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.[a]**

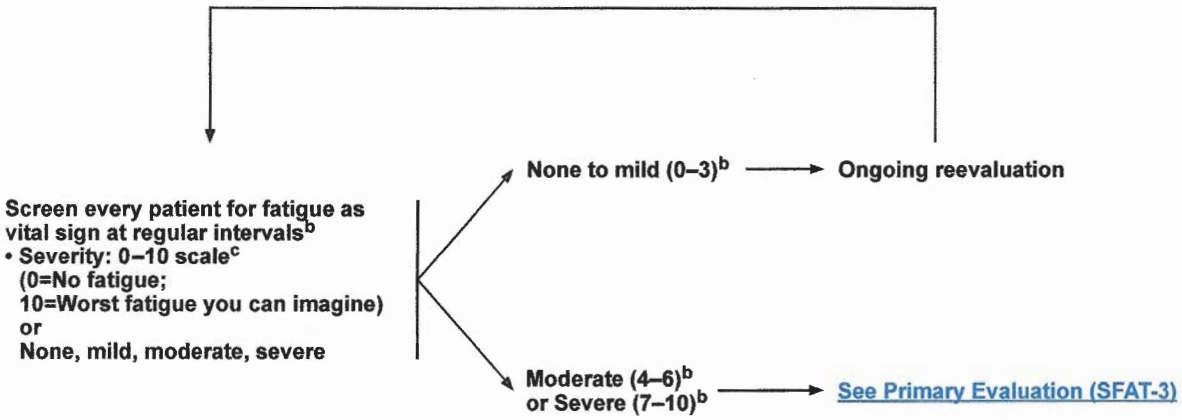
CONSIDERATIONS FOR FATIGUE IN CANCER SURVIVORS

- **Fatigue is a common complaint in individuals undergoing cancer therapy and can be a persistent problem for some cancer survivors in the months and years after cancer diagnosis.**
  - **Receipt of chemotherapy and radiation are both predisposing factors for cancer-related fatigue, but it can be seen in some patients who are treated with surgery alone.**
  - **The time-course of fatigue is unique to the survivor and his or her treatment plan, but some general principles apply. Mild to moderate fatigue is common in cancer survivors who undergo chemotherapy and/or radiation; mild to moderate fatigue lasting up to one year can occur in a proportion of cancer survivors.**
  - **Fatigue that initially presents months after the completion of adjuvant therapy or fatigue that worsens over this period warrants additional evaluation.**

[a]See the NCCN Guidelines for Cancer-Related 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.

SCREENING



[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, Wagner LI, Beaumont JL, et al. Use of a single-item screening tool to detect clinically significant fatigue, pain, distress, and anorexia in ambulatory cancer practice. J Pain Symptom Manage 2008;35:20-30.

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PRIMARY EVALUATION FATIGUE SCORE: MODERATE OR SEVERE (4–10)

EVALUATION

H&P:

- Focused fatigue history
  - Onset, pattern, duration
  - Change over time
  - Associated or alleviating factors
  - Interference with function
- Evaluate disease status
  - Evaluate risk of recurrence based on stage, pathologic factors, and treatment history
  - Perform review of systems to determine if other symptoms substantiate suspicion for recurrence
- Assessment of treatable contributing factors:
  - Comorbidities
    - ◊ Alcohol/substance abuse
    - ◊ Cardiac dysfunction
    - ◊ Endocrine dysfunction (eg, hypothyroidism, hypogonadism, adrenal insufficiency)
    - ◊ Gastrointestinal dysfunction
    - ◊ Hepatic dysfunction
    - ◊ Infection
    - ◊ Pulmonary dysfunction
    - ◊ Renal dysfunction
    - ◊ Anemia
    - ◊ Arthritis
  - Prescribed or OTC medications (eg, sleep aids, pain medications, antiemetics)
  - Emotional distress- screen for anxiety and depression (See SANXDE-1)
  - Sleep disturbance (eg, insomnia, sleep apnea, vasomotor symptoms, restless legs syndrome [RLS]) (See SSD-1)
  - Pain (See SPAIN-1)
  - Nutritional issues
    - ◊ Weight/caloric intake changes (See SNWM-1)
  - Deconditioning/loss of muscle mass

