



A pan-Canadian practice guideline and algorithm: screening, assessment, and supportive care of adults with cancer-related fatigue

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ABSTRACT

Purpose

The purpose of the present systematic review was to develop a practice guideline to inform health care providers about screening, assessment, and effective management of cancer-related fatigue (CRF) in adults.

Methods

The internationally endorsed ADAPTE methodology was used to develop a practice guideline for pan-Canadian use. A systematic search of the literature identified a broad range of evidence: clinical practice guidelines, systematic reviews, and other guidance documents on the screening, assessment, and management of CRF. The search included MEDLINE, EMBASE, CINAHL, the Cochrane Library, and other guideline and data sources to December 2009.

Results

Two clinical practice guidelines were identified for adaptation. Seven guidance documents and four systematic reviews also provided supplementary evidence to inform guideline recommendations. Health professionals across Canada provided expert feedback on the adapted recommendations in the practice guideline and algorithm through a participatory external review process.

Conclusions

Practice guidelines can facilitate the adoption of evidence-based assessment and interventions for adult cancer patients experiencing fatigue. Development of an algorithm to guide decision-making in practice may also foster the uptake of a guideline into routine care.

KEY WORDS

Fatigue, cancer, survivor, survivorship, screening, assessment, supportive care, adapted guideline

1. INTRODUCTION

Cancer-related fatigue (CRF) can be experienced at all phases of the disease trajectory. Prevalence rates for CRF are reported to range from 70% to 100% during active treatment and to be about 30% in post-treatment survivors^{1–5}. Although definitions of CRF vary, elements include a subjective feeling of tiredness or exhaustion, prompted by cancer or treatment and disproportionate to the level of recent exertion, that is not relieved by rest and that interferes with usual daily activities^{6,7}. Cancer-related fatigue is differentiated from fatigue experienced in the daily life of the general adult population⁶. For most, CRF is the most distressing side effect of cancer—more distressing than pain or nausea—and it causes significant disruption of normal functioning^{8–10}. Because CRF interferes with daily living and personal and social roles within family and community, it has a negative effect on quality of life^{8–10}.

The causes of CRF are multifactorial, arising from a complex interplay of physical, psychological, environmental, physiologic, and pathologic factors^{11–13}. Disease and treatment factors (for example, anemia as a side effect of cancer treatment), comorbid conditions, and inflammatory cytokines contribute to fatigue occurrence^{11–13}. Other factors may include poor nutrition, deconditioning¹³, and interrelationships with other symptoms that cluster with fatigue, such as insomnia, pain, and depression^{14,15}. Despite CRF being a devastating symptom, it remains a largely unrecognized and poorly managed problem for cancer patients and survivors^{6–8,10,16}. Routine screening and assessment are essential so that best practices for management of fatigue can be initiated early in the course of treatment to minimize negative effects^{6–8}.

In spite of the multifactorial nature of CRF, a body of evidence is available to guide health professionals in the assessment and management of fatigue. Use of the best evidence is a fundamental aspect of quality health care, and valid clinical practice guidelines are an important tool to inform evidence-based practice¹⁷. The purpose of the present paper was to summarize, for pan-Canadian use in routine supportive care, the adaptation of evidence for a clinical practice guideline and algorithm for the screening, assessment, and management of CRF in adults.

The specific question that guided the literature search and development of the practice recommendations was this: What are the optimal assessment parameters and effective interventions for management of fatigue in adults with cancer? Outcomes of interest included reduction or improvement in CRF or energy (vigour or vitality), or both. The specific aims of the review were to

- adapt evidence-based recommendations as action statements to create a knowledge product practical for use in clinical practice, and
- develop an algorithm as an intervention and care pathway to guide clinical practice in the supportive care of adults with CRF, based on severity cut-offs in the Edmonton Symptom Assessment System (ESAS)¹⁸.

2. METHODS

2.1 Synthesis of Evidence

Clinical practice guidelines are “systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances”¹⁹. *De novo* guideline development is time-consuming, requires significant resources, and often duplicates efforts because a wealth of guidelines usually exists for a topic area²⁰. The present practice guideline was developed using the ADAPTE methodology^{17,21} and the AGREE II convention for guideline appraisal^{22,23}. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high-quality guidelines tailored for use in a specific health care context¹⁷. The ADAPTE process consists of 3 main phases (planning and set-up, adaptation, and development of the final product), with 27 steps embedded across the phases. An algorithm, being a quick summary of evidence-based recommendations from a full technical document, was also developed, because algorithms are shown to facilitate uptake of guidelines by clinicians²⁴.

