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Clinical Practice Guidelines

Screening and Assessment of Cancer-Related Fatigue: A Clinical Practice Guideline for Health Care Providers

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Abstract

Cancer-related fatigue (CRF) is the most common side effect of cancer treatment. Regular surveillance is recommended, but few clinical practice guidelines transparently assess study bias, quality, and clinical utility in deriving recommendations of screening and assessment methods. The purpose of this clinical practice guideline (CPG) is to provide recommendations for the screening and assessment of CRF for health care professions treating individuals with cancer. Following best practices for development of a CPG using the Appraisal of Guidelines for Research and Evaluation (AGREE) Statement and Emergency Care Research Institute (ECRI) Guidelines Trust Scorecard, this CPG included a systematic search of the literature, quality assessment of included evidence, and stakeholder input from diverse health care fields to derive the final CPG. Ten screening and 15 assessment tools supported by 114 articles were reviewed. One screen (European Organisation for Research and Treatment of Cancer–Quality of Life Questionnaire–30 Core Questionnaire) and 3 assessments (Piper Fatigue Scale–Revised, Functional Assessment of Chronic Illness Therapy–Fatigue, and Patient Reported Outcome Measurement Information System [PROMIS] Fatigue-SF) received an A recommendation ("should be used in clinical practice"), and 1 screen and 5 assessments received a B recommendation ("may be used in clinical practice"). Health care providers have choice in determining appropriate screening and assessment tools to be used across the survivorship care continuum. The large number of tools available to screen for or assess CRF may result in a lack of comprehensive research evidence, leaving gaps in the body of evidence for measurement tools. More research into the responsiveness of these tools is needed in order to adopt their use as outcome measures.

Impact. Health care providers should screen for and assess CRF using one of the tools recommended by this CPG.

Keywords: Neoplasm, Outcome Assessment, Psychometrics

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Introduction

By the year 2026, an estimated 20.6 million people in the United States will be living with and beyond a diagnosis of cancer.[1] One of the most commonly reported side effects of cancer treatment is cancer-related fatigue (CRF), which impacts nearly all individuals with cancer at some point in the care continuum.[2] CRF is defined as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" by the National Comprehensive Cancer Network (NCCN).[3] This fatigue is considered to be multidimensional in nature and a hallmark feature is that CRF is not generally relieved by rest.[3,4] Cancer-related fatigue may result from the disease itself or from treatments such as chemotherapy or radiation and often worsens during the acute treatment timeframe.[5]

Estimates of the prevalence of CRF range from 25% to 99%, depending on the type and stage of cancer, type of treatment received, or method of assessment.[4] CRF is associated with significant physical and psychological impairments and a decrease in overall quality of life during and after cancer treatment[6] and can persist up to 5 years or more after completion of treatment.[7–9]

A stakeholder survey—including both health care providers and those with a diagnosis of cancer, completed to inform the development of this clinical practice guideline (CPG)—highlighted the challenge and lack of consistent attention to CRF.[10] Only 36% of health care providers screen for CRF at each visit and only 37% of those who screen use a standardized questionnaire. Additionally, the most common barriers to receiving treatment for CRF were lack of physician referrals and time constraints. These barriers limit accessibility to adequate care and often have a negative impact on quality of life. Among patients, 84% reported that CRF is an important issue, and 77% reported that they had initiated discussion about fatigue with their health care provider.[10] Low rates of detection and treatment of CRF are not unique to this sample. Other research indicates that detection and treatment of CRF are often driven by the individual with cancer rather than the health care provider.[11,12] Furthermore, these findings conflict with implementation of leading cancer organizations' recommendations for routine screening for CRF.[13] These results suggest that few individuals with CRF are routinely screened, making the potential for overlooking this important problem significant with negative consequences for those diagnosed with cancer.

Because CRF is multidimensional, the diagnosis is challenging. In 1998, the Fatigue Coalition, a multidisciplinary group of medical practitioners, researchers, and patient advocates, proposed that CRF involved 4 criteria: (1) a 2-week period of daily fatigue, with 5 of the 10 additional fatigue-related symptoms (weakness, diminished concentration, decreased motivation, insomnia, nonrestorative sleep, memory difficulties, malaise, difficulty completing tasks because of fatigue, inability or struggle to overcome inactivity); (2) fatigue resulting in distress or impaired social or occupational function; (3) clinical evidence that fatigue is related to cancer or cancer treatment; and (4) fatigue not due to a psychiatric condition, such as depression.[14] Although depression may mimic the symptoms of CRF, depression rates are reportedly low (9%–17%) among those with a cancer diagnosis, in contrast to the significantly higher numbers of those reporting fatigue.[15] Using the Fatigue Coalition criteria to diagnose CRF requires an interview by a physician with appropriate medical testing to rule out manageable cancer treatment side effects such as anemia, dehydration, malnutrition, and infection as well as necessary screening to rule out depression.[14] These diagnostic criteria helped establish that CRF is different from typical tiredness on the basis of activity levels or lifestyle factors. However, in the 2 decades since they were established, these criteria appear to have limited clinical impact because of the onerous nature in diagnosing CRF,[16] and efforts to more easily diagnose CRF have emerged with the development of more than 50 different self-report questionnaires for fatigue. Yet, CRF screening and assessment remain challenging and are often overlooked despite the high prevalence of CRF, making identification and treatment of this pervasive issue difficult.

Physicians typically diagnose CRF after a patient report of fatigue, followed by a performance of a comprehensive medical examination including lab work to identify possible medical causes of fatigue, such as anemia, malnutrition, pharmacological effects, or psychological conditions such as depression.[17,18] Because the primary method of diagnosing CRF is self-report, the majority of the tools to screen for and assess CRF are questionnaires. An understanding of the science of questionnaire development is important to be able to critically assess the tools available.

Questionnaire development is a multistep process. Generally, item generation is completed by a team of content experts in an iterative process. Resulting items are then tested in a sample population, using factor analysis methodology in which item-loading eigen factors are calculated to identify how many factors, or constructs, the questionnaire portrays. In the case of CRF, a unidimensional scale generally portrays only fatigue severity or intensity, whereas a multidimensional scale portrays the different aspects of fatigue such as physical, emotional, and cognitive aspects. The reliability of each item is assessed using Cronbach α to determine whether each item reliably portrays the intent of the scale—in this case, assessment of CRF. Validity testing is also a part of questionnaire development and goes beyond the simplistic concern of whether the tool measures what it is supposed to measure. Given that most tools used to screen for and assess CRF are self-report questionnaires, multiple tests for validity are necessary. This includes construct validity, which indicates whether the questions in the measure evaluate the construct of interest—in this case fatigue—and is often measured using factor analysis.[19] Convergent and discriminant validity evaluate the level to which a measure is similar or dissimilar, respectively, to another reference standard measure, using correlational statistics.[19] The challenge with CRF is that there is no established reference standard against which all tests should be measured. Ideally, diagnostic accuracy, such as sensitivity and specificity, as well as responsiveness, should be studied. Responsiveness measures include minimal detectable change (MCD), the amount of change that exceeds error, and minimal clinically important difference, which denotes the amount of change necessary to see a clinical change in an individual. Clinical utility, such as time to complete, available languages, and cost to use, should be assessed as well. It is with this understanding of questionnaire development and psychometric study that the Guideline Development Group (GDG) assessed measures of CRF.

Oncology care providers must be able to properly evaluate CRF within their respective scopes of practice. The comprehensive care of the individual with cancer depends on each health care provider having an awareness of the likelihood of developing CRF and the steps necessary to screen and assess this condition to drive intervention approaches. Accurate screening and assessment of CRF depend on measures that demonstrate strong psychometric properties as well as efficient clinical administration.[20] Multiple systematic reviews such as the Evidence Database to Guide Effectiveness Task Force of the Academy of Oncologic Physical Therapy (APTA Oncology) have reported on the myriad of instruments used to measure CRF.[3,20–22] What is lacking in many of these systematic reviews is a stringent assessment of the quality of the evidence, a hallmark of a high-quality systematic review.[23] Guidance on which measures to use to screen and assess CRF should be based on the highest-quality evidence. What is needed for today's health care providers is a CPG for the screening and assessment of CRF.

APTA Oncology commissioned the writing of an evidence-based CPG for CRF. A team of physical therapist researchers with expertise in oncology (M.I.F., S.E.H., J.Q.L.), cardiopulmonary disease (D.M.), and an expert clinician with more than 30 years of experience in treating individuals with cancer (J.C.C.) comprise the GDG. A CPG is needed to address the shortfalls of previous systematic reviews and guidelines. The goals of this CPG are to:

1. Provide recommendations for measures to be used by health care providers treating individuals with cancer, based on a systematic review and quality assessment of the body of literature related to the screening and assessment of CRF.
2. Identify gaps in the research for screening and assessment of CRF to encourage further investigation.

