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ASCO SPECIAL ARTICLE

Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation

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Editor's note: This American Society of Clinical Oncology Clinical Practice Guideline provides recommendations, with review and analysis of the relevant literature for each recommendation. Additional information, which may include data supplements, slide sets, patient versions, frequently asked questions, and clinical tools and resources, is available at www.asco.org/adaptations/fatigue.

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A B S T R A C T

Purpose

This guideline presents screening, assessment, and treatment approaches for the management of adult cancer survivors who are experiencing symptoms of fatigue after completion of primary treatment.

Methods

A systematic search of clinical practice guideline databases, guideline developer Web sites, and published health literature identified the pan-Canadian guideline on screening, assessment, and care of cancer-related fatigue in adults with cancer, the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines In Oncology (NCCN Guidelines) for Cancer-Related Fatigue and the NCCN Guidelines for Survivorship. These three guidelines were appraised and selected for adaptation.

Results

It is recommended that all patients with cancer be evaluated for the presence of fatigue after completion of primary treatment and be offered specific information and strategies for fatigue management. For those who report moderate to severe fatigue, comprehensive assessment should be conducted, and medical and treatable contributing factors should be addressed. In terms of treatment strategies, evidence indicates that physical activity interventions, psychosocial interventions, and mind-body interventions may reduce cancer-related fatigue in post-treatment patients. There is limited evidence for use of psychostimulants in the management of fatigue in patients who are disease free after active treatment.

Conclusion

Fatigue is prevalent in cancer survivors and often causes significant disruption in functioning and quality of life. Regular screening, assessment, and education and appropriate treatment of fatigue are important in managing this distressing symptom. Given the multiple factors contributing to post-treatment fatigue, interventions should be tailored to each patient's specific needs. In particular, a number of nonpharmacologic treatment approaches have demonstrated efficacy in cancer survivors.

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INTRODUCTION

Recent advances in cancer screening and treatment have resulted in an expanding number of cancer survivors. The American Cancer Society estimates that as of January 2012, there were 13.7 million cancer survivors in the United States, and this number is estimated to rise to nearly 18 million by 2022.[1] The American Society of Clinical Oncology (ASCO) has taken steps to address the recommendations made by the Institute of Medicine (IOM)[2] to promote evidence-based, comprehensive, compassionate, and coordinated survivorship care.[3-5] More specifically, the ASCO Cancer Survivorship Committee has mobilized to address recommendation three of the IOM, which calls for the "use of systematically developed evidence-based clinical practice guidelines, assessment tools, and screening instruments to help identify and manage late effects of cancer and its treatment. Existing guidelines should be refined and new evidence-based guidelines should be developed through public-and private-sector efforts."[2(p155)] This guideline addresses one of a series of topics that have been identified and prioritized for development in cancer survivorship.

A majority of patients will experience some level of fatigue during their course of treatment; however, approximately 30% of patients will endure

THE BOTTOM LINE

GUIDELINE QUESTION

What are the screening, assessment, and treatment approaches to the management of adult cancer survivors who are experiencing symptoms of fatigue after completion of primary treatment?

Target Population

- This practice guideline pertains to cancer survivors diagnosed at age ≥ 18 years who have completed primary cancer treatment with curative intent and are in clinical remission off therapy as well as patients who are disease free and have transitioned to maintenance or adjuvant therapy (eg, patients with breast cancer receiving hormonal therapy, patients with chronic myelogenous leukemia receiving tyrosine kinase inhibitors).

Target Audience

- This guidance is intended to inform health care professionals (eg, medical, surgical, and radiation oncologists, psychosocial and rehabilitation professionals, primary care providers, nurses, and others involved in the delivery of care for survivors) as well as patients, family members, and caregivers of patients who have survived cancer.

Recommendations

Screening

- All health care providers should routinely screen for the presence of fatigue from the point of diagnosis onward, including after completion of primary treatment.
- All patients should be screened for fatigue as clinically indicated and at least annually.
- Screening should be performed and documented using a quantitative or semiquantitative assessment.

Comprehensive and Focused Assessment

History and Physical

- Perform a focused fatigue history
- Evaluate disease status
- Assess treatable contributing factors.
- As a shared responsibility, the clinical team must decide when referral to an appropriately trained professional (eg, cardiologist, endocrinologist, mental health professional, internist, and so on) is needed.

