General

Guideline Title
Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical Oncology Clinical Practice guideline adaptation.

Bibliographic Source(s)

Guideline Status
This is the current release of the guideline.

Recommendations

Major Recommendations
The recommendations were adapted from the three guidelines (original recommendation matrix provided in the Methodology Supplement [see the “Availability of Companion Documents” field]) by a multidisciplinary group of experts using evidence from the supplementary literature search and clinical experience as a guide. The majority of the recommendation text is listed verbatim from the three guidelines; however, there are some instances where the American Society of Clinical Oncology (ASCO) expert panel made modifications or additions to the recommendations to reflect local context, practice beliefs, and updated empiric evidence. These changes are identified with the words "modified from" preceding the guideline title after each subsection heading. Figure 1 in the original guideline document presents a two-page screening, assessment, treatment, and care map algorithm for fatigue adapted from the pan-Canadian guideline. Copyright permission for the adaption was obtained from the authors of the pan-Canadian and National Comprehensive Cancer Network (NCCN) guidelines.

Definition
(Modified from NCCN Guideline for Cancer-Related Fatigue and NCCN Guideline for Survivorship)
Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment that is not proportional to recent activity and interferes with usual functioning. These guidelines are focused on fatigue in patients who have completed primary cancer treatment and/or are in clinical remission.)
**Recommendations**

**Screening**

*Modified from pan-Canadian guideline and NCCN Guideline for Cancer-Related Fatigue*

All health care providers should routinely screen for the presence of fatigue from the point of diagnosis onward, including after completion of primary treatment. All patients should be screened for fatigue as clinically indicated and at least annually. Screening should be performed and documented using a quantitative or semi-quantitative assessment. For example, on a 0 to 10 numeric rating scale (0, no fatigue; 10, worst fatigue imaginable), mild fatigue is indicated as a score of 1 to 3, moderate fatigue as 4 to 6, and severe fatigue as 7 to 10. Because fatigue is rarely an isolated symptom, a multi-symptom screening tool may have greater clinical utility. Patients who report moderate to severe fatigue should undergo a comprehensive and focused assessment.

Table 1 in the original guideline document lists selected instruments for the measurement of fatigue, which could be used to supplement initial screening with the 0 to 10 numeric scale.

**Comprehensive and Focused Assessment**

*Modified from NCCN Guideline for Survivorship*

Regarding history and physical, first, perform a focused fatigue history, including:

- Onset, pattern, and duration
- Change over time
- Associated or alleviating factors

Second, evaluate disease status by:

- Evaluating risk of recurrence based on stage, pathologic factors, and treatment history
- Performing a review of systems to determine if other symptoms substantiate suspicion for recurrence

Third, assess treatable contributing factors, including:

- Comorbidities (see Table 2 in the original guideline document)
- Medications (consider persistent use of sleep aids, pain medications, or antiemetics)
- Alcohol/substance abuse
- Nutritional issues (including weight/caloric intake changes)
- Decreased functional status
- Deconditioning/decreased activity level

As a shared responsibility, the clinical team must decide when referral to an appropriately trained professional (e.g., cardiologist, endocrinologist, mental health professional, internist, and so on) is needed.

**Laboratory Evaluation**

*NCCN Guideline for Survivorship Verbatim*

Consider performing laboratory evaluation based on presence of other symptoms, onset, and severity of fatigue.

- Complete blood cell count with differential: compare end-of-treatment hemoglobin/hematocrit with current values; assess other cell lines (white blood cells [WBC] and platelets).
- Comprehensive metabolic panel: assess electrolytes; assess hepatic and renal function.
- Endocrinologic evaluation: TSH (thyroid-stimulating hormone); consider more comprehensive evaluation or referral to specialist if other symptoms present.

**Treatment and Care Options**
**Modified from Pan-Canadian Guideline and NCCN Guideline for Cancer-Related Fatigue**

Regarding education and counseling:

All patients should be offered specific education about fatigue after treatment (e.g., information about the difference between normal and cancer-related fatigue, persistence of fatigue after treatment, and causes and contributing factors).

Patients should be offered advice on general strategies that help manage fatigue (e.g., physical activity, guidance on self-monitoring of fatigue levels).

If treated for fatigue, patients should be observed and reevaluated on a regular basis to determine whether treatment is effective or needs to be reassessed.

