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EDUCATIONAL OBJECTIVES:
After reading the article “Screening, Evaluation, and Management of Cancer-Related Fatigue: Ready for Implementation to Practice?” the learner should be able to:
1. Describe the prevalence and risk factors associated with cancer-related fatigue.
2. Discuss what is known regarding the biologic mechanisms of cancer-related fatigue.
3. Review guideline recommendations regarding screening and evaluation of patients for cancer-related fatigue.
4. Describe evidence-based pharmacologic and nonpharmacologic interventions for cancer-related fatigue.

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AUTHOR DISCLOSURES
Ann M. Berger, PhD, APRN, AOCNS, FAAN, Sandra A. Mitchell, PhD, CRNP, AOCN, Paul Jacoebse, PhD, and William F. Pirl, MD, MPH, have nothing to disclose.

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Evidence regarding cancer-related fatigue (fatigue) has accumulated sufficiently such that recommendations for screening, evaluation, and/or management have been released recently by 4 leading cancer organizations. These evidence-based fatigue recommendations are available for clinicians, and some have patient versions; but barriers at the patient, clinician, and system levels hinder dissemination and implementation into practice. The underlying biologic mechanisms for this debilitating symptom have not been elucidated completely, hindering the development of mechanistically driven interventions. However, significant progress has been made toward methods for screening and comprehensively evaluating fatigue and other common symptoms using reliable and valid self-report measures. Limited data exist to support the use of any pharmacologic agent; however, several nonpharmacologic interventions have been shown to be effective in reducing fatigue in adults. Never before have evidence-based recommendations for fatigue management been disseminated by 4 premier cancer organizations (the National Comprehensive Cancer, the Oncology Nursing Society, the Canadian Partnership Against Cancer/Canadian Association of Psychosocial Oncology, and the American Society of Clinical Oncology). Clinicians may ask: Are we ready for implementation into practice? The reply: A variety of approaches to screening, evaluation, and management are ready for implementation. To reduce fatigue severity and distress and its impact on functioning, intensified collaborations and close partnerships between clinicians and researchers are needed, with an emphasis on system-wide efforts to disseminate and implement these evidence-based recommendations. CA Cancer J Clin 2015;65:190-211. © 2015 American Cancer Society.

Keywords: cancer-related fatigue, evidence-based interventions, multidisciplinary management, patient-reported outcomes, screening

Introduction
Cancer-related fatigue (fatigue) is the symptom reported more frequently than any other symptom by patients with cancer and is often the symptom that causes the most suffering and interference with function during both the treatment and survivorship phases.1 In response to the critical need to reduce this pervasive and debilitating symptom, the National Cancer Institute’s (NCI) Symptom Management and Quality of Life Steering Committee constituted a working group to identify gaps in knowledge about fatigue and to advance the science and research of symptom intervention. The committee’s main recommendations were to continue to address measurement issues and to adopt the Patient Reported Outcomes Measurement Information System (PROMIS) fatigue scale in clinical research; to examine biobehavioral mechanisms of fatigue, and to test interventions that are based on hypothesized mechanisms.2 Recommendations from a 2012 international collaboration on fatigue and its impact on functioning parallel those of the NCI in recommending the need to increase knowledge of fatigue’s underlying mechanisms, improve the measurement of fatigue in clinical and research contexts, and promote the use of manuals and protocols to permit fidelity of interventions and to allow fidelity across diverse contexts.3

1University of Nebraska Medical Center College of Nursing, Fred and Pamela Buffett Cancer Center, Omaha, NE; 2Outcomes Research Branch, Applied Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD; 3Division of Population Science, Moffitt Cancer Center and Research Institute, Tampa, FL; 4Center for Psychiatric Oncology and Behavioral Sciences, Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA

Corresponding author: Ann M. Berger, PhD, University of Nebraska Medical Center, 985330 Nebraska Medical Center, Omaha, NE 68198-5330; aberger@unmc.edu

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A body of evidence from rigorously conducted studies has provided sufficient evidence regarding cancer-related fatigue such that recommendations for screening, evaluation, and interventions have been released by several leading organizations. Table 1 provides a comparison across these fatigue management recommendations, including differences in the processes used to summarize the evidence and develop the guideline recommendations. The National Comprehensive Cancer Network (NCCN) guidelines for fatigue and survivorship remain the most frequently updated and widely circulated resources for multidisciplinary clinician decision-making about screening, evaluating, and managing fatigue throughout the course of cancer.\textsuperscript{4,5} The Oncology Nursing Society (ONS) disseminates the Puting Evidence Into Practice (PEP) resources and emphasizes fatigue interventions that are “recommended for practice” and “likely to be effective.”\textsuperscript{6-8} The NCI supports a Physician Data Query (PDQ) website that summarizes general information about cancer-related fatigue for patients and provides health professionals with up-to-date information about its causes, assessment, and treatment. However, the NCI PDQ website does not provide formal guidelines or recommendations for making decisions about health care.\textsuperscript{9,10} A collaborative partnership in Canada and the American Society of Clinical Oncology (ASCO) both recently released their initial guidelines for fatigue. Both groups adapted existing recommendations (ie, NCCN, ONS) to enhance efficiency and reduce duplication\textsuperscript{9,10} and also conducted systematic searches for current evidence.

It is clear that there has been significant progress made to support evidence-based screening, evaluation, and management of fatigue,\textsuperscript{12} and clinicians have available to them several evidence-based guidelines with concordant recommendations based on current evidence. It is now time to test system-wide efforts to promote the dissemination and implementation of these recommendations in clinical practice and to develop and test evidence-based programs and policies designed to improve fatigue management. Although evidence-based recommendations for fatigue are available for clinicians, and some have patient versions, barriers remain at the patient, provider, and system levels that hinder adoption in clinical practice. Implementation of the recommended interventions by multidisciplinary providers and patients remains haphazard, and the challenges to guideline implementation include attitudes, knowledge, and resources (both time and expertise).

In this article, first, we summarize the evidence base supporting effective fatigue management, including the prevalence, underlying biology, and causative factors. Then, we describe established methods for screening and measurement of fatigue. The next section provides a synthesis of the research that supports current guidelines for the pharmacologic, behavioral, and supportive care management of cancer-related fatigue. The final section discusses approaches to accelerate the translation of evidence into clinical practice and health care delivery systems to achieve improved fatigue outcomes.

### Prevalence

Cancer-related fatigue is highly prevalent in patients during and after cancer treatment. Fatigue reportedly occurs in 70\% to 80\% of patients in the clinical trial setting and varies according to the type of cancer, treatments, and method of assessment.\textsuperscript{13}

Of patients undergoing active treatment, those most likely to report moderate/severe fatigue were patients being treated with opioids, with poor performance status, and those who had a greater than 5\% weight loss within 6 months.\textsuperscript{1} Among 121 East Asian Indian patients, severe fatigue was more prevalent among patients who were receiving chemotherapy (98\%) and concurrent chemoradiation (79\%) compared with those who were receiving radiotherapy (45\%); these percentages are similar to those for patients treated in the United States.\textsuperscript{14} Men with prostate cancer reported a prevalence of any fatigue as high as 74\%, and 39\% reported chronic fatigue when hormone therapy was combined with radiotherapy.\textsuperscript{15} About one-third of cancer survivors, most of whom had breast cancer, reported persistent fatigue during the first 10 years post-treatment.\textsuperscript{13} Wang and colleagues also found that about one-third of cancer survivors reported moderate/severe fatigue and that fatigue was most likely to occur in patients with poor performance status and a history of depression.\textsuperscript{1} Fatigue is highly prevalent among patients, and several factors that predict those at higher risk have been identified.

A recent research priority has been to determine prevalence based on the use of diagnostic criteria for a syndrome of cancer-related fatigue. Results of a systematic review showed wide variability in the prevalence of fatigue based on diagnostic criteria, reflecting a lack of consistency in how these diagnostic criteria are applied.\textsuperscript{16} More research is needed to revise these criteria to enhance their usefulness. This review highlights the need to improve measurements that use consistent diagnostic criteria for a syndrome of cancer-related fatigue.

### Causes and Biology

Fatigue is a common medical complaint across many illnesses, and its causes may vary in different diseases and settings. Persistent chronic fatigue is reported by approximately 15\% of primary care patients.\textsuperscript{17} If no medical causes are identified, a diagnosis of chronic fatigue syndrome is often considered. Although chronic fatigue syndrome may share some characteristics with cancer-related fatigue, they should be considered distinct entities. Some of their definitions are similar, such as persistent fatigue that is not the result of exertion, not relieved by rest, and causes
| TITLE                                                                 | FIRST RELEASE | LAST UPDATE | SPONSORING ORGANIZATION (SOURCE) | SOURCE OF EVIDENCE | CRITERIA USED TO GRADE EVIDENCE | STRENGTHS                                                                 | LIMITATIONS                                                                 |
|----------------------------------------------------------------------|---------------|-------------|----------------------------------|--------------------|---------------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines) | 2000          | October 2014| NCCN (NCCN 2015)                 | Research studies and meta-analyses; expert consensus | NCCN categories of evidence and consensus | Annual updates; panel members represent 21 leading cancer centers; interventions divided into 3 phases: during treatment, post-treatment, and end of life | NCCN criteria for grading nonspecific; most of the evidence comes from women with early stage breast cancer |
| NCCN Guidelines for Survivorship                                      | 2013          | July 2014   | NCCN (NCCN 2014)                 | Research studies and meta-analyses; expert consensus | NCCN categories of evidence and consensus | Focus on survivorship phase; late effects/long-term psychosocial and physical problems and prevention, healthy lifestyle | Covers individual symptoms; but lacks a focus on symptom clusters |
| Putting Evidence Into Practice                                         | 2006          | October 2014| Oncology Nursing Society (ONS) (Mitchell & Friese 2014,7 ONS 2014,7 Inuin & Johnson 20148) | Research studies and meta-analyses; expert consensus | Weight of evidence classification | Rigorous review and evaluation schema; each team is led by a researcher; comprehensive search strategy for all articles that meet criteria; one of 20 supportive care symptoms that used weight of evidence classification | No content on screening or assessment; focus is on weight of evidence for interventions |
| Pan-Canadian Practice Guideline: Screening, assessment and care of cancer-related fatigue in adults with cancer | 2011          | February 2011| Collaborative partnership between the Canadian Partnership Against Cancer and the Canadian Association of Psychosocial Oncology (Howell 20139) | NCCN Guidelines, ONS evidence synthesis | ADAPTE methodology | Recommends all health care professionals should routinely screen adult cancer patients for fatigue using standardized screening tools; if positive, conduct comprehensive, focused assessments; treatment options include those included in NCCN 1 and 2A and ONS categories “recommended for practice” and “likely to be effective” | Has not been updated since initial release in 2011; scheduled for update August 2015 |
| American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Adaptation | 2014          | April 2014  | ASCO (Bower 201410)              | Pan-Canadian, NCCN Guidelines, NCCN Guidelines/Survivorship, ONS evidence synthesis | ADAPTE methodology | This method takes advantage of existing guidelines to enhance efficient production, reduce duplication, and promote the local update of quality guideline recommendations; used Pan-Canadian in addition to NCCN and ONS information | Focus is on survivors who are experiencing symptom of fatigue post-treatment |
a reduction in functioning. Poor memory or concentration, unrefreshing sleep, and postexertion malaise also are frequently experienced in both entities. However, individuals with cancer-related fatigue may not report enough of the other required symptoms for a diagnosis of chronic fatigue syndrome, such as sore throat, tender cervical or axillary lymph nodes, muscle pain, multijoint pain without redness or swelling, and new or severe headaches. Most importantly, the key distinction is that the fatigue with chronic fatigue syndrome is "unexplained," and the other is cancer-related by definition. Cancer-related fatigue can be the result of cancer treatments, including surgery, chemotherapy, and radiation, and the impact of the cancer itself, both physical and psychological. This fatigue can persist many years into survivorship. In addition, fatigue can occur in individuals with cancer from other causes, such as comorbidities and their treatments.

Although the underlying mechanisms for cancer-related fatigue have not been fully elucidated, research suggests that there may be some common underlying biologic alterations. Similar to the symptoms, these physiological findings might even persist for years after cancer treatment has been completed. Work over the last decade has identified several interconnected processes that are correlated with fatigue in individuals with cancer. These have led to current hypotheses about the etiology of cancer-related fatigue that include elevations in levels of proinflammatory cytokines, 5-hydroxytryptophan (5-HT) dysregulation, hypothalamic-pituitary-adrenal axis dysfunction, circadian rhythm disturbances, and increased vagal tone. Although correlations cannot speak to causation, a compelling story can be told by starting with any one of these processes. For example, one hypothesized pathway could be that the administration of chemotherapy elevates levels of tumor necrosis factor-alpha, which might then lead to changes in diurnal levels of cortisol and circadian rhythm disturbances resulting in sleep disturbance and fatigue, increased release of peripheral 5-HT, activation of afferent vagal nerves and decreased skeletal muscle tone resulting in general weakness, and altered skeletal muscle metabolism resulting in wasting. However, biomarkers have yet to enter into the clinical diagnosis and management of cancer-related fatigue.

