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EDUCATIONAL OBJECTIVES:

After reading the article "American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline," the learner should be able to:

1. Discuss the most frequent and relevant long-term and late effects of cancer and its treatment occurring in women with a history of breast cancer.
2. Review recommendations of the American Cancer Society (ACS)/American Society of Clinical Oncology (ASCO) Breast Cancer Survivorship Care Guideline.

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

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The purpose of the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline is to provide recommendations to assist primary care and other clinicians in the care of female adult survivors of breast cancer. A systematic review of the literature was conducted using PubMed through April 2015. A multidisciplinary expert workgroup with expertise in primary care, gynecology, surgical oncology, medical oncology, radiation oncology, and nursing was formed and tasked with drafting the Breast Cancer Survivorship Care Guideline. A total of 1073 articles met inclusion criteria; and, after full text review, 237 were included as the evidence base. Patients should undergo regular surveillance for breast cancer recurrence, including evaluation with a cancer-related history and physical examination, and should be screened for new primary breast cancer. Data do not support performing routine laboratory tests or imaging tests in asymptomatic patients to evaluate for breast cancer recurrence. Primary care clinicians should counsel patients about the importance of maintaining a healthy lifestyle, monitor for post-treatment symptoms that can adversely affect quality of life, and monitor for adherence to endocrine therapy. Recommendations provided in this guideline are based on current evidence in the literature and expert consensus opinion. Most of the evidence is not sufficient to warrant a strong evidence-based recommendation. Recommendations on surveillance for breast cancer recurrence, screening for second primary cancers, assessment and management of physical and psychosocial long-term and late effects of breast cancer and its treatment, health promotion, and care coordination/practice implications are made. **CA Cancer J Clin 2016;66:43-73.**

Keywords: breast cancer, survivorship, clinical care, follow-up, guideline, primary care, quality of life, survivorship care plan, long-term effects, late effects, care coordination

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Introduction

Breast cancer is the most common noncutaneous malignancy among women, representing 4 in 10 female cancer survivors in the United States.[1] Long-term survival is common after breast cancer treatment, with a 5-year survival rate of almost 90%[2]; thus, addressing survivors' unique post-treatment needs is critical to providing quality health care.[3]

Nearly a decade ago, two landmark publications from the Institute of Medicine highlighted the importance of surveillance, health promotion, and assessing and managing the myriad of physical, psychological, spiritual, social, and practical long-term and late effects faced by many cancer survivors after completing active treatment.[4,5] Recent publications affirm the importance of addressing health, wellness, and quality of life (QoL) concerns of post-treatment cancer survivors.[3,6,7] In recognition of the increasing need for information to support primary care clinicians who care for breast cancer survivors, this guideline was developed to provide recommendations to enhance the quality of clinical follow-up care for those who have completed initial treatment for female breast cancer (eg, surgery, radiation, targeted therapy, and/or chemotherapy).[8]

Although many evidence-based clinical guidelines exist for diagnosis and treatment, there are few evidence-based clinical care guidelines addressing life-long follow-up care for survivors by cancer type. The National Comprehensive Cancer Network® (NCCN®) guidelines are evidence- and consensus-based for the treatment of patients with breast cancer[9] that include information on recommended surveillance for cancer recurrence or new cancers. The NCCN also has symptom-specific survivorship care guidelines addressing anthracycline-induced cardiac toxicity, anxiety and depression, cognitive function, fatigue, pain, sexual function, sleep disorders, healthy lifestyles and immunizations and infections.[10] In addition, the American Society of Clinical Oncology (ASCO) has guidelines for the follow-up and management of patients with breast cancer[11,12] as well as symptom-based guidelines specific to fatigue,[13] chemotherapy-induced peripheral neuropathy (CIPN),[14] and anxiety and depressive symptoms[15]; ASCO is also developing guidelines on the prevention and monitoring of cardiac dysfunction in survivors of adult cancers and on the management of chronic pain. Furthermore, ASCO recently endorsed the American Cancer Society (ACS) guideline on prostate cancer survivorship.[16] The ACS/ASCO Breast Cancer Survivorship Care Guideline builds upon prior guidelines by providing comprehensive, holistic recommendations specific to post-treatment breast cancer clinical care to help primary care clinicians better manage potential long-term and late effects and to provide timely and appropriate screening and surveillance to improve the overall health and QoL of breast cancer survivors.

This year, approximately 231,840 women will be newly diagnosed with breast cancer, and an estimated 3.1 million breast cancer survivors are alive in the United States.[17] The median age at diagnosis is 61 years, and 43% are older than 65 years at diagnosis; thus, cancer survivorship must be managed in coordination with comorbidities associated with aging.[1] Approximately 61% will have localized disease, for which survival outcomes are highest (5-year relative survival rates: 99% for localized-stage breast cancer vs 25% for distant-stage breast cancer).[2]

Breast cancer treatment depends on the stage at diagnosis, the size and location of the tumor, and tumor characteristics. Those who have stage II or III disease at diagnosis may receive more involved cancer treatment, which can result in greater likelihood and severity of the impact of treatment. Treatment generally includes two key components—treatment of the breast and local lymph nodes with surgery either with or without radiation therapy ("local therapy") and drug treatments for cancer cells that may have spread ("adjuvant systemic therapy") outside the breast. Surgical treatment for breast cancer includes breast-conserving surgery with radiation or mastectomy with or without radiation and with or without immediate/delayed reconstruction. In women with a very high risk of contralateral cancer from inherited susceptibility (eg, patients with mutations in the breast and ovarian cancer susceptibility genes *BRCA1*/*BRCA2*), contralateral prophylactic mastectomy may be performed.[18,19] Systemic therapy may precede ("neoadjuvant") or follow ("adjuvant") local therapy and consists of combinations of hormonal therapy, chemotherapy, and biological agents.

There is no standardized follow-up model for patients with early stage breast cancer who have completed surgery,

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This guideline was developed through a collaboration between the American Cancer Society and the American Society of Clinical Oncology and has been published jointly by invitation and consent in both *CA: A Cancer Journal for Clinicians* and the *Journal of Clinical Oncology*.

chemotherapy, and radiation. Most of these women will have endocrine-responsive tumors and will require endocrine therapy for a total of 5 to 10 years. Randomized trials have shown equivalent outcomes with follow-up by either the oncologist or a primary care physician.[20] Shared follow-up care between one or more oncologists and the primary physician is an additional possibility. However, the great majority of these patients will eventually be discharged back to their primary clinician for ongoing follow-up. It should be noted that these patients remain at risk indefinitely for complications of their previous cancer treatment. Most also remain at risk indefinitely for local and/or systemic recurrence of their breast cancer.

Gaps in post-treatment cancer survivorship resources and clinical follow-up care were identified through the work of the National Cancer Survivorship Resource Center (The Survivorship Center; cancer.org/survivorshipcenter), which is a collaboration between the ACS, The George Washington University (GW) Cancer Institute, and the Centers for Disease Control and Prevention (CDC) funded by a 5-year cooperative agreement from the CDC. The overarching goals of The Survivorship Center are to improve individual-level, system-level, and policy-level post-treatment survivorship clinical care, to develop resources to help survivors achieve optimal health and QoL, as well as to highlight the importance of post-treatment survivorship as a public health issue.[8] A strategic partnership with ASCO was formed to optimize consistent, evidence-based recommendations for survivorship care in patients with breast cancer.