The GDG used the National Academies' definition of a CPG—recommendations considering the benefits and harms of alternative options while optimizing care on the basis of a systematic review of the evidence—as a framework to develop this guideline and followed the Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument and Emergency Care Research Institute (ECRI) Guidelines Trust Scorecard criteria.[24–26] This CPG reflects the work of the GDG in developing recommendations for the screening and assessment of CRF.

Methods

Clinical Question

As this CPG focuses on screening and assessment of CRF, use of a typical PICO (Population, Intervention, Comparator, Outcome) framework was adapted to PACO, in which Assessment replaces Intervention, to derive the following clinical question: Which methods/tools/measurements are indicated for use to screen for and assess CRF in individuals with cancer? The Population includes adults diagnosed with any type of cancer at any point in the care continuum. The Assessment(s) in question are any methods used to screen for and assess CRF; no comparison is included. The Outcome is a fatigue score denoting the presence and/or severity of CRF.

Data Sources and Searches

In consultation with a University of Dayton academic librarian, medical subject headings (MeSH) search terms were identified and deployed in searching PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Cochrane databases and in using the Google Scholar search engine. The initial search focused broadly on *cancer related fatigue* or *cancer-related fatigue* to survey the literature. Because of the large yield, the search terms were modified to *cancer related fatigue* or *cancer-related fatigue* and *assessment* or *screening* or *diagnosis*. The search was limited to peer-reviewed articles from January 1, 2000 through September 30, 2017, available in English, and including adults over the age of 18 years. A secondary search was conducted in March 2019 to identify new research published between the dates of October 1, 2017, and February 28, 2019. Because of the delays in manuscript production as a result of the COVID-19 pandemic, a final literature search was performed from the dates of March 1, 2019, through August 31, 2020.

Study Selection

The GDG completed title and abstract review to select studies that met inclusion criteria while ensuring they reported on the process of questionnaire design, development, and psychometric evaluation of these survey instruments. Inclusion criteria were as follows: study population including adults ≥18 years of age with a diagnosis of any cancer type, tools or methods used to screen for or assess CRF, report on the psychometric evaluation of the measure, and full text available in English. Studies that evaluated fatigue in noncancer populations or focused on treatment were excluded. Full-text review was completed utilizing Covidence software (Veritas Health Innovation Ltd, Melbourne, Victoria, Australia). Two GDG members reviewed each article to ensure that inclusion and exclusion criteria were met; any disagreement was reviewed by a third GDG member for final determination of study selection.

Data Extraction and Quality Assessment

The GDG utilized a 3-step process to evaluate the body of evidence for each tool. These steps included assessment of bias present in each study by trained reviewers (1 of whom was a GDG member), assignment of a Center for Evidence Based Medicine level, and data extraction of relevant psychometric properties. Bias was assessed using questionnaires recommended by the American Physical Therapy Association's (APTA) manual for CPG development.[27]

Study reviewers were recruited via electronic newsletters, via listservs, and by word of mouth through the APTA Oncology membership. Training covered the purpose and methodology of developing a CPG, specific training in bias assessment using the Scottish Intercollegiate Guideline Network (SIGN) risk-of-bias questionnaire, use of the Consensus-Based Standards for the Selection of Health Status Measurement Instruments (COSMIN) for internal consistency and structural validity, and use of Covidence software for conducting systematic reviews. Each reviewer was assessed for reliability on 2 test articles to ensure consistency in application of bias criteria.

Step 1: Assessment of Bias

Two reviewers assessed study bias (a minimum of 1 GDG member for each study). One or both of the following

risk-of-bias questionnaires were used to assess the bias of each individual article: the SIGN and, for those studies examining internal consistency and structural validity, the COSMIN checklist. The SIGN is aimed at evaluating studies of diagnostic accuracy and assesses 5 domains: patient selection, index test, reference test, flow and timing, and overall assessment of the study (Suppl. Appendix 1).[28] Questionnaire reliability focuses largely on internal consistency, whereas validity focuses on construct validity, and, in particular, structural validity. The COSMIN has 3 questions to assess internal consistency and 2 questions to assess structural validity (Suppl. Appendix 2).[29] Two questions on the SIGN were not considered in assessing bias. These questions related to the timing of the interpretation of index and reference standard tests (questions 2.1 and 3.2 on the SIGN) and were excluded because the order of self-administered tests would not influence the evaluator score. Overall study quality was determined on the basis of the results of bias assessment. Disagreement between reviewers on any domain was discussed until consensus was achieved. If no consensus could be achieved, a third reviewer completed bias assessment with discussion until consensus was reached.

Step 2: Level of Evidence Assignment

The Oxford Centre for Evidence-Based Medicine levels of evidence were used to categorize and assign each study a level of evidence (Suppl. Appendix 3).[30] The diagnosis/diagnostic accuracy column was used to assign a preliminary Oxford Centre for Evidence-Based Medicine level of evidence based on the study design.

Step 3: Data Extraction

Each article was reviewed for relevant data to be extracted which included: type of cancer, stage of cancer, index test, reference tests, and relevant psychometric properties including reliability, validity, responsiveness, and diagnostic accuracy. Data related to clinical utility, such as time to complete, effort (inclusive of complexity), accessibility of tool, and cost for use, was extracted as well. These data were utilized in determining strength of recommendation.

Data Synthesis and Analysis

Determining Overall Level of Evidence

In addition to data extraction, a determination of the final overall level of the evidence of each included article was made on the basis of the synthesis of study design and bias assessment, using the APTA CPG process manual.[27] The final level of evidence assessment allowed the team to determine the amount of confidence they had in the study results. The design of each study was categorized as prospective/retrospective, cohort/case–control, and consecutive/nonconsecutive. Combining the study design with the bias assessment results allowed each team member to assign a final level of evidence using the Oxford Centre for Evidence-Based Medicine's level of evidence 2009 reference.[30]

The evidence related to each measure of CRF was combined into a measurement summary form that contained information about the measure, the populations studied, clinical utility, relevant psychometrics, and the level of evidence. This information was then evaluated by a GDG member to assign a recommendation grade and level of obligation, using the methods outlined in the APTA CPG process manual.[27] The level of obligation refers to language associated with the recommendation. Supplementary Appendix 4 shows the grade assignments for level-of-evidence recommendations.

Organization of Findings

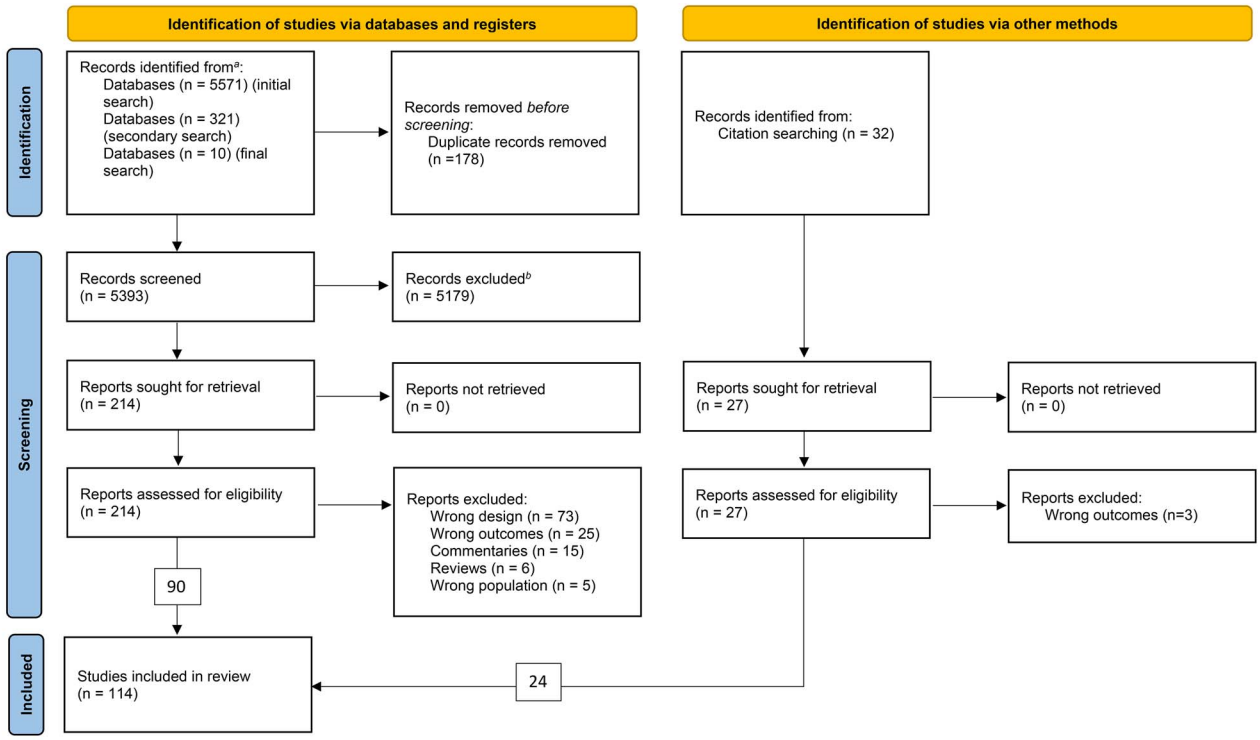
Given that the purpose of this CPG is to identify the best ways to screen for and assess CRF, the tools evaluated were categorized either as a screening tool—an efficient unidimensional way to identify CRF and prioritize intervention—or as an assessment tool, used to direct intervention. Assessments can be used by health care providers to provide an in-depth evaluation of the CRF experience and, ultimately, to direct treatment focus based on findings.