Fatigue in individuals with cancer can be the end result of many causal pathways; often more than one causal, contributing, or modulating factor may be present. In evaluating a patient with cancer-related fatigue, clinicians must consider all potential factors that could be contributing to fatigue. NCCN and recent ASCO guidelines recommend that the clinical evaluation for fatigue consider changes in disease status along with pain, emotional distress, anemia, sleep disturbance, nutrition deficits/imbalance, decreased functional status, medications/side effects, and comorbidities, including alcohol and substance abuse. Although clinicians may be familiar with the evaluation of many of these issues, they may have less experience evaluating the factors that contribute to fatigue, such as emotional distress, sleep disturbance, nutritional deficits/imbalance, decreased functional status, and the complexities of pain.

Psychiatric symptoms and disorders can both cause fatigue and have fatigue as a manifestation. Depression and anxiety are the 2 most common psychiatric comorbidities that occur in individuals with cancer-related fatigue. Recent ASCO guidelines for the management of depression recommend using the Patient Health Questionnaire-2 (PHQ-2) to screen patients for possible depression. The PHQ-2 has only 2 questions; and, when a "help" question was added, the PHQ-2 was both sensitive and specific in identifying depression. Patients with both fatigue and depression also may report greater functional impairment than other patients with the same fatigue severity level, suggesting that mood disturbance is an important intervention target in all patients with cancer-related fatigue. The Fatigue Symptom Inventory (FSI) may be a particularly helpful measure in isolating fatigue and depression; depression is suggested when scores on the FSI impairment subscale are greater than those on the severity subscale. Another 2-question screening measure for anxiety, the generalized anxiety disorder 2 (GAD-2) scale, is comprised of the first 2 items from the GAD-7. Both of these screening measures for anxiety and depression are available without cost online. Patients who screen positive on the PHQ-2 or GAD-2 should receive further evaluation and appropriate treatment. Referrals to mental health professionals can be useful to guide further evaluation and multidisciplinary management of mood disturbances that accompany fatigue.

Disrupted sleep can result in daytime tiredness, sleepiness, and difficulty with cognitive function. Sleep problems are common in individuals with cancer and are likely under-reported. Fatigue from sleep problems often can present as excessive daytime sleepiness. Helpful questions can be, “Does your fatigue feel like you are struggling to stay awake? Do you sometimes fall asleep by accident?” Insomnia can be managed with behavioral interventions as well as medications. Multiple awakenings over the course of a night can be common. These awakenings can be caused by other symptoms or side effects of treatments, such as the need to frequently use the bathroom or to clear nasopharyngeal secretions at night.

Sometimes, patients might not even be aware of a sleep disruption other than experiencing fatigue and an increased need for sleep. These symptoms could suggest an underlying sleep disorder, such as sleep apnea or periodic limb movements during sleep, both of which are associated with arousals. Obstructive sleep apnea can develop with age, weight gain, and airway changes. Central apnea can sometimes be present in patients who are receiving narcotics. Periodic limb movements during sleep are associated with

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iron deficiency and with some classes of medications, including antiemetics and antidepressants. Referral for polysomnography is needed to make these diagnoses and determine appropriate treatment. However, a simple sleep history can reveal potential contributors to insomnia, such as napping and poor sleep habits. Although primary care providers often manage sleep disorders, a referral to a sleep specialist or behavior sleep therapist may be needed.

Nutritional deficits also can contribute to fatigue. Poor appetite, gastrointestinal symptoms, weight loss, and low albumin may signal a nutritional problem. A referral to a registered dietitian may be helpful for both assessment and dietary recommendations, but the primary team also could do further assessments with tools validated in patients with cancer, such as the Patient-Generated Subject Global Assessment.

Deconditioning is often observed in patients with cancer-related fatigue. Deconditioning could be the result of poor nutrition, inactivity, cardiopulmonary dysfunction, and/or medications that can cause sarcopenia (glucocorticoids and androgen-deprivation therapy). Performance-based evaluations and questions about how an individual typically spends their day and any limitations that result from fatigue can provide a sense of an individual’s functional status and gauge the extent of debilitation from fatigue. Referrals to physical therapy can offer more detailed assessments of the extent of cardiopulmonary deconditioning and sarcopenia and are helpful in prescribing and advancing a safe and effective regimen of physical activity to build strength and stamina.

Pain can have a complex relationship with cancer-related fatigue. Pain often co-occurs with fatigue and may be part of a symptom cluster, suggesting some possible underlying connections. Pain itself can be exhausting, and it also can lead to fatigue by interfering with sleep and decreasing abilities for physical activity. Although the treatment of pain often improves fatigue, sedating side effects of the pain medications can amplify fatigue. Opioids may not only cause sedation, they also can disrupt sleep by causing central apnea and alterations in sleep architecture leading to unrefreshing sleep.

After evaluating and treating physical and psychological contributors to fatigue, it may still persist in some individuals. This does not necessarily mean for these individuals that their fatigue is any less real. Patient self-report is our only method of detecting fatigue, and many times a specific cause for fatigue cannot be identified. Nonetheless, exploring any secondary gain an individual may be receiving from remaining fatigued should be considered.

Screening for Cancer-Related Fatigue

Clinical practice guidelines for cancer-related fatigue developed by the NCCN and the Canadian Partnership Against Cancer and Canadian Association of Psychosocial Oncology (CPAC/CAPO) and adapted by ASCO for cancer survivors recommend that all cancer patients be screened for fatigue at their initial visit, at appropriate intervals during and after cancer treatment, and as clinically indicated. All of these guidelines also recommend that screening of adults with cancer be conducted using brief, quantitative, self-report measures with empirically established cutoff scores.

With regard to specific measures for use with adults, the CPAC/CAPO guidelines recommend administration of the 10-item Edmonton Symptom Assessment System (ESAS) as part of a broader multisymptom screening strategy. In terms of fatigue, the ESAS includes an item asking respondents to rate their current level of tiredness on a scale from 0 (“no fatigue”) to 10 (“worst fatigue you can imagine”). Ratings are categorized as mild (score, 1-3), moderate (score, 4-6), or severe (score, 7-10) and then are used to recommend different care pathways.

The NCCN and ASCO guidelines, in contrast, recommend administration of an item asking respondents to rate their level of fatigue over the past 7 days on a scale from 0 (“no fatigue”) to 10 (“worst fatigue you can imagine”). Ratings are categorized as none to mild (score, 0-3), moderate (score, 4-6) or severe (score, 7-10) and, like the CPAC/CAPO guidelines, are then used to suggest different care pathways. There is no empirical evidence to show that one of these screening methods is clearly superior to the other. This situation reflects, in large part, the general lack of research on the screening properties of brief fatigue measures. A recent systematic review of research with cancer patients on numeric rating scales from 0 to 10 identified only 10 studies that evaluated cutoff points for fatigue. Those studies used a variety of rating formats as well as several different analytic strategies to select cutoff points. Lending confidence to the NCCN and CPAC/CAPO guidelines, a score of 4 was most frequently the optimal cutoff point for identifying moderate or clinically significant fatigue, and scores of 7 and 8 were most frequently the optimal cutoff points for identifying severe fatigue.

Unlike the CPAC/CAPO and ASCO guidelines, the NCCN guidelines also address screening for fatigue in children. For children ages 5 to 6 years, the recommendation is to ask about feeling “tired” or “not tired”; and, for children ages 7 to 12 years, the recommendation is to obtain a rating for fatigue on a scale from 1 (“no fatigue”) to 5 (“worst fatigue”). Ratings are categorized for children ages 5 to 6 years as tired or not tired and, for children ages 7 to 12 years, as 1 or 2 (none to mild), 3 (moderate), or 4 or 5 (severe) and are then used to recommend different care pathways.

Measurement and Clinical Evaluation of Cancer-Related Fatigue

The NCCN, CPAC/CAPO, and ASCO clinical practice guidelines recommend an in-depth clinical evaluation of fatigue for adults with moderate or severe fatigue, and the
NCCN guidelines recommend an in-depth evaluation for older children with moderate or severe fatigue and for younger children with any fatigue. As part of this clinical evaluation, each set of guidelines recommends a focused assessment designed to evaluate various characteristics of the patient’s fatigue, including onset, variability, duration, provoking factors, consequences for function, and symptom features of the fatigue experience (eg, cognitive dysfunction).

In contrast to the paucity of research on single-item screening measures, there is an abundant literature on multi-item self-report measurements that can be used to conduct a focused assessment of cancer-related fatigue. Indeed, a systematic review identified 40 measurements that have been used to assess cancer-related fatigue in research studies. The primary evidence to support use of these measures comes from studies that were designed specifically to evaluate their psychometric properties (eg, reliability and validity). Additional evidence comes from observational research in which the measures were used to identify the course, characteristics, and correlates of cancer-related fatigue and interventional research in which they were used to evaluate the impact of interventions expected to prevent or alleviate fatigue.

Table 2 provides a summary of the most widely used, multi-item, self-report instruments for assessing cancer-related fatigue. The instruments listed in Table 2 emphasize measures: 1) that have been used frequently in studies of patients with cancer and 2) for which information is available about their basic psychometric properties. As described below, we have also included several newly developed measures that have strong psychometric properties, address issues of patient burden, and, thus, hold potential for adoption in both clinical practice and research. A review of the psychometric properties and strengths and weaknesses of each measure is beyond the scope of this report; readers seeking such information should consult recent systematic and qualitative reviews of self-report instruments for measuring fatigue in cancer and chronic disease.

Several reviews of instruments for assessing cancer-related fatigue have attempted to distinguish between unidimensional and multidimensional measures. However, comparisons across these reviews reveal no clear operational definitions of the terms unidimensional and multidimensional and very little consistency in the categorization of measures as either unidimensional or multidimensional. Our approach in this report is to list the outcomes that can be derived from each measure to identify patterns. Inspection of Table 2 suggests that these measures can be grouped into 3 categories.

One category consists of measures yielding a single overall score that reflects the severity of fatigue. Examples include the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) Fatigue scale, the Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F) scale, the Profile of Moods States Fatigue (POMS-F) scale for use with adults; the Fatigue Scale-Adolescent (FS-A) for use with adolescents; and the Fatigue Scale-Child (FS-C) for use with children. In general, use of multi-item rather than single-item measures to assess fatigue severity is likely to yield scores with higher reliability. This issue is particularly important both in clinical care and in research when seeking to evaluate the effects of interventions designed to relieve cancer-related fatigue.

A recent and important development in this category is the creation of fatigue questionnaire item banks and fatigue short forms as part of the PROMIS initiative. Development began with the formation of a bank of 95 items for measuring fatigue in adults and a bank of 23 items for measuring fatigue in children. Items from these banks can be administered in one of two ways. In both instances, item selection is based on Item Response Theory, in which statistical models are used to link individual items to the underlying construct represented by all items in the bank.

One way for researchers to use the banks is through computer-adaptive testing, in which a participant’s responses to earlier items inform selection of subsequent items from the banks using an automated system. The ability to select the most informative item at each step has the potential to improve both the efficiency and the precision with which a construct is measured.

The other way for researchers to use the item banks is to select one of the short forms also developed using Item Response Theory. The 4-item, 6-item, and 8-item short forms for adults are nested such that the 6-item version includes the 4-item version, and the 8-item version includes the 6-item version. There also is a 7-item short form that was developed specifically for use in oncology populations based on psychometric considerations and clinician input. PROMIS measures merit consideration from both clinicians and researchers given their sound psychometric foundation, flexible measurement approach, use in a variety of other clinical populations, and placement within the larger family of PROMIS measures.

A second category consists of measures yielding scores about the extent to which fatigue interferes with daily functioning as well as fatigue severity. Examples include the Brief Fatigue Inventory (BFI) and the Fatigue Symptom Inventory (FSI) for use with adults. These types of measures can be particularly useful as part of clinical evaluation, because, in addition to providing information about the impact of fatigue, they yield separate patient ratings of fatigue right now and worst and usual fatigue in the past 24 hours (BFI) or the past week (FSI). The FSI also provides scores that describe the duration of fatigue and possible diurnal variation in fatigue (ie, the extent to which it is typically worse at the beginning or end of the day).
A third category consists of measures yielding scores for various manifestations of cancer-related fatigue. Examples include the Fatigue Questionnaire for use with adults, which yields scores for physical and mental fatigue, and the Pediatric Quality of Life Inventory Multidimensional Fatigue Scale for use with children and adolescents, which yields scores for general, sleep/rest, and cognitive fatigue. Additional manifestations measured by instruments in this category as reflected by their scores include emotional, behavioral, sensory, and perceptual fatigue (Table 2).

Among the newest measures in this category is the EORTC Quality of Life Questionnaire-Fatigue (EORTC QLQ-FA13). Creation of this measure was based on a multidimensional model of fatigue that included physical, emotional, and cognitive domains. In a preliminary evaluation of the measure, there was adequate evidence of unidimensionality for scales labeled physical fatigue (eg, “Have you felt exhausted?”), emotional fatigue (eg, “Did you feel discouraged?”), and cognitive fatigue (eg, “Did you have trouble thinking clearly?”). In addition, a recent study based on a sample of breast cancer patients yielded factor analytic results consistent with the 3-dimensional model on which the measure is based. Although final psychometric testing by its developers is still in progress, the EORTC QLQ-FA13 merits consideration based on these promising initial results and the ability to use this measure in conjunction with the EORTC QLQ-C30, which includes a scale measuring overall fatigue severity.

