HAM-A) https://egret.psychol.cam.ac.uk/medicine/scales/HAM_A.pdf	14 items	A clinician-rated scale consisting of multiple-choice response option graded on a 5 pt scale.	0 to 56 (score range 0-4 for each items)	Validity and reliability estimates reported here are from the general population **Construct validity:** Correlates with other self-reported measure of anxiety, such as the Beck Anxiety Inventory (r=0.51) (Beck et al. 1988) **Interrater reliability**: HAM-A has good interrater reliability among experienced (r=0.74 to 0.86) and less experienced (r=0.74 to 0.93) raters. (Gjerris et al. 1983)	Each item is scored on a 5-point scale, ranging from 0 = not present to 4 = severe. From the sum from all 14 parameters: 14-17 = mild anxiety; 18-24 moderate anxiety; 25-30 severe anxiety Note: scale was developed as a rating for severity among individuals known to have anxiety, not as a mean of diagnosing anxiety.	There are no published reports of the sensitivity and specificity of the HAM-A in screening for post-stroke anxiety. The major value of the HAM-A is to document the results of pharmaco- or psychotherapy, rather than as diagnostic or screening tool.
State-Trait Anxiety Inventory (STAI) http://www.mindgarden.com/index.htm	40 items (20 items per subscale)	Self-report consisting of multiple-choice questions	40 to 80 (range score for each subtest is 20-80)	Validity and reliability estimates reported here are from the general population **Construct validity:** Limited in discriminating anxiety from depression (Kabacoff et al. 1997) **Test-retest reliability:** Test-retest coefficients range from 0.31 to 0.86 with intervals ranging from 1 hour to 104 days. (note the S-Anxiety scale tends to detect transitory states, thus test-retest coefficients are lower from the S-Anxiety vs. to the T-Anxiety scale)	A cut point of 39-40 is suggested to detect clinically significant symptoms for the S-Anxiety scale A higher cut point of 54-55 is suggested for older adults	There are no published reports of the sensitivity and specificity of the STAI in screening for post-stroke anxiety in the general population

Assessment Tool and Link	# of Items	Response Format	Total Score	Reliability & Validity	Interpretation of Scores	Sensitivity & Specificity
				Since the T-Anxiety scale is to characterize "proneness" as a characteristic of anxiety, the T-Anxiety scale is less responsive to change vs. S-Anxiety		
Zung Self-Rating Anxiety Scale https://psychology-tools.com/zung-anxiety-scale/	20 items	Self-report consisting for multiple choice questions for each item	20 to 80	There are no published reports of the reliability and validity of the Zung in the general population	Each item is score on a 4-point scale from 1 to 4. The sum of all 20 items: 20-40 = Normal range;45-59 = Mild to moderate anxiety levels; 60-74 = marked to severe anxiety levels; 75-80 = Extreme anxiety levels	There are no published reports of the sensitivity and specificity of the Zung in screening for post-stroke anxiety

References for Tables 1A & 1B

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Table 1C: Summary Table for Selected Pharmacotherapy for Post-Stroke Depression

This table provides a summary of the pharmacotherapeutic properties, side effects, drug interactions and other important information on selected classes of medications available for use in Canada and more commonly recommended for post-stroke depression. This table should be used as a reference guide by health care professionals when selecting an appropriate agent for individual patients. Patient compliance, patient preference and/or past experience, side effects, and drug interactions should all be taken into consideration during decision-making, in addition to other information provided in this table and available elsewhere regarding these medications.