Guideline Questions

The clinical practice guideline addresses 5 key areas of breast cancer survivorship to provide recommendations on best practice in the management of adult women after breast cancer treatment, focusing on the role of primary care clinicians and other clinicians who care for post-treatment breast cancer survivors. The 5 areas covered include 1) surveillance for breast cancer recurrence, 2) screening for second primary cancers, 3) assessment and management of physical and psychosocial long-term and late effects of breast cancer and treatment, 4) health promotion, and 5) care coordination and practice implications (see Table 1).[21-23]

Methods

The methods used to develop this guideline reflect an evolving process that was influenced by ACS screening[24] and survivorship[16] guidelines. Where appropriate, this guideline builds upon the recently published ASCO symptom-based guidelines for adult cancer survivors.[14,15,25]

Panel Formation

A multidisciplinary expert workgroup was formed and tasked with drafting the Breast Cancer Survivorship Care Guideline. Workgroup members had expertise in primary care, gynecology, surgical oncology, medical oncology, radiation oncology, and nursing. In addition, a cancer survivor was included to provide a patient perspective.

Literature Review

The literature review began with an environmental scan of existing guidelines and guidance developed by other organizations (eg, the NCCN,[9,10,26] ASCO,[11,14,15,25,27] and the Children's Oncology Group *Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* [survivorshipguidelines.org]), specific medical centers (eg, The University of Texas MD Anderson Clinical Tools and Resources Breast Cancer Survivorship algorithm,[28] the US Preventive Services Task Force,[22,29,30] and the American Association of Clinical Endocrinologists[31]), individual publications[32-35] available from other countries (eg, the Australian Cancer Survivorship Center), and publications from other expert panels (eg, the Breast Health Global Initiative guidelines[36]).

Literature Search Strategy

A systematic review of the literature was conducted using PubMed through April 2015. Studies on childhood cancers, qualitative studies, and non-English publications were excluded. Search terms included: cancer survivor AND review OR meta-analysis OR systematic review OR guidelines; guidance AND breast cancer OR breast cancer survivor; breast cancer patient post-treatment AND symptom management OR late effects OR long-term effects OR psychosocial care OR palliative care OR health promotion OR surveillance OR screening for new cancers OR self-management OR guidelines OR guidance OR follow-up OR follow-up OR side effects OR (chemotherapy AND side effects) OR (radiation AND side effects), OR surgery OR treatment complications OR genetic counseling and testing OR survivor or patient interventions OR provider interventions OR provider education OR barriers. Additional search attempts included breast cancer OR breast cancer survivor OR breast cancer patient post-treatment AND (symptom-specific terms, such as lymphedema, body image, early menopause, etc).

The highest priority was given to articles that met the following criteria: peer reviewed publication in English since 2004, unless a seminal article published before that date still carried the most weight, including randomized controlled trials (RCTs), prospective cohort studies, and well-conducted, population-based, case-control studies; large studies of more than 100 cancer cases analyzed and with high-quality assessment of covariates and analytic methods; and analyses controlled for important confounders (eg, pre-existing comorbid conditions) (Table 2).

TABLE 1. The Bottom Line: Recommendations for the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline

Target population: Female adult breast cancer survivors
Target audience: Primary care providers, medical oncologists, radiation oncologists, and other clinicians caring for breast cancer survivors
Methods: An expert panel was convened to develop clinical practice guideline recommendations based on a systematic review of the medical literature
ACS/ASCO key recommendations for breast cancer survivorship care
Surveillance for breast cancer recurrence
History and physical
Recommendation 1.1: It is recommended that primary care clinicians (a) should individualize clinical follow-up care provided to breast cancer survivors based on age, specific diagnosis, and treatment protocol and as recommended by the treating oncology team (LOE = 2A); and (b) should make sure the patient receives a detailed cancer-related history and physical examination every 3 to 6 mo for the first 3 y after primary therapy, every 6-12 mo for the next 2 y, and annually thereafter (LOE = 2A).
Screening the breast for local recurrence or a new primary breast cancer
Recommendation 1.2: It is recommended that primary care clinicians (a) should refer women who have received a unilateral mastectomy for annual mammography on the intact breast and, for those with lumpectomies, an annual mammography of both breasts (LOE = 2A); and (b) should not refer for routine screening with MRI of the breast unless the patient meets high-risk criteria for increased breast cancer surveillance as per ACS guidelines (Saslow 2007[21]; LOE = 2A).
Laboratory tests and imaging
Recommendation 1.3: It is recommended that primary care clinicians should not offer routine laboratory tests or imaging, except mammography if indicated, for the detection of disease recurrence in the absence of symptoms (LOE = 2A).
Signs of recurrence
Recommendation 1.4: It is recommended that primary care clinicians should educate and counsel all women about the signs and symptoms of local or regional recurrence (LOE = 2A).
Risk evaluation and genetic counseling
Recommendation 1.5: It is recommended that primary care clinicians (a) should assess the patient's cancer family history; and (b) should offer genetic counseling if potential hereditary risk factors are suspected (eg, women with a strong family history of cancer [breast, colon, endometrial] or age 60 y or younger with triple-negative breast cancer; Moyer 2014[22]; LOE = 2A).
Endocrine treatment impacts, symptom management
Recommendation 1.6: It is recommended that primary care clinicians should counsel patients to adhere to adjuvant endocrine (antiestrogen) therapy (LOE = 2A).
Screening for second primary cancers
Cancer screenings in the average-risk patient
Recommendation 2.1: It is recommended that primary care clinicians (a) should screen for other cancers as they would for patients in the general population; and (b) should provide an annual gynecologic assessment for postmenopausal women on selective estrogen receptor modulator therapies.
Assessment and management of physical and psychosocial long-term and late effects of breast cancer and treatment
Body image concerns
Recommendation 3.1: It is recommended that primary care clinicians (a) should assess for patient body image/appearance concerns (LOE = 0); (b) should offer the option of adaptive devices (eg, breast prostheses, wigs) and/or surgery when appropriate (LOE = 0); and (c) should refer for psychosocial care as indicated (LOE = IA).
Lymphedema
Recommendation 3.2: It is recommended that primary care clinicians (a) should counsel survivors on how to prevent/reduce the risk of lymphedema, including weight loss for those who are overweight or obese (LOE = 0); and (b) should refer patients with clinical symptoms or swelling suggestive of lymphedema to a therapist knowledgeable about the diagnosis and treatment of lymphedema, such as a physical therapist, occupational therapist, or lymphedema specialist (LOE = 0).
Cardiotoxicity
Recommendation 3.3: It is recommended that primary care clinicians (a) should monitor lipid levels and provide cardiovascular monitoring, as indicated (LOE = 0); and (b) should educate breast cancer survivors on healthy lifestyle modifications, potential cardiac risk factors, and when to report relevant symptoms (shortness of breath or fatigue) to their health care provider (LOE = I).
Cognitive impairment
Recommendation 3.4: It is recommended that primary care clinicians (a) should ask patients if they are experiencing cognitive difficulties (LOE = 0); (b) should assess for reversible contributing factors of cognitive impairment and optimally treat when possible (LOE = IA); and (c) should refer patients with signs of cognitive impairment for neurocognitive assessment and rehabilitation, including group cognitive training if available (LOE = IA).