An important unresolved issue with the last category of measures is the extent to which they possess incremental validity beyond the first category of measures that yields...
scores only for fatigue severity. That is, to what extent does measuring various manifestations of fatigue provide additional useful information or better predict clinical outcomes than simply measuring overall fatigue severity? Surprisingly, a MEDLINE library search identified no studies with cancer patients that have directly addressed this issue. A related issue is whether measures yielding scores for several manifestations of fatigue are tapping different aspects of the fatigue experience. Of relevance to this issue is a review of 56 studies that assessed physical and mental fatigue in cancer patients. Findings suggested that measures of physical and mental fatigue often behave similarly. For example, both tend to be higher in cancer patients than in healthy controls. However, there was evidence suggesting that physical fatigue is more severe than mental fatigue in patients with more advanced disease. Although useful clinically to characterize features of a patient’s fatigue experience, additional study is needed (especially on the issue of incremental validity) to better identify the role that measures in this third category should play in research on cancer-related fatigue. Consequently, measures in the second category (e.g., BFI and FSI) can be viewed as having greater utility for clinical practice given their ability to provide information about the range of fatigue and its interference with daily functioning during a defined time period.

**Evidence-Based Summary of Pharmacologic Interventions**

The primary use of medications for cancer-related fatigue is the treatment of comorbidities and other contributors, for example, the treatment of hypothyroidism with levothyroxine. However, caution should guide the use of erythropoiesis-stimulating agents for fatigue given their association with thromboembolism and shortened survival.

The use of medications for fatigue, beyond those agents that are prescribed to treat a specific comorbidity, is still considered investigational. At this time, there are no US Food and Drug Administration-approved medications for the treatment of cancer-related fatigue. Results from clinical trials of selected pharmacologic agents in general have been mixed, and interpretation of the trial outcomes is challenged by methodological flaws that include small samples, short length of follow-up, nonblinding of outcome assessors, and low intervention potency. Without a clear physiologic mechanism, there has been little guidance for the selection of agents to study. In clinical trials, very high rates of placebo response also have made it difficult to observe a significant difference in benefit. Therefore, limited data exist to support the use of any pharmacologic agents for fatigue.

However, there is some evidence that 2 agents may be helpful. Considerations for using these medications should include a careful weighing of potential benefits against side effects. The first is methylphenidate, a stimulant medication. A recent update of a systematic review concluded that methylphenidate may provide some benefit, although other reviews have concluded that psychostimulants should only be used in the context of a clinical trial. Clinically, methylphenidate is typically started at a dose from 2.5 to 5.0 mg once or twice a day and is then increased, balancing response with side effects. Side effects of methylphenidate include anxiety, poor sleep, and, in higher doses, decreased appetite. Another medication that is similar to a stimulant, modafinil, has been repeatedly found to have no benefit on cancer-related fatigue.

The second agent that may be helpful is methylprednisolone. In a recent randomized controlled trial (RCT) that included almost 600 patients with advanced cancer who were receiving opioids, methylprednisolone 16 mg twice a day did not decrease pain intensity but significantly improved fatigue, appetite, and patient satisfaction. A recent review focused on the role of corticosteroids for fatigue in advanced cancer concluded that there is a short-term benefit for fatigue and anorexia in this setting. However, long-term use of corticosteroids was not recommended because of the lack of evidence of long-term benefits and safety. Corticosteroids can interfere with sleep, increase appetite, cause mood disturbances, and, with longer term use, may lead to muscle wasting, all of which, in turn, may amplify fatigue.

**Evidence-Based Summary of Nonpharmacologic Interventions**

A wide range of nonpharmacologic interventions have been shown to be effective in managing fatigue in adults. Table 3 summarizes those fatigue management interventions that have been identified as likely to be beneficial across the 4 published fatigue guidelines. Comparatively fewer studies have been conducted in samples of children or adolescents and young adults, and this represents an important gap in the evidence base. A recent systematic review has summarized the evidence for the effectiveness of fatigue intervention in pediatric or adolescent and young adult populations.

There is expert consensus that patients with fatigue should be evaluated for potentially treatable etiologic factors and managed as indicated. Examples of factors that may contribute to fatigue include endocrinopathies (hypothyroidism, hypogonadism, adrenal insufficiency), cardiopulmonary dysfunction, impaired sleep quality, medications with fatigue or sedation as side effects (e.g., opiates, antidepressants, antiemetics, antihistamines), deconditioning, asthenia, sarcopenia, anemia, and concurrent symptoms such as pain, nausea, or depression. There is also some empirical evidence that the management of concurrent symptoms,
including depression, pain, cognitive dysfunction, and sleep disturbance, helps to alleviate fatigue. A randomized trial of an Advanced Practice Nurse fatigue intervention that incorporated systematic symptom monitoring and targeted management\textsuperscript{91} had beneficial effects. Improved fatigue outcomes also were seen in a single-arm cohort study of a palliative care clinic consultation designed to address concurrent symptoms.\textsuperscript{92}

More than 40 meta-analyses or systematic reviews of RCTs have confirmed the effectiveness of physical activity/exercise to improve fatigue outcomes; with 8 of those published in the past 2 years.\textsuperscript{93-100} Study populations in which effectiveness has been demonstrated include patients with breast, colon, and prostate cancer; patients undergoing treatment with radiation, chemotherapy, or hematopoietic stem cell transplantation; young adults with cancer; and survivors who have been treated for either a solid tumor or a hematologic malignancy. Across studies, effect sizes were generally small, and positive results for the outcome of fatigue were not consistently observed.\textsuperscript{101-103} In their meta-analysis, Puetz and Herring note that exercise exerts a palliative effect on fatigue during active treatment and provides a rehabilitative effect after treatment.\textsuperscript{104} The exercise modalities that have been examined differ in content (walking, cycling, swimming, resistive exercise, or combined exercise interventions) as well as frequency, duration, intensity, and degree of supervision (fully supervised group vs self-directed exercise). Knowledge about the type, intensity, and duration of physical exercise most beneficial in reducing fatigue at different stages of disease and treatment is still being developed,\textsuperscript{104} and more research is needed to systematically assess the

For the purposes of this analysis, rehabilitation is defined as a structured, multicomponent intervention that is \textit{1)} delivered and individualized under the supervision of a health care professional with specialized skills and \textit{2)} combines a physical therapy modality (exercise, physical activity, and cardiopulmonary and strength training) together with individual or group psychoeducational support (education, nutritional counseling, mind–body interventions, and cognitive–behavioral therapy) along with physical modalities (massage, manual lymph drainage).\textsuperscript{106} Structured rehabilitation is designed to prevent or ameliorate physical impairments (eg, muscle weakness), preserve or restore functional capacity needed for purposeful activity, and address restrictions in activity and role performance (eg, self-care limitations, vocational limitations). The effects of rehabilitation on fatigue outcomes have been evaluated in 11 RCTs,\textsuperscript{107-117} conducted predominantly in Scandinavia and Canada. Study samples represented both advanced disease and survivors and included participants with varied tumor types. In all but one randomized trial,\textsuperscript{116} these multicomponent rehabilitation interventions demonstrated beneficial effects on fatigue outcomes. The effect of rehabilitation on fatigue endpoints also has been examined in several single-arm and quasi-experimental trials.\textsuperscript{118-132} Two systematic reviews recently concluded that rehabilitation is a promising intervention to improve fatigue endpoints as well as other outcomes, such as physical function, mood, and nutritional status.\textsuperscript{133,134}

Psychoeducational interventions have demonstrated positive effects on fatigue outcomes in more than a dozen RCTs or quasi-experimental studies.\textsuperscript{135-158} In addition, several systematic reviews have concluded that psychoeducational interventions are efficacious for fatigue management.\textsuperscript{159-164} At the same time, a few trials failed to confirm the benefits of psychoeducational interventions for fatigue, although, in some instances, favorable effects on other outcomes were seen that may relate to fatigue, including psychological symptoms, activity levels, or sleep quality.\textsuperscript{165-168} Psychoeducational interventions typically incorporate anticipatory guidance about patterns of fatigue and tailored recommendations for self-management of fatigue, including increased activity/exercise, measures to address sleep dysregulation, coaching and emotional support to enhance motivation, self-care and active coping, and praise and encouragement to promote self-efficacy and goal-setting and to augment feelings of control. Many of the effective psychoeducational interventions also include components whereby patients are taught methods of energy conservation and activity management (ECAM). One RCT delivered the ECAM intervention as a single intervention and had beneficial effects on fatigue outcomes.\textsuperscript{169}

| TABLE 3. Interventions Recommended for Cancer-Related Fatigue in Adults |

| INTERVENTIONS IDENTIFIED AS LIKELY TO BE BENEFICIAL BY THE NCCN (NCCN 2015\textsuperscript{100}), ONS (ONS 2014\textsuperscript{14}), CPAC/CAPO (HOWELL 2013\textsuperscript{9}), AND ASCO (BOWER 2014\textsuperscript{14}) |
|---|
| Address treatable contributors to fatigue |
| Manage concurrent symptoms |
| Physical activity/exercise |
| Rehabilitation |
| Psychoeducation |
| Meditation, mindfulness-based stress reduction, and cognitive-behavioral stress management |
| Relaxation |
| Cognitive-behavioral therapy for fatigue, depression, and pain |
| Cognitive-behavioral therapy for sleep |
| Yoga |

Abbreviations: ASCO, American Society of Clinical Oncology; CPAC/CAPO, Canadian Partnership Against Cancer/Canadian Association of Psychosocial Oncology; NCCN, National Comprehensive Cancer Network; ONS, Oncology Nursing Society.
whereas a second RCT testing the ECAM intervention did not confirm a benefit for fatigue.\textsuperscript{170} The investigators speculated that low baseline fatigue scores and low intervention potency may have eroded statistical power and diminished the effect size. In a recently released practice guideline from the Society for Integrative Oncology, energy conservation was the only therapy recommended as a supportive care intervention for fatigue during treatment for breast cancer.\textsuperscript{171}

Meditation, mindfulness-based stress reduction (MBSR), and cognitive-behavioral stress management (CBT for stress) improved both fatigue severity and fatigue-related daytime interference in 5 RCTs during and after treatment for breast cancer\textsuperscript{172-176} and in one RCT among patients who had mixed tumor sites.\textsuperscript{177} Secondary analyses suggest that the improvement in fatigue outcomes in those receiving the MBSR intervention may have been greatest in those who had a fatigue-related biomarker abnormality at study baseline.\textsuperscript{178} However, 3 RCTs and 3 single-arm trials in patients with mixed solid tumors showed inconsistent effects on fatigue outcomes.\textsuperscript{179-184} To permit unequivocal conclusions about the effectiveness of CBT for stress and MBSR in reducing fatigue, further research is warranted.

In 6 small RCTs, progressive muscle relaxation with or without imagery, relaxation breathing, coping skills training, or distraction delivered in a series of sessions improved fatigue in outpatients undergoing radiotherapy,\textsuperscript{185} allogeneic hematopoietic stem cell transplantation recipients,\textsuperscript{186} women with breast cancer undergoing surgical or systemic treatment,\textsuperscript{187-189} and patients with solid tumors who had the symptom cluster of fatigue, pain, and sleep disturbance.\textsuperscript{190} Two randomized trials comparing the effects of relaxation versus progressive resistance training on fatigue outcomes are in progress.\textsuperscript{191,192}

CBT interventions for fatigue, depression, and pain and CBT combined with hypnosis improved fatigue outcomes in 7 RCTs and one single-arm trial. Populations in which CBT with or without hypnosis has been studied include depressed cancer patients\textsuperscript{193,194} or survivors,\textsuperscript{195} a young and cancer survivors,\textsuperscript{196-198} and women undergoing breast cancer radiotherapy.\textsuperscript{199,200} However, in one RCT of CBT that was tailored to symptom profiles, investigators observed no statistically significant differences in fatigue, although the intervention did improve pain outcomes.\textsuperscript{201} Hypnosis alone also improved fatigue outcomes in women undergoing excisional breast biopsy or lumpectomy in 2 RCTs with an attentional control.\textsuperscript{202,203} Evidence-based interventions to manage cognitive fatigue recently have been published.\textsuperscript{204}

Four RCTs and a recent systematic review provide evidence that cognitive-behavioral interventions for sleep (CBT for sleep) exert a beneficial effect on fatigue outcomes.\textsuperscript{205-209} Components of CBT for sleep include relaxation training, sleep consolidation, stimulus control, and reducing cognitive-emotional arousal and may be effectively delivered individually, in a group, or via the web.\textsuperscript{209}

There is emerging evidence that yoga may be effective in treating fatigue, particularly in breast cancer survivors. Three RCTs confirm that yoga practices significantly improve fatigue in women with breast cancer who were undergoing radiotherapy\textsuperscript{210} and women in the post-treatment survivorship phase.\textsuperscript{211,212} Several small or single-arm trials also suggest that yoga may have beneficial effects in reducing fatigue in other populations, although additional confirmatory evidence is needed.\textsuperscript{213-218} Furthermore, 5 systematic reviews\textsuperscript{219-223} concluded that the effectiveness of yoga on fatigue outcomes has not been consistently established across a wide range of cancer patient populations or at all points in the cancer continuum and pointed out that many yoga studies have a high risk of bias because of sampling, inconsistent methods, short duration of follow-up, and nonblinding of participants and outcome assessors.

