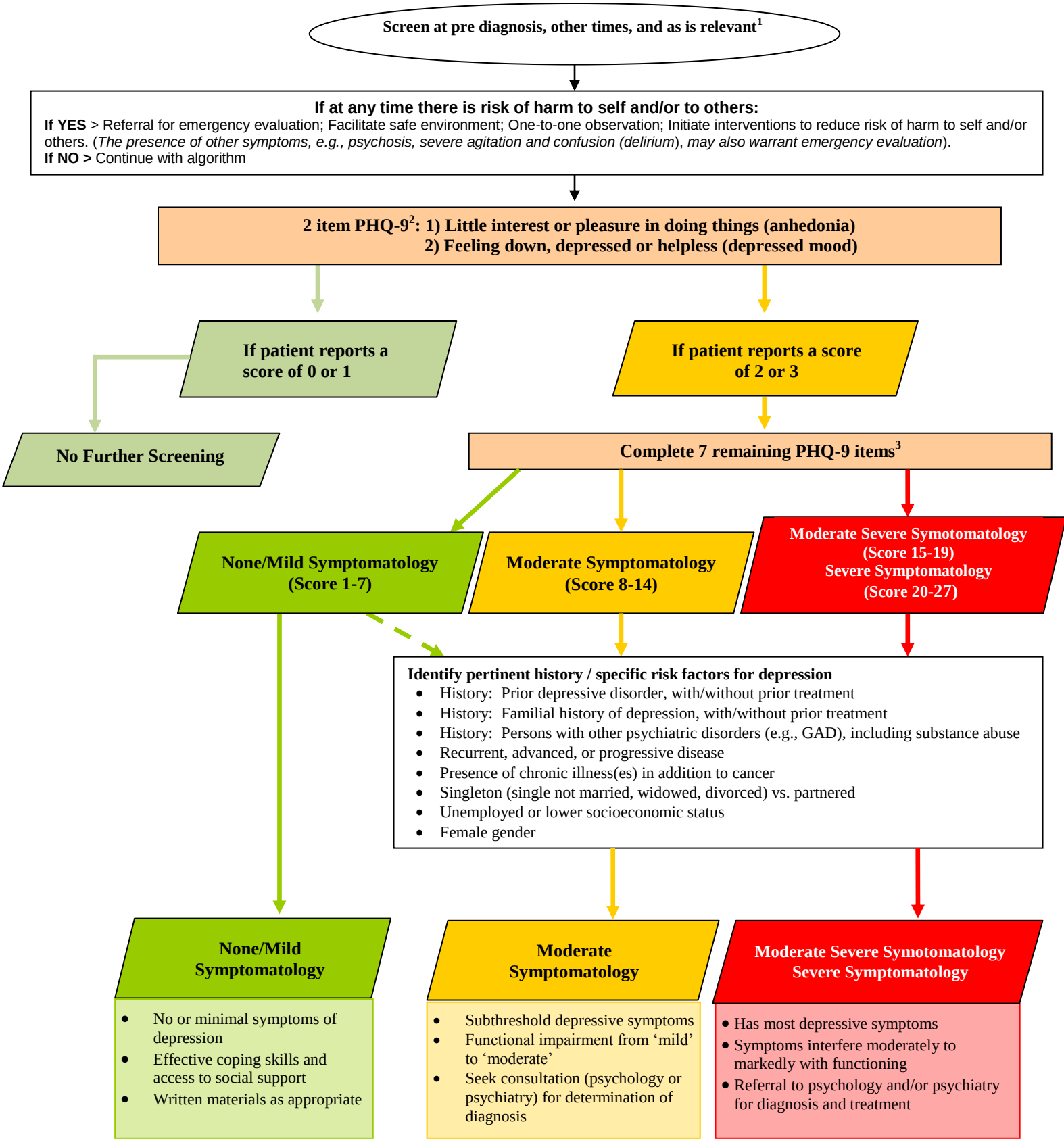
Data Supplement

American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline

Table of Contents

Screening and Assessment – Depression in Adults with Cancer



***In this algorithm the use of the word depression refers to the PHQ-9screening scale and not to a clinical diagnosis**

1. Initial diagnosis/start of treatment, regular intervals during treatment, 3, 6, and 12 months post treatment, diagnosis of at recurrence or progression, when approaching death and during times of personal transition or re-appraisal such as family crisis (CAPO guideline: "Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient" by Howell et al, 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2010).
2. Presence of symptom in the last two weeks, rated as follows: 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day.
3. Content of remaining 7 Items: sleep problems, low energy, appetite, low self view, concentration difficulties, motor retardation or agitation, and thoughts of self harm.