Laboratory Evaluation

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

Treatment and Care Options

Education and Counseling

- All patients should be offered specific education about fatigue after treatment (eg, information about the difference between normal and cancer-related fatigue, persistence of fatigue after treatment, and causes and contributing factors).
- Patients should be offered advice on general strategies that help manage fatigue.
- If treated for fatigue, patients should be observed and re-evaluated on a regular basis to determine whether treatment is effective or needs to be reassessed.

Contributing Factors

- Address all medical and treatable contributing factors first (eg, pain, depression, anxiety, emotional distress, sleep disturbance, nutritional deficit, activity level, anemia, medication adverse effects, and comorbidities).

Physical Activity

- Initiating/maintaining adequate levels of physical activity can reduce cancer-related fatigue in post-treatment survivors.

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THE BOTTOM LINE (CONTINUED)

- Actively encourage all patients to engage in a moderate level of physical activity after cancer treatment (eg, 150 minutes of moderate aerobic exercise [such as fast walking, cycling, or swimming] per week with an additional two to three 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 physicians but without any formal exercise testing (such as a stress test).
- Survivors at higher risk of injury (eg, those living with neuropathy, cardiomyopathy, or other long-term effects of therapy) and patients with severe fatigue interfering with function should be referred to a physical therapist or exercise specialist. Breast cancer survivors with lymphedema should also consider meeting with an exercise specialist before initiating upper-body strength training.

Psychosocial Interventions

- Cognitive behavioral therapy/behavioral therapy can reduce cancer-related fatigue in post-treatment survivors.
- Psychoeducational therapies/educational therapies can reduce cancer-related fatigue in post-treatment 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 and other organizations.

Mind-Body Interventions

- There is some evidence that mindfulness-based approaches, yoga, and acupuncture can reduce fatigue in cancer survivors.
- Additional research, particularly in the post-treatment population, is needed for biofield therapies (touch therapy), massage, music therapy, relaxation, reiki, and qigong.
- Survivors should be referred to practitioners who specialize in cancer and who use protocols that have been empirically validated in cancer survivors.

Pharmacologic Interventions

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

persistent fatigue for a number of years after treatment.[6,7] Fatigue is one the most prevalent and distressing long-term effects of cancer treatment, significantly affecting patients' quality of life.[6] The objective of this guideline is to identify evidence-based clinical practice guidelines, assessment tools, and screening instruments to help health care professionals care for survivors of adult-onset cancers who are experiencing symptoms of fatigue after completion of primary treatment.

ASCO has established a process for adapting other organizations' clinical practice guidelines. This article summarizes the results of that process and presents the adapted practice recommendations.

The clinical question of focus is: What are the optimal screening, assessment, and treatment approaches in the management of adult cancer survivors who are experiencing symptoms of fatigue after completion of primary treatment? This practice guideline pertains to cancer survivors diagnosed at age $\geq$ 18 years who have completed primary cancer treatment with curative intent and are in clinical remission off therapy as well as patients who are disease free and have transitioned to maintenance or prophylactic therapy (eg, patients with breast cancer receiving hormonal therapy, patients with chronic myelogenous leukemia receiving tyrosine kinase inhibitors). This guidance is intended to inform professional health care providers (eg, medical, surgical, and radiation oncologists, psychosocial and rehabilitation professionals, primary care providers, nurses, and others involved in the delivery of care for survivors) as well as patients, family members, and caregivers of patients who have survived cancer.

METHODS

This guideline adaptation was informed by the ADAPTE methodology,[8] which was used as an alternative to de novo guideline development for this guideline. Adaptation of guidelines is considered by ASCO in selected circumstances, when one or more quality guidelines from other organizations already exist on the same topic. The objective of the ADAPTE process (http://www.adapte.org/) is to take advantage of existing guidelines to enhance efficient production, reduce duplication, and promote the local uptake of quality guideline recommendations.