This concludes information regarding fatigue management interventions that are identified as likely to be beneficial in the fatigue guidelines. Next, we provide content on fatigue management interventions that currently lack evidence of effectiveness and need to undergo further testing.

A broad array of complementary and alternative medicine approaches, including acupuncture, morning exposure to bright light, massage, and biofield therapies like myotherapy, qigong, tai chi, herbal remedies, and nutritional supplements have been evaluated for their effects on fatigue. Nine meta-analyses or systematic reviews have appraised the evidence for the effectiveness of acupuncture, electroacupuncture, acupressure, and self-acupuncture as supportive care interventions during and after cancer treatment; all reached the conclusion that these strategies are feasible, well accepted, and safe.\textsuperscript{224-232} The majority of RCTs demonstrated a positive effect on fatigue outcomes.\textsuperscript{142,233-236} However, interpretation of these results is complicated by the fact that several the trials had a high risk of bias because of design flaws, such as short duration of follow-up and nonblinding of outcome assessors. Several of the reviews and meta-analyses from the literature have drawn conflicting conclusions\textsuperscript{237-241} in part because of differing inclusion criteria and review methodologies; all have urged additional study using rigorous trial designs.

Morning exposure to bright light may protect recipients from circadian rhythm desynchronization\textsuperscript{242} and has been shown in 2 small RCTs to mitigate fatigue during chemotherapy for breast cancer\textsuperscript{243} and to reduce fatigue in cancer survivors with breast or gynecologic cancer who have completed treatment.\textsuperscript{244} Based on evidence from several RCTs and quasi-experimental studies, NCCN guidelines for fatigue recommend that clinicians consider whether massage and biofield therapies such as Reiki, healing touch, polarity therapy, or haptotherapy may be helpful components of comprehensive
fatigue management. Several systematic reviews have concluded that, based on currently available studies, definitive statements about the effectiveness of massage and biofield therapies must be tempered by potential study limitations, including short duration of follow-up, small sample sizes, and the absence of a sham or active control condition. The recent ONS PEP guidelines for fatigue classified these interventions as effectiveness not established.

Qigong has shown beneficial effects on fatigue outcomes in 3 RCTs, and tai chi improved fatigue in a small single-arm trial; however, a recent meta-analysis concluded that, owing to heterogeneous study quality, these trials should be interpreted cautiously.

In a large, rigorously conducted, double-blind, placebo-controlled trial in cancer survivors, Wisconsin ginseng (an 8-week course of 2000 mg daily) improved fatigue outcomes and was well tolerated. However, inconsistent effects on fatigue outcomes have been observed in studies of other nutritional supplements and herbal remedies, including vitamin supplements, multicomponent nutritional supplementation, coenzyme Q10, levocarnitine, lectin-standardized mistletoe, omega-3 fatty acid supplements in combination with megestrol acetate, protein supplementation in combination with nutritional counseling, gaurana, Chinese herbal medicine, essiac, and valerian.

There is preliminary evidence that expressive writing, art, music, dance, or animal-assisted therapy, exposure to nature and green space, moxibustion, distraction-virtual reality immersion, and a combined-modality intervention that included aromatherapy, lavender foot soak, and reflexology may be helpful in managing fatigue. Conclusions about efficacy are limited by potential study design flaws, including the use of open-label and/or uncontrolled study designs, small sample sizes, and testing of multiple secondary endpoints. In addition, because many of these interventions were delivered as a combined-modality treatment, disentangling the effects of the separate components presents an additional constraint when interpreting the findings.

In summary, there is strong and consistent evidence that nonpharmacologic interventions like psychoeducation, cognitive-behavioral therapies, MBSR, yoga, Wisconsin ginseng, rehabilitation, and relaxation are effective for fatigue. Although evidence of the beneficial effects on fatigue outcomes is not particularly strong for interventions such as acupuncture, massage, or bright light, use of these therapies in clinical practice for fatigue management can be rationalized based on the fact that they are generally well tolerated and may be efficacious in particular fatigue contexts or may favorably affect symptoms that amplify fatigue, including anxiety, depression, sleep disturbance, and pain.

Evidence-Based Fatigue Management Across the Cancer-Care Continuum

Table 3 summarizes multidisciplinary fatigue management interventions identified as likely to be beneficial across a majority of the fatigue guidelines. The goals of fatigue management at the individual level include reducing fatigue severity, lowering distress, and decreasing interference with daily or usual activities. In some clinical situations (eg, patients undergoing hematopoietic stem cell transplantation or beginning a course of radiation therapy), the achievable clinical goal is to mitigate worsening in fatigue across the course of treatment. Programmatic goals of fatigue management include systematic implementation of approaches to ensure that all patients with cancer are screened for fatigue at regular intervals while on active treatment and during long-term follow-up. In patients with moderate to severe fatigue, the presence of fatigue contributing factors (eg, concurrent symptoms, emotional distress, sleep disturbances, anemia, nutritional alterations, inactivity/deconditioning, and comorbidities, such as hypothyroidism and cardiomyopathy) and the management plan to address these issues should be documented at regular intervals. Evidence-based guidelines that support achievement of these expected outcomes were published by NCCN and ONS and provided the foundation for the fatigue multidisciplinary management guidelines articulated by CPAC/CAPO and ASCO. Evidence-based information about managing fatigue also is available for patients from NCCN and NCI PDQ.

All patients who are beginning any fatigue-inducing treatment should be provided with education and counseling about fatigue and its anticipated characteristics, pattern of onset, duration, and consequences for mood, physical, and role function. Patients and their families should be made aware that several interventions have been shown to be effective in limiting the severity of fatigue during treatment. This information should be reinforced at regular intervals across the treatment course. Incorporating knowledge of the effectiveness of these interventions, patients should be encouraged to develop their own individualized plan for fatigue self-management. Fatigued patients should be encouraged to participate in a consistent program of gentle exercise that is individualized to the patient’s age, condition, and physical fitness level. Referral to physical therapy, occupational therapy, or physical medicine and rehabilitation should be considered, especially for those patients with significant comorbidities and deconditioning. Patients’ responses to fatigue interventions should be monitored closely, because there is evidence that programs that are lengthy or include frequent treatment sessions may exacerbate fatigue levels in some patient populations, for example, those receiving radiation therapy or those with advanced cancers.
The transition to long-term follow-up is another important point at which to provide anticipatory guidance concerning the expected course and continued self-management of fatigue. Survivors and their families should be aware that the resolution of moderate to severe fatigue may require several months to a year of recovery, and they should be prepared with the knowledge that a subset of survivors may experience prolonged fatigue that interferes with function. The development of a survivorship care plan offers an opportunity to review strategies that may be effective for long-term fatigue management during survivorship (eg, exercise, MBSR, yoga, psychosocial support interventions, measures to improve sleep quality, and screening for treatable etiologies, such as hypothyroidism).

Individuals with fatigue who have advanced cancer or are at the end of life and those who care for them will benefit from education to understand the multiple causes and consequences of fatigue at this point in the disease trajectory. It may be helpful to normalize the reality that fatigue may increase substantially or become more unpredictable as the disease progresses and that the effects of fatigue (eg, sadness, isolation, fear) on well-being may become more prominent. Intervention strategies that may have worked in the past (eg, distraction, exercise) may no longer be feasible, and patients and their families will benefit from guidance about options that may be helpful in managing fatigue and alleviating suffering through the end of life, such as energy conservation, massage, aromatherapy, relaxation, meditation and MBSR, acupuncture, psychosocial support, and aggressive management of concurrent symptoms. Future studies are needed to develop and test novel palliative treatment approaches (eg, meaning-centered psychotherapy) that may help address the existential suffering associated with severe fatigue, particularly at the end of life.

**Translation Into Practice**

This report has provided clinicians with current knowledge about the prevalence and causes of cancer-related fatigue. Measures to screen and evaluate fatigue have been recommended. Current information about interventions with the highest level of evidence has been presented. We have shared recommendations issued by 4 leading organizations (NCCN, ONS, CPAC/CAPO, and ASCO) for interventions likely to be beneficial for managing fatigue. Now, we ask the clinician: “Are you ready to implement guidelines for fatigue into your practice?”

Using the framework of the translational science continuum, Figure 1 illustrates a modified model for improving fatigue outcomes by accelerating the translational science continuum.** During recent decades, scientific efforts have emphasized the T0 level of scientific discovery to build theories, develop measures, and identify underlying mechanisms and biomarkers related to fatigue. Despite considerable efforts, a specific etiology of, and biomarker for, fatigue has not been discovered. The lack of mechanism-driven fatigue interventions is a major barrier to better symptom control.

Scientists have worked simultaneously at the T1 level to conduct tests of promising interventions. These combined efforts have led to recent progress at the T2 level. Never before have evidence-based recommendations for improving fatigue been disseminated by 4 premier cancer organizations. As a collective group focusing on improving fatigue outcomes, considerable work is underway to promote researcher-clinician partnerships and to evaluate each intervention’s feasibility, effectiveness, acceptability, and cost. A decade of grant funding by the NCI has supported implementation science in cancer prevention and control. Studies positioned from T2 to T4 on the translational continuum address issues of each intervention’s feasibility, effectiveness, acceptability, and cost.

At this time, we are at the tipping point between T2 and T3 on the translational science continuum. A significant evidence base of more than 200 RCTs has identified those interventions that are likely to be beneficial for relieving cancer-related fatigue. Several interventions have been given the “green light” for implementation in oncology practice and policy (Table 3). Two examples of models to accelerate the implementation of interventions for fatigue into practice are physical activity/exercise in cancer survivorship and physical rehabilitation for women with breast cancer. More exemplars are needed. The discussion below will focus on the challenges and potential solutions to promote the implementation of guideline recommendations. We will conclude with implications for the future goal of sustained adoption and integration into policies and quality standards.

Effective oncology leaders are essential to overcoming challenges in implementing fatigue guidelines into practice. The value that oncology leaders place on these symptom and supportive care services influences progress. Oncology leaders face daily challenges in prioritizing and balancing the resources devoted to screening, evaluating, and managing fatigue. This is true particularly as other quality-of-care issues receive attention, such as distress screening, survivorship care planning, referrals to palliative care, and monitoring adherence to oral chemotherapy. These issues represent high priorities in oncology care that must be addressed to improve cancer care outcomes.

Most clinical settings only introduce and maintain a few major initiatives each year. Initiatives tied to accreditations tend to receive the highest priority, such as the American College of Surgeons Commission on Cancer’s standard for distress screening and survivorship and the ASCO Quality Oncology Practice Initiative certification program, which requires a process to monitor adherence
with oral chemotherapy. Unless a leader in a clinic is an early adopter of a new initiative, it may seem like the clinic is falling behind when a new competing project is started before a previous project is adopted, resulting in delays or inadequate support of one or both projects. Oncology leaders, clinicians, and patients all may become discouraged when trying to reduce a symptom like fatigue, which may only be modified to a minimal degree and may not assist patients in achieving goals, such as returning to full-time work.

Numerous challenges and barriers to guideline implementation have been identified at the patient, clinician, and system levels. These include, but are not limited to, patient’s attitudes and beliefs about fatigue; clinician’s lack of knowledge and ability to provide evidence-based interventions; and a health care system’s lack of access to, and reimbursement for, integrated supportive care services. Clinics specifically focused on symptom control have potential for the greatest impact but are not widely available for patients at all stages of the cancer trajectory. This may be because fatigue is complicated, and we do not know the mechanism(s) or have a taxonomy to classify it. Multi-component interventions are complex and, because of a lack of knowledge of the effective ingredient, are difficult to deliver with fidelity in routine clinical care.

Once fatigue is selected as a priority symptom for implementation, it is imperative to identify strategies to improve the capacity of clinicians to screen, evaluate, and deliver evidenced-based interventions to reduce its severity. Strategies for screening, such as the inclusion of electronic symptom measurements and PROMIS computer-adaptive tests imbedded into the electronic health record, have been shown to facilitate ongoing cancer symptom screening and reporting and serve as the basis for psychosocial and supportive care referrals. The provision of support at a distance has been facilitated by access to electronic health records, accessible team members, available technology, and ease of documentation.

Focusing on interventions that have been given the “green light” for dissemination and implementation, it is necessary to overcome the “black box,” or unknown critical elements, of its effectiveness. Interventions using protocols that are ready to be adapted for local use and diverse populations in a variety of settings will promote evaluation for effectiveness, acceptability, and cost in the real world. Interventions like exercise can be tailored to the individual and the phase of treatment (active, post-treatment, end of life). The Livestrong program at the YMCA, which was designed for adult cancer survivors, is one example of a program that implements guidelines for exercise.

We offer numerous implications for the translation and implementation of guidelines for cancer-related fatigue. Widespread uptake of feasible strategies at the systems level is needed for clinicians to screen for fatigue at every encounter. Leaders of systems need to exploit technology to improve the capacity of clinicians to screen, evaluate, and deliver interventions and follow-up in a timely manner to reduce fatigue and improve physical, mental, emotional, and social functioning.