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Medication Generic and Trade Names *recommended	*citalopram – Celexa *escitalopram – Cipralex fluoxetine – Prozac fluvoxamine – Luvox paroxetine – Paxil *sertraline – Zoloft	*duloxetine – Cymbalta *venlafaxine – Effexor	methylphenidate – Ritalin (amphetamine) nortriptyline – Aventyl (tricyclic antidepressant) trazodone – Desyrel (tetracylic antidepressant) *mirtazapine – Remeron (NASSA, noradrenaline and specific serotonin antagonist)
Contra-indications	concurrent monoamine oxidase inhibitor (MAOI) use	concurrent monoamine oxidase inhibitor (MAOI) use	nortriptyline – cardiac conduction abnormalities, uncontrolled narrow angle glaucoma, or concurrent monoamine oxidase inhibitor (MAOI) use
Side Effects	Serotonin syndrome, sedation (fluvoxamine, paroxetine), bleeding, and hyponatremia Fluoxetine, fluvoxamine, paroxetine: interact with certain cardiac medication e.g. clopidogrel and beta-blockers Generally reported: dry mouth, loss of appetite and weight-loss, nausea, dizziness, loss of libido, constipation or diarrhea, insomnia or somnolence, sweating	Increases in heart rate, hypertension (venlafaxine), serotonin syndrome Generally reported: dry mouth, loss of appetite and weight-loss, loss of libido, constipation, nausea, insomnia, dizziness anxiety, sweating	nortriptyline – potential effects on cognition and may increase risk of delirium (anticholinergic); serotonin syndrome, ventricular arrhythmias and orthostatic hypotension Generally reported: dry mouth, loss of appetite and weight-loss, loss of libido, constipation, nausea, dizziness, anxiety, somnolence, sweating
Landmark Trials	citalopram[6,14], fluvoxamine[8] , fluoxetine[1-5] sertraline[7,14] paroxetine[9]	reboxetine[10] , milnacipran[11], venlafaxine[12] , duloxetine[14]	trazodone[15,16] , nortriptyline[17,18] methylphenidate[19]

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Inclusion Criteria & Depression Severity	First ever and recurrent strokes Mild depression[5, 7, 8] Moderate depression[1,2,4,5,6] Severe depression [3, 9, 14]	SNRI: PSD following from first ever stroke. Venlafaxine: moderate depression Duloxetine: severe depression	First ever and recurrent strokes trazodone: mild[15] and moderate[16] depression nortriptyline: mild[17] and moderate[18] depression methylphenidate: moderate depression
Dose Ranges Tested	fluoxetine: 10 - 40mg/day (including variable dose study) citalopram: 10 – 40mg/day[6,10,14,20, 21] Maximum doses: 40mg/day adults, 20mg/day geriatric[22] escitalopram: 10 – 20mg/day Maximum doses: 20 mg/day adults,10 mg/day geriatric[22] sertraline: 50 - 200mg/day[14]	venlafaxine: 75 – 150 mg/day duloxetine: 60 – 120mg/day	trazodone: 200 – 300mg/day mirtazapine: 30mg/day nortriptyline: 20 – 100mg/day
Summary of Findings	Level 1 RCT evidence supports the efficacy of SSRIs fluoxetine and citalopram for treatment of moderate to severe post-stroke depression.	Studies were open-label or uncontrolled; no level 1 RCT evidence available to support efficacy of SNRI for treatment of post-stroke depression.	Level 1 RCT evidence available to support nortriptyline and methylphenidate for treatment of post-stroke depression.
Other Outcomes	Prevention of PSD: fluoxetine, escitalopram and sertraline effective in prophylaxis Mortality & PSD: increased survival of depressed and non-depressed treated with fluoxetine or nortriptyline over placebo in 9-year follow-up[23]. Cognitive function: maintenance of executive function compared to placebo over 21 months	Anxiety in PSD: duloxetine more effective than citalopram in treating anxiety symptoms Alexithymia: venlafaxine results in greater improvement of emotional awareness than fluoxetine	Prevention of PSD: mirtazapine efficacious in preventing PSD[9] Mortality & PSD: increased survival of depressed and non-depressed treated with fluoxetine or nortriptyline over placebo in 9-year follow-up[23] Functional status (ADLs): trazodone treatment resulted in trending improvement