TABLE 1. *Continued*

Distress, depression, anxiety
Recommendation 3.5: It is recommended that primary care clinicians (a) should assess patients for distress, depression, and/or anxiety (LOE = I); (b) should conduct a more probing assessment for patients at a higher risk of depression (eg, young patients, those with a history of prior psychiatric disease, and patients with low socioeconomic status; LOE = III); and (c) should offer in-office counseling and/or pharmacotherapy and/or refer to appropriate psycho-oncology and mental health resources as clinically indicated if signs of distress, depression, or anxiety are present (LOE = I).
Fatigue
Recommendation 3.6: It is recommended that primary care clinicians (a) should assess for fatigue and treat any causative factors for fatigue, including anemia, thyroid dysfunction, and cardiac dysfunction (LOE = 0); (b) should offer treatment or referral for factors that may impact fatigue (eg, mood disorders, sleep disturbance, pain, etc) for those who do not have an otherwise identifiable cause of fatigue (LOE = I); and (c) should counsel patients to engage in regular physical activity and refer for cognitive behavioral therapy as appropriate (LOE = I).
Bone health
Recommendation 3.7: It is recommended that primary care clinicians (a) should refer post-menopausal breast cancer survivors for a baseline DEXA scan (LOE = 0); and (b) should refer for repeat DEXA scans every 2 y for women taking an aromatase inhibitor, premenopausal women taking tamoxifen and/or a GnRH agonist, and women who have chemotherapy-induced, premature menopause (LOE = 0).
Musculoskeletal health
Recommendation 3.8: It is recommended that primary care clinicians (a) should assess for musculoskeletal symptoms, including pain, by asking patients about their symptoms at each clinical encounter (LOE = 0); and (b) should offer one or more of the following interventions based on clinical indication: acupuncture, physical activity, and referral for physical therapy or rehabilitation (LOE = III).
Pain and neuropathy
Recommendation 3.9: It is recommended that primary care clinicians (a) should assess for pain and contributing factors for pain with the use of a simple pain scale and comprehensive history of the patient's complaint (LOE = 0); (b) should offer interventions, such as acetaminophen, nonsteroidal anti-inflammatory drugs, physical activity, and/or acupuncture, for pain (LOE = I); (c) should refer to an appropriate specialist, depending on the etiology of the pain once the underlying etiology has been determined (eg, lymphedema specialist, occupational therapist, etc; LOE = 0); (d) should assess for peripheral neuropathy and contributing factors for peripheral neuropathy by asking the patient about their symptoms, specifically numbness and tingling in their hands and/or feet, and the characteristics of the symptoms (LOE = 0); (e) should offer physical activity for neuropathy; and (f) should offer duloxetine for patients with neuropathic pain, numbness, and tingling (LOE = IB).
Infertility
Recommendation 3.10: It is recommended that primary care clinicians should refer survivors of childbearing age who experience infertility to a specialist in reproductive endocrinology and infertility as soon as possible (LOE = 0).
Sexual health
Recommendation 3.11: It is recommended that primary care clinicians (a) should assess for signs and symptoms of sexual dysfunction or problems with sexual intimacy (LOE = 0); (b) should assess for reversible contributing factors to sexual dysfunction and treat, when appropriate (LOE = 0); (c) should offer nonhormonal, water-based lubricants and moisturizers for vaginal dryness (LOE = IA); and (d) should refer for psychoeducational support, group therapy, sexual counseling, marital counseling, or intensive psychotherapy when appropriate (LOE = IA).
Premature menopause/hot flashes
Recommendation 3.12: It is recommended that primary care clinicians should offer selective serotonin-norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, gabapentin, lifestyle modifications, and/or environmental modifications to help mitigate vasomotor symptoms of premature menopausal symptoms (LOE = IA).
Health promotion
Information
Recommendation 4.1: It is recommended that primary care clinicians (a) should assess the information needs of the patient related to breast cancer and its treatment, side effects, other health concerns, and available support services (LOE = 0); and (b) should provide or refer survivors to appropriate resources to meet these needs (LOE = 0).
Obesity
Recommendation 4.2: It is recommended that primary care clinicians (a) should counsel survivors to achieve and maintain a healthy weight (LOE = III); and (b) should counsel survivors if overweight or obese to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss (LOE = IA, III).
Physical activity
Recommendation 4.3: It is recommended that primary care clinicians should counsel survivors to engage in regular physical activity consistent with the ACS guideline (Rock 2012[23]) and specifically: (a) should avoid inactivity and return to normal daily activities as soon as possible after diagnosis (LOE = III); (b) should aim for at least 150 min of moderate or 75 min of vigorous aerobic exercise per wk (LOE = I, IA); and (c) should include strength training exercises at least 2 d per wk and emphasize strength training for women treated with adjuvant chemotherapy or hormone therapy (LOE = IA).
Nutrition
Recommendation 4.4: It is recommended that primary care clinicians should counsel survivors to achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; low in saturated fats; and limited in alcohol consumption (LOE = IA, III).

TABLE 1. *Continued*

Smoking cessation
Recommendation 4.5: It is recommended that primary care clinicians should counsel survivors to avoid smoking and refer survivors who smoke to cessation counseling and resources (LOE = I).
Care coordination/practice implications
Survivorship care plan
Recommendation 5.1: It is recommended that primary care clinicians should consult with the cancer treatment team and obtain a treatment summary and survivorship care plan (LOE = 0, III).
Communication with oncology team
Recommendation 5.2: It is recommended that primary care clinicians should maintain communication with the oncology team throughout the patient's diagnosis, treatment, and post-treatment care to ensure care is evidence-based and well-coordinated (LOE = 0).
Inclusion of family
Recommendation 5.3: It is recommended that primary care clinicians should encourage the inclusion of caregivers, spouses, or partners in usual breast cancer survivorship care and support (LOE = 0).
Additional resources
More information, including a data supplement with additional evidence tables, is available with the online version of this article at asco.org/guidelines/breastsurvivorship and asco.org/guidelineswiki; patient information is available at onlinelibrary.wiley.com/doi/10.3322/caac.21319/pdf; journal-based continuing education is available at acsjournals.com/ce

ACS indicates American Cancer Society; ASCO, American Society of Clinical Oncology; DEXA, dual-energy x-ray absorptiometry; GnRH, gonadotropin-releasing hormone; LOE, level of evidence.

Workgroup members were also asked to consider the specific level of evidence (LOE) criteria along with consistency across studies and study designs, dose-response when presenting treatment impacts, race/ethnicity differences, and second primary cancers for which survivors are at high risk because of treatment and genetic considerations. After finalization by the workgroup, the guideline manuscript was sent to additional internal and external experts for review and comment before submission for publication. The guideline summarizes literature with the highest level of evidence (ie, RCTs). A comprehensive list of evidence is available online (see online supporting information).

This is the most recent information as of the publication date. For updates, the most recent information, and to submit new evidence, please visit asco.org/guidelines/breastsurvivorship and the ASCO Guidelines Wiki (asco.org/guidelineswiki). On the basis of formal review of the emerging literature, ACS/ASCO will determine the need to update on a regular basis. At minimum, it will be updated every 5 years.

Guideline Disclaimer

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Guideline and Conflicts of Interest

The expert panel was assembled in accordance with the ACS Conflict of Interest Procedures and the ASCO

TABLE 2. Levels of Evidence

LEVEL OF EVIDENCE	CRITERIA
I	Meta-analyses of RCTs
IA	RCT of breast cancer survivors
IB	RCT based on cancer survivors across multiple cancer sites
IC	RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing menopausal symptoms, sexual dysfunction, etc)
IIA	Non-RCTs based on breast cancer survivors
IIB	Non-RCTs based on cancer survivors across multiple sites
IIC	Non-RCTs not based on cancer survivors but on general population experiencing a specific long-term or late effect
III	Case-control study or prospective cohort study
0	Expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study
2A	NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

non-RCTs indicates nonrandomized controlled trials; RCTs, randomized controlled trials.

Conflict of Interest Management Procedures for Clinical Practice Guidelines ("Procedures"; summarized at asco.org/rwc). Members of the panel completed the ACS Guidelines Development Participant Disclosure Form, the ASCO disclosure form, and the International Committee of Medical Journal Editors Form for Disclosure of Potential Conflicts of Interest, 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 a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Procedures, the majority of the members of the panel did not disclose any such relationships.