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

Disclaimer

The information contained in this article, including but not limited to clinical practice guidelines and other guidance, is based on the best available evidence at the time of creation and is provided by ASCO to assist providers in clinical decision making. The information should not be relied on as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified herein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular product or course of medical treatment. Furthermore, the information is not intended to substitute for the independent professional judgment of the treating provider, because the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like must, must not, should, and should not indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an as is basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

Guideline and Conflicts of Interest

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

RESULTS

GUIDELINE SEARCH AND ASCO PANEL CONTENT REVIEW

As mentioned, the adaptation process starts with a literature search to identify candidate guidelines for adaptation on a given topic. The systematic search of clinical practice guideline databases, guideline developer Web sites, and published health literature was conducted to identify clinical practice guidelines, systematic reviews, meta-analyses, and other guidance documents addressing the screening, assessment, and care of cancer-related fatigue (see the Data Supplement on www.asco.org/guidelines for details of the search). On the basis of content review of the search yield, the ad hoc panel selected the pan-Canadian guideline on fatigue published in 2011,[9] which is informed by recommendations from the Oncology Nursing Society[10] and National Comprehensive Cancer Network (NCCN).[11] The panel also considered two NCCN Guidelines[12,13] that had been created or updated since 2009. These guidelines were selected because they were comprehensive and recently developed by multidisciplinary panels of experts.

Overview of Pan-Canadian and NCCN Guidelines

Clinical questions and target populations. The pan-Canadian guideline[9] describes assessment after screening and effective interventions for management of fatigue in adults with cancer who are identified as experiencing symptoms of fatigue or tiredness using the Edmonton Symptom Assessment System (ESAS; further information on ESAS can be found in pan-Canadian guideline[9]). This practice guideline pertains to adults with cancer at any phase of the cancer continuum, regardless of cancer type, disease stage, or treatment modality. This practice guideline is intended to inform Canadian health authorities, program leaders, and administrators as well as health care professionals who provide care to adults with cancer. The guideline is interprofessional in focus, and the recommendations are applicable to direct-care providers (eg, nurses, social workers, family practitioners) in diverse care settings.

The NCCN Guideline for Cancer-Related Fatigue[12] describes procedures for the assessment and management of fatigue in patients with cancer. The target population includes children, adolescents, and adults, and the guideline is intended to provide guidance for health care professionals as they implement it in their respective institutions and clinical practice. The NCCN Guideline for Survivorship[13] consists of screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment. The target population for this guideline is survivors who have completed treatment and are in clinical remission. It is intended for health care professionals who work with survivors of adult-onset cancer in the post-treatment period.

Summary of development methodology and key evidence of pan-Canadian and NCCN guidelines. The pan-Canadian guideline[9] used systematic methods to search for evidence and clearly describes the strengths and limitations of the body of evidence and the methods used for formulating recommendations. The NCCN guidelines[12,13]

represent a consensus of experts; they are based on evidence, well respected, and widely used, and as such, they were included as supplementary evidence. All three guidelines offer comprehensive and user-friendly algorithms helpful in informing screening, assessment, and treatment options.

ASCO METHODOLOGIC REVIEW

From the identified guidelines and reviews, the pan-Canadian guideline on screening, assessment, and care of cancer-related fatigue in adults with cancer[9] was singled out and underwent an expedited review by two content experts, who suggested that the guideline be accepted with modifications. After a second review, the ASCO panel suggested that the more recent NCCN Guideline for Cancer-Related Fatigue[12] and NCCN Guideline for Survivorship[13] also be included in the adaptation. A methodologic review of the three guidelines was completed by two ASCO staff members using the Rigour of Development subscale of the AGREE II (Appraisal of Guidelines for Research and Evaluation II) instrument[14] (www.agreecollaboration.org). The Rigour of Development subscale consists of seven items that assess the quality of processes used to gather and synthesize relevant data and methods used to formulate guideline recommendations (Data Supplement; detailed results of scoring for this guideline are available on request to guidelines@asco.org). Briefly, the pan-Canadian guideline[9] received a score of 86.5%, the NCCN Guideline for Cancer-Related Fatigue[12] received a score of 47%, and the NCCN Guideline for Survivorship[13] received a score of 44%.