Role of the Funding Source

APTA provided funding for the development of this CPG. In addition, APTA's CPG process manual[27] was utilized to guide the development of this CPG.

Results

The initial broad search resulted in 5571 articles; the secondary and tertiary searches resulted in 331 additional articles. Following removal of duplicates, 5393 articles were screened; many of these included pharmaceutical and other intervention studies. After exclusions, 214 articles were retrieved for full-text review by 2 GDG members. After applying all inclusion and exclusion criteria to each article, 90 articles were included. Following this review, the GDG removed the review time frame to capture questionnaires developed prior to 2000, resulting in 24 additional entries. A total of 114 articles are included in the final review for assessment or screening of CRF (Figure). A total of 55 questionnaires that assessed CRF were identified in the literature search. Twenty measurements were eliminated as they did not specifically screen or assess cancer-related fatigue, or the study population was not cancer related. Further, 10 of the remaining measurements were eliminated due to lack of evidence to evaluate for this review, leaving 25 remaining measurements included and reviewed for this clinical practice guideline (10 screening and 15 assessment). Because of the large number of questionnaires identified, the GDG narrowed the number of recommended tools to those which had the highest-quality evidence supporting use, or greatest clinical applicability. Tools that were rated Recommendation Level A or B and Best Practice are described below and are recommended for use (4 screening tools and 8 assessments); the total bank of tools is identified in Table 1. Because CRF can impact individuals at different points in the survivorship care continuum, it is important that the chosen tool reflect that time period. Table 2 identifies the usefulness of each tool at each stage of survivorship. Because some measures were investigated in specific cancer populations, different measures may be used for different cancer diagnoses. The types of cancer in which the tools are validated are presented in Table 3. Although no tool has been investigated in every possible cancer diagnosis population, this table provides an overview of the breadth of the types of cancer in which the scales were investigated. Lastly, the GDG acknowledges that not all individuals with cancer are fluent in the English



[a]Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
[b]If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Figure. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71. For more information: http://www.prisma-statement.org/

language, and Table 4 provides a list of known languages in which each tool is available. Together, these considerations—point in the survivorship care continuum, diagnosis, and cultural presentation—must be evaluated by the provider in deciding which is the best measure to use to screen for or assess CRF. The included tables are intended to guide this clinical decision-making process. Supplementary Table 1 provides the bias assessment for each study reviewed for this clinical practice guideline. The recommended tools in this CPG present with low bias and, therefore, are considered high-quality studies.

CPG Review

Practice recommendations were presented at the APTA Combined Sections Meeting in February of 2020, and at the American Congress of Rehabilitation Medicine Annual Meeting in October of 2020; feedback from these conference presentations was included in this manuscript. The last step prior to completing this guideline was to have the full text reviewed for scientific and clinical content by content experts including oncologists and other physicians and nurses, physical and occupational therapists practicing in oncology, and by individuals with a history of cancer. In particular, feedback focused on whether this guideline addressed the knowledge gaps identified in our stakeholder survey. This expert panel input was synthesized and incorporated as appropriate in the final version of this manuscript.

Screening Tools

European Organisation for Research and Treatment of Cancer–Quality of Life Questionnaire–30 Core Questionnaire (EORTC-QLQ-C30)

The EORTC-QLQ-C30 should be used to screen for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: A). On the basis of a preponderance of level I evidence, strong psychometrics, and good clinical utility, the EORTC-QLQ-C30 is an effective tool to identify the presence of CRF.

Description of Measure and Psychometric Properties

The EORTC-QLQ-C30 is a 30-item quality-of-life questionnaire with 3 fatigue-specific questions: (1) Did you need to rest? (2) Have you felt weak? and (3) Were you tired? An affirmative response to any of these questions within the total tool indicates the presence of fatigue and warrants further assessment. The EORTC-QLQ-C30 has acceptable levels of internal consistency, with Cronbach α values ranging from 0.67 to 0.84, and established test–retest reliability.[31,32] Confirmatory factor analysis revealed strong global fit (0.84) with the item analysis of the 3 fatigue questions demonstrating moderate relationships ($r = 0.71$, 0.54, and 0.77, respectively).[31] Convergent validity was established between burden limitations and need for help (Spearman $\rho = 0.98$ and 0.63, respectively).[33] Divergent validity was established comparing high and low Karnofsky Performance Scores and long versus short survival time.[32] The EORTC-QLQ-C30 also has undergone responsiveness testing, and has a sensitivity of 86%

Table 1. Final Recommendations for Cancer-Related Fatigue

Type and Name of Tool	Grade[a]	Notes on Recommendation
Screening		
European Organisation for Research and Treatment of Cancer–Quality of Life Questionnaire–30 Core Questionnaire[31–35,37,107]	A	Health care providers should use for screening cancer-related fatigue
MD Anderson Symptom Inventory[38–42]	B	May be used for screening cancer-related fatigue
Distress Thermometer and Associated Problem List[44]	P	Limited evidence (1 study); good screening tool for severe fatigue; should be followed up with a more thorough assessment if positive
One-Item Fatigue Scale[45]	P	Limited evidence (1 study); should be used for screening cancer-related fatigue
Bidimensional Fatigue Scale[105]	R	Limited evidence (1 study); originally intended for chronic fatigue syndrome
Daily Fatigue Cancer Scale[106]	R	Limited evidence (1 study); currently in the development phase; shows promising construct validity and diagnostic accuracy; further psychometrics and normative data need reported
Four-Item Fatigue Scale[108]	R	Limited evidence (1 study); correlated reasonably well with a single point in time, but not over time; limited number of subjects
ICD-10 Criteria for Fatigue[109,110]	R	Limited evidence (2 studies); limited psychometrics; not easy to access and unclear use; poor quality studies
Muscle and Joint Measure[111]	R	Limited evidence (1 study); trialed in the Hematopoietic cell transplantation population; symptom score to screen
Perform Questionnaire[112]	R	Limited evidence (1 study); Spanish speaking population only
Assessment		
Functional Assessment of Chronic Illness Therapy–Fatigue[47–51,117]	A	High level of evidence; good overall psychometrics; widely used with multiple validated translations; missing useful elements such as responsiveness measures
Piper Fatigue Scale–Revised[54–61,122–124]	A	Should be used for initial assessment of cancer-related fatigue if at risk or referred for cancer-related fatigue; strong psychometric data; some controversy on the factor solution in different cultures
Patient-Reported Outcomes Measurement Information System Fatigue–Short Forms[63,64,66,96,97,125–127]	A	Short Form – Fatigue has significant evidence with strong psychometric support for use as initial or ongoing assessment of CRF. The measure is easy to use and translated into multiple languages
Brief Fatigue Inventory[5,67–75]	B	Health care providers should use to assess cancer-related fatigue when a patient has a history of cancer
Cancer Fatigue Scale[76–80,92,113]	B	Instrument designed to assess three separate domains of fatigue; concerns with level of evidence for psychometric properties; challenges with translation to other languages and cultures
Fatigue Symptom Inventory[79,80,88,90–93]	B	Useful to assess fatigue but has a lower number of high-quality studies. Concern about translation in other languages that do not capture fatigue the same as English does
Multidimensional Fatigue Inventory 20[81–87]	B	High quality (primarily Level II studies) with good ease of use. Some challenges with structural validity in languages other than English
Patient-Reported Outcomes Measurement Information System Bank v1.0–Fatigue CAT	B	This computer-adapted testing form for Fatigue is available for use on several platforms, however, psychometrics are emerging and the cost associated with use is high
European Organisation for Research and Treatment of Cancer–Quality of Life Questionnaire–FA12[114–116]	C	Low evidence available in studies; may use to assess cancer-related fatigue
Schwartz Cancer Fatigue Scale[79,80,92,128–130]	C	May use for assessment of cancer-related fatigue; low preponderance of evidence acceptable; mixed quality of studies
General Fatigue Scale[118]	R	Limited evidence (1 study); unable to locate tool; R; Taiwanese version is a reliable and valid instrument for assessing fatigue among cancer patients; additional information needed for scoring; need psychometric development
Hirai Cancer Fatigue Scale[119]	R	Limited evidence (1 study); in development phase; study had some unclear details that may affect quality of evidence; scale developed specifically for Japan and has not been translated
Illness Perception Questionnaire[120]	R	Limited evidence (1 study); appears to be in development phase at time of review
Multidimensional Fatigue Symptom Inventory–Short Form[121]	R	Limited evidence (1 study); unable to accurately determine usefulness in this population
Taiwan Cancer-Related Fatigue Cognition Questionnaire–Version 1.0[131]	R	Limited evidence (1 study); limited applicability; has not been validated against a reference standard
Wu Cancer Fatigue Scale[132,133]	R	Limited evidence (2 studies); still in the development phase; scale constructed at 42 items, but revised to 9; further psychometric data needed

[a]A = strong obligation: should be used; B = moderate obligation: may be used; C = weak obligation: may be used; P = best practice: may be used; R = research: unable to recommend.