Results

In total, 1073 articles (the list is available online; see online supporting information) met inclusion criteria; and, after full text review, 237 were included as the evidence base. Only 2% of eligible articles were rated as level I evidence, 7% were rated as level IA evidence, and 2% were rated as level IIA evidence. The majority of evidence was rated as level III (26%) and level 0 (64%). Recommendations provided in this guideline are based on current evidence in the

TABLE 3. Guideline for Surveillance for Breast Cancer Recurrence and Genetic Counseling

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 1.1: History and physical	
(a) Should individualize clinical follow-up care provided to breast cancer survivors based on age, specific diagnosis, and treatment protocol as recommended by the treating oncology team	2A[b,c]
(b) Should make sure the patient receives a detailed cancer-related history and physical examination every 3-6 mo for the first 3 y after primary therapy, every 6-12 mo for the next 2 y, and annually thereafter by the treating oncology team	
Recommendation 1.2: Screening the breast for local recurrence or a new primary breast cancer	2A[b,c]
(a) Should refer women who have received a unilateral mastectomy for annual mammography on the intact breast and for those with lumpectomies an annual mammography of both breasts	
(b) Should not refer for routine screening with MRI of the breast unless the patient meets high risk criteria for increased breast cancer surveillance as per ACS guidelines	
Recommendation 1.3: Laboratory tests and imaging	2A[b,c]
Should not offer routine laboratory tests or imaging, except mammography if indicated, for the detection of disease recurrence in the absence of symptoms	
Recommendation 1.4: Signs of recurrence	2A[b,c]
Should educate and counsel all women about the signs and symptoms of local or regional recurrence	
Recommendation 1.5: Risk evaluation and genetic counseling	2A[b,c]
(a) Should assess your patient's cancer family history	
(b) Should offer genetic counseling if potential hereditary risk factors are suspected (eg, women with a strong family history of cancer [breast, colon, endometrial], or age 60 y or younger with triple-negative breast cancer)	
Recommendation 1.6: Endocrine treatment impacts, symptom management	2A[b,c]
Should counsel patients to adhere to adjuvant endocrine (antiestrogen) therapy	

ACS indicates American Cancer Society; MRI, magnetic resonance imaging. [a]Levels of evidence: I indicates meta-analyses of randomized controlled trials (RCTs); IA, RCT of breast cancer survivors; IB, RCT based on cancer survivors across multiple sites; IC, RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing fatigue, lymphedema, etc); IIA, nonrandomized controlled trial (non-RCT) based on breast cancer survivors; IIB, non-RCT based on cancer survivors across multiple sites; IIC, non-RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing urinary incontinence, erectile dysfunction, etc); III, case-control or prospective cohort study; 0, expert opinion, observation, clinical practice, literature review, or pilot study. [b]National Comprehensive Cancer Network category 2A indicates that "based upon lower-level evidence, there is uniform consensus that the intervention is appropriate." Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NCCN Clinical Practice Guidelines in Oncology, Breast Cancer, V.2.2015. © National Comprehensive Cancer Network, Inc 2015. All rights reserved. Accessed August 3, 2015. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc. [c]Referenced with permission from the American Society of Clinical Oncology (ASCO).

literature and expert consensus opinion. Most of the evidence is not sufficient to warrant a strong, evidence-based recommendation. Rather, recommendations should be largely viewed as possible management strategies given the current limited evidence base and the logistical challenges of comprehensively adhering to these recommendations.

Recommendations

Surveillance for Breast Cancer Recurrence

The guiding principle of surveillance is that it should consider a patient's risk of recurrence in the context of functional status and patient preferences (see Table 3: Guideline for Surveillance for Breast Cancer Recurrence and Genetic Counseling). In asymptomatic patients, routine screening tests to detect recurrence are not recommended. However, a careful history is often needed to assure that patients are indeed asymptomatic. Patients at a higher risk for local recurrence should have appropriate screening.

History and physical

Recommendation 1.1. It is recommended that primary care clinicians (a) should individualize clinical follow-up care provided to breast cancer survivors based on age, specific diagnosis, and treatment protocol as recommended by the treating oncology team (LOE = 2A); and (b) should make sure the patient receives a detailed cancer-related history and physical examination every 3 to 6 months for the first 3 years after primary therapy, every 6 to 12 months for the next 2 years, and annually thereafter by the treating oncology team (LOE = 2A).

Clinical interpretation. Perform periodic history and physical examination on all breast cancer survivors. In a previous ASCO guideline, ASCO recommended that all female breast cancer survivors have a detailed history and physical examination every 3 to 6 months for the first 3 years after primary therapy, every 6 to 12 months for the next 2 years, and annually thereafter to detect cancer recurrence at an early stage.[11,12] Frequency should be determined by the treating oncologist and should be based on the individual risk profile and perspective of the patient. This can be done in collaboration with the primary care clinician. Patients should be made aware of the signs and symptoms of disease recurrence and should be instructed to seek medical attention if any of the signs or symptoms occur between scheduled follow-up visits. If one or more additional oncology health care providers are following the patient, the frequency of the primary physician's visits should be adjusted accordingly. Clinicians can recommend vaccinations to their patients with a breast cancer history as appropriate based on guidelines; they can receive flu (shot, not nasal) or pneumonia vaccine at any time, including during chemotherapy, and zoster vaccine when not receiving chemotherapy.[37]

Screening the breast for local recurrence or a new primary breast cancer

Recommendation 1.2. It is recommended that primary care clinicians (a) should refer women who have received a unilateral mastectomy for annual mammography on the intact breast and for those with lumpectomies an annual mammography of both breasts (LOE = 2A); and (b) *should not* refer for routine screening with magnetic resonance imaging (MRI) of the breast unless the patient meets high risk criteria for increased breast cancer surveillance as per ACS guidelines[21] (LOE = 2A).

Clinical interpretation. Mammography should be performed yearly on the breast treated by breast conserving surgery and on the intact contralateral breast. More frequent mammography is only warranted for evaluation or follow-up of a suspicious finding.[11] After mastectomy, the site of the reconstructed breast does not require imaging. While MRI of the breast is more sensitive than mammography, there is an increased risk of false-positive findings that may lead to unnecessary additional imaging and often unnecessary biopsies. The use of MRI can only be justified if the probability of missing a cancer with mammography alone is sufficiently high. In women who have not undergone bilateral mastectomy, the use of MRI of the breasts in screening for local recurrence or a new primary cancer should be restricted to women who meet the high-risk criteria of the ACS or ASCO.[11,21,38] High risk is defined as a woman with a lifetime risk of a second primary breast cancer >20%, such as a woman with a *BRCA1*/*BRCA2* mutation or a very strong family history of breast cancer.[21]

Laboratory tests and imaging

Recommendation 1.3. It is recommended that primary care clinicians *should not* offer routine laboratory tests or imaging, except mammography if indicated, for the detection of disease recurrence in the absence of symptoms (LOE = 2A).

Clinical interpretation. Consistent with ASCO Guidelines and NCCN Guidelines®, routine testing with breast cancer tumor markers or imaging studies (eg, bone scan, chest x-ray, positron emission tomography-computed tomography [CT] scans, MRI scans, biomarkers) should not be performed for screening purposes, because they have not been shown to improve survival outcomes or QoL in asymptomatic patients.[9,11] Chest x-rays and advanced body imaging (eg, CT, MRI, positron emission tomography-CT, bone scan) should be ordered only if disease recurrence is suspected.[39] Randomized trials in the 1980s that compared clinical follow-up with periodic advanced imaging did not demonstrate a survival advantage with advanced imaging

and did show a significant rate of false-positive findings with additional testing.[40-42]

Signs of recurrence

Recommendation 1.4. It is recommended that primary care clinicians should educate and counsel all women about the signs and symptoms of local or regional recurrence (LOE = 2A).