2.2 Expert Panel Review

Using a participatory approach, a national expert panel comprising nurses, psychologists, administrators, a

patient education specialist, a dietician, researchers, a pharmacist, a research coordinator, and a guideline methodologist from across Canada acted in an advisory capacity at all stages of guideline development. To ensure that the views of consumers also informed the final guideline, two members of the group were cancer survivors. A draft of the guideline technical report was distributed on several occasions to the expert panel for feedback concerning the collection, interpretation, and synthesis of the evidence, as well as the adaptation of the recommendations and the summarized content in the algorithm. As part of an external review process, content experts and key stakeholders across the country were invited to review and provide input on the guideline. A nominal group consensus method was used to reach final expert panel agreement on the guideline recommendations, taking into consideration the findings of the external review ($n = 14$, 1 requested a minor edit).

2.3 Literature Search

To ensure the currency of the evidence, a broad systematic search of the literature identified guidelines and systematic reviews for fatigue. Electronic databases—MEDLINE, EMBASE, CINAHL, the Cochrane Library, the Guidelines International Network (<http://www.g-i-n.net>), the National Guidelines Clearinghouse (<http://www.guideline.gov>), and the Canadian Partnership Against Cancer SAGE Inventory of Cancer Guidelines (<http://www.cancerview.ca>)—were searched to December 2009. In addition, the Web sites of the U.K. National Institute for Health and Clinical Excellence, the Scottish Intercollegiate Guideline Network, the U.S. National Comprehensive Cancer Network (NCCN), and provincial guideline organizations [Cancer Care Ontario (CCO), the Vancouver Island Health Authority and Fraser Health in British Columbia, and Cancer Care Nova Scotia] were searched for additional guidelines. The search used separate or combined terms, including “cancer,” “neoplasm,” “fatigue,” “asthenia,” “cancer fatigue,” “screening,” “assessment,” “interventions,” “guidelines,” “recommendations,” “practice guidelines,” “management of CRF,” “pharmacological treatments,” and “nonpharmacological treatments.”

2.4 Study Selection Criteria

Clinical practice guidelines, systematic reviews, and other guidance documents with explicit links to the evidence and a focus on any one or a combination of screening, assessment, or management of adult CRF (pharmacologic or nonpharmacologic) were included. Outcomes of interest were improvement in CRF (occurrence, duration, intensity) or energy (vigour or vitality) using validated fatigue scales or subscales from other patient-reported outcome measures. Additional criteria for inclusion were patients

18 years of age or older, any cancer type, published after 2003, English, and systematic reviews (with or without meta-analyses) published during 2004–2009.

3. RESULTS

3.1 Literature Review

The review identified nineteen guidelines, guidance documents, or systematic reviews that met the inclusion criteria. Twelve guidelines were excluded: five because they either were based on data produced before 2003 or were not guidelines for practice (for example, they contained lay information or a clinical knowledge summary, or they discussed guidelines); four, because they were not specific to cancer patients (for example, they addressed chronic fatigue syndrome); and three, because they did not address CRF management in a comprehensive manner (for example, they consisted of curriculum information and guidelines focused on a different topic). As shown in Table 1, two clinical practice guidelines identified in the literature search comprised the primary evidence base for the present practice guideline: an NCCN guideline⁶ and the Oncology Nursing Society (ONS) guideline⁷. In addition, seven guidance documents^{25–31} and four systematic reviews^{32–35} provided supplementary,

but mainly indirect, evidence to inform the guideline recommendations. Supporting documents were included to clarify background information, to provide additional detail in the guidelines, and to ensure the incorporation of recent evidence. Since completion of the original literature search, an updated NCCN fatigue guideline³⁶ has been released; however, the new text was not substantively different from the earlier version, suggesting currency of the earlier guideline.

3.2 Critical Appraisal

Table 11 shows the results of the critical appraisal of the guidelines conducted using the AGREE II criteria and instrument^{22,23}. The AGREE II instrument is a critical appraisal tool that guides the selection of the best-quality guidelines for use in an adapted guideline²³. It evaluates the quality of the guidelines being adapted based on 6 domains: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence. A decision was made to include both of the appraised guidelines, because the NCCN guideline is widely endorsed for use in comprehensive cancer centres in the United States⁶ and because the ONS guideline scored 50% on rigour, demonstrating methodologic quality⁷. Both were also based on expert consensus.

