National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Cancer-Related Fatigue

Version 2.2024 — October 30, 2023

NCCN.org

Continue

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Cancer-Related Fatigue

NCCN Guidelines Index
Table of Contents
Discussion

***Catherine Jankowski, PhD/Chair £**
University of Colorado Cancer Center

***Kristen M. Carpenter, PhD/Vice-Chair θ**
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Olivia Aranha, MD, PhD † ‡
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Tarah Ballinger, MD †
Indiana University Melvin and Bren Simon Comprehensive Cancer Center

Chandana Banerjee, MD £
City of Hope National Medical Center

William S. Breitbart, MD θ Þ £
Memorial Sloan Kettering Cancer Center

Young Chang, MD £
Moffitt Cancer Center

Dana Chase, MD Ω
UCLA Jonsson Comprehensive Cancer Center

Erin Davis, MSN, CRNP §
Abramson Cancer Center at the University of Pennsylvania

Vanna Dest, MSN, APRN †
Yale Cancer Center/Smilow Cancer Hospital

Kristin Dickinson, PhD, RN §
Fred & Pamela Buffett Cancer Center

Lori L. DuBenske, PhD θ
University of Wisconsin Carbone Cancer Center

Carmen P. Escalante, MD Þ
The University of Texas MD Anderson Cancer Center

Michael Fediw, MD £
UT Southwestern Simmons Comprehensive Cancer Center

Sofia Garcia, PhD θ
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Annemarie Hargadon, MD Þ
UC Davis Comprehensive Cancer Network

Aminah Jatoi, MD †
Mayo Clinic Comprehensive Cancer Center

Leigh E. Kinczewski, DNP, CRNP £
Fox Chase Cancer Center

Cristina Kline-Quiroz, DO £
Vanderbilt-Ingram Cancer Center

Sheila Lahijani, MD θ
Stanford Cancer Institute

Elizabeth Trice Loggers, MD, PhD † £
Fred Hutchinson Cancer Center

Belinda Mandrell, PhD, RN €
St. Jude Children's Research Hospital/ The University of Tennessee Health Science Center

Susan McInnes, MD £
Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Kathi Mooney, PhD, RN † #
Huntsman Cancer Institute at the University of Utah

Hitendra Patel, MD †
UC San Diego Moores Cancer Center

Michelle B. Riba, MD, MS θ
University of Michigan Rogel Cancer Center

Hope S. Rugo, MD † ‡
UCSF Helen Diller Family Comprehensive Cancer Center

Wil L. Santivasi, MD Þ £
Duke Cancer Institute

Keith M. Swetz, MD, MA £
O'Neal Comprehensive Cancer Center at UAB

Nina Wagner-Johnston, MD † ‡
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Eric S. Zhou, PhD £
Dana-Farber/Brigham and Women's Cancer Center/Mass General Cancer Center

NCCN
Cindy Hochstetler, PhD
Ryan Schonfeld, BA

Ω Gynecologic oncology
‡ Hematology/Hematology oncology
Þ Internal medicine
† Medical oncology
# Nursing
€ Pediatric oncology
θ Psychiatry, psychology, including health behavior
§ Radiotherapy/Radiation oncology
£ Supportive care including palliative, pain management, pastoral care, and oncology social work
* Discussion Section Writing Committee

NCCN Guidelines Panel Disclosures

Continue

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Cancer-Related Fatigue

NCCN Guidelines Index
Table of Contents
Discussion

Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Find an NCCN Member Institution: https://www.nccn.org/home/member-institutions.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.

See NCCN Categories of Evidence and Consensus.

Terminologies in all NCCN Guidelines are being actively modified to advance the goals of equity, inclusion, and representation.

Updates in Version 2.2024 of the NCCN Guidelines for Cancer-Related Fatigue from Version 1.2024 include:

MS-1
• The discussion was updated to reflect the changes in the algorithm.

Updates in Version 1.2024 of the NCCN Guidelines for Cancer-Related Fatigue from Version 2.2023 include:

FT-2
• Standards of Care for Cancer-Related Fatigue in Children/Adolescents and Adults
  ▸ Bullet 7 revised: Implementation of guidelines for fatigue evaluation and management is best accomplished by interdisciplinary teams who are able to tailor interventions to the needs of the individual patient. Consider referral to an appropriate specialist or supportive care provider (eg, survivorship, palliative care, integrative oncology, psychology, psychiatry, physical therapy, *exercise specialist,* occupational therapy, physical medicine) *from diagnosis to end of life*.
  ▸ Bullet removed: Consider referral to rehabilitation as indicated: physical therapy, occupational therapy, and physical medicine from diagnosis to end of life.

FT-4
• Primary Evaluation for Fatigue Score: Moderate or Severe Age >12 y (4–10), Age 7–12 y (3–5), or Age 5–6 y (Tired)
  ▸ Assessment of Treatable Contributing Factors
    ◊ Comorbidities/Cancer treatment sequelae
      – Bullet 10 added: Rheumatologic or autoimmune disorders

FT-6
• Interventions for Patients on Active Treatment
  ▸ Nonpharmacologic
    ◊ Bullet 3 added: Acupuncture
• Footnotes
  ▸ Footnote k added: Consider referral to appropriate specialist or supportive care provider. (Also for FT-7 and FT-8; this text was separated from footnote f)

FT-7
• Interventions for Patients Post-Treatment
  ▸ Nonpharmacologic
    ◊ Bullet 1, 1st sub-sub bullet revised: *Persistent and ~~L~~late* effects of treatment (eg, cardiomyopathy)

FT-8
• Interventions for Patients at the End of Life
  ▸ Footnote u revised: Yennurajalingam S, et al. J Clin Oncol 2013;31:3076-3082; Paulsen O, et al. J Clin Oncol 2014;32:3221-3228; *Yennurajalingam S, et al. Cancers (Basel) 2023;15:91.*

DEFINITION OF CANCER-RELATED FATIGUE

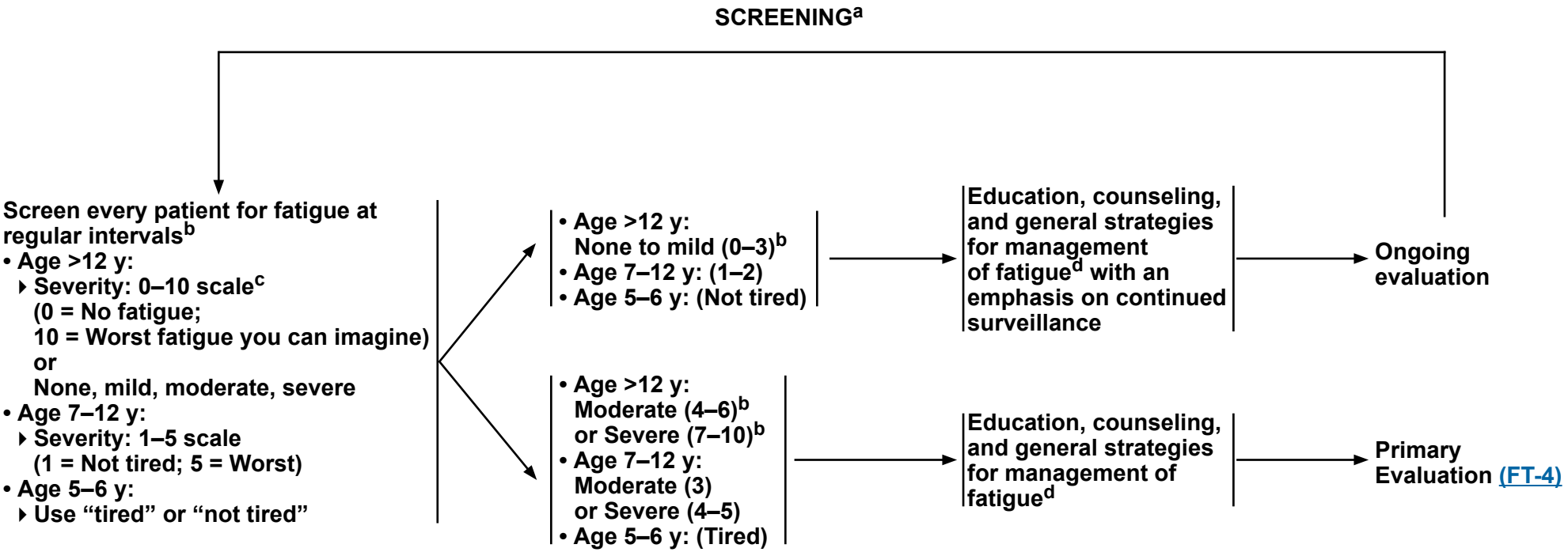
Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

STANDARDS OF CARE FOR CANCER-RELATED FATIGUE IN CHILDREN/ADOLESCENTS AND ADULTS

- **Fatigue is rarely an isolated symptom and most commonly occurs with other symptoms and signs, such as pain, emotional distress, anemia, and sleep disturbances, in symptom clusters. Therefore, patients should be screened for multiple symptoms and signs that may vary according to diagnosis, treatment, and stage of disease.**
- **Fatigue is a subjective experience that should be systematically assessed using patient self-reports and other sources of data.**
- **Fatigue should be screened, assessed, and managed according to clinical practice guidelines.**
- **All patients should be screened using age-appropriate measures for fatigue at their initial visit, at regular intervals during and following cancer treatment, and as clinically indicated.**
- **Fatigue should be recognized, evaluated, monitored, documented, and treated promptly for all age groups, at all stages of disease, prior to, during, and following treatment.**
- **Patients and family/caregiver(s) should be informed that management of fatigue is an integral part of total health care and that fatigue can persist following treatment.**
- **Implementation of guidelines for fatigue evaluation and management is best accomplished by interdisciplinary teams who are able to tailor interventions to the needs of the individual patient. Consider referral to an appropriate specialist or supportive care provider (eg, survivorship, palliative care, integrative oncology, psychology, psychiatry, physical therapy, exercise specialist, occupational therapy, physical medicine) from diagnosis to end of life.**
- **Educational and training programs should be implemented to ensure that health care professionals have knowledge and skills in the assessment and management of fatigue.**
- **Cancer-related fatigue should be included in clinical health outcome studies as an independent variable and potential moderator of outcome.**
- **Quality of fatigue management should be included in institutional continuous quality improvement projects.**
- **Medical care contracts should include reimbursement for the management of fatigue.**
- **Disability insurance should include coverage for the continuing effects of fatigue.**

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



[a] See Discussion Appendix for screening resources.
[b] Recommended screen and re-evaluation: "How would you rate your fatigue on a scale of 0–10 over the past 7 days?"
[c] Butt Z, et al. J Pain Symptom Manage 2008;35:20-30.
[d] General Strategies for the Management of Fatigue/Patient and Family/Caregiver Education and Counseling (FT-5).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PRIMARY EVALUATION FOR FATIGUE SCORE: Moderate or Severe Age >12 y (4–10), Age 7–12 y (3–5), or Age 5–6 y (Tired)

Focused History

- Disease status, treatments, and recent hospitalizations
  - Cancer treatment (eg, radiation therapy, systemic therapy)
  - Consider recurrence and/or progression
- Medications/side effects/drug interactions/misuse
  - See NCCN Guidelines for Older Adult Oncology (OAO-H)
- Review of systems
- In-depth fatigue history
  - Onset, pattern, and duration
  - Change over time
  - Associated or alleviating factors
  - Interference with function
- Social support status/availability of caregivers
- Economic status and resources for obtaining tangible support

Assessment of Treatable Contributing Factors

- Pain
- Emotional distress
  - Depression
  - Anxiety
- Anemia
- Sleep disturbance (eg, insomnia, hypersomnia/narcolepsy, obstructive sleep apnea, restless legs syndrome, circadian rhythm sleep-wake disorders)
- Nutritional deficits/imbalance
  - Vitamin imbalance
  - Weight/caloric intake changes
  - Fluid electrolyte imbalance: sodium, potassium, calcium, and magnesium
- Decreased functional status
  - Physical activity level
  - Deconditioning
- Comorbidities/Cancer treatment sequelae
  - Alcohol and drug misuse and illicit substance use
  - Cardiac dysfunction
  - Endocrine dysfunction (eg, hot flashes, hypothyroidism, hypogonadism, adrenal insufficiency), with special concern for people receiving immunotherapy
  - Gastrointestinal dysfunction
  - Hepatic dysfunction
  - Infection
  - Neurologic dysfunction
  - Pulmonary dysfunction
  - Renal dysfunction
  - Rheumatologic or autoimmune disorders

→ Management of concurrent symptoms and treatable contributing factors

- Medications/side effects/drug interactions
- Pain
  See NCCN Guidelines for Adult Cancer Pain
- Emotional distress
  See NCCN Guidelines for Distress Management
- Anemia
  See Management of Cancer- and Chemotherapy-Induced Anemia in the NCCN Guidelines for Hematopoietic Growth Factors
- Sleep disturbance/ poor sleep hygiene
  See NCCN Guidelines for Survivorship
- Nutritional deficit/ imbalance
- Decreased functional status
- Comorbidities
  See NCCN Guidelines for Management of Immunotherapy-Related Toxicities

→ See (FT-5) for General Strategies for the Management of Fatigue/Patient and Family/Caregiver Education and Counseling

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

GENERAL STRATEGIES FOR THE MANAGEMENT OF FATIGUE/ PATIENT AND FAMILY/CAREGIVER EDUCATION AND COUNSELING

- Information about known pattern of fatigue during and following treatment
- Reassurance that treatment-related fatigue is not necessarily an indicator of disease progression

→ **Active Treatment**[e,f,g]
- Consider initiation and/or encourage maintenance of a physical activity/exercise program
- Self-monitor fatigue levels
- Energy conservation[h]
  - Set priorities and realistic expectations
  - Pace
  - Delegate
  - Schedule activities at times of peak energy
  - Use labor-saving and assistive devices[i]
  - Postpone nonessential activities
  - Limit naps to not interfere with night-time sleep quality
  - Have a structured daily routine
  - Attend to one activity at a time
- Consider referral to appropriate specialist or supportive care provider
- Review list of medications to identify agents that may be contributing to fatigue and adjust accordingly

→ FT-6

- Information about known pattern of fatigue during and following treatment

→ **Post-Treatment**[e,f,g]
- See above (Active Treatment)

→ FT-7

- Information about known pattern of fatigue during and following treatment
  - Expected end-of-life symptom
  - May vary in intensity

→ **End of Life**[e,f,g,j]
- See above (Active Treatment)
- Eliminate nonessential activities
- Conserve energy for valued activities

→ FT-8

[e] See Discussion for information on differences between active treatment, post-treatment, and end-of-life treatment.
[f] Interventions should be culturally specific and tailored to the needs of patients and families along the illness trajectory, because not all patients may be able to integrate these options due to variances in individual circumstances and resources.
[g] There is limited scientific evidence for children.
[h] There is a lack of scientific evidence in this area.
[i] Examples include use of reachers for grasping items beyond arm's length, sock aids for pulling on socks, rolling carts for transporting items, wheelchairs, walkers, commodes, escalators and elevators for traveling between building floors, and electrical appliances for performing common household tasks (eg, opening cans).
[j] NCCN Guidelines for Palliative Care.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

INTERVENTIONS FOR PATIENTS ON ACTIVE TREATMENT[e,f,g,k]

Nonpharmacologic

- **Physical activity (category 1)**
  - **Maintain optimal level of activity**
  - **Cautions in determining level of activity:**
    - ◊ **Bone metastases**
    - ◊ **Thrombocytopenia[l]**
    - ◊ **Anemia**
    - ◊ **Fever, active infection, or post surgery**
    - ◊ **Limitations secondary to metastases or other comorbid illnesses**
    - ◊ **Safety issues (ie, assessment of risk of falls)**
  - **Consider initiation and/or encourage maintenance of a physical activity/exercise program, as appropriate per health care provider, consisting of cardiovascular endurance (walking, jogging, or swimming) and resistance (weights) training.[m]**
  - **Consider referral to rehabilitation: physical therapy, occupational therapy, and physical medicine**
  - **Yoga (category 1)**
- **Massage therapy (category 1)**
- **Acupuncture**
- **Psychosocial interventions**
  - **Cognitive behavioral therapy (CBT)[n]/Behavioral therapy (BT)[o] (category 1)**
  - **Psycho-educational therapies/Educational therapies (category 1)**
  - **Supportive expressive therapies[p]**
- **Nutrition consultation**
- **CBT[n] for insomnia (CBT-I)**
  - **Stimulus control/Sleep restriction/Sleep hygiene**
- **Bright white light therapy[q]**

Pharmacologic

- **Consider psychostimulants[r] (methylphenidate) in consideration of other modifiable causes**

→ **Repeat screening and evaluation (FT-3) and (FT-4)**
See (FT-5) for General Strategies for the Management of Fatigue/Patient and Family/Caregiver Education and Counseling

[e] See Discussion for information on differences between active treatment, post-treatment, and end-of-life treatment.
[f] Interventions should be culturally specific and tailored to the needs of patients and families along the illness trajectory, because not all patients may be able to integrate these options due to variances in individual circumstances and resources.
[g] There is limited scientific evidence for children.
[k] Consider referral to appropriate specialist or supportive care provider.
[l] Morishita S, et al. Hematology 2020;25:95-100.
[m] NCCN Guidelines for Survivorship: Physical Activity.
[n] A type of psychotherapy that focuses on recognizing and changing maladaptive thoughts and behaviors to reduce negative emotions and behaviors and to facilitate psychological adjustment. Trial evidence shows CBT-I can improve fatigue among participants with insomnia symptoms.
[o] CBT/BT influences thoughts and promotes changes in behavior; it includes a variety of strategies (eg, cognitive restructuring, relaxation, mindfulness).
[p] Supportive expressive therapies (eg, support groups, counseling, journal writing) facilitate expression of emotion and foster support from one or more people.
[q] Bright white light therapy of 1250–10,000 lux is most frequently self-administered in the early morning for 30–40 minutes. Timing needs to be adjusted for those who sleep during the day (Xiao P, et al. J Pain Symptom Manage 2022;63:e188-e202).
[r] Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded. Optimal dosing and schedule have not been established for use of psychostimulants in older adults and patients with cancer.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

INTERVENTIONS FOR PATIENTS POST-TREATMENT[e,f,g,k]

Nonpharmacologic

- **Physical activity (category 1)**
  - **Maintain optimal level of activity**
  - **Consider initiation and/or encourage maintenance of a physical activity/exercise program, as appropriate per health care provider, consisting of cardiovascular endurance (walking, jogging, or swimming) and resistance (weights) training[m]**
  - **Cautions in determining level of activity:**
    - ◊ **Persistent and late effects of treatment (eg, cardiomyopathy)**
    - ◊ **Safety issues (ie, assessment of risk of falls)**
  - **Consider referral to rehabilitation: physical therapy, occupational therapy, and physical medicine**
  - **Yoga (category 1)**
- **Psychosocial interventions (category 1)**
  - **CBT[n]/BT[o] (category 1)**
  - **Mindfulness-based stress reduction (category 1)**
  - **Psycho-educational therapies/Educational therapies (category 1)**
  - **Supportive expressive therapies[p] (category 1)**
- **CBT-I[n] (category 1)**
  - **Stimulus control/Sleep restriction/Sleep hygiene**
- **Bright white light therapy**
- **Acupuncture**
- **Nutrition consultation**

Pharmacologic[s]

- **Consider psychostimulants[r] (methylphenidate) in consideration of other modifiable causes**

→ **Repeat screening and evaluation (FT-3) and (FT-4)**
See (FT-5) for General Strategies for the Management of Fatigue/Patient and Family/Caregiver Education and Counseling

[e] See Discussion for information on differences between active treatment, post-treatment, and end-of-life treatment.
[f] Interventions should be culturally specific and tailored to the needs of patients and families along the illness trajectory, because not all patients may be able to integrate these options due to variances in individual circumstances and resources.
[g] There is limited scientific evidence for children.
[k] Consider referral to appropriate specialist or supportive care provider.
[m] NCCN Guidelines for Survivorship: Physical Activity.
[n] A type of psychotherapy that focuses on recognizing and changing maladaptive thoughts and behaviors to reduce negative emotions and behaviors and to facilitate psychological adjustment. Trial evidence shows CBT-I can improve fatigue among participants with insomnia symptoms.
[o] CBT/BT influences thoughts and promotes changes in behavior; it includes a variety of strategies (eg, cognitive restructuring, relaxation, mindfulness).
[p] Supportive expressive therapies (eg, support groups, counseling, journal writing) facilitate expression of emotion and foster support from one or more people.
[r] Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded. Optimal dosing and schedule have not been established for use of psychostimulants in older adults and patients with cancer.
[s] Adjust current treatments for pain, sleep disturbances, and other symptoms and comorbidities, including drugs. Nonpharmacologic management of pain may be considered, such as palliative radiation, nerve blocks, or epidural management.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

INTERVENTIONS FOR PATIENTS AT THE END OF LIFE[e,f,g,j,k]

Nonpharmacologic

- **Physical activity[t]**
  - **Optimize level of activity with careful consideration of the following:**
    - ◊ **Patient goals**
    - ◊ **Bone metastases**
    - ◊ **Thrombocytopenia**
    - ◊ **Anemia**
    - ◊ **Fever or active infection**
    - ◊ **Limitations secondary to metastases or other comorbid illnesses**
    - ◊ **Recommendations for physical and occupational therapy**
    - ◊ **Safety issues (ie, assessment of risk of falls)**

Pharmacologic

- **Consider psychostimulants[r] (methylphenidate) in consideration of other modifiable causes**
- **Consider short-term use of corticosteroids[u] (prednisone or dexamethasone [adults only]) for patients with advanced cancer**

→ **Repeat screening and evaluation (FT-3) and (FT-4)**
See (FT-5) for General Strategies for the Management of Fatigue/ Patient and Family/Caregiver Education and Counseling

[e] See Discussion for information on differences between active treatment, post-treatment, and end-of-life treatment.
[f] Interventions should be culturally specific and tailored to the needs of patients and families along the illness trajectory, because not all patients may be able to integrate these options due to variances in individual circumstances and resources.
[g] There is limited scientific evidence for children.
[j] NCCN Guidelines for Palliative Care.
[k] Consider referral to appropriate specialist or supportive care provider.
[r] Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded. Optimal dosing and schedule have not been established for use of psychostimulants in older adults and patients with cancer.
[t] A structured exercise protocol depending on the patient's tolerance level can be used to improve fatigue experienced by patients with advanced cancer in hospice care (Vira P, et al. Am J Hosp Palliat Care 2021;38:503-511).
[u] Yennurajalingam S, et al. J Clin Oncol 2013;31:3076-3082; Paulsen O, et al. J Clin Oncol 2014;32:3221-3228; Yennurajalingam S, et al. Cancers (Basel) 2023;15:91.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

ABBREVIATIONS

BT	**behavioral therapy**
CBT	**cognitive behavioral therapy**
CBT-I	**cognitive behavioral therapy for insomnia**

NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

Discussion

This discussion corresponds to the NCCN Guidelines for Cancer-Related Fatigue. Last updated: October 30, 2023.