Clinical interpretation. Physicians should educate and counsel patients about the signs and symptoms of local or regional recurrence, including new lumps (eg, in underarm or neck), rash or skin changes on the breast or chest wall, chest pain, changes in the contour/shape/size of the breast, and swelling of the breast or arm.[11] Evaluation of patient-reported symptoms is essential in detecting a recurrence as early as possible, which may impact survival.

Risk evaluation and genetic counseling

Recommendation 1.5. It is recommended that primary care clinicians (a) should assess the patient's cancer family history; and (b) should offer genetic counseling if potential hereditary risk factors are suspected (eg, women with a strong family history of cancer [breast, colon, endometrial], or age 60 years or younger with triple-negative breast cancer)[22] (LOE = 2A).

Clinical interpretation. To identify those women with breast cancer who have a high risk of a second primary breast cancer and/or may have a genetic susceptibility to cancer that may affect other family members, a detailed history, including key risk factors and paternal and maternal family history, should be obtained for all patients. Those with a family history of breast or ovarian cancer or with cancer in a certain age group and/or cancer type should be referred for genetic counseling for consideration of testing for hereditary predisposition to genetic mutations. Specifically, genetic counseling for consideration of testing for hereditary predisposition to gene mutations should be recommended for breast cancer survivors with in the following characteristics: those with at least one grandparent of Ashkenazi Jewish heritage, younger than age 50 years at diagnosis, with a history of ovarian cancer at any age or in any first-degree or second-degree relative, with a first-degree relative who had breast cancer diagnosed before age 50 years, with two or more first-degree or second-degree relatives diagnosed with breast cancer at any age, with a diagnosis of bilateral breast cancer, with a history of breast cancer in a male relative, or any survivor diagnosed at age 60 years or younger with triple-negative breast cancer.[22] It is important to periodically review these issues with the patient, because some survivors may not have been offered genetic counseling or testing at the time of diagnosis, and/or new cancer events may have occurred in the family after the initial diagnosis and treatment. Because new primary cancers may be associated with some hereditary syndromes, identifying the risk of genetic mutations in the survivor may help to formulate a prevention strategy to reduce the risk of a new cancer. In addition, this information also could be helpful to family members.

Genetic testing should be preceded by consultation with a genetics counselor or other trained professional to assure full discussion of the risks and benefits and to assure that other genetic syndromes beyond *BRCA1* and *BRCA2* breast/ovarian syndromes are considered. Depending on the hereditary gene that is identified, different screening and prevention strategies may be offered. Recommendations for alternate screening and prevention strategies depend on the specific genetic syndrome and should be left to a trained professional in coordination with the oncology team and the primary care clinician.

Endocrine treatment impacts, symptom management

Recommendation 1.6. It is recommended that primary care clinicians should counsel patients to adhere to adjuvant endocrine (antiestrogen) therapy (LOE = 2A).

Clinical interpretation. Endocrine therapy (tamoxifen, aromatase inhibitors, or ovarian suppression therapy) used as adjuvant systemic therapy for 5 to 10 years reduces the risk of recurrence and of subsequent second primary breast cancers and improves overall survival. Adherence to endocrine therapy is necessary to achieve its survival benefits. Unfortunately, some women discontinue endocrine therapy because of cost, side effects, and other reasons. Reported adherence to a 5-year course of therapy ranges from 50% to 92% of breast cancer patients.[43] Primary care clinicians should assess and encourage adherence to adjuvant endocrine therapy at each visit.[9]

Screening for Second Primary Cancers

Cancer screenings in the average risk patient

Recommendation 2.1. It is recommended that primary care clinicians (a) should screen for other cancers, as they would for patients in the general population; and (b) should provide an annual gynecologic assessment for postmenopausal women on selective estrogen receptor modulator therapies (SERMs) (see Table 4).

Clinical interpretation. Women should be advised to follow the ACS screening and early detection guidelines for cervical, colorectal, endometrial, and lung cancers detailed in Table 4.[44] Postmenopausal women who are taking SERMS, such as tamoxifen, should be advised to report any vaginal spotting or bleeding, because these drugs slightly increase the risk of endometrial cancer in postmenopausal women. In the absence of abnormal vaginal spotting or bleeding, periodic imaging is not of value and may lead to unwarranted biopsies.[45] Discuss the risks, benefits, and limitations of screening modalities with your patients.

TABLE 4. American Cancer Society Guidelines for the Early Detection of Cancer in Average Risk, Asymptomatic Individuals[a]

CANCER SITE	POPULATION	TEST OR PROCEDURE	FREQUENCY
Cervix	Women, ages 21-65 y	Pap test and HPV DNA test	Cervical cancer screening should begin at age 21 y; for women ages 21-29 y, screening should be done every 3 y with conventional or liquid-based Pap tests; for women ages 30-65 y, screening should be done every 5 y with both the HPV test and the Pap test (preferred) or every 3 y with the Pap test alone (acceptable); women older than 65 y who have had $\geq$3 consecutive negative Pap tests or $\geq$2 consecutive negative HPV and Pap tests within the last 10 y, with the most recent test occurring within the last 5 y, and women who have had a total hysterectomy should stop cervical cancer screening if they no longer have a cervix and are without a history of cervical intraepithelial lesion grade 2 or a more severe diagnosis in the past 20 y or if they have ever had cervical cancer; women at any age should not be screened annually by any screening method
Colorectal	Women aged 50 y and older	FOBT with at least 50% test sensitivity for cancer, or FIT with at least 50% test sensitivity for cancer, or	Annual, starting at age 50 y; testing at home with adherence to manufacturer's recommendation for collection techniques and number of samples is recommended; FOBT with the single stool sample collected on the clinician's fingertip during a DRE in the health care setting is not recommended; guaiac-based toilet bowl FOBT tests also are not recommended; compared with guaiac-based tests for the detection of occult blood, immunochemical tests are more patient-friendly and are likely to be equal or better in sensitivity and specificity; there is no justification for repeating FOBT in response to an initial positive finding
		Stool DNA test,[b] or	Interval uncertain, starting at age 50 y
		FSIG, or	Every 5 y, starting at age 50 y; FSIG can be performed alone or consideration can be given to combining FSIG performed every 5 y with a highly sensitive guaiac-based FOBT or FIT performed annually
		DCBE, or	Every 5 y, starting at age 50 y
		Colonoscopy	Every 10 y, starting at age 50 y
		CT colonography	Every 5 y, starting at age 50 y
Endometrial	Women, at menopause		At the time of menopause, women at average risk should be informed about the risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting to their physicians
Lung	Current or former smokers ages 55-74 y in good health with at least a 30 pack-y history	LDCT	Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about lung cancer screening with apparently healthy patients ages 55-74 y who have at least a 30 pack-y smoking history and who currently smoke or have quit within the past 15 y; a process of informed and shared decision-making with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with LDCT should occur before any decision is made to initiate lung cancer screening; smoking-cessation counseling remains a high priority for clinical attention in discussions with current smokers, who should be informed of their continuing risk of lung cancer; screening should not be viewed as an alternative to smoking cessation
Cancer-related checkup	Women, aged 20 y and older		On the occasion of a periodic health examination, the cancer-related checkup should include examination for cancers of the thyroid, ovaries, lymph nodes, oral cavity, and skin as well as health counseling about tobacco, sun exposure, diet and nutrition, risk factors, sexual practices, and environmental and occupational exposures

CT indicates computed tomography; DCBE, double-contrast barium enema; DRE, digital rectal examination; FIT, fecal immunochemical test; FOBT, fecal occult blood test; FSIG, flexible sigmoidoscopy; HPV, human papillomavirus; LDCT, low-dose helical computed tomography; Pap, Papanicolaou. [a]Recommendation 2.1: Among average-risk patients, it is recommended that primary care clinicians (a) should screen for other cancers as they would for patients in the general population; and (b) should provide an annual gynecological assessment for postmenopausal women on selective estrogen receptor modulator therapies. [b]The stool DNA test approved for colorectal cancer screening in 2008 is no longer commercially available; new stool DNA tests are presently undergoing evaluation and may become available at some future time.

