HEART & STROKE FOUNDATION

CANADIAN Stroke BEST PRACTICE RECOMMENDATIONS

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Mood, Cognition and Fatigue Following Stroke

Fifth Edition

Update 2015

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January 2015

Canadian Stroke Best Practice Recommendations

Mood, Cognition and Fatigue Following Stroke

FIFTH EDITION (Updated January 2015)

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Canadian Stroke Best Practice Recommendations

Mood, Cognition and Fatigue Following Stroke
Fifth Edition (Updated AUGUST 2014)

Section One: INTRODUCTION and OVERVIEW

Introduction

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, Canada (HSF), following the 2013 transition of Canadian stroke best practices and quality activities to the HSF from the Canadian Stroke Network.

The goal of disseminating and implementing these recommendations is to reduce practice variations in the care of stroke patients across Canada, reduce the gap between current knowledge and clinical practice, and increase consistency in care across Canada.

Why is better stroke management important?

- Every year, approximately 60,000 people with stroke and transient ischemic attack are treated in Canadian hospitals. Moreover, it is estimated that for each symptomatic stroke, there are nine “silent” 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.
- Stroke is a leading cause of adult disability, with some 315,000 Canadians living with the effects of stroke.
- The annual cost of stroke is approximately $3.6 billion, taking into account both healthcare costs and lost economic output.
- The human cost of stroke is immeasurable.

The HSF 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 *Canadian Stroke Best Practice Recommendations* 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 results 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.

This is the fifth edition of the *Canadian Stroke Best Practice Recommendations,* which were first released in 2006. The theme for the 2014 – 2015 update is ***Working Together with Stroke Survivors and their Caregivers to Achieve Optimal Outcomes***. This theme emphasizes the need for a committed interprofessional team approach to stroke care across the continuum, and to ensure consistent patient-centred care delivery. With stroke patients and family members at the core, the entire team must be supported and actively engaged at every stage of care and in every setting. The HSF *Canadian Stroke Best Practice Recommendations* provide healthcare professionals with the most current evidence and expert guidance on how to engage in patient-centred optimal stroke care for patients and family members. Patients and family caregivers particularly should receive education and be empowered as active participants throughout their journey of recovery to ensure meaningful contributions to goal setting and treatment planning. This theme aligns with and supports the new HSF survivorship mission priority and is included as part of each module for the 2014-15 update of the *Canadian Stroke Best Practice Recommendations.*

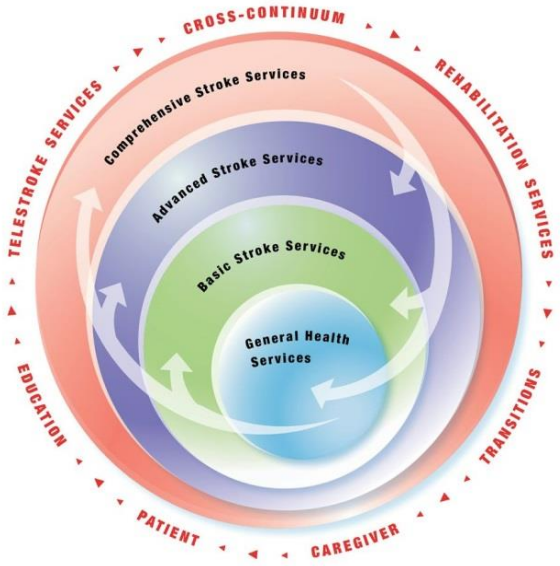
Organization of Stroke Care in Canada

The Heart and Stroke Foundation, in collaboration with the CSBPR advisory committee and key stakeholders have developed a framework to facilitate system improvement through the adoption of evidence-based best practices in stroke across the continuum of care.

Optimal stroke services include access to stroke experts, diagnostic equipment and expertise, and a range of emergent and timely evidence-based acute and rehabilitation treatment options. These services can be arranged along a continuum from minimal, non-specialized services in organizations that provide general health care, to providing basic diagnostic services and management, then advanced care at a single site, and on to comprehensive stroke care across a region.

Figure 1: Canadian Stroke Best Practices Optimal Stroke Services Framework

The Canadian Stroke Best Practices Optimal Stroke Services Framework, as visualized in Figure 1 is meant to organize and prioritize stroke services based on resource availability for a regional or geographic area. The goal set forth within this framework is for each organization involved in the delivery of stroke care services to engage in an ongoing cycle of developing the expertise, processes and protocols needed to provide optimal stroke patient care, taking into consideration the organization's geographic location, patient population, structural and human resources, and relationship to other centres within their healthcare region or system. Once a level of stroke services has been achieved, the organization should strive to develop and incorporate components of the next higher level for ongoing growth of stroke services where appropriate, as well as continuous quality improvement within the level of service currently provided.



For more information, refer to the Canadian Stroke Best Practices Overview and Methodology Module at http://www.strokebestpractices.ca/wp-content/uploads/2010/10/CSBPR-2014_Overview_Methodology_ENG.pdf

Mood, Cognition and Fatigue following Stroke Module Overview

Working Together with Stroke Survivors and their Caregivers to Achieve Optimal Outcomes 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, affect up to 30% to 60% of patients who have experienced a stroke within the first year after onset. 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.

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 to identify risk areas, agree on goals for treatment and recovery, and implement appropriate management strategies. This theme applies across the system of care, and emphasizes the participation of individuals with stroke, their families and caregivers, healthcare providers, and the broader community.

The first steps for healthcare professionals in ***Working Together*** for mood and cognition 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. ***Achieving optimal outcomes*** for stroke survivors and their families requires ongoing screening and assessment for mood and cognitive changes. Screening should occur through all stages and settings following a stroke, including in acute care, rehabilitation, prevention clinics and outpatient community settings (including primary care, home care and long-term care).

Working Together involves healthcare providers, policy makers, individuals with stroke, their families and caregivers, and the public. It should ensure timely access to clinicians with expertise in treating these issues, and ongoing monitoring of the effects of treatment and goal attainment. Ideally, when screening is suggestive of a mood or cognition issue, patients 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 patient 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.

Recent reports on the quality of stroke services across Canada and within specific provinces have shown that there is inconsistent screening and monitoring of patients for post-stroke depression 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 2014 Update of Mood, Cognition and Fatigue Following Stroke

The 2014 update of the *Canadian Stroke Best Practice Recommendations* Mood, Cognition and Fatigue 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 some of 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 Mood, Cognition and Fatigue module recommendations for 2014 include:

- ✓ Updated recommendations on the timing of screening for depression and VCI
- ✓ New literature incorporated which suggests that prophylactic antidepressant medication can be effective in some stroke patients.
- ✓ New comparison table of selected antidepressants for management of post-stroke depression;
- ✓ New information on cognitive rehabilitation strategies for patients with vascular cognitive impairment;
- ✓ Updated comparison table of assessment tools for screening for vascular cognitive impairment
- ✓ Addition of post-stroke fatigue recommendations to this module (previously included in Transitions of Care following Stroke module)

Guideline Development Methodology:

The *Canadian Stroke Best Practice Recommendations* 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 closing 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 useful 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
2. Systematic search, appraisal and update of research literature
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, 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.
9. Update of educational materials and implementation resources
10. Final approvals, endorsement and translation of chapter
11. Public release & 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 *Canadian Stroke Best Practice Recommendations* is available in the *Canadian Stroke Best Practice Recommendations Overview and Methodology* manual available on the Canadian stroke best practices website at http://www.strokebestpractices.ca/wp-content/uploads/2014/08/CSBPR2014_Overview_Methodology_ENG.pdf

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 Advisory committee and appropriate HSF 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 membership.

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). Recommendations with this level of evidence may also be made in response to requests from a range of healthcare professionals who seek guidance and direction from the experts in the absence of strong evidence on certain topics that are faced on a regular basis.

Table 1: Summary of Criteria for Levels of Evidence Reported in the *Canadian Best Practice Recommendations for Stroke Care* (Update 2014)

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. Desirable effects outweigh or are closely balanced with undesirable effects or vice versa.
C	Writing group consensus and/or supported by limited research evidence. Desirable effects outweigh or are closely balanced with undesirable effects or vice versa, as determined by writing group consensus.

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

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Citing the Mood, Cognition and Fatigue following Stroke 2014 Module

Eskes G, Lanctot K on behalf of the Mood, Cognition and Fatigue following Stroke Writing Group. *Mood, Cognition and Fatigue following Stroke Module 2014*. In Lindsay MP, Gubitz G, Bayley M, and Smith EE (Editors), on behalf of the Canadian Stroke Best Practices and Advisory Committee. *Canadian Stroke Best Practice Recommendations*, 2014; Ottawa, Ontario Canada: Heart and Stroke Foundation.

Comments

We invite comments, suggestions, and inquiries on the development and application of the *Canadian Stroke Best Practice Recommendations.*

Please forward comments to the Heart and Stroke Foundation's Stroke Team at strokebestpractices@hsf.ca.

Canadian Stroke Best Practice Recommendations

Mood, Cognition and Fatigue FOLLOWING STROKE

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Canadian Stroke Best Practice Recommendations

Mood, Cognition and Fatigue FOLLOWING STROKE

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Canadian Stroke Best Practice Recommendations

Mood, Cognition and Fatigue FOLLOWING STROKE

Section Two: RECOMMENDATIONS

1. Post-Stroke Depression

Mood, Cognition and Fatigue **1. Post-Stroke Depression**

Update 2014

1.0 All patients with stroke should be considered to be at high risk for post-stroke depression (PSD), which can occur at any stage of recovery [Evidence Level A].

1.1 Screening for Post-stroke Depression:

i. All patients with stroke should be screened for depressive symptoms, given the high prevalence of depression post stroke, the need for screening to detect depression, and the strong evidence for treating symptomatic depression post stroke [Evidence Level B]. *For palliative care patients, refer to Acute Care Module Section 4.*

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

iii. Stroke patient assessments should include evaluation of risk factors for depression, particularly a history of depression [Evidence Level C].

iv. For patients who experience some degree of communication challenge or deficits following stroke, appropriate strategies for screening of possible PSD should be implemented to ensure adequate assessment and access to appropriate treatment [Evidence Level C]. *Refer to the Stroke Rehabilitation Module for further information.*

Side note: Common risk factors associated with PSD 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 PSD. Communication deficits and social isolation may also be considered as possible risk factors for depression. Refer to Transitions of Care Module for information on depression in family and informal caregivers of people with stroke.

1.2 TIMING of Screening for Post-Stroke Depression:

i. Screening for post-stroke depression may take place at various stages throughout the continuum of stroke care, particularly at transition points [Evidence Level C]. Repeated screening may be required since the ideal timing for screening for post-stroke depression is unclear.

ii. Screening for depressive symptoms could be considered during acute care stay in patients at high risk for depression, particularly if evidence of depression or mood changes is noted. Stroke patients who are identified as at-risk could be screened before discharge from acute care [Evidence Level C].

iii. Screening for depressive symptoms should be considered during transition points in care; such as from an inpatient acute setting to an inpatient rehabilitation setting, and or before return to the

community [Evidence Level C].

iv. Screening for depressive symptoms should be considered following discharge to the community, at stroke prevention clinic assessments, during follow-up appointments, and during periodic health assessments with primary care practitioners and consulting specialists [Evidence Level C].