Strategies to embed supportive care monitoring into the electronic health record are needed. A system-wide process using electronic health records is needed that uses built-in triggers of meaningful alerts and provides decision support to help clinicians evaluate and manage patients with moderate to severe fatigue. Support for accessing these resources needs to be available in the health system, through community agencies, and/or on the World Wide Web.
Key components that represent the effective component(s) of a fatigue intervention need to be included in manuals and standardized for delivery. To date, interventions have shown the best evidence of effectiveness in breast cancer patients in the post-treatment phase, and we have gaps of knowledge to determine what works, for whom, and in what settings along the cancer treatment continuum (active, post-treatment, end of life). Major organizations that have published recommendations for clinicians are urged to improve access to services by disseminating interventions with the strongest evidence in patient-focused, online versions. There is a need to test telehealth approaches for making effective interventions widely available, such as cognitive behavioral therapy for sleep. These products can be used by a variety of professionals to develop programs delivered in local health care and community settings and/or at a distance.

Translation of fatigue recommendations can benefit from recent advancements in other areas, such as psychosocial care and distress.134 One widely used technique to measure and provide feedback on the implementation of recommendations is through audit and feedback.135 The American College of Surgeons Commission on Cancer’s release of Cancer Program Standards, titled Ensuring Patient-Centered Care, includes a standard for psychosocial distress screening, but not for fatigue screening. Integrating the distress thermometer as a standard for psychosocial distress screening has led to database development to demonstrate outcomes, such as the proportion screened for distress at baseline and follow-up. Databases have the highest potential when they are integrated into the electronic health record and provide opportunities to examine trends among several symptoms and in various settings.

Another step toward progress in reducing fatigue is to support policy work and quality standards. Areas ripe for policy work include reimbursement for cancer-related fatigue interventions and payment mechanisms to assure sustained adoption. Multidisciplinary cancer rehabilitation models that are similar to cardiac rehabilitation models are needed for patients with moderate to severe fatigue to reduce symptoms and increase function during and after treatment.

Currently, patient satisfaction surveys do not routinely measure satisfaction with the management of symptoms other than pain. The cost of providing informal supportive care services is not quantified routinely, but clinicians are aware that poor fatigue management can lead to decreased satisfaction with care by both the patient and the caregiver. Severe fatigue also can lead to increased costs related to the number of telephone calls, clinic visits, and emergency room visits and delayed timing and dose of treatments.136 Teaching and reinforcing self-management strategies to reduce fatigue and adopt healthy lifestyle behaviors early in the cancer treatment trajectory may result in reduced costs and numbers of survivors who report chronic fatigue and poor functioning.

Conclusion
Although improved processes and policies can facilitate the dissemination of cancer-related fatigue guidelines, individual clinicians remain the access point for patient care. On an individual level, clinicians may ask: How do I assist patients to select a recommended intervention for cancer-related fatigue? Or, on a systems level, what will it take to accelerate translation and implementation of fatigue interventions into practice? We call for integrated and multi-component approaches to the screening, evaluation, and management of fatigue and other symptoms in various clinical settings. When patients report moderate to severe fatigue, clinicians can assist them to select an intervention likely to be beneficial and to receive adequate instruction to execute the intervention in a safe and effective manner. Ongoing reassessment will assist in documenting both short-term and long-term outcomes of the intervention on fatigue and various functional outcomes.

References
1. Wang XS, Zhao F, Fisch MJ, et al. Prevalence and characteristics of moderate to severe fatigue: a multicenter study in cancer patients and survivors. Cancer. 2014;120:425-432.
2. Barsevick AM, Irwin MR, Hinds P, et al. Recommendations for high-priority research on cancer-related fatigue in children and adults. J Natl Cancer Inst. 2013;105:1432-1440.
3. Minton O, Berger A, Barsevick A, et al. Cancer-related fatigue and its impact on functioning. Cancer. 2013;119:2124-2130.
4. National Comprehensive Cancer Network (NCCN). Cancer-related fatigue (version 2.2015). nccn.org/professionals/physician_gls/pdf/fatigue.pdf. Accessed February 5, 2015.
5. National Comprehensive Cancer Network (NCCN). Survivorship (version 2.2014). nccn.org/professionals/physician_gls/pdf/survivorship.pdf. Accessed December 14, 2014.
6. Mitchell S, Friese CR. Oncology Nursing Society PEP (Putting Evidence Into Practice) weight of evidence classification schema: decision rules for summative evaluation of a body of evidence. ons.org/practice-resources/pep/evaluation-process. Accessed December 14, 2014.
7. Oncology Nursing Society. Putting Evidence Into Practice (PEP): fatigue. ons.org/practice-resources/pep. Accessed December 14, 2014.
8. Irwin M, Johnson LA, eds. Putting Evidence Into Practice: A Pocket Guide to Cancer Symptom Management. Pittsburgh, PA: Oncology Nursing Society; 2014.
9. Howell D, Keller-Olaman S, Oliver TK, et al. A pan-Canadian practice guideline and algorithm: screening, assessment, and supportive care of adults with cancer-related fatigue. Curr Oncol. 2013;20:e233-e246.
10. Bower JE, Bak K, Berger A, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical Oncology clinical practice guideline algorithm. J Clin Oncol. 2014;32:1840-1850.
11. National Cancer Institute. Fatigue (PDQ). cancer.gov/cancertopics/pdq/supportive-care/fatigue/HealthProfessional/. Accessed October 5, 2014.
12. Bower JE. Cancer-related fatigue—mechanisms, risk factors, and treatments. Nat Rev Clin Oncol. 2014;11:597-609.
13. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-
related fatigue: the scale of the problem. Oncologist. 2007;12(suppl 1):4-10.

14. Karthikeyan G, Jummani D, Prabhhu R, Manoor UK, Supe SS. Prevalence of fatigue among cancer patients receiving various anticancer therapies and its impact on quality of life: a cross-sectional study. Indian J Palliat Care. 2012;18:165-175.

15. Langston B, Armes J, Levy A, Tidey E, Ream E. The prevalence and severity of fatigue in men with prostate cancer: a systematic review of the literature. Support Care Cancer. 2013;21:1761-1771.

16. Donovan KA, McGinty HL, Jacobsen PB. A systematic review of research using the diagnostic criteria for cancer-related fatigue. Psychooncology. 2013;22:737-744.

17. Bates DW, Schmitt W, Buchwald D, et al. Marked 24-h rest/activity rhythms of cancer-related fatigue. Clin Cancer Res. 2000;6:3038-3045.

18. Fukuoka S, Maitani T, Sakamoto K, Matsunaga T, Seike M. Fatigue in cancer patients: a systematic review of research using the diagnostic criteria for cancer-related fatigue. Psychooncology. 2013;22:737-744.

19. Bates DW, Schmitt W, Buchwald D, et al. Marked 24-h rest/activity rhythms of cancer-related fatigue. Clin Cancer Res. 2000;6:3038-3045.

20. Andersen BL, DeRubeis RJ, Berman BS, et al. Sleep disturbances in adults with cancer: an American Society of Clinical Oncology guideline administration. J Clin Oncol. 2014;32:1600-1619.

21. Ailawadi R, Karthikeyan G, Jumnani D, Prabhu R, et al. Chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med. 1994;121:953-959.

22. Rich T, Innominato PF, Roener J, et al. Elevated serum cytokines correlated with altered behavior, serum cortisol rhythm, and damped 24-hour rest-activity patterns in patients with metastatic colorectal cancer. Clin Cancer Res. 2005;11:1757-1764.

23. Bower JE, Larkin DM. Inflammation and cancer-related fatigue: mechanisms, contributory factors, and treatment implications. Brain Behav Immun. 2013;30(suppl):S48-S57.

24. Ryan JL, Carroll JK, Ryan EP, Mustian KM, Fiscella K, Morrow GR. Mechanisms of cancer-related fatigue. Oncologist. 2007;12(suppl 1):22-34.

25. Bower JE, Marshall J, Ganz PA, Etzioni AD, Code K, Irwin MR. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med. 1994;121:953-959.

26. Berger A, Farr L. The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. Oncol Nurs Forum. 1999;26:1663-1671.

27. Mork R, McLeod HL, Harstad A, et al. Fatigue in patients with breast cancer: a randomized controlled trial comparing two interventions. J Clin Oncol. 2004;22:777-785.

28. Barter PV, Renfrew DP, Rutledge R, et al. A randomized controlled trial of a behavioral intervention for cancer survivors with fatigue. Cancer. 2004;101:1016-1025.

29. Zubi B, Blakely RD, Hewlett WA. The proinflammatory cytokines interleukin-1beta and tumor necrosis factor-alpha activate serotonin transporters. Neuropsychopharmacology. 2006;31:1211-1231.

30. Andrews P, Morrow GR, Hickok J, Roscoe J, Stone P. Mechanisms and models of fatigue associated with cancer and its treatment: evidence from preclinical and clinical studies. In: Armes J, Krishnasamy M, Higgins J, eds. Fatigue in Cancer. Oxford, UK: Oxford University Press; 2004:51-87.

31. Argiles JM, Busquets S, Lopez-Soriano FJ. Cytokines as mediators and targets for cancer cachexia. Cancer J. 2005;11:1757-1764.

32. Andersen BL, DeRubeis RJ, Berman BS, et al. Sleep disturbances in adults with cancer: an American Society of Clinical Oncology guideline administration. J Clin Oncol. 2014;32:1600-1619.

33. Hoque R, Cheson AL. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med. 2010;6:79-83.

34. Huang X, Zhang Q, Kang X, Song Y, Zhao W. Factors associated with cancer-related fatigue in breast cancer patients undergoing endocrine therapy in an urban setting: a cross-sectional study [serial online]. BMC Cancer. 2010;10:453-453.

35. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

36. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

37. Neil SE, Klika RJ, Garland SJ, McKenzie DC, Campbell KL. Cardiorespiratory and neuromuscular deconditioning in fatigued and non-fatigued breast cancer survivors. Support Care Cancer. 2013;21:873-881.

38. Andrews P, Morrow GR, Hickok J, Roscoe J, Stone P. Mechanisms and models of fatigue associated with cancer and its treatment: evidence from preclinical and clinical studies. In: Armes J, Krishnasamy M, Higgins J, eds. Fatigue in Cancer. Oxford, UK: Oxford University Press; 2004:51-87.

39. Maitani T, Seike M. Fatigue in cancer patients: a systematic review of research using the diagnostic criteria for cancer-related fatigue. Psychooncology. 2013;22:737-744.

40. Hoque R, Cheson AL. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med. 2010;6:79-83.

41. Huang X, Zhang Q, Kang X, Song Y, Zhao W. Factors associated with cancer-related fatigue in breast cancer patients undergoing endocrine therapy in an urban setting: a cross-sectional study [serial online]. BMC Cancer. 2010;10:453-453.

42. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

43. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

44. Neil SE, Klika RJ, Garland SJ, McKenzie DC, Campbell KL. Cardiorespiratory and neuromuscular deconditioning in fatigued and non-fatigued breast cancer survivors. Support Care Cancer. 2013;21:873-881.

45. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

46. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

47. Neil SE, Klika RJ, Garland SJ, McKenzie DC, Campbell KL. Cardiorespiratory and neuromuscular deconditioning in fatigued and non-fatigued breast cancer survivors. Support Care Cancer. 2013;21:873-881.

48. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

49. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

50. Neil SE, Klika RJ, Garland SJ, McKenzie DC, Campbell KL. Cardiorespiratory and neuromuscular deconditioning in fatigued and non-fatigued breast cancer survivors. Support Care Cancer. 2013;21:873-881.

51. Kim HJ, Barsevick AM, Fang CY, Miaskowski C. Common biological pathways underlying the psychoneurological symptom cluster in cancer patients. Cancer Nurs. 2012;35:E1-E20.

52. Watanabe SM, Nekolaichuk C, Beaumont C, Johnson L, Myers J, Strasser F. A multicenter study comparing two numerical versions of the Edmonton Symptom Assessment System in palliative care patients. J Pain Symptom Manage. 2011;44:5-21.

53. Watanabe SM, Nekolaichuk C, Beaumont C, Johnson L, Myers J, Strasser F. A multicenter study comparing two numerical versions of the Edmonton Symptom Assessment System in palliative care patients. J Pain Symptom Manage. 2011;44:5-21.

54. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

55. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

56. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

57. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.

58. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0–10 numeric rating scales for symptom assessment in cancer patients: a systematic review. Support Care Cancer. 2012;20:1155-1163.

59. Capra S, Ferguson M, Ried K. Cancer: Impact of nutrition intervention outcome—nutrition issues for patients. Nutrition. 2001;17:769-772.
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59. Chalder T, Belerowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res. 1993;37:147-153.

60. Mandrell BN, Yang J, Hooke MC, et al. Psychometric and clinical assessment of the 13-item reduced version of the fatigue scale-adolescent instrument. J Pediatr Oncol Nurs. 2011;28:287-294.

61. Hinds PS, Yang J, Gattuso JS, et al. Psychometric and clinical assessment of the 10-item reduced version of the Fatigue Scale-Child instrument. J Pain Symptom Manage. 2010;39:572-578.