Assessment and Management of Physical and Psychosocial Long-Term and Late Effects of Breast Cancer and Treatment

The risk of physical long-term and late effects after therapy for breast cancer is associated with several factors, including: (a) type of treatment, (b) duration and dose of treatment(s) (increasing cumulative dose and duration of therapy increase the potential risk), (c) specific type of chemotherapy, (d) receipt of and type of hormone treatment, and (e) age of patient during treatment. Modalities of treatment include surgery, radiation therapy, chemotherapy, targeted therapy, and/or endocrine therapy. Primary care clinicians should refer to the patient's cancer treatment summary, if available, for specific drugs and doses (see Recommendation 5.1). Table 5 lists potential physical and psychosocial long-term and late effects associated with surgery, radiation, chemotherapy, hormone therapy, and targeted treatment. Long-term effects are medical problems that develop during active treatment and persist after the completion of treatment, whereas late effects are medical problems that develop or become apparent months or years after treatment is completed. Recommendations for the assessment and management of specific physical and psychosocial long-term and late effects most commonly experienced by breast cancer survivors are detailed in Table 6.

Body image concerns

Recommendation 3.1. It is recommended that primary care clinicians (a) should assess for patient body image/appearance concerns (LOE = 0); (b) should offer the option of adaptive devices (eg, breast prostheses, wigs) and/or surgery when appropriate (LOE = 0); and (c) should refer for psychosocial care as indicated (LOE = IA).

Clinical interpretation. Body image/appearance changes can be a major area of concern, affecting from 31% to 67% of breast cancer survivors.[46] Factors such as the loss of a breast, scarring and/or lymphedema after surgery, hair loss or sexual dysfunction/chemotherapy-related early menopause, skin changes from radiation, and weight gain can all lead to changes in body image with negative implications on short-term and long-term QoL.[47] These body image implications are especially relevant for young breast cancer survivors.[47-50] Among female breast cancer survivors who are sexually active, greater body image problems have been associated with mastectomy with or without reconstruction, hair loss from chemotherapy, concern with weight change, decreased self-esteem before the time of cancer diagnosis, poorer mental health, and a partner's difficulty understanding one's feelings.[49]

Patients with radiation-associated breast/soft-tissue fibrosis should be considered for therapy with oral pentoxifylline (Trental) and vitamin E.[51-54] A radiation oncologist should evaluate such patients to assure that the clinical findings are consistent with the radiation treatment delivered. Recurrent cancer or infection can sometimes be mistaken for radiation-associated fibrosis. Primary care clinicians should refer back to the oncologist (medical, surgical, or radiation) if they ever are uncertain about potential recurrence.

Breast-reconstructive surgery should be considered in women who do not feel comfortable with the results of their initial breast surgery, whether lumpectomy or mastectomy, because there may be ways to improve symmetry or appearance. Breast forms/prostheses or bras are options that are available to survivors who have undergone mastectomy or nonbreast-conserving therapies and generally require a prescription from a physician. Special lingerie, attachable nipples, and other resources can help the survivor regain self-esteem. Most insurance plans cover mastectomy prostheses and specialty bras. In addition, wigs, hats, scarves, and other accessories are available for survivors who experience permanent hair loss (alopecia is a rare complication of chemotherapy) or changes in hair color or texture. Women should check with their insurance company and obtain a prescription from their physicians. Breast cancer care centers or specialists often maintain directories of resources in their community where patients can find these products.

Primary care clinicians should refer patients who have body image concerns that are not corrected by the above options for psychosocial care. For example, for women who experience early menopause or for those with sexual concerns, support groups, psychotherapy, cognitive behavioral therapy, couple-based interventions, or sex therapy may be helpful. Couple-based interventions can promote coping skills and provide specific techniques to address body image issues.[55]

Lymphedema

Recommendation 3.2. It is recommended that primary care clinicians (a) should counsel survivors on how to prevent/reduce risk of lymphedema, including weight loss for those who are overweight or obese (LOE = 0); and (b) should refer patients with clinical symptoms or swelling suggestive of lymphedema to a therapist knowledgeable about the diagnosis and treatment of lymphedema, such as a physical therapist, occupational therapist, or lymphedema specialist (LOE = 0).

Clinical interpretation. All breast cancer survivors who undergo breast surgery and/or radiation are at risk for lymphedema. This is arm, breast, or chest wall swelling as a result of a blockage of the lymphatic fluid from the arm and/or breast, leading to retention of fluid and swelling. The incidence of lymphedema among breast cancer survivors varies widely,[56] although it is estimated that over 40% of survivors will experience lymphedema to some degree.[57,58] The risk of

TABLE 5. Summary of Long-Term and Late Effects by Treatment Type[a]

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Surgery	• Lack of skin sensitivity	• Lymphedema
	• Body image issues	• Neuropathy
	• Sexual dysfunction	
	• Numbness	
	• Pain	
	• Limited range of motion	
	• Weakness	
	• Poor cosmetic outcome	
Radiation therapy to the breast/chest wall/regional lymph nodes	• Fatigue[b,c]	• Skin discoloration
	• Skin sensitivity/pain	• Breast may be slightly smaller and firmer than the nonirradiated side (breast asymmetry)
	• Sexual dysfunction	• Skin sensitivity/pain
	• Pain	• Telangiectasia
	• Pneumonitis[b,c]	• Sexual dysfunction
	• Poor cosmetic outcome	• Lymphedema[b]
	• Breast atrophy/asymmetrical breast volume	• Shortness of breath (lung pneumonitis or fibrosis)[b,c]
	• Lymphedema[b]	• Cardiovascular disease (eg, pericardial effusion, pericarditis)[c]
	• Numbness or weakness of the upper extremity[b]	• Numbness or weakness of the upper extremity[c,d]
		• Second primary cancers (eg, soft-tissue sarcomas of thorax, shoulder, and pelvis; lung cancer)[b,c]
Chemotherapy	• Cognitive impairment	• Osteoporosis/osteopenia
	• Fatigue	• Increased risk of cardiovascular disease (cardiomyopathy, congestive heart failure) with anthracycline-based chemotherapy
	• Ovarian failure with or without menopausal symptoms	• Increased risk of leukemia and myelodysplastic syndrome with alkylating agents, anthracyclines, other topoisomerase II inhibitors, and other agents with immunosuppressive potential
	• Sexual dysfunction	
	• Change in libido	
	• Infertility	
	• Weight gain	
	• Obesity	
	• Neuropathy, especially after taxanes	
	• Oral health issues	
	• Hair loss	
Hormonal therapy		
• Tamoxifen	• Hot flashes	• Increased risk of stroke
	• Changes in menstruation	• Increased risk of endometrial cancer
	• Mood changes	• Increased risk of blood clots
	• Increased triglycerides	• Osteopenia in premenopausal women
• Aromatase inhibitors	• Vaginal dryness	• Increased risk of osteoporosis
	• Decreased libido	• Increased risk of fractures
	• Musculoskeletal symptoms/pain	
	• Cholesterol elevation	