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
	follow-up[24]; improvement in verbal and visual memory[25] Sleep: fluvoxamine improved sleep disturbances as measured by peripheral melatonin blood levels. Functional status: **fluoxetine** associated with improved motor recovery (FLAME trial)[25] Other: fluoxetine improved quality of life[2]		
Safety All antidepressants have Health Canada Warnings regarding increased risk of suicidal thinking and behavior (particularly in children, adolescents and young adults)	Discontinuation: Discontinuation of escitalopram may increase post stroke depressive symptoms over 6 months[26] Cerebrovascular AE: rare (<1/1000) in fluoxetine, infrequent to rare (1/100 to 1/1000) for other SSRIs but vigilance required for use in high-risk bleeding & vasoconstrictive stroke.[27] SSRIs lower risk of cardiovascular events but increase bleeding and mortality. [28] Potential risk of hemorrhagic stroke with SSRIs[29] Delirium : anticholinergic effects (paroxetine) may play role in delirium in acute stroke patients[30] QTc prolongation: Health Canada warnings regarding citalopram. Minimal QT effect with escitalopram and sertraline. Fluvoxamine, fluoxetine and paroxetine minimal concern. [31]	QTc prolongation: Among SNRIs, venlafaxine has the greatest risk [31]	Trazodone: serious warning for priapism, associated with increased risk of syncope and falls, particularly in older patients Nortriptyline: special consideration for geriatric population with orthostatic hypotension and anticholinergic effects; caution is advised if used in patients with a personal or family history of cardiovascular disease, arrhythmias or conduction disturbances

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Cost per month/ coverage in Canada	citalopram $0.33/day (regular benefit) escitalopram $1.84 (regular benefit) fluoxetine (20mg) $0.46 (regular benefit) paroxetine – (20mg) $0.45 and (30mg) $0.4796 sertraline - (25mg) $0.20 and ~(100mg) $0.40 fluvoxamine - (50mg) $0.21 and (100mg) $0.38	duloxetine – Cymbalta (30mg) $1.89 and (60mg) $3.79 milnacipran – not available reboxetine - not readily available, not covered by provincial drug coverage plans venlafaxine $0.3469/day (regular benefit)	methylphenidate – $0.28-$4.18 (10-80mg) trazodone ~$0.10/day (regular benefit)

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Table 2B: Summary of Select Screening and Initial Assessment Tools for Vascular Cognitive Impairment in People Who Have Experienced a Stroke (Sixth Edition, 2019)

In 2024, a new stand-alone module was released on Vascular Cognitive Impairment as part of the 7th edition update of the CSBPR. The new 7th edition VCI CSBPR module is available here on the CSBPR website, as well as published in the journal Alzheimer's & Dementia.

Table 3A: Summary of Selected Validated Screening and Assessment Tools for Post-Stroke Fatigue

This table provides a summary of the psychometric properties of a selected set of screening and assessment tools that have been validated for use in persons following stroke, or frequently reported in the stroke literature. This list is not exhaustive, rather it highlights the more commonly used and validated tools. It is recommended that these tools be considered as first line options for all stroke services.

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSF
Fatigue Severity Scale (FSS) http://www.scireproject.com/sites/default/files/worksheet_fatigue_severity_scale_fss.docx	9	Self-report Each item is scored on a scale from 1 (disagree) to 7 (agree) with each statement	9-63	**Internal consistency**: Nadarajah et al. 2017 found that the FSS had excellent internal consistency for both stroke patients and healthy controls (Cronbach's α > 0.90). Likewise, Ozyemisci-Taskiran et al. (2019) found similar results with a Cronbach's α or 0.93. **Test-retest reliability:** The FSS scale demonstrated excellent for both stroke and healthy controls with interclass coefficient (ICC) of 0.93 (95% CI: 0.88 to 0.96) and 0.93 (95% CI: 0.82 to 0.94), respectively. **Criterion validity:** Lerdal et al. (2011) found that the SFF has adequate criterion validity with a Cronbach's α of 0.86. **Concurrent Validity**: Nadarajah et al. (2017) found that the FSS scale had good concurrent validity with the VAS-Fatigue (all r > 0.60, p < 0.01) and moderate validity with the SF36-vitatlity scale (r = 0.32, p = 0.02) *Lerdal et al. found that items 1 and 2 in the FSS should not be used in a mean score, and that a seven item FSS (FSS-7) demonstrated better validity and reliability, and likely more sensitive for measuring change in fatigue. Ozyemisci-Taskiran, et al. (2019) however, found that the ICC values for individual items of the FSS were good expect for item 6.	A score of ≥36 is suggestive of the need for further assessment	There are no studies examining the sensitivity and specificity of the FSS in the stroke population. Anton et al. found that among male patients with motor complete SCI in tertiary care, the area under the curve (AUC) was 0.80. Assuming a FSS cut-score of 4 to indicate significant fatigue and a WAS-F score of over 6 to indicate severe fatigue: • Sensitivity = 75% • Specificity = 67%