Table of Contents

Overview

Fatigue in patients with cancer has been underreported, underdiagnosed, and undertreated. Fatigue is a common symptom in patients with cancer and is nearly universal in those receiving cytotoxic chemotherapy, RT, bone marrow transplantation, or treatment with biological response modifiers.[1-9] The specific mechanisms involved in the pathophysiology of cancer-related fatigue (CRF) are unknown. Proposed mechanisms include pro-inflammatory cytokines,[9-12] hypothalamic-pituitary-adrenal (HPA) axis dysregulation,[12] circadian rhythm desynchronization,[13] skeletal muscle wasting,[14] and genetic dysregulation.[15] These mechanisms may be interdependent.[16] Ultimately, there is limited evidence to support a firm conclusion regarding underlying causes of CRF, and longitudinal studies that evaluate fatigue before, during, and after cancer treatment are needed.[16]

CRF is very common. A systematic review and meta-analysis of 129 studies with 71,568 patients reported a 49% prevalence of fatigue but noted a significant degree of heterogeneity among studies.[17] The prevalence of fatigue decreased from 65% in 1996 to 44% in 2020. A contributing factor could be the publication and implementation of multiple guidelines on CRF.[17] According to a survey of 1569 patients with cancer, the symptom is experienced by 80% of individuals who receive chemotherapy and/or radiotherapy.[18,19] In patients with metastatic disease, the prevalence of CRF exceeds 75%.[20-23] Moderate or severe fatigue was reported by 983 of 2177 patients (45%) who were undergoing active outpatient treatment and 150 of 515 survivors (29%) with complete remission from breast, prostate, colorectal, or lung cancer.[24] Results from a 1-year longitudinal study comparing 68 patients with non-metastatic breast cancer undergoing chemotherapy treatment to 60 cancer-free control participants showed that fatigue increased during chemotherapy treatment ($P = .003$) and was significantly greater for patients, relative to controls ($P < .01$ for all time points).[25] A meta-analysis including 27 studies of 12,237 breast cancer survivors showed that predictors of severe fatigue include higher disease stage (II or III vs. 0 or I; relative risk [RR], 1.18; 95% CI, 1.08–1.28) and chemotherapy treatment (RR, 1.12; 95% CI, 1.06–1.19).[26] A study including 1869 patients treated with hematopoietic cell transplantation (HCT) showed that female sex and chronic pain are associated with greater fatigue.[5]

Cancer survivors report that fatigue is a disruptive symptom months or even years after treatment ends.[6,26-35] Persistent CRF affects quality of life (QOL), as patients become too tired to fully participate in the roles and activities that make life meaningful.[28,36-38] CRF may also influence the time it takes to return to work following treatment.[39] Patients perceive fatigue to be the most distressing symptom associated with cancer and its treatment, more distressing even than pain or nausea and vomiting, which can generally be managed by medications.[40]

Health care professionals have been challenged in their efforts to help patients manage CRF and to remain as fully engaged in life as possible. Because of the successes in cancer treatment, health care professionals are now likely to see patients with prolonged states of fatigue related to the lasting effects of treatment. Disability-related issues are relevant and often challenging, especially for patients with cancer who are cured of their malignancy but have continued fatigue.[41] It is often difficult for patients with CRF to obtain or retain disability benefits from insurers. Health care professionals should advocate for patients who require disability benefits and educate insurers about this issue.

To address the important problem of CRF, NCCN convened a panel of experts. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Related Fatigue, first published in 2000[42] and updated annually, synthesize the available research and clinical experience in this field and provide recommendations for patient care. The

complete details of the Development and Update of the NCCN Guidelines are available on the NCCN website at www.NCCN.org.

Guidelines Update Methodology

The complete details of the Development and Update of the NCCN Guidelines are available at www.NCCN.org.

Literature Search Criteria

Prior to the update of this version of the NCCN Guidelines for Cancer-Related Fatigue®, an electronic search of the PubMed database was performed to obtain key literature in cancer-related fatigue published since the previous Guidelines update using the following search term: cancer fatigue. The PubMed database was chosen as it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.[43]

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Practice Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies.

The data from key PubMed articles as well as articles from additional sources deemed as relevant to these Guidelines as discussed by the panel during the Guidelines update have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

Sensitive/Inclusive Language Usage

NCCN Guidelines strive to use language that advances the goals of equity, inclusion, and representation.[44] NCCN Guidelines endeavor to use language that is person-first; not stigmatizing; anti-racist, anti-classist, anti-misogynist, anti-ageist, anti-ableist, and anti-weight biased; and inclusive of individuals of all sexual orientations and gender identities. NCCN Guidelines incorporate non-gendered language, instead focusing on organ-specific recommendations. This language is both more accurate and more inclusive and can help fully address the needs of individuals of all sexual orientations and gender identities. NCCN Guidelines will continue to use the terms men, women, female, and male when citing statistics, recommendations, or data from organizations or sources that do not use inclusive terms. Most studies do not report how sex and gender data are collected and use these terms interchangeably or inconsistently. If sources do not differentiate gender from sex assigned at birth or organs present, the information is presumed to predominantly represent cisgender individuals. NCCN encourages researchers to collect more specific data in future studies and organizations to use more inclusive and accurate language in their future analyses.

Defining Cancer-Related Fatigue

The distinction between tiredness, fatigue, and exhaustion is generally not made in practice, despite conceptual differences.[45,46] The Cancer-Related Fatigue Guidelines Panel defines CRF as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. Compared with the fatigue experienced by healthy individuals, CRF is more severe, more distressing, and less likely to be relieved by rest. In terms of the defining characteristics, it is important to note the subjective sense of tiredness reported by the patient. As with pain, the clinician must rely on the description of fatigue and accompanying distress provided by the patient. Fatigue that interferes with usual functioning is another substantial component of the definition for CRF and the source of much distress for patients.[47]

Standards of Care for Assessment and Management

The panel developed the Standards of Care for CRF using the NCCN Guidelines for Adult Cancer Pain and the NCCN Guidelines for Distress Management (both available at www.NCCN.org) as exemplar models (see *Standards of Care for Cancer-Related Fatigue in Children/Adolescents and Adults* in the algorithm). These fatigue standards represent the best level of care for the assessment and management of fatigue in patients with cancer, including children, adolescents, and adults, and should provide guidance for health care professionals as they implement these guidelines in their respective institutions and clinical settings. The overall goal of the standards and guidelines is to ensure that all patients with cancer experiencing fatigue are identified and given prompt, effective treatment. The NCCN Guidelines provide "best care" information based on current evidence to support treatment.[48]

Fatigue should be screened, assessed, and managed for most patients according to the clinical practice guidelines. It is a subjective experience that should be systematically assessed using patient self-reports and other sources of data. However, because it is a symptom that is perceived by the patient, fatigue can be described most accurately by self-report. Patients should be screened for the presence and severity of fatigue at their initial clinical visit, at regular intervals during and/or following cancer treatment, and as clinically indicated.[49] The history and physical examination, laboratory data, and descriptions of patient behavior by family members/caregivers, especially regarding children, are important sources of additional information.

Patients and families should be informed that managing fatigue is an integral part of total health care and all patients should receive symptom management. If patients cannot tolerate their cancer treatment or if they must choose between treatment and QOL, control of their disease may be diminished.[50]

The guidelines for fatigue evaluation and management are best implemented by an interdisciplinary institutional committee, including experts in medicine, nursing, social work, physical therapy, and nutrition.[51] However, current practices in assessing and treating fatigue are inadequate and inconsistent at many institutions.[52] The panel recognizes that education and training programs are needed to prepare oncology experts in fatigue management. These are now being offered, but much more attention to these programs within the institutional setting is necessary if professionals are to become skilled in managing fatigue.[53] There is variation among institutions regarding which professional disciplines and staff can provide appropriate specialized consultation for fatigue. Therefore, in addition to implementation of fatigue treatment guidelines, health care providers should familiarize themselves with the type of supportive care staff available at their institution. Referral to an appropriate specialist or supportive care provider should be considered from the time of diagnosis to the end of life. Supportive care staff may include experts in survivorship, palliative care, integrative oncology, psychology, psychiatry, physical therapy, exercise therapy, occupational therapy, and physical medicine among others.

The NCCN Panel recommends that assessment of CRF levels be included in outcomes research. Quality of fatigue management should be included in institutional continuous quality improvement projects. Institutions can make faster progress in implementing these guidelines if they monitor adherence and progress with the guidelines.[53] Medical care contracts should reimburse for managing fatigue, including referrals to a physical therapist, dietitian, or the institution's symptom management service. Disability insurance should include coverage for the continuing effects of fatigue that lead to persistent disability.

Guidelines for Evaluation and Treatment

The general schema of the fatigue algorithm defines four phases: screening, primary evaluation, intervention, and re-evaluation. During the first phase, the health care professional must screen for fatigue and, if present, assess intensity level. If the intensity level is moderate to severe, the health care professional is directed during the primary evaluation phase of the algorithm to conduct a more focused history and physical examination. This phase includes an evaluation of concurrent symptoms and contributing factors frequently associated with fatigue, and can be treated as an initial step in managing fatigue. If, however, a patient either does not have one of these treatable contributing factors or continues to have moderate-to-severe fatigue after treatment of the factors, the health care professional should recommend additional treatment based on the NCCN Guidelines for Cancer-Related Fatigue.

After the evaluation phase, the guidelines delineate a set of interventions for the amelioration of fatigue based on clinical status (ie, active cancer treatment, post-treatment, end of life). Education and counseling are believed to be central to the effective management of fatigue. Additional interventions that are both nonpharmacologic and pharmacologic may be introduced; in many instances a combination of approaches must be used. The treatment of fatigue is continuous and, as indicated by the re-evaluation of patients, leads to an iterative loop in fatigue screening and management. Regardless of whether a patient demonstrates moderate-to-severe fatigue, health care professionals should continue to monitor for fatigue both throughout and after treatment, as fatigue symptoms have been shown to persist for years. While there are no studies that have evaluated the long-term treatment of fatigue, it should be assessed, and measures should be taken to reduce its impact on QOL.

Screening

The first phase of the algorithm emphasizes the screening of every patient for the presence or absence of fatigue using age-appropriate measures. Valid and reliable instruments are available to measure fatigue in children, adolescents, and adults (see *Appendix*); however, the effectiveness of these methods is limited without adequate implementation. If fatigue is present, a quantitative or semi-quantitative assessment should be performed and documented. For example, on a 0 to 10 numeric rating scale (0 = no fatigue and 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. The evaluation of fatigue in children may be simplified to a scale of 1 to 5 and modified even further in young children (aged 5–6 years) who may be asked more simply if they are “tired” or “not tired.” If the screening process determines that fatigue is absent or at a mild level, the patient and family/caregiver should receive education, counseling, and common management strategies for fatigue. Periodic re-screening and re-evaluation are recommended. It should be emphasized that survivors or patients who have completed treatment must still be monitored for fatigue, because fatigue may exist beyond the period of active treatment.[6,26]

Currently, screening is not systematic nor effective in many practice settings for various reasons, which often include patient or family/caregiver barriers and clinician barriers. For example, patients may not want to bother their health care professional in the clinic or office or when they are hospitalized. Patients may also be concerned that if they report high levels of fatigue, they might have their treatment altered. Patients do not want to be perceived as complaining and, therefore, may not mention fatigue. Patients may also assume that they must live with fatigue, because they believe there is no treatment for it. Health care professionals may not initiate a discussion about fatigue for many of the same reasons. First, clinicians may not recognize that fatigue is a problem for the patient. As a symptom, fatigue has been unrecognized and untreated, whereas medical

advances have led to better control over the more noticeable or less subtle acute symptoms of nausea, vomiting, and pain. Second, health care professionals may not be aware that there are effective treatments for fatigue, despite the lack of understanding about the underlying pathophysiology and mechanisms responsible for CRF.

Given these barriers, screening for CRF must be emphasized.[54] Clinical experience with fatigue assessment has shown that some patients cannot put a numeric value on their fatigue. Consequently, some patients may need to rate fatigue as mild, moderate, or severe. In some circumstances, other sources of data must be used. For example, patients may not be aware that fatigue has negatively affected their lives; however, spouses, parents, or other family members/caregivers may be more cognizant of these changes and the effect of fatigue. An appendix to this discussion provides additional information and resources to assist in the selection of instruments to measure CRF. Amarsheda et al[55] described multiple instruments used to assess CRF in breast cancer.

Using the numeric rating scale (ie, 0–10 scale), fatigue studies in patients with cancer have revealed a marked decrease in physical functioning at the level of 7 or higher.[56] In another study, ratings of symptom interference guided the selection of numeric rating cutpoints for the levels of mild, moderate, and severe fatigue. Interference levels on the MD Anderson Symptom Inventory (MDASI) scale were found to be well differentiated with the cutpoints for mild, moderate, or severe fatigue.[24] Based on these validated levels of fatigue intensity, the panel believes that the numeric rating scale can be used as a guide in practice settings and decision-making.

Primary Evaluation Phase

Focused History

When fatigue is rated as moderate to severe, with a score of 4 to 10, a more focused history and physical examination should be conducted as part of the primary evaluation phase outlined in the algorithms. One component of this evaluation is an assessment of the patient's current disease status, which encompasses the type and length of treatment, its capacity to induce fatigue, the patient's response to treatment (see *Primary Evaluation* in the algorithm), and recent hospitalizations. If possible, it should be determined whether the fatigue is related to a recurrence of the malignancy for those patients assumed to be disease-free or whether it is related to a progression of the malignancy for patients with underlying disease. Disease recurrence or progression is often an important factor causing patients with fatigue to seek further evaluation. If the fatigue is determined not to be related to disease recurrence or progression, informing patients and family members/caregivers may substantially reduce their anxiety levels.

Review and adjustment of current medications (including over-the-counter, herbals, vitamins, and other supplements) is essential. In addition, recent medication changes should be noted. Medications and medication interactions and/or misuse may contribute to the worsening of fatigue. For example, certain cardiac medications (such as beta-blockers) may elicit bradycardia and subsequent fatigue. Combinations of different classes of medications (such as narcotics, antidepressants, antiemetics, and antihistamines) may contribute to excessive drowsiness and increased fatigue. Polypharmacy (ie, use of ≥4 medications) and potentially inappropriate medication use is common among older adults with cancer.[57] It may be appropriate to adjust the dose of medications to treat fatigue. In some patients, altering either the dosage or dosing interval of a medication may be sufficient to improve the condition.

As part of a focused history, a review of systems should also be completed. This review may be helpful in determining the various organ systems affected and in directing the physical evaluation and diagnostic workup. Another component of the focused history is an in-depth fatigue assessment that includes evaluation of several aspects of fatigue: onset, pattern, duration, change over time, associated or alleviating factors, and interference with function. Other physical, emotional, and cognitive symptoms may be associated with fatigue. Because fatigue is a subjective condition involving a combination of symptoms and is experienced and reported differently by each person, it is important that the in-depth assessment includes the patient's self-assessment of the causes of fatigue.

The panel also recognizes the important role of social support throughout the course of cancer treatment and survivorship.[58] Fatigue is a major cause of functional dependence for patients with cancer, especially among older adults.[59] Besides assisting with daily living, caregivers provide cancer-specific support such as monitoring treatment side effects, aiding in fatigue and pain management, and administering medicine, among other forms of support.[60] The availability of dependable caregivers can significantly impact the functional, emotional, and financial capacity of a patient coping with cancer and the pursuant fatigue. A support network can also be provided when the patient lacks the economic and supportive resources to obtain tangible support.

Assessment of Treatable Contributing Factors

The panel identified factors that are often causative elements in the fatigue experience and, therefore, should be specifically assessed during the focused evaluation. These factors include pain, emotional distress, anemia, sleep disturbance, nutritional deficits/imbalance, decreased functional status, and comorbidities/cancer treatment sequelae. In a randomized controlled trial (RCT) of 152 patients with advanced cancer, protocolized patient-tailored treatment of the accompanying physical symptoms was coordinated by a nurse and resulted in a higher impact on fatigue than standard oncologic care.[61]

Descriptive studies have shown that, in both adults and children, fatigue seldom occurs by itself and more commonly clusters with sleep disturbance, emotional distress (eg, depression, anxiety), or pain.[62-65] Assessment of pain along with emotional distress and institution of effective treatment are essential. Fatigue and depression have also been documented as concurrent symptoms in patients with cancer.[5,66,67]

Sleep disturbances are a neglected problem in oncology[68] and may range from hypersomnia to insomnia.[69,70] Sleep disturbances are prevalent in 30% to 75% of patients with cancer.[71] Several studies have shown that patients with cancer experiencing fatigue during active treatment spend increased time resting and sleeping, but their sleep pattern is often severely disrupted. Patients may benefit from evaluation and education to improve sleep quality. In addition, sleep apnea can develop as a consequence of cancer treatment in surgery settings that affect the upper airway, changes in body composition, and alterations in hormone status (eg, thyroid, estrogen, testosterone); therefore, obstructive sleep apnea should also be evaluated.

Poor sleep hygiene may contribute to fatigue in patients with cancer. Factors associated with poor sleep hygiene include poor individual habits, a poor sleep environment, and an inability to decompress before bedtime. Habits that may also contribute include deviating from a regular sleep schedule, napping during the daytime, and ingesting caffeine, alcohol, or high-sugar foods before bed. An environment conducive to sleep should be dark, quiet, and comfortable to improve sleep quality. Stress-reducing activities prior to bed such as reading, journaling, yoga, meditation, or quiet music also contribute to positive sleep hygiene. While all patients should be aware of factors that hinder sleep hygiene, younger patients are

especially prone to some of these factors, including late-night gaming, television watching, computer and cell phone usage, and social media use in the hours that interfere with sleep.

Patients should undergo a nutritional assessment to evaluate weight gain and loss, caloric intake changes, impediments to nutritional intake, anemia, vitamin imbalance/intake, and fluid and electrolyte imbalances. Weight and weight changes should be carefully noted. The health care provider should review and discuss changes in caloric intake with the patient. If there are substantial abnormalities, a consultation with a nutrition expert may be appropriate. Often fatigue symptoms can be lessened by improving anemia and modifying dietary intake with appropriate caloric exchanges. Imbalances in sodium, potassium, calcium, iron, and magnesium serum levels are often reversible and, with appropriate supplementation, may reduce fatigue. Nutritional intake may be affected by nausea, vomiting, loss of appetite, food disinterest, mucositis, odynophagia, bowel obstruction, diarrhea, and constipation.

CRF is associated with decreased functional status. A survey conducted by Mustian and colleagues that included 753 patients receiving systemic chemotherapy showed that CRF interfered with physical functioning in the majority of patients.[72] Interference was moderate, and was noted to be higher in females, non-whites, and patients with metastatic disease. Patients with moderate-to-severe fatigue should be queried about their functional status, including changes in exercise or activity patterns and the influence of deconditioning. Can patients accomplish normal daily or enjoyable activities? Can they participate in formal or informal exercise programs? What is the amount and frequency of exercise? Has the patient modified exercise or other activity patterns since the development of fatigue? This assessment is important when formulating a treatment plan that may include exercise. Exercise has been beneficial in lowering fatigue levels in certain populations of patients with cancer.[73,74] However, before recommending an exercise program, the health care provider or exercise expert (eg, physiatrist, physical therapist) should assess the conditioning level of the patient. It is often difficult to convince patients with fatigue that exercise will improve their symptoms. It may be best to begin with discussions and low-level activities, which can gradually be increased over a period of time. This is especially important if the patient is significantly deconditioned.

Cancer treatment sequelae and non–cancer-related comorbidities may contribute substantially to symptoms of fatigue in patients with cancer. Therefore, the status of comorbidities must be reviewed in conjunction with the present treatment management strategies. If the comorbidity is not optimally managed, it may be necessary to further evaluate and improve management. For example, if a patient has underlying congestive heart failure secondary to anthracycline cardiomyopathy and is experiencing symptoms of dyspnea and angina, fatigue may often be improved by stabilizing the condition and decreasing the frequency of episodes of congestive heart failure. This may entail introduction of new medications, titration of current medications, or both. It may also involve an invasive interventional assessment of the patient's cardiac status.

Comorbidities that need review and assessment include cardiac, pulmonary, renal, gastrointestinal, hepatic, and neurologic dysfunction, rheumatologic or immune disorders, as well as infection. In patients receiving immunotherapy treatment, fatigue may be a presenting symptom of an endocrine disorder secondary to immunotherapy, such as a thyroid or pituitary disorder.[75] There is also a high incidence of thyroid dysfunction in normal individuals and in patients receiving thyroid medications.[76] Development of hypothyroidism occurs after RT for Hodgkin disease and other non-Hodgkin lymphomas, head and neck cancers, and breast cancer, as well as after total body irradiation in bone marrow transplantation. Hypogonadism is commonly seen in patients with

advanced cancer. A cross-sectional pilot study including males with advanced cancer showed that abnormally low levels of testosterone may be associated with fatigue.[77] However, additional research in a larger patient population is needed to clarify the incidence of hypogonadism and its association with specific malignancies and neurotoxic chemotherapy. Therefore, attention should be given to thyroid and endocrine problems (including hot flashes, hypothyroidism, hypogonadism, or adrenal insufficiency) in patients with cancer. Finally, health care providers should also be alert for signs of alcohol and drug misuse and illicit substance use. These detrimental habits can often lead to or aggravate other health problems such as sleep disturbance and result in fatigue.

Patient Clinical Status

After the primary fatigue evaluation is completed, the patient's clinical status (active cancer treatment, post-treatment with no active treatment except hormonal therapy or long-term maintenance, or end of life) should be determined due to its influence on CRF management and treatment strategies. As cancer treatment paradigms have changed, the use of these categories is not always clear. However, some general treatment guidelines apply across all clinical categories.[78]

If any treatable contributing factor discussed above is identified during the primary evaluation phase, it should be treated as an initial approach to fatigue management. Other NCCN Guidelines are also available to guide supportive care, including the NCCN Guidelines for Adult Cancer Pain, Distress Management, Hematopoietic Growth Factors (Cancer- and Chemotherapy-Induced Anemia), Antiemesis, Survivorship, Palliative Care, and Prevention and Treatment of Cancer-Related Infections (available at www.NCCN.org).