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Laboratory Evaluation:

- Consider performing laboratory evaluation based on presence of other symptoms, onset, and severity of fatigue
  - CBC with differential
    - ◊ Compare end-of-treatment hemoglobin/hematocrit with current values
    - ◊ Assess other cell lines (WBC and platelets)
  - Comprehensive metabolic panel
    - ◊ Assess electrolytes
    - ◊ Assess hepatic and renal function
  - Endocrine evaluation
    - ◊ TSH, especially in patients who have received prior head/neck, torso, or breast radiation
    - ◊ Consider more comprehensive evaluation or referral to specialist if other symptoms present
    - ◊ Cortisol stimulation test, if history of prolonged steroid use

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Other Diagnostic Testing:

- Consider radiologic assessment only if high risk of disease recurrence OR if accompanying signs and symptoms suggest presence of metastatic disease
- Consider cardiac testing (ECHO) for patients treated with an anthracycline (See SCARDIO-1), trastuzumab, bevacizumab, other VEGF- or HER2-targeted therapy, or other therapy known to cause cardiac dysfunction
- Chest x-ray and oxygen saturation testing for pulmonary complaints[d]

→ See Treatment of Contributing Factors (SFAT-4)

[d]Refer to a pulmonologist for pulmonary complaints.

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TREATMENT OF CONTRIBUTING FACTORS

- **Treat contributing factors:**
  - ***Medications/side effects***
  - **Pain** (See SPAIN-1)
  - **Emotional distress** (See SANXDE-1) **and** NCCN Guidelines for Distress Management
  - **Anemia**
    - ◊ **Treat iron, B_{12}, folate deficiency, if present**
    - ◊ **Consider referral/*further evaluation* for anemia or cytopenias**
  - **Sleep disturbance** (See SSD-1)
  - **Nutritional deficit/imbalance**
  - **Comorbidities**

→ See Interventions for Cancer Survivors (SFAT-5)

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INTERVENTIONS FOR CANCER SURVIVORS

Patient/Family Education and Counseling

Provide information about patterns of fatigue during and after treatment
- Self-monitoring of fatigue levels
- Energy conservation
  - Set priorities
  - Pace
  - Schedule activities at times of peak energy

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Physical Activity

- Maintain adequate levels of physical activity (category 1) (See SPA-1 and SPA-4)
- Survivors at higher risk of injury (eg, those living with neuropathy, cardiomyopathy, lymphedema, or other long-term effects of therapy or other comorbidities) should be referred to a physical therapist or exercise specialist
- Make use of local resources to help patients increase exercise (eg, aerobics, strength training, yoga)
  - Community exercise programs or classes, preferably those focused on cancer survivors
  - Exercise professional certified by the American College of Sports Medicine
  - For patients with fatigue interfering with function, consider referral to a physical therapist or physiatrist

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Other Interventions[e]

- Psychosocial interventions (category 1)
  - CBT[f]/Behavioral therapy (category 1)
  - Mindfulness-based stress reduction (category 1)
  - Psycho-educational therapies/Educational therapies (category 1)
  - Supportive expressive therapies (category 1)[g]
- Nutrition consultation
- CBT[f] for sleep (category 1) (See SSD-1)
  - Stimulus control
  - Sleep restriction
  - Sleep hygiene
- Acupuncture

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Pharmacologic[h]

Consider psychostimulants[i] (methylphenidate[j]) after ruling out other causes of fatigue and failure of other interventions

[e]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.
[f]A type of psychotherapy that focuses on recognizing and changing maladaptive thoughts and behaviors to reduce negative emotions and facilitate psychological adjustment.
[g]Supportive expressive therapies (such as support groups, counseling, and journal writing) facilitate expression of emotion and foster support from one or more people.
[h]Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients.
[i]Psychostimulants are at times used to treat cancer-related fatigue. A number of studies have evaluated their efficacy in the setting of active treatment and results have been mixed. There are extremely limited data regarding the use of these agents in the post-treatment setting.
[j]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 patients with cancer.

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