Table 2. Tool Applicability Across the Care Continuum[a]

Type and Name of Tool	Active Treatment	Immediate Posttreatment Period	Long-Term Survivorship
Screening			
Bidimensional Fatigue Scale[105]			✓
Daily Fatigue Cancer Scale[106]		✓	
Distress Thermometer & Associated Problem List[44]	✓	✓	
European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire – Core 30[31–35,37,107]	✓		
Four-Item Fatigue Scale[108]	✓	✓	✓
ICD-10 Criteria for Fatigue[109,110]	✓		
MD Anderson Symptom Inventory[38–42]	✓	✓	✓
Muscle and Joint Measure[111]			✓
One-Item Fatigue Screen[45]	✓	✓	✓
Perform Questionnaire[112]	✓		
Assessment			
Brief Fatigue Inventory[5,67–75]	✓	✓	
Cancer Fatigue Scale[76–80,92,113]	✓		
European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire - FA12[114–116]	✓	✓	✓
Functional Assessment of Chronic Illness Therapy – Fatigue[47–51,117]	✓		
Fatigue Symptom Inventory[79,80,88,90–93]	✓	✓	✓
General Fatigue Scale[118]	✓		
Hirai Cancer Fatigue Scale[119]	✓		
Illness Perception Questionnaire[120]	✓	✓	
Multidimensional Fatigue Inventory-20[81–87]	✓	✓	✓
Multidimensional Fatigue Symptom Inventory – Short Form[121]	✓		
Piper Fatigue Scale – Revised[54–61,122–124]	✓	✓	
Patient-Reported Outcomes Measurement Information System[63,64,66,96,97,125–127]		✓	
Schwartz Cancer Fatigue Scale[79,80,92,128–130]	✓	✓	✓
Taiwan Cancer-Related Fatigue Cognition Questionnaire-Version 1.0[131]	✓		
Wu Cancer Fatigue Scale[132,133]	✓		

[a]Active treatment = surgery, chemotherapy, or radiation; immediate posttreatment period = completion of primary adjuvant treatment in the first year of recovery[134]; long-term survivorship = ≥1 year after diagnosis.

and a specificity of 78%.[33] The minimal detectable change of the EORTC-QLQ-C30 is 11 points; the minimally clinically important difference for improving fatigue is 12 points and worsening fatigue is 9 points.[34,35]

Clinical Utility

The clinical utility of the EORTC-QLQ-C30 is good. Although the questionnaire is 30 items, it takes less than 10 minutes to complete. It has been translated and validated into at least 110 languages.[36] Although the tool covers a multitude of possible symptoms and side effects related to cancer and cancer treatment, making it a broad-based tool, examination of the 3 questions related to fatigue show that the use is valid to screen for the presence of CRF among those treated for cancer.[31–35,37] The EORTC-QLQ-C30 is free for clinical use; users simply need to register at the EORTC website as an academic user (https://qol.eortc.org/questionnaire/eortc-qlq-c30/).

MD Anderson Symptom Inventory (MDASI)

The MDASI may be used to screen for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: B). On the basis of a preponderance of level II evidence, and strong psychometrics, but somewhat limited clinical utility, the MDASI is an effective tool to identify the presence of CRF.

Description of Measure and Psychometric Properties

The MDASI is a 13-item questionnaire designed to evaluate the severity and impact of symptoms related to cancer and cancer treatment. Each item represents a symptom and is rated on a scale from 0 ("not present") to 10 ("as bad as you can imagine") in the last 24 hours. It is scored by calculating the total and mean score. Subscale mean scores can be calculated as well on the basis of items of interest to researchers. A higher score means greater symptom burden. Three of the items, questions 2, 4, and 9, relate to fatigue. Question 2 asks the participant to rate "Your fatigue (tiredness) at its WORST;" question 4 asks the participant to rate "Your disturbed sleep at its WORST;" and question 9 is "Your feeling drowsy (sleepy) at its WORST." These fatigue-related questions are routinely reported as being rated as the most severe symptoms in psychometric testing.[38–41]

The psychometrics reported for the MDASI are robust. Internal consistency was tested in 5 studies by Cronbach alphas and were reported as ranging from 0.68 to 0.96 with the majority 0.8 or greater, indicating good to excellent internal consistency.[38–40,42,43] Test–retest reliability was also

Table 3. Cancer-Related Fatigue Measurements Used in Various Types of Cancer

Type and Name of Tool	Breast	Prostate	Colorectal	Lung	Head and Neck	Urogenital	Brain	Myeloma	Blood	Lymphoma	Bone	Gynecologic	Skin	Liver	Stomach	Pancreas	Not Specified
Screening																	
Bidimensional Fatigue Scale[105]																	✓
Daily Fatigue Cancer Scale[106]	✓		✓	✓	✓							✓		✓	✓	✓	
Distress Thermometer & Associated Problem List[44]	✓		✓														
European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire – Core 30[31–35,37,107]	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓					
Four-Item Fatigue Scale[108]																	✓
ICD-10 Criteria for Fatigue[109,110]																	✓
MD Anderson Symptom Inventory[38–42]	✓		✓	✓	✓	✓		✓	✓	✓		✓					
Muscle and Joint Measure[111]									✓	✓							
One-Item Fatigue Screen[45]				✓	✓												
Perform Questionnaire[112]	✓	✓	✓	✓		✓											
Assessment																	
Brief Fatigue Inventory[5,67–75]	✓		✓	✓	✓				✓	✓	✓	✓	✓	✓			
Cancer Fatigue Scale[76–80,92,113]	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓		✓		
European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire - FA12[114–116]	✓	✓	✓		✓	✓			✓	✓	✓	✓	✓		✓		
Functional Assessment of Chronic Illness Therapy - Fatigue[47–51,117]	✓	✓	✓	✓	✓	✓			✓	✓							
Fatigue Symptom Inventory[79,80,88,90–93]	✓		✓	✓	✓	✓			✓	✓		✓			✓		
General Fatigue Scale[118]	✓																
Hirai Cancer Fatigue Scale[119]	✓		✓	✓	✓	✓			✓	✓					✓		
Illness Perception Questionnaire[120]	✓		✓	✓	✓	✓	✓		✓	✓	✓	✓			✓		
Multidimensional Fatigue Inventory-20[81–87]	✓	✓	✓	✓	✓	✓				✓		✓	✓	✓	✓		
Multidimensional Fatigue Symptom Inventory – Short Form[121]	✓	✓	✓	✓		✓				✓		✓					
Piper Fatigue Scale – Revised[54–61,122–124]	✓	✓	✓	✓	✓				✓		✓						
Patient-Reported Outcomes Measurement Information System[63,64,66,96,97,125–127]	✓	✓	✓	✓	✓	✓				✓		✓					
Schwartz Cancer Fatigue Scale[79,80,92,128–130]	✓		✓	✓	✓	✓						✓			✓		
Taiwan Cancer-Related Fatigue Cognition Questionnaire-Version 1.0[131]	✓		✓	✓					✓						✓		
Wu Cancer Fatigue Scale[132,133]	✓																