62. Hannon D, Jacobsen P, Azzarello L, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. Qual Life Res. 1998;7:301-310.

63. Smets E, Garssen B, De Haes JH, et al. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res. 1995;39:315-325.

64. Stein KD, Martin SC, Hannon DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. Cancer Pract. 1998;6:143-152.

65. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer. Cancer. 2002;94:2090-2106.

66. Reeve BB, Stover AM, Alfano CM, et al. The Piper Fatigue Scale-12 (PFS-12): psychometric findings and item reduction in a cohort of breast cancer survivors. Breast Cancer Res Treat. 2012;136:9-20.

67. McNair D, Lorr M, Droppleman L, eds. Profile of Mood States (POMS). San Diego, CA: Educational and Industrial Testing Services; 1971.

68. PROMIS. A brief guide to the PROMIS fatigue instruments. assessmentcenter.net. Accessed December 14, 2014.

69. Schwartz A, Meek P. Additional construct validity of the Schwartz Cancer Fatigue Scale. J Nurs Meas. 1999;7:35-45.

70. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue. Version 1.2014. nccn.org/professionals/ default.aspx. Accessed October 10, 2014.

71. Hjollund NH, Andersen JH, Bech P. Assessment of fatigue in chronic disease: a bibliographic study of fatigue measurement scales. Health Qual Life Outcomes. 2007;5:1-5.

72. Jean-Pierre P, Figueroa-Moseley CD, Kohli S, Fiscella K, Palesh O, Morrow GR. Assessment of cancer-related fatigue: implications for clinical diagnosis and treatment. Oncologist. 2007;12(suppl 1):11-21.

73. Minton O, Stone P. A systematic review of the scales used for the measurement of cancer-related fatigue (CRF). Ann Oncol. 2009;20:17-25.

74. Tomlinson D, Hinds PS, Ethier MC, Ness KK, Zupanec S, Sung L. Psychometric properties of instruments used to measure fatigue in children and adolescents with cancer: a systematic review. J Pain Symptom Manage. 2013;45:83-91.

75. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85:365-376.

76. Fries J, Bruce B, Cella D. The promise of PROMIS: Using item response theory to improve assessment of patient-reported outcomes. Clin Exp Rheumatol. 2009;23:S33-S57.

77. Lai J, Cella D, Choi S, et al. How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example. Arch Phys Med Rehabil. 2011;92:S20-S27.

78. Garcia SF, Cella D, Clauser SB, et al. Standardizing patient-reported outcomes assessment in cancer clinical trials: a patient-reported outcomes measurement information system initiative. J Clin Oncol. 2007;25:5106-5112.

79. Feuer KD, Mehner A, Geue K, Hinz A. Fatigue in breast cancer patients: psychometric evaluation of the fatigue questionnaire EORTC QLQ-FAT13 [published online ahead of print 2014]. Breast Cancer. 2014.

80. de Raaf PJ, de Klerk C, van der Rijt CC. Elucidating the behavior of physical fatigue and mental fatigue in cancer patients: a review of the literature. Psychooncology. 2013;22:1919-1929.

81. Rizzo JD, Bowers M, Hurley P, et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guidelines update on the use of epoetin and darbepoetin in adults with cancer. J Clin Oncol. 2010;28:4996-5010.

82. Gong S, Sheng P, Jin H, et al. Effect of methylphenidate in patients with cancer-related fatigue: a systematic review and meta-analysis [serial online]. PLoS One. 2014;9:e84391.

83. Sathith S, Aife K, Blackhall F, et al. Modafinil for the treatment of fatigue in lung cancer: results of a placebo-controlled, double-blind, randomized trial. J Clin Oncol. 2014;32:1882-1888.

84. Hovey E, de Souza P, Marx G, et al. Phase III, randomized, double-blind, placebo-controlled study of modafinil for fatigue in patients treated with docetaxel-based chemotherapy. Support Care Cancer. 2014;22:1233-1242.

85. Paulsen O, Klepstad P, Rosland JH, et al. Efficacy of methylprednisolone on pain, fatigue, and appetite loss in patients with advanced cancer using opioids: a randomized, placebo-controlled, double-blind trial. J Clin Oncol. 2014;32:3221-3228.

86. Yennurajalingam S, Frisbee-Hume S, Palmer J, et al. Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized, placebo-controlled trial in patients with advanced cancer. J Clin Oncol. 2013;31:3076-3082.

87. Yennurajalingam S, Bruea E. Review of clinical trials of pharmacologic interventions for cancer-related fatigue: focus on psychostimulants and steroids. Cancer J. 2014;20:319-324.

88. Yennurajalingam S, Bruea E. Role of corticosteroids for fatigue in advanced incurable cancer: is it a “wonder drug” or “deal with the devil.” Curr Opin Support Palliat Care. 2014;8:346-351.
mendations for cancer-related fatigue, cognitive impairment, sleep problems, depression, pain, anxiety, and physical dysfunction: a review. Oncol Hematol Rev. 2012;8:81-88.

104. Puetz TW, Herring DP. Differential effects of exercise on cancer-related fatigue during and following treatment: a meta-analysis. Am J Prev Med. 2012;43:e1-e24.

105. Wolin KY, Schwartz AL, Matthews CE, de Pra C, Clark AM, van der Salm C, et al. Implementing exercise guidelines for cancer survivors. J Prev Oncol. 2012;10:171-177.

106. Mitchell SA, Hoffman AJ, Clark JC, et al. Putting evidence into practice: an update of evidence-based interventions for cancer-related fatigue during and following treatment. Clin J Oncol Nurs. 2014;18:38-58.

107. van Weert E, van der Malsburg M, van den Berge B, Knaapen M, Oostrom J. The effect of a multimodal exercise intervention in cancer patients undergoing chemotherapy. Phys Ther. 2010;90:1413-1425.

108. Cantarero-Villanueva I, Fernandez-Lao C, Del Moral-Avila R, Fernandez-de-Las-Penas C, Feriche-Fernandez-Castanys MB, Arroyo-Morales M. Effectiveness of core stability exercises for myofascial release massage on fatigue in breast cancer survivors: a randomized controlled clinical trial [serial online]. Evid Based Complement Alternat Med. 2012;2012:620619.

109. Gagnon B, Murphy J, Eades M, et al. A prospective evaluation of an interdisciplinary nutrition-rehabilitation program for patients with advanced cancer. Curr Oncol. 2013;20:310-318.

110. Chasen MR, Feldstain A, Gravelle D, Macdonald N, Pereira J. An interprofessional palliative care oncology rehabilitation program: effects on function and predictors of program completion. Curr Oncol. 2013;20:301-309.

111. Bertheussen G, Assa S, Hokstad A, et al. Feasibility and changes in symptoms and functioning following inpatient cancer rehabilitation. Acta Oncol. 2012;51:1070-1080.

112. Swenson KK, Nissen MJ, Knippenberg K, et al. Cancer rehabilitation: outcome evaluation of a strengthening and conditioning program. Cancer Nurs. 2014;37:162-169.

113. Riesenberg H, Lubbe AS. Inpatient rehabilitation of lung cancer patients—a prospective study. Support Care Cancer. 2010;18:877-882.

114. van Weert E, Hoekstra-Weebes J, Otter R, Postema K, Sanderman R, van der Schans C. Cancer-related fatigue: predictors and effects of rehabilitation. Oncologist. 2006;11:184-196.

115. Strauss-Blasche G, Gnad E, Ekmekcioglu C. Cancer-related fatigue: predictors and following treatment: a meta-analyses. J Pain Symptom Manage. 2008;31:145-159.

116. Bjorneklett HG, Lindemalm C, Ojutkangas E, Shohet R. Relationship between cancer-related fatigue and physical activity in inpatient cancer rehabilitation. Support Care Cancer. 2006;14:116-127.

117. Adamson J, Quist M, Midtgard J, et al. The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue. Eur J Oncol Nurs. 2013;17:331-339.

118. Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial [serial online]. BMJ. 2009;339:b4310.

119. Cheville A. Therapeutic exercise during outpatient radiation therapy for advanced cancer: feasibility and impact on physical well-being. Am J Phys Med Rehabil. 2010;89:611-619.

120. Spahn G, Choi KE, Kennemann C, et al. Multidisciplinary rehabilitation can impact on health-related quality of life outcome in radical cystectomy: secondary reported outcome of a randomized controlled trial. J Multidiscip Healthc. 2014;7:301-311.

121. Cantarero-Villanueva I, Fernandez-Lao C, Del Moral-Avila R, Fernandez-de-Las-Penas C, Feriche-Fernandez-Castanys MB, Arroyo-Morales M. Effectiveness of core stability exercises for myofascial release massage on fatigue in breast cancer survivors: a randomized controlled clinical trial [serial online]. Evid Based Complement Alternat Med. 2012;2012:620619.

122. Riesenberg H, Lubbe AS. Inpatient rehabilitation of lung cancer patients—a prospective study. Support Care Cancer. 2010;18:877-882.

123. van Weert E, Hoekstra-Weeebers J, Otter R, Postema K, Sanderman R, van der Schans C. Cancer-related fatigue: predictors and effects of rehabilitation. Oncologist. 2006;11:184-196.

124. Strauss-Blasche G, Gnad E, Ekmekcioglu C. Cancer-related fatigue: predictors and following treatment: a meta-analyses. J Pain Symptom Manage. 2008;31:145-159.

125.FromClassen MR, Feldstain A, Gravelle D, Macdonald N, Pereira J. An interprofessional palliative care oncology rehabilitation program: effects on function and predictors of program completion. Curr Oncol. 2013;20:301-309.

126. Bertheussen G, Assa S, Hokstad A, et al. Feasibility and changes in symptoms and functioning following inpatient cancer rehabilitation. Acta Oncol. 2012;51:1070-1080.

127. Swenson KK, Nissen MJ, Knippenberg K, et al. Cancer rehabilitation: outcome evaluation of a strengthening and conditioning program. Cancer Nurs. 2014;37:162-169.

128. Riesenberg H, Lubbe AS. Inpatient rehabilitation of lung cancer patients—a prospective study. Support Care Cancer. 2010;18:877-882.

129. van Weert E, Hoekstra-Weebes J, Otter R, Postema K, Sanderman R, van der Schans C. Cancer-related fatigue: predictors and effects of rehabilitation. Oncologist. 2006;11:184-196.

130. Strauss-Blasche G, Gnad E, Ekmekcioglu C. Cancer-related fatigue: predictors and following treatment: a meta-analyses. J Pain Symptom Manage. 2008;31:145-159.

131. Windsor PM, Potter J, Mcdonald K, McCowan C. Evaluation of a fatigue intervention: information on exercise for patients receiving cancer treatment. Clin Oncol (R Coll Radiol). 2009;21:473-482.
noma: a replication study. J Clin Oncol. 2005;23:1270-1277.

146. Yates P, Aranda S, Hargraves M, et al. Randomized controlled trial of an educational intervention for managing fatigue in women receiving adjuvant chemotherapy for early stage breast cancer. J Clin Oncol. 2005;23:6027-6036.

147. Allison PJ, Edgar L, Nicolau B, Archer J, Black M, Hier M. Results of a feasibility study for a psycho-educational intervention in head and neck cancer. Psychooncology. 2004;13:482-485.

148. Given B, Given C, McCorkle R, et al. Pain. Cancer. 2002;10:416-421.

149. Given B, Given C, McCorrke R, et al. Pain and fatigue management: results of a nursing randomized clinical trial. Oncol Nurs Forum. 2002;29:949-956.

150. Fawzy FI, Cousins N, Fawzy NW, Kemeny ME, Elashoff R, Morton D. A structured psychiatric intervention for cancer patients. I. Changes over time in methods of coping and effective avoidance. Arch Gen Psychiatry. 1990;47:720-725.

151. Dolbeault S, Cayrou S, Brédart A, et al. The effectiveness of a psycho-educational group after early stage breast cancer treatment: results of a randomized French study. Psychooncology. 2009;18:647-656.

152. Vilela LD, Nicolau B, Mahmud S, et al. Comparison of psychosocial outcomes in head and neck cancer patients receiving a coping strategies intervention and control subjects receiving no intervention. J Otalaryngol. 2006;35:88-96.

153. Vesibalkan OU, Karadakovan A, Goker E. The effectiveness of nursing education as an intervention to decrease fatigue in Turkish patients receiving chemotherapy. Oncol Nurs Forum. 2009;36:E215-E222.

154. Chan CW, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy: results of a psychoeducational randomized controlled trial. J Pain Symptom Manage. 2011;41:347-357.

155. Lee H, Lim Y, Yoo MS, Kim Y. Effects of a nurse-led cognitive-behavior therapy on fatigue and quality of life of patients with breast cancer undergoing radiotherapy: an exploratory study. Cancer Nurs. 2011;34: E22-E30.

156. Goedendorp MM. Is increasing physical activity necessary to diminish fatigue during cancer treatment comparing cognitive behavior therapy and a brief nursing intervention with usual care in a multicenter randomized controlled trial. Oncologist. 2010;15:1122-1132.

157. Badger TA, Segrin C, Figueredo AJ, et al. Psychosocial interventions to improve quality of life in prostate cancer survivors and their intimate or family partners. Qual Life Res. 2011;20:833-844.