ASCO UPDATED LITERATURE SEARCH

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

FINAL RECOMMENDATIONS

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

DEFINITION

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

RECOMMENDATIONS

Screening

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

- All health care providers should routinely screen for the presence of fatigue from the point of diagnosis onward, including after completion of primary treatment.
- All patients should be screened for fatigue as clinically indicated and at least annually.
- Screening should be performed and documented using a quantitative or semiquantitative assessment. For example, on a 0 to 10 numeric rating scale (0, no fatigue; 10, worst fatigue imaginable), mild fatigue is indicated as a score of 1 to 3, moderate fatigue as 4 to 6, and severe fatigue as 7 to 10.[15,16] Because fatigue is rarely an isolated symptom, a multisymptom screening tool may have greater clinical utility. Patients who report moderate to severe fatigue should undergo a comprehensive and focused assessment.

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

Comprehensive and Focused Assessment

Modified from NCCN Guideline for Survivorship. Regarding history and physical, first, perform a focused fatigue history, including:

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

Second, evaluate disease status by:

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

Third, assess treatable contributing factors, including:

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

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

Laboratory Evaluation

NCCN Guideline for Survivorship verbatim.

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

Treatment and Care Options

Modified from pan-Canadian guideline and NCCN Guideline for Cancer-Related Fatigue. Regarding education and counseling:

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

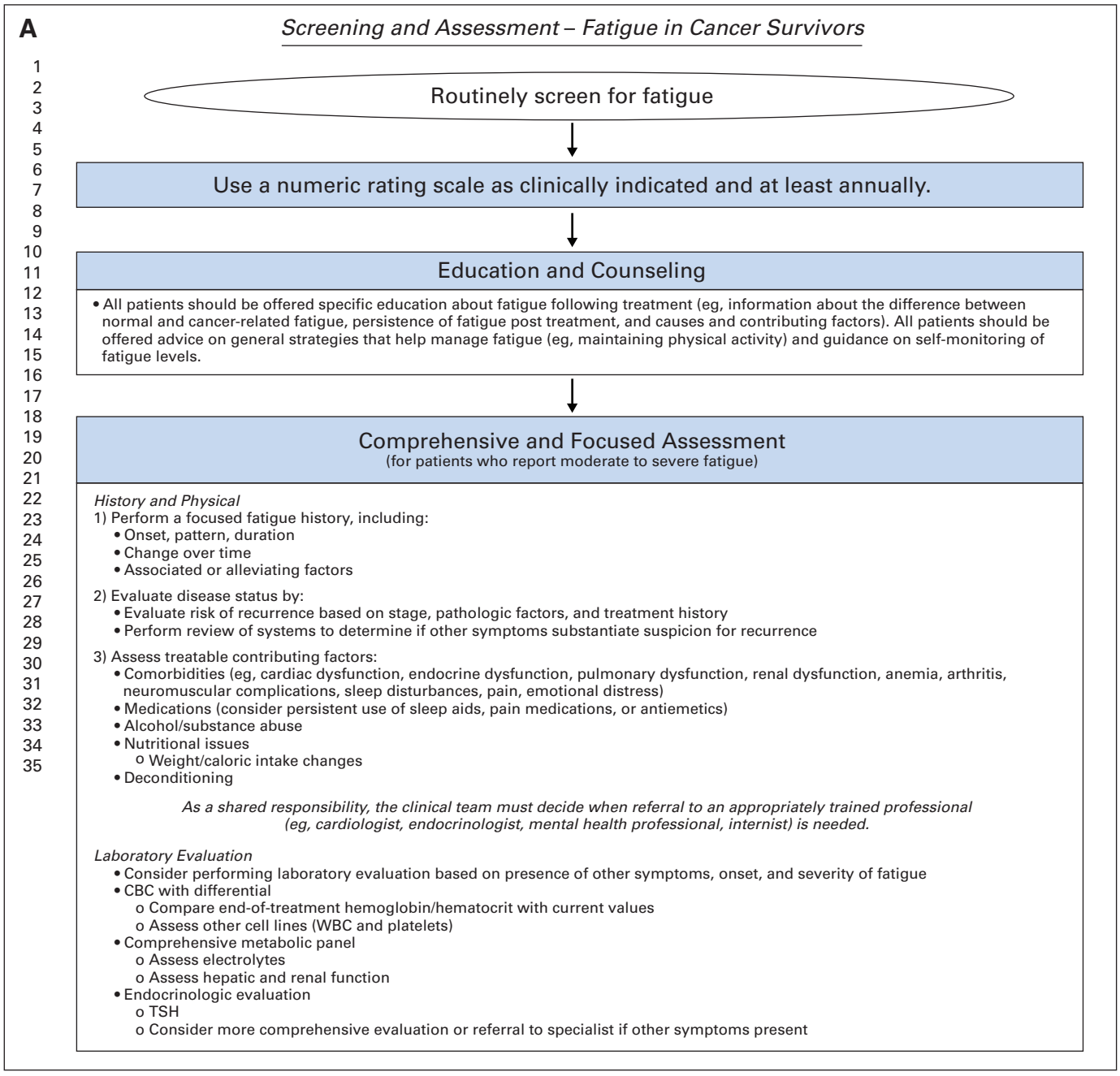

Fig 1. Screening and assessment of fatigue in cancer survivors. CBC, complete blood cell count; TSH, thyroid-stimulating hormone. Data adapted with permission.[9]