1.3 Assessment for Post stroke Depression:

i. Patients identified with a high probability of clinically significant post-stroke depression during screening should be assessed in a timely manner by a healthcare professional with expertise in diagnosis, management and follow-up of depression in patients following stroke [Evidence Level C].

1.4 Non-Pharmacological Management of Post-Stroke Depression

i. There is a lack of evidence to support use of psychotherapy as a monotherapy in the treatment of PSD (Evidence Level C). However it is reasonable to consider these therapies (either cognitive-behavioural therapy or interpersonal therapy]) as one of the first line treatments for acute major depressive disorders post stroke, given their demonstrated efficacy in primary depressive disorders [Evidence Level A]. *Refer to the CANMAT Guidelines for additional information.*

ii. Treatment for PSD may include psychotherapy as an adjunct in combination with antidepressants [Evidence Level B], as appropriate to the patients' health state and other deficits (e.g., communication and other cognitive deficits).

iii. Treatment should be provided with the goal of preventing relapse [Evidence Level B].

iv. Other approaches to adjunctive treatment of PSD are emerging, but require more research. These include physical exercise, music, mindfulness, acupuncture, deep breathing, meditation, visualization, and Repetitive Transcranial Magnetic Stimulation. These could be considered on an individual basis at the discretion of the treating healthcare professional in consultation with the patient. [Evidence Level C].

1.5 Pharmacotherapy for Post-Stroke Depression

i. Patients 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.*

   a. Pharmacological treatment should be considered/started if the depression is persistent and interferes with clinical goals, or worsens [Evidence Level B].

ii. Patients ***diagnosed*** with a depressive disorder following formal assessment 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 PSD treatment. Side effect profiles, however, suggest that some selective serotonin reuptake inhibitors may be favoured in this patient population [Evidence Level A]. *Refer to Table 1B for a summary of suggested pharmacotherapy agents for the treatment of PSD.*

   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.

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 twelve months. [Evidence Level C].

   a. 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.

b. If the patient's mood has not improved 2–4 weeks after initiating treatment, check that the patient is taking the medicine as prescribed. If yes, then consider increasing the dose or changing to another antidepressant [Evidence Level B].
c. 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].
d. 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 PSD, patients should continue to be monitored for recurrence of depressive symptoms, as part of ongoing comprehensive stroke management [Evidence Level C]. The involvement and feedback of patients, family and caregivers can be an important component of ongoing monitoring.

vii. **Pseudobulbar Affect:** In cases of severe, persistent or troublesome tearfulness (emotional incontinence or lability), patients may be given a trial of antidepressant medication [Evidence Level A]. Side effect profiles suggest that some selective serotonin reuptake inhibitors may be preferred over others for this patient population. There is no evidence for non-pharmacotherapy for this condition. *Refer to Table 1B for a summary of suggested pharmacotherapy agents for the treatment of PSD.*

**Note: Watchful waiting is defined as a period of time when the patient who 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 somewhere between 2 to 4 weeks. It is often described as including suggestions to the patient for self-help strategies and participation in physical exercise.*

1.6 Prophylactic Treatment for Post-Stroke Depression

i. At this time the routine use of prophylactic use of antidepressants for ALL patients is not recommended as the risk – benefit has not been clearly established [Evidence Level B].

ii. Emerging data on the use of pharmacotherapy to prevent post-stroke depression suggests that pharmacotherapy may be reasonable for some patients [Evidence Level A].

iii. Further research is required to define *at risk* patients, choice of antidepressant agents, optimal timing and duration of intervention.

1.7 Other Mood States (Anxiety)

i. Anxiety frequently co-exists with depression following stroke or may appear in patients not clinically depressed. For patients with marked anxiety with or without clinical depression, it is reasonable to offer psychotherapy [Evidence level C].

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

ii. Apathy frequently co-exists with depression following stroke or may appear in patients not clinically depressed. For patients with marked apathy, with or without clinical depression, it is reasonable to offer psychotherapy [Evidence level C].

1.8 Ongoing Monitoring, Support and Education

i. Patients and families should be given information and education about the potential impact of stroke on their mood and that of family and caregivers; patients 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 Transitions of Care Module for further information on Patient and Family Education.*

ii. Patients and their caregivers should have their psychosocial and support needs assessed as part

of ongoing stroke management [Evidence level C].

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). The majority of cases of post-stroke depression (PSD) may develop in the first 3 months of stroke, and incidence rates of depression tend to decline over time, although research reports have indicated symptoms have emerged up to two years after index stroke. In one study, post-stroke depression (PSD) also was reported in 48% of 71 young stroke patients after at least 1 year of follow-up. PSD 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 and a previous history of depression have all been identified as important risk factors for the development of PSD.

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

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

System Implications

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

- Screening tools should be available that are sensitive to unique patient circumstances such as patients with communication deficits and tools that may be culturally appropriate.
- Education for primary care practitioners and healthcare providers across the continuum of stroke care on recognition, assessment, and management of post-stroke depression.
- 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.
- Timely access to and availability of specialized therapies to manage post-stroke depression, including medication, counseling and psychotherapy as required.
- 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).
- Process for ongoing monitoring of any patient with positive screening for depression during screening and assessment process.
- Education and support for caregivers of stroke survivors
- 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.
- Optimization of strategies to prevent the recurrence of stroke.

Performance Measures

1. **Proportion of acute stroke patients 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 acute stroke patients referred for additional assessment or intervention for a suspected diagnosis of depression.
3. Proportion of stroke patients diagnosed with PSD and treated with antidepressants and/or psychotherapy at one month, three months, six months, and one year following the initial stroke event.

Measurement Notes

- Recommendations for screening and assessment of PSD and corresponding performance measures apply across the continuum of stroke care and should be considered in the acute, early rehabilitation and longer-term recovery phases and in 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.
- Data for measurement may be found through primary chart audit. Data quality will be dependent on the quality of documentation by healthcare professionals.
- For patients referred to psychiatry, information may be available through provincial physician billing databases.
- 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 issue addressed is to increase the number of patients with PSD who are adequately treated, and reduce the number of patients 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 Depression Screening Tools
- Table 1B: Summary Table for Selected Pharmacotherapy for Post-Stroke Depression
- Evidence-based Review of Post-Stroke Depression (EBRSR) http://www.ebrsr.com/evidence-review/18-post-stroke-depression
- StrokEngine, Depression section http://strokengine.ca/
- NHS Psychological care after stroke: http://webarchive.nationalarchives.gov.uk/20130221101407/http://www.improvement.nhs.uk/stroke/NationalProjects1011/Psychologicaltherapy/tabid/177/Default.aspx
- APA Diagnostic and Statistical Manual of Mental Disorders (DSM) http://www.psychiatry.org/practice/dsm

Patient Information

- "Taking Charge of Your Stroke Recovery: A survivor's guide to the Canadian Stroke Best Practice Recommendations": http://www.strokebestpractices.ca/wp-content/uploads/2014/08/HSF_SBP_PatientsGuide_F14_EN_July2014-FINAL.pdf
- Your Stroke Journey: http://www.strokebestpractices.ca/wp-content/uploads/2015/03/YOURSTROKEJOURNEY.FINAL_.ENGLISH..pdf
- Stroke Engine: http://strokengine.ca/
- Getting on With The Rest of Your Life After Stroke: http://strokebestpractices.ca/wp-content/uploads/2010/11/Getting-on-with-the-Rest-of-Your-Life-After-Stroke.pdf
- Emotions, moods and relationships: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.8570109/k.41F2/Emotions_moods_and_relationships.htm

- The Heart & Stroke Living with Stroke™ program: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3936679/k.7231/Stroke__Living_with_StrokeTM_program.htm
- Canadian Partnership for Stroke Recovery - Life after Stroke: http://www.lifeafterstroke.ca
- Stroke Care Tips and Tools - A Guide for Stroke Caregivers: http://www.heartandstroke.on.ca/site/c.pvI3IeNWJwE/b.6194819/k.9B09/Tips_and_Tools.htm
- Coping with stress: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.5590155/k.3B4A/Heart_disease__Coping_with_stress.htm
- Post-Stroke Checklist: http://www.strokebestpractices.ca/wp-content/uploads/2014/06/HSF%20Post%20Stroke%20Checklist_WEB.pdf

Summary of the Evidence

Post-Stroke Depression and Mood Evidence Tables and Reference List (hyperlink)

Post-stroke depression is a common consequence of stroke. In a systematic review of 51 prospective, observational studies of post-stroke depression conducted in hospital-, rehabilitation-, and population-based settings, Hackett et al (2005) estimated that approximately one-third of all individuals who experience stroke exhibit depressive symptoms at some point following the event (i.e., at acute, sub-acute or long-term follow-up). The authors suggest that this proportion is likely an underestimation of prevalence, given possible under-reporting of unusual mood, difficulty in the assessment of depression within the stroke population, and the variability in the methods used to assess and define cases of depression within the literature (Hackett et al. 2005).

In a systematic review intended to establish risk factors for the development of PSD, Hackett and Anderson (2005) included data from a total of 21 studies. Of the many different variables assessed, physical disability, stroke severity and cognitive impairment were most consistently associated with the development of depression following a stroke event. The authors noted that major methodological limitations within the available literature made it difficult to form a definitive conclusion. As part a multi-centred, observational study of depression in stroke, Paolucci and colleagues (2005) identified female sex (OR=1.49), previous stroke (OR = 1.55), previous depression (OR=3.97) and severe disability (Modified Rankin Scale score >3, OR = 2.70) as variables associated with increased odds for the development of PSD. In addition, the risk for post-stroke depression was found to increase exponentially in individuals with more than one risk factor (Paolucci et al. 2005).

Depression and anxiety may also be increased in parents of children with stroke (Goodman 2000; Gordon, 2002). PSD in survivors of childhood stroke is not well studied but appears to be common based on preliminary evidence (Elbers, 2013). In young adults with stroke, PSD risk factors are localization of the infarct in a carotid territory, severe disability, bad general outcome and absence of return to work (Neau et al., 1992).

In a report from the Auckland Regional Community Stroke Study (Hackett and Anderson 2006), the authors described an attempt to create a simple, predictive tool for the identification of individuals most at risk for abnormal mood. Of the factors included in the model, only two were significant predictors of mood; prior treatment for depression (OR = 2.4, 95% CI 1.34 – 3.43) and requiring “much help” with activities of daily living (OR = 2.35, 95% CI 1.33 – 4.14).The ability of the model to predict risk for depression might be increased by the inclusion of other factors such as fatigue and performance of instrumental activities of daily living. However, Van de Port et al. (2007) demonstrated that use of these two predictors (prior treatment for depression and requiring much help with ADLs) in a multivariate model could correctly

classify depression in 76% of patients 3 years post stroke.

Examination of the results of multiple meta-analyses (Mitchell and Kakkadasam 2011; Mitchell et al. 2011; Mitchell et al. 2010; Mitchell et al. 2009; Cepoiu et al. 2007) revealed that non-psychiatric physicians, nurses, and therapists demonstrate poor sensitivity relative to gold standard psychiatric interviews and standardized formal rating scales when using clinical observation to identify depression in individuals who have experienced stroke in both inpatient and community-based settings. By comparison, use of standardized screening tools is associated with significantly greater sensitivity (Lowe et al. 2004). As in the recent CANMAT task force recommendations, it is noted that the use of formal instruments is a key component in the diagnostic process required to promote early detection of depression.