158. Donnelly CM, Blaney JM, Lowe-Strong A, et al. A randomised controlled trial testing the feasibility and efficacy of a physical activity behaviour change intervention in managing fatigue with gynaecological cancer survivors. Gynecol Oncol. 2011;122:618-624.

159. Larkin D, Lopez V, Aromataris E. Managing cancer-related fatigue in men with prostate cancer: a systematic review of non-pharmacological interventions. Int J Nurs Pract. 2013;20:549-560.

160. Jacobsen PN, Donovan KA, Vadaparampil S, Small RR. Examining fatigue and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. Health Psychol. 2007;26:660-667.

161. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Psychosocial interventions for fatigue during cancer treatment in adults [serial online]. Cochrane Database Syst Rev. 2009;1: CD006953.

162. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull. 2008;134:700-741.

163. Foris EA, Bertheussen GF, Thune I, et al. Psychosocial interventions as part of breast cancer rehabilitation programs: Results from a systematic review. Psychooncology. 2011;20:909-918.

164. Duits SJ, Faber MM, Oldenburg HS, van Beurden M, Aaronsin NK. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. Psychooncology. 2011;20:115-126.

165. Armes J, Chaldler T, Addington-Hall J, Richardson A, Hotopf M. A randomized controlled trial to evaluate the effectiveness of a brief, behaviorally oriented intervention for cancer-related fatigue. Cancer. 2007;110:1385-1395.

166. Purcell A, Fleming J, Burmeister B, Bennett S, Haines T. Is education an effective management strategy for reducing cancer-related fatigue? Support Care Cancer. 2011;19:1429-1439.

167. Goodwin PJ, Leszcz M, Ennis M, et al. The effect of group psychosocial support on survival of metastatic breast cancer. N Engl J Med. 2001;345:1719-1726.

168. O’Brien L. Education for cancer-related fatigue: could talking about it make people more likely to report it? Support Care Cancer. 2014;22:209-215.

169. Barsevick A, Dudley WN, Beck SL, Sweeney C, Whitmer K, Nall L. A randomized clinical trial of energy conservation for patients with cancer-related fatigue. Cancer. 2004;100:1302-1310.

170. Barsevick A, Beck SL, Dudley WN, et al. Efficacy of an intervention for fatigue and sleep disturbance during cancer chemotherapy. J Pain Symptom Manage. 2010;40:200-216.

171. Greenlee H, Balneaves LG, Carlson LE, et al. Clinical practice guidelines on the use of integrative therapies as supportive care in patients treated for breast cancer. J Natl Cancer Inst Monogr. 2014;50:346-358.

172. Vargas S, Antoni MH, Carver CS, et al. Sleep quality and fatigue after a stress management intervention for women with early stage breast cancer in southern Florida. Int J Behav Med. 2014;21:971-981.

173. Lengacher CA, Reich RR, Post-White J, et al. Mindfulness-based stress reduction in post-treatment breast cancer patients: an examination of symptoms and symptom clusters. J Behav Med. 2012;35:86-94.

174. Hoffman CI, Ersser SJ, Hopkinson JB, Nicholls PG, Harrington JE, Thomas PW. Effectiveness of mindfulness-based stress reduction in mood, breast- and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: a randomized, controlled trial. J Clin Oncol. 2012;30: 1335-1342.

175. Lengacher CA, Johnson-Mallard V, Post-White J, et al. Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. Psychooncology. 2009;18:1261-1272.

176. Kim YH, Kim HJ, Ahn SD, Seo YJ, Kim SH. Effects of meditation on anxiety, depression, fatigue, and quality of life of women undergoing radiation therapy for breast cancer. Complement Ther Med. 2013;21:379-387.

177. van der Lee ML, Garssen B. Mindfulness-based cognitive therapy reduces chronic cancer-related fatigue: a treatment study. Psychotherapy. 2012;21:264-272.

178. Reich RR, Lengacher CA, Kip KE, et al. Baseline immune biomarkers as predictors of MBSR(BC) treatment success in off-treatment breast cancer patients. Biol Res Nurs. 2014;16:429-437.

179. Speca M, Carlson LE, Goodey E, Angen M. A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. Psychosom Med. 2000; 62:613-622.

180. Kiviet-Stijnen A, Visser A, Garssen B, Hudig W. Mindfulness-based stress reduction training for oncology patients: patients’ appraisal, and changes in well-being. Patient Educ Couns. 2008;72:436-442.

181. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Psychosocial interventions as part of breast cancer rehabilitation programs. Psychooncology. 2011;20:115-126.

182. Barsevick A, Dudley WN, Beck SL, Sweeney C, Whitmer K, Nall L. A randomized clinical trial of energy conservation for patients with cancer-related fatigue. Cancer. 2004;100:1302-1310.

183. Barsevick A, Beck SL, Dudley WN, et al. Efficacy of an intervention for fatigue and sleep disturbance during cancer chemotherapy. J Pain Symptom Manage. 2010;40:200-216.

184. Greenlee H, Balneaves LG, Carlson LE, et al. Clinical practice guidelines on the use of integrative therapies as supportive care in patients treated for breast cancer. J Natl Cancer Inst Monogr. 2014;50:346-358.

185. Vargas S, Antoni MH, Carver CS, et al. Sleep quality and fatigue after a stress management intervention for women with early stage breast cancer in southern Florida. Int J Behav Med. 2014;21:971-981.

186. Lengacher CA, Reich RR, Post-White J, et al. Mindfulness-based stress reduction in post-treatment breast cancer patients: an examination of symptoms and symptom clusters. J Behav Med. 2012;35:86-94.

187. Kim SD, Kim HS. Effects of a relaxation breathing exercise on fatigue in haemo-poietic stem cell transplantation patients. J Clin Nurs. 2005;14:51-55.

188. Garssen B, Boomsma MF, Meezenbroek Ede J, et al. Stress management training
for breast cancer surgery patients. Psychon- 
ology. 2013;2.2:572-580.

188. Cohen M, Fried G. Comparing relaxation training and cognitive-behavioral group therapy for women with breast cancer. Res Soc Work Pract. 2007;17:313-323.

189. Demiralp M, Oflaz F, Komuru S. Effects of relaxation training on sleep quality and fatigue in patient with breast cancer undergoing adjuvant chemotherapy. J Clin Nurs. 2010;19(7–8):1073-1083.

190. Kwekkeboom KL, Abbott-Anderson K, Cherwin C, Rolland R, Serlin RC, Ward SE. Pilot randomized controlled trial of a person-centered, cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. J Pain Symptom Manage. 2012;44:810-822.

191. Pothoff K, Schmidt ME, Wiskemann J, et al. Randomized controlled trial to evaluate the effects of progressive resistance training compared to progressive muscle relaxation training for breast cancer patients undergoing adjuvant radiotherapy: the BEST study [serial online]. BMC Cancer. 2013; 13:2407.

192. Schmidt ME, Wiskemann J, Krakowski- Roosen H, et al. Progressive resistance versus relaxation training for breast cancer patients undergoing adjuvant chemother- apy: design and rationale of a randomized controlled trial (BEATE study). Contemp Clin Trials. 2013;34:117-125.

193. Strong V, Waters R, Hibberd C, et al. Management of depression for people with cancer (SmA/R oncology 1): a randomised trial. Lancet. 2008;372:40-48.

194. Savard J, Simard S, Giguere I, et al. Randomized clinical trial on cognitive therapy for depression in women with metastatic breast cancer: psychological and immunological effects. Palliat Support Care. 2006;4:219-237.

195. Brothers BM, Yang HC, Strunk DR, Andersen BL. Cancer patients with major depressive disorder: testing a biobehavio- ral/cognitive behavior intervention. J Consult Clin Psychol. 2011;79:253-260.

196. Gießen MF, Wilborg JF, Verhagen CA, Knoop H, Bleijenberg G. Examining the role of physical activity in reducing study- post cancer fatigue. Support Care Cancer. 2012;20:1441-1447.

197. Gießen MF, Verhagen S, Witjes F, Bleijenberg G. Effects of cognitive behav- ior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. J Clin Oncol. 2006;24:4882-4887.

198. Prinsen H, Bleijenberg G, Heijmen L, et al. The role of physical activity and physical fatigue in post cancer fatigue: a random- ized controlled trial. Support Care Cancer. 2013;21:2279-2288.

199. Montgomery GH, David D, kangas M, et al. Randomized controlled trial of a cognitively-based behavioral therapy plus hypnosis intervention to control fatigue in patients undergoing radiotherapy for breast cancer. J Clin Oncol. 2014;32:557-563.

200. Montgomery GH, Kangas M, David D, et al. Fatigue during breast cancer radio- therapy: an initial randomized study of cognitive-behavioral therapy plus hypno- sis. Health Psychol. 2009;28:317-322.
231. Ling W, Lui LY, So KWK, Chan K. Effects of acupuncture and acupressure on cancer-related fatigue: a systematic review. Oncol Nurs Forum. 2014;41:581-592.

232. Zeng Y, Luo T, Finneghan-John J, Cheng ASK. Meta-analysis of randomized controlled trials of acupuncture for cancer-related fatigue. Integr Cancer Ther. 2013;13:193-200.

233. Molassiotis A, Bardy J, Finneghan-John J, et al. Acupuncture for cancer-related fatigue in patients with breast cancer: a pragmatic randomized controlled trial. J Clin Oncol. 2012;30:4470-4476.

234. Molassiotis A, Bardy J, Finneghan-John J, et al. A randomized, controlled trial of acupuncture self-needling as maintenance therapy for cancer-related fatigue after therapist-delivered acupuncture. Ann Oncol. 2013;24:1645-1652.

235. Mao JJ, Farrar JT, Bruner D, et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with/without aromatase inhibitor-related arthralgia: a randomized trial. Cancer. 2014;120:3471-3472.

236. Smith C, Carmady B, Thornton C, Perz J, Shepherd A. Multivitamins do not improve radiation therapy-related fatigue: results of a double-blind, randomized crossover trial. Am J Clin Oncol. 2012;35:105:1230-1238.

237. Azad A, John T. Do randomized acupuncture studies in patients with cancer need a sham acupuncture control arm? J Natl Cancer Inst. 2013;105:2057-2058.

238. Molassiotis A. Managing cancer-related fatigue with acupuncture: is it all good news for patients? Acupunct Med. 2013;31:3-4.

239. Ernst E, Posadzki P, Reply to Molassiotis [letter]. Support Care Cancer. 2013;21:3257.

240. Molassiotis A. Evidence is in the eye of the beholder. Support Care Cancer. 2013;21:3259-3260.

241. Molassiotis A, Richardson A. Reply to A. Azad, et al. J Clin Oncol. 2013;31:2058-2059.

242. Neikrug AB, Rissling M, Tofersen V, et al. Bright light therapy protects women from circadian rhythm desynchronization during chemotherapy for breast cancer. Behav Sleep Med. 2012;10:202-216.

243. Ancoli-Israel S, Rissling M, Neikrug A, et al. Light treatment prevents fatigue in women undergoing chemotherapy for breast cancer. Support Care Cancer. 2012;20:1211-1219.

244. Redd WH, Valdimarsdottir H, Wu LM, et al. Systematic light exposure in the treatment of cancer-related fatigue: a preliminary study. Psychoneuroendocrinology. 2014;23:1431-1434.

245. Pan YQ, Yang KH, WangYL, Zhang LP, Liang HQ. Massage interventions and treatment-related side effects of breast cancer: a systematic review and meta-analysis. Int J Clin Oncol. 2014;19:829-841.

246. Myers CD, Walton T, Bratsman L, Wilson J, Small B. Massage modalities and symptoms reported by cancer patients: narrative review. Soc Integr Oncol. 2008;6:19-28.

247. Jain S, Mills PJ. Biofield therapies: Helpful or full of hype? A best evidence synthesis. Int J Behav Med. 2010;17:1-16.

248. Ernst E. Massage therapy for cancer palliation and supportive care: a systematic review of randomised clinical trials. Support Care Cancer. 2009;17:333-337.

249. Oh B, Butow P, Mullan B, et al. Impact of medical Qigong on quality of life, fatigue, mood, and treatment-related fatigue in cancer patients: a randomized controlled trial. Ann Oncol. 2010;21:608-614.

250. Campo RA, Agarwal N, LaStayo PC, et al. Levels of fatigue and distress in senior prostate cancer survivors enrolled in a 12-week intervention trial of Qigong. J Cancer Surviv. 2014;8:60-69.

251. Chen Z, Meng Z, Milbury K, et al. Qigong improves quality of life in women undergoing radiotherapy for breast cancer: results of a randomized controlled trial. Cancer. 2013;119:160-1698.

252. Galantino ML, Callens ML, Cardena GJ, Piel A, Mao JJ. Tai chi for well-being of breast cancer survivors with aromatase inhibitor-related arthralgias: a feasibility study. Altern Ther Health Med. 2013;19:38-44.

253. Zeng Y, Luo T, Xie H, Huang M, Cheng A. Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses. Complement Ther Med. 2014;22:173-184.

254. Barton DL, Liu H, Dakhil SR, et al. Wisconsin ginseng (Panax quinquefolius) to improve cancer-related fatigue: a randomized, double-blind trial, N07C2. J Natl Cancer Inst. 2013;105:1230-1238.