Note: Reference for PHQ-9 cutoff ≥8 is Thekkkumpurath et al., (2011). Screening for MDD in CA outpatients. *Cancer*.

Care Map – Depression in Adults with Cancer

None/Mild Symptoms

Care Pathway 1
Supportive Care and Prevention

- Offer referral to supportive care services

Moderate Symptoms

Care Pathway 2
Psychological (group) or Psychosocial

Intervention Options (low intensity)

- Individual guided self-help (or computerized) based on cognitive behavior therapy (CBT); including behavioral activation and problem solving)
- Group based CBT for depression
- Psychosocial interventions (group)
- Structured physical activity program
- Pharmacologic, as appropriate

Moderate Severe to Severe Symptoms

Care Pathway 3
Psychological (individual) and/or Psychiatric

Intervention Options (high intensity)

- Psychological (individual: CBT, Interpersonal Therapy)
- Pharmacologic
- Combined

Psychological (individual)

- Delivered by licensed mental health professionals using relevant treatment manuals which may include some or all of the following content: cognitive change, behavioral activation, biobehavioral strategies, education, and/or relaxation strategies.
- Relapse prevention additions are also important.
- Monitor for efficacy.
- Behavioral couples' therapy can be considered for people with a regular partner and where the relationship may contribute to the development or maintenance of depression.

Pharmacological

- Anti-depressants, with choice informed by side effect profiles, interactions, response, patient age and preference.
- Consider interventions with short term duration.
- Monitor regularly for adherence, side effects, and adverse events.

Psychosocial (group)

- Structured, professionally led, with topics such as: stress reduction, positive coping (seeking information, problem solving, assertive communication), enhancing social support from friends/family, coping with physical symptoms (e.g., fatigue, sexual dysfunction) and bodily changes, and health behavior change (diet, activity level, tobacco use).
- Consider for individual treatment should depressive symptoms not remit or worsen.

Supportive Care Services for All Patients, As Available and Appropriate

Provide education and information (verbal plus any relevant materials) for the patient and family about:

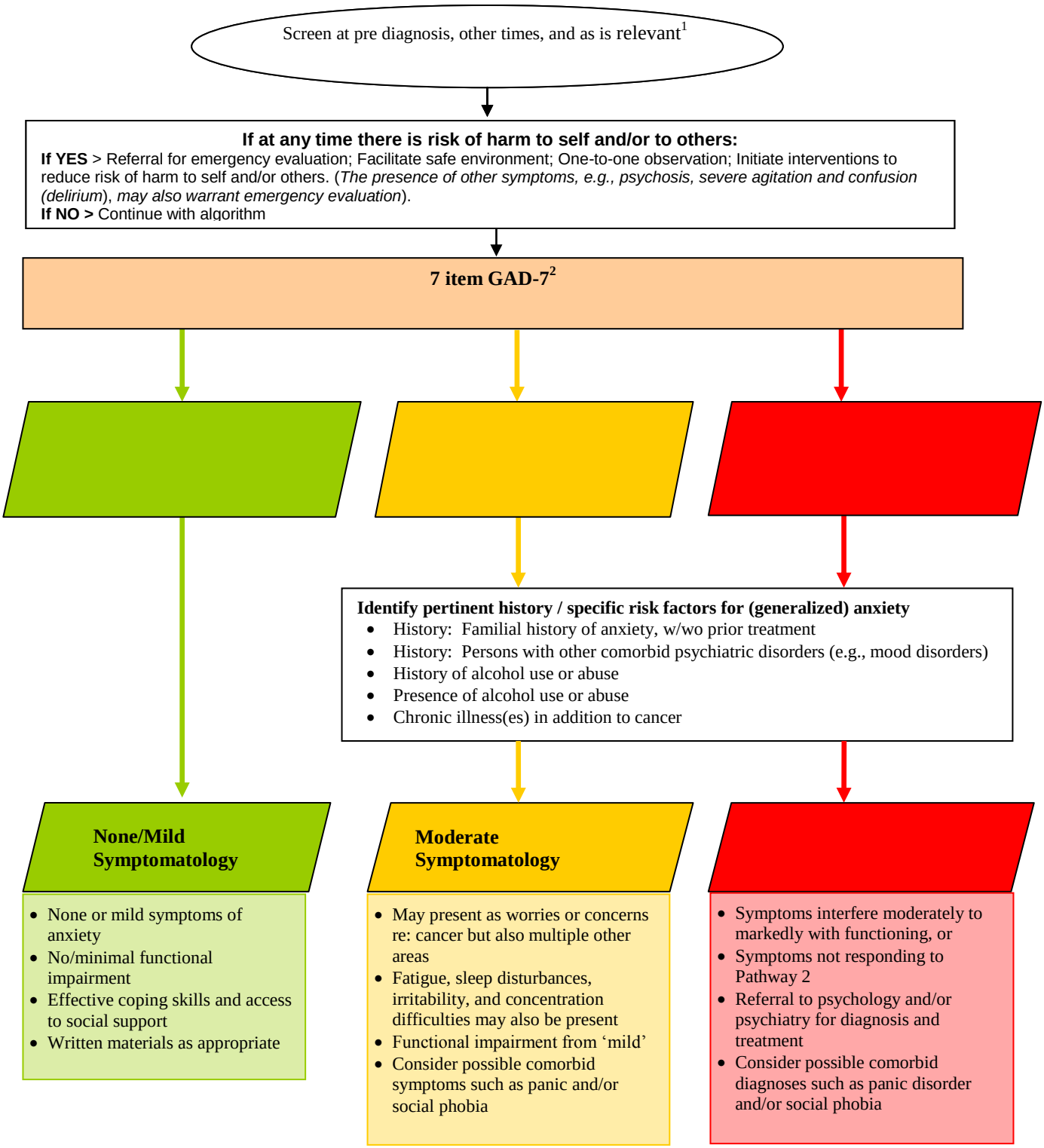
- Normalcy of stress in the context of cancer
- Specific stress reduction strategies (e.g., progressive muscle relaxation)
- Sources of informational support/resources (patient library, reliable internet sites)
- Availability of supportive care services (e.g., professionally led groups, informational lectures, volunteer organizations) for the patient and family at the institution or in the community
- Availability of financial support (e.g., accommodations, transportation, health/drug benefits)
- Information about signs and symptoms of depression if stress or distress worsen and avenues for care
- Information on sleep hygiene and self-management of fatigue
- Information on other non-pharmacological interventions (physical activity, nutrition)

Follow-up and ongoing re-assessment

It is common for persons with depressive symptoms to lack the motivation necessary to follow through on referrals and/or to comply with treatment recommendations. With this in mind, on a bi-weekly or monthly basis, until symptoms have remitted:

- Assess follow-through and compliance with individual or group psychological/psychosocial referrals, as well as satisfaction with these services.
- Assess compliance with pharmacologic treatment, patient's concerns about side effects, and satisfaction with the symptom relief..
- If compliance is poor, assess and construct a plan to circumvent obstacles to compliance, or discuss alternative interventions that present fewer obstacles.
- After 8 weeks of treatment, if symptom reduction and satisfaction with treatment are poor, despite good compliance, alter the treatment course (e.g., add a psychological or pharmacological intervention; change the specific medication; refer to individual psychotherapy if group therapy has not proved helpful).

Screening and Assessment – Anxiety in Adults with Cancer



***In this algorithm the use of the word anxiety refers to the GAD-7 scale and not to a clinical diagnosis of anxiety disorder(s).**

1. Initial diagnosis/start of treatment, regular intervals during treatment, 3, 6, and 12 months post treatment, diagnosis of at recurrence or progression, when approaching death and during times of personal transition or re-appraisal such as family crisis (CAPO guideline: "Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient" by Howell et al, 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2010).
2. Presence of symptom in the last two weeks, rated as follows: 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day. Content of items: feeling nervous, anxious, on edge; cannot stop/control worry; worry too much; trouble relaxing; restlessness; easily annoyed, irritable; and, feeling afraid. Final item regarding difficulty of the problems

Note: Reference for GAD-7 cutoffs is Spitzer, R.L. et al. (2006). A brief measure for assessing generalized anxiety disorder. *Arch Intern. Med*.