The best time to screen formally for the possible presence of PSD is not certain and incident rates of post-stroke depression are not stable over time. Bour and colleagues (2011) reported a decrease in incident cases of depression over the course of the first year following the stroke event. Cumulative incidence of PSD was 18.8% at 1month and 23.1%, 26.7%, 31%, and 36.2% at 3, 6, 9 and 12 months, respectively. Although incident rates decline over time and a general trend toward improvement in depressive symptomatology is evident in the first year post stroke, PSD may prove to be persistent for a longer duration for a significant proportion of individuals identified as depressed (Ostir et al. 2011, Ayerbe et al. 2011, Farner et al. 2010, Berg et al. 2003).

In 2006, the Canadian Stroke Strategy and Heart and Stroke Foundation of Ontario supported a consensus process to identify a standardized basket of outcome assessment tools that could be used to across the stroke continuum of care. Included in the resulting collection of measures were the following screening tools for the identification of possible depression in individuals with stroke: The Hospital Anxiety and Depression Scale (HADS), the Geriatric Depression Scale (GDS) and the Stroke Aphasic Depression Questionnaire (SADQ-10). Additional tools for consideration include the 9-item Patient Health Questionnaire (PHQ-9), and the Children's Depression Inventory (CDI). A brief description of these and several additional tools may be found in the accompanying summary table.

Once possible depression has been detected via formal screening and a diagnosis made by an experienced healthcare professional, treatment via pharmacotherapy has been associated with reduction of depressive symptomatology (Chen et al. 2006, Hackett et al. 2008). However, these findings should be considered in light of reports of adverse effects associated with the use of antidepressant medications. Whereas selective serotonin reuptake inhibitors are among the most commonly prescribed pharmacological agents for the treatment of PSD, they may also be associated with increased risk for mortality and stroke (Coupland et al. 2011, Wu et al. 2011). In addition, pharmacodynamic interactions between antidepressants and cardiovascular agents have been noted for several antidepressant classes including SSRIs, which may result in significant adverse events (Tuunainen et al. 2009).

Whereas psychotherapeutic approaches such as cognitive behavioural therapy or interpersonal therapy may be accepted treatment approaches for acute major depressive disorders in general, based on the results of available meta-analyses (Wilson et al. 2009, Hackett et al. 2008), there is insufficient evidence to support their application as monotherapy for the treatment of PSD. However, talk-based therapy, such as problem-solving therapy, when used in combination with pharmacotherapy may be an effective means to promote the reduction of symptoms of depression (Mitchell et al. 2009, Alexopoulos et al. 2012, Lincoln and Flanaghan 2003). The use of other, non-pharmacological strategies, such as light therapy (Tuuainen et al. 2009, Sondergaard et al. 2006), physical exercise (Graven et al. 2011), music therapy (Jun et al. 2012, Sarkamo et al. 2008), and acupuncture (Zhang et al. 2010) have all been demonstrated to have a positive effect on mood within the population of individuals with stroke.

For individuals who, following screening and appropriate follow-up assessment, experience mild symptoms of depression, watchful waiting may be the most appropriate strategy. Although there is no direct evidence of the effectiveness of this approach as an intervention within the stroke population, it has been used with good results as part of interventions, such as stepped care management (van't Veer-Tazelaar et al. 2009, Dozeman et al. 2012), undertaken in populations of older individuals. A single randomized controlled trial examined the use of pharmacotherapy for individuals with mild depression and

found a significant reduction in depressive symptomatology associated with the use of antidepressant therapy; however, study participants were not drawn from the stroke population (Williams et al. 2000).

Prevention of PSD

Given the high prevalence of PSD and the negative consequences associated with it, there has been increasing attention paid to strategies for its prevention. The most commonly studied strategy has been universal pharmacologic prophylaxis, although discussions have expanded to include selected and/or indicated prophylaxis (Salter et al. 2013), problem-solving therapy (Robinson et al. 2008) and motivational interviewing (Watkins et al. 2007, 2011). Results of recent meta-analyses have provided encouraging results in favour of pharmacotherapy for the prevention of post-stroke depression (Salter et al. 2013, Yi et al. 2010, Chen et al. 2007); however, the individual studies within these analyses were small and provided conflicting results. In addition, little is known about how many individuals in these studies might have been experiencing subsyndromal depression, or had the greatest risk for PSD over time, and what the optimal timing and duration of preventative interventions might be whether using a universal, selected or indicated approach. In each case, the potential benefits associated with the use of prophylactic prevention of PSD must be weighed against the risks associated with the use of antidepressive agents, particularly among older individuals (Coupland et al. 2011).

Pseudobulbar Affect (Post Stroke Emotional Incontinence-PSEI)

Reported frequency of pseudobulbar affect (PBA) post-stroke ranges from 11%-35% depending upon the criteria used to define the condition and time elapsed since stroke onset (House et al. 1989, Kim and Choi-Kwon 2000). Although an association has been reported between PBA and PSD, many individuals with emotionalism may not end up with significant or diagnosable depression (Kim and Choi-Kwon 2000, Tang et al. 2004). In a recent Cochrane review (Hackett et al. 2010), pooled analyses were reported for data gathered from 5 randomized controlled trials examining antidepressant therapy for post-stroke PBA. Large treatment effects in terms of emotionalism, reduced tearfulness, clinical impressions of change and Lability Scale scores were reported in favour of antidepressant treatment when compared to control conditions. Given methodological limitations, the authors conclude that the existing literature does not provide definitive evidence that pharmacotherapy is effective in the treatment of PBA post-stroke. The combination medication dextromethorphan/quinidine (DM/Q) is available and approved in the US for the treatment of PBA. The combination is not approved in Canada, but both components are available as they are approved for other indications. As yet, DM/Q has not been evaluated in post-stroke PBA, and tolerability, particularly cardiac toxicity must be considered (Patatanian & Cassellman 2014 PMID:24704895; Schoedel et al 2014 PMID:25061302).

Anxiety Following Stroke

Anxiety following stroke occurs more often in women than in men. In the Perth Community Stroke Study, it was reported that 20% of women who experienced stroke developed symptoms of anxiety following the event while, in the same sample, only 9% of men experienced post-stroke anxiety (Burvill et al. 1995). However, individuals who experienced post-stroke anxiety often reported having anxiety or depression at the time of the stroke event (Burvill et al. 1995). Individuals with generalized anxiety disorder (GAD) after stroke may often experience co-morbid depression. Castillo et al. (1995) reported that, in a sample of individuals with post-stroke GAD approximately 75% were also depressed. Despite the prevalence of post-stroke anxiety, very few studies have included evaluation of the effectiveness of potential treatments. A recent Cochrane review (Campbell Burton et al. 2011) identified only 2 RCTs suggesting a positive effect associated with the provision of pharmacotherapy with or without the addition of psychotherapy. Further research in this area is certainly indicated in this post-stroke population.

Post-Stroke Depression and Mood Evidence Tables and Reference List (hyperlink)

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 recently Sagen et al (2009) reported α=0.83. **Construct validity**: Reported satisfactory on confirmatory factor analysis (Johnston et al.	Scale authors recommended either 8/9 (high sensitivity) or 10/11 (high specificity) be used to identify the presence of depression using the depression subscale of	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. 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

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
				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 HADS (Zigmond and Snaith 1983). Alternate cut-off points have been evaluated for the post stroke population.	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 of ≥11), 79% and 85% (cut off of ≥12) respectively. For the HADS-D, sensitivity = 79% and specificity = 82% (cut off of ≥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 with the PHQ-2 increased the accuracy of identification (sensitivity = 87%) (de man-van Ginkel et al. 2012).
Additional Tools for Consideration						

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
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 (McDowell et al. 1996)	Using the suggested cut-off score, Shinar et al. and Parikh et al. reported sensitivity of 73% and 86%, and specificity of 100% and 90% respectively (relative to the DSM-III-R).
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	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%).

Assessment Tool and Link	# of Items	Response Format	Total Score	Stroke-specific reliability/validity	Interpretation of Scores*	Sensitivity/Specificity for PSD
				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).		
Aphasia Depression Rating Scale (ADRS) http://strokengine.ca/assess/module_adrs_intro-en.html	9	Observer rating based on interview & observation Rating scale varies per item	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 with results of HRSD (Benaim et al. 2004).	Scores of ≥ 9 are used to indicate the presence of depression (Benaim et al. 2004).	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).
Tools for Consideration in Children						
Children's Depression Inventory (CDI) this scale has been revised and CDI 2 is now used. This information needs to be updated. http://www.mhs.com/product.aspx?gr=edu&id=overview&prod=cdi2#description	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/english/project/	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: 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. (Table completed by Dr. Krista Lanctot, Dr. Nathan Herrmann and team at Sunnybrook Health Sciences Centre, Toronto, Canada).

	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 QTc lengthening possible	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

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Landmark Trials	citalopram[6,14], fluvoxamine[8] , fluoxetine[1-5,14] sertraline[7,14] paroxetine[9]	reboxetine[10] , milnacipran[11], venlafaxine[12] , duloxetine[14]	trazodone[15,16] , nortriptyline[17,18] methylphenidate[19] [Niedermaier]
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: 20 – 60mg/ day escitalopram: 10 – 20mg/day sertraline: 50 - 100mg/day	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	Anxiety in PSD: duloxetine more effective than citalopram in treating anxiety symptoms Alexithymia: venlafaxine results in greater improvement of emotional	Mortality & PSD: increased survival of depressed and non-depressed treated with fluoxetine or nortriptyline over placebo in 9-year follow-up[c] Functional status (ADLs): trazodone

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
	fluoxetine or nortriptyline over placebo in 9-year follow-up[a] Executive function: maintenance of executive function compared to placebo over 21 months follow-up[b]; no improvement of executive function Sleep: fluvoxamine improved sleep disturbances as measured by peripheral melatonin blood levels. Functional status: fluoxetine treatment associated with improved motor recovery (FLAME trial)	awareness than fluoxetine	treatment resulted in trending improvement
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[d] 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.[e] Delirium : anticholinergic effects (paroxetine) may play role in delirium in acute stroke patients[f]		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

[c] Jorge, *Am J Psychiatry* 2003 Oct;160(10):1823-9
[i] Jorge, *Am J Psychiatry* 2003 Oct;160(10):1823-9
[b] Narushima, *B J Psych* 2007, 190:260-265
[d] Mikami, *Stroke* 2011*; Aug 42:3281-3283*
[e] Ramasubbu, *J Clin Psychiatry* 2004; 64:1642-1653
[f] Caeiro, *Eur J. of Neurology* 2004; 11: 699–704

	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)

2. Vascular Cognitive Impairment

Definition of Vascular Cognitive Impairment: (update 2014)

Vascular Cognitive Impairment (VCI) includes the cognitive and behavioural disorders associated with cerebrovascular disease and risk factors, from mild cognitive deficits to frank dementia. VCI is a syndrome with cognitive impairment affecting at least one cognitive domain (e.g., attention, memory, language, perception or executive function) and with evidence of clinical stroke or subclinical vascular brain injury. VCI encompasses a large range of cognitive deficits, from relatively mild cognitive impairment of vascular origin (VaMCI) to Vascular Dementia (VaD), the most severe form of VCI. VCI also plays an important role in patients with Alzheimer's disease (AD) pathology who have coexisting vascular lesions.