Table 4. Foreign Language Translations

Type and Name of Tool	Spanish	French	Dutch	Chinese	Korean	Arabic	Russian	Japanese	Greek	Filipino	Taiwanese	Swedish	Italian	Portuguese	Ethiopian	Indonesian	Polish	German
Screening																		
Bidimensional Fatigue Scale[105]																		
Daily Fatigue Cancer Scale[106]		✓																
Distress Thermometer & Associated Problem List[44]																		
European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire – Core 30[31–35,37,107]	✓					✓												
Four-Item Fatigue Scale[108]																		
ICD-10 Criteria for Fatigue[109,110]		✓	✓								✓							
MD Anderson Symptom Inventory[38–42]		✓		✓	✓		✓	✓	✓	✓	✓							
Muscle and Joint Measure[111]																		
One-Item Fatigue Screen[45]																		
Perform Questionnaire[112]	✓																	
Assessment																		
Brief Fatigue Inventory[5,67–75]				✓	✓			✓	✓	✓	✓		✓		✓	✓		
Cancer Fatigue Scale[76–80,92,113]				✓				✓	✓					✓				✓
European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire - FA12[114–116]																		
Functional Assessment of Chronic Illness Therapy - Fatigue[47–51,117]														✓			✓	
Fatigue Symptom Inventory[79,80,88,90–93]				✓														
General Fatigue Scale[118]											✓							
Hirai Cancer Fatigue Scale[119]								✓										
Illness Perception Questionnaire[120]																		
Multidimensional Fatigue Inventory-20[81–87]		✓		✓										✓				
Multidimensional Fatigue Symptom Inventory – Short Form[121]																		
Piper Fatigue Scale – Revised[54–61,122–124]	✓	✓										✓	✓	✓				
Patient-Reported Outcomes Measurement Information System[63,64,66,96,97,125–127]	✓			✓														
Schwartz Cancer Fatigue Scale[79,80,92,128–130]				✓														
Taiwan Cancer-Related Fatigue Cognition Questionnaire-Version 1.0[131]											✓							
Wu Cancer Fatigue Scale[132,133]																		

good to excellent, (ICCs = 0.88–0.98).[40] Convergent validity was reported as acceptable ($r = -0.63$ to -0.76) in testing against the 36-Item Short-Form Survey (SF-36)–Revised (SF-36R) subscales[42] and EORTC-QLQ-C30 with $r = -0.60$ versus Global Health Status Scale and the Brief Pain Inventory with $r = 0.84$ for the item "Pain at its worst in the past 24 hours."[39] Concurrent validity was demonstrated with significant correlations with the Functional Assessment of Cancer Therapy–Ovarian ($r = -0.48$ to -0.64) and quality of life ($r = -0.23$ to -0.39) scores.[40] Divergent validity was acceptable at $r = -0.63$ as compared to the SF-36R vitality subscale.[42] Furthermore, diagnostic accuracy was assessed and reported as a significant difference in mean severity and interference if the Eastern Cooperative Oncology Group performance score was ≤ 1 versus ≥ 2.[38] Importantly, cutoff points are available for the MDASI and were reported in 2 studies as 5 or 6, indicating moderate symptoms, and ≥ 7, indicating severe symptoms.[38,42]

Clinical Utility

The MDASI takes 2 to 5 minutes to complete. It is available in pen and paper; interactive voice response; tablet; and web-based forms. Disease site–specific and treatment-specific add-on modules are available. The MDASI may not be used or reproduced without permission, and fees are a minimum of $100 for clinical use but can vary on the basis of the size of the clinic and the number of practitioners. The MDASI has been translated and validated in Chinese, Russian, Japanese, Greek, Korean, Filipino, Taiwanese, German, and French, with additional translations into other languages. For further information, see https://www.mdanderson.org/content/dam/mdanderson/documents/Departments-and-Divisions/Symptom-Research/MDASI_userguide.pdf.

Two other tools were graded Best Practice, for their ease of use and common presence in cancer care, but which lack strong evidence for use. The Distress Thermometer and Associated Problem List (Distress Thermometer) and the One-Item Fatigue Scale are included in this category.

Distress Thermometer

The Distress Thermometer may be used to screen for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: P). On the basis of a limited amount of evidence, but good clinical utility, the Distress Thermometer is often used clinically to screen for CRF.

Description of Measure and Psychometric Properties

The Distress Thermometer was developed by the NCCN to assess distress and identify problems that individuals living with or beyond a cancer diagnosis face. The Distress Thermometer is a 1-item 11-point Likert scale pictured as a thermometer with 0 equating to no distress and 10 equating to severe distress. A cutoff point of 4 is generally accepted as the score that would trigger completion of the second part of the questionnaire.[44] The second part of the questionnaire is a 40-item checklist covering practical problems, family problems, emotional problems, spiritual/religious concerns, and physical problems. Fatigue is one of the items under physical problems. Minimal psychometric testing has been conducted on the Distress Thermometer, but the sensitivity is 89% to 91%, the specificity is 75% to 77%, the positive predictive value is 0.53 to 0.64, and the negative predictive value is 0.95.[44]

Clinical Utility

The clinical utility of the Distress Thermometer is good. Although the problem list includes 40 items, the tool takes less than 5 minutes to complete and is free to use. Positive findings should trigger a more comprehensive assessment.

One-Item Fatigue Scale

The One-Item Fatigue Scale may be used to screen for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: P). Although the psychometric properties of the One-Item Fatigue Scale are promising, and the clinical utility is high, a limited number of studies have examined its use in screening for CRF.

Description of Measure and Psychometric Properties

The One-Item Fatigue Scale is either a numeric or verbal rating scale on which an individual answers the question "Since your last visit, how would you rate your worst fatigue on a scale of 0 to 10?" The NCCN cutoff points are identified as 0 = no fatigue, 1 to 3 = mild fatigue, 4 to 6 = moderate fatigue, and 7 to 10 = severe fatigue. Test–retest reliability was good ($r = 0.88$) in a group of individuals with mixed cancer diagnoses, and convergent validity was established with the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) ($r = -0.75$[45] and 0.56[46]) and the Fatigue Symptom Inventory (FSI) ($r = 0.87$[45]). Divergent validity was established with the Hospital Anxiety and Depression Scale (HADS) ($r = 0.56$). Diagnostic accuracy was examined in 2 studies using the FACIT-F as comparison, with a sensitivity of 69% to 85% and a specificity of 61% to 71%.[45,46] Furthermore, a cutoff point of 3 to 5 is considered indicative of fatigue.[45,46]

Clinical Utility

The clinical utility of the One-Item Fatigue Scale is good. The tool is free, takes less than 1 minute to complete and the visual or numeric versions are easily understood. Positive findings should trigger a more comprehensive assessment.

Assessment Tools

Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F)

The FACIT-F should be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: A). On the basis of a preponderance of high-quality evidence, robust psychometrics, extensive testing and validation, and good clinical utility, the FACIT-F is an effective tool for the initial or ongoing assessment of CRF.

Description of Measure and Psychometric Properties

The FACIT-F is part of the FACIT system, which assesses chronic illness, with an emphasis on cancer therapy, cancer subtypes and symptoms (https://www.facit.org/). The instrument is a 41-item questionnaire, consisting of the FACT-G plus a fatigue subscale, which measures health-related quality of life covering 5 domains—physical well-being (7 items), family/social well-being (7 items), emotional well-being (6 items), functional well-being (7 items), and fatigue-specific items (13 items).[47] These items are scored on a 5-point Likert scale, where 0 = "not at all" and 5 = "very much," with a recall period over the past 7 days. Domain scores can be calculated by summing the scores for each domain, and/or a total score

by summing the scores for all domains, with higher scores representing better functioning or less fatigue.

Internal consistency was excellent, with Cronbach α values ranging from 0.74 to 0.96 for the total FACIT-F and from 0.91 to 0.96 for the fatigue subscale.[47–50] Test–retest reliability was likewise excellent (ICC = 0.91; 95% CI = 0.86–0.94) for the total FACIT-F and fatigue subscale (ICC = 0.90; 95% CI = 0.81–0.92).[48] Convergent and divergent validity was established with the Piper Fatigue Scale (PFS), Profile of Mood States (POMS)–Fatigue, POMS–Vigor, Edmonton Symptom Assessment System, and the SF-36.[47–49,51] On the basis of a global perception of fatigue improvement, a change in FACIT-F score of 10 points had a sensitivity of 73% and a specificity of 78% and was best able to predict a clinically important improvement.[51] A cutoff score of 34 was diagnostic of cancer-related fatigue on the basis of a total available score of 0 to 52 for the fatigue subscale.[47]

Clinical Utility

The FACIT-F has been used across a variety of settings, as well as cancer diagnoses and stages of treatment. The instrument can be completed in about 15 minutes,[47,52,53] either as a patient self-report or via patient interview. It has been translated into several languages. The English version of the FACIT-F is available for free (www.facit.org), but users are required to register their project or study on the FACIT.org website and to notify the website as reports or publications become available. Translated versions may require a fee for use on a case-to-case basis, for example, for pharmacological trials of a commercial nature.

PFS–Revised (PFS-R)

The PFS-R should be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: A). On the basis of a prevalence of strong level I evidence, robust psychometrics, and good clinical utility, the PFS-R is an effective tool for the initial or ongoing assessment of CRF.