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSF
Multidimensional Fatigue Symptom Inventory (MFSI)	83	Self report Each item is rated on a 5-point scale indicating how true each statement was for the respondent during the last week (0=not at all; 4=extremely).	0-332	**Internal consistency:** Among stroke patients, the MFSI demonstrated a Cronbach's α of 0.91 and 0.93 for first and second interviews, respectively. (Mead et al. 2007) **Test-retest reliability:** Among stroke patients, the MSFI demonstrated moderate to good test-retest reliability across scale items, with Kappa (*k)* ranging from 0.48 (95% CI: 0.27 to 0.69) to 0.69 (95% CI: 0.53 to 0.85) (Mead et al. 2007). For total score, the ICC was 0.76 (95% CI: 0.55 to 0.87) **Interrater reliability:** Among stroke patients, The MSFI demonstrated very good interrater reliability across scale items with *k* ranging from 0.82 (85% CI: 0.63 to 1.00) to 0.92 (95% CI: 0.83 to 1.00). For total score, the ICC was 0.88 (95% CI: 0.78 to 0.93) **Convergent construct validity:** Among stroke patients, the convergent construct validity of the MFSI was high. The construct validity for MFSI was higher was when measured against the SF-36v2 (r= -0.47, p <0.001)	Higher scores indicate more fatigue	There are no studies examining the sensitivity and specificity of the MFSI in the stroke population. Stein et al. (1998) found that the MFSI was sensitive to fatigue, accurately discriminating cancer patients from control subjects and between patients with varying levels of performance status.
SF-36v2	36	35 items are rated on a Likert scale with varying number of response categories. Vitality component is used to measure fatigue in stroke patients	0-100%	**Internal consistency:** Among stroke patients, the SF36v2 demonstrated a Cronbach's α of 0.76 and 0.78 for first and second interviews, respectively. (Mead et al. 2007) **Test-retest reliability:** Among stroke patients, the SF36v2 demonstrated fair to moderate test-retest reliability across scale items, with *k* ranging from 0.35 (95% CI: 0.07 to 0.63) to 0.47 (95% CI: 0.25 to 0.70) (Mead et al.2007). For total score, the ICC was 0.51 (95% CI: 0.27 to 0.69)	Higher vitality indicates less fatigues	There are no studies examining the sensitivity and specificity of the SF-36v2 in the stroke population.