TABLE 1 Sources of evidence

Reference	Title
<i>Clinical practice guidelines</i>	
Mitchell <i>et al.</i> , 2007 ⁷	Putting Evidence into Practice: evidence-based interventions for fatigue during and following cancer and its treatment
National Comprehensive Cancer Network, 2009 ⁶	<i>Cancer-Related Fatigue</i>
<i>Supporting guidance documents</i>	
Cancer Care Ontario, 2004 ²⁷	<i>Telephone Nursing Practice and Symptom Management Guidelines</i>
Cancer Care Ontario, 2005 ²⁸	<i>Palliative Care Collaborative Care Plan: Fatigue (Cancer Patients)</i>
Fraser Health, 2006 ³⁰	<i>Fatigue</i> . Series: Hospice Palliative Care Program: Symptom Guidelines
CPAC/CAPO 2009	<i>A Pan-Canadian Clinical Practice Guideline: Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient</i>
Eaton and Tipton, eds., 2009 ²⁵	<i>Putting Evidence into Practice: Improving Oncology Patient Outcomes</i>
Canadian Partnership Against Cancer, 2009 ²⁹	<i>Guide to Implementing Screening for Distress, the 6th Vital Sign. Moving Towards Person-Centered Care</i> . Part A: Background, Recommendations and Implementation
U.S. National Cancer Institute, 2010 ³¹	Fatigue (PDQ). Health Professional Information
<i>Systematic reviews</i>	
Kirkova <i>et al.</i> , 2006 ³⁵	Cancer symptom assessment instruments: a systematic review
Cramp and Daniel, 2008 ³³	Exercise for the management of cancer-related fatigue in adults
Brown and Kroenke, 2009 ³²	Cancer-related fatigue and its association with depression and anxiety: a systematic review
Goedendorp <i>et al.</i> , 2009 ³⁴	Psychosocial interventions for reducing fatigue during cancer treatment in adults

CAPO = Canadian Association of Psychosocial Oncology

TABLE II Critical appraisal of clinical practice guidelines

Domain (AGREE II)	Score (%)	
	National Comprehensive Cancer Network, 2009 ⁶ (2 reviewers)	Oncology Nursing Society, 2007 ⁷ (2 reviewers)
1. Scope and purpose	58	53
2. Stakeholder involvement	42	31
3. Rigour of development	24	50
4. Clarity of presentation	86	72
5. Applicability	44	29
6. Editorial independence	79	29

Of the four systematic reviews identified^{32–35}, checks were made to ensure that all had explicit study selection criteria (clear inclusion and exclusion criteria) against which the evidence was assessed, that they were clear about attempts to minimize biases, and that they were specific about how studies were integrated to form the recommendations. However, a formal critical appraisal was not conducted.

3.3 Routine Screening for CRF

Routine screening to ensure early detection and management of CRF was uniformly recommended across guidelines and supporting documents. According to the NCCN⁶ and the CCO telephone practice guidelines²⁷, routine screening should occur at the initial cancer clinic visit and at intervals during management (at every clinic visit: CCO^{27,28}), at post-treatment follow-up visits, and as clinically indicated using an intensity scale with validated cut-offs. The ONS guideline⁷ and the CCO document²⁷ both reinforced the idea that patient self-report of intensity is the best choice, given the subjectivity of the fatigue experience.

Consistent across guidelines was a recommendation to use a valid intensity scale for screening and assessment of fatigue. Screening includes asking patients “How would you rate your fatigue on a scale of 0–10 over the past 7 days” (0 = no fatigue, 10 = worst fatigue you can imagine), with the use of cut-off scores of 0–3 (none to mild), 4–6 (moderate), and 7–10 (severe). The NCCN⁶ noted that, if patients are unable to assign a numeric value to their fatigue, they can rate the fatigue as mild, moderate, or severe, and that family members may also provide useful information about the effect of fatigue on the patient’s functioning over time.

The use of the ESAS (0 = no fatigue, 10 = worse fatigue)¹⁸ at every clinic visit was recommended in the CCO guidance^{27,28}, and in Canada, the ESAS is endorsed as a screening tool for cancer programs

alongside the Canadian Problem Checklist²⁹. The ESAS is a valid and reliable assessment tool for early-stage and advanced disease that rates severity for 9 common cancer symptoms (pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath)^{18,37–39}. The ESAS range (0–10) and recommended cut-off scores for tiredness are similar to those recommended by the NCCN guideline⁶. Regardless of tool or approach, comparable data to reliably detect changes over time is critical.

In terms of who performs the screening, the NCCN guideline⁶ indicates that a health care professional should screen for CRF. The ONS guideline⁷ and the CCO telephone symptom management guidelines²⁷ primarily target nurses as screeners. Other supporting documents were not explicit about who should screen for fatigue. Tailoring of guidelines to local health care environments is a critical step in guideline implementation^{17,40}, and as part of that process, a determination of who is accountable for screening for and assessing fatigue should be clarified.

3.4 Parameters of CRF Assessment

There is consensus in North America that identification of a problem through systematic screening (ESAS score ≥ 4) should be followed by a comprehensive and focused assessment to clarify the nature and extent of the problem, with the aim of guiding selection of appropriate and relevant interventions^{6,26}. The NCCN guideline⁶ recommends that a health professional trained in fatigue evaluation complete an in-depth fatigue history, including a review of clinical status and medications, and a physical exam. The physical exam should include an examination of gait, posture, and range of motion and observation of the eyes (conjunctiva pallor if anemic) and mouth [cheilosis or angular cheilitis and angular stomatitis (reddened shiny tongue)] for vitamin deficiencies. A focused assessment of fatigue to determine its onset, duration, pattern, change over time, associated or alleviating factors, and interference with function was also recommended. Taken together, the two main sources of guideline evidence and the supporting documents were consistent in the parameters of fatigue assessment that should follow a positive screen (Table III).