Cognitive deficits: The pattern of cognitive deficits in VCI may encompass all cognitive domains, including focal stroke syndromes. Attention and executive function deficits include functions such as slowed information processing, impairments in the ability to maintain task set or shift from one task to another and deficits in the ability to hold and manipulate information (e.g., working memory).

Vascular pathology: Cognitive impairment can result from a range of vascular pathology, including multiple cortical infarcts, multiple subcortical infarcts, covert ("silent") infarcts, strategic infarcts, small-vessel disease with white matter lesions and lacunae, and brain hemorrhage.

Diagnostic criteria for vascular cognitive impairment following stroke has been defined by Gorelick et al (2011) and can be found in Table 2A (Hyperlink).

Mood, Cognition and Fatigue **2. Vascular Cognitive Impairment**

Update 2014

2.0 All patients with clinically evident stroke or transient ischemic attack should be considered at risk for vascular cognitive impairment (VCI) [Evidence Level A].

2.1 Screening and Assessment for Vascular Cognitive Impairment

i. Patients with stroke and transient ischemic attack should be considered for screening for vascular cognitive impairment [Evidence Level C].

ii. Patients with other significant risk factors for vascular disease and VCI post-stroke, such as neuroimaging findings of covert stroke or white matter disease, hypertension, diabetes, atrial fibrillation, other cardiac disease, and/or sleep apnea should be considered for screening for vascular cognitive impairment, particularly those patients with cognitive, perceptual or functional changes that are clinically evident or reported during history taking [Evidence Level C].

iii. Screening for VCI should be conducted using a validated screening tool, such as the Montreal Cognitive Assessment test [Evidence Level C].

Refer to Table 2B for a summary of suggested VCI screening and assessment tools, and their psychometric properties, which may help to guide decision making about the appropriate tool for individual patients.

2.2 **Assessment for Vascular Cognitive Impairment**

i. Patients who demonstrate cognitive impairments in the screening process should be managed by healthcare professionals with expertise in the assessment and management of neurocognitive functioning.* *If required*, a referral could be made to an appropriate cognitive specialist [Evidence Level C].

a. Vascular cognitive impairment is associated with a range of potential deficits thus a detailed cognitive screen and/or assessment could address arousal, alertness, sensorimotor function, attention, orientation, memory, language, agnosia, visual-spatial/perceptual function, praxis, and executive function. [Evidence Level B].
b. Executive function assessment may include assessment of initiation, inhibition, shifting, insight, planning and organization, judgment, problem solving, abstract reasoning, and social cognition [Evidence Level B].
c. Additional assessments could be undertaken to determine the nature and severity of cognitive impairments, as well as the presence of remaining cognitive abilities and strengths [Evidence Level C].
d. The impact of deficits on function and safety in activities of daily living and instrumental activities of daily living, and occupational and school functioning should also be assessed (e.g., driving, home safety) [Evidence Level C]. *Refer to Transitions of Care following Stroke Module for more information on driving.*
e. The results of these assessments should be used to guide selection and implementation of appropriate remedial, compensatory and/or adaptive intervention strategies according to client-centered goals and current or anticipated living environment (e.g., to help with discharge planning) [Evidence Level B]. *Refer to Sections 2.3 and 2.4 for more information on management of patients with stroke and VCI.*

***** *Note: Experts in neurocognitive assessment may include neuropsychologist, psychologist, occupational therapist, speech-language pathologist, clinical nurse specialist, psychiatrist, physiatrist, geriatrician, neurologist, memory specialists, and developmental pediatricians. Experts require specific qualifications to administer many of the identified assessments.*

2.3 Other considerations related to Screening and Assessments

A. Comorbidities

i. Screening for VCI should take into account any immediate factors that may impact assessment results, such as communication and sensorimotor deficits (speech and language, vision, hearing), delirium, hypoarousal, and other medical conditions that may have temporary impact on cognition [Evidence Level B].
ii. Post-stroke patients with suspected cognitive impairment should also be screened for depression, given that depression has been found to contribute to vascular cognitive impairment [Evidence Level A] *Refer to Recommendation 1.0 on Post Stroke Depression for additional information.*

B. Timing

i. The impact and presentation of VCI evolves over time. All patients considered at risk for cognitive impairment should be screened and/or assessed periodically to detect changes over time in cognition, perceptual deficits, depression, and/or changes in function [Evidence Level C].
ii. Screening and assessment could occur at different stages of care as indicated by the severity of clinical presentation, history and/or imaging abnormalities [Evidence Level C].

C. Age

i. Effects of age or developmental stage must also be considered when deciding when and what to assess [Evidence Level C].
    a. For example, in children with stroke, outcomes will evolve in parallel with development and deficits may not be fully realized until many years later [Evidence Level C].
    b. In Young adults, decisions about what to assess should take into consideration age-specific goals such as educational and vocational needs [Evidence Level C].

D. Multiple Assessments

i. Although screening or conducting assessments at different stages of care is important for guiding diagnosis and management, it is also important to be aware of the potential impact of multiple assessments on both the validity of the results as well as on the patient (e.g., practice effects, test fatigue) [Evidence Level B]. Thus, use of different equivalent assessment forms is recommended when available (e.g., MOCA has 3 versions).

2.4 Management of Vascular Cognitive Impairment following Stroke

i. Vascular risk factors (e.g., hypertension, diabetes) should be managed aggressively to achieve maximum risk reduction for future strokes) [Evidence Level B].
   a. Treatment of hypertension reduces cognitive decline, even in the absence of stroke events and should be addressed for all patients with stroke and elevated blood pressure [Evidence Level A].
   b. The benefits of vascular risk reduction on cognitive decline in older populations suggest extrapolation to individuals post stroke is warranted and should be addressed [Evidence Level B]. *Refer to Prevention of Stroke module for additional information.*

ii. Interventions for cognitive impairment should be tailored according to the following considerations
   a. Goals should be patient-centered and sensitive to the values and expectations of patient, family and caregivers [Evidence Level B].
   b. Goals and interventions should take into account the strengths and weaknesses of the cognitive profile and communication abilities [Evidence Level C].
   c. Patients with communication or cognitive issues may require additional support (e.g., family involvement) to optimize patient participation in goal-setting and/or engagement in rehabilitation [Evidence Level C].
   d. Interventions should be individualized, based on best available evidence, and have the long-term aim to facilitate resumption of desired activities and participation (e.g., self-care, home and financial management, leisure, driving, return to work) [Evidence Level C].
   e. Severity of impairments: If the level of impairment has reached the moderate dementia stage, it is reasonable for interventions to be more focused on providing education and support for the caregiver in addition to, or in lieu of, cognitive rehabilitation with the patient (Evidence Level C].

Refer to Stroke Rehabilitation Module for additional information.

NOTE: Issues such as intensity and dose of therapy, stage of treatment, and impact of severity of deficits can modify effectiveness of therapy, and require more research.

iii. Interventions with the patient can be broadly classified as either compensation strategies training, or direct remediation/cognitive skill training. These approaches are not mutually exclusive, and, depending upon the impairments, activity limitations and goals may be offered together.
   a. Compensation strategy training should focus on teaching strategies to manage impairments and is often directed at specific activity limitations to promote independence. It can include environmental changes or changing the way one performs an activity [Evidence Level B].
   b. Direct remediation/cognitive skill training should focus on providing intensive specific training to directly improve the impaired cognitive domain. It can include drill and practice exercises, mnemonic strategies (ex: acronyms, songs), or computer based

tools directed at specific deficits [Evidence Level B].

c. It is reasonable to treat attention impairments with computerized skill training under the supervision of a therapist aimed at specific aspects of attention [Evidence Level B].

d. Evidence for impact on activity or participation limitations is limited, however and requires more research. [Evidence Level C].

iv. Memory impairments may be treated with compensation using external strategies (e.g. assistive electronic and non-electronic devices,) and using internal strategies (e.g., encoding and retrieval strategies, self-efficacy training), with some evidence for benefits to activity limitations [Evidence Level B].

v. Executive function deficits may be treated with computerized skill training under the supervision of a therapist and/or compensation strategies, depending upon the specific impairment. There is some evidence for benefits to activity limitations [Evidence Level B].

a. Targetted computerized skill training directed by a therapist may be considered for working memory deficits [Evidence Level B]

b. Internal strategy training may be considered and includes strategies to improve goal management, problem solving, time pressure management, and metacognitive reasoning [Evidence Level B].

vi. Aerobic exercise can be considered for treatment of cognitive impairments including attention, memory and executive function [Evidence Level B], although evidence for benefits to physical activity and/or participation limitations is limited.

a. Exercise may be considered to slow cognitive decline in those with vascular disease without presence of stroke [Evidence Level B]

vii. New developments in cognitive intervention that may be of potential benefit include repetitive transcranial magnetic stimulation or direct stimulation, the use of virtual reality environments, and application of constraint-induced approaches for the impaired cognitive domain. These strategies require more research before recommendations can be developed on their use [Evidence Level C].

viii. Patients with cognitive impairment and evidence of changes in mood (e.g., depression, anxiety), or other behavioural changes on screening could be referred and managed by an appropriate mental healthcare professional [Evidence Level B]. *Refer to Recommendation 1 on Post Stroke Depression for additional information.*

Refer to Stroke Rehabilitation module for additional information related to treatment of other domains, including communication, visual-perceptual disorders and neglect in patients with stroke and vascular cognitive impairment.

2.5 Pharmacotherapy for Vascular Cognitive Impairment following Stroke

i. Cholinesterase inhibitors (donepezil, rivastigmine and galantamine) and the NMDA receptor antagonist memantine may be considered in individual stroke patients with vascular dementia, based on randomized trials showing small magnitude benefits in cognitive outcomes. However, the clinical relevance of these benefits remains controversial; therefore, the use of these medications should be based on clinical judgment that small improvements in cognition would have a meaningful impact on the patient's quality of life [Evidence level B].

ii. For patients with evidence of vascular cognitive impairment a referral to a healthcare professional or team with expertise in vascular cognitive impairment should be considered for further assessment and recommendations regarding pharmacotherapy [Evidence Level C].

Clinical Considerations:

- It should be noted that most of the available evidence is based on people who meet the criteria for vascular dementia or mixed dementia. Thus, evidence for pharmacological treatment effects in

VCI-ND is limited at this time.

- Severity should be taken into account in decisions for pharmacological management.
- VCI patients may be susceptible to AEs given the frequent medical comorbidities and concomitant medications
- Stages of care across the continuum may include:
    - during presentation to emergency when cognitive, perceptual or functional concerns are noted;
    - during acute care stay, particularly if cognitive, perceptual or functional concerns, in the absence of delirium is noted;
    - during rehabilitation within inpatient, outpatient, and home-based settings, according to client progress; ,
    - following hospital discharge from the emergency department or inpatient setting to an outpatient or community-based healthcare setting.

- *Note: These medications are currently approved by Health Canada for the treatment of Alzheimer's Disease. They have not yet received approval for the indication of vascular cognitive impairment.*

Rationale

Vascular cognitive impairment affects up to 60 percent of stroke survivors and is associated with poorer recovery and decreased function in activities of daily living and instrumental activities of daily living. Patients may require long-term, ongoing intervention and rehabilitation (Teasell et al, 2009; Madureira et al 2001). Cognitive abilities in the areas of executive function, attention and memory appear important in predicting functional status at discharge. In addition, cognitive impairment can be chronic and progressive after stroke; post-stroke dementia is estimated to occur in 26 percent of stroke patients by three months (95% CI 3% in age-matched controls) and adversely affects recovery. Cognitive impairment increases long-term dependence and is associated with increased mortality rates (61 percent versus 25 percent) (Black, 2007).