Care Map – Generalized Anxiety in Adults with Cancer

None/Mild Symptoms

Care Pathway 1

Supportive Care and Prevention

- Offer referral to supportive care services

Moderate Symptoms

Care Pathway 2

Psychological (group) or Psychosocial

Intervention Options (low intensity)

- Education and active monitoring
- Non facilitated or guided self-help (or computerized) based on cognitive behavior therapy (CBT; including behavioral activation and problem solving)
- Psychosocial interventions (group)
- Pharmacologic, as appropriate

Moderate Severe to Severe Symptoms

Care Pathway 3

Psychological (individual) and/or Psychiatric

Intervention Options (high intensity)

- Psychological (individual: CBT or applied relaxation)
- Pharmacologic
- Combined

Psychological (individual)

- Delivered by licensed mental health professionals using relevant treatment manuals which may include some or all of the following content: cognitive change, behavioral activation, biobehavioral strategies, education, and/or relaxation strategies.
- Relapse prevention additions are also important as GAD is most often chronic.
- Monitor for efficacy.

Pharmacological

- SSRIs or anxiolytics with choice informed by side effect profiles, interactions, response, patient age and preference.
- Consider interventions with short term duration.
- Monitor regularly for adherence, side effects, and adverse events.

Psychosocial (group)

- Structured, professionally led, with topics such as: stress reduction, positive coping (seeking information, problem solving, assertive communication), enhancing social support from friends/family, coping with physical symptoms (e.g., fatigue, sexual dysfunction) and bodily changes.
- Consider for care pathway 3 should anxiety symptoms not remit or worsen.

Supportive Care Services for All Patients, As Available and Appropriate

Provide education and information (verbal plus any relevant materials) for the patient and family about:

- Normalcy of stress and anxiety in the context of cancer
- Specific stress reduction strategies (e.g., progressive muscle relaxation)
- Sources of informational support/resources (patient library, reliable internet sites)
- Availability of supportive care services (e.g., professionally led groups, informational lectures, volunteer organizations) for the patient and family at the institution or in the community
- Availability of financial support (e.g., accommodations, transportation, health/drug benefits)
- Information about signs and symptoms of anxiety disorders and their treatment
- Information on sleep hygiene and self-management of fatigue
- Information on other non-pharmacological interventions (physical activity, nutrition)

Follow-up and ongoing re-assessment

As cautiousness and a tendency to avoid threatening stimuli are cardinal features of anxiety pathology, it is common for persons with symptoms of anxiety to not to follow through on potentially helpful referrals or treatment recommendations. With this in mind, on a monthly basis or until symptoms have subsided:

- Assess follow-through and compliance with individual or group psychological/ psychosocial referrals, as well as satisfaction with these services.
- Assess compliance with pharmacologic treatment, patient's concerns about side effects, and satisfaction with symptom relief.
- Consider tapering the patient from any antidepressant medications if anxiety symptoms are under control and if the primary environmental sources of anxiety are no longer present.
- If compliance is poor, assess and construct a plan to circumvent obstacles to compliance, or discuss alternative interventions that present fewer obstacles.
    - After 8 weeks of treatment, if symptom reduction and satisfaction with treatment are poor, despite good compliance, alter the treatment course (e.g., add a psychological or pharmacological intervention; change the specific medication; refer to individual psychotherapy if group therapy has not proved helpful).

Screening and Assessment – Fatigue in Cancer Survivors

Routinely screen for fatigue

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Use a numeric rating scale as clinically indicated and at least annually.

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Education and Counseling

- All patients should be offered specific education about fatigue following treatment (e.g. information about the difference between normal and cancer related fatigue, persistence of fatigue post treatment, and causes and contributing factors).All patients should be offered advice on general strategies that help manage fatigue (e.g., maintaining physical activity) and guidance on self-monitoring of fatigue levels.