Descriptions of fatigue by patients in their own words can be helpful to reflect subjective experience, and the patient should be asked to describe their pattern of fatigue⁴¹. The pattern typical of CRF is described as a sensation of tiredness that is persistent, not linked to activity or exertion, and not relieved by sleep or rest. It can include tiredness or exhaustion disproportionate to recent activity, impairment in important areas of functioning (for example, daily tasks, work, social life, other), diminished concentration or attention, significant distress or negative

TABLE III Parameters of assessment for cancer-related fatigue

1. Pattern of fatigue	Onset, duration, change over time, relationship to treatment
2. Description of fatigue in patient's own words and intensity	Use a valid tool for assessing intensity of fatigue—that is, the Brief Fatigue Inventory
3. Factors that alleviate or aggregate fatigue	Disease status, treatment history, treatment-related symptoms Sleep or rest patterns, relaxation habits Current medications, including alcohol and other risk substances Possible stressors (for example, life events: recent bereavement or loss; change in home setting, financial resources, or support systems) Nutrition intake and any appetite or weight changes, muscle wasting Level of activity or exercise
4. Effects of fatigue on daily living and lifestyle	Determine the activities with which fatigue interferes; impact on work, participation in social life, and other leisure activities; work; concentration; short-term memory
5. Possible contributing factors	Consider anemia, depression, anxiety, pain, dehydration, nutritional deficiencies (for example, protein, calories, vitamins), sedating medications (for example, opioids, benzodiazepines), neurotoxic therapies, infection, fever, sleep disturbances, inactivity, or other symptoms (for example, dyspnea)
6. Physical exam	Check for signs of nutritional deficiencies, gait and posture, muscle wasting

mood related to feeling fatigued (for example, sad, frustrated, irritable), sleep disturbance (insomnia or hypersomnia, sleep as non-restorative or not refreshing), decreased motivation or interest in engaging in usual activities, or disturbance in quality of life⁶. The clinician must be knowledgeable concerning the variance of fatigue patterns with clinical status and specific treatment regimens. For example, fatigue often peaks near the end of radiation therapy and tapers off over several months, but patients receiving cytotoxic chemotherapy may experience daily variation in fatigue and increasing severity of fatigue with each subsequent treatment cycle, with gradual tapering of fatigue in the first year after treatment^{42,43}.

3.5 Risk Factors for Fatigue

A number of risk factors were also identified as part of CRF assessment by NCCN⁶ and ONS⁷ (Table IV). The U.S. National Cancer Institute³¹ also recommended asking patients specifically about job performance and inclusion of a psychiatric evaluation (including evaluation for depression) to meet criteria for fatigue as a syndrome according to the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision⁴⁴. The CCO practice guidance²⁸ also includes disease stage, stress, changes in activity or exercise patterns, and other symptoms as risk factors. The assessment of other symptoms as a risk factor is critical, given that a large body of research shows that CRF is usually part of a symptom cluster with sleep disturbance, emotional distress (depression or anxiety, or both), and pain^{14,15}.

3.6 Treatment and Supportive Care

A key principle for the management of any symptom is first to address causes that are amenable to medical treatment⁴⁵. The ONS and NCCN guidelines both recommended medical treatment or prevention of anemia, nutrition deficiencies, and other symptoms contributing to fatigue. Referral to specialist services (for example, a social worker or dietician depending on the problems uncovered) before follow-up and re-evaluation was also recommended by NCCN⁶. Other interventions for the management of CRF from the review are identified below.

3.6.1 Nonpharmacologic Interventions

The NCCN guideline reported that randomized controlled trial (RCT) data indicate that enhanced physical activity or exercise, cognitive-behavioural therapy (CBT), and psychosocial interventions improve fatigue⁶. Exercise was the only intervention recommended by ONS based on RCT data⁷. Recent reviews support the latter finding and show higher effects for reduction in CRF severity with exercise than with psychosocial interventions⁴⁶. The ONS⁷ guideline recommend 30 minutes of moderate-intensity activity on most days of the week (for example, walking, swimming, cycling, resistance training), which is consistent with the U.S. Surgeon General recommendations for all populations⁴⁷. Other considerations identified by the NCCN for an exercise regime included disease status (active cancer treatment, long-term follow-up, advanced disease, or end of life) and the presence of bone metastases, neutropenia, low platelet count,