Cognitive impairment due to covert vascular pathology is also increasing. Covert strokes, visualized as lacunes or white matter hyperintensities on T2-weighted images, are common (23 percent of community elderly) and are associated with cognitive decline, dementia, and stroke. Evidence is emerging that demonstrates that for every clinically evident stroke, there may be up to ten covert strokes. Intracerebral small-vessel disease is a disorder that is on the rise with the aging of the population, leading to an increase in the need support services over the long term.

Emotional and related behavioural changes are known to occur following stroke, with specific behaviours linked to the affected hemisphere and stroke location. Disorders such as apathy, anxiety, labile laughing and crying, and other behaviours such as disinhibition, denial, indifference, overt sadness, and aggressiveness can occur in the early days following stroke. Some of these behaviours may be related to later development of depression; however, prospective studies of mood changes during and immediately after stroke are limited as yet.

In most population studies, vascular dementia is the second most common cause of dementia, after Alzheimer disease. The combination of Alzheimer disease and vascular disease results in the commonest substrate of dementia in the elderly. A single macroscopic hemispheric infarct is sufficient to cause dementia in people with intermediate Alzheimer pathology.

System Implications

- Public education to increase awareness that cognitive changes may be considered as manifestations of vascular disease and stroke.
- Public education to increase awareness of untreated or uncontrolled hypertension and other vascular risk factors and their relationship to cognitive changes and dementia.

- Professional education to increase awareness among family physicians and primary care health professionals that patients with vascular risk factors, if not treated, will be at high risk for cognitive deficits.
- Professional education across specialties (e.g., nephrology, ophthalmology, family medicine) to increase awareness that patients with small-vessel disease should be investigated for stroke risk factors and cognitive impairment.
- Access to interprofessional teams with the expertise to appropriately manage patients with vascular cognitive impairment across the continuum of stroke care and in the community.
- 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).
- Continuing professional education to ensure proficiency in assessment administration, interpretation and management of patients demonstrating post stroke and vascular cognitive impairment or at risk of vascular cognitive impairment

Performance Measures

1. **Percentage of patients with stroke or stroke risk factors who undergo a brief cognitive screening at each transition point along the continuum of stroke care (i.e., acute inpatient care, inpatient rehabilitation, outpatient clinics and programs, home-based services, and stroke prevention clinics) and in the community following inpatient discharge and at any time when there is a suspected change in cognitive status. (Core indicator)**
2. Percentage of patients with stroke who are referred for more in-depth cognitive or neuropsychological assessment throughout the continuum of stroke care (for example, during inpatient care, inpatient rehabilitation, outpatient and ambulatory clinics or programs (stroke prevention clinics) and/or following inpatient discharge to the community.
3. Percentage of change in cognition, e.g. Montreal Cognitive Assessment (MoCA) or other recommended measure scores at baseline and three months, six months and one year following initiation of therapy.
4. Percentage improvement in control of high blood pressure and other vascular risk factors in patients with vascular cognitive impairment.
5. Proportion of stroke patients diagnosed with VCI and according to cognitive domain at one month, 6 months and one year following stroke.

Measurement notes

- Recommendations for VCI and corresponding performance measures apply across the continuum of stroke care and should be considered in acute inpatient care, inpatient rehabilitation, outpatient clinics, home-based services, and stroke prevention clinics and/or following inpatient discharge to the community.
- When using these performance measures it is important to record when and in what context (continuum of care) the measurements were conducted. Data for measurement may be found through primary chart audit. Data quality will be dependent on the quality of documentation by healthcare professionals.
- Performance Measure 3: Change will occur due to natural recovery in the absence of therapy, so for this measure to be meaningful this should be considered, and when possible conduct a comparison of change due to natural recovery versus change due to therapy.
- This is a new area and will require a great deal of education for healthcare professionals especially in the area of documentation.

Implementation Resources and Knowledge Transfer Tools

Health Care Provider Information

- Table 2A: Diagnostic Criteria for Vascular Cognitive Impairment and Dementia
- Table 2B: Select Tools for the Screening and Initial Assessment for Vascular Cognitive Impairment in Stroke Patients
- Vascular Harmonization Guidelines http://stroke.ahajournals.org/content/37/9/2220.full
- Evidence-based Review of Cognitive Disorders and Apraxia (EBRSR): http://www.ebrsr.com/evidence-review/12-cognitive-disorders-and-apraxia
- Canadian Partnership for Stroke Recovery: http://www.canadianstroke.ca/
- AHA/ASA Scientific Statement on Vascular Contributions to Cognitive Impairment and Dementia http://stroke.ahajournals.org/content/early/2011/07/21/STR.0b013e3182299496
- Evidence- based Review of Post-Stroke Depression (EBRSR): http://www.ebrsr.com/evidence-review/18-post-stroke-depression
- NHS Psychological care after stroke: http://webarchive.nationalarchives.gov.uk/20130221101407/http://www.improvement.nhs.uk/stroke/NationalProjects1011/Psychologicaltherapy/tabid/177/Default.aspx
- Winnipeg Regional Health Authority Occupational Therapy Cognition Toolkit: http://www.wrha.mb.ca/professionals/cognition/index.php

Patient Information

- 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
- Your Stroke Journey: http://www.strokebestpractices.ca/wp-content/uploads/2015/03/YOURSTROKEJOURNEY.FINAL_.ENGLISH..pdf
- StrokeEngine http://strokengine.ca/
- Behaviour, thinking and memory: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.8566601/k.3748/Behaviour_thinking_and_memory.htm
- Changes in mood: Depression: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.8570109/k.41F2/Emotions_moods_and_relationships.htm
- The Heart & Stroke Living with Stroke™ program: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3936679/k.7231/Stroke__Living_with_StrokeTM_program.htm
- Let's Talk About Stroke http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3882223/k.3FC6/Stroke__Lets_Talk_about_Stroke.htm
- Canadian Partnership for Stroke Recovery - Life after Stroke: http://www.lifeafterstroke.ca
- Getting on With The Rest of Your Life After Stroke: http://strokebestpractices.ca/wp-content/uploads/2010/11/Getting-on-with-the-Rest-of-Your-Life-After-Stroke.pdf

- Coping with stress: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.5590155/k.3B4A/Heart_disease__Coping_with_stress.htm
- Post-Stroke Checklist: http://www.strokebestpractices.ca/wp-content/uploads/2014/06/HSF%20Post%20Stroke%20Checklist_WEB.pdf

Summary of the Evidence (2014 Version)

Vascular Cognitive Impairment Evidence Tables and Reference List (hyperlink)

It has been estimated that 5% of all people over the age of 65 years, in Canada, have evidence of vascular cognitive impairment (VCI). Vascular cognitive impairment refers to cognitive impairment due to all forms of cerebral vascular disease, including stroke, with severity that ranges from mild cognitive impairment to dementia (Gorelick et al., 2011, Rockwood et al. 2000). However, in individuals who have experienced stroke, reported VCI prevalence rates tend to be much greater, depending upon time post stroke, number of strokes and method of assessment, with values ranging from 61% in the acute phase (Hoffmann et al., 2001 to 21%-66% from 3 months to 14 years (e.g., Patel et al., 2003, Delgado et al, 2010, Douiri et al., 2013). While the risk for cognitive impairment is greater following stroke and, certainly, not all individuals with cognitive impairment have dementia, post-stroke cognitive impairment is associated with an increased risk for dementia.

Pendlebury and Rothwell (2009) conducted a systematic review and meta-analysis of 73 published studies examining prevalence and predictors of dementia in individuals with stroke. Overall, pooled prevalence of pre-stroke dementia was 14.4% in hospital-based cohorts (n=22) and 9.1% in community-based studies (n=8). Prevalence of post-stroke dementia ranged from 7.4% in population-based studies of individuals with first-ever stroke and no existing dementia to 41.3% in hospital-based studies of individuals with recurrent stroke (both with and without existing dementia). Rates of dementia were at least doubled following recurrent stroke when compared to first-ever stroke and were higher in hospital-based than in community-based studies. At 3- 6 months, post-stroke incidence of dementia was approximately 20%; this increased linearly at a rate of 3.0% in hospital-based studies of either first or recurrent stroke. Incidence rates were lower in population-based studies of first-ever stroke and when cases with recurrent stroke were excluded.

In the review by Pendlebury and Rothwell (2009), multivariate analyses were identified in 19 studies. From these 19 studies, the most commonly reported independent predictors of post-stroke dementia were older age, lower education level, previous stroke, diabetes, atrial fibrillation, pre-existing cognitive impairment and stroke severity. In summary, Pendlebury and Rothwell (2009) suggest that approximately 10% of patients have existing dementia at the time of stroke. An additional 10% develop new dementia shortly after a first-ever stroke while more than one-third of patients may experience dementia following a recurrent stroke. Recurrent stroke was identified as an important, and commonly cited, predictor of dementia. Gorelick (1997, 2004) reported on the risk factors for vascular dementia in 4 categories: demographic (older age, male sex, lower level of education), atherosclerotic (hypertension, smoking, myocardial infarction, diabetes, hyperlipidemia), genetic (cerebral autosomal dominant arteriopathy with subcortical infarct, leukoencephalopathy, apolipoprotein) and stroke-related (volume of cerebral tissue loss, evidence of bilateral cerebral infarction, strategic infarction, white matter disease).

Cognitive impairment following stroke has been associated with reduction in functional ability, and increased risk for depression (ebrsr.com). Individuals with cognitive impairments have greater functional impairment (Racic et al., 2011, Mok et al., 2004), increased dependency (Narasimhalu et al., 2011), show less clinical improvement (Cristea et al., 2006), and may require more therapy over longer periods of time (Zinn et al. 2004). In addition, the presence of executive dysfunction may have a negative impact on engagement in rehabilitation (Skidmore et al. 2010). A review by Leys et al. (2005) reported that higher

rates of mortality have also been found among patients with post stroke dementia in both community-based and hospital-based studies. Overall, mortality rates are reported to be 2 to 6 times higher among individuals with post stroke dementia after adjusting for demographic factors, associated cardiac disease, stroke severity and stroke recurrence (Leys et al. 2005).

At present, there is no 'gold standard' for the diagnosis of vascular cognitive impairment. However, it has been recommended that given the anticipated presence of attention and executive dysfunction in cases of vascular cognitive impairment post stroke, any assessment used to detect the presence of VCI be appropriate to the assessment of these domains. As part of the development of the Canadian Stroke Network vascular cognitive impairment harmonization standards, Hachinski et al. (2006) outlined an assessment approach that provided recommended tests for a 5-min, 30-min or 60-minute testing protocol for the screening and assessment of VCI. The 5-minute and 30-minute testing protocols were intended for initial VCI screening (see Table 3 in Hachinski et al., 2006), while the 60 minute battery (Table 2) was provided to allow a breakdown of abilities by domain when needed for rehabilitation or other assessment purposes. Psychometric properties of the recommended tests are reviewed in Hachinski et al., 2006 and further information on screening tests used in stroke populations can be found in Table 2B of these guidelines. More research on the sensitivity and specificity of these protocols in screening for VCI is needed. Overall, the Montreal Cognitive Assessment (MoCA) test appears more sensitive to the presence of VCI compared to the Mini Mental State Examination (MMSE), particularly with mild deficits (e.g., Pendlebury et al., 2012, Godefroy et al., 2011, Toglia et al., 2011, Dong et al., 2010), although equivalence has been noted in other studies, notably with patients of moderate to severe strokes (Dong et al., 2012). Inclusion of the Mini Mental Status Examination in the initial 5-minute Harmonization protocol was rejected, as it does not provide adequate assessment of executive function and is insensitive to mild memory impairment (Hachinski et al. 2006).