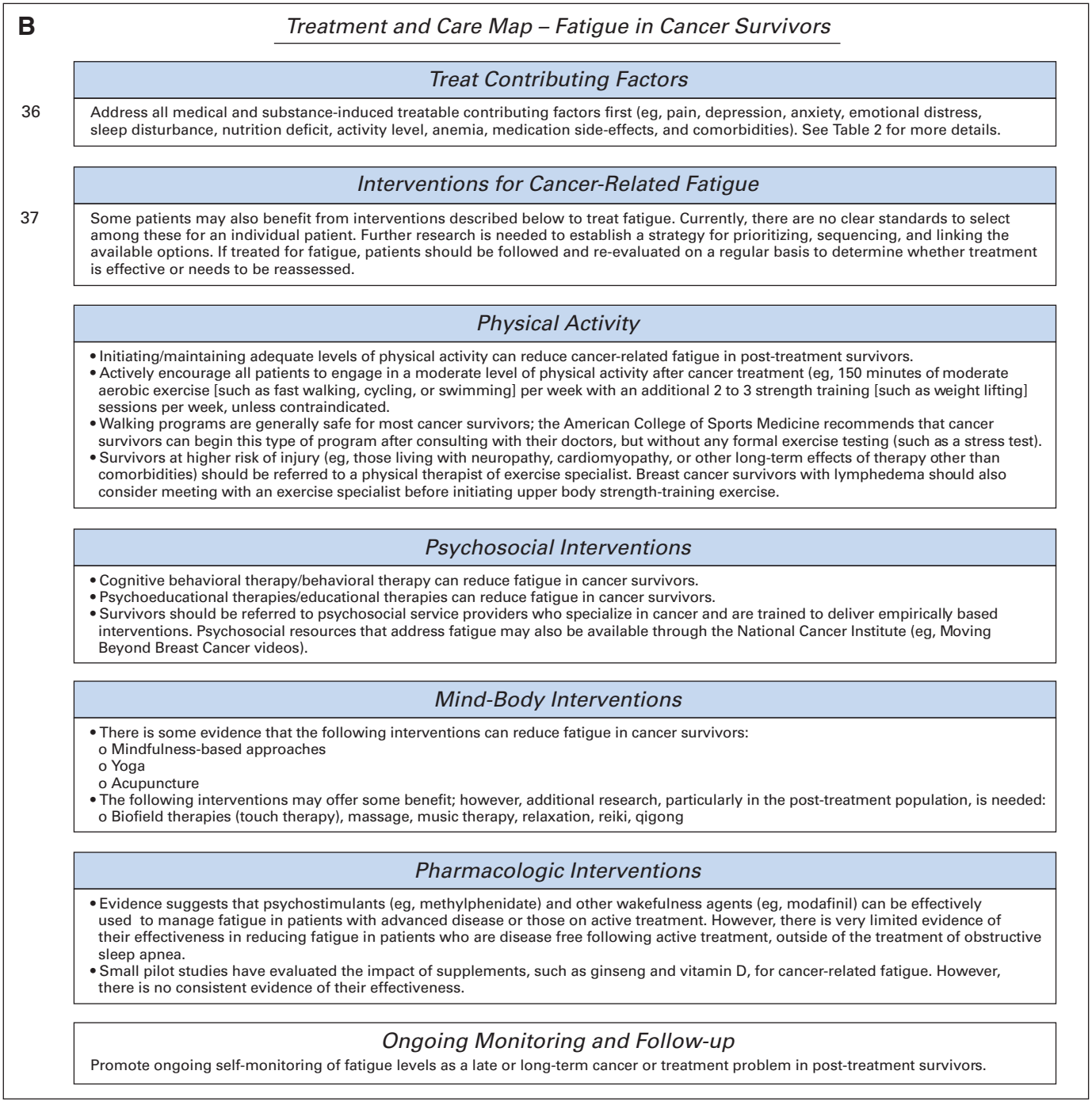

Fig 1. Treatment and care map for fatigue in cancer survivors. Data adapted with permission.[9]

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

Treatment of Contributing Factors

Modified from pan-Canadian guideline and NCCN Guideline for Survivorship. Address all medical and substance-induced treatable contributing factors first (eg, comorbidities, medications, nutritional issues, activity level). Table 2 provides more details. Some patients can also benefit from interventions described in this article to treat fatigue. Currently, there are no clear standards for selecting among these to treat an individual patient. Further research is needed to establish a strategy for prioritizing, sequencing, and linking the available options.

Physical Activity

Modified from pan-Canadian guideline and NCCN Guideline for Survivorship. Several meta-analyses, systematic reviews, and randomized

Table 1. Selected Instruments Used to Measure Cancer-Related Fatigue[17]

Scale	Description
Unidimensional*	
FACT-F[18]	13-item standalone questionnaire that is part of larger FACIT series of quality-of-life and tumor-specific symptom questionnaires
	Studied in mixed cancer population
	Dimension: severity
EORTC QLQ C30[19]	30-item quality-of-life questionnaire with three-item fatigue subscale (independently validated as separate fatigue measure)
	Psychometric properties weaker than more extensive scales, but it is brief and easy to use
	Independently assessed in lung cancer, bone marrow transplantation, and metastatic cancer
	Dimension: severity
POMS-F[20]	65-item questionnaire with seven-item fatigue subscale
	Assessed in both noncancer and cancer populations
	Has defined minimum clinically significant difference
	Dimension: severity
Multidimensional†	
BFI[15]	Nine-item numeric scale
	Validated for use in mixed cancer population
	Reasonable psychometric properties but limited ongoing use
	Cutoff scores to differentiate between mild, medium, and severe fatigue, but it has not been validated and is likely to be of use for screening purposes only
	Dimensions: severity and interference
Chalder Fatigue Scale (also called FQ)[21]	11-item scale
	Validated in general practice setting but widely used for chronic fatigue syndrome
	Brief and easy to administer
	Dimensions: physical and mental
FSI[22]	13-item scale
	Validated in breast cancer population and mixed cancers
	Reasonable psychometric properties, but there is some concern regarding its test/retest reliability
	Dimensions: severity, duration, and interference
MFI-20[23]	20-item scale
	Designed for use in patients with cancer
	Validated in Army trainees and physicians undertaking shift work as well as in patients with cancer
	Dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity
MFSI-30[24]	30-item scale
	Investigated in patients with breast cancer undergoing treatment and in mixed cancer population
	Favorable psychometric properties
	Dimensions: general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor
Revised Piper Fatigue Scale[25]	22-item revised version of original scale
	Validated in breast cancer survivors
	Dimensions: behavioral, severity, affective meaning, sensory, cognitive/mood
Schwartz Cancer Fatigue Scale[26]	28-item scale
	Validated in mixed cancer population undergoing treatment
	Psychometric properties examined in mixed cancer population
	Limited use; hence, its usefulness despite extensive psychometric data must therefore be questioned
	Dimensions: total score and physical and perceptual subscores

Abbreviations: BFI, Brief Fatigue Inventory; EORTC QLQ C30, European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30; FACIT, Functional Assessment of Chronic Illness Therapy; FACT-F, Functional Assessment of Cancer Therapy–Fatigue; FQ, Fatigue Questionnaire; FSI, Fatigue Symptom Inventory; MFI-20, 20-item Multidimensional Fatigue Inventory; MFSI-30, Multidimensional Fatigue Symptom Inventory 30-item short form; POMS-F, Profile of Mood States–Fatigue.

*Tend to measure physical impact of fatigue.