TABLE IV Risk factors for cancer-related fatigue

<i>Factor</i>	<i>National Comprehensive Cancer Network, 2009⁶</i>	<i>Oncology Nursing Society, 2007⁷</i>	<i>Supporting</i>
<i>Physical symptoms</i>			
Shortness of breath	—	X	X
Heart palpitations	—	X	—
General lack of energy	X	X	—
<i>Contributing risk factors</i>			
Anemia	X	X	X
Endocrine dysfunction ^a	X	X	X
Cardiac dysfunction ^b	X	X	X
Pulmonary dysfunction	X	X	X
Fluid and electrolyte imbalances	X	X	X
Weight, caloric intake, or nutritional deficiencies	X	—	X
Pain	X	X	X
Depressed mood or depression	X	X	X
Emotional distress	X	X	X
Sleep disturbances	X	X	X
Medication side-effects profile (that is, sedation)	X	X	X
Infection	X	—	X
Nausea	—	X	—
Hepatic, renal, neurologic dysfunction	X	—	X
Decreased activity or fitness	X	—	X
Pain	—	—	X
Fever	—	—	X
Treatment side effects	—	—	X
<i>Individual risk factors</i>			
Disease status ^c	X	—	—
History of psychiatric problems ^d	X	—	X
Coping methods and cancer-related stressors	X	—	—
Pre-treatment activity levels	X	—	—

^a For example, hypothyroidism, hypogonadism, adrenal insufficiency.

^b For example, cardiomyopathy.

^c For example, on active treatment, at end of life.

^d For example, depression, anxiety.

anemia or fever⁶. The risks and benefits must be weighed, and in some cases, a modified exercise regimen can be recommended. For example, a neutropenic patient should avoid environments carrying a high risk for infection (for example, gyms and swimming pools). Exercise regimens must be tailored to the individual, taking into account factors such as age, disease status, treatment modalities, pre-treatment activity levels, and comorbidities⁴⁸.

Other supportive care interventions described by the ONS as likely to be effective included energy

conservation, education, CBT (for example, sleep hygiene strategies and strategies to influence sleep-disrupting thoughts), and relaxation training⁷. The goal of energy conservation and activity management is to balance rest and activities so that prioritized activities are more likely to be achieved. The main focus of CBT is on the reframing of negative thinking patterns that influence the perception of problems and, subsequently, behaviour⁴⁹. Negative attributions for CRF are reported⁵⁰, and perceptions about fatigue are emerging as a potential contributor to fatigue

severity⁵¹. The ONS also indicated that education benefits all patients, including coping strategies, counseling and support, coaching in fatigue management, and provision of information⁷. A recent Cochrane review reported that traditional patient education alone is less effective than education focused on behaviour change⁵². The ONS also reported that progressive muscle relaxation is likely to be effective, although the percentage of fatigued individuals who learn and routinely practice this intervention may be very small.

At the time that the ONS conducted its evidence summary, it reported insufficient or poor-quality data to establish the effectiveness of various pharmacologic, psycho-educational, CBT, or complementary interventions⁷. In contrast, the more recent NCCN guideline reports level 1 evidence for CBT³⁶. A Cochrane review by Zhang *et al.*⁵³ concurs with the ONS findings. Although promising, the evidence supporting the use of complementary interventions—that is, Chinese medicinal herbs—to treat the side effects of chemotherapy in breast cancer populations (for example, nausea, vomiting, fatigue) is limited. Another Cochrane review examined the effectiveness of psychosocial interventions in RCTs designed to reduce CRF (for example, facilitated support groups, CBT, psychotherapy with a trained professional, and fatigue intervention during home visits)³⁴. Overall, fatigue reduction was more pronounced and effective with interventions targeting fatigue as a primary outcome (for example, education about fatigue and activity management).

3.6.2 Pharmacologic Interventions

In agreement with the NCCN⁶ and ONS guidelines⁷, a recent Cochrane review considered evidence for the use of drug therapy in the management of CRF to be inconclusive⁵⁴. The Cochrane review of twenty-seven interventional RCTs for CRF detected mixed results, with methylphenidate (Ritalin; Novartis Pharmaceuticals, St. Louis, MO, U.S.A.) appearing to be effective for CRF; however, because of small sample sizes, more research is needed to confirm the role of that drug⁵⁴.

The National Cancer Institute document reported that, based on limited experience, psychostimulants may be considered only in the treatment of severe fatigue³¹. According to the NCCN guideline, no RCTs had determined whether psychostimulants were useful for treating fatigue in cancer survivors, and optimal dosing and schedules were not yet established⁶. Erythropoietin and darbepoetin (for anemia) were reported to be effective for CRF in patients who were anemic as a result of chemotherapy⁵⁴. Concurring with the ONS guideline⁷, Minton *et al.* cautioned about the use of erythropoietin and darbepoetin, reporting that the optimal dose, treatment duration, and maintenance level associated with better quality of life and relief of CRF were not clearly established⁵⁴.

Additionally, progestational steroids and paroxetine, an antidepressant, were found to be no better than placebo⁵⁴. The NCCN guideline also did not recommend the use of antidepressants to reduce fatigue⁶; however, underlying clinical depression, a contributing factor in CRF, should still be treated according to best practices. Treatment and care recommendations from the National Cancer Institute³⁶, plus other supporting documents that focus on palliative patients^{28,30}, are, overall, consistent with the NCCN⁶ and ONS⁷ guideline recommendations.