255. Yeom CH, Jung GC, Song KJ. Changes of clinical and health-related quality of life after high dose vitamin C administration. J Korean Med Sci. 2007;22:7-11.

256. de Souza Fede AB, Bensi CG, Trufelli DC, et al. Multivitamins do not improve radiation therapy-related fatigue: results of a double-blind randomized crossover trial. Am J Clin Oncol. 2007;30:432-436.

257. Vollbracht C, Schneider B, Reich G, et al. Influence of postoperative completeronon on quality of life in breast cancer patients during chemo-/radiotherapy and aftercare: results of a retrospective, multicentre, comprehensive cohort study in Germany. In Vivo. 2011;25:983-990.

258. Carr AC, Vissers MCM, Cook JS. The effect of intravenous vitamin C on cancer- and chemotherapy-related fatigue and quality of life [serial online]. Front Oncol. 2014;4:283.

259. Mantovani G, Maccio A, Madeddu C, et al. Randomized phase III clinical trial of five different arms of treatment for patients with cancer cachexia: interim results. Nutrition. 2008;24:305-313.

260. Schumacher K, Schneider B, Reich G, et al. Influence of postoperative completeronon with l-carnitine supplemen- tary treatment with l-carnitine in patients with cancer cachexia: interim results. J Pain Symptom Manage. 2007;32:551-559.

261. Mantovani G, Zang JJ, Manola J, Cella D, Ansari B, Fisch MJ. L-carnitine supplementation for the management of fatigue in patients with cancer: a randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2012;30:3864-3869.

262. Cruciucari RA, Dvorin E, Homel P, et al. Safety, tolerability and symptom outcomes associated with L-carnitine in patients with cancer and with cancer cachexia: a preliminary analysis. Ann NY Acad Sci. 2004;1033:168-176.

263. Cruciucari RA, Dvorin E, Homel P, et al. L-carnitine supplementation in patients with advanced cancer and cancer cachexia: a double-blind, placebo-controlled study. J Pain Symptom Manage. 2009;37:622-631.

264. Cruciucari RA, Dvorin E, Homel P, et al. L-carnitine supplementation for the treatment of fatigue and depressed mood in cancer patients with cancer cachexia: a preliminary analysis. Ann NY Acad Sci. 2004;1033:168-176.

265. Cruciucari RA, Dvorin E, Homel P, et al. Safety, tolerability and symptom outcomes associated with L-carnitine in patients with cancer and with cancer cachexia: a preliminary analysis. Ann NY Acad Sci. 2004;1033:168-176.

266. Cruciucari RA, Dvorin E, Homel P, et al. Safety, tolerability and symptom outcomes associated with L-carnitine in patients with cancer and with cancer cachexia: a preliminary analysis. Ann NY Acad Sci. 2004;1033:168-176.

267. Cruciucari RA, Dvorin E, Homel P, et al. L-carnitine supplementation in patients with advanced cancer and cancer cachexia: a double-blind, placebo-controlled study. J Pain Symptom Manage. 2009;37:622-631.

268. Cruciucari RA, Dvorin E, Homel P, et al. L-carnitine supplementation for the treatment of fatigue and depressed mood for patients with cancer and with cancer cachexia: a randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2012;30:3864-3869.

269. Mantovani G, Maccio A, Madeddu C, et al. Randomized phase III clinical trial of five different arms of treatment for patients with cancer cachexia: interim results. Nutrition. 2008;24:303-313.

270. Schumacher K, Schneider B, Reich G, et al. Influence of postoperative completeronon with l-carnitine supplemen- tary treatment with l-carnitine in patients with cancer cachexia: interim results. J Pain Symptom Manage. 2007;32:551-559.

271. Mantovani G, Maccio A, Madeddu C, et al. Randomized phase III clinical trial of five different arms of treatment for patients with cancer cachexia: interim results. Nutrition. 2008;24:303-313.

272. Jensen MB, Hessov I. Randomization to nutritional intervention at home did not improve postoperative function, fatigue, or well-being. Br J Surg. 1997;84:113-118.

273. da Costa Miranda V, Trufelli DC, Santos J, et al. Effectiveness of guarana (Paullinia cupana) for postradation fatigue and depression: results of a pilot double-blind randomized study. J Altern Complement Med. 2009;15:431-433.

274. de Oliveira Campos MP, Riechermann R, Martins LC, Hassan BJ, Casa FB, Del Giglio A. Guarana (Paullinia cupana) improves fatigue in breast cancer patients undergoing systemic chemotherapy. J Altern Complement Med. 2011;17:505-512.
275. del Giglio AB, Cubero Dde I, Lerner TG, et al. Purified dry extract of Paulinia cupana (guarana) (PC-18) for chemotherapy-related fatigue in patients with solid tumors: an early discontinuation study. J Diet Suppl. 2013;10:325-334.

276. Su CX, Wang LQ, Grant SJ, Liu JP. Chinese herbal medicine for cancer-related fatigue: a systematic review of randomized clinical trials. Complement Ther Med. 2014;22:567-579.

277. Zick SM, Sen A, Feng Y, Green J, Olatunde S, Boon H. Trial of Essiac to ascertain its effect in women with breast cancer (TEA-BC). J Altern Complement Med. 2006;12:971-980.

278. Barton DL, Atherton PJ, Bauer BA, et al. Purified dry extract of Paullinia cupana (Guarana) PC-18 in improving sleep in patients who are undergoing treatment for cancer: a phase III randomized, placebo-controlled, double-blind study (NCCTG trial, N01C5). J Support Oncol. 2011;9:24-31.

279. Lu Q, Zheng D, Young L, Kagawa-Singer K. Fatigue: a systematic review of randomised controlled trials. J Diet Suppl. 2008;5:225-232.

280. Sturm J, Baak J, Storbek B, Traore A, Thuss-Patience F. Effect of dance on cancer-related fatigue and quality of life. Support Care Cancer. 2014;22:2241-2249.

281. Nakau M, Imanishi J, Imanishi J, et al. Spiritual care of cancer patients by integrated medicine in urban green space: a pilot study. Explore (NY). 2013;9:87-90.

282. de Moor C, Sterner J, Hall M, et al. A pilot study of expressive writing intervention among Chinese-speaking breast cancer survivors. Health Psychol. 2012;31:548-551.

283. Archer S, Buxton S, Sheffield D. The effect of music interventions for improving psycho-somatic outcomes for adult cancer patients: a systematic review and meta-analyses. J Clin Oncol. 2013;31:663-670.

284. Milbury K, Spelman A, Wood C, et al. Randomized controlled trial of expressive writing for patients with renal cell carcinoma. J Clin Oncol. 2014;32:663-670.

285. Milbury K, Spelman A, Wood C, et al. Randomized controlled trial of expressive writing for distressed metastatic breast cancer patients. Psychol Health. 2012;27:88-100.

286. de Moor C, Sterner J, Hall M, et al. A pilot study of the effects of expressive writing on psychological and behavioral adjustment in patients enrolled in a phase II trial of vaccine therapy for metastatic renal cell carcinoma. Health Psychol. 2002;21:615-619.

287. Clark M, Isacks-Downton G, Wells N, et al. Use of preferred music to reduce emotional distress and symptom activity during radiation therapy. J Music Ther. 2006;43:247-265.

288. Archer S, Buxton S, Sheffied D. The effect of creative psychological interventions on psychological outcomes for adult cancer patients: a systematic review of randomised controlled trials. Psychooncology. 2015;24:1-10.

289. Tsai HF, Chen YK, Chung MH, et al. Effectiveness of music intervention in ameliorating cancer patients’ anxiety, depression, pain, and fatigue: a meta-analyses. Cancer Nurs. 2014;37:E35-E50.

290. Bradt J, Dileo C, Grocke D, Magill L. Music interventions for improving psychological and physical outcomes in cancer patients [serial online]. Cochrane Database Syst Rev. 2011;8:CD006911.

291. Bozucuk H, Artac M, Kara A, et al. Does music exposure during chemotherapy improve quality of life in early breast cancer patients? A pilot study. Med Sci Monit. 2006;12:200-205.

292. Bar-Sela G, Atid L, Danos S, Gabay N, Epelbaum R. Art therapy improved depression and influenced fatigue levels in cancer patients on chemotherapy. Psychooncology. 2007;16:980-984.

293. Johnson RA, Meadows RL, Hauzer JS, Sevedge K. Animal-assisted activity among patients with cancer: effects on mood, fatigue, self-perceived health, and sense of coherence. Oncol Nurs Forum. 2008;35:225-232.

294. Sturm J, Baak J, Storbek B, Traore A, Thuss-Patience F. Effect of dance on cancer-related fatigue and quality of life. Support Care Cancer. 2014;22:2241-2249.

295. Nakau M, Imanishi J, Imanishi J, et al. Spiritual care of cancer patients by integrated medicine in urban green space: a pilot study. Explore (NY). 2013;9:87-90.

296. Lee S, Jerng UM, Liu Y, Kang JW, Nam D, Lee JD. The effectiveness and safety of moxibustion for treating cancer-related fatigue: a systematic review and meta-analyses. Support Care Cancer. 2014;22:1429-1440.

297. Archer S, Buxton S, Sheffield D. The effect of music interventions for improving psycho-somatic outcomes for adult cancer patients: a systematic review and meta-analyses. J Clin Oncol. 2013;31:663-670.

298. Barton DL, Atherton PJ, Bauer BA, et al. Purified dry extract of Paullinia cupana (Guarana) PC-18 in improving sleep in patients who are undergoing treatment for cancer: a phase III randomized, placebo-controlled, double-blind study (NCCTG trial, N01C5). J Support Oncol. 2011;9:24-31.

299. Lu Q, Zheng D, Young L, Kagawa-Singer K. Fatigue: a systematic review of randomised controlled trials. J Diet Suppl. 2008;5:225-232.

300. Sturm J, Baak J, Storbek B, Traore A, Thuss-Patience F. Effect of dance on cancer-related fatigue and quality of life. Support Care Cancer. 2014;22:2241-2249.

301. Nakau M, Imanishi J, Imanishi J, et al. Spiritual care of cancer patients by integrated medicine in urban green space: a pilot study. Explore (NY). 2013;9:87-90.

302. Lee S, Jerng UM, Liu Y, Kang JW, Nam D, Lee JD. The effectiveness and safety of moxibustion for treating cancer-related fatigue: a systematic review and meta-analyses. Support Care Cancer. 2014;22:1429-1440.

303. Breitbart W, Rosenfeld B, Gibson C, Pessin H, Poppiuo S, Nelson C. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. Psychoonology. 2010;19:21-28.

304. Alfano CM, Smith T, de Moor JS, et al. An action plan for translating cancer survivorship research into care [serial online]. J Natl Cancer Inst. 2014;106:628-287.

305. Neta G, Sanchez MA, Chambers DA, et al. Implementation science in cancer prevention and control: a decade of grant funding by the national cancer institute and future directions [serial online]. Implement Sci. 2015;10:4.

306. Phillips SM, Alfano CM, Perna FM, Glasgow RE. Accelerating translation of physical activity and cancer survivorship research into practice: recommendations for a more integrated and collaborative approach. Cancer Epidemiol Biomarkers Prev. 2014;23:687-699.

307. Stout NL, Binkley JM, Schmitz KH, et al. A prospective surveillance model for habilitation for women with breast cancer. Cancer. 2012;118(suppl):2191-2200.

308. Bornehan T. Reducing patient barriers to pain and fatigue management. J Pain Symptom Manage. 2010;39:486-501.

309. Strasser F, Sweeney C, Willey J, Benisch-Tolley S, Palmer JL, Bruera E. Impact of a half-day multidisciplinary symptom control and palliative care outpatient clinic in a comprehensive cancer center on recommendations, symptom intensity, and patient satisfaction: a retrospective descriptive study. J Pain Symptom Manage. 2004;27:481-491.

310. Wagner LI, Schink J, Bass M, et al. Bringing PROMIS to practice: brief and precise symptom screening in ambulatory cancer care [published online ahead of print November 6, 2014]. Cancer. 2014: doi:10.1002/cncr.29104.

311. Macartney G, Stacey D, Carley M, Harrison MB. Priorities, barriers and facilitators for remote support in improving symptom management: a survey of Canadian oncology nurses. Can Oncol Nurs J. 2012;22:235-247.

312. Stacey D, Bakker D, Ballantyne B, et al. Managing symptoms during cancer treatment: Evaluating the implementation of evidence-informed remote support protocols [serial online]. Implement Sci. 2012;7:110.

313. Livestrong Foundation. Livestrong at the YMCA. livestrong.org/what-we-do/our-actions/programs-partnerships/livestrong-at-the-ymca/. Accessed December 14, 2014.

314. Jacobsen PB, Holland JC, Steensma DP. Caring for the whole patient: the science of psychosocial care. J Clin Oncol. 2012;30:1151-1155.

315. Jacobsen PB, Wagner LI. A new quality standard: the integration of psychosocial care into routine cancer care. J Clin Oncol. 2012;30:1154-1159.

316. Graze L, Brady-Copertino C, Varner A, Stiver WS. The development of a nursing assessment and symptom management clinic. Clin J Oncol Nurs. 2014;18(suppl):12-16.