TABLE 5. *Continued*

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Targeted therapy		
• Trastuzumab	• Increased risk of cardiac dysfunction	
General psychosocial long-term and late effects	• Depression	
	• Distress—multifactorial unpleasant experience of psychological, social, and/or spiritual nature	
	• Worry, anxiety	
	• Fear of recurrence	
	• Fear of pain	
	• End-of-life concerns: Death and dying	
	• Loss of sexual function and/or desire	
	• Challenges with body image	
	• Challenges with self-image	
	• Relationship and other social role difficulties	
	• Return-to-work concerns and financial challenges	

[a]Note: Long-term effect is something that starts during treatment and does not subside, such as pain, fatigue, cognitive changes. In contrast, a late effect is something that develops much later, such as a second malignancy, heart failure, lymphedema. Some long-term effects are the same or overlap with late effects; for example, lymphedema can be either. [b]Risks are increased in patients who also received radiotherapy to the supraclavicular lymph nodes. [c]Risks are increased in patients who also received radiotherapy to the internal mammary lymph nodes. [d]There is a need to be careful, because these can also be signs of recurrent cancer, typically with pain; an appropriate consultation with the radiation oncologist may be warranted.

lymphedema is much lower with sentinel lymph node dissections than with the full axillary lymph node dissection previously performed in all cases.[59] Lymphedema may occur immediately after treatment or develop after many years. Radiation treatment may cause or exacerbate lymphedema, especially radiation to the supraclavicular lymph nodes or axilla.[60]

The degree of swelling associated with lymphedema varies widely, even for those who receive similar surgery and/or radiation. In most cases, it is generally limited in extent and is not disabling. In some cases, the swelling is extensive and leads to significant disability, such as limitation of the ability to perform fine motor functions with the hand as well as limited range of motion of other affected joints.[61] In addition, the swelling may cause symptoms ranging from mild discomfort to overt pain. The swelling may be of a noticeable degree, making clothes difficult to fit and causing pain from the added weight of the arm. The International Society of Lymphology provides a staging system to categorize the extent of lymphedema.[62] Patients with lymphedema are also at greater risk for the development of cellulitis of the breast, arm, or chest, which, especially if not promptly treated with antibiotics, may exacerbate lymphedema.

More studies are needed in the area of lymphedema prevention above and beyond biopsy types and surgical strategies (sentinel lymph node dissections and axillary reverse mapping).[63] Obesity is also a risk factor for lymphedema,[64,65] so physicians should recommend weight loss for those who are overweight or obese and emphasize the importance of maintaining a normal weight (see also Recommendation 5.2). Historically, patients with axillary lymphadenectomies/radiation have been advised to avoid physical activity and heavy lifting with the arm on the affected side. However, one study has shown that supervised, slowly progressive resistance training is safe and effective for breast cancer survivors with regard to lymphedema development. Furthermore, this type of physical activity may reduce the likelihood of arm swelling among breast cancer survivors at high risk for lymphedema who have had five or more lymph nodes removed and may improve the symptoms and severity for those in whom the condition was already present.[66] While the results of this study suggest a promising intervention for lymphedema, additional research is warranted. Therefore, primary care clinicians should focus on the early identification and management of lymphedema among their patients with breast cancer.[67]

Patients who develop clinical symptoms or swelling suggestive of lymphedema should be referred to a therapist knowledgeable about the diagnosis and treatment of lymphedema. Depending on available resources in a community, this may be a physical[68] or occupational[69] therapist or a specialist therapist trained in lymphedema management.

Cardiotoxicity

Recommendation 3.3. It is recommended that primary care clinicians (a) should monitor lipid levels and provide

TABLE 6. Guideline for Assessment and Management of Physical and Psychosocial Long-Term/Late Effects

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 3.1: Body image concerns	
(a) Should assess for patient body image/appearance concerns	0 (Assessment)
(b) Should offer the option of adaptive devices (eg, breast prostheses, wigs) and/or surgery when appropriate	0 (Adaptive devices)
(c) Should refer for psychosocial care as indicated	IA (Couple-based intervention)
Recommendation 3.2: Lymphedema	
(a) Should counsel survivors on how to prevent/reduce the risk of lymphedema, including weight loss for those who are overweight or obese	0 (Prevention)
(b) Should refer patients with clinical symptoms or swelling suggestive of lymphedema to a therapist knowledgeable about the diagnosis and treatment of lymphedema, such as a physical therapist, occupational therapist, or lymphedema specialist	0 (Referral)
Recommendation 3.3: Cardiotoxicity	
(a) Should monitor lipid levels and provide cardiovascular monitoring, as indicated	0 (Monitoring)
(b) Should educate breast cancer survivors on healthy lifestyle modifications, potential cardiac risk factors, and when to report relevant symptoms (shortness of breath or fatigue) to their health care provider	I (Lifestyle modifications)
Recommendation 3.4: Cognitive impairment	
(a) Should ask patients if they are experiencing cognitive difficulties	0 (Assessment)
(b) Should assess for reversible contributing factors of cognitive impairment and optimally treat when possible	IA (Contributing factors)
(c) Should refer patient with signs of cognitive impairment for neurocognitive assessment and rehabilitation, including group cognitive training if available	IA (Group cognitive rehabilitation)
Recommendation 3.5: Distress, depression, and anxiety	
(a) Should assess patients for distress, depression, and/or anxiety	I (Assessment)
(b) Should conduct a more probing assessment for patients at a higher risk of depression (eg, young patients, those with a history of prior psychiatric disease, and patients with low socioeconomic status)	III (At-risk groups)
(c) Should offer in-office counseling and/or pharmacotherapy and/or refer to appropriate psycho-oncology and mental health resources as clinically indicated if signs of distress, depression, or anxiety are present	I (Interventions)
Recommendation 3.6: Fatigue	
(a) Should assess for fatigue and treat any causative factors for fatigue, including anemia, thyroid dysfunction, and cardiac dysfunction	0 (Assessment)
(b) Should offer treatment or referral for factors that may impact fatigue (eg, mood disorders, sleep disturbance, pain, etc) for those who do not have an otherwise identifiable cause of fatigue	I (Causative factors)
(c) Should counsel patients to engage in regular physical activity and refer for cognitive behavioral therapy (CBT) as appropriate	I (Physical activity, CBT)
Recommendation 3.7: Bone health	
(a) Should refer postmenopausal breast cancer survivors for a baseline DEXA scan	0 (Baseline DEXA)
(b) Should refer for repeat DEXA scans every 2 y for women taking an aromatase inhibitor, premenopausal women taking tamoxifen and/or a GnRH agonist, and women who have chemotherapy-induced premature menopause	0 (High risk)
Recommendation 3.8: Musculoskeletal health	
(a) Should assess for musculoskeletal symptoms, including pain, by asking patients about their symptoms at each clinical encounter	0 (Assessment)
(b) Should offer one or more of the following interventions based on clinical indication: acupuncture, physical activity, and referral for physical therapy or rehabilitation	III (Interventions)
Recommendation 3.9: Pain and neuropathy	
(a) Should assess for pain and contributing factors for pain with the use of a simple pain scale and comprehensive history of the patient's complaint	0 (Assessment)