4. EXTERNAL REVIEW

Feedback from health care professionals was obtained through an online survey of 14 purposively selected interdisciplinary practitioners from across Canada (Table v). External reviewers were initially contacted by e-mail, followed by three reminder e-mail messages. The survey consisted of 20 items asking for the respondent's current professional role and use of cancer fatigue guidelines and evaluating the relevance of the recommendations, the methods used to search and synthesize the literature, the agreement of the respondents with the results and recommendations, and their likely use of the guideline in current practice. Of 25 practitioners approached, 14 responded, including health professionals from Alberta ($n = 2$), British Columbia ($n = 1$), Nova Scotia ($n = 1$), Ontario ($n = 9$), and Quebec ($n = 1$). More than half the respondents (57.1%) indicated that they do not currently follow a CRF guideline. Of those that did, 1 reported using a variety of sources, 1 reported using the ESAS, and 3 reported using the NCCN guideline⁶ as a source. Most respondents were in agreement about the need for and appropriateness of the guideline, and most indicated that they would likely, or very likely, apply the recommendations in clinical practice.

5. ADAPTED GUIDELINE AND ALGORITHM

Based on a synthesis of the evidence reviewed, we developed, for pan-Canadian use, an adapted set of recommendations for the screening, assessment, and supportive care of adult cancer patients with fatigue (Table vi). Additionally, as shown in Figures 1 and 2, we developed an algorithm based on those recommendations to guide clinical practice. The algorithm is colour-coded to reflect the basis of the assessment and interventions in the ESAS severity cut-off scores: 0–3 (mild), green; 4–6 (moderate), yellow; and 7–10 (severe), red. The literature suggests that clinicians will not even read a guideline if it is more than 1 or 2 pages in length⁵⁵. Although the NCCN guideline⁶ distinguished recommendations for the management of fatigue in terms of a clinical diagnosis of mild, moderate, or severe fatigue as an assessment outcome, that distinction was not explicitly reported

TABLE V Summary of external review survey results

Survey item	Response [n (%)]			
	Strongly agree	Agree	Somewhat agree	Other ^a
The overall objective of the fatigue guideline is specifically described.	6 (42.9)	6 (42.9)	0 (0.0)	2 (14.2)
The target population for the fatigue guideline is clearly described.	5 (35.7)	6 (42.9)	2 (14.2)	1 (7.1)
The target users of the fatigue guideline are clearly described.	6 (42.9)	6 (42.9)	0 (0.0)	2 (14.2)
Systematic search methods for identifying relevant guidelines for adaptation were used.	6 (42.9)	6 (42.9)	1 (7.1)	1 (7.1)
The methods for formulating the fatigue recommendations are clearly described.	5 (35.7)	5 (35.7)	2 (14.2)	2 (14.2)
The recommendations for fatigue are easily identifiable.	7 (50.0)	4 (28.6)	1 (7.1)	2 (14.2)
The recommendations for fatigue are appropriate.	3 (21.4)	10 (71.4)	0 (0.0)	1 (7.1)
The recommendations for fatigue are feasible.	2 (14.2)	8 (57.1)	2 (14.2)	2 (14.2)
When applied, the fatigue guideline will produce more benefits than harms.	8 (57.1)	4 (28.6)	1 (7.1)	1 (7.1)
The fatigue guideline is supported with tools for application.	3 (21.4)	5 (35.7)	4 (28.6)	2 (14.2)
	<i>Very likely</i>	<i>Likely</i>	<i>Somewhat likely</i>	<i>Other^b</i>
How likely would you be able to apply the recommendations in the fatigue guideline in clinical practice?	2 (14.2)	8 (57.1)	1 (7.1)	3 (21.4)

^a Respondents replied Disagree, Undecided, or Not Applicable.

^b Respondents replied Undecided or Not Applicable.

in the ONS guideline⁷. The CCO report distinguishes between nonurgent, urgent, and emergent fatigue in palliative patients, in which nonurgent patients can carry out their activities of daily life, and emergent (severe) fatigue is characterized by shortness of breath at rest, chest pain, tachycardia, sudden onset of severe fatigue, or rapid blood loss²⁸.

There was strong consensus by the expert panel that, given the prevalence of CRF, all patients should receive preparatory education and supportive care early in the disease and treatment trajectory. Thus, based on the evidence reviewed, we included a set of recommendations to be considered part of routine supportive care for patients experiencing CRF.