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSF
		(Dorman et al.1999)		**Interrater reliability:** Among stroke patients, The SF36v2 demonstrated good to very good interrater reliability across scale items with *k* ranging from 0.72 (85% CI: 0.45 to 0.99) to 0.89 (95% CI: 0.75 to 1.00). For total score, the ICC was 0.92 (95% CI: 0.86 to 0.96) **Convergent construct validity:** Among stroke patients, the convergent construct validity of the SF-36v2 was high. The construct validity was lower when compared against the FAS (r = -0.41, p = 0.003) and the MFSI (r = -0.47, p <0.001)		
Profile of Mood States-fatigue subscale (POMS-fatigue)	7	Self-report Items are rated on a 5-point Likert scale indicating how one has been feeling during the past week, including today (0 = not at all; 4 = extremely)	0-28	**Internal consistency:** Among stroke patients, the POMS-Fatigue demonstrated a Cronbach's α of 0.89 and 0.88 for first and second interviews, respectively. (Mead et al. 2007) **Test-retest reliability:** Among stroke patients, the MSFI demonstrated moderate to good test-retest reliability across scale items, with Kappa (*k*) ranging from 0.45 (95% CI: 0.19 to 0.72) to 0.61 (95% CI: 0.42 to 0.80) (Mead et al.2007). For total score, the ICC was 0.74 (95% CI: 0.56 to 0.85) **Interrater reliability:** Among stroke patients, The MSFI demonstrated good to very good interrater reliability across scale items with *k* ranging from 0.71 (85% CI: 0.45 to 0.97) to 0.89 (95% CI: 0.75 to 1.00). For total score, the ICC was 0.84 (95% CI: 0.72 to 0.91) **Convergent construct validity:** Among stroke patients, the convergent construct validity of the POMS-fatigue was high. The construct validity was higher was	Higher scores on the POMS-fatigue reflect a greater agreement with the mood state during the past week.	There are no studies examining the sensitivity and specificity of the FSS in the stroke population.

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSF
				when measured against the SF-36v2 (r= -0.58, p <0.001) (Mead et al.2007). The POMS-fatigue has been found to be correlated with other measures of fatigue including the Functional Assessment of Cancer Therapy fatigue subscale (r=-0.74 p<0.05), the revised Piper Fatigue Scale (r=0.75, p=0.01) ad the Lee Fatigue Scale (r=0.78, p<0.01) (Yellen et al 1997; Lee et al. 1991) *Systematic review of fatigue questionnaires in across multiple disease states recommended the use of POMS-F for the stroke population (Elbers et al.2012)		
Fatigue Assessment Scale (FAS)	10 items	Self report Each item is answered using a five-point Likert scale ranging from 1 (never) to 5 (always). Items 4 and 10 are reverse-scored	Total scores range from 10 to 50	**Internal consistency:** Among the non-stroke population, scale developer Michielsen et al. (2003) found then internal consistency to be 0.90. Among stroke patients, Cronbach's α for first and second interview were 0.58 and 0.62, respectively (Mead et al. 2007) **Test-Retest reliability:** Among stroke patients, kappa values across scales items ranged from fair to good, with a interclass correlation coefficient for total test-retest of 0.77 (95% CI: 0.62 to 0.86). (Mead et al.2007) **Concurrent validity:** Results of the scale correlated highly with the fatigue-related subscales of the Checklist Individual Strength among non-stroke patients. (Michielsen et al.2003) **Convergent construct validity:** Construct validity was ranged from fair to good against the SF-36v2 (r=-0.41, p=0.003), POMS (r=0.59, p < 0.001) and MFSI (r=0.71, p < 0.001)	The low score of 10 is indicative of the lowest level of fatigue, and 50 indictive of the highest level of fatigue. No potential cut-off for fatigue was noted in the original development of the scale. (Michielsen et al. 2003) A cut-off score of ≥24 is proposed for classifying post-stroke fatigue (Cummings et al.2017) FAS-3: With a possible range of 3 to 15, a cut-off score of ≥8 is indicative of post-stroke fatigue.	Among stroke patients, using a cut-off score of ≥24 yielded an area under the curve (AUC) of 0.83 (95% CI: 0.71 to 0.94) with a sensitivity and specificity of 0.84 and 0.67, respectively. (Cummings et al.2017) **FAS-3** At a cut-off of ≥8, AUC was 0.81 (95% CI: 0.73 to 0.89) with a sensitivity and specificity of 0.83 and 075, respectively. (Cummings et al. 2017)

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSF
				FAS-3 Post hoc analysis of the scale among stroke patients found that 3 scale items were most predictive of fatigue: "I am bothered by fatigue"; "I get tried very quickly"; and "Physically, I feel exhausted." The FAS-3 score was derived by aggregating the scores on these items. (Cummings et al. 2017)		

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