†Tend to measure cognitive or affective symptoms.

trials[27-36] have demonstrated that initiating or maintaining adequate levels of physical activity can reduce cancer-related fatigue in post-treatment patients. For example, a recent meta-analysis of 27 exercise intervention trials conducted with patients after treatment completion found that exercise training significantly reduced fatigue, with a mean effect size of 0.38 (95% CI, 0.21 to 0.43).[27]

Actively encourage all patients to engage in a moderate level of physical activity after cancer treatment (eg, 150 minutes of moderate aerobic exercise, such as fast walking, cycling, or swimming, per week with an additional two to three sessions per week of strength training, such as weight lifting, unless contraindicated).[27-31]

Walking programs are generally safe for most cancer survivors; the American College of Sports Medicine recommends that cancer survivors begin this type of program after consulting with their physician but without any formal exercise testing (such as a stress test).[30]

Survivors at higher risk of injury (eg, those living with neuropathy, cardiomyopathy, or other long-term effects of therapy

Table 2. Potential Comorbid Conditions and Other Treatable Contributing Factors Possibly Associated With Fatigue Symptoms

Treatable Contributing Factor	Examples of Possible Diagnostic Evaluation*
Cardiac dysfunction (eg, arrhythmia, hypertension, coronary artery disease, congestive heart failure)	Consider echocardiogram, exercise test for cardiopulmonary reserve
Endocrine dysfunction (eg, diabetes, hypothyroidism, hypogonadism, adrenal insufficiency)	Consider measuring HgbA1C, TSH, glucose, and testosterone, conduct dexamethasone suppression test
Pulmonary dysfunction	Consider chest x-ray, 6-minute walk test, pulmonary function tests, oxygen saturation
Renal dysfunction	Consider kidney and electrolyte chemistries
Anemia	Consider CBC
Arthritis	Consider sedimentation rate, serologies
Neuromuscular complications (neuromuscular, neuropathy)	Consider grip strength test, neuropathy sensory testing, electromyography
Sleep disturbances (eg, insomnia, sleep apnea, vasomotor symptoms, restless leg syndrome)	Consider assessing sleep with standardized questionnaire, possible sleep study
Pain	Evaluate with standardized assessment tool
Emotional distress (eg, anxiety, depression)	Evaluate with standardized assessment tool or diagnostic interview

NOTE. This list is not meant to be exhaustive. Data adapted.[13]
Abbreviations: CBC, complete blood cell count; HgbA1C, hemoglobin A1C; TSH, thyroid-stimulating hormone.
*Should be undertaken only when clinically appropriate.

other than comorbidities) should be referred to a physical therapist or exercise specialist. Breast cancer survivors with lymphedema should also consider meeting with an exercise specialist before initiating upper-body strength training.

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

Common barriers to physical activity in cancer survivors include physical and disease-related limitations (eg, illness, pain, fatigue, weakness) as well as lack of time, lack of interest/motivation, lack of facilities, and lack of encouragement from family or friends.[37-40] To overcome these barriers, survivors should be encouraged to avoid inactivity by, at the minimum, engaging in exercises such as walking or using a stationary bicycle or cycle ergometer, beginning at an easy pace and progressing gradually to moderate intensity.[41] Counseling and motivational interviewing have also been shown to encourage exercise adherence.[41-43]

Psychosocial Interventions

Modified from NCCN Guideline for Survivorship. Several meta-analyses, systematic reviews, and randomized trials[32,44-48] have indicated that cognitive behavioral therapy/behavioral therapy can reduce fatigue in cancer survivors. For example, a cognitive behavioral intervention that targeted dysfunctional thoughts about fatigue, poor coping strategies, and dysregulated sleep and activity patterns in a mixed sample of fatigued cancer survivors led to significant improvements in fatigue that were sustained over long-term follow-up.[45]

Several systematic reviews and randomized trials have suggested that psychoeducational/educational therapies may reduce fatigue in cancer survivors.[32,48,49] For example, an Internet-based educational program that provided tailored information on cancer-related fatigue, physical activity, pain control, distress management, sleep hygiene, nutrition, and energy conservation led to significant improvements in fatigue in a mixed sample of fatigued cancer survivors.[50]

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

Mind-Body Interventions

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

- Mindfulness-based approaches.[44,51,52]
- Yoga.[53,54]
- Acupuncture.[55,56]

The following interventions may also offer some benefit[57-61]; however, additional research, particularly in the post-treatment period, is needed:

- Biofield therapies (touch therapy), massage, music therapy, relaxation, reiki, and qigong.
- Survivors should be referred to practitioners specializing in cancer and using protocols that have been empirically validated in cancer survivors.