Description of Measure and Psychometric Properties

The PFS-R is a 22-item numerically scaled self-report measure designed to measure the current levels of fatigue a person is experiencing.[54] The PFS was originally developed with 42 items in 1989 and revised to its current 22 items on the basis of a study of women with breast cancer.[54] The PFS-R is designed to assess multidimensional fatigue; each item is rated on a scale from 0 to 10, with varying descriptors at either end, for example 0 = "none," 10 = "a great deal," measuring 4 dimensions of subjective fatigue. The behavioral/severity subscale (6 items) consists of items related to the impact of activities of daily living; the affective subscale (5 items) relate to the emotional aspects of fatigue; the sensory subscale (5 items) consists of items related to the physical symptoms of fatigue, and the cognitive/mood subscale (6 items) are related to mental and mood status. Four additional short answer questions were designed to obtain qualitative information. The score is calculated for subscales and total score by adding the sum of the scores and dividing by number of items to obtain a score between 0 and 10, with higher scores corresponding to more fatigue.

The PFS-R has acceptable reliability ranging from Pearson $r = 0.60$ to 0.95.[55–58] Test–Retest reliability was good ($r > 0.86$).[55,56] Factor analyses have demonstrated good internal reliability with differences on factor solutions related to cultural contextual elements. The PFS-R has shown good predictive validity ($r = 0.74$),[56] and concurrent validity with the POMS–Fatigue, $r = 0.50$ to 0.80, and the Multidimensional Fatigue Inventory (MFI), from $r = 0.49$ to $r = 0.84$[55,56,59] Discriminant validity was established with the POMS Vigor.[55,56] Although the sensitivity and specificity of the PFS-R have not been demonstrated, cutoff points for categorizing patients by fatigue severity level have been published but require additional research.[60]

Clinical Utility

The PFS-R has been used with various cancer diagnoses, and in early cancer survivorship. It has been translated and validated in several languages including Italian, Spanish, Portuguese, Dutch and Swedish.[55,57–59,61] Other versions of the PFS—the QuickPiper (15 items)[56] and the 12-item PFS—have also been explored, with varying levels of evidence or reliability.[60,61] The pen and paper version of the instrument takes less than 10 minutes to complete, and is available for free (https://geriatrictoolkit.missouri.edu/fatigue/PiperFatigueScale.pdf).

Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue–Short Forms v1.0–Fatigue (4a, 6a, 7a, 7b, 8a, 13a)

The PROMIS Fatigue–Short Forms v1.0–Fatigue (4a, 6a, 7a, 7b, 8a, 13a) should be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: A). On the basis of a large amount of level I evidence, sound psychometrics, and good clinical utility, the PROMIS Fatigue–Short Forms v1.0–Fatigue (4a, 6a, 7a, 7b, 8a, 13a) is an effective tool for the initial or ongoing assessment of CRF.

Description of Measure and Psychometric Properties

There are 6 adult PROMIS Fatigue–Short Forms, and the number (eg, 4a) designates how many questions are in each form. The original adult short-form instrument was the 7a and measures fatigue in the past 7 days, as do forms 4a, 6a and 8a.[62] Short Forms 7b and 13a are instruments that measure daily fatigue.[62] The PROMIS Fatigue–Short Forms assess the experience of fatigue and the interference of fatigue on daily activities. Items are scored on a 5-point Likert scale, where 1 = not at all and 5 = very much, and summed; some items are reverse scored, such as item 7 in form 7a. We recommend referring to the online guidance for further information at https://www.assessmentcenter.net/ac_scoringservice as well as the scoring manual.[62] The PROMIS Fatigue–Short Forms are part of the PROMIS system of self-report measures developed by the National Institutes of Health to evaluate and monitor physical, mental, and social health in adults and children in the general population and living with chronic conditions (http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis).

Excellent internal consistency has been reported ($\alpha = 0.99$) and acceptable item–total correlation was found (range: 0.51–0.85) for the fatigue item bank.[63] The 72-item bank reported a Cronbach α value of 0.98, with corrected item-total correlations ranging from 0.47 to 0.80.[64] All items in the bank have significant factor loadings ranging from 0.60 to 0.87 showing acceptable construct validity.[63] The PROMIS Fatigue–Short

Forms 7a T-score minimally important difference ranges from 3.0 to 5.0 points.[65]

Clinical Utility

The PROMIS Fatigue–Short Forms instruments are short, are easy to complete, and have been translated into several languages (http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/available-translations). The instruments are available for free, though commercial users must seek permission to use, reproduce, or distribute the instrument. The PROMIS Fatigue–Short Forms are part of the PROMIS system of self-report measures and are available through a number of different platforms[63,64,66] (http://www.healthmeasures.net/index.php?option=com_content&view=category&layout=blog&id=71&Itemid=817).

Brief Fatigue Inventory (BFI)

The BFI may be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: B). On the basis of the large number of high-quality studies, extensive validation and sound psychometrics, the BFI is a valuable tool for the initial or ongoing assessment of CRF. However, the potential costs associated with its use impact its clinical utility.

Description of Measure and Psychometric Properties

The BFI was specifically developed for rapid assessment of CRF levels in patients with cancer, with the aim of identifying those with severe fatigue.[67] It evaluates fatigue severity and the impact of fatigue on daily functioning in the last 24 hours. Key advantages of the BFI are that it is short and easy to answer, it is easily translated into other languages, and it includes an interference (impact) assessment.[68] The term used to describe fatigue is often difficult to translate, but the BFI assesses the intensity of fatigue and its impact on daily activities by using simple words.[68]

The BFI has 3 questions that ask about fatigue severity, and 6 questions to determine the amount that fatigue interferes with daily activities, including walking ability, normal work, and mood. Items are scored on a scale from 0 to 10, where 0 is "no fatigue" or "fatigue does not interfere" and 10 is "fatigue as bad as you can imagine" or "[fatigue] completely interferes." Higher scores indicate more severe fatigue or more interference with activity. A fatigue severity or interference score can be calculated by averaging the subscale scores, or a global score can be calculated by averaging all items of the BFI.[67,68] The BFI can be administered as a self-report, via interview with research or clinical staff, or via an interactive voice response system (https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools/brief-fatigue-inventory.html). The BFI has been tested in a wide variety of patients with cancer, in varying stages of treatment. It has been validated in several languages, including Korean, Taiwanese, Japanese, Greek, German, Filipino, and Italian.[69]

Internal consistency of the BFI has been consistently excellent (Cronbach $\alpha > 0.9$) across the various translations.[5,68–75] Test–retest reliability was also excellent.[71,72] BFI scores were significantly correlated with other fatigue and/or vigor subscales of instruments such as the POMS, and the SF-36.[68,71,73] The BFI was able to distinguish between patients who had poorer performance status on the Eastern Cooperative Oncology Group performance scale.[68,69,73,75] Factor analysis of the BFI suggested a 1-factor loading for most of the versions suggesting unidimensionality[70–73,75] though the Chinese version suggested a 2-factor solution—fatigue severity and fatigue interference.[74] BFI cutoff scores of 1 to 3 indicated mild fatigue, 4 to 6 indicated moderate fatigue, and 7 to 10 indicated severe fatigue.[5,67]

Clinical Utility

The BFI is a simple, easily administered and scored, fatigue scale. Although there is no cost to use the BFI, there appears to be a US $100 licensing or processing fee associated with its use (https://www4.mdanderson.org/symptomresearch/index.cfm?), which impacts the clinical utility of this instrument.

Cancer Fatigue Scale (CFS)

The CFS may be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: B). On the basis of 6 psychometric studies ranging in quality from high (1), acceptable (2), to low (3), this 15-item multidimensional scale measuring physical, affective, and cognitive fatigue may be useful for clinical use, with promising psychometric results. The lower-quality evidence is related to challenges of translation validation; nuances of language and semantics may not adequately represent some concepts within each of the 3 domains.

Description of Measure and Psychometric Properties

Each question of the CFS is assessed on a 5-point Likert scale where 1 = no and 5 = very much; this can be completed through self-report or via interview and takes only a few minutes to complete. Higher scores indicate greater fatigue.

Studies have examined multiple types of reliability and validity. In the questionnaire development phase, the internal consistency of the items was examined in 4 studies; Cronbach α values ranged from 0.79 to 0.94 among the studies with acceptable quality, indicating good to excellent internal consistency.[76,77] Test–retest reliability was also good, with $r = 0.79$ for the total scale and $r = 0.80$, 0.84, and 0.75 for the physical, affective, and cognitive subscales, respectively. Construct validity was established showing that the CFS items positively correlate with the construct of fatigue.[76] Convergent and divergent validity have also been investigated. The CFS has established convergent validity with the visual analog scale for fatigue (the One-Item Fatigue Scale), a low Karnofsky Performance Score, the FSI, the Schwartz Cancer Fatigue Scale, the HADS, the Mini-Mental State Examination, and the global health status of the EORTC-QLQ-C30.[76–78] The CFS divergent validity was established with the Herth Hope Index, and discriminant validity showed that the scale could distinguish between Karnofsky Performance Scores of >80% and those of <80% as well as between no depression, doubtful depression, and clinical cases of depression on the HADS.[79] Although no cutoff points are reported, some evidence suggests that the CFS is responsive to change with a minimally important difference ranging from 0.3 to 0.5.[80]

Clinical Utility

The CFS is estimated to take less than 5 minutes to complete and has been translated into multiple languages. There is evidence that some aspects of fatigue may not be fully represented in translated versions due to cultural and linguistic differences. Cost information could not be determined.