6. DISCUSSION

Across the disease and treatment trajectory, CRF is a prevalent symptom with profound effects on emotional distress, daily living, and health-related quality of life^{4,8,14}. Based on an internationally endorsed methodology for adapting guideline evidence^{17,21}, we developed a pan-Canadian practice guideline and algorithm for use in cancer programs. However, to ensure the provision of optimal care, the adoption

of these recommendations as part of routine clinical practice will require more than passive dissemination of the guideline⁵⁶. Putting knowledge into action is a complex process that requires an understanding of knowledge translation, including paying attention to the multifactorial barriers to practice change and using systematic implementation processes that incorporate multifaceted change strategies known to work in translating evidence into effective care^{56–59}. The Knowledge-to-Action Framework, a prominent knowledge translation framework, can be used to guide planning and to systematize the implementation process¹⁷. As noted in the framework, further tailoring of the guideline to each practice setting may still be necessary based on local health care resources and organizational cultures with incorporation of expectations or standards of the clinical team, including processes that delineate the person responsible for assessing fatigue, the scope of practice for management of fatigue, and clear pathways for referral to fatigue specialists.

More important, it must be recognized that, as part of knowledge translation efforts, patients are responsible for the daily monitoring and management of fatigue. Studies show that cancer patients are often

TABLE VI Cancer-related fatigue recommendations

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1. Screening for cancer-related fatigue
(based on the expert consensus of the National Advisory Group and informed by National Comprehensive Cancer Network category 2A, Oncology Nursing Society expert opinion^{1,2})
 - All health care providers should routinely screen for the presence of fatigue from the point of diagnosis onward.
 - All patients should be screened for fatigue at their initial visit, at appropriate intervals (for example, daily for inpatients, routine and follow-up visits for outpatients, and self-monitoring during post-treatment) and as clinically indicated, especially with changes in disease status.
 - Screen with a valid and reliable tool that includes reportable scores (dimensions) that are clinically meaningful and have established cut-offs—for example, Screening for Distress Tool, which includes the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist (CPC).
 - For inpatients unable to assign a numeric value to rate their fatigue, a rating of mild, moderate, or severe may be used.

 2. Comprehensive and focused assessment of cancer-related fatigue
(based on the expert consensus of the National Advisory Group and informed by National Comprehensive Cancer Network category 2A, ONS category “likely to be effective”, Oncology Nursing Society expert opinion)
 - Screen for fatigue, and if moderate or severe fatigue is detected through screening (ESAS tiredness greater than 4), individuals should have a comprehensive and a focused assessment to identify the nature and extent of the fatigue symptoms.
 - Medical and substance-induced causes of fatigue should be ruled out (for example, anemia, infection, nutrition deficiencies, medication, or treatment side effects).
 - Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments based on scope of practice.
 - Assessment should include a history of fatigue (for example, disease status, pretreatment activity levels, fatigue onset, pattern, duration, changes over time, interference with function and daily living), contributing risk factors (for example, depression, anemia, pain, nausea, sleep disturbance, comorbidities), a physical exam, a review of symptoms, and a self-assessment of causes contributing to fatigue.
 - Promote open communication between the patient, family members, and the clinical team to facilitate discussions about the experience of fatigue and its effects on daily functioning.
 - As a shared responsibility, the clinical team must decide when referral to an appropriately trained professional is needed (that is, all patients with an ESAS score in the severe range, or with certain accompanying factors or symptoms, or with a cut-off score identified using valid and reliable tools for assessment of symptoms of fatigue).