**Treatment of Contributing Factors**

*Modified from Pan-Canadian Guidelines and NCCN Guideline for Survivorship*

Address all medical and substance-induced treatable contributing factors first (e.g., comorbidities, medications, nutritional issues, activity level). Table 2 in the original guideline document provides more details. Some patients can also benefit from interventions described in this article to treat fatigue.

Currently, there are no clear standards for selecting among these to treat an individual patient. Further research is needed to establish a strategy for prioritizing, sequencing, and linking the available options.

**Physical Activity**

*Modified from Pan-Canadian Guideline and NCCN Guideline for Survivorship*

Several meta-analyses, systematic reviews, and randomized trials have demonstrated that initiating or maintaining adequate levels of physical activity can reduce cancer-related fatigue in post-treatment patients. For example, a recent meta-analysis of 27 exercise intervention trials conducted with patients after treatment completion found that exercise training significantly reduced fatigue, with a mean effect size of 0.38 (95% confidence interval [CI], 0.21 to 0.43).

Actively encourage all patients to engage in a moderate level of physical activity after cancer treatment (e.g., 150 minutes of moderate aerobic exercise, such as fast walking, cycling, or swimming, per week with an additional two to three sessions per week of strength training, such as weight lifting, unless contraindicated).

Walking programs are generally safe for most cancer survivors; the American College of Sports Medicine recommends that cancer survivors begin this type of program after consulting with their physician but without any formal exercise testing (such as a stress test).

Survivors at higher risk of injury (e.g., those living with neuropathy, cardiomyopathy, or other long-term effects of therapy other than comorbidities) should be referred to a physical therapist or exercise specialist. Breast cancer survivors with lymphedema should also consider meeting with an exercise specialist before initiating upper-body strength training.

Encourage survivors to make use of empirically based programs and local resources that are consistent with guideline recommendations. For patients with severe fatigue interfering with function, consider referral to a physical therapist or physiatrist.

Common barriers to physical activity in cancer survivors include physical and disease-related limitations (e.g., illness, pain, fatigue, weakness) as well as lack of time, lack of interest/motivation, lack of facilities, and lack of encouragement from family or friends. To overcome these barriers, survivors should be encouraged to avoid inactivity by, at the minimum, engaging in exercises such as walking or using a stationary bicycle or cycle ergometer, beginning at an easy pace and progressing gradually to moderate intensity. Counseling and motivational interviewing have also been shown to encourage exercise adherence.

**Psychosocial Interventions**
Several meta-analyses, systematic reviews, and randomized trials have indicated that cognitive behavioral therapy/behavioral therapy can reduce fatigue in cancer survivors. For example, a cognitive behavioral intervention that targeted dysfunctional thoughts about fatigue, poor coping strategies, and dysregulated sleep and activity patterns in a mixed sample of fatigued cancer survivors led to significant improvements in fatigue that were sustained over long-term follow-up.

Several systematic reviews and randomized trials have suggested that psychoeducational/educational therapies may reduce fatigue in cancer survivors. For example, an Internet-based educational program that provided tailored information on cancer-related fatigue, physical activity, pain control, distress management, sleep hygiene, nutrition, and energy conservation led to significant improvements in fatigue in a mixed sample of fatigued cancer survivors.

Survivors should be referred to psychosocial service providers specializing in cancer and trained to deliver empirically based interventions. Psychosocial resources that address fatigue may also be available through the National Cancer Institute (http://www.cancer.gov), the American Cancer Society (http://www.cancer.org), LIVESTRONG (http://www.livestrong.org), the Cancer Support Community (http://www.cancersupportcommunity.org/), CancerCare (http://www.cancercare.org), Cancer.Net (http://www.cancer.net), and the American Psychosocial Oncology Society (http://www.apossociety.org/survivors/helpline/ helpline.aspx).

Mind-Body Interventions

There is evidence from randomized trials that the following interventions may relieve fatigue in cancer survivors:

- Mindfulness-based approaches
- Yoga
- Acupuncture

The following interventions may also offer some benefit; however, additional research, particularly in the post-treatment period, is needed:

- Biofield therapies (touch therapy), massage, music therapy, relaxation, reiki, and qigong

Survivors should be referred to practitioners specializing in cancer and using protocols that have been empirically validated in cancer survivors.

Pharmacologic Interventions

Evidence suggests that psychostimulants (e.g., methylphenidate) and other wakefulness agents (e.g., modafinil) can be effectively used to manage fatigue in patients with advanced disease or those receiving active treatment. However, there is limited evidence of their effectiveness in reducing fatigue in patients who are disease free after active treatment, outside of the treatment of obstructive sleep apnea.

Small pilot studies have evaluated the impact of supplements, such as ginseng and vitamin D, for cancer-related fatigue. However, there is no consistent evidence of their effectiveness.

Ongoing Monitoring and Follow-Up

Promote ongoing self-monitoring of fatigue levels, using a symptoms diary or other methods, because fatigue can be a late or long-term problem in post-treatment survivors.

Clinical Algorithm(s)

An algorithm titled "Screening and Assessment - Fatigue in Cancer Survivors" is provided in the original.
Scope

Disease/Condition(s)
Fatigue

Guideline Category
Counseling
Evaluation
Management
Screening

Clinical Specialty
Internal Medicine
Oncology
Radiation Oncology

Intended Users
Advanced Practice Nurses
Allied Health Personnel
Nurses
Patients
Physician Assistants
Physicians

Guideline Objective(s)
To present screening, assessment, and treatment approaches for the management of adult cancer survivors who are experiencing symptoms of fatigue after completion of primary treatment

Target Population
Cancer survivors diagnosed at age ≥18 years who have completed primary cancer treatment with curative intent and are in clinical remission off therapy as well as patients who are disease free and have transitioned to maintenance or adjuvant therapy (e.g., patients with breast cancer receiving hormonal therapy, patients with chronic myelogenous leukemia receiving tyrosine kinase inhibitors)
Interventions and Practices Considered

1. Routine screening for fatigue
   - At least annually from the point of diagnosis onward
   - Quantitative or semiquantitative assessment

2. History and physical
   - Evaluation of disease status
   - Assessment of treatable contributing factors
   - Referral as needed

3. Laboratory evaluations as indicated

4. Education and counseling
   - Education on normal vs. cancer-related fatigue, causes and contributing factors
   - Fatigue management advice

5. Observation and re-evaluation on a regular basis

6. Treatment
   - Management of contributing factors
   - Physical activity
   - Psychosocial interventions (e.g., cognitive behavioral therapy)
   - Mind-body interventions (e.g., yoga, acupuncture)
   - Pharmacologic interventions (e.g., psychostimulants)

7. Promotion of ongoing self-monitoring

Major Outcomes Considered

- Treatment efficacy
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

American Society of Clinical Oncology (ASCO) Updated Literature Search

Because the literature search included in the pan-Canadian guideline was only current to 2009, an additional search was undertaken. The MEDLINE and EMBASE databases were systematically searched by one reviewer from January 2009 to March 2013 using a combination of the following search terms: fatigue, cancer, survivor, post-treatment, late effects, and long-term effects. Reference lists of reviews were also extensively searched for studies on fatigue in the cancer survivor population. The located meta-analyses, systematic reviews, and randomized controlled trials were used as a supplementary evidence base for the recommendations and are cited where appropriate in the text.

Guideline Search and ASCO Panel Content Review

As mentioned, the adaptation process starts with a literature search to identify candidate guidelines for adaptation on a given topic. The systematic search of clinical practice guideline databases, guideline developer Web sites, and published health literature was conducted to identify clinical practice guidelines, systematic reviews, meta-analyses, and other guidance documents addressing the screening,
assessment, and care of cancer-related fatigue (see the Data Supplement [see the "Availability of Companion Documents" field] for details of the search). On the basis of content review of the search yield, the ad hoc panel selected the pan-Canadian guideline on fatigue published in 2011, which is informed by recommendations from the Oncology Nursing Society and National Comprehensive Cancer Network (NCCN). The panel also considered two NCCN Guidelines that had been created or updated since 2009. These guidelines were selected because they were comprehensive and recently developed by multidisciplinary panels of experts.

Number of Source Documents
Not stated

Methods Used to Assess the Quality and Strength of the Evidence
Not stated

Rating Scheme for the Strength of the Evidence
Not applicable

Methods Used to Analyze the Evidence
Review of Published Meta-Analyses
Systematic Review

Description of the Methods Used to Analyze the Evidence
From the identified guidelines and reviews, the pan-Canadian guideline on screening, assessment, and care of cancer-related fatigue in adults with cancer was singled out and underwent an expedited review by two content experts, who suggested that the guideline be accepted with modifications. After a second review, the ASCO panel suggested that the more recent NCCN Guideline for Cancer-Related Fatigue and NCCN Guideline for Survivorship also be included in the adaptation. A methodologic review of the three guidelines was completed by two ASCO staff members using the Rigour of Development subscale of the AGREE II (Appraisal of Guidelines for Research and Evaluation II) instrument (www.agreetrust.org). The Rigour of Development subscale consists of seven items that assess the quality of processes used to gather and synthesize relevant data and methods used to formulate guideline recommendations (see the Data Supplement [see the "Availability of Companion Documents" field]; detailed results of scoring for this guideline are available on request to guidelines@asco.org). Briefly, the pan-Canadian guideline received a score of 86.5%, the NCCN Guideline for Cancer-Related Fatigue received a score of 47%, and the NCCN Guideline for Survivorship received a score of 44%.

Methods Used to Formulate the Recommendations
Expert Consensus

Description of Methods Used to Formulate the Recommendations
The guideline adaptation was informed by the ADAPTE methodology, which was used as an alternative to de novo guideline development for this guideline. Adaptation of guidelines is considered by the American Society of Clinical Oncology (ASCO) in selected circumstances, when one or more quality guidelines from...
other organizations already exist on the same topic. The objective of the ADAPTE process is to take advantage of existing guidelines to enhance efficient production, reduce duplication, and promote the local uptake of quality guideline recommendations.

The American Society of Clinical Oncology (ASCO) adaptation process begins with a literature search to identify candidate guidelines for adaptation. Adapted guideline manuscripts are reviewed and approved by the ASCO Clinical Practice Guidelines Committee (CPGC). The review includes two parts: methodologic review and content review. The methodologic review is completed by a member of the CPGC Methodology Subcommittee and/or by ASCO senior guideline staff. The content review is completed by an ad hoc panel (see Appendix Table A1 in the original guideline document) with guidance from an advisory group (see Appendix Table A2 in the original guideline document), convened by ASCO that includes multidisciplinary representation. Additional details on the methods used for the development of this guideline are reported in an online Methodology Supplement (see the "Availability of Companion Documents" field).

The Panel is led by two Co-Chairs who have the primary responsibility for the development and timely completion of the guideline adaptation. Recommendations from the source guidelines are extracted into a summary matrix (see Appendix II of the Methodology Supplement [see the "Availability of Companion Documents" field]).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

All members of the Expert Panel participated in the preparation of the draft guideline document, which was then disseminated for external review and submitted to the Journal of Clinical Oncology (JCO) for peer review and publication. All ASCO guidelines are reviewed and approved by the ASCO Clinical Practice Guideline Committee prior to publication.

The Clinical Practice Guideline Committee approved this guideline update on July 29, 2013.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations
Potential Benefits
Appropriate screening, assessment and management of fatigue in adult cancer survivors

Potential Harms
Not stated

Qualifying Statements

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Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, please see the ASCO Web site.

Implementation Tools

Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides
Slide Presentation
Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better
Living with Illness
Staying Healthy

IOM Domain

Effectiveness
Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

The guidelines were adapted from the following sources:

- Pan-Canadian Guideline on Screening, Assessment, and Care of Cancer-Related Fatigue in Adults with Cancer
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines In Oncology (NCCN Guidelines) for Cancer-Related Fatigue
- NCCN Guidelines for Survivorship

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Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

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American Society of Clinical Oncology (ASCO)

Guideline Committee

American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee

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Financial Disclosures/Conflicts of Interest

The expert panel was assembled in accordance with the American Society of Clinical Oncology (ASCO) Conflicts of Interest Management Procedures for Clinical Practice Guidelines (summarized at http://www.asco.org/guidelinescoi). Members of the panel completed the ASCO disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with these procedures, the majority of the members of the panel did not disclose any such relationships.

Authors' Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following author(s) and/or an author's immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: None Consultant or Advisory Role: None Stock Ownership: None Honoraria: None Research Funding: Carmelita P. Escalante, Pfizer; Patricia A. Ganz, Amgen; Gary Lyman, Amgen; Paul Jacobsen, Pfizer Expert Testimony: None Patents, Royalties, and Licenses: None Other Remuneration: None

Guideline Status

This is the current release of the guideline.
Guideline Availability
Available from the Journal of Clinical Oncology Web site.

Availability of Companion Documents
The following are available:


Patient Resources
The following is available:


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NGC Status
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