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Comprehensive and Focused Assessment

(for patients who report moderate to severe fatigue)

History and Physical

1) Perform a focused fatigue history, including:
   - Onset, pattern, duration
   - Change over time
   - Associated or alleviating factors

2) Evaluate disease status by:
   - 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

3) Assess treatable contributing factors:
   - Comorbidities (e.g, cardiac dysfunction, endocrine dysfunction, pulmonary dysfunction, renal dysfunction, anemia, arthritis, neuromuscular complications, sleep disturbances, pain, emotional distress)
   - Medications (consider persistent use of sleep aids, pain medications, or antiemetics)
   - Alcohol/substance abuse
   - Nutritional Issues
     - Weight/caloric intake changes
   - Deconditioning

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

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
- Endocrinologic evaluation
  - TSH
  - Consider more comprehensive evaluation or referral to specialist if other symptoms present

Treatment and Care Map – Fatigue in Cancer Survivors

Treat Contributing Factors

Address all medical and substance-induced treatable contributing factors first (e.g., pain, depression, anxiety, emotional distress, sleep disturbance, nutrition deficit, activity level, anemia, medication side-effects, and comorbidities). See Table 2 for more details.

Interventions for Cancer-Related Fatigue

Some patients may also benefit from interventions described below to treat fatigue. Currently, there are no clear standards to select among these for an individual patient. Further research is needed to establish a strategy for prioritizing, sequencing, and linking the available options. If treated for fatigue, patients should be followed and re-evaluated on a regular basis to determine whether treatment is effective or needs to be reassessed.

Physical Activity

- Initiating/maintaining adequate levels of physical activity can reduce cancer-related fatigue in post-treatment survivors.
- Actively encourage all patients to engage in a moderate level of physical activity after cancer treatment (e.g., 150 minutes of moderate aerobic exercise (such as fast walking, cycling, or swimming) per week with an additional 2 to 3 strength training (such as weight lifting) sessions per week, unless contraindicated.
- Walking programs are generally safe for most cancer survivors; the American College of Sports Medicine recommends that cancer survivors can begin this type of program after consulting with their doctors, but without any formal exercise testing (such as a stress test).
- Survivors at higher risk of injury (e.g., those living with neuropathy, cardiomyopathy, or other long-term effects of therapy other than comorbidities) should be referred to a physical therapist of exercise specialist. Breast cancer survivors with lymphedema should also consider meeting with an exercise specialist before initiating upper body strength-training exercise.

Psychosocial Interventions

- Cognitive behavioral therapy/behavioral therapy can reduce fatigue in cancer survivors.
- Psycho-educational therapies/educational therapies can reduce fatigue in cancer survivors.
- Survivors should be referred to psychosocial service providers who specialize in cancer and are trained to deliver empirically-based interventions. Psychosocial resources that address fatigue may also be available through the National Cancer Institute (e.g., Moving Beyond Breast Cancer videos).

Mind-Body Interventions

- There is some evidence that the following interventions can reduce fatigue in cancer survivors:
  - Mindfulness-based approaches
  - Yoga
  - Acupuncture
- The following interventions may offer some benefit, however additional research, particularly in the post-treatment population, is needed:
  - Biofield therapies (touch therapy), massage, music therapy, relaxation, reiki, qigong

Pharmacologic Interventions

- Evidence suggests that psychostimulants (e.g., methylphenidate) and other wakefulness agents, eg., modafinil can be effectively used to manage fatigue in patients with advanced disease or those on active treatment. However, there is very limited evidence of their effectiveness in reducing fatigue in patients who are disease free following active treatment, outside of the treatment of obstructive sleep apnea.
- Small pilot studies have evaluated the impact of supplements, such as ginseng and vitamin D, for cancer-related fatigue. However, there is no consistent evidence of their effectiveness.

Ongoing Monitoring and Follow-up

Promote ongoing self-monitoring of fatigue levels as a late or long-term cancer or treatment problem in post-treatment survivors.

ASCO GUIDELINES

PREVENTION AND MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN SURVIVORS OF ADULT CANCERS: AMERICAN SOCIETY OF CLINICAL ONCOLOGY CLINICAL PRACTICE GUIDELINE		
Clinical Question	**Recommendation**	**Evidence Rating**
What are the optimum *prevention* approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?	There are no established agents recommended for the prevention of CIPN in cancer patients undergoing treatment with neurotoxic agents. This is based on the paucity of high-quality, consistent evidence and a balance of benefits versus harms.	Type: Evidence-based Harms outweigh benefits Evidence quality: Ranges from low to high Strength of Recommendation: Ranges from inconclusive to strong against
	Clinicians should not offer the following agents for the prevention of CIPN to cancer patients undergoing treatment with neurotoxic agents: • acetyl-L-carnitine (ALC) • amifostine • amitriptyline • CaMg for patients receiving oxaliplatin-based chemotherapy • diethyldithio-carbamate (DDTC) • glutathione (GSH) for patients receiving paclitaxel/carboplatin chemotherapy • nimodipine • Org 2766 • all-*trans* retinoic acid • rhuLIF • vitamin E	