Multidimensional Fatigue Inventory 20 (MFI-20)

The MFI-20 may be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: B). On the basis of high-quality (although mostly level II) studies, ease of use, and availability, the MFI-20 is a useful tool for the initial or ongoing assessment of CRF. However, there are noted challenges with structural validity when translated into other languages.

Description of Measure and Psychometric Properties

The MFI-20 is a 20-item self-report that addresses fatigue as a "multidimensional construct" with 5 dimensions—general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity. Each dimension contains 4 questions, scored on a Likert scale from 1 to 5, where higher scores indicate greater fatigue. The tool is free to use and is estimated to take between 5 and 10 minutes to complete.[81] The MFI-20 was originally developed in Dutch, but has been translated into several languages, including French, English, Chinese and Brazilian Portuguese.[81–87]

The MFI-20 was tested in patients with various cancer diagnoses and varying stages of disease and treatment. It had good overall internal consistency, with Cronbach α ranging from 0.84 to 0.93 overall and from 0.59 to 0.81 for each subscale.[84–87] The MFI-20 showed expected relationships between measures of fatigue/vigor, physical and mental subscales of quality-of-life measures and depression/anxiety instruments.[83–85,87] A 5-factor solution was identified in early testing,[81] however, translated versions revealed challenges with items loading on multiple factors, with multiple validation versions loading into as few as 3 factors compared to the original version.[83,85–87] These questions of structural validity create uncertainty into the named dimensions and constructs of the MFI-20.

Clinical Utility

The clinical utility of the MFI-20 is good. The tool is free after contacting the developer and typically takes 5 to 10 minutes to complete. The tool is typically completed as a pen and paper measure and is available in multiple languages. Similar to other instruments, translated versions have noted challenges with factor analysis and questions loading onto multiple dimensions.

Fatigue Symptom Inventory (FSI)

The FSI may be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength: B). The FSI is a useful tool for the initial or ongoing assessment of CRF. However, there was a relatively low number of available high-quality studies, as well as concerns about its use in other languages (ie, Taiwanese Chinese) that potentially impact its validity and clinical utility in those languages.

Description of Measure and Psychometric Properties

The FSI is a 14-item self-report designed to assess the severity, frequency, diurnal variation of fatigue, along with its perceived interference with quality of life.[88] Fatigue severity is assessed using 4 items on a scale from 0 to 10 (0 = "not at all fatigued;" 10 = "as fatigued as I could be") within 4 areas: most, least, average, and current fatigue. Frequency is measured using 2 items: the number of days in the past week (0–7) that a patient felt fatigued and the extent of each day on average they felt fatigued (0 = none of the day; 10 = the entire day). Perceived interference is measured diurnal using 7 items on a separate scale from 0 to 10 (0 = no interference, 10 = extreme interference) that assess the degree to which fatigue in the past week was judged to interfere with various aspects of life such as general activity, ability to dress and bathe, ability to concentrate, etc. The final item provides qualitative information about potential daily diurnal patterns of fatigue. Each item on the FSI can be scored individually, and the frequency and interference ratings can be summed to yield a total subscale score.[89]

The FSI exhibited good internal consistency, with Cronbach α values ranging from 0.89 to 0.95 for the overall, severity and interference subscale scores.[79,88,90–92] Test–retest reliability among patients with cancer assessed on 3 separate occasions were low to adequate (range $r = 0.35$ to 0.75).[91] Convergent and divergent validity was demonstrated using the fatigue subscale of the POMS–Fatigue, SF-36 vitality subscale, Satisfaction With Life Domains Scale for Cancer, Schwartz Cancer Fatigue Scale, and CFS, with correlations in the expected directions.[79,88,90,91] The FSI was able to discriminate between high and low performance status on the Karnofsky Performance Score, treatment stage, and between patients with cancer and healthy subjects ($P < .05$).[79,91] The reported minimal detectable change is ≥ 3.[93] Validity testing in the Taiwanese Chinese version resulted in a 12-item questionnaire compared to the original, as well as some contextual challenges in translation.[79] This and a relatively low number of high-quality studies available about the FSI may potentially impact its recommendation strength.

Clinical Utility

The FSI is free to use and takes less than 5 minutes to complete.[94] The tool has been translated for use in Chinese populations.

Patient-Reported Outcomes Measurement Information System Computerized Adaptive Testing for Fatigue (PROMIS Bank v1.0–Fatigue CAT)

The PROMIS Bank v1.0–Fatigue CAT may be used to assess for CRF in individuals living with or beyond a cancer diagnosis (Recommendation Strength:B).

Description of Measure and Psychometric Properties

The PROMIS Bank v1.0–Fatigue CAT is part of the PROMIS system of self-report measures developed by the National Institutes of Health to evaluate and monitor population health. The PROMIS Bank v1.0–Fatigue CAT is available via several web-based platforms or applications, using computerized adaptive testing (CAT). However, although psychometrics are promising, they are still in the relatively early stages, and access might be a limiting factor for some patients; this factor might affect its clinical utility.

The PROMIS Bank v1.0–Fatigue CAT item bank includes 95 items (ie, questions and their respective response options) that have been reviewed qualitatively and quantitatively as reliable and valid indicators of fatigue. The items have been item response theory calibrated as a unidimensional measure of fatigue,[95] including both fatigue experiences (eg, severity) and impact on patient's lives (eg, physical, emotional, social). Period of recall is over 7 days. With the CAT, the patient's responses guide the system's subsequent choices from the full

item bank. Initial items target moderate symptom severity, then, on the basis of response, the succeeding questions tap higher or lower symptom levels.[96] This allows for fast identification, between 4 and 12 items, of where the patient scores on the domain continuum (https://www.healthmeasures.net/resource-center/measurement-science/computer-adaptive-tests-cats).

PROMIS Bank v1.0–Fatigue CAT scores were significantly correlated with FACIT-F scores ($r = -0.83$).[96] Researchers have identified challenges with reliability when using the PROMIS Bank v1.0–Fatigue CAT when measuring intraindividual change in fatigue with a level of confidence required for intervention.[97] The area under the curve using receiver operating characteristic analysis for fatigue was 0.95 with a FACIT-F cutoff of ≤30, and the recommended T-score cutoff point was reported to be 57.[96]

Clinical Utility

The PROMIS Bank v1.0–Fatigue CAT is intended to be completed by the patient without assistance, though a proxy is also acceptable should the patient be unable to report on their own. However, because the tool is housed in a web-based or app-based format, access might be limited for some patients and providers. Moreover, use of the CAT system may have a relatively high cost, ranging from $5000 annually for single institutions and up to $15,000 annually for most distributors/vendors; additional fees and programming time may apply for use of foreign languages.[98] The developers also note that use of the CAT in a system such as REDCap is strictly for research studies only and not ongoing clinical use.[98] Computer adapted tests are designed to have fewer items than conventional measures, decreasing patient burden. It is important to note that there is a PROMIS cancer-specific fatigue CAT (PROMIS–Cancer Bank v1.0 Fatigue); however, because of limited reported psychometric properties, we can only provide a grade of "R" for this measure.

Discussion

Importance of Clinical Practice Guideline for Screening of and Assessing Cancer-Related Fatigue

This clinical practice guideline provides a current critical review of the literature related to the screening and assessment of CRF by evaluating the strength and quality of the available evidence and making recommendations for clinical use by health care providers. Bias assessment, psychometric strength, and clinical utility were evaluated by the GDG in making final recommendations. The NCCN CPG for CRF strongly recommends that screening for CRF take place at every visit with a health care provider, and should the fatigue be deemed moderate to severe, a comprehensive assessment should take place.[3] The NCCN guideline provides multiple tools for screening and assessment in the appendix, but the critical analysis of the literature supporting the use of such tools is not transparent. Another guideline by the American Society of Clinical Oncology also recommends such screening and assessment yet fails to individually assess the available evidence supporting particular methods for screening and assessment.[99] The Pan-Canadian CRF Guideline has not had an update since 2013.[100] The current CPG addresses a significant gap in the literature by assessing and critically analyzing the psychometric properties of tools currently used for screening and assessment of CRF. This in-depth analysis has allowed the GDG to make recommendations regarding the clinical utility of 25 screening and assessment tools for CRF.