Pharmacologic Interventions

Modified from NCCN Guideline for Cancer-Related Fatigue and NCCN Guideline for Survivorship. Evidence suggests that psychostimulants (eg, methylphenidate) and other wakefulness agents (eg, modafinil) can be effectively used to manage fatigue in patients with advanced disease or those receiving active treatment.[62-64] However, there is limited evidence of their effectiveness in reducing fatigue in patients who are disease free after active treatment, outside of the treatment of obstructive sleep apnea.[65]

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.[57]

Ongoing Monitoring and Follow-Up

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

SPECIAL COMMENTARY

Although there are a number of guidelines and systematic reviews offering recommendations on the management of cancer-related fatigue, there is still relatively little guidance available for the management of fatigue in cancer survivors. The purpose of this guideline is to tailor the available information to this distinct population, because follow-up care for cancer survivors is often challenging, especially if they are dealing with comorbidities and receiving care from multiple providers. Patient follow-up and ongoing care should be individualized based on type of cancer, treatments received, overall health, and personal preferences. In many cases, the patient will be transitioned post-treatment to his or her primary care provider or a survivorship clinic. This transition may be eased with the use of survivorship care plans, which contain personalized information about the patient's treatment and follow-up plans (examples provided in ASCO templates at http://www.cancer.net/survivorship/asco-cancer-treatment-summaries). It is estimated that by 2022, the number of cancer survivors in the United States will exceed 18 million.[1] Therefore, there is a need for greater coordination of care among oncologists and primary care providers, development of evidence-based resources, and ongoing research focusing on the survivor population as well as education, training, and clinical tools that will improve overall patient experience and well-being. The cornerstone of progress for the patient with cancer is the rapport established with his or her health care team. Open and engaging communication will assist both the patient and health care providers in assessing the patient's experience of fatigue and in determining an appropriate management strategy. ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

Additional information, including data supplements, evidence tables, and clinical tools and resources, can be found at www.asco.org/guidelines/. Patient information is available there and at www.cancer.net. The complete adapted guideline can be accessed at http://www.capo.ca/Fatigue_Guideline.pdf and http://www.nccn.org.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Table A1. Members of Fatigue Panel

Panel Member	Institution
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William Breitbart, MD, psychiatry	Memorial Sloan-Kettering Cancer Center, New York, NY
Carmelita P. Escalante, MD, internal medicine	University of Texas MD Anderson Cancer Center, Houston, TX
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Hester Hill Schnipper, LICSW, BCD, patient representative, oncology social work	Beth Israel Deaconess Medical Center, Boston, MA
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Christina Lacchetti, MHSc	ASCO, Alexandria, VA

Abbreviations: ASCO, American Society of Clinical Oncology; PGIN, Practice Guidelines Implementation Network.

Table A2. Members of Survivorship Guideline Advisory Group

Member	Institution
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Smita Bhatia (cochair)	City of Hope Comprehensive Cancer Center, Duarte, CA
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Julia Howe Rowland	National Institutes of Health, Bethesda, MD/Department of Health and Human Services, Washington, DC
Kevin C. Oeffinger	Memorial Sloan-Kettering Cancer Center, New York, NY
Donna E. Maziak	The Ottawa Hospital, General Campus, Ottawa, ON
Larissa Nekhlyudov	Harvard Medical School, Boston, MA
Wendy Landier	City of Hope, Duarte, CA
Paul B. Jacobsen	H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL
Mark Gorman	Patient Representative, Silver Spring, MD
Anthony Magdalinski	ASCO PGIN; Abington Health Lansdale Hospital, Lansdale, PA; Doylestown Hospital, Doylestown, PA; Grand View Hospital, Sellersville, PA; St Luke's Quakertown Hospital, Quakertown, PA

Abbreviations: ASCO, American Society of Clinical Oncology; PGIN, Practice Guidelines Implementation Network.