TABLE 6. *Continued*

RECOMMENDATION	LEVEL OF EVIDENCE[a]
(b) Should offer interventions, such as acetaminophen, nonsteroidal anti-inflammatory drugs, physical activity, and/or acupuncture, for pain	I (Interventions)
(c) Should refer to an appropriate specialist, depending on the etiology of the pain once the underlying etiology has been determined (eg, lymphedema specialist, occupational therapist, etc)	0 (Referral)
(d) Should assess for peripheral neuropathy and contributing factors for peripheral neuropathy by asking the patient about their symptoms, specifically numbness and tingling in their hands and/or feet, and the characteristics of those symptoms	0 (Assessment)
(e) Should offer physical activity for neuropathy.	IA (Physical activity)
(f) Should offer duloxetine for patients with neuropathic pain, numbness, and tingling	IB (Duloxetine)
Recommendation 3.10: Infertility	
Should refer survivors of childbearing age who experience infertility to a specialist in reproductive endocrinology and infertility as soon as possible	0
Recommendation 3.11: Sexual health	
(a) Should assess for signs and symptoms of sexual dysfunction or problems with sexual intimacy	0 (Assessment)
(b) Should assess for reversible contributing factors to sexual dysfunction and treat when appropriate	0 (Contributing factors)
(c) Should offer nonhormonal, water-based lubricants and moisturizers for vaginal dryness	IA (Nonhormonal lubricants and moisturizers)
(d) Should refer for psychoeducational support, group therapy, sexual counseling, marital counseling or intensive psychotherapy, when appropriate	IA (Counseling)
Recommendation 3.12: Premature menopause/hot flashes	
Should offer selective serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), gabapentin, lifestyle modifications and/or environmental modifications to help mitigate vasomotor symptoms of premature menopausal symptoms	IA (SNRI and SSRI use)

DEXA indicates dual-energy x-ray absorptiometry; GnRH, gonadotropin-releasing hormone.
[a]Level of evidence: I indicates meta-analyses of randomized controlled trials (RCTs); IA, RCT of breast cancer survivors; IB, RCT based on cancer survivors across multiple sites; IC, RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing fatigue, lymphedema, etc); IIA, nonrandomized controlled trial (non-RCT) based on breast cancer survivors; IIB, non-RCT based on cancer survivors across multiple sites; IIC, non-RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing urinary incontinence, erectile dysfunction, etc); III, case-control or prospective cohort study; 0, expert opinion, observation, clinical practice, literature review, or pilot study.

cardiovascular monitoring, as indicated (LOE = 0); and (b) should educate breast cancer survivors on healthy lifestyle modifications, potential cardiac risk factors, and when to report relevant symptoms (shortness of breath or fatigue) to their health care provider (LOE = I).

Clinical interpretation. Radiation, chemotherapy, and hormonal/endocrine therapy with aromatase inhibitors have been associated with an increased risk of cardiovascular disease in patients with breast cancer.[70,71] The risk of heart disease increases in postmenopausal women, as endogenous estrogens in younger women contribute to the low prevalence of cardiovascular disease in that population. Therefore, breast cancer patients who experience treatment-related early menopause may be at higher risk for heart disease than age-matched women in the general population. The chemotherapeutic agents epirubicin and doxorubicin are associated with a low but real risk of cardiomyopathy[72]; similarly, trastuzumab is associated with an increased risk of cardiac dysfunction, most notably when given concomitantly or after an anthracycline, as has been detailed by the European Society for Medical Oncology.[73] Aromatase inhibitors can raise cholesterol levels[74,75] and the risk of diabetes. Significant weight gain may lead to hypertension and insulin resistance, which further elevate the risk of cardiovascular disease. Primary care clinicians should monitor lipid levels and engage in cardiovascular monitoring consistent with clinical standards for other high-risk populations (eg, US Preventive Services Task Force recommendations[29]).

It is important to educate breast cancer survivors about lifestyle modifications, including smoking cessation, diet, and exercise (see Recommendations 4.3-4.5), that may reduce the risk or severity of cardiotoxicity or cardiovascular diseases in general. Patients should be advised to be aware of the potential risk for cardiotoxicities and report symptoms such as shortness of breath or fatigue (without an otherwise identifiable cause) to their health care provider. However, routine screening or testing for cardiovascular disease in asymptomatic patients beyond careful history and physical examination are not warranted. ASCO is currently developing a guideline on the prevention and monitoring of cardiac dysfunction in survivors of adult cancers.

Cognitive impairment

Recommendation 3.4. It is recommended that primary care clinicians (a) should ask patients if they are experiencing cognitive difficulties (LOE = 0); (b) should assess for reversible contributing factors of cognitive impairment and optimally treat when possible (LOE = IA); and (c) should refer patients with signs of cognitive impairment for neurocognitive assessment and rehabilitation, including group cognitive training if available (LOE = IA).

Clinical interpretation. Impairment in cognitive function as a result of cancer and its treatment can lead to distress and impaired QoL in breast cancer survivors. Up to 75% of breast cancer patients in treatment and 35% after treatment report cognitive impairment, including problems with concentration, executive function, and memory.[76-78] Cognitive impairment can also have detrimental effects on the survivor's role within the family, in the workplace, and in society.[79,80] Clinicians should ask patients if they are having cognitive difficulties and listen to family members' reporting of patient cognitive symptoms. If this is an issue, consultation with a neuropsychologist for assessment and referral for cognitive rehabilitation strategies should be offered as one would do with the general population.

The causes of cognitive impairment are thought to be multifactorial and may include treatable conditions, such as fatigue, insomnia, and depression. Links have been suggested between cognitive impairment and adjuvant chemotherapy,[81-84] surgery/anesthesia, endocrine therapy,[76,85] as well as cancer itself.[76] Research suggests that older adults and/or those with lower cognitive reserves may be more susceptible to cognitive impairment from treatment[86] and that there may also be genetic factors associated with certain estrogen metabolism genes.[87,88]

The treatment of cognitive impairment in the breast cancer survivor is not well established. A few studies have shown some success with pharmaceuticals, such as modafinil,[89] that have helped improve cognitive impairment, but the data are not consistent.[90] Cognitive rehabilitation strategies, including the practice of group cognitive training (ie, interventions geared toward improving, restoring, or maintaining mental function through structured, repetitive practice of tasks posing a mental challenge or requiring the person to problem solve) has been found to be helpful at reducing cognitive impairment in breast cancer survivors.[91,92] Primary care clinicians should provide referral for neurocognitive assessment and rehabilitation as clinically indicated.

Distress, depression, and anxiety

Recommendation 3.5. It is recommended that primary care clinicians (a) should assess patients for distress, depression, and/or anxiety (LOE = I); (b) should conduct a more probing assessment for patients at a higher risk of depression (eg, young patients, those with a history of prior psychiatric disease, and patients with low socioeconomic status; LOE = III); and (c) should offer in-office counseling and/or pharmacotherapy and/or refer to appropriate psycho-oncology and mental health resources as clinically indicated if signs of distress, depression, or anxiety are present (LOE = I).

Clinical interpretation. Many cancer survivors report ongoing difficulties in recovery and returning to "normal" after treatment.[1,2,17,93] Some survivors of cancer experience fear of recurrence (FOR),[94] which contributes to significant mental health problems for which they may already have an increased risk, including distress, depression, and anxiety.[95,96] African American breast cancer survivors and those who are older have been found to have less FOR. A shorter interval of time since diagnosis, having received chemotherapy, and having more symptoms, especially pain, have been related to higher levels of FOR.[97] Prevalence estimates for anxiety, depression, and distress in cancer survivors vary widely as a result of inconsistency in the use of measurement tools and differences in methodological approaches, such as the choice of comparators from the general population. The estimated prevalence of anxiety and depression is 17.9% and 11.6%, respectively, among the general cancer survivor population.[98] In a systematic review of observational studies, the prevalence of depression and anxiety specifically among breast cancer survivors was 22% (range, 13%-56%) using the Center for Epidemiological Studies for Depression, 22% (range, 17%-48%) using the Beck Depression Inventory, and 10% (range, 1%-22%) using the Hospital Anxiety and Depression Scale.[99]

To provide timely and appropriate support for their patients with a history of breast cancer, primary care clinicians should be familiar with the mental health concerns they may experience, the tools to screen for and assess these problems, and the resources to care for their patients. A tool for initial screening is the distress thermometer (NCCN.org), with scores from 0 (no distress) to 10 (extreme distress). A score of 4 or