When formulating recommendations for the screening and assessment of CRF, it is important to be mindful of the benefits and harms associated with the use of these clinical tools. Certainly, the benefits are apparent; if CRF can be identified, it can be addressed. Appropriate referrals can be made, and intervention initiated. The potential harm is that some tools may create respondent burden potentiating fatigue itself. Yet, given the availability of simple and quick measurement tools, the harm of not detecting and treating CRF is too significant to ignore. Screening and assessment should follow NCCN recommendations to be done at every visit with a health care provider;[3] all health care providers involved in the care of a person with cancer are able to utilize the recommended screening tools here, and once referral for treatment is made to an appropriate health care provider such as rehabilitation or counseling, a more in-depth assessment can be administered to drive intervention decisions.

Recommendations for Screening

Only 1 screening tool rises to the level of grade A evidence for screening CRF. The EORTC-QLQ-C30 is a general symptom inventory that can be used to screen for fatigue and other problems those with cancer may have. The MDASI, also a general symptom inventory in which the individual with cancer assesses their present symptom burden, is graded B. Positive responses on the questions related to fatigue can be used to trigger a more in-depth assessment. The limitation of both self-report questionnaires is also their strength; they survey a broad number of possible symptoms. These tools do not solely focus on fatigue. Should fatigue be the primary problem an individual faces, there are extraneous questions. As screens, neither tool addresses the multidimensional nature of CRF in depth. Yet as a screen, appropriate referral for assessment can be made.

Both questionnaires can be completed in 10 minutes or less, with the MDASI having fewer questions. A primary limitation to possible adoption of these questionnaires is both the cryptic cost related to use—websites for the questionnaires do not provide a definitive answer to how much the questionnaire costs to use but instead require a form to be completed and sent to the authoring body—as well as the potential high cost associated with use. This group reached out to both the European Organisation for Research and Treatment of Cancer and the University of Texas–MD Anderson Cancer Center (UTMDACC) regarding costs. The authors confirmed that the EORTC-QLQ-C30 can be utilized for academic research and clinical use free of charge, but this took extra effort to confirm. UTMDACC responded that the charges for use of the MDASI are dependent on the number of health providers in a practice; for large hospital-based rehabilitation practices, this cost could be prohibitive, negatively impacting clinical utility.

The One-Item Fatigue Scale is a variation of a numeric rating scale or a visual analog scale. As such, it is easy to administer, free, and has established psychometrics in pain assessment. Although this group recommends this as best practice for screening for its simplicity and high clinical utility, it cannot be rated strongly due to a lack of specific research in the CRF realm. Likewise, the Distress Thermometer, which has widespread use in cancer centers, is easy to use to screen

for problems related to cancer and cancer treatment, including fatigue, yet lacks any significant psychometric research to establish its reliability and validity. For these reasons, this GDG recommends additional research into these promising tools to screen for CRF.

Recommendations for Assessing CRF

Several tools are available for health care providers to assess the multidimensional nature of CRF. These include the Grade A scales of the PFS-R, the FACIT–Fatigue, and the PROMIS Fatigue–Short Forms. These scales address the multidimensional nature of CRF while having excellent psychometrics in high-quality studies and good to excellent clinical utility. The PFS-R assesses fatigue in the behavioral, affective (emotional), sensory and the cognitive (mood) domains. FACIT-F assesses fatigue and its impact on daily activity. The PROMIS Fatigue–Short Forms assesses the physical, mental, and social impact of fatigue.

Likewise, 4 scales are graded B and may be used to assess CRF among individuals diagnosed with cancer. These include the BFI, the MFI-20, the FSI, and the PROMIS Bank v1.0–Fatigue CAT. These scales fail to reach the level of an A recommendation because of either lower-quality evidence or unsettled clinical utility. Indeed, although the PROMIS Bank v1.0–Fatigue CAT scores high for quality evidence and ease of completion, it has drawbacks in clinical utility, including the requirement for computer access to the internet and, more significantly, the cost. The BFI, too, has excellent evidence for use, but has a significant cost associated with use, lowering the grade from A to B. Although both the MFI-20 and the FSI are promising, they lack the strength of evidence to move the recommendation for use to an A. It is possible that higher-quality studies examining the psychometric qualities of these tools will be conducted in the future.

This number of potential tools from which a health care provider can choose to assess CRF is substantial. Although the authors presented alternative choices with a grade of B, they recommend that any of the 3 tools graded A, strongly recommended, should be used to assess CRF. Choosing which one will depend on the clinical situation and the point of recovery for those with cancer; only the MFI-20 covers all points in the care continuum. Yet decreasing the variation in assessment can provide the research community with a clearer picture of fatigue in those with cancer. Since each of these tools, the PFS-R, the FACIT-F, and the PROMIS Fatigue–Short Forms, are multidimensional in nature, they provide the health care provider with rich information regarding the type, severity, and impact of fatigue on individuals with cancer.

Constraints of this Clinical Practice Guideline

The survey of the literature and evaluation of the multiple scales for CRF have led the GDG to identify several limitations in the current evidence database. Although 25 self-report questionnaires are included in this review, the survey of the literature found 55 different fatigue assessment tools. Not all were included as only those tools evaluated in a population of individuals with cancer with research support were included. Even with this strict inclusion, 25 different tools provide too many choices. Although the authors acknowledge that different populations may require different tools, the sheer number of tools results in a lack of a consistent benchmark against which to measure. Furthermore, the numerous tools seem to have resulted in less in-depth research as the research efforts are spread out over many possibilities. Prior to further new tool development, this GDG proposes increased research into the recommended tools to determine which tools are best suited to screen for and assess CRF. This research should focus on whether certain tools are more sensitive in a specific population or at a specific time point in care (ie, chemotherapy or radiation therapy treatment) or survivorship.

One of the important aspects of the use of questionnaires as screening and assessment is determining diagnostic cutoff points. Although the NCCN CRF Guideline stipulates that a score of 1 to 3 on a scale from 0 to 10 is mild fatigue, 4 to 6 is moderate, and > 7 is severe, these cutoff points appear to be based on research on values from the MDASI, rather than specific cutoff points for the scale from 0 to 10. Additionally, there is limited evaluation of cutoff points for most of the other scales in this review and demonstrates a dearth of research into tool responsiveness. Most tools have no established minimal detectable change or minimally clinically important difference. With the limited information on responsiveness, caution should be exercised in using these tools as outcome measures. Further research is needed to establish the responsiveness of these recommended tools so that they can be used as outcome measures over time.

Another area to consider is the widespread use of translated versions of multiple scales. That scales are translated into many languages increasing the accessibility of the scales. However, the health care provider must understand the difference between validation in another language and a simple translation. Validation requires psychometric study of the translated instrument in the population of interest. Although multiple translations of questionnaires exist, not all are validated in the translated language. This is an area of further research.

One of the primary areas of weakness of all screening and assessments of CRF is that they rely on patient self-report since no objective diagnostic standard test exists. This is in part because of the difficulty in determining causes of CRF, and debate about whether CRF is a centrally mediated phenomenon or is peripherally related to changes due to cancer and the effects of treatment is ongoing.[94,101–104] Until the cause of CRF is established, objective assessment may remain elusive.

Limitations

There are several limitations to this systematic review that serve as the basis of this clinical practice guideline. First, although the initial literature search was comprehensive, and multiple secondary searches were carried out to find studies evaluating the psychometrics of tools used to screen for and assess CRF, it is possible that studies were missed that met inclusion criteria, either because they were published outside of the review window or failure to be identified during the MeSH term search. Additionally, only studies that included individuals with cancer were included. Any articles or tools not published in English were excluded; it is possible that strong evidence for use may be overlooked. It is possible that other fatigue measures may be suitable for screening and assessing fatigue in individuals with cancer that are used in other populations. Until psychometric evaluation of these tools in a population of individuals with cancer is conducted, these tools should not be used to screen for or assess CRF.

Implementation of and Procedure to Update this Guideline

The preliminary findings of this guideline were presented at the APTA Combined Sections Meeting and the American College of Rehabilitation Medicine conference. Additionally, the GDG with support of APTA Oncology and APTA is committed to open access publication in order to reach the broadest possible audience. An executive summary of this guideline is published in *Rehabilitation Oncology* and is freely available. Digital tools including a podcast, social media highlights, Academy newsletters, and other means will be employed to increase awareness of this guideline. Additional implementation practices including decision-making trees and other clinical decision-making will be developed.

This guideline should be reviewed and updated 5 years after publication in accordance with best practices for guideline development and implementation set forth by *Clinical Practice Guidelines We Can Trust*, AGREE II, and ECRI.[24,25] This update will consist of an updated search for contemporary evidence, combined with a review of recommendations, to provide current best practice recommendations.

Conclusion

CRF should be screened on each patient encounter by all health care providers. Positive screens should be followed up by referral to appropriate health care providers for assessment using 1 of several strong assessment tools.

Author Contributions

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