Cognitive rehabilitation interventions for VCI within the stroke population, focusing on common deficits of attention, memory or executive function are limited, but growing. In general, interventions may be considered to have one of two objectives: 1) to reinforce or re-establish previous behavioural skills or function (e.g., to remediate with computerized exercises) or 2) to teach compensatory mechanisms (e.g., strategy training) that may be either internal or external to the individual (Cicerone 2000, 2005). Systematic reviews of cognitive rehabilitation interventions conducted by Cicerone et al. (2000, 2005) and updated in 2011, reported effect sizes for cognitive interventions in attention, visuospatial, language, memory and comprehensive training. Studies of attention or executive function, memory or comprehensive cognitive function were focused more often on individuals with TBI or other brain injury. Although generally positive results have been reported for studies examining the use of attention training, memory strategy training, use of mnemonic devices (e.g. personal pagers), and problem-solving training for study participants who have experienced brain injury (including stroke) evidence from randomized controlled trials specific to the stroke population was more limited (Cicerone et al, 2011; ebrsr.com). More recently, a systematic review by Cha & Kim, 2013 of the efficacy of computer-based cognitive rehabilitation revealed an overall effect size of 0.54 (medium effect), with no difference in acute or chronic stroke patients. Likewise, a recent Cochrane review (Loetscher & Lincoln, 2013) of attention rehabilitation (using various approaches) in stroke reported a significant treatment effect on specific, but not global, attention function, but with no evidence for impact on activities of daily living. In contrast, memory self-efficacy training was reported to improve subjective daily memory reports and quality of life in one RCT with 153 stroke patients in the chronic phase of stroke (Aben et al., 2013). Cicerone et al., 2011 also recommend use of external aids to improve function directly (e.g., alarms, pagers, notebooks) for severe memory impairment following stroke or TBI. In terms of executive dysfunction, while several small studies have reported benefits of meta-cognitive strategy training (Skidmore et al., 2014), goal management training (Levine et al., 2011) and problem solving skill training (Man et al., 2006) in stroke, recent reviews highlight the lack of strong evidence for these interventions at this time (Chung et al., 2013, Poulin et al, 2012).

Finally, physical exercise may also be beneficial for cognitive impairment post stroke as seen in a recent systematic review by Cumming et al., 2012. On the basis of 9 trials investigating the effect of exercise on cognition in stroke patients, they reported a significant, but small, pooled treatment effect (standardized mean difference = 0.2, 95%, CI 0.04 to 0.36, p=0.015).

Pharmacotherapy

Cholinergic agents have been used in the treatment of dementia of the Alzheimer's type. Three such agents, donepezil, rivastigmine and galantamine, have also been investigated for use in the treatment of vascular dementia. Donepezil, a selective acetylcholinesterase inhibitor, has been the subject of 3 large randomized controlled trials (Black et al. 2003, Wilkinson et al. 2003, Roman et al. 2010). A meta-analysis of the first 2 trials demonstrated significant improvements in cognitive and global function, including improvements in the performance of activities of daily living associated with use of donepezil in the treatment of patients with mild to moderate vascular dementia (Passmore et al. 2005). The most recent trial also reported significant improvement in cognitive outcomes associated with treatment (Roman et al. 2010).

In randomized controlled trials, benefits on global function and functional status were not always congruent with benefits on cognition. A study of Vascular Dementia, which include pure and mixed cases showed beneficial effects in both cognition and function, but this was driven by the mixed Alzheimer and vascular cases. The pure Vascular Dementia subgroup showed only modest effects (Erkinjuntti, Lancet 2002, Craig Cochrane review, 2006). There was an attempt to replicate the study in pure Vascular Dementia, but only modest efficacy was shown for the cognitive measure and not for functional outcomes (Auchus, Neurology 2007).

Children and Vascular Cognitive Impairment

Cognitive outcomes for children with stroke must be considered differently. Covert VCI is not a common issue except in select disease states (moyamoya, sickle-cell, small vessel vasculitis). Most importantly, cognitive outcomes must be considered within the context of constantly evolving neurodevelopment. Thus, outcomes must use developmentally and age-appropriate outcome measures. Deficits in cognition and higher brain functions may not be evident until the relevant stage of development is reached, whereby young children "grow into" their deficits over time.[Westmacott *et al.* 2007a;Westmacott *et al.* 2009]

About 1 in 3 children with stroke have cognitive deficits at outcome, limiting academic, social, and independent functional success [Friefeld *et al.* 2004;Nass and Trauner 2004](Carr L 2011). Adverse cognitive outcomes from childhood cerebral sinus venous thrombosis (CSVT) [Wasay *et al.* 2008;deVeber *et al.* 2001;Moharir *et al.* 2010;Berfelo *et al.* 2010] and hemorrhagic stroke [Blom *et al.* 2003;Meyer-Heim and Boltshauser 2003] are also common. Overall cognitive function including intelligence, verbal ability, working memory, and processing speed are lower than average in children with stroke. (Westmacott, 2009), [Hetherington *et al.* 2005; McLinden *et al.* 2007] [Max 2004; Lansing *et al.* 2004].

Post-stroke psychiatric/behavioural disorders also appear to be common in childhood stroke (Max, 2002; Elbers 2013). Difficulties with social and behavioral development are also increased in children after stroke with secondary impact on parental mental health (De Schryver, 2002; Goodman, 2000). Limited studies suggest that social function is commonly impaired following stroke in childhood [Mosch *et al.* 2005]. Rates of potentially treatable Attention Deficit Hyperactivity Disorder (ADHD) are increased [Max *et al.* 2002;Max *et al.* 2003;Max *et al.* 2004], particularly with lesions involving the putamen [Teicher *et al.* 2000].

Contradicting the idea that the immature brain may be more plastic with a greater capacity for recovery, a younger age at stroke onset may be associated with worse cognitive and behavioural outcomes. (Westmacott, 2009; Everts, 2008)[Stiles 2000;Lansing, Max, Delis, Fox, Lancaster, Manes, and Schatz2004;Westmacott *et al.* 2007b]. There is also evidence for late emergence of cognitive deficits after perinatal stroke, with IQ measured in the preschool period higher than that measured later.(Westmacott, 2011) About one third of childhood stroke survivors require specialized education (Delsing, 2001). Regular, age-appropriate neuropsychological evaluations should be considered in all at-risk children to determine educational and support needs.

TABLE 2A: DIAGNOSTIC CRITERIA FOR VASCULAR COGNITIVE IMPAIRMENT AND DEMENTIA (GORELICK ET AL, 2011)

1. The term *VCI* characterizes all forms of cognitive deficits from Vascular Dementia (VaD) to Mild Cognitive Impairment (MCI) of vascular origin
2. These criteria cannot be used for subjects who have an active diagnosis of drug or alcohol abuse/dependence. Subjects must be free of any type of substance for at least 3 months.
3. These criteria cannot be used for subjects with delirium.

Dementia

1. The diagnosis of dementia should be based on a decline in cognitive function from a prior baseline and a deficit in performance in 2 cognitive domains that are of sufficient severity to affect the subject's activities of daily living.
2. The diagnosis of dementia must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions.
3. The deficits in activities of daily living are independent of the motor/sensory sequelae of the vascular event.

Probable Vascular Dementia (VaD)

1. There is cognitive impairment and imaging evidence of cerebrovascular disease and
    a. There is a clear temporal relationship between a vascular event (e.g., clinical stroke) and onset of cognitive deficits, or
    b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (e.g., as in CADASIL).
2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder.

Possible Vascular Dementia (VaD)

There is cognitive impairment and imaging evidence of cerebrovascular disease but

1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (e.g., silent infarcts, subcortical small-vessel disease) and the cognitive impairment.
2. There is insufficient information for the diagnosis of VaD (e.g., clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available).
3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (e.g., annual cognitive evaluations) before the clinical event that caused aphasia *could* be classified as having probable VaD.
4. There is evidence of other neurodegenerative diseases or conditions in addition to cerebrovascular disease that may affect cognition, such as
    a. A history of other neurodegenerative disorders (e.g., Parkinson disease, progressive supranuclear palsy, dementia with Lewy bodies);

b. The presence of Alzheimer disease biology is confirmed by biomarkers (e.g., PET, CSF, amyloid ligands) or genetic studies (e.g., *PS1* mutation); or

c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function.

Vascular Mild Cognitive Impairment (VaMCI)

1. VaMCI includes the 4 subtypes proposed for the classification of MCI: amnestic, amnestic plus other domains, nonamnestic single domain, and nonamnestic multiple domain.
2. The classification of VaMCI must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions. The classification should be based on an assumption of decline in cognitive function from a prior baseline and impairment in at least 1 cognitive domain.
3. Instrumental activities of daily living could be normal or mildly impaired, independent of the presence of motor/sensory symptoms.

Probable Vascular Mild Cognitive Impairment (VaMCI)

1. There is cognitive impairment and imaging evidence of cerebrovascular disease and
    a. There is a clear temporal relationship between a vascular event (e.g., clinical stroke) and onset of cognitive deficits, or
    b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (e.g., as in CADASIL).
2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder.

Possible Vascular Mild Cognitive Impairment (VaMCI)

There is cognitive impairment and imaging evidence of cerebrovascular disease but

1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (e.g., silent infarcts, subcortical small-vessel disease) and onset of cognitive deficits.
2. There is insufficient information for the diagnosis of VaMCI (e.g., clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available).
3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (e.g., annual cognitive evaluations) before the clinical event that caused aphasia *could* be classified as having probable VaMCI.
4. There is evidence of other neurodegenerative diseases or conditions in addition to cerebrovascular disease that may affect cognition, such as
    a. A history of other neurodegenerative disorders (e.g., Parkinson disease, progressive supranuclear palsy, dementia with Lewy bodies);
    b. The presence of Alzheimer disease biology is confirmed by biomarkers (e.g., PET, CSF, amyloid ligands) or genetic studies (e.g., *PS1* mutation); or
    c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function.

Unstable Vascular Mild Cognitive Impairment (VaMCI)

1. Subjects with the diagnosis of probable or possible VaMCI whose symptoms revert to normal should be classified as having “unstable VaMCI.”

Notes: VCI indicates vascular cognitive impairment; VaD, vascular dementia; MCI, mild cognitive impairment; CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CT/MRI, computed tomography/magnetic resonance imaging; PET, positron emission tomography; CSF, cerebrospinal fluid; and VaMCI, vascular mild cognitive impairment.

Additional Diagnostic Criteria:

- Refer to the American Psychological Association *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) for Updated Criteria for Classification of Vascular Dementia (available at http://www.dsm5.org/Pages/Default.aspx).

- Also see: Perminder S. Sachdev, Deborah Blacker, Dan G. Blazer, Mary Ganguli, Dilip V. Jeste, Jane S. Paulsen, Ronald C. Petersen. Classifying neurocognitive disorders: the DSM-5 approach. *Nature Reviews Neurology, 2014;* 10:634–642.
  Available at http://www.pubfacts.com/fulltext_frame.php?PMID=25266297&title=Classifying neurocognitive disorders: the DSM-5 approach.