PREVENTION AND MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN SURVIVORS OF ADULT CANCERS: AMERICAN SOCIETY OF CLINICAL ONCOLOGY CLINICAL PRACTICE GUIDELINE		
Clinical Question	**Recommendation**	**Evidence Rating**
Continued, **What are the optimum *prevention* approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?**	Venlafaxine is not recommended for routine use in clinical practice. While the venlafaxine data supports its potential utility, the data were not strong enough to recommend its use in clinical practice, until additional supporting data become available.	Type: Evidence-based Balance of benefits and harms Evidence quality: Intermediate Strength of Recommendation: Inconclusive
	No recommendations can be made on the use of N-acetylcysteine, carbamazepine, glutamate, glutathione for patients receiving cisplatin or oxaliplatin-based chemotherapy, goshajinkigan (GJG), omega-3 fatty acids, or oxycarbazepine for the prevention of CIPN at this time.	Type: Evidence-based Balance of benefits and harms Evidence quality: Low Strength of recommendation: Inconclusive
What are the optimum *treatment* approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?	For cancer patients experiencing CIPN, clinicians may offer duloxetine.	Type: Evidence-based Benefits outweigh harms Evidence quality: Intermediate Strength of Recommendation: Moderate
	No recommendations can be made on the use of acetyl-L-carnitine, noting that a positive phase III abstract supported its value, but this work has not yet been published in a peer-reviewed journal and a prevention trial suggested that this agent was associated with worse outcomes.	Type: Evidence-based Harms outweigh benefits Evidence quality: Low Strength of Recommendation: Inconclusive

PREVENTION AND MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN SURVIVORS OF ADULT CANCERS: AMERICAN SOCIETY OF CLINICAL ONCOLOGY CLINICAL PRACTICE GUIDELINE		
Clinical Question	**Recommendation**	**Evidence Rating**
Continued, **What are the optimum *treatment* approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?**	No recommendations can be made on the use of tricyclic antidepressants. However, based on the limited options that are available for this prominent clinical problem and the demonstrated efficacy of these drugs for other neuropathic pain conditions, it is reasonable to try a tricyclic antidepressant (e.g., nortriptyline or desipramine) in patients suffering from CIPN following a discussion with the patients about the limited scientific evidence for CIPN, potential harms, benefits, cost, and patient preferences.	Type: Evidence-based Balance of benefits and harms Evidence quality: Intermediate Strength of Recommendation: Inconclusive
	No recommendations can be made on the use of gabapentin, noting that the available data were limited regarding its efficacy for treating CIPN. However, the panel felt that this agent is reasonable to try for selected patients with CIPN pain given that only a single negative randomized trial for this agent was completed, given the established efficacy of gabapentin and pregabalin for other forms of neuropathic pain, and given the limited CIPN treatment options. Patients should be informed about the limited scientific evidence for CIPN, potential harms, benefits, and costs.	Type: Evidence-based Balance of benefits and harms Evidence quality: Intermediate Strength of Recommendation: Inconclusive

PREVENTION AND MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN SURVIVORS OF ADULT CANCERS: AMERICAN SOCIETY OF CLINICAL ONCOLOGY CLINICAL PRACTICE GUIDELINE		
Clinical Question	**Recommendation**	**Evidence Rating**
	No recommendations can be made on the use of a topical gel treatment containing baclofen (10 mg), amitriptyline HCL (40 mg), and ketamine (20 mg), noting that a single trial supported that this product did decrease CIPN symptoms. Given the available data, the panel felt that this agent is reasonable to try for selected patients with CIPN pain. Patients should be informed about the limited scientific evidence for the treatment of CIPN, potential harms, benefits, and costs.	Type: Evidence-based Benefits outweigh harms Evidence quality: Intermediate Strength of Recommendation: Inconclusive