 3. Treatment and care options for cancer-related fatigue
(based on the expert consensus of the National Advisory Group and informed by National Comprehensive Cancer Network categories 1 and 2A, Oncology Nursing Society categories “recommended for practice” and “likely to be effective”, Oncology Nursing Society expert opinion)
 - Address all medical and substance-induced treatable contributing factors first (for example, pain, depression, anxiety, anemia, sleep disturbance, nutrition, activity level, medication side effects, and comorbidities).
 - Actively encourage all patients to engage in a moderate level of physical activity during and after cancer treatment (for example, 30 minutes of moderate-intensity activity most days) unless contraindicated. Moderate activity includes aerobic (for example, fast walking, cycling, or swimming) and resistance (for example, weights) training.
 - Additional nonpharmacologic interventions include nutrition consultation, optimizing sleep quality, psychosocial interventions to improve coping with fatigue (for example, cognitive behavioural therapy, stress management, or support groups), relaxation, massage and attention-restoring therapy (for example, exposure to natural environments).
 - For patients on active treatment or on long-term follow-up post treatment who have moderate-to-severe fatigue, consider referral to rehabilitation (for example, physical or occupational therapy, and physical medicine).
 - All patients should be offered specific education about fatigue before the start of treatment and when fatigue is identified, plus advice on strategies (for example, physical activity, energy conservation, stress reduction, and distraction) to manage fatigue.
 - At this time, the use of pharmacologic agents to treat cancer-related fatigue is considered experimental and is therefore not recommended (for example, psychostimulants, sleep medications, trials of low-dose corticosteroids such as prednisone or dexamethasone), except for selected patients at the end of life with severe fatigue.
 - Promote ongoing self-monitoring of fatigue levels as a late or long-term cancer or treatment problem in post-treatment survivors.
 - For those on active treatment and those with advanced, progressive disease, repeat ESAS screening and assessment as needed to determine any change in both subjective and objective aspects of fatigue.
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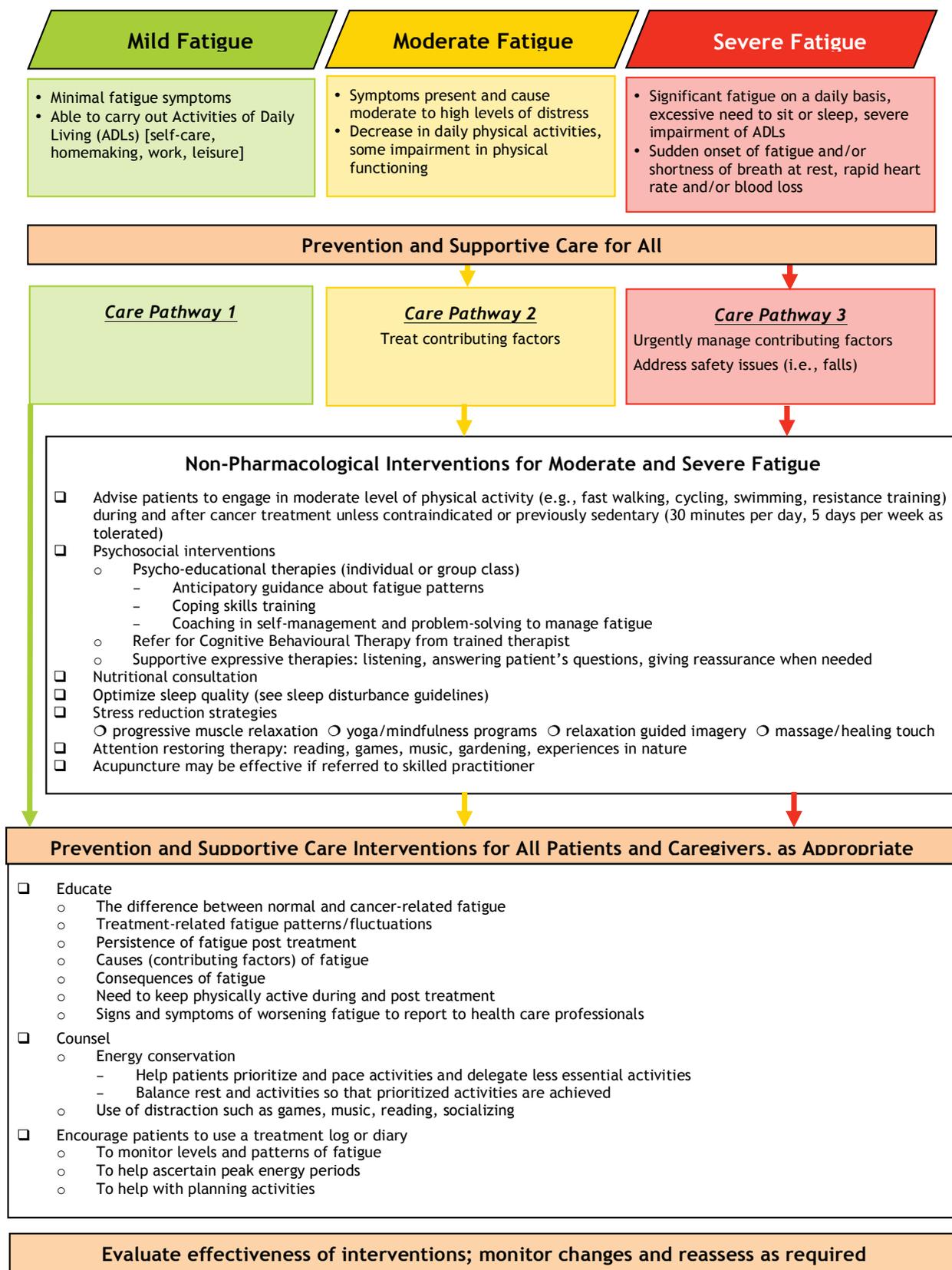


FIGURE 2 Care map—cancer-related fatigue in adults with cancer (please see the full guideline for copyright and disclaimer before use).

left isolated in coping with this symptom because health professionals seldom discuss the potential implications and management of CRF, and the advice given is often unhelpful or counterproductive^{9,16}. Consequently, patients may not initiate active management of CRF, potentially exacerbating CRF severity and related psychological distress. Future research should address implementation of these recommendations for management of CRF as part of routine care that include specific evidence-based protocols based on recommendations in guidelines that patients can follow to foster adoption of behaviours to reduce CRF and its impact.

7. CONCLUSIONS

The significant and disabling problem of CRF requires that clinicians ensure its early detection and management throughout all phases of the cancer trajectory. The use of effective knowledge translation strategies will still be required to ensure consistent and optimal management of CRF by clinicians and patients based on evidence synthesized in this pan-Canadian practice guideline.

8. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to declare.

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