Table 2B: Summary of Select Screening and Initial Assessment tools for vascular cognitive impairment in stroke patients (Updated 2014)

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
Recommended First Line Screening and Assessment Tools					
Montreal Cognitive Assessment Tool (MoCA) The MoCA is available for free in several languages for educational and clinical purposes at: http://www.mocatest.org/ http://strokengine.ca/assess/module_moca_intro-en.html	Designed as a rapid screen for mild cognitive impairment	**Content:** The items of the MoCA examine attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation **Population:** Can be used in patients with stroke and any individual who is experiencing memory difficulties but scores within the normal range on the MMSE	5-10 minutes	**Reliability:** The MoCA has been demonstrated to have high internal consistency in patients with stroke or vascular dementia in at least 3 studies with Cronbach alpha scores > 0.75 (Cumming et al., 2011; Toglia et al., 2011; Freitas et al., 2012) **Validity:** Convergent: Strong correlations with the Mini Mental State Examination (MMSE) have been reported (e.g. Freitas et al., 2012) Construct: Known groups. One study reported that the MoCA can distinguish between patients with mild cognitive impairment and healthy controls.	**Sensitivity:** Many studies of the MoCA in patients with stroke or vascular dementia report high sensitivity (with most values > 80%) (e.g. Wong et al., 2013; Dong et al., 2012; Freitas et al., 2012; Pendlebury et al., 2012) . However, the optimal cutoff reported varies between studies and ranges from 17 (Freitas et al., 2012) to the standard cutoff of 26. **Specificity:** Most studies report lower specificity for the MoCA (specifically compared to the MMSE), however this ranges from 35% (Luis et al., 2009) to 97% (Freitas et al., 2012) depending on the population and cutoffs used.
NINDS-CSN Harmonization VCI Neuropsychology Protocols Black SE, Ganda A, Gao F, Gibson E, Graham S, Honjo K, Lobaugh NJ,	Designed to measure vascular cognitive impairment in stroke patients	**Content:** Three different versions: 60 Minute - executive/activation function, visuospatial, language/lexical retrieval, memory and learning, and neuropsychiatric/depressive symptoms.	60, 30, or 5 minute versions available	**Validity:** All three versions of the NINDS-CSN translated to Chinese were tested in a group of ischemic stroke patients and controls (Wong et al., 2013). All protocols differentiated patients from controls (area under ROC for the three protocols between 0.77 to 0.79, $p<0.001$), and significantly correlated with the functional measures (Pearson r ranged from 0.37 to 0.51). A cut-off of 19/20 on MMSE identified only one-	

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
Marola J, Pedelty L, Rangwala N, Scott CJ, Stebbins GT, Stuss DT, Zhou XJ, Nyenhuis D. Validation of the NINDS-CSN harmonization VCI neuropsychology protocols in an ischemic stroke sample. Stroke, 2011;42:e586-e629.		30 Minute - semantic and phonemic fluency, Digit Symbol-Coding, revised Hopkins Verbal Learning Test, CES-D, and Neuropsychiatric Inventory. 5 Minute - subtests from the Montreal Cognitive Assessment, including a 5-word immediate and delayed memory test, a 6-item orientation task and a 1-letter phonemic fluency test (F). **Population:** Patients with stroke		tenth of patients classified as impaired on the 5-min protocol. Cronbach's α across the four cognitive domains of the 60-min protocol was 0.78 for all subjects and 0.76 for stroke patients.	
Additional Screening and Assessment Tools for Vascular Cognitive Impairment and Dementia					
Cognitive- Functional Independence Measure (Cognitive- FIM) http://www.strokengine.ca/assess/fim/ http://www.rehabmeasures.org/Lists/RehabMeasures/DispForm.aspx?ID=889	Designed to offer a uniform system of measurement for disability based on the International Classification of Impairment, Disabilities and Handicaps.	**Content:** 5 cognitive items: comprehension, expression, social interaction, problem solving, and memory. The level of a patient's disability indicates the burden of caring for them and items are scored on the basis of how much assistance is required for the individual to carry out activities of daily living. **Population**: Patients with stroke, traumatic brain injury, spinal cord injury, multiple sclerosis,	30-45 minutes to administer the full test (Motor and Cognitive)	**Reliability:** In a review of 11 studies, Ottenbacher et al., 1996 reported a mean inter-observer reliability value of 0.95; a median test-retest reliability of 0.95 and a median equivalence reliability (across versions) of 0.92. Reliability was higher for items in the motor domain than for those in the social/cognitive domain. Internal consistency: - alpha of 0.93 – 0.95 reported at admission vs. discharge (Dodds et al. 1993); alpha = 0.88 to 0.91(Hsueh et al. 2002); Hobart et al. (2001) reported item-to-total correlations ranging from 0.53 to 0.87 for FIM total, 0.60 for FIM motor and 0.63 cognitive FIM – mean inter-item correlations were 0.51 for FIM, 0.56 – 0.91 for motor FIM and 0.72 – 0.80 for cognitive FIM, alpha = 0.95, 0.95 and 0.89	

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
		and elderly individuals undergoing inpatient rehabilitation. Has been used with children as young as 7 years old.		for FIM, motor FIM and cognitive FIM respectively. **Validity:** Content: The FIM was created based on a literature review of measures and expert panels and was piloted in 11 centers. The Delphi method was applied, using rehabilitation expert opinion to establish the inclusiveness and appropriateness of the items. Criterion: Excellent correlations with the BI; MRS; DRS. FIM scores predict home care required; admission scores many functional outcomes. Construct: FIM scores discriminated between groups based on spinal cord injury and stroke severity, and the presence of comorbid illness both at admission and discharge. Concurrent. Found to have an excellent correlation with the DRS; adequate correlation with the Montebello Rehabilitation Factor Score (MRFS) (efficacy); and a poor correlation with the MRFS (efficiency). Convergent/Discriminant. The Cognition-FIM was found to demonstrate an excellent correlation with the MMSE; adequate correlation with the Lowenstein Occupational Therapy Cognitive Assessment (LOTCA), Office of Population Censuses and Surveys Disability scores, and the revised Wechsler Adult Intelligence Test-verbal IQ; and a poor correlation with the London Handicap Scale, SF-36 Physical and Mental components, and the General Health Questionnaire.	

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
				Ecological: The Cognition-FIM demonstrated adequate correlations with the OT-APST.	
Cambridge Cognition Examination (CAMCOG) The CAMCOG can be obtained by purchasing the entire CAMDEX from the Cambridge University Department of Psychiatry http://strokengine.ca/assess/module_camcog_intro-en.html	Designed to be a standardized assessment instrument for diagnosis and grading of dementia	**Content:** The CAMCOG consists of 67 items. It is divided into 8 subscales: orientation, language (comprehension and expression), memory (remote, recent and learning), attention, praxis, calculation, abstraction and perception. R-CAMCOG was developed as a shortened version of the original CAMCOG. **Population:** The CAMCOG can be used with, but is not limited to clients with stroke.	Original CAMCOG: 20 to 30 minutes R-CAMCOG: 10 minutes	**Reliability:** No studies have examined the internal consistency of the CAMCOG in clients with stroke. No studies have examined the reliability of the CAMCOG in clients with stroke. **Validity:** Predictive Validity. At least 6 studies have examined the predictive validity of the CAMCOG and reported that the CAMCOG can be predicted by age, the R-CAMCOG, the MMSE and cognitive and emotional impairments. Additionally, the CAMCOG was an excellent predictor of dementia 3 to 9 months post-stroke (de Koning et al., 1998). Another study demonstrated one year post stroke, the CAMCOG dimensions of orientation (b = – 0.21), Perception (b = – 0.16) and Memory (b = – 0.16), were significant predictors of health status (Verhoeven et al., 2011) Convergent validity: Excellent correlations have been reported between the CAMCOG and the R-CAMCOG and the MMSE shortly after and 1 year post-stroke. Correlations between the CAMCOG and the FIM Measure range from adequate after stroke to poor at 1 year post-stroke (Winkel-Witlox et al., 2008). Correlations have also been demonstrated with the Raven's Test and Weigl Test (0.59, 0.65) (Leeds et al., 2001)	**Sensitivity & Specificity:** The CAMCOG has been demonstrated to be a more accurate screening tool than the MMSE (area under the curve for CAMCOG, 0.95; for MMSE, 0.90) (de Koning et al., 1998) The diagnostic accuracy at the pre-specified cut-off point for the R-CAMCOG of 33/ 34 was established through receiver operating characteristic (ROC) analyses (sensitivity 66%, specificity 94%). At a cut-off point of 36/37 sensitivity would be 83% and specificity 78% (de Koning et al., 2005). .
Frontal Assessment Battery Dubois, B. ; Litvan, I.; The FAB: A frontal assessment battery at	Designed to be a brief tool to be used at the bedside or in a clinic setting to	**Content:** conceptualization, mental flexibility, programming, sensitivity to interference, inhibitory control, and environmental autonomy	~ 10 minutes	**Reliability**: Chinese FAB: In stroke patients with small sub-cortical infarct (Mok et al., 2004), the CFAB had low to good correlation with various executive measures: MDRS I/P ($r = 0.63$, $p < 0.001$), number of category completed ($r = 0.45$, $p < 0.001$), and number	

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
bedside. Neurology. 55(11): 1621-1626, 2000. http://www.docstoc.com/docs/46935262/Frontal-Assessment-Battery---Content_-instructions_-and-scoring Oguro, H., Yamaguchi, S., Abe, S., Ishida, Y., Bokura, H., & Kobayashi, S. (2006). Differentiating Alzheimer's disease from subcortical vascular dementia with the FAB test. *Journal of neurology*, *253*(11), 1490-1494.	discriminate between dementias with a frontal dysexecutive phenotype and Dementia of Alzheimer's Type (DAT).			of preservative errors ($r = -0.37$, $p < 0.01$) of WCST. Among the executive measures, only number of category completed had significant but small contribution (6.5%, $p = 0.001$) to the variance of CFAB. A short version of CFAB using three items yielded higher overall classification accuracy (86.6%) than that of CFAB full version (80.6%) and MMSE (77.6%). In another test, which compared the Chinese FAB to the Mattis Dementia Rating Scale Initiation/Perseveration subset: Both tests showed comparably good ability in Receiver Operating Characteristics curves analysis (AUCMDRS I/P = 0.887; AUC FAB = 0.854, $p = .833$) in discriminating between controls and patients and correctly classified over 78% of subjects. Verbal fluency and motor programming contributed most to the discriminating power in the two tests. Validity: Chinese FAB: Internal consistency (alpha = 0.77), test-retest reliability (rho = 0.89, $p < 0.001$), and inter-rater reliability (rho = 0.85, $p < 0.001$) of CFAB were good (Mok et al., 2004)	
Mini-Mental State Exam (MMSE) http://strokengine.ca/assess/module_mmse_intro-en.html	Designed to screen for cognitive impairment .	**Content:** The MMSE consists of 11 simple questions or tasks that look at various functions including: arithmetic, memory and orientation. **Population:** Population While originally used to detect dementia within a psychiatric setting, its use is now widespread and is available with an attached table that	~ 10 minutes	**Reliability:** Out of 9 studies examining the internal consistency of the MMSE, 3 reported poor internal consistency, 1 reported adequate internal consistency, 2 reported poor to excellent internal consistency, 2 reported excellent internal consistency, 1 reported excellent internal consistency in patients with Alzheimer's Disease and poor internal consistency in patients with cognitive impairment. Out of 6 studies examining the test-rest reliability of the MMSE, 2 studies reported excellent test-rest, 1 reported adequate test-retest, 1 reported adequate to excellent test. retest, 1 reported poor to	