General Strategies for Management of Fatigue/Patient and Family/Caregiver Education and Counseling

Education about fatigue and its natural history should be offered to all patients with cancer,[54] especially patients beginning potential fatigue-inducing treatments (such as radiation, chemotherapy, or biotherapy) before fatigue onset. A Cochrane systematic review including 14 RCTs with 2213 patients with cancer showed that educational interventions may impact CRF (standardized mean difference [SMD], -0.27; 95% CI, -0.51 to -0.04), CRF intensity (SMD, -0.28; 95% CI, -0.52 to -0.04), and interference of CRF on daily life (SMD, -0.35; 95% CI, -0.54 to -0.16), although the quality of evidence was sometimes low.[79] Patients should be informed that if fatigue occurs, it may be a consequence of the treatment and is not necessarily an indication that the treatment is not working or that the disease is progressing. This reassurance is important, as fear of progression is a main reason for the underreporting of fatigue.

Patients who are completing treatment and their families should be educated about the pattern and level of fatigue that can be expected during this period. Although a significant subset of patients continues to experience distressing levels of fatigue that interfere with function, most patients experience a gradual decrease in fatigue and return of energy to normal levels.[80,81] Regular monitoring of fatigue levels can document the decrease in fatigue that normally occurs after treatment. Health care providers should continue to screen regularly for fatigue during follow-up visits.

In addition to education, the panel recommends counseling for patients about general strategies (physical activity and energy conservation) useful for coping with fatigue.[54,82] A meta-analysis including eight studies with 478 breast cancer survivors showed that exercise might improve CRF by counteracting low-grade inflammatory mediators (eg, interleukin 6).[83]

Energy conservation is defined as the deliberately planned management of one's personal energy resources to prevent their depletion. It encompasses a common sense approach that helps patients set realistic expectations, prioritize and pace activities, and delegate less essential activities.[84] A multisite clinical trial of energy conservation in 296 patients receiving cancer treatment reported significantly lower fatigue in patients receiving the experimental intervention.[85] However, evidence supporting energy conservation in patients with CRF is generally lacking. Patients should be counseled that it is permissible to postpone all nonessential activities if they are experiencing moderate-to-severe fatigue. In a situation of escalating fatigue at the end of life, family members/caregivers may wish to designate individuals to assume activities relinquished by the individual with cancer. Daytime naps can replenish energy, but it is advisable to limit these to not interfere with night-time sleep quality. Patients may also use labor-saving techniques such as wearing a bathrobe instead of drying off with a towel or assistive devices such as a walker, grabbing tools, and a bedside commode. One useful plan is to maintain a daily and weekly log or diary that allows the patient to self-monitor fatigue levels and ascertain peak energy periods and then plan activities accordingly within a structured routine.

Patients may be referred to exercise specialists (eg, physical therapist, physical medicine, rehabilitation specialist) as indicated for assessment and an exercise prescription. The American College of Sports Medicine has developed a certification program for cancer rehabilitation that is available for exercise professionals who specialize in the care of patients with cancer. It also convened a roundtable discussion and published specific guidelines for physical activity testing and exercise programs for patients with cancer.[86] Education and counseling could potentially be delivered via telehealth and/or the internet, especially for patients in the palliative care setting and for patients who are not under active treatment.[87-91]

Interventions for Patients on Active Treatment

Nonpharmacologic Interventions

Nonpharmacologic treatment of fatigue is beneficial in patients with cancer.[92-94] A meta-analysis including 113 studies and 11,525 patients showed that nonpharmacologic interventions, specifically exercise (weighted effect size [WES], 0.30; 95% CI, 0.25–0.36; $P < .001$) and psychological interventions (WES, 0.27; 95% CI, 0.21–0.33; $P < .001$), improve CRF, while pharmacologic interventions do not significantly improve CRF (WES, 0.09; 95% CI, 0.00–0.19; $P = .05$).[95] Of the specific nonpharmacologic interventions during active cancer treatment, the panel recommends physical activity (category 1), massage therapy (category 1), acupuncture, and psychosocial interventions. There is also supporting evidence for nutrition consultation, cognitive behavioral therapy (CBT) for insomnia, and bright white light therapy (BWLT) for CRF treatment in patients on active cancer treatment.[96] These interventions align with recommendations from the European Society for Medical Oncology (ESMO) Clinical Practice Guidelines[97] and the Oncology Nursing Society (ONS).[98-100] Both American Society of Clinical Oncology (ASCO)[101] and the pan-Canadian practice guidelines[102] used the ADAPTE method to take advantage of these existing guidelines (ie, NCCN, ONS) to enhance efficient production, reduce duplication, and promote the local update of quality guideline recommendations by their organizations.

Physical Activity

A large number of small- to moderate-sized studies have been performed to evaluate the feasibility of interventions designed to increase physical activity during therapy, and to explore the impact of increased activity upon CRF, QOL, treatment-related side effects, and other endpoints. Systematic reviews have associated exercise with improvement in fatigue for patients with breast cancer,[103,104] prostate cancer,[105,106] colorectal cancer,[107] lymphoma,[108] and hematologic malignancies[109,110]; in patients

who are undergoing adjuvant RT[111]; and in patients who have undergone HCT.[112]

A thorough review of the impact of physical activity on CRF (measured using various outcomes) is beyond the scope of this discussion. However, several meta-analyses have been conducted to provide a comprehensive evaluation of the impact of increased activity upon CRF.[113-118] Other smaller analyses confirmed a significant effect of exercise intervention on fatigue.[119-131] A systematic review of 16 meta-analyses showed a general benefit of exercise for CRF, but the ability to draw definitive conclusions about this benefit is limited by the variety of participant characteristics, fatigue measurement tools, and intervention characteristics evaluated in these meta-analyses.[132] A systematic review of systematic reviews and meta-analysis of 10 studies reported that physical training had a beneficial effect on fatigue in all cancer populations (SMD, -0.33; 95% CI, -0.43 to -0.23).[133] Wolvers and colleagues identified three main physical behavior profiles, suggesting that treatment options should be better tailored to suit specific needs.[134]

It is reasonable to encourage all patients to engage in a moderate level of physical activity during and after cancer treatment. Currently there is no sufficient evidence to recommend a specific amount of physical activity. The U.S Department of Health and Human Services recommends at least 150 minutes to 300 minutes of moderate intensity or 75 minutes to 150 minutes of vigorous intensity aerobic physical activity weekly, or an equivalent combination of both.[135] Some observational and interventional studies have suggested that patients with cancer who engage in at least 3 to 5 hours of moderate activity per week may experience better outcomes and have fewer side effects of therapy, including fatigue.[73,136-140]

Exercise interventions must be used with caution in patients with any of the following:

- Bone metastases
- Thrombocytopenia[141] (low platelets)
- Anemia (low red blood cells)
- Fever, active infection, or post-surgery
- Limitations secondary to metastasis or other comorbid illnesses
- Safety issues (ie, risk of falls)

The exercise program itself should be individualized based on the patient's age, gender, type of cancer, and physical fitness level. Both cardiovascular endurance (eg, walking,[142,143] swimming) and resistance exercise (ie, weight training) may be encouraged. Consider cancer-specific exercise programs if available. The program should begin at a low level of intensity and duration, progress slowly, and be modified as the patient's condition changes.

Yoga

A Cochrane review including 24 studies with 2166 patients with breast cancer showed that there is moderate-quality evidence that yoga reduces CRF, compared to no therapy (pooled SMD, -0.48; 95% CI, -0.75 to -0.20) and psychoeducation (pooled SMD, -0.90; 95% CI, -1.31 to -0.50).[144] When compared to exercise, however, this review showed that yoga did not significantly reduce CRF, although the quality of evidence was low. Several RCTs have demonstrated that yoga intervention impacts CRF during treatment.[145-152] Three of these studies targeted patients undergoing RT.[145,146,151] In an RCT including 352 females with non-metastatic breast cancer undergoing chemotherapy, a Tibetan yoga program did not significantly impact CRF compared to a stretching program and usual care.[153] However, exploratory analyses (n = 74) showed that practicing yoga at least twice per week was associated with better sleep-related outcomes 6 months after intervention completion (ie, fewer daily disturbances and better sleep quality and efficiency) when compared to participants who practiced yoga less than twice per week.

Another RCT targeted 60 patients with breast cancer who were undergoing adjuvant chemotherapy.[154] Fatigue was improved in patients randomized to receive 8 weeks of Anusara yoga sessions, twice per week ($P < .001$).

Some randomized trials have shown some benefit of tai chi and qigong, a practice involving movement, posture, and breathing, to CRF.[155-159] These benefits have also been observed in two systematic reviews.[160,161] However, one of these reviews showed that tai chi has a significant short-term benefit on CRF but that the long-term benefit is less clear.[160] A systematic review and meta-analysis of 1268 patients with breast cancer suggest that at 3-month follow-up, tai chi did not alleviate fatigue when compared to conventional supportive care interventions, such as CBT.[162] However, tai chi along with conventional supportive care interventions significantly reduced symptoms of fatigue.

The panel recommends yoga for treatment of CRF in patients on active cancer treatment (category 1). More data are needed to establish the effectiveness of yoga in reducing fatigue in males and in other cancers besides breast cancer.[163] An RCT including 54 patients with non-metastatic colorectal cancer randomized patients to either weekly yoga (for 10 weeks) or to a waitlist control group.[149] Modest group differences were found for sleep disturbances 3 months after intervention completion ($P = .04$). Study results may have been affected by attrition and poor intervention adherence rates.

Massage Therapy

Physically based therapies are those performed on a patient by a therapist or lay person, and include massage therapy or acupuncture. Massage therapy may be effective in reducing CRF,[164-167] with one meta-analysis including five RCTs with 667 patients showing favorable effects on CRF (SMD, -0.61; 95% CI, -1.09 to -0.13; $P = .01$).[168] The panel recommends massage therapy as a category 1 recommendation for treatment of CRF in patients on active treatment.

Acupuncture/Acupressure

Seven systematic reviews suggest that acupuncture and acupressure may have beneficial properties, although the studies acknowledge that a paucity of data makes it difficult to definitively evaluate the benefits.[169-175] Positive effects of acupuncture on fatigue have been reported in small samples but need to be confirmed in larger RCTs.[176,177] These small trials were conducted during active non-palliative RT,[178,179] and during and after chemotherapy treatment.[180-182] A small RCT showed that patients with CRF ($N = 78$) who received infrared laser moxibustion, a type of acupuncture in which the herb moxa (*Artemisia vulgaris*) is burned on or near the skin at acupoints, had less fatigue, compared to patients who received sham laser moxibustion ($P = .002$).[183] Significant group differences persisted up to 4 weeks after intervention completion ($P = .006$). Another RCT examining the effects of transcutaneous electrical acupoint stimulation (TEAS) on CRF in patients with non-small cell lung cancer (NSCLC) receiving chemotherapy showed that patients randomized to receive TEAS reported less fatigue than patients randomized to receive sham TEAS ($P = .005$) or routine nursing care ($P < .01$).[184] The panel recommends acupuncture as an option for patients on active treatment.

Psychosocial Interventions

Although a strong correlation exists between emotional distress and fatigue, the precise relationship is not clearly understood. Current psychosocial interventional studies may target one or more biologic mechanisms (eg, 5-HT3 neurotransmitter deregulation, vagal afferent activation, alteration in muscle and adenosine triphosphate metabolism, HPA axis dysfunction, circadian rhythm dysfunction, cytokine deregulation); however, most studies to date do not identify the underlying

targeted mechanism. The exception includes interventions aimed at increasing relaxation, thereby diminishing stress and activation of the HPA axis. Because of the inherent difficulty of conducting mechanistically based interventions, the majority of studies to date have been designed to address educational and coping deficits in order to optimize the patient's ability to deal with this often-debilitating symptom. Patients should be counseled regarding coping with fatigue and educated about anxiety and depression, which are commonly associated with fatigue during cancer treatment.[185]

Several meta-analyses evaluated the impact of psychosocial interventions on CRF. Analyzing 41 studies on 3620 patients with cancer, Kangas et al[121] reported a weighted pooled mean effect of -0.31 for psychosocial interventions on fatigue. Goedendorp et al[186] reported that, of 27 RCTs included in their analysis, seven showed significantly reduced fatigue. Of interest, 80% of fatigue-specific interventions were effective, compared to 14% of non-specific strategies. Jacobsen et al[187] analyzed 30 RCTs and found a significant effect for psychological interventions but not for activity-based programs.

Studies testing interventions to decrease fatigue can be grouped as CBT/behavioral therapy (BT), psycho-educational therapies/educational therapies, and supportive expressive therapies, based on review of three meta-analyses.[121,186,187] Of note, the categories in which interventions have been grouped are different in each of the meta-analyses and have been compared to the work reported by the ONS Putting Evidence into Practice (PEP).[99,100,188] These studies can be categorized based on their primary outcome parameter: fatigue or other. In many studies, fatigue was a secondary endpoint measured by a single item or a subscale of an instrument designed to measure emotional distress, QOL, or general symptom burden. Furthermore, fatigue was not an eligibility requirement. In studies specifically designed to measure fatigue, no severity cut-off score was used. Thus, patients enrolled in these studies may or may not have had significant levels of fatigue, thereby limiting the potential impact of the intervention.

A meta-analysis by Duijts and colleagues[120] reported that, like exercise programs, behavioral techniques including CBT, relaxation techniques, counseling, social support, hypnosis, and biofeedback are beneficial in improving fatigue among patients with breast cancer during and after treatment. Substantial data in literature provide high-level evidence during active treatment for CBT/BT[189-196] and psycho-educational therapies/educational therapies,[96,197-208] and these psychosocial interventions are recommended by the panel for treatment of CRF (category 1). However, one RCT in which patients with cancer were randomized to receive either a fatigue management education program or standard of care did not demonstrate an effect on CRF.[209] Potential explanations by the study investigators for the negative results include the program's inability to capture the complexity of CRF, contamination bias, measurement response shift, and patient reluctance regarding patient education. Supportive expressive therapies (eg, in-person or online support groups, counseling, journal writing) may serve as an emotional outlet and as a support network. There is less robust evidence for supportive expressive therapies during active treatment and it is therefore a category 2A recommendation.

Complementary therapies such as muscle relaxation, music therapy, hypnosis, arts therapy, and stress reduction based on mindfulness have been evaluated in combination with CBT approaches, although some of these therapies have also been evaluated on their own.[196,210-221] The data suggest that these therapies may be effective in reducing fatigue in patients with cancer. For example, education regarding stress management may help improve sleep quality. Secondary analyses from a 10-week cognitive behavioral stress management program for females

undergoing adjuvant treatment for breast cancer (N = 240) showed that those randomized to receive the stress management intervention reported a reduction in fatigue-related daytime interference, relative to participants randomized to a psychoeducational control group (P < .05).[222] Mediation analyses showed that these results were accounted for by self-reported improvements in sleep quality. Another RCT including 155 patients with breast cancer found no statistically significant difference in fatigue between those randomized to a stress management group and those in a control group.[223] A systematic review and analysis of 29 studies with 3476 participants or survivors diagnosed with different cancers found that mindfulness-based stress reduction, especially for breast cancer, improved multiple physiological parameters such as fatigue and stress.[224] However, the benefits might not be long-lasting.[225] The results of a Bayesian network meta-analysis that examined multiple interventions irrespective of the cancer stage determined that mindfulness-based stress reduction therapy, psychoeducational therapy, and CBT improved CRF.[226] Stress management and meditation interventions did not significantly improve CRF, nor did multimodal interventions. One RCT with 116 patients with breast or gynecologic cancer determined that music therapy during radiation treatment could alleviate CRF and depression.[227] However, larger studies are needed. An e-health–based self-management system can help alleviate fatigue but does not improve overall QOL.[228]

Nutrition Consultation

Many patients with cancer have changes in nutritional status. Because cancer and treatment can interfere with dietary intake, nutrition consultation may be helpful in managing the nutritional deficiencies that result from anorexia, diarrhea, nausea, and vomiting.[229] Adequate hydration and electrolyte balance are also essential in preventing and treating fatigue.[106] Large RCTs are needed to determine the impact of nutrition therapy on CRF.

Sleep Therapy

There are numerous types of CBT for insomnia; the most frequently used include stimulus control, sleep restriction, and sleep hygiene. Stimulus control includes going to bed when sleepy, going to bed at approximately the same time each night, and maintaining a regular rising time each day. Getting out of bed after 20 minutes if unable to fall asleep, both when first going to bed and when awakening during the night, is a key aspect of stimulus control. Sleep restriction requires avoiding long or late afternoon naps and limiting total time in bed.[230] Techniques to promote a good night's sleep and optimal functioning the next day, such as avoiding caffeine after noon and establishing an environment that is conducive to sleep (eg, dark, quiet, comfortable), are components of sleep hygiene. These strategies were used in a pilot study with females during adjuvant breast cancer treatment with chemotherapy. Sleep/wake patterns remained consistent with normal values except for increased number and length of nighttime awakenings.[231] For children with cancer, a consistent bedtime and routine, an environment conducive to sleep, and the presence of security objects (such as blankets and toys) are effective measures (see *Assessment of Treatable Contributing Factors*).

Bright White Light Therapy

BWLT involves exposure to very high fluorescent light (typically 1250–10,000 lux) emitted from a "light box" that is usually purchased for at-home use. This type of therapy has been used for the treatment of mood disorders and sleep disturbances in the general population and in older adults.[232-235] BWLT stimulates the suprachiasmatic nucleus of the hypothalamus, which regulates circadian rhythms.

BWLT has been associated with positive changes in fatigue in females with breast cancer during treatment with chemotherapy.[236,237] Thus far, samples have been small, and the risks associated with BWLT need to be balanced with the benefits. Further, the optimal timing and length of

treatment require further study, although BWLT is most commonly administered in the early morning for 30 to 40 minutes, and timing may be adjusted for those who sleep during the day.[238] A systematic review and meta-analysis of 13 RCTs reported that light therapy, at an intensity of 417.9 to 12,000 lux, alleviated CRF (SMD = 0.45; *P* = .007).[238] In a meta-analysis of nine studies, Hung et al[239] reported that compared to dim red light, daily BWLT for 30 minutes in the morning was associated with an amelioration in CRF severity (*k* = 5; Hedges' *g* = -0.414; 95% CI, -0.740 to -0.087; *P* = .013). The panel recommends that home-based BWLT be included as a nonpharmacologic strategy for treating CRF in patients on active treatment.

Pharmacologic Interventions

There is some evidence for pharmacologic therapy as treatment for fatigue, although a significant placebo response has been observed in a randomized trial.[240] A systematic review and meta-analysis demonstrated that 26% of patients treated with a placebo reported an improvement in CRF compared to 36% in patients treated by other means.[241] Another study found that the placebo response is non-trivial and statistically significant.[242] An open-label RCT by Yennurajalingam et al[243] also reported a significant placebo effect in patients with advanced cancer. As such, studies need to have sufficient power to account for the placebo effect. This should be taken into consideration when designing a clinical trial.

Although a wide variety of prescription pharmacologic options are available to improve sleep quality, there is little empirical evidence for the use of these agents in patients with cancer, and their use may be associated with adverse side effect profiles. Clinicians need to be aware of the potential risks of sedative-hypnotic drugs, which include severe allergic reactions and complex sleep-related behaviors, including sleep-driving. A table summarizing the medications commonly used to promote sleep is provided at the NCI Physician Data Query website (http://www.cancer.gov/cancertopics/pdq/supportivecare/sleepdisorders/HealthProfessional). Prescribing considerations for these classes of agents include increased likelihood of problems with daytime sleepiness, fatigue, withdrawal symptoms, dependency, rebound insomnia, sleep maintenance, memory, anticholinergic symptoms, orthostasis, and the potential for drug-drug interactions involving the cytochrome p450 isoenzyme system.

A systematic review of systematic reviews and pooled meta-analysis of six studies comprising patients undergoing cancer treatment and/or after treatment determined that psychostimulants may be moderately effective in reducing CRF (SMD, -0.20; 95% CI, -0.32 to 0.08; *P* < .0001).[244] The psychostimulant methylphenidate significantly reduced fatigue (SMD, -0.69; 95% CI, -1.29 to -0.09; *P* < .0001). Other studies that evaluated methylphenidate for its effect on CRF yielded mixed results in patients undergoing cancer therapy.[245-248] A meta-analysis including seven studies showed that methylphenidate reduces CRF compared to a placebo (SMD, -0.28; 95% CI, -0.44 to -0.12).[249] Analyzing five RCTs, Minton et al[250] attributed a significant benefit to psychostimulants in alleviating fatigue compared to placebo (Z-score [Z] = 2.83; *P* = .005). Patients have reported minor side effects with methylphenidate, including headache and nausea.

The wakefulness-promoting non-amphetamine psychostimulant, modafinil, has been approved for use in narcolepsy. In a large RCT, Jean-Pierre et al[251] randomized 867 patients undergoing chemotherapy to 200 mg of modafinil per day or placebo. Of the 631 evaluable patients, 315 received modafinil and 316 received placebo. Improvement in fatigue was observed in patients with severe fatigue (*P* = .017), but not in patients with mild or moderate fatigue. Toxicity was similar between the two arms. Secondary analyses from this study showed that, among patients with severe fatigue, depression improved in those randomized to receive modafinil [*t*(54) =

4.79; $P < .001$], compared to those randomized to receive a placebo [$t(73) = 3.56$; $P < .01$], potentially due to impact on positive affect ($P = .007$).[252] A phase III randomized, placebo-controlled trial assessing the effect of modafinil measured the improvement in fatigue in patients with metastatic prostate or breast cancer undergoing chemotherapy.[253] Fatigue was measured using the MDASI and no statistically significant difference was seen between treatment arms (35.9 vs. 39.6; 95% CI, -8.9 to 1.4; $P = .15$). There was an increase in toxicity with patients experiencing grade 2 or higher nausea and vomiting in the modafinil arm (45.4% vs. 25%). A phase II RCT conducted with 54 patients receiving RT for primary brain tumors showed that armodafinil was well-tolerated and improved fatigue after RT completion in those who reported greater fatigue at baseline assessment, although overall between-group differences did not reach statistical significance.[254] A meta-analysis including three studies showed that modafinil did not significantly reduce CRF, compared to placebo treatment.[249] Due to the limited number of studies and the marginal improvement in CRF in response to modafinil and armodafinil, it is not a recommended treatment.

The use of dietary supplements to alleviate the symptoms of fatigue has yielded mixed results. Although one review showed no benefit of coenzyme Q10 and guarana,[213] another systematic review showed that guarana extract combined with a fatigue reduction diet may successfully treat CRF.[255] There may also be some data to support the use of American ginseng.[213] In a phase III RCT of 364 patients experiencing CRF, symptom improvement as measured by the Multidimensional Fatigue Symptom Inventory Short Form (MFSI-SF) following treatment with 2000 mg of Wisconsin ginseng was observed.[256] In the overall population, improvement at 4 weeks was not statistically significant (ginseng, 14.4 points; standard deviation [SD], 27.1 vs. placebo, 8.2 points; SD, 24.8; $P = .07$). However, at 8 weeks, a statistically significant improvement ($P = .003$) in patients receiving ginseng (20 points; SD, 27) versus patients given the placebo (10.3 points; SD, 26.1) was observed. Furthermore, improvement was greatest in patients undergoing active cancer treatment compared to patients who had completed treatment. A phase II randomized study examining the effect of ginger extract (6-gingerol) in 88 patients receiving moderately to highly emetogenic adjuvant chemotherapy showed that patients who received the ginger extract reported significantly less grade 3 fatigue compared to patients who received a placebo (2% vs. 20%, respectively; $P = .02$).[257] A systematic review of seven clinical trials and one retrospective study concluded that although there is some evidence that ginseng is effective at combating CRF, there are insufficient high-quality trials to fully support the inclusion of ginseng as a standard treatment option for CRF.[258] Although an RCT showed that L-carnitine may be associated with improved fatigue in patients with hypothyroidism who underwent surgery for thyroid cancer ($n = 27$; $P < .05$),[259] other studies have shown no significant benefit of this dietary supplement on CRF.[213,260,261]

Based on currently available data, the panel included consideration of the psychostimulant methylphenidate in consideration of other modifiable causes of fatigue for patients undergoing active cancer treatment. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded. Use of psychostimulants in older adults should be treated with caution, as older adults may need a lower dosage than younger adults.[262] The data were not sufficient to support the recommendation for modafinil. Studies on the selective serotonin reuptake inhibitor paroxetine showed no influence by this antidepressant on fatigue in patients receiving chemotherapy.[263,264] One small study ($N = 40$) showed improved CRF after 4 weeks of treatment with 150 mg of the bupropion sustained-release antidepressant.[265] Antidepressants are not recommended to reduce fatigue.

Interventions for Patients Post-Treatment

Improvements in cancer survival rates have led to efforts to enhance symptom management, QOL, and overall functioning of individuals post-treatment. As previously mentioned, fatigue can be an acute effect of cancer or treatment, but it can also be a long-term or late effect.[266] Patients may continue to report unusual fatigue for months or years after treatment cessation.[27,29-32,80,267] The cause of fatigue during post-treatment is unclear and probably multifactorial.[268] Researchers have suggested that such fatigue may be due to persistent activation of the immune system[27,269] or to other factors, including the late effects of treatment on major organ systems.[269] One cross-sectional comparative study investigated fatigue and physiologic biomarkers of immune system activation in 20 breast cancer survivors who were fatigued (mean, 5 years since diagnosis) and in 20 non-fatigued survivors.[269] Fatigued survivors had significantly higher serum markers (interleukin-1 receptor antagonist [IL-1ra], soluble tumor necrosis factor type II, and neopterin) and lower cortisol levels when compared with non-fatigued survivors. Significantly higher numbers of circulating T lymphocytes that correlated with elevated serum IL-1ra levels also suggest that persistent fatigue in survivors may be caused by a chronic inflammatory process involving the T-cell compartment.[27] Longitudinal studies examining fatigue in long-term disease-free survivors are needed.

To date, most research reports of incidence and prevalence rates of fatigue during post-treatment are limited by their cross-sectional designs,[266,270-273] lack of comparison groups,[271] heterogeneous samples,[270] differing fatigue scales, lack of consistency in applying diagnostic criteria,[274] small sample sizes,[269] varying baseline survivorship definitions (ie, time since diagnosis vs. time since treatment cessation), and different mean survivorship durations. Additionally, most fatigue studies of patients who are post-treatment and disease-free have been conducted in white, English-speaking patients with breast cancer,[27,269,272] and in patients treated with peripheral stem cell or bone marrow transplant[275,276] with few exceptions.[29,31,32] These design issues make it difficult to reach conclusions about the prevalence, incidence, and duration of fatigue; the associated risk factors; and QOL. Incidence and prevalence rates for fatigue in this population range from 17% to 21% when strict *International Classification of Diseases, Tenth Revision* (ICD-10) diagnostic criteria are applied,[270] and range from 33% to 53% when other criteria (such as a score of 4 or more on the 0–10 fatigue scale) are used.[277] In contrast to these findings, Canadian and U.S. ovarian cancer survivors (n = 100), who were diagnosed a mean of 7.2 years before the survey, reported equivalent energy levels when compared with the general population.[81] As a consequence, what constitutes valid incidence and prevalence rates in patients who are disease-free requires more study.

Risk factors associated with fatigue during post-treatment of patients who are disease-free include pretreatment fatigue, anxiety and depression levels,[278] physical activity levels,[279,280] coping methods and cancer-related stressors, comorbidities, type of malignancy, prior treatment patterns, and treatment late effects. In a Norwegian study of Hodgkin disease survivors in remission for more than 5 years, higher fatigue levels were documented in those who had pulmonary dysfunction; the prevalence of chronic fatigue was two to three times higher than in survivors without pulmonary dysfunction.[277] No significant correlations in this study were found between fatigue and cardiac sequelae as measured by echocardiography, exercise testing, and chest radiography.[277]

Nonpharmacologic Interventions

Specific interventions recommended to manage fatigue during active cancer treatment are also recommended for the post-treatment of patients who are disease-free[78]; however, there are fewer studies of physically based therapies post-treatment, compared to studies of patients actively undergoing treatment.

Physical Activity

Physical activity is a category 1 recommendation for patients who have completed treatment. Improving strength, energy, and fitness through regular exercise has been shown to facilitate the transition from patient to survivor, decrease anxiety and depression, improve body image, and increase tolerance for physical activity even in patients who implement a moderate walking exercise program. However, if the patient is significantly deconditioned, weak, or has relevant late effects of treatment (such as cardiopulmonary limitations), referral to a physiatrist or a supervised rehabilitation program may be indicated. Exercise should be recommended with caution in patients with persistent and late effects of treatment (eg, cardiomyopathy) and those with safety issues (ie, risk of falls). Both cardiovascular endurance (eg, walking, swimming) and resistance exercise (ie, weight training) may be encouraged.

Of the nonpharmacologic approaches for managing CRF, exercise has the best evidence to support its effectiveness.[78,86,281-291] A meta-analysis of 44 studies including 3254 cancer survivors concluded that exercise reduced fatigue, especially in programs that involved moderate-intensity resistance exercise among older cancer survivors.[292] A systematic review of 140 independent meta-analyses by Fuller et al found a significant beneficial effect of aerobic and resistance exercises in 75% of the studies.[293] The results from a systematic review and meta-analysis of RCTs that included individuals with colorectal cancer pre-treatment, during treatment, or following treatment determined that compared to usual care, exercise improved health outcomes such as fatigue (SMD, 0.23; 95% CI, 0.01–0.45; $P = .04$) and QOL (SMD, 0.21; 95% CI, 0.05–0.37; $P < .01$).[107] A Cochrane systematic review including 26 studies of physical activity interventions for females with breast cancer who completed adjuvant therapy showed small improvements in CRF upon intervention completion (SMD, -0.32; 95% CI, -0.47 to -0.18), with results from four trials showing that improvements are sustained for at least 3 months post-intervention (SMD, -0.47; 95% CI, -0.84 to -0.11).[294] A meta-analysis including nine RCTs with 1156 breast cancer survivors showed that supervised exercise may improve CRF (SMD, -0.51; 95% CI, -0.81 to -0.21).[295] Two studies testing the effects of physical activity interventions on fatigue in breast cancer survivors found that individualized, prescriptive exercise reduced fatigue. However, researchers emphasize it is critical that exercise be individualized to the survivor's abilities to prevent exacerbation of cancer treatment toxicities.[279,280] Tailored exercise programs delivered using the internet may also help reduce fatigue, based on results of a randomized trial including 81 survivors of breast cancer who were treated with adjuvant therapy ($P < .001$).[285]

Yoga may also reduce fatigue in cancer survivors, and it is recommended for these patients by the Society for Integrative Oncology.[213] A systematic review including 14 trials with 828 patients showed that yoga may successfully reduce CRF following completion of cancer treatment (SMD, -0.68; 95% CI, -0.93 to -0.43).[93] An RCT including 200 survivors of breast cancer showed that those assigned to hatha yoga sessions twice per week for 12 weeks reported less fatigue at 3-month follow-up, relative to a wait-list control group ($P = .002$).[147] Frequency of yoga practice was strongly associated with less fatigue at 3-month follow-up ($P < .001$). In another RCT including 97 older cancer survivors, the effects of a 4-week yoga intervention on CRF were assessed.[148] After 4 weeks, participants receiving the yoga intervention reported less fatigue, relative to a standard care group ($P = .03$). In a small randomized trial including 34 breast cancer survivors, a yoga intervention delivered via DVD improved CRF, although effects were not significantly different from participants who received a strength training intervention.[296] The panel recommends yoga for patients who have completed treatment (category 1).

A systematic review and meta-analysis of 22 RCTs found that that there was low-level evidence that tai chi can improve QOL and sleep and

moderate-level evidence that tai chi can reduce fatigue.[297] Another systematic review also reported improved fatigue and sleep quality in cancer survivors who underwent tai chi training but indicated that the evidence level was low.[298] Qigong was found to ameliorate sleep and fatigue post-intervention in a systematic review and meta-analysis.[299] However, the beneficial effects were not significant after a period of 3 months. Chinese traditional wushu was evaluated in a systematic review and meta-analysis of 18 studies.[300] While no benefit was noted in terms of CRF in patients who are breast cancer survivors, the researchers found an improvement in sleep quality.

For further guidance on physical activity, see the NCCN Guidelines for Survivorship (available at www.NCCN.org).

Psychosocial Interventions

Psychosocial interventions, including CBT/BT, mindfulness-based stress reduction, psycho-educational therapies/educational therapies, and supportive expressive therapies are category 1 recommendations.[120,197,268,301-310] An RCT including 322 breast cancer survivors showed that a mindfulness-based stress reduction program improved self-reported fatigue interference and severity, compared to that reported by a usual care group ($P < .01$).[311] Another intervention including 252 distressed (ie, score of 4 or higher on the NCCN Distress Thermometer) breast cancer survivors showed that females randomized to receive a mindfulness-based intervention reported a significantly greater reduction in fatigue, compared to females who were randomized to receive a supportive expressive group therapy intervention, with between-group effects being large ($d = 0.45$).[312] Additional small RCTs also support the use of mindfulness-based interventions for CRF in cancer survivors.[313,314] However, the beneficial effects of CBT diminish over long periods of time. Van Gessel et al followed up with patients from two RCTs and found that only about half of the participants still reported comparable fatigue levels as they did immediately post-CBT.[315] One RCT with 89 breast cancer survivors assessed the benefits of *Reimagine*, an online symptom self-management curriculum, and determined that *Reimagine* has a strong impact on fatigue and depression.[316] Further studies are needed to further evaluate the impact of psychoeducation therapies.

Additional details on these interventions are provided in the preceding pages in the section on *Psychosocial Interventions* under *Interventions for Patients on Active Treatment*.

Additional Nonpharmacologic Approaches

CBT for insomnia (category 1) and nutrition consultation may be helpful for fatigue management during post-treatment.[188,317] A number of published studies support the conclusion that CBT interventions designed to optimize sleep quality in patients who completed cancer treatment may improve fatigue.[318-322] Positive effects on both sleep and fatigue after four to five weekly BT sessions have been reported in RCTs of patients in the survivorship phase who reported chronic insomnia.[323-325] Two smaller studies of patients with current complaints of insomnia in the survivorship phase reported improved sleep and fatigue.[318,319] Two other studies found positive benefits of a behavioral intervention on sleep and fatigue that were not sustained over time.[231,320] The American Academy of Sleep Medicine (AASM) has recommended three specific therapies for chronic insomnia in healthy individuals: relaxation training, CBT, and stimulus control therapy.[326] AASM has also published clinical guidelines for the management of chronic insomnia in adults.[327]

A randomized study determined that patients aged ≥65 years who received acupressure had a significant decrease in the severity and level of fatigue.[328] Another RCT also reported that acupressure or reiki significantly alleviated fatigue in patients receiving palliative care ($P < .001$).[329] A meta-analysis including 10 RCTs (about half included patients with breast cancer only) with 1327 patients with various malignancies

showed that acupuncture reduced CRF (SMD, -1.26; 95% CI, -1.80 to -0.71; *P* < .01).[174] This finding persisted when including only patients who are no longer undergoing treatment (*n* = 4; 285 patients; SMD, -1.38; 95% CI, -2.16 to -0.61; *P* < .01). ASCO and the Society for Integrative Oncology recommend acupuncture for patients who have completed cancer treatment, although the benefit of this intervention is potentially small.[213,330] The panel recommends acupuncture for cancer survivors.

The panel currently does not recommend BWLT for cancer survivors. However, emerging data from RCTs show that BWLT may reduce CRF in this population.[331-333] Large randomized trials are needed in this area.

Pharmacologic Interventions

Some evidence exists to support the use of psychostimulants following cancer therapy. A 54% response rate to methylphenidate has been reported in a phase II trial of 37 patients with breast cancer in remission.[334] An RCT of 154 patients post-chemotherapy also found an improvement in fatigue symptoms in the active arm.[335] Similarly to patients receiving active treatment, modafinil has limited study data in patients post-treatment. Although pilot studies suggested that modafinil may be associated with reduced fatigue,[336,337] the improved outcome was not maintained in larger trials[253,338] (see *Interventions for Patients on Active Treatment*). The panel agrees that methylphenidate may be considered in consideration of other modifiable causes of fatigue but does not recommend the use of modafinil. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded.

In one small RCT whereby cancer survivors (*N* = 40) were given open-label placebo drugs or no treatment, the results showed that placebos improved CRF.[339] A phase II study investigating the efficacy of American ginseng in head and neck cancer survivors concluded that the evidence was insufficient for ginseng to be recommended as a treatment modality.[340]

Interventions for Patients at the End of Life

Although the assessment and management of fatigue at the end of life parallels the general principles of this guideline, there are a few issues that are specific to this population. Factors that have a greater likelihood of association with fatigue at the end of life include anemia, medication adverse effects and polypharmacy, cognitive impairment, adverse effects of recent treatment, and malnutrition.[341] Evaluating and correcting these contributing factors could reduce fatigue severity.

It is likely that fatigue will increase substantially as disease progresses; however, patterns of fatigue are variable. For some adults, fatigue may be characterized as constant and unrelenting; for others, it is unpredictable and may come on suddenly.[342,343] At the end of life, most research has demonstrated that patients with cancer experience fatigue in the context of multiple symptoms. In a study of 278 Swedish adults admitted to a palliative care unit, 100% reported fatigue; other symptoms included pain (83%), dyspnea (77%), and appetite loss (75%).[344] In a large sample of adults receiving palliative care (N = 1000), Walsh and colleagues[345] noted that individuals with advanced cancer had multiple symptoms. Pain was the most prevalent (84%), followed by fatigue (69%), weakness (66%), and lack of energy (61%). Walsh and Rybicki[346] cluster-analyzed 25 symptoms in 1000 consecutive admissions to a palliative care program and found seven symptom clusters. The fatigue cluster included easy fatigue, weakness, anorexia, lack of energy, dry mouth, early satiety, weight loss, and taste changes. Pain and fatigue could have a synergistic effect that worsens the overall symptom experience in older patients with cancer.[47,347] In a case study of 15 adults with advanced disease, fatigue resulted in substantial regret, sadness, and sense of loss due to the deterioration of one's health.[343] Mystakidou and colleagues[348] reported that

a patient's desire for hastened death was predicted by feelings of sadness, a lack of appetite, pain, and fatigue.

Children with advanced cancer also experienced multiple symptoms at the end of life, most commonly fatigue, pain, and dyspnea.[349] According to parents who cared for a child at the end of life, more than 90% of the children experienced fatigue and almost 60% experienced significant suffering from it.[349]

Individuals with advanced cancer and their caregivers need information about the management of symptoms, including fatigue.[350] This includes information about the causes, patterns, and consequences of fatigue during treatment for advanced cancer and end-of-life care. Several major consequences of fatigue have been described, including its effect on functional status, emotional distress, and suffering. As fatigue escalates, it is likely to increasingly interfere with usual activities.[343] Families need to be apprised of this issue so they can plan accordingly. Fatigue is likely to have a significant effect on emotional well-being.[343,349]

Given the high prevalence of fatigue and other symptoms at the end of life, symptom management needs to be a major focus of care. Active commitment by the health care team to palliative care is critical when aggressive cancer therapy is given to patients with a low likelihood of long-term survival.[349] Interventions for fatigue should be initiated to relieve or diminish suffering, although it is recognized that some causes of fatigue cannot be assuaged.[78] See the NCCN Guidelines for Palliative Care for more information on intervention for patients receiving end-of-life care (available at www.NCCN.org).

Nonpharmacologic Interventions

There is currently no category 1 evidence for nonpharmacologic interventions at the end of life. Psychosocial interventions for these patients may focus on meaning and dignity, and gaining acceptance of the limitations imposed by fatigue. This may include a re-emphasis on meaningful family interactions that do not require high-level physical activity.[351] However, a Cochrane systematic review including 14 studies with 3077 participants showed that there is little evidence to support psychosocial interventions for CRF in patients with incurable cancer receiving palliative care.[352]

Although fatigue may increase at the end of life, some individuals may choose to be active despite declining health. There is some evidence that exercise is beneficial to individuals with incurable cancer and short life expectancies, although it is important to consider patients' goals (see section regarding *Physical Activity* under *Interventions for Patients on Active Treatment*). A structured exercise protocol depending on the patient's tolerance level can be used to improve fatigue experienced by patients with advanced cancer in hospice care.[353] Based on a systematic review of 20 exercise studies relevant to fatigue and muscle wasting in multiple myeloma, Strong[354] summarized weight-bearing precautions for bone metastases and exercise guidelines for adults with solid tumors and hematologic cancers, older cancer survivors, and individuals with CRF. An exercise protocol for multiple myeloma that incorporated aerobic, resistance, and flexibility exercises was also recommended. Three systematic reviews including patients with advanced cancer showed that exercise interventions improved CRF.[355-357] However, these results were not always consistent.[358] Smaller studies assessing the impact of physical activity in patients with cancer at the end of life have been conducted.[359-361] Although more research is needed, physical activity, which may include both endurance and resistance exercise as deemed appropriate by the health care provider, shows promise as a fatigue management strategy at the end of life; psychosocial interventions, sleep therapy, family interaction, and nutritional therapy are also helpful.

Pharmacologic Interventions

There continues to be interest in psychostimulant drugs for patients with cancer at the end of life, although studies have had mixed results. Methylphenidate has been shown to yield improvement in fatigue in patients with advanced cancer in two pilot studies.[362,363] Two RCTs reported an improvement in fatigue in both the methylphenidate and placebo arms.[364,365] However, another RCT found no significant difference between methylphenidate and placebo in patients with advanced cancer.[366] An RCT in patients with advanced NSCLC (n = 160) showed no significant improvement between patients treated with modafinil (n = 75) versus placebo (n = 85). Although well-tolerated, the mean score change between groups as measured by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT)-F scale was not significant (0.20; 95% CI, -3.56 to 3.97).[338] Overall, methylphenidate may be considered with caution for select patients with terminal cancer. Another psychostimulant, dexamphetamine, was evaluated for fatigue in patients with advanced cancer.[367] The results of an RCT showed tolerance of the drug and short-term improvement in fatigue at the second day, but no long-term benefit by the end of the 8-day study.

There is evidence supporting the effectiveness of corticosteroids (ie, prednisone and its derivative, dexamethasone) in adults in providing short-term relief of fatigue and improving QOL.[368-371] An RCT in patients with advanced cancer demonstrated significant improvement of fatigue in patients receiving dexamethasone (n = 43) compared to patients receiving placebo (n = 41) for 14 days (P = .008).[372] Improved outcomes were determined from the FACIT-F subscale as the primary endpoint. An assessment of overall QOL showed improvement at day 15 (P = .03) and in physical well-being measured at day 8 (P = .007) and day 15 (P = .002) by the Edmonton Symptom Assessment System for physical distress. This study was effective as a short-term therapy, but the long-term effects were not evaluated.[372] In an RCT investigating the effects of methylprednisolone in patients with advanced cancer receiving opioids, fatigue was measured in patients given methylprednisolone twice a day (n = 26) versus patients in the placebo group (n = 24).[373] Patients receiving methylprednisolone experienced a 17-point improvement on the EORTC-QOL Questionnaire C30 compared to the 3-point decline recorded by the placebo group (-17 vs. 3 points; P = .003). The results of a meta-analysis showed that treatment with corticosteroids significantly improved CRF (treatment effects of 0.94; P < .0001).[374] A prospective observational study from Japan including 179 patients with advanced cancer who received corticosteroids showed that treatment response to corticosteroids was associated with greater baseline fatigue, fair general condition, and absence of fluid retention symptoms.[375]

Given the toxicity associated with long-term use, consideration of short-term use of corticosteroids (prednisone or dexamethasone) is restricted to the terminally ill, adult patients with fatigue and concomitant anorexia, and patients with pain related to brain or bone metastases. Effects of the progestational agent megestrol acetate have been investigated in these patients. A systematic review demonstrated the safety and efficacy of megestrol acetate in treating cachexia for patients with cancer.[376] However, a second systematic review and meta-analysis of four studies revealed no benefit of progestational steroids compared with placebo for treatment of CRF (Z = 0.78; P = .44).[250,377] Double-blind RCTs have shown that melatonin[378] and Panax ginseng extract[379] do not significantly improve fatigue in patients with advanced cancer receiving palliative care.

Re-Evaluation Phase

Because fatigue may arise at many points during the course of a patient's disease and treatment, ongoing re-evaluation of the patient's status (with appropriate modifications and institution of new treatments) is an integral part of effective, overall fatigue management.

Summary

The NCCN Guidelines for Cancer-Related Fatigue recommend that patients be evaluated regularly for fatigue using a brief screening instrument and be treated as indicated by their fatigue level. Fatigue should be minimally evaluated with the scale outlined in the algorithm; however, there are additional tools for the measurement of fatigue that may be used to identify fatigue as appropriate (see *Appendix*).

Management of fatigue begins with primary oncology team members who perform the initial screening and either provide basic education and counseling or expand the initial screening to a more focused evaluation for moderate or higher levels of fatigue. The focused evaluation includes assessment of current disease and treatment status, a review of body systems, and an in-depth fatigue evaluation. In addition, the patient is assessed for the presence of treatable factors known to contribute to fatigue. If present, factors should be treated according to practice guidelines, with referral to other care professionals as appropriate, and the patient's fatigue should be re-evaluated regularly. If none of the factors is present or if the fatigue is unresolved, appropriate fatigue management and treatment strategies are selected within the context of the patient's clinical status (active treatment, post-treatment, or end-of-life care). Management of fatigue is cause-specific when conditions known to induce fatigue can be identified and treated. When specific causes of fatigue cannot be identified and corrected, nonpharmacologic and pharmacologic treatment of fatigue should be initiated.

Nonpharmacologic interventions may include a physical activity program to improve functional capacity and activity tolerance; psychosocial programs to manage stress and increase support; implementation of energy conservation strategies; and nutrition consultation, sleep, massage, and acupuncture as appropriate. Pharmacologic therapy may include drugs used to treat comorbidities. A 2014 update on the use of the psychostimulant methylphenidate suggests that it may provide some benefit.[380] A second agent that may be helpful for short-term use in advanced cancer is the corticosteroid methylprednisolone.[49,372-374] However, potential treatment modalities in managing fatigue require further research.

Effective management of CRF involves an informed and supportive oncology care team that assesses fatigue levels regularly, counsels and educates patients regarding strategies for coping with fatigue, and uses institutional experts for referral of patients with unresolved fatigue.[51] The oncology care team must recognize the many patient-, provider-, and system-related behaviors that can impede effective fatigue management.[53] Reducing barriers by use of available resources and evidence-based guidelines increases benefits to patients experiencing fatigue. [381,382]

Appendix

Fatigue Measurement for the Health Care Professional

A resource to facilitate selection of instruments to measure fatigue

Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. Lancet 2003;362:640-650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12944066.

- *This resource provides a detailed description of six scales [PFS, FACT-F, SCFS, MFI-20, BFI, and CLAS] frequently used in patients with cancer to measure fatigue.*

Jacobsen PB. Assessment of fatigue in cancer patients. J Natl Cancer Inst Monogr 2004:93-97. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15263047.

- *This resource includes factors to consider when selecting a fatigue measure.*

Meek PM, Nail LM, Barsevick A, et al. Psychometric testing of fatigue instruments for use with cancer patients. Nurs Res 2000;49:181-190. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10929689.

- *This study evaluates psychometric properties of several commonly used fatigue measures (POMS-F, MAF, LFS, and MFI).*

National Cancer Institute. Fatigue (PDQ) Health Professional Version. 2023. Available at: http://www.cancer.gov/cancertopics/pdq/supportivecare/fatigue/HealthProfessional. Accessed September 11, 2023.

- *This resource describes and provides references to 8 commonly used scales to measure fatigue (VAS, NCCN intensity tool, BFI, FSI, FACIT-F, MFI, EORTC QLQ-FA13, and PFS-R).*

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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22933027.

- *This resource provides psychometric properties for a shortened version of a commonly used fatigue measure.*

Stover AM, Reeve BB, Piper BF, et al. Deriving clinically meaningful cut-scores for fatigue in a cohort of breast cancer survivors: a Health, Eating, Activity, and Lifestyle (HEAL) Study. Qual Life Res 2013;22:2279-2292. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23420495.

- *This resource provides information about clinically meaningful cut-scores for fatigue using the PFS-R.*

Commonly Used Tools to Assess Cancer-Related Fatigue[P]

Screening Tool/ Assessment	Number/Type of Dimensions	Type of Scale	No. of Items	Length/ Ease of Use	Validated in Patients with Cancer	A/P/E[§]	Reliability/ Internal Consistency	Other
Brief Fatigue Inventory[56]	1 (severity)	11-point Likert	9	Short, easy to use	Yes, mixed cancers[56,383]	A,P,E	α=0.82–0.97	Questions about general activity, mood, walking ability, normal work, relationships, overall QOL; hard to distinguish between mild and moderate; validated in other languages
Daily Fatigue Cancer Scale[384]	1 (severity)	10-point Likert	3	Short, easy to use	Yes, mixed cancers[384]	A	N/A	Items measure tiredness, lacking energy, and feeling weary
EORTC QLQ-C30[‡,370]	1 (severity)	4-point Likert	3	Easy to use	Yes, mixed cancers[385,386]	A,P,E	α=0.80–0.85	Measures physical fatigue; not recommended as the only scale for end-of-life fatigue[387]
EORTC QLQ-FA12[*,388,389]	3 (physical, emotional, cognitive)	4-point Likert	12	Easy to use	Yes, mixed cancers[388,389]	A,P,E	α=0.79–0.90	To be used in conjunction with EORTC QLQ-C30
Fatigue Questionnaire[390]	1 (severity)	4-point Likert	11	Easy to use	Yes, cancer vs. normal population,[390] Hodgkin lymphoma[391]	A,P,E	α=0.88–0.90	Measures physical and mental fatigue
Visual Analogue Fatigue Scale[392]	1 (severity)	Analogue	18	Short, easy to use	Yes, patients with cancer compared to healthy controls[392]	A,P,E	α=0.91–0.96	Measures physical and mental fatigue; may help measure fatigue in 24-hour period but less effective over longer time periods

Screening Tool/ Assessment	Number/Type of Dimensions	Type of Scale	No. of Items	Length/ Ease of Use	Validated in Patients with Cancer	A/P/E§	Reliability/ Internal Consistency	Other
Fatigue Symptom Inventory[393]	4 (severity, frequency, diurnal variation, interference)	11-point Likert	14	Reasonable	Yes, breast,[393-396] metastatic,[397] and mixed cancers[398]	A,P	r=0.35–0.75 α=0.92–0.95	Two additional quantifiable fatigue questions; able to distinguish change over time; weak test-retest reliability
Functional Assessment of Cancer Therapy, Fatigue[399]	5 (physical, social/family, emotional, functional, fatigue)	5-point Likert	41/13	Long but subscale is reasonable and simple	Yes, breast[400] and mixed cancers[273,401-403]	A,P,E	r=0.90 α=0.93–0.95	Items consist of general health-related QOL (28 items) plus fatigue subscale of 13 items; lacks construct validity; measures change over time
Multi-Dimensional Fatigue Inventory-20[404]	5 (general, physical, mental, reduced activity, reduced motivation)	5-point Likert	20	Reasonable	Yes, breast,[405,406] uterine,[407,408] and mixed cancers[404,409-411]	A,P,E	α=0.65–0.80	Likert scale incorporates VAS
Multi-Dimensional Fatigue Symptom Inventory[412]	5 (general, physical, mental emotional, vigor)	5-point Likert	83/30	Variable length, can be complicated	Yes, mixed[412,413] and breast cancer[414]	A,P	r>0.50 α=0.87–0.96	Full version is long (83 items) but short form is a reasonable alternative[415]
Piper Fatigue Score-12[416]	4 (sensory, behavioral/ severity, affective meaning, cognitive/mood)	11-point Likert	12	Easy to use	Yes, breast cancer[416,417]	P	r=0.87–0.89	Shortened from revised Piper Fatigue Score that has been tested more extensively[198,416-424]; reliability is based on subscales in single study
NCCN Problem List	1 (general)	Dichotomous (yes/no)	1	Easy to use	Yes, breast cancer and colorectal cancer[425]	A	N/A	Taken from NCCN Distress Thermometer and Problem List

Screening Tool/ Assessment	Number/Type of Dimensions	Type of Scale	No. of Items	Length/ Ease of Use	Validated in Patients with Cancer	A/P/E[§]	Reliability/ Internal Consistency	Other
PROMIS CAT[426]	3 (fatigue, sleep disturbance, sleep impairment)	1 (never) to 5 (always)	Up to 20	Not burdensome	Yes, mixed cancers[426]	A	α=0.92–0.94	Scores correlate significantly with FACIT-Fatigue and the Insomnia Severity Index (r = -0.57 to 0.83; P < .001)[426]
Schwartz Cancer Fatigue Scale, Revised[427]	2 (physical and perceptual)	5-point Likert	6	Reasonable and clear	Yes, mixed cancers[427,428]	A	α=0.90	Shortened from the original 28-item Schwartz Cancer Fatigue Scale[429]

[Ꝑ] Tools are grouped as unidimensional tools followed by multidimensional tools and listed in alphabetical order within each subset.
[§] A/P/E, active treatment/post-treatment/end-of-life.
[‡] EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30.
* EORTC QLQ-FA12, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Cancer-Related Fatigue module.

References

1. Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. Lancet 2003;362:640-650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12944066.

2. Collins JJ, Devine TD, Dick GS, et al. The measurement of symptoms in young children with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7-12. J Pain Symptom Manage 2002;23:10-16. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11779663.

3. Wagner LI, Cella D. Fatigue and cancer: causes, prevalence and treatment approaches. Br J Cancer 2004;91:822-828. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15238987.

4. Silver JK, Baima J, Mayer RS. Impairment-driven cancer rehabilitation: an essential component of quality care and survivorship. CA Cancer J Clin 2013;63:295-317. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23856764.

5. Jim HS, Sutton SK, Jacobsen PB, et al. Risk factors for depression and fatigue among survivors of hematopoietic cell transplantation. Cancer 2016;122:1290-1297. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26814442.

6. Vardy JL, Dhillon HM, Pond GR, et al. Fatigue in people with localized colorectal cancer who do and do not receive chemotherapy: A longitudinal prospective study. Ann Oncol 2016;27:1761-1767. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27443634.

7. Kreissl S, Mueller H, Goergen H, et al. Cancer-related fatigue in patients with and survivors of Hodgkin's lymphoma: a longitudinal study of the German Hodgkin Study Group. Lancet Oncol 2016;17:1453-1462. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27612583.

8. Ramsenthaler C, Kane P, Gao W, et al. Prevalence of symptoms in patients with multiple myeloma: a systematic review and meta-analysis. Eur J Haematol 2016;97:416-429. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27528496.

9. Holliday EB, Dieckmann NF, McDonald TL, et al. Relationship between fatigue, sleep quality and inflammatory cytokines during external beam radiation therapy for prostate cancer: A prospective study. Radiother Oncol 2016;118:105-111. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26743832.

10. Miller AH, Ancoli-Israel S, Bower JE, et al. Neuroendocrine-immune mechanisms of behavioral comorbidities in patients with cancer. J Clin Oncol 2008;26:971-982. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18281672.

11. Tariman JD, Dhorajiwala S. Genomic variants associated with cancer-related fatigue: a systematic review. Clin J Oncol Nurs 2016;20:537-546. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27668374.

12. Bower JE. The role of neuro-immune interactions in cancer-related fatigue: Biobehavioral risk factors and mechanisms. Cancer 2019;125:353-364. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30602059.

13. Berger AM, Wielgus K, Hertzog M, et al. Patterns of circadian activity rhythms and their relationships with fatigue and anxiety/depression in women treated with breast cancer adjuvant chemotherapy. Support Care Cancer 2010;18:105-114. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19381692.

14. al-Majid S, McCarthy DO. Cancer-induced fatigue and skeletal muscle wasting: the role of exercise. Biol Res Nurs 2001;2:186-197. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11547540.

15. Rich TA. Symptom clusters in cancer patients and their relation to EGFR ligand modulation of the circadian axis. J Support Oncol 2007;5:167-174; discussion 176-167. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17500504.

16. O'Higgins CM, Brady B, O'Connor B, et al. The pathophysiology of cancer-related fatigue: current controversies. Support Care Cancer 2018;26:3353-3364. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29961146.

17. Al Maqbali M, Al Sinani M, Al Naamani Z, et al. Prevalence of fatigue in patients with cancer: A systematic review and meta-analysis. J Pain Symptom Manage 2021;61:167-189 e114. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32768552.

18. Henry DH, Viswanathan HN, Elkin EP, et al. Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. Support Care Cancer 2008;16:791-801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18204940.

19. Hofman M, Ryan JL, Figueroa-Moseley CD, et al. Cancer-related fatigue: the scale of the problem. Oncologist 2007;12 Suppl 1:4-10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573451.

20. Portenoy RK, Kornblith AB, Wong G, et al. Pain in ovarian cancer patients. Prevalence, characteristics, and associated symptoms. Cancer 1994;74:907-915. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8039118.

21. Ventafridda V, De Conno F, Ripamonti C, et al. Quality-of-life assessment during a palliative care programme. Ann Oncol 1990;1:415-420. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1707297.

22. Curtis EB, Krech R, Walsh TD. Common symptoms in patients with advanced cancer. J Palliat Care 1991;7:25-29. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1870042.

23. Portenoy RK, Thaler HT, Kornblith AB, et al. Symptom prevalence, characteristics and distress in a cancer population. Qual Life Res 1994;3:183-189. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7920492.

24. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24436136.

25. Ancoli-Israel S, Liu L, Rissling M, et al. Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. Support Care Cancer 2014;22:2535-2545. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24733634.

26. Abrahams HJ, Gielissen MF, Schmits IC, et al. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. Ann Oncol 2016;27:965-974. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26940687.

27. Bower JE, Ganz PA, Aziz N, et al. T-cell homeostasis in breast cancer survivors with persistent fatigue. J Natl Cancer Inst 2003;95:1165-1168. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12902446.

28. Crom DB, Hinds PS, Gattuso JS, et al. Creating the basis for a breast health program for female survivors of Hodgkin disease using a participatory research approach. Oncol Nurs Forum 2005;32:1131-1141. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16270109.

29. Fossa SD, Dahl AA, Loge JH. Fatigue, anxiety, and depression in long-term survivors of testicular cancer. J Clin Oncol 2003;21:1249-1254. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12663711.

30. Haghighat S, Akbari ME, Holakouei K, et al. Factors predicting fatigue in breast cancer patients. Support Care Cancer 2003;11:533-538. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12730728.

31. Ruffer JU, Flechtner H, Tralls P, et al. Fatigue in long-term survivors of Hodgkin's lymphoma; a report from the German Hodgkin Lymphoma Study Group (GHSG). Eur J Cancer 2003;39:2179-2186. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14522376.

32. Servaes P, Verhagen S, Schreuder HW, et al. Fatigue after treatment for malignant and benign bone and soft tissue tumors. J Pain Symptom

Manage 2003;26:1113-1122. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14654263.

33. Jones JM, Olson K, Catton P, et al. Cancer-related fatigue and associated disability in post-treatment cancer survivors. J Cancer Surviv 2016;10:51-61. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25876557.

34. Joly F, Ahmed-Lecheheb D, Kalbacher E, et al. Long-term fatigue and quality of life among epithelial ovarian cancer survivors: a GINECO case/control VIVROVAIRE I study. Ann Oncol 2019;30:845-852. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30851097.

35. Mounier N, Anthony S, Busson R, et al. Long-term fatigue in survivors of non-Hodgkin lymphoma: The Lymphoma Study Association SIMONAL cross-sectional study. Cancer 2019;125:2291-2299. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30901086.

36. Janda M, Gerstner N, Obermair A, et al. Quality of life changes during conformal radiation therapy for prostate carcinoma. Cancer 2000;89:1322-1328. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11002229.

37. Behringer K, Goergen H, Muller H, et al. Cancer-related fatigue in patients with and survivors of Hodgkin lymphoma: the impact on treatment outcome and social reintegration. J Clin Oncol 2016;34:4329-4337. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27998235/.

38. Jung JY, Lee JM, Kim MS, et al. Comparison of fatigue, depression, and anxiety as factors affecting posttreatment health-related quality of life in lung cancer survivors. Psychooncology 2018;27:465-470. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28755492.

39. Islam T, Dahlui M, Majid HA, et al. Factors associated with return to work of breast cancer survivors: a systematic review. BMC Public Health 2014;14 Suppl 3:S8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25437351.

40. Hinds PS, Quargnenti A, Bush AJ, et al. An evaluation of the impact of a self-care coping intervention on psychological and clinical outcomes in adolescents with newly diagnosed cancer. Eur J Oncol Nurs 2000;4:6-17; discussion 18-19. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12849624.

41. Morrow GR, Andrews PL, Hickok JT, et al. Fatigue associated with cancer and its treatment. Support Care Cancer 2002;10:389-398. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12136222.

42. Mock V, Atkinson A, Barsevick A, et al. NCCN practice guidelines for cancer-related fatigue. Oncology (Williston Park) 2000;14:151-161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11195408.

43. PubMed Overview. Available at: https://pubmed.ncbi.nlm.nih.gov/about/. Accessed January 4, 2022.

44. Freedman-Cass DA, Fischer T, Alpert AB, et al. The value and process of inclusion: Using sensitive, respectful, and inclusive language and images in NCCN content. J Natl Compr Canc Netw 2023;21:434-441. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37156485.

45. Olson K. A new way of thinking about fatigue: a reconceptualization. Oncol Nurs Forum 2007;34:93-99. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17562637.

46. Olson K, Krawchuk A, Quddusi T. Fatigue in individuals with advanced cancer in active treatment and palliative settings. Cancer Nurs 2007;30:E1-10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17666968.

47. Given CW, Given B, Azzouz F, et al. Comparison of changes in physical functioning of elderly patients with new diagnoses of cancer. Med Care 2000;38:482-493. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10800975.

48. Nail LM. Fatigue in patients with cancer. Oncol Nurs Forum 2002;29:537. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11979285.

49. Berger AM, Mitchell SA, Jacobsen PB, Pirl WF. Screening, evaluation, and management of cancer-related fatigue: Ready for implementation to

practice? CA Cancer J Clin 2015;65:190-211. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25760293.

50. Malik UR, Makower DF, Wadler S. Interferon-mediated fatigue. Cancer 2001;92:1664-1668. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11598884.

51. Escalante CP, Grover T, Johnson BA, et al. A fatigue clinic in a comprehensive cancer center: design and experiences. Cancer 2001;92:1708-1713. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11598891.

52. Pearson EJ, Morris ME, McKinstry CE. Cancer-related fatigue: a survey of health practitioner knowledge and practice. Support Care Cancer 2015;23:3521-3529. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25847296.

53. Berger AM, Mooney K. Dissemination and implementation of Guidelines for Cancer-Related Fatigue. J Natl Compr Canc Netw 2016;14:1336-1338. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27799505.

54. Pachman DR, Price KA, Carey EC. Nonpharmacologic approach to fatigue in patients with cancer. Cancer J 2014;20:313-318. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25299140.

55. Amarsheda S, Bhise AR. Systematic review of cancer-related fatigue instruments in breast cancer patients. Palliat Support Care 2022;20:122-128. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33947504.

56. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. Cancer 1999;85:1186-1196. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10091805.

57. Maggiore RJ, Dale W, Gross CP, et al. Polypharmacy and potentially inappropriate medication use in older adults with cancer undergoing chemotherapy: effect on chemotherapy-related toxicity and hospitalization during treatment. J Am Geriatr Soc 2014;62:1505-1512. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25041361.

58. Given BA, Given CW, Kozachik S. Family support in advanced cancer. CA Cancer J Clin 2001;51:213-231. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11577488.

59. Luciani A, Jacobsen PB, Extermann M, et al. Fatigue and functional dependence in older cancer patients. Am J Clin Oncol 2008;31:424-430. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18838877.

60. van Ryn M, Sanders S, Kahn K, et al. Objective burden, resources, and other stressors among informal cancer caregivers: a hidden quality issue? Psychooncology 2011;20:44-52. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20201115.

61. de Raaf PJ, de Klerk C, Timman R, et al. Systematic monitoring and treatment of physical symptoms to alleviate fatigue in patients with advanced cancer: a randomized controlled trial. J Clin Oncol 2013;31:716-723. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23284036.

62. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. Eur J Cancer Care (Engl) 2001;10:245-255. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11806675.

63. Berger AM, Walker SN. An explanatory model of fatigue in women receiving adjuvant breast cancer chemotherapy. Nurs Res 2001;50:42-52. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19785244.

64. Dodd MJ, Miaskowski C, Paul SM. Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum 2001;28:465-470. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11338755.

65. Hinds PS, Hockenberry M, Rai SN, et al. Nocturnal awakenings, sleep environment interruptions, and fatigue in hospitalized children with cancer. Oncol Nurs Forum 2007;34:393-402. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573303.

66. Hopwood P, Stephens RJ. Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. J Clin Oncol 2000;18:893-903. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10673533.

67. Loge JH, Abrahamsen AF, Ekeberg, Kaasa S. Fatigue and psychiatric morbidity among Hodgkin's disease survivors. J Pain Symptom Manage 2000;19:91-99. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10699536.

68. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. J Clin Oncol 2001;19:895-908. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11157043.

69. Berger AM, Mitchell SA. Modifying cancer-related fatigue by optimizing sleep quality. J Natl Compr Canc Netw 2008;6:3-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18267055.

70. Roscoe JA, Kaufman ME, Matteson-Rusby SE, et al. Cancer-related fatigue and sleep disorders. Oncologist 2007;12 Suppl 1:35-42. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573454.

71. Berger AM, Parker KP, Young-McCaughan S, et al. Sleep wake disturbances in people with cancer and their caregivers: state of the science. Oncol Nurs Forum 2005;32:E98-126. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16270104.

72. Mustian K, Palesh OG, Heckler CE, et al. Cancer-related fatigue interferes with activities of daily living among 753 patients receiving chemotherapy: A URCC CCOP study [abstract]. J Clin Oncol 2008;26 (15s):Abstract 9500. Available at: https://ascopubs.org/doi/abs/10.1200/jco.2008.26.15_suppl.9500.

73. Mock V, Frangakis C, Davidson NE, et al. Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. Psychooncology 2005;14:464-477. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15484202.

74. Schwartz AL. Daily fatigue patterns and effect of exercise in women with breast cancer. Cancer Pract 2000;8:16-24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10732535.

75. Linardou H, Gogas H. Toxicity management of immunotherapy for patients with metastatic melanoma. Ann Transl Med 2016;4:272. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27563659.

76. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000;160:526-534. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10695693.

77. Strasser F, Palmer JL, Schover LR, et al. The impact of hypogonadism and autonomic dysfunction on fatigue, emotional function, and sexual desire in male patients with advanced cancer: a pilot study. Cancer 2006;107:2949-2957. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17103445.

78. Mitchell SA, Beck SL, Hood LE, et al. Putting evidence into practice: evidence-based interventions for fatigue during and following cancer and its treatment. Clin J Oncol Nurs 2007;11:99-113. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17441401.

79. Bennett S, Pigott A, Beller EM, et al. Educational interventions for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev 2016;11:CD008144. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27883365.

80. Bower JE, Ganz PA, Desmond KA, et al. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. J Clin Oncol 2000;18:743-753. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10673515.

81. Stewart DE, Wong F, Duff S, et al. "What doesn't kill you makes you stronger": an ovarian cancer survivor survey. Gynecol Oncol 2001;83:537-542. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11733968.

82. 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;2014:346-358. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25749602.

83. Meneses-Echavez JF, Correa-Bautista JE, Gonzalez-Jimenez E, et al. The effect of exercise training on mediators of inflammation in breast cancer survivors: a systematic review with meta-analysis. Cancer Epidemiol Biomarkers Prev 2016;25:1009-1017. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27197276.

84. Barsevick AM, Whitmer K, Sweeney C, Nail LM. A pilot study examining energy conservation for cancer treatment-related fatigue. Cancer Nurs 2002;25:333-341. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12394560.

85. Barsevick AM, Dudley W, Beck S, et al. A randomized clinical trial of energy conservation for patients with cancer-related fatigue. Cancer 2004;100:1302-1310. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15022300.

86. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc 2019;51:2375-2390. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31626055.

87. Steel JL, Geller DA, Kim KH, et al. Web-based collaborative care intervention to manage cancer-related symptoms in the palliative care setting. Cancer 2016;122:1270-1282. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26970434.

88. Foster C, Grimmett C, May CM, et al. A web-based intervention (RESTORE) to support self-management of cancer-related fatigue following primary cancer treatment: a multi-centre proof of concept randomised controlled trial. Support Care Cancer 2016;24:2445-2453. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26643072.

89. Bruggeman-Everts FZ, Wolvers MDJ, van de Schoot R, et al. Effectiveness of two web-based interventions for chronic cancer-related fatigue compared to an active control condition: results of the "fitter na kanker" randomized controlled trial. J Med Internet Res 2017;19:e336. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29051138.

90. Seiler A, Klaas V, Troster G, Fagundes CP. eHealth and mHealth interventions in the treatment of fatigued cancer survivors: A systematic review and meta-analysis. Psychooncology 2017;26:1239-1253. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28665554.

91. Willems RA, Mesters I, Lechner L, et al. Long-term effectiveness and moderators of a web-based tailored intervention for cancer survivors on social and emotional functioning, depression, and fatigue: randomized controlled trial. J Cancer Surviv 2017;11:691-703. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28698999.

92. Tang NK, Lereya ST, Boulton H, et al. Nonpharmacological treatments of insomnia for long-term painful conditions: a systematic review and meta-analysis of patient-reported outcomes in randomized controlled trials. Sleep 2015;38:1751-1764. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25902806.

93. Hilfiker R, Meichtry A, Eicher M, et al. Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: A systematic review incorporating an indirect-comparisons meta-analysis. Br J Sports Med 2018;52:651-658. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28501804.

94. Wu C, Zheng Y, Duan Y, et al. Nonpharmacological interventions for cancer-related fatigue: A systematic review and bayesian network meta-analysis. Worldviews Evid Based Nurs 2019;16:102-110. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30919569.

95. Mustian KM, Alfano CM, Heckler C, et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: A meta-analysis. JAMA Oncol 2017;3:961-968. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28253393.

96. Mustian KM, Morrow GR, Carroll JK, et al. Integrative nonpharmacologic behavioral interventions for the management of cancer-

related fatigue. Oncologist 2007;12 Suppl 1:52-67. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573456.

97. Fabi A, Bhargava R, Fatigoni S, et al. Cancer-related fatigue: ESMO Clinical Practice Guidelines for diagnosis and treatment. Ann Oncol 2020;31:713-723. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32173483.

98. 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 Suppl:38-58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25427608.

99. Oncology Nursing Society Putting Evidence into Practice (PEP). Fatigue. Available at: https://www.ons.org/practice-resources/pep. Accessed May 1, 2015.

100. Irwin M, Johnson LA, editors. Putting evidence into practice: A pocket guide to cancer symptom management. Pittsburgh: Oncology Nursing Society; 2014.

101. 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 adaptation. J Clin Oncol 2014;32:1840-1850. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24733803.

102. 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:e233-246. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23737693.

103. Singh B, Spence RR, Steele ML, et al. A systematic review and meta-analysis of the safety, feasibility, and effect of exercise in women with stage II+ breast cancer. Arch Phys Med Rehabil 2018;99:2621-2636. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29730319.

104. Ehlers DK, DuBois K, Salerno EA. The effects of exercise on cancer-related fatigue in breast cancer patients during primary treatment: a meta-analysis and systematic review. Expert Rev Anticancer Ther 2020;20:865-877. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32842816.

105. Gardner JR, Livingston PM, Fraser SF. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: a systematic review. J Clin Oncol 2014;32:335-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24344218.

106. Baguley BJ, Bolam KA, Wright ORL, Skinner TL. The effect of nutrition therapy and exercise on cancer-related fatigue and quality of life in men with prostate cancer: A systematic review. Nutrients 2017;9:1003. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28895922.

107. Singh B, Hayes SC, Spence RR, et al. Exercise and colorectal cancer: a systematic review and meta-analysis of exercise safety, feasibility and effectiveness. Int J Behav Nutr Phys Act 2020;17:122. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32972439.

108. Vermaete N, Wolter P, Verhoef G, Gosselink R. Physical activity, physical fitness and the effect of exercise training interventions in lymphoma patients: a systematic review. Ann Hematol 2013;92:1007-1021. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23408096.

109. Bergenthal N, Will A, Streckmann F, et al. Aerobic physical exercise for adult patients with haematological malignancies. Cochrane Database Syst Rev 2014;11:CD009075. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25386666.

110. Knips L, Bergenthal N, Streckmann F, et al. Aerobic physical exercise for adult patients with haematological malignancies. Cochrane Database Syst Rev 2019;1:CD009075. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30702150.

111. Lipsett A, Barrett S, Haruna F, et al. The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: A systematic review and meta-analysis. Breast 2017;32:144-155. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28189100.

112. van Haren IE, Timmerman H, Potting CM, et al. Physical exercise for patients undergoing hematopoietic stem cell transplantation: systematic review and meta-analyses of randomized controlled trials. Phys Ther 2013;93:514-528. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23224217.

113. Puetz TW, Herring MP. Differential effects of exercise on cancer-related fatigue during and following treatment: a meta-analysis. Am J Prev Med 2012;43:e1-24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22813691.

114. Tomlinson D, Diorio C, Beyene J, Sung L. Effect of exercise on cancer-related fatigue: a meta-analysis. Am J Phys Med Rehabil 2014;93:675-686. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24743466.

115. Mishra SI, Scherer RW, Snyder C, et al. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev 2012;8:CD008465. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22895974.

116. Tian L, Lu HJ, Lin L, Hu Y. Effects of aerobic exercise on cancer-related fatigue: a meta-analysis of randomized controlled trials. Support Care Cancer 2016;24:969-983. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26482381.

117. Oberoi S, Robinson PD, Cataudella D, et al. Physical activity reduces fatigue in patients with cancer and hematopoietic stem cell transplant recipients: A systematic review and meta-analysis of randomized trials. Crit Rev Oncol Hematol 2018;122:52-59. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29458789.

118. Medeiros Torres D, Jorge Koifman R, da Silva Santos S. Impact on fatigue of different types of physical exercise during adjuvant chemotherapy and radiotherapy in breast cancer: Systematic review and meta-analysis. Support Care Cancer 2022;30:4651-4662. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35064331.

119. Cramp F, Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev 2008:CD006145. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18425939.

120. Duijts SF, Faber MM, Oldenburg HS, et al. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20336645.

121. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18729569.

122. McMillan EM, Newhouse IJ. Exercise is an effective treatment modality for reducing cancer-related fatigue and improving physical capacity in cancer patients and survivors: a meta-analysis. Appl Physiol Nutr Metab 2011;36:892-903. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22067010.

123. Velthuis MJ, Agasi-Idenburg SC, Aufdemkampe G, Wittink HM. The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of randomised controlled trials. Clin Oncol (R Coll Radiol) 2010;22:208-221. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20110159.

124. Steindorf K, Schmidt ME, Klassen O, et al. Randomized, controlled trial of resistance training in breast cancer patients receiving adjuvant radiotherapy: results on cancer-related fatigue and quality of life. Ann Oncol 2014;25:2237-2243. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25096607.

125. van Waart H, Stuiver MM, van Harten WH, et al. Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial. J Clin Oncol 2015;33:1918-1927. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25918291.

126. Gokal K, Wallis D, Ahmed S, et al. Effects of a self-managed home-based walking intervention on psychosocial health outcomes for breast cancer patients receiving chemotherapy: a randomised controlled trial. Support Care Cancer 2016;24:1139-1166. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26275768.

127. Baumann FT, Bieck O, Oberste M, et al. Sustainable impact of an individualized exercise program on physical activity level and fatigue syndrome on breast cancer patients in two German rehabilitation centers. Support Care Cancer 2017;25:1047-1054. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27942857/.

128. Rogers LQ, Courneya KS, Anton PM, et al. Effects of a multicomponent physical activity behavior change intervention on fatigue, anxiety, and depressive symptomatology in breast cancer survivors: Randomized trial. Psychooncology 2017;26:1901-1906. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27530961.

129. Hoffman AJ, Brintnall RA, Given BA, et al. Using perceived self-efficacy to improve fatigue and fatigability in postsurgical lung cancer patients: a pilot randomized controlled trial. Cancer Nurs 2017;40:1-12. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27135752.

130. Van Vulpen JK, Velthuis MJ, Steins Bisschop CN, et al. Effects of an exercise program in colon cancer patients undergoing chemotherapy. Med Sci Sports Exerc 2016;48:767-775. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26694846.

131. Hojan K, Kwiatkowska-Borowczyk E, Leporowska E, et al. Physical exercise for functional capacity, blood immune function, fatigue, and quality of life in high-risk prostate cancer patients during radiotherapy: a prospective, randomized clinical study. Eur J Phys Rehabil Med 2016;52:489-501. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26761561.

132. Kelley GA, Kelley KS. Exercise and cancer-related fatigue in adults: a systematic review of previous systematic reviews with meta-analyses. BMC Cancer 2017;17:693. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29058631.

133. Belloni S, Arrigoni C, Caruso R. Effects from physical exercise on reduced cancer-related fatigue: a systematic review of systematic reviews and meta-analysis. Acta Oncol 2021;60:1678-1687. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34396915.

134. Wolvers MDJ, Bussmann JBJ, Bruggeman-Everts FZ, et al. Physical behavior profiles in chronic cancer-related fatigue. Int J Behav Med 2018;25:30-37. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28699090.

135. Physical Activity Guidelines for Americans, 2nd edition. 2018. Available at: https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf. Accessed September 7, 2023.

136. Courneya KS, Friedenreich CM, Sela RA, et al. The group psychotherapy and home-based physical exercise (group-hope) trial in cancer survivors: physical fitness and quality of life outcomes. Psychooncology 2003;12:357-374. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12748973.

137. Courneya KS, Mackey JR, Bell GJ, et al. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol 2003;21:1660-1668. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12721239.

138. Drouin JS, Armstrong H, Krause S. Effects of aerobic exercise training on peak aerobic capacity, fatigue, and psychological factors during radiation for breast cancer. Rehab Oncol 2005;23:11-17. Available at: http://www.highbeam.com/doc/1P3-823983201.html.

139. Schwartz AL, Mori M, Gao R, et al. Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. Med Sci Sports Exerc 2001;33:718-723. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11323538.

140. Segal RJ, Reid RD, Courneya KS, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol

2003;21:1653-1659. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12721238.

141. Morishita S, Nakano J, Fu JB, Tsuji T. Physical exercise is safe and feasible in thrombocytopenic patients with hematologic malignancies: A narrative review. Hematology 2020;25:95-100. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32075567.

142. Wang P, Wang D, Meng A, et al. Effects of walking on fatigue in cancer patients: A systematic review and meta-analysis. Cancer Nurs 2022;45:E270-E278. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34870943.

143. Yuan Y, Lin L, Zhang N, et al. Effects of home-based walking on cancer-related fatigue in patients with breast cancer: A meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 2022;103:342-352. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34302791.

144. Cramer H, Lauche R, Klose P, et al. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev 2017;1:CD010802. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28045199.

145. Chakrabarty J, Vidyasagar M, Fernandes D, et al. Effectiveness of pranayama on cancer-related fatigue in breast cancer patients undergoing radiation therapy: A randomized controlled trial. Int J Yoga 2015;8:47-53. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25558133.

146. Chandwani KD, Perkins G, Nagendra HR, et al. Randomized, controlled trial of yoga in women with breast cancer undergoing radiotherapy. J Clin Oncol 2014;32:1058-1065. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24590636.

147. Kiecolt-Glaser JK, Bennett JM, Andridge R, et al. Yoga's impact on inflammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial. J Clin Oncol 2014;32:1040-1049. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24470004.

148. Sprod LK, Fernandez ID, Janelsins MC, et al. Effects of yoga on cancer-related fatigue and global side-effect burden in older cancer survivors. J Geriatr Oncol 2015;6:8-14. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25449185.

149. Cramer H, Pokhrel B, Fester C, et al. A randomized controlled bicenter trial of yoga for patients with colorectal cancer. Psychooncology 2016;25:412-420. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26228466.

150. Bower JE, Garet D, Sternlieb B, et al. Yoga for persistent fatigue in breast cancer survivors: a randomized controlled trial. Cancer 2012;118:3766-3775. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22180393.

151. Ben-Josef AM, Chen J, Wileyto P, et al. Effect of Eischens yoga during radiation therapy on prostate cancer patient symptoms and quality of life: a randomized phase II trial. Int J Radiat Oncol Biol Phys 2017;98:1036-1044. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28721886.

152. Danhauer SC, Addington EL, Cohen L, et al. Yoga for symptom management in oncology: A review of the evidence base and future directions for research. Cancer 2019;125:1979-1989. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30933317.

153. Chaoul A, Milbury K, Spelman A, et al. Randomized trial of Tibetan yoga in patients with breast cancer undergoing chemotherapy. Cancer 2018;124:36-45. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28940301.

154. Taso CJ, Lin HS, Lin WL, et al. The effect of yoga exercise on improving depression, anxiety, and fatigue in women with breast cancer: a randomized controlled trial. J Nurs Res 2014;22:155-164. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25111109.

155. Yeh ML, Chung YC. A randomized controlled trial of qigong on fatigue and sleep quality for non-Hodgkin's lymphoma patients undergoing

chemotherapy. Eur J Oncol Nurs 2016;23:81-86. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27456379.

156. Chuang TY, Yeh ML, Chung YC. A nurse facilitated mind-body interactive exercise (Chan-Chuang qigong) improves the health status of non-Hodgkin lymphoma patients receiving chemotherapy: randomised controlled trial. Int J Nurs Stud 2017;69:25-33. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28122280.

157. Zhang LL, Wang SZ, Chen HL, Yuan AZ. Tai chi exercise for cancer-related fatigue in patients with lung cancer undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2016;51:504-511. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26721747.

158. Zhou W, Wan YH, Chen Q, et al. Effects of tai chi exercise on cancer-related fatigue in patients with nasopharyngeal carcinoma undergoing chemoradiotherapy: a randomized controlled trial. J Pain Symptom Manage 2018;55:737-744. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29122618.

159. McQuade JL, Prinsloo S, Chang DZ, et al. Qigong/tai chi for sleep and fatigue in prostate cancer patients undergoing radiotherapy: a randomized controlled trial. Psychooncology 2017;26:1936-1943. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27548839.

160. Song S, Yu J, Ruan Y, et al. Ameliorative effects of Tai Chi on cancer-related fatigue: a meta-analysis of randomized controlled trials. Support Care Cancer 2018;26:2091-2102. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29564620.

161. Wayne PM, Lee MS, Novakowski J, et al. Tai Chi and Qigong for cancer-related symptoms and quality of life: a systematic review and meta-analysis. J Cancer Surviv 2018;12:256-267. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29222705.

162. Liu L, Tan H, Yu S, et al. The effectiveness of tai chi in breast cancer patients: A systematic review and meta-analysis. Complement Ther Clin Pract 2020;38:101078. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32056814.

163. Buffart LM, van Uffelen JG, Riphagen, II, et al. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC Cancer 2012;12:559. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23181734.

164. Cassileth BR, Vickers AJ. Massage therapy for symptom control: outcome study at a major cancer center. J Pain Symptom Manage 2004;28:244-249. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15336336.

165. Post-White J, Kinney ME, Savik K, et al. Therapeutic massage and healing touch improve symptoms in cancer. Integr Cancer Ther 2003;2:332-344. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14713325.

166. Lopez G, Liu W, Milbury K, et al. The effects of oncology massage on symptom self-report for cancer patients and their caregivers. Support Care Cancer 2017;25:3645-3650. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28660350.

167. Kinkead B, Schettler PJ, Larson ER, et al. Massage therapy decreases cancer-related fatigue: Results from a randomized early phase trial. Cancer 2018;124:546-554. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29044466.

168. Pan YQ, Yang KH, Wang YL, et al. Massage interventions and treatment-related side effects of breast cancer: a systematic review and meta-analysis. Int J Clin Oncol 2014;19:829-841. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24275985.

169. Towler P, Molassiotis A, Brearley SG. What is the evidence for the use of acupuncture as an intervention for symptom management in cancer supportive and palliative care: an integrative overview of reviews. Support Care Cancer 2013;21:2913-2923. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23868190.

170. Posadzki P, Moon TW, Choi TY, et al. Acupuncture for cancer-related fatigue: a systematic review of randomized clinical trials. Support Care

Cancer 2013;21:2067-2073. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23435597.

171. Ling WM, Lui LY, So WK, Chan K. Effects of acupuncture and acupressure on cancer-related fatigue: a systematic review. Oncol Nurs Forum 2014;41:581-592. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25355016.

172. Lau CH, Wu X, Chung VC, et al. Acupuncture and related therapies for symptom management in palliative cancer care: systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e2901. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26945382.

173. Pan Y, Yang K, Shi X, et al. Clinical benefits of acupuncture for the reduction of hormone therapy-related side effects in breast cancer patients: A systematic review. Integr Cancer Ther 2018;17:602-618. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30117343.

174. Zhang Y, Lin L, Li H, et al. Effects of acupuncture on cancer-related fatigue: a meta-analysis. Support Care Cancer 2018;26:415-425. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29128952.

175. Hsieh SH, Wu CR, Romadlon DS, et al. The effect of acupressure on relieving cancer-related fatigue: A systematic review and meta-analysis of randomized controlled trials. Cancer Nurs 2021;44:E578-E588. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34380961.

176. Sood A, Barton DL, Bauer BA, Loprinzi CL. A critical review of complementary therapies for cancer-related fatigue. Integr Cancer Ther 2007;6:8-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17351022.

177. Li H, Schlaeger JM, Jang MK, et al. Acupuncture improves multiple treatment-related symptoms in breast cancer survivors: A systematic review and meta-analysis. J Altern Complement Med 2021;27:1084-1097. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34449251.

178. Balk J, Day R, Rosenzweig M, Beriwal S. Pilot, randomized, modified, double-blind, placebo-controlled trial of acupuncture for cancer-related fatigue. J Soc Integr Oncol 2009;7:4-11. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19476729.

179. Mao JJ, Styles T, Cheville A, et al. Acupuncture for nonpalliative radiation therapy-related fatigue: feasibility study. J Soc Integr Oncol 2009;7:52-58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19476739.

180. Molassiotis A, Sylt P, Diggins H. The management of cancer-related fatigue after chemotherapy with acupuncture and acupressure: a randomised controlled trial. Complement Ther Med 2007;15:228-237. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18054724.

181. Vickers AJ, Straus DJ, Fearon B, Cassileth BR. Acupuncture for postchemotherapy fatigue: a phase II study. J Clin Oncol 2004;22:1731-1735. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15117996.

182. Tang WR, Chen WJ, Yu CT, et al. Effects of acupressure on fatigue of lung cancer patients undergoing chemotherapy: an experimental pilot study. Complement Ther Med 2014;22:581-591. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25146059.

183. Mao H, Mao JJ, Guo M, et al. Effects of infrared laser moxibustion on cancer-related fatigue: A randomized, double-blind, placebo-controlled trial. Cancer 2016;122:3667-3672. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27495269.

184. Hou L, Zhou C, Wu Y, et al. Transcutaneous electrical acupoint stimulation (TEAS) relieved cancer-related fatigue in non-small cell lung cancer (NSCLC) patients after chemotherapy. J Thorac Dis 2017;9:1959-1966. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28839994.

185. Stark D, Kiely M, Smith A, et al. Anxiety disorders in cancer patients: their nature, associations, and relation to quality of life. J Clin Oncol 2002;20:3137-3148. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12118028.

186. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Psychosocial interventions for reducing fatigue during cancer treatment in

adults. Cochrane Database Syst Rev 2009:CD006953. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19160308.

187. Jacobsen PB, Donovan KA, Vadaparampil ST, Small BJ. Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. Health Psychol 2007;26:660-667. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18020836.

188. Eaton LH, Tipton JM, eds. Oncology Nursing Society Putting Evidence into Practice: Improving oncology patient outcomes. Pittsburgh, PA: Oncology Nursing Society; 2009.

189. Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med 2005;12:278-285. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16262547.

190. Armes J, Chalder T, Addington-Hall J, et al. A randomized controlled trial to evaluate the effectiveness of a brief, behaviorally oriented intervention for cancer-related fatigue. Cancer 2007;110:1385-1395. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17661342.

191. Luebbert K, Dahme B, Hasenbring M. The effectiveness of relaxation training in reducing treatment-related symptoms and improving emotional adjustment in acute non-surgical cancer treatment: a meta-analytical review. Psychooncology 2001;10:490-502. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11747061.

192. Montgomery GH, Kangas M, David D, et al. Fatigue during breast cancer radiotherapy: an initial randomized study of cognitive-behavioral therapy plus hypnosis. Health Psychol 2009;28:317-322. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19450037.

193. Haller H, Winkler MM, Klose P, et al. Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. Acta Oncol 2017:1-12. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28686520.

194. Abrahams HJG, Gielissen MFM, Donders RRT, et al. The efficacy of Internet-based cognitive behavioral therapy for severely fatigued survivors of breast cancer compared with care as usual: A randomized controlled trial. Cancer 2017;123:3825-3834. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28621820.

195. Kwekkeboom KL, Abbott-Anderson K, Cherwin C, et al. Pilot randomized controlled trial of a patient-controlled cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. J Pain Symptom Manage 2012;44:810-822. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22771125.

196. Mendoza ME, Capafons A, Gralow JR, et al. Randomized controlled trial of the Valencia model of waking hypnosis plus CBT for pain, fatigue, and sleep management in patients with cancer and cancer survivors. Psychooncology 2017;26:1832-1838. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27467589.

197. Boesen EH, Ross L, Frederiksen K, et al. Psychoeducational intervention for patients with cutaneous malignant melanoma: a replication study. J Clin Oncol 2005;23:1270-1277. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15718325.

198. Gaston-Johansson F, Fall-Dickson JM, Nanda J, et al. The effectiveness of the comprehensive coping strategy program on clinical outcomes in breast cancer autologous bone marrow transplantation. Cancer Nurs 2000;23:277-285. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10939175.

199. Given B, Given CW, McCorkle R, et al. Pain and fatigue management: results of a nursing randomized clinical trial. Oncol Nurs Forum 2002;29:949-956. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12096292.

200. Kim Y, Roscoe JA, Morrow GR. The effects of information and negative affect on severity of side effects from radiation therapy for prostate cancer. Support Care Cancer 2002;10:416-421. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12136225.

201. Lindemalm C, Strang P, Lekander M. Support group for cancer patients. Does it improve their physical and psychological wellbeing? A pilot study. Support Care Cancer 2005;13:652-657. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16041464.

202. Ream E, Richardson A, Alexander-Dann C. Supportive intervention for fatigue in patients undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2006;31:148-161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16488348.

203. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16135471.

204. Allison PJ, Edgar L, Nicolau B, et al. Results of a feasibility study for a psycho-educational intervention in head and neck cancer. Psychooncology 2004;13:482-485. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15227717.

205. Godino C, Jodar L, Duran A, et al. Nursing education as an intervention to decrease fatigue perception in oncology patients. Eur J Oncol Nurs 2006;10:150-155. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16618589.

206. Williams SA, Schreier AM. The role of education in managing fatigue, anxiety, and sleep disorders in women undergoing chemotherapy for breast cancer. Appl Nurs Res 2005;18:138-147. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16106331.

207. Yesilbalkan 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:E215-222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19581225.

208. Yun YH, Lee KS, Kim YW, et al. Web-based tailored education program for disease-free cancer survivors with cancer-related fatigue: a randomized controlled trial. J Clin Oncol 2012;30:1296-1303. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22412149.

209. Bourmaud A, Anota A, Moncharmont C, et al. Cancer-related fatigue management: evaluation of a patient education program with a large-scale randomised controlled trial, the PEPs fatigue study. Br J Cancer 2017;116:849-858. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28196066.

210. Dobos G, Overhamm T, Bussing A, et al. Integrating mindfulness in supportive cancer care: a cohort study on a mindfulness-based day care clinic for cancer survivors. Support Care Cancer 2015;23:2945-2955. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25711654.

211. Charalambous A, Giannakopoulou M, Bozas E, et al. Guided imagery and progressive muscle relaxation as a cluster of symptoms management intervention in patients receiving chemotherapy: a randomized control trial. PLoS One 2016;11:e0156911. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27341675.

212. Bradt J, Dileo C, Magill L, Teague A. Music interventions for improving psychological and physical outcomes in cancer patients. Cochrane Database Syst Rev 2016:CD006911. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27524661.

213. Greenlee H, DuPont-Reyes MJ, Balneaves LG, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J Clin 2017;67:194-232. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28436999.

214. Duong N, Davis H, Robinson PD, et al. Mind and body practices for fatigue reduction in patients with cancer and hematopoietic stem cell transplant recipients: A systematic review and meta-analysis. Crit Rev Oncol Hematol 2017;120:210-216. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29198334.

215. Shaw JM, Sekelja N, Frasca D, et al. Being mindful of mindfulness interventions in cancer: a systematic review of intervention reporting and

study methodology. Psychooncology 2018;27:1162-1171. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29377335.

216. Gregoire C, Faymonville ME, Vanhaudenhuyse A, et al. Effects of an intervention combining self-care and self-hypnosis on fatigue and associated symptoms in post-treatment cancer patients: A randomized-controlled trial. Psychooncology 2020;29:1165-1173. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32297396.

217. Witek Janusek L, Tell D, Mathews HL. Mindfulness based stress reduction provides psychological benefit and restores immune function of women newly diagnosed with breast cancer: A randomized trial with active control. Brain Behav Immun 2019;80:358-373. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30953776.

218. Zhang Q, Zhao H, Zheng Y. Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related quality of life in breast cancer patients-a systematic review and meta-analysis. Support Care Cancer 2019;27:771-781. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30488223.

219. Qi Y, Lin L, Dong B, et al. Music interventions can alleviate cancer-related fatigue: a metaanalysis. Support Care Cancer 2021;29:3461-3470. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33481115.

220. Cheng P, Xu L, Zhang J, et al. Role of arts therapy in patients with breast and gynecological cancers: A systematic review and meta-analysis. J Palliat Med 2021;24:443-452. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33507828.

221. Jiang XH, Chen XJ, Xie QQ, et al. Effects of art therapy in cancer care: A systematic review and meta-analysis. Eur J Cancer Care (Engl) 2020;29:e13277. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32542749.

222. 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. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24318654.

223. Rissanen R, Arving C, Ahlgren J, Nordin K. Group versus individual stress management intervention in breast cancer patients for fatigue and emotional reactivity: a randomised intervention study. Acta Oncol 2014;53:1221-1229. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25007225.

224. Xunlin NG, Lau Y, Klainin-Yobas P. The effectiveness of mindfulness-based interventions among cancer patients and survivors: a systematic review and meta-analysis. Support Care Cancer 2020;28:1563-1578. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31834518.

225. Schell LK, Monsef I, Wockel A, Skoetz N. Mindfulness-based stress reduction for women diagnosed with breast cancer. Cochrane Database Syst Rev 2019;3:CD011518. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30916356.

226. Yuan Y, Lin L, Xie C, et al. Effectiveness comparisons of various psychosocial therapies for cancer-related fatigue: A Bayesian network meta-analysis. J Affect Disord 2022;309:471-481. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35504400.

227. Alcantara-Silva TR, de Freitas-Junior R, Freitas NMA, et al. Music therapy reduces radiotherapy-induced fatigue in patients with breast or gynecological cancer: A randomized trial. Integr Cancer Ther 2018;17:628-635. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29633652.

228. Xu A, Wang Y, Wu X. Effectiveness of e-health based self-management to improve cancer-related fatigue, self-efficacy and quality of life in cancer patients: Systematic review and meta-analysis. J Adv Nurs 2019;75:3434-3447. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31566769.

229. Brown JK. A systematic review of the evidence on symptom management of cancer-related anorexia and cachexia. Oncol Nurs Forum 2002;29:517-532. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11979284.

230. Morin C, Espie C. Insomnia: A clinical guide to assessment and treatment. New York: Kluwer Academic; 2003.

231. Berger AM, VonEssen S, Khun BR, et al. Feasibilty of a sleep intervention during adjuvant breast cancer chemotherapy. Oncol Nurs Forum 2002;29:1431-1441. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12432414.

232. Golden RN, Gaynes BN, Ekstrom RD, et al. The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence. Am J Psychiatry 2005;162:656-662. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15800134.

233. Pail G, Huf W, Pjrek E, et al. Bright-light therapy in the treatment of mood disorders. Neuropsychobiology 2011;64:152-162. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21811085.

234. Montgomery P, Dennis J. A systematic review of non-pharmacological therapies for sleep problems in later life. Sleep Med Rev 2004;8:47-62. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15062210.

235. Forbes D, Blake CM, Thiessen EJ, et al. Light therapy for improving cognition, activities of daily living, sleep, challenging behaviour, and psychiatric disturbances in dementia. Cochrane Database Syst Rev 2014;2:CD003946. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24574061.

236. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21660669.

237. Jeste N, Liu L, Rissling M, et al. Prevention of quality-of-life deterioration with light therapy is associated with changes in fatigue in women with breast cancer undergoing chemotherapy. Qual Life Res 2013;22:1239-1244. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22865153.

238. Xiao P, Ding S, Duan Y, et al. Effect of light therapy on cancer-related fatigue: A systematic review and meta-analysis. J Pain Symptom Manage 2022;63:e188-e202. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34563631.

239. Hung CM, Zeng BY, Zeng BS, et al. Cancer-related fatigue: light therapy: updated meta-analysis of randomised controlled trials. BMJ Support Palliat Care 2021. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34266911.

240. de la Cruz M, Hui D, Parsons HA, Bruera E. Placebo and nocebo effects in randomized double-blind clinical trials of agents for the therapy for fatigue in patients with advanced cancer. Cancer 2010;116:766-774. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19918921.

241. Junior PNA, Barreto CMN, de Iracema Gomes Cubero D, Del Giglio A. The efficacy of placebo for the treatment of cancer-related fatigue: a systematic review and meta-analysis. Support Care Cancer 2020;28:1755-1764. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31302766.

242. Roji R, Stone P, Ricciardi F, Candy B. Placebo response in trials of drug treatments for cancer-related fatigue: A systematic review, meta-analysis and meta-regression. BMJ Support Palliat Care 2020;10:385-394. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32046962.

243. Yennurajalingam S, Azhar A, Lu Z, et al. Open-label placebo for the treatment of cancer-related fatigue in patients with advanced cancer: A randomized controlled trial. Oncologist 2022;27:1081-1089. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36106759.

244. Belloni S, Arrigoni C, de Sanctis R, et al. A systematic review of systematic reviews and pooled meta-analysis on pharmacological interventions to improve cancer-related fatigue. Crit Rev Oncol Hematol 2021;166:103373. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34051301.

245. Butler JM, Jr., Case LD, Atkins J, et al. A phase III, double-blind, placebo-controlled prospective randomized clinical trial of d-threo-methylphenidate HCl in brain tumor patients receiving radiation therapy.

Int J Radiat Oncol Biol Phys 2007;69:1496-1501. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17869448.

246. Mar Fan HG, Clemons M, Xu W, et al. A randomised, placebo-controlled, double-blind trial of the effects of d-methylphenidate on fatigue and cognitive dysfunction in women undergoing adjuvant chemotherapy for breast cancer. Support Care Cancer 2008;16:577-583. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17972110.

247. Moraska AR, Sood A, Dakhil SR, et al. Phase III, randomized, double-blind, placebo-controlled study of long-acting methylphenidate for cancer-related fatigue: North Central Cancer Treatment Group NCCTG-N05C7 trial. J Clin Oncol 2010;28:3673-3679. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20625123.

248. Schwartz AL, Thompson JA, Masood N. Interferon-induced fatigue in patients with melanoma: a pilot study of exercise and methylphenidate. Oncol Nurs Forum 2002;29:E85-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12183762.

249. Qu D, Zhang Z, Yu X, et al. Psychotropic drugs for the management of cancer-related fatigue: a systematic review and meta-analysis. Eur J Cancer Care (Engl) 2016;25:970-979. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26490083.

250. Minton O, Richardson A, Sharpe M, et al. Drug therapy for the management of cancer-related fatigue. Cochrane Database Syst Rev 2010;7:CD006704. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20614448.

251. Jean-Pierre P, Morrow GR, Roscoe JA, et al. A phase 3 randomized, placebo-controlled, double-blind, clinical trial of the effect of modafinil on cancer-related fatigue among 631 patients receiving chemotherapy: a University of Rochester Cancer Center Community Clinical Oncology Program Research base study. Cancer 2010;116:3513-3520. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20564068.

252. Conley CC, Kamen CS, Heckler CE, et al. Modafinil moderates the relationship between cancer-related fatigue and depression in 541 patients receiving chemotherapy. J Clin Psychopharmacol 2016;36:82-85. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26658264.

253. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24337761.

254. Page BR, Shaw EG, Lu L, et al. Phase II double-blind placebo-controlled randomized study of armodafinil for brain radiation-induced fatigue. Neuro Oncol 2015;17:1393-1401. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25972454.

255. Pereira P, Reis AD, Diniz RR, et al. Dietary supplements and fatigue in patients with breast cancer: a systematic review. Breast Cancer Res Treat 2018;171:515-526. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29915949.

256. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23853057.

257. Konmun J, Danwilai K, Ngamphaiboon N, et al. A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy. Med Oncol 2017;34:69. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28349496.

258. Sadeghian M, Rahmani S, Zendehdel M, et al. Ginseng and cancer-related fatigue: A systematic review of clinical trials. Nutr Cancer 2021;73:1270-1281. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32691627.

259. An JH, Kim YJ, Kim KJ, et al. L-carnitine supplementation for the management of fatigue in patients with hypothyroidism on levothyroxine treatment: a randomized, double-blind, placebo-controlled trial. Endocr J 2016;63:885-895. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27432821.

260. Hershman DL, Unger JM, Crew KD, et al. Randomized double-blind placebo-controlled trial of acetyl-L-carnitine for the prevention of taxane-induced neuropathy in women undergoing adjuvant breast cancer therapy. J Clin Oncol 2013;31:2627-2633. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23733756.

261. Marx W, Teleni L, Opie RS, et al. Efficacy and effectiveness of carnitine supplementation for cancer-related fatigue: A systematic literature review and meta-analysis. Nutrients 2017;9:1224. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29112178.

262. Franzen JD, Padala PR, Wetzel MW, Burke WJ. Psychostimulants for older adults. Current Psychiatry 2012;11:23-32. Available at: https://www.mdedge.com/psychiatry/article/64585/depression/psychostimulants-older-adults.

263. Morrow GR, Hickok JT, Roscoe JA, et al. Differential effects of paroxetine on fatigue and depression: a randomized, double-blind trial from the University of Rochester Cancer Center Community Clinical Oncology Program. J Clin Oncol 2003;21:4635-4641. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14673053.

264. Roscoe JA, Morrow GR, Hickok JT, et al. Effect of paroxetine hydrochloride (Paxil) on fatigue and depression in breast cancer patients receiving chemotherapy. Breast Cancer Res Treat 2005;89:243-249. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15754122.

265. Ashrafi F, Mousavi S, Karimi M. Potential role of bupropion sustained release for cancer-related fatigue: a double-blind, placebo-controlled study. Asian Pac J Cancer Prev 2018;19:1547-1551. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29936730.

266. Knobel H, Loge JH, Nordoy T, et al. High level of fatigue in lymphoma patients treated with high dose therapy. J Pain Symptom Manage 2000;19:446-456. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10908825.

267. Servaes P, Verhagen S, Bleijenberg G. Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann Oncol 2002;13:589-598. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12056710.

268. Gielissen MF, Verhagen S, Witjes F, Bleijenberg G. Effects of cognitive behavior 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17050873.

269. Bower JE, Ganz PA, Aziz N, Fahey JL. Fatigue and proinflammatory cytokine activity in breast cancer survivors. Psychosom Med 2002;64:604-611. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12140350.

270. Cella D, Davis K, Breitbart W, et al. Cancer-related fatigue: prevalence of proposed diagnostic criteria in a United States sample of cancer survivors. J Clin Oncol 2001;19:3385-3391. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11454886.

271. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. Oncologist 2000;5:353-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11040270.

272. Servaes P, Prins J, Verhagen S, Bleijenberg G. Fatigue after breast cancer and in chronic fatigue syndrome: similarities and differences. J Psychosom Res 2002;52:453-459. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12069869.

273. Stone P, Richardson A, Ream E, et al. Cancer-related fatigue: inevitable, unimportant and untreatable? Results of a multi-centre patient survey. Cancer Fatigue Forum. Ann Oncol 2000;11:971-975. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11038033.

274. Donovan KA, McGinty HL, Jacobsen PB. A systematic review of research using the diagnostic criteria for cancer-related fatigue. Psychooncology 2013;22:737-744. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22544488.

275. Hann DM, Jacobsen PB, Martin SC, et al. Fatigue in women treated with bone marrow transplantation for breast cancer: a comparison with women with no history of cancer. Support Care Cancer 1997;5:44-52. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9010989.

276. Mock V, Cameron L, Tompkins C. Every step counts: A walking exercise program for persons living with cancer. Baltimore: Johns Hopkins University; 1997.

277. Knobel H, Havard Loge J, Lund MB, et al. Late medical complications and fatigue in Hodgkin's disease survivors. J Clin Oncol 2001;19:3226-3233. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11432890.

278. Geinitz H, Zimmermann FB, Thamm R, et al. Fatigue in patients with adjuvant radiation therapy for breast cancer: long-term follow-up. J Cancer Res Clin Oncol 2004;130:327-333. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15007642.

279. Schneider CM, Hsieh CC, Sprod LK, et al. Effects of supervised exercise training on cardiopulmonary function and fatigue in breast cancer survivors during and after treatment. Cancer 2007;110:918-925. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17582616.

280. Vallance JK, Courneya KS, Plotnikoff RC, et al. Randomized controlled trial of the effects of print materials and step pedometers on physical activity and quality of life in breast cancer survivors. J Clin Oncol 2007;25:2352-2359. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17557948.

281. Knols R, Aaronson NK, Uebelhart D, et al. Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. J Clin Oncol 2005;23:3830-3842. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15923576.

282. McNeely ML, Campbell KL, Rowe BH, et al. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 2006;175:34-41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16818906.

283. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Development of fatigue in cancer survivors: a prospective follow-up study from diagnosis into the year after treatment. J Pain Symptom Manage 2013;45:213-222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22926087.

284. Cantarero-Villanueva I, Fernandez-Lao C, Cuesta-Vargas AI, et al. The effectiveness of a deep water aquatic exercise program in cancer-related fatigue in breast cancer survivors: a randomized controlled trial. Arch Phys Med Rehabil 2013;94:221-230. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23017985.

285. Galiano-Castillo N, Cantarero-Villanueva I, Fernandez-Lao C, et al. Telehealth system: A randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. Cancer 2016;122:3166-3174. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27332968.

286. Kampshoff CS, Chinapaw MJ, Brug J, et al. Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study. BMC Med 2015;13:275. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26515383.

287. Hagstrom AD, Marshall PW, Lonsdale C, et al. Resistance training improves fatigue and quality of life in previously sedentary breast cancer survivors: a randomised controlled trial. Eur J Cancer Care (Engl) 2016;25:784-794. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26593858.

288. Cuesta-Vargas AI, Buchan J, Arroyo-Morales M. A multimodal physiotherapy programme plus deep water running for improving cancer-related fatigue and quality of life in breast cancer survivors. Eur J Cancer Care (Engl) 2014;23:15-21. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23947581.

289. Furzer BJ, Ackland TR, Wallman KE, et al. A randomised controlled trial comparing the effects of a 12-week supervised exercise versus usual

care on outcomes in haematological cancer patients. Support Care Cancer 2016;24:1697-1707. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26423617.

290. Rogers LQ, Courneya KS, Oster RA, et al. Physical activity and sleep quality in breast cancer survivors: a randomized trial. Med Sci Sports Exerc 2017;49:2009-2015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28538261.

291. Liu L, He X, Feng L. Exercise on quality of life and cancer-related fatigue for lymphoma survivors: a systematic review and meta-analysis. Support Care Cancer 2019;27:4069-4082. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31300873.

292. Brown JC, Huedo-Medina TB, Pescatello LS, et al. Efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2011;20:123-133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21051654.

293. Fuller JT, Hartland MC, Maloney LT, Davison K. Therapeutic effects of aerobic and resistance exercises for cancer survivors: a systematic review of meta-analyses of clinical trials. Br J Sports Med 2018;52:1311. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29549149.

294. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity for women with breast cancer after adjuvant therapy. Cochrane Database Syst Rev 2018;1:CD011292. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29376559.

295. Meneses-Echavez JF, Gonzalez-Jimenez E, Ramirez-Velez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC Cancer 2015;15:77. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25885168.

296. Stan DL, Croghan KA, Croghan IT, et al. Randomized pilot trial of yoga versus strengthening exercises in breast cancer survivors with cancer-related fatigue. Support Care Cancer 2016;24:4005-4015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27129840.

297. Ni X, Chan RJ, Yates P, et al. The effects of Tai Chi on quality of life of cancer survivors: a systematic review and meta-analysis. Support Care Cancer 2019;27:3701-3716. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31236699.

298. Yang L, Winters-Stone K, Rana B, et al. Tai Chi for cancer survivors: A systematic review toward consensus-based guidelines. Cancer Med 2021;10:7447-7456. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34533284.

299. Cheung DST, Takemura N, Smith R, et al. Effect of qigong for sleep disturbance-related symptom clusters in cancer: A systematic review and meta-analysis. Sleep Med 2021;85:108-122. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34303913.

300. Ren T, Rong S, Wang H, et al. Effect of chinese traditional wushu on cancer-related fatigue, sleep quality and upper limb dysfunction of breast cancer survivors: A systematic review and meta-analysis. Biomed Res Int 2022;2022:6879566. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35342756.

301. Dolbeault S, Cayrou S, Bredart 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19039808.

302. Fillion L, Gagnon P, Leblond F, et al. A brief intervention for fatigue management in breast cancer survivors. Cancer Nurs 2008;31:145-159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18490891.

303. Hoffman CJ, Ersser SJ, Hopkinson JB, et al. 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. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22430268.

304. 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. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21506018.

305. Soares A, Biasoli I, Scheliga A, et al. Association of social network and social support with health-related quality of life and fatigue in long-term survivors of Hodgkin lymphoma. Support Care Cancer 2013;21:2153-2159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23475196.

306. Garssen B, Boomsma MF, Meezenbroek Ede J, et al. Stress management training for breast cancer surgery patients. Psychooncology 2013;22:572-580. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22383279.

307. Reif K, de Vries U, Petermann F, Gorres S. A patient education program is effective in reducing cancer-related fatigue: a multi-centre randomised two-group waiting-list controlled intervention trial. Eur J Oncol Nurs 2013;17:204-213. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22898654.

308. Wangnum K, Thanarojanawanich T, Chinwatanachai K, et al. Impact of the multidisciplinary education program in self-care on fatigue in lung cancer patients receiving chemotherapy. J Med Assoc Thai 2013;96:1601-1608. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24511726.

309. Willems RA, Bolman CA, Mesters I, et al. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: Randomized controlled trial. Psychooncology 2017;26:222-230. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26988800.

310. Ferguson RJ, Sigmon ST, Pritchard AJ, et al. A randomized trial of videoconference-delivered cognitive behavioral therapy for survivors of breast cancer with self-reported cognitive dysfunction. Cancer 2016;122:1782-1791. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27135464.

311. Lengacher CA, Reich RR, Paterson CL, et al. Examination of broad symptom improvement resulting from mindfulness-based stress reduction in breast cancer survivors: A randomized controlled trial. J Clin Oncol 2016;34:2827-2834. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27247219.

312. Carlson LE, Tamagawa R, Stephen J, et al. Randomized-controlled trial of mindfulness-based cancer recovery versus supportive expressive group therapy among distressed breast cancer survivors (MINDSET): long-term follow-up results. Psychooncology 2016;25:750-759. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27193737.

313. Bower JE, Crosswell AD, Stanton AL, et al. Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. Cancer 2015;121:1231-1240. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25537522.

314. Johns SA, Brown LF, Beck-Coon K, et al. Randomized controlled pilot study of mindfulness-based stress reduction for persistently fatigued cancer survivors. Psychooncology 2015;24:885-893. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25132206.

315. Van Gessel LD, Abrahams HJG, Prinsen H, et al. Are the effects of cognitive behavior therapy for severe fatigue in cancer survivors sustained up to 14 years after therapy? J Cancer Surviv 2018;12:519-527. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29651784.

316. Smith SK, MacDermott K, Amarasekara S, et al. Reimagine: a randomized controlled trial of an online, symptom self-management curriculum among breast cancer survivors. Support Care Cancer 2019;27:1775-1781. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30146666.

317. Page MS, Berger AM, Johnson LB. Putting evidence into practice: evidence-based interventions for sleep-wake disturbances. Clin J Oncol Nurs 2006;10:753-767. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17193942.

318. Davidson JR, Waisberg JL, Brundage MD, MacLean AW. Nonpharmacologic group treatment of insomnia: a preliminary study with cancer survivors. Psychooncology 2001;10:389-397. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11536417.

319. Quesnel C, Savard J, Simard S, et al. Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. J Consult Clin Psychol 2003;71:189-200. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12602439.

320. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. J Clin Oncol 2005;23:6083-6096. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16135475.

321. Heckler CE, Garland SN, Peoples AR, et al. Cognitive behavioral therapy for insomnia, but not armodafinil, improves fatigue in cancer survivors with insomnia: a randomized placebo-controlled trial. Support Care Cancer 2016;24:2059-2066. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26542272.

322. Irwin MR, Olmstead R, Carrillo C, et al. Tai chi chih compared with cognitive behavioral therapy for the treatment of insomnia in survivors of breast cancer: a randomized, partially blinded, noninferiority trial. J Clin Oncol 2017;35:2656-2665. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28489508.

323. Dirksen SR, Epstein DR. Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. J Adv Nurs 2008;61:664-675. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18302607.

324. Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. Oncol Nurs Forum 2007;34:E51-59. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17878117.

325. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. J Clin Oncol 2008;26:4651-4658. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18591549.

326. Morgenthaler T, Kramer M, Alessi C, et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An american academy of sleep medicine report. Sleep 2006;29:1415-1419. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17162987.

327. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med 2008;4:487-504. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18853708.

328. Ozdemir U, Tasci S. Acupressure for cancer-related fatigue in elderly cancer patients: A randomized controlled study. Altern Ther Health Med 2023;29:57-65. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33891570.

329. Utli H, Dinc M, Utli MDA. The effect of acupressure or reiki interventions on the levels of pain and fatigue of cancer patients receiving palliative care: A randomized controlled study. Explore (NY) 2023;19:91-99. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36476354.

330. Lyman GH, Bohlke K, Cohen L. Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO Clinical Practice Guideline summary. J Oncol Pract 2018;14:495-499. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30096271.

331. Redd WH, Valdimarsdottir H, Wu LM, et al. Systematic light exposure in the treatment of cancer-related fatigue: a preliminary study. Psychooncology 2014;23:1431-1434. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24798589.

332. Wu LM, Amidi A, Valdimarsdottir H, et al. The effect of systematic light exposure on sleep in a mixed group of fatigued cancer survivors. J Clin Sleep Med 2018;14:31-39. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29198295.

333. Johnson JA, Garland SN, Carlson LE, et al. Bright light therapy improves cancer-related fatigue in cancer survivors: a randomized controlled trial. J Cancer Surviv 2018;12:206-215. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29127575.

334. Hanna A, Sledge G, Mayer ML, et al. A phase II study of methylphenidate for the treatment of fatigue. Support Care Cancer 2006;14:210-215. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16096772.

335. Lower EE, Fleishman S, Cooper A, et al. Efficacy of dexmethylphenidate for the treatment of fatigue after cancer chemotherapy: a randomized clinical trial. J Pain Symptom Manage 2009;38:650-662. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19896571.

336. Morrow GR, Gillies LJ, Hickok JT, et al. The positive effect of the psychostimulant modafinil on fatigue from cancer that persists after treatment is completed [abstract]. J Clin Oncol 2005;23(Suppl 16):Abstract 8012. Available at: https://ascopubs.org/doi/10.1200/jco.2005.23.16_suppl.8012.

337. Kaleita TA, Wellisch DK, Graham CA, et al. Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors [abstract]. J Clin Oncol 2006;24:Abstract 1503. Available at: https://ascopubs.org/doi/10.1200/jco.2006.24.18_suppl.1503.

338. Spathis A, Fife 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24778393.

339. Zhou ES, Hall KT, Michaud AL, et al. Open-label placebo reduces fatigue in cancer survivors: a randomized trial. Support Care Cancer 2019;27:2179-2187. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30298411.

340. Guglielmo M, Di Pede P, Alfieri S, et al. A randomized, double-blind, placebo controlled, phase II study to evaluate the efficacy of ginseng in reducing fatigue in patients treated for head and neck cancer. J Cancer Res Clin Oncol 2020;146:2479-2487. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32617701.

341. Yennurajalingam S, Bruera E. Palliative management of fatigue at the close of life: "it feels like my body is just worn out". JAMA 2007;297:295-304. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17227981.

342. Barsevick AM, Whitmer K, Walker L. In their own words: using the common sense model to analyze patient descriptions of cancer-related fatigue. Oncol Nurs Forum 2001;28:1363-1369. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11683307.

343. Krishnasamy M. Fatigue in advanced cancer -- meaning before measurement? Int J Nurs Stud 2000;37:401-414. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10785531.

344. Lundh Hagelin C, Seiger A, Furst CJ. Quality of life in terminal care--with special reference to age, gender and marital status. Support Care Cancer 2006;14:320-328. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16189646.

345. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer 2000;8:175-179. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10789956.

346. Walsh D, Rybicki L. Symptom clustering in advanced cancer. Support Care Cancer 2006;14:831-836. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16482450.

347. Given B, Given C, Azzouz F, Stommel M. Physical functioning of elderly cancer patients prior to diagnosis and following initial treatment. Nurs Res 2001;50:222-232. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11480531.

348. Mystakidou K, Parpa E, Katsouda E, et al. The role of physical and psychological symptoms in desire for death: a study of terminally ill cancer patients. Psychooncology 2006;15:355-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16184617.

349. Wolfe J, Grier HE, Klar N, et al. Symptoms and suffering at the end of life in children with cancer. N Engl J Med 2000;342:326-333. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10655532.

350. Wong RK, Franssen E, Szumacher E, et al. What do patients living with advanced cancer and their carers want to know? - a needs assessment. Support Care Cancer 2002;10:408-415. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12136224.

351. Miovic M, Block S. Psychiatric disorders in advanced cancer. Cancer 2007;110:1665-1676. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17847017.

352. Poort H, Peters M, Bleijenberg G, et al. Psychosocial interventions for fatigue during cancer treatment with palliative intent. Cochrane Database Syst Rev 2017;7:CD012030. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28708236.

353. Vira P, Samuel SR, Amaravadi SK, et al. Role of physiotherapy in hospice care of patients with advanced cancer: A systematic review. Am J Hosp Palliat Care 2021;38:503-511. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32829651.

354. Strong A, Karavatas G, Reicherter EA. Recommended exercise protocol to decrease cancer-related fatigue and muscle wasting in patients with multiple myeloma: an evidence-based systematic review. Topics in Geriatric Rehabilitation 2006;22:172-186. Available at: http://www.nursingcenter.com/lnc/journalarticle?Article_ID=647880.

355. Dittus KL, Gramling RE, Ades PA. Exercise interventions for individuals with advanced cancer: A systematic review. Prev Med 2017;104:124-132. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28716654.

356. Heywood R, McCarthy AL, Skinner TL. Efficacy of exercise interventions in patients with advanced cancer: A systematic review. Arch Phys Med Rehabil 2018;99:2595-2620. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29738745.

357. Chen YJ, Li XX, Ma HK, et al. Exercise training for improving patient-reported outcomes in patients with advanced-stage cancer: A systematic review and mta-analysis. J Pain Symptom Manage 2020;59:734-749.e710. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31546002.

358. Peddle-McIntyre CJ, Singh F, Thomas R, et al. Exercise training for advanced lung cancer. Cochrane Database Syst Rev 2019;2:CD012685. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30741408.

359. Oldervoll LM, Loge JH, Paltiel H, et al. The effect of a physical exercise program in palliative care: A phase II study. J Pain Symptom Manage 2006;31:421-430. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16716872.

360. Pyszora A, Budzynski J, Wojcik A, et al. Physiotherapy programme reduces fatigue in patients with advanced cancer receiving palliative care: randomized controlled trial. Support Care Cancer 2017;25:2899-2908. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28508278.

361. Porock D, Kristjanson LJ, Tinnelly K, et al. An exercise intervention for advanced cancer patients experiencing fatigue: a pilot study. J Palliat Care 2000;16:30-36. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11019505.

362. Sarhill N, Walsh D, Nelson KA, et al. Methylphenidate for fatigue in advanced cancer: a prospective open-label pilot study. Am J Hosp Palliat Care 2001;18:187-192. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11406895.

363. Bruera E, Driver L, Barnes EA, et al. Patient-controlled methylphenidate for the management of fatigue in patients with advanced cancer: a preliminary report. J Clin Oncol 2003;21:4439-4443. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14645434.

364. Bruera E, Valero V, Driver L, et al. Patient-controlled methylphenidate for cancer fatigue: a double-blind, randomized, placebo-controlled trial. J Clin Oncol 2006;24:2073-2078. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16648508.

365. Bruera E, Yennurajalingam S, Palmer JL, et al. Methylphenidate and/or a nursing telephone intervention for fatigue in patients with advanced cancer: a randomized, placebo-controlled, phase II trial. J Clin Oncol 2013;31:2421-2427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23690414.

366. Centeno C, Roji R, Portela MA, et al. Improved cancer-related fatigue in a randomised clinical trial: Methylphenidate no better than placebo. BMJ Support Palliat Care 2022;12:226-234. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33168668.

367. Auret KA, Schug SA, Bremner AP, Bulsara M. A randomized, double-blind, placebo-controlled trial assessing the impact of dexamphetamine on fatigue in patients with advanced cancer. J Pain Symptom Manage 2009;37:613-621. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18790598.

368. Peuckmann V, Elsner F, Krumm N, et al. Pharmacological treatments for fatigue associated with palliative care. Cochrane Database Syst Rev 2010:CD006788. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21069692.

369. Matsuo N, Morita T, Iwase S. Physician-reported corticosteroid therapy practices in certified palliative care units in Japan: a nationwide survey. J Palliat Med 2012;15:1011-1016; quiz 1117-1018. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22734663.

370. Matsuo N, Morita T, Iwase S. Efficacy and undesirable effects of corticosteroid therapy experienced by palliative care specialists in Japan: a nationwide survey. J Palliat Med 2011;14:840-845. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21631371.

371. Begley S, Rose K, O'Connor M. The use of corticosteroids in reducing cancer-related fatigue: assessing the evidence for clinical practice. Int J Palliat Nurs 2016;22:5-9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26804950.

372. Yennurajalingam S, Frisbee-Hume S, Palmer JL, 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23897970.

373. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25002731.

374. Yennurajalingam S, Lu Z, Rozman De Moraes A, et al. Meta-analysis of pharmacological, nutraceutical and phytopharmaceutical interventions for the treatment of cancer related fatigue. Cancers (Basel) 2023;15:91. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36612088.

375. Matsuo N, Morita T, Matsuda Y, et al. Predictors of responses to corticosteroids for cancer-related fatigue in advanced cancer patients: a multicenter, prospective, observational study. J Pain Symptom Manage 2016;52:64-72. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27233138.

376. Pascual Lopez A, Roque i Figuls M, Urrutia Cuchi G, et al. Systematic review of megestrol acetate in the treatment of anorexia-cachexia syndrome. J Pain Symptom Manage 2004;27:360-369. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15050664.

377. Minton O, Richardson A, Sharpe M, et al. A systematic review and meta-analysis of the pharmacological treatment of cancer-related fatigue. J Natl Cancer Inst 2008;100:1155-1166. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18695134.

378. Lund Rasmussen C, Klee Olsen M, Thit Johnsen A, et al. Effects of melatonin on physical fatigue and other symptoms in patients with advanced cancer receiving palliative care: A double-blind placebo-controlled crossover trial. Cancer 2015;121:3727-3736. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26178160.

379. Yennurajalingam S, Tannir NM, Williams JL, et al. A double-blind, randomized, placebo-controlled trial of Panax ginseng for cancer-related

fatigue in patients with advanced cancer. J Natl Compr Canc Netw 2017;15:1111-1120. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28874596.

380. Gong S, Sheng P, Jin H, et al. Effect of methylphenidate in patients with cancer-related fatigue: a systematic review and meta-analysis. PLoS One 2014;9:e84391. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24416225.

381. Borneman T, Piper BF, Sun VC, et al. Implementing the fatigue guidelines at one NCCN member institution: process and outcomes. J Natl Compr Canc Netw 2007;5:1092-1101. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18053431.

382. Piper BF, Borneman T, Sun VC, et al. Cancer-related fatigue: role of oncology nurses in translating National Comprehensive Cancer Network assessment guidelines into practice. Clin J Oncol Nurs 2008;12:37-47. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18842523.

383. Mystakidou K, Tsilika E, Parpa E, et al. Psychometric properties of the brief fatigue inventory in Greek patients with advanced cancer. J Pain Symptom Manage 2008;36:367-373. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18440770.

384. Baussard L, Stoebner-Delbarre A, Bonnabel L, et al. Development and validation of the daily fatigue cancer scale (DFCS): Single-item questions for clinical practice. Eur J Oncol Nurs 2017;26:42-48. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28069151.

385. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8433390.

386. Storey DJ, Waters RA, Hibberd CJ, et al. Clinically relevant fatigue in cancer outpatients: the Edinburgh Cancer Centre symptom study. Ann Oncol 2007;18:1861-1869. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17804467.

387. Knobel H, Loge JH, Brenne E, et al. The validity of EORTC QLQ-C30 fatigue scale in advanced cancer patients and cancer survivors. Palliat Med 2003;17:664-672. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14694917.

388. Weis J, Tomaszewski KA, Hammerlid E, et al. International psychometric validation of an EORTC quality of life module measuring cancer related fatigue (EORTC QLQ-FA12). J Natl Cancer Inst 2017;109. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28376231.

389. Weis J, Wirtz MA, Tomaszewski KA, et al. Sensitivity to change of the EORTC quality of life module measuring cancer-related fatigue (EORTC QlQ-Fa12): Results from the international psychometric validation. Psychooncology 2019;28:1753-1761. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31225669.

390. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res 1993;37:147-153. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8463991.

391. Loge JH, Abrahamsen AF, Ekeberg O, Kaasa S. Hodgkin's disease survivors more fatigued than the general population. J Clin Oncol 1999;17:253-261. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10458240.

392. Glaus A. Assessment of fatigue in cancer and non-cancer patients and in healthy individuals. Support Care Cancer 1993;1:305-315. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8156248.

393. Hann DM, Jacobsen PB, Azzarello LM, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. Qual Life Res 1998;7:301-310. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9610214.

394. Hann DM, Denniston MM, Baker F. Measurement of fatigue in cancer patients: further validation of the Fatigue Symptom Inventory. Qual Life Res 2000;9:847-854. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11297027.

395. Donovan KA, Jacobsen PB, Andrykowski MA, et al. Course of fatigue in women receiving chemotherapy and/or radiotherapy for early stage breast cancer. J Pain Symptom Manage 2004;28:373-380. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15471655.

396. Kumar N, Allen KA, Riccardi D, et al. Fatigue, weight gain, lethargy and amenorrhea in breast cancer patients on chemotherapy: is subclinical hypothyroidism the culprit? Breast Cancer Res Treat 2004;83:149-159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14997046.

397. Respini D, Jacobsen PB, Thors C, et al. The prevalence and correlates of fatigue in older cancer patients. Crit Rev Oncol Hematol 2003;47:273-279. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12962901.

398. Jacobsen PB, Garland LL, Booth-Jones M, et al. Relationship of hemoglobin levels to fatigue and cognitive functioning among cancer patients receiving chemotherapy. J Pain Symptom Manage 2004;28:7-18. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15223080.

399. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage 1997;13:63-74. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9095563.

400. Wratten C, Kilmurray J, Nash S, et al. Fatigue during breast radiotherapy and its relationship to biological factors. Int J Radiat Oncol Biol Phys 2004;59:160-167. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15093912.

401. Hwang SS, Chang VT, Rue M, Kasimis B. Multidimensional independent predictors of cancer-related fatigue. J Pain Symptom Manage 2003;26:604-614. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12850643.

402. Hwang SS, Chang VT, Cogswell J, Kasimis BS. Clinical relevance of fatigue levels in cancer patients at a Veterans Administration Medical Center. Cancer 2002;94:2481-2489. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12015774.

403. Kallich JD, Tchekmedyian NS, Damiano AM, et al. Psychological outcomes associated with anemia-related fatigue in cancer patients. Oncology (Williston Park) 2002;16:117-124. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12380961.

404. Smets EM, Garssen B, Bonke B, De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res 1995;39:315-325. Available at: https://www.ncbi.nlm.nih.gov/pubmed/7636775.

405. de Jong N, Candel MJ, Schouten HC, et al. Prevalence and course of fatigue in breast cancer patients receiving adjuvant chemotherapy. Ann Oncol 2004;15:896-905. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15151946.

406. de Jong N, Candel MJ, Schouten HC, et al. Course of mental fatigue and motivation in breast cancer patients receiving adjuvant chemotherapy. Ann Oncol 2005;16:372-382. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15677622.

407. Ahlberg K, Ekman T, Gaston-Johansson F. Levels of fatigue compared to levels of cytokines and hemoglobin during pelvic radiotherapy: a pilot study. Biol Res Nurs 2004;5:203-210. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14737921.

408. Ahlberg K, Ekman T, Gaston-Johansson F. The experience of fatigue, other symptoms and global quality of life during radiotherapy for uterine cancer. Int J Nurs Stud 2005;42:377-386. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15847900.

409. Smets EM, Visser MR, Willems-Groot AF, et al. Fatigue and radiotherapy: (A) experience in patients undergoing treatment. Br J Cancer 1998;78:899-906. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9764581.

410. Furst CJ, Ahsberg E. Dimensions of fatigue during radiotherapy. An application of the Multidimensional Fatigue Inventory. Support Care Cancer 2001;9:355-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11497389.

411. Holzner B, Kemmler G, Greil R, et al. The impact of hemoglobin levels on fatigue and quality of life in cancer patients. Ann Oncol 2002;13:965-973. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12123343.

412. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. Cancer Pract 1998;6:143-152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9652245.

413. Stein KD, Jacobsen PB, Blanchard CM, Thors C. Further validation of the multidimensional fatigue symptom inventory-short form. J Pain Symptom Manage 2004;27:14-23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14711465.

414. Mills PJ, Parker B, Dimsdale JE, et al. The relationship between fatigue and quality of life and inflammation during anthracycline-based chemotherapy in breast cancer. Biol Psychol 2005;69:85-96. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15740827.

415. Donovan KA, Stein KD, Lee M, et al. Systematic review of the multidimensional fatigue symptom inventory-short form. Support Care Cancer 2015;23:191-212. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25142703.

416. 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. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22933027.

417. Stover AM, Reeve BB, Piper BF, et al. Deriving clinically meaningful cut-scores for fatigue in a cohort of breast cancer survivors: a Health, Eating, Activity, and Lifestyle (HEAL) Study. Qual Life Res 2013;22:2279-2292. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23420495.

418. Can G, Durna Z, Aydiner A. Assessment of fatigue in and care needs of Turkish women with breast cancer. Cancer Nurs 2004;27:153-161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15253173.

419. Berger AM. Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. Oncol Nurs Forum 1998;25:51-62. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9460773.

420. Berger AM, Farr L. The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. Oncol Nurs Forum 1999;26:1663-1671. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10573683.

421. Piper BF, Dibble SL, Dodd MJ, et al. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. Oncol Nurs Forum 1998;25:677-684. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9599351.

422. Monga U, Kerrigan AJ, Thornby J, Monga TN. Prospective study of fatigue in localized prostate cancer patients undergoing radiotherapy. Radiat Oncol Investig 1999;7:178-185. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10406060.

423. Shun SC, Lai YH, Jing TT, et al. Fatigue patterns and correlates in male liver cancer patients receiving transcatheter hepatic arterial chemoembolization. Support Care Cancer 2005;13:311-317. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15611851.

424. Trask PC, Paterson AG, Esper P, et al. Longitudinal course of depression, fatigue, and quality of life in patients with high risk melanoma receiving adjuvant interferon. Psychooncology 2004;13:526-536. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15295774.

425. Abrahams HJG, Gielissen MFM, de Lugt M, et al. The Distress Thermometer for screening for severe fatigue in newly diagnosed breast and colorectal cancer patients. Psychooncology 2017;26:693-697. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27362532.

426. Leung YW, Brown C, Cosio AP, et al. Feasibility and diagnostic accuracy of the Patient-Reported Outcomes Measurement Information

System (PROMIS) item banks for routine surveillance of sleep and fatigue problems in ambulatory cancer care. Cancer 2016;122:2906-2917. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27351521.

427. Schwartz A, Meek P. Additional construct validity of the Schwartz Cancer Fatigue Scale. J Nurs Meas 1999;7:35-45. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10394773.

428. Shun SC, Beck SL, Pett MA, Richardson SJ. Assessing responsiveness of cancer-related fatigue instruments: distribution-based and individual anchor-based methods. Oncologist 2007;12:495-504. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17470692.

429. Schwartz AL. The Schwartz Cancer Fatigue Scale: testing reliability and validity. Oncol Nurs Forum 1998;25:711-717. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9599354.