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
		enables patient-specific norms		adequate test-rest, 1 reported poor test-retest. Out of 3 studies examining the inter-rater reliability of the MMSE, 1 reported excellent inter-rater, 2 reported adequate inter-rater. **Validity:** Criterion: The MMSE can discriminate between patients with Alzheimer's Disease and frontotemporal dementia; can discriminate between patients with left- and right-hemispheric stroke. Construct: Concurrent. MMSE had a poor correlation with the Mattis Dementia Rating Scale; poor to excellent correlations with the Wechsler Adult Intelligence Test; adequate correlation with the FIM; significant correlations with the Montgomery Asberg Depression Rating Scale and the Zung Depression Scale. Predictive. MMSE scores found to be predictive of functional improvement in patients with stroke following rehabilitation; discharge destination; developing functional dependence at a 3-year follow-up interval; ambulatory level; length of hospital stay such that for patients with moderate dementia; death. Floor/Ceiling effects: Folstein, Folsten, and McHugh (1998) reported that the MMSE demonstrates marked ceiling effects in younger intact individuals and marked floor effects in individuals with moderate to severe cognitive impairment.	
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) http://www.pearsonclinic	Designed to be a brief neurocognitive battery with four alternate forms	**Content:** The content of the RBANS consists of neurocognitive test paradigms including tests for: immediate memory, visuospatial/construction	25 min	**Reliability:** NA in a stroke population **Validity:** Construct validity: Supported by strong convergent validity demonstrated for the Language, Visuospatial/Constructional,	Sensitivity & Specificity: In a group of participants with Subcortical Vascular Dementia, RBANS found to have higher specificity (subtest range: 76.9 –

Assessment Tool and Reference	Purpose	Content & Population	Length of Test	Reliability & Validity	Sensitivity & Specificity
al.com/psychology/products/100000726/repeatable-battery-for-the-assessment-of-neuropsychological-status-update-rbans-update.html Wagle, J., Farner, L., Flekkøy, K., Bruun Wyller, T., Sandvik, L., Fure, B., ... & Engedal, K. (2011). Early post-stroke cognition in stroke rehabilitation patients predicts functional outcome at 13 months. *Dementia and geriatric cognitive disorders*, *31*(5), 379-387.		al, language, attention, and delayed memory. **Population:** Not specific		Immediate Memory and Delayed Memory indexes in individuals with stroke (Larson, 2005). Attention index did not demonstrate significant convergent validity. Discriminant Validity: Challenged by the finding that the RBANS Attention, Visuospatial/Constructional and Immediate Memory indices correlate with several measures of language ability in individuals post stroke (Larson, 2005). Further challenged by the finding that the RBANS had difficulty differentiating between Alzheimer's Disease and Subcortical Vascular Dementia (McDermott & DeFilippis, 2010)	92.3%) than sensitivity (subtest range: 48.3 – 62.1%) (McDermott & DeFilippis, 2010).

NOTE: Patient factors such as communication challenges should be taken into account during screening and assessment. Refer to Recommendation 2.3A for additional information.

3. Post Stroke Fatigue

Mood, Cognition and Fatigue **3. Post-Stroke Fatigue**
Update 2014

3.0 Post-stroke fatigue is a common condition, and can be experienced after TIA and 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 patients and families to mitigate fatigue through assessment, education, and interventions at any point during the stroke-recovery continuum.

3.1 Screening and Assessment

ii. Stroke and TIA survivors should be routinely asked about post-stroke fatigue during healthcare visits (e.g., primary care, home care, and outpatient) following return to the community and at transition points [Evidence Level C].

i. Prior to discharge from hospital ward, stroke unit or the emergency department, stroke survivors, their families and informal caregivers should be provided with basic information regarding the frequency and experience of post-stroke fatigue [Evidence Level B].

a. Post-stroke fatigue experience includes:

- Overwhelming tiredness and lack of energy to perform daily activities
- Abnormal need for extended sleep
- More easily tired by activities than pre-stroke and abnormal need for naps or rest
- Unpredictable feelings of fatigue without apparent reason

iii. Stroke survivors 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, including [Evidence Level B].

a. Signs of depression or other mood-related conditions
b. Sleep disorders or factors that decrease quality of sleep (e.g. sleep apnea, pain)
c. Other common post-stroke medical conditions and medications that increase fatigue, e.g. systemic infection such as UTI, dehydration, sedating drugs.

3.2 Management of Post-Stroke Fatigue

i. Management strategies for post-stroke fatigue can vary, and are not mutually exclusive, due to the potential multifactorial nature of post-stroke fatigue. In addition to education of both patient and caregivers about post-stroke fatigue, and treatment of any co-morbid condition that could cause/exacerbate fatigue (as above), strategies can include the following categories:

a. Strategies for energy conservation and fatigue management that take into account optimizing daily function in high priority activities (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 techniques.*
b. Engaging in planned exercise schedules with increasing physical demands appropriate to tolerance level to improve deconditioning and physical tolerance [Evidence Level C].
c. Education in, and establishment of good sleep hygiene behaviours [Evidence Level B]); *Refer to Prevention of Stroke module Section 10 on Sleep Apnea for more information.*
d. Communicating energy status and rest needs to family members, caregivers,

employers and social groups [Evidence Level C].

ii. Stroke patients should be cared for by healthcare professionals who are knowledgeable in the symptoms of fatigue and its management. [Evidence Level C].

iii. There is insufficient evidence to recommend specific pharmacological treatment for post-stroke fatigue at this time [Evidence Level B].

Box 3: Examples of More Specific Energy Conservation Strategies

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

- Structuring 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 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 patients to use appropriate body mechanics, posture and sitting positions and locations (i.e. rest in bed, rather than 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 stroke survivor 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 patients who have experienced a stroke. However, symptoms of fatigue are often reported by patients in both the acute and chronic stages of recovery following a stroke. Prevalence rates of post stroke fatigue (HSF) 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 stroke patient 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 patient's ability to actively participate in rehabilitation, which has been associated with poorer long-term outcomes. Therefore, new recommendation shave been added to the Canadian Stroke Best Practice Recommendations to raise awareness of the frequency of post-stroke fatigue, the physical and emotional impact of PSF on patients and the negative impact on recovery and outcomes.

System Implications

i. Protocols for the inclusion of post-stroke fatigue in patient screening and assessments at all transition points and stages of care following a stroke.

ii. 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).

iii. 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.
iv. Education and increased awareness about post-stroke fatigue and management strategies for patients, caregivers, employers and health care professionals.

Performance Measures

1. The number and proportion of patients who report symptoms of post-stroke fatigue, measured at each transition point as a proportion of all stroke patients.
2. The proportion of stroke patients 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

- CSBPR Summary Table: Tools to Assess Participation, QoL and Fatigue (Transitions of Care module)
- Multidimensional Fatigue Symptom Inventory: http://www.cas.usf.edu/~jacobsen/HANDOUT.FSI&MFSI.pdf
- Fatigue severity scale: http://www.healthywomen.org/sites/default/files/FatigueSeverityScale.pdf

Patient Information

- 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
- Your Stroke Journey: http://www.strokebestpractices.ca/wp-content/uploads/2015/03/YOURSTROKEJOURNEY.FINAL_.ENGLISH..pdf
- Fatigue After Stroke: http://www.stroke.org.uk/sites/default/files/Fatigue%20after%20stroke.pdf
- Fatigue http://www.stroke.org.uk/about/fatigue
- Fatigue http://www.stroke.org/site/PageServer?pagename=fatigue
- Lets Talk About Feeling Tired After Stroke: http://www.strokeassociation.org/idc/groups/stroke-public/@wcm/@hcm/documents/downloadable/ucm_309719.pdf
- Activity Journal: http://www.cdc.gov/healthyweight/pdf/physical_activity_diary_cdc.pdf
- Post-Stroke Checklist: http://www.strokebestpractices.ca/wp-content/uploads/2014/06/HSF%20Post%20Stroke%20Checklist_WEB.pdf

Summary of the Evidence

Post-Stroke Fatigue Evidence Tables and Reference List (hyperlink)

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 post-stroke fatigue 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 6 months and 1 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 1 year, 29.3% were also depressed. Van der Port et al. (2007) reported that the percentages of patients considered fatigued at 6, 12 and 36 months were 68%, 74% and 58%, respectively, in 223 acute stroke patients followed prospectively. In all of these studies, the presence of fatigue was identified based on a score of 4 or greater 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, 10% and 29.2% of respondents reported “always” or “often” being tired (Glader et al. 2002) in a postal survey. 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 2 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 9 studies, the percentage of patients reporting fatigue increased from assessment time 1 to time 2, while it had decreased between assessment points in 2 studies. Independent predictors of fatigue that have been identified include depression, low levels of physical functioning, and pre-stroke fatigue (Lerdal et al. 2011). Predictors of fatigue are somewhat unclear as 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 (Gladder et al. 2002) sex.

A few controlled studies have been conducted comparing fatigue in persons recovering from stroke with persons from the general population and in cases of TIA. When compared with 1,069 person 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 5 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 3 months (Christensen et al. 2008). Winward et al. (2009) compared 73 subjects with minor stroke and 76 subjects with TIA who were participants in the Oxford Vascular study. At 6 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 TIAs 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 (McGeough et al. 2009) included the results from 3 RCTs, each examining different therapy approaches. The results from all 3 were equivocal. In one trial, 83 subjects 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 3 months (Choi-Kwon et al. 2007). At the end of treatment, there were no significant differences in the number of patients with PSF. At 6 months, 34 patients (85%) in the fluoxetine group reported PSF compared with 40 (93%) in the control group. However, at 3 months, fewer patients in the fluoxetine group reported excessive/inappropriate crying (n=16, 40% vs. n=27, 62.8%, p=0.038), and at 6 months fewer patients in the fluoxetine group were identified with depression (n=5, 12.5% vs. n=13,

30.2%, p=0.05). In another trial, 831 participants with a variety of chronic disease conditions who may or may not have suffered from fatigue at study entry were randomized to participate in a 6-month chronic disease self-management program (CDSMP) immediately after randomization, or after a 6 month delay (Lorig et al. 2001). The program was provided over 7 weeks, for 2.5 hours weekly. The authors acquired data reporting on the subset of 125 patients with stroke in the trial. The mean fatigue scale change scores (1-5) at 6 months were 0.246 for controls and 0.087 for those who received the active treatment condition, indicating that fatigue became worse for wait list controls, although the difference was not significant (p=0.253). Finally, in the third study, 31 women in the acute stage of SAH who may or may not have suffered from fatigue were randomized to receive tirilazad mesylate vs. placebo for 10 consecutive days. In women who survived and could be assessed for fatigue at 3 months, significantly fewer patients in the intervention group reported debilitating fatigue (4/9 vs. 9/9, p<0.01).

Two RCTs that evaluated therapy programs designed specifically to treat fatigue following stroke 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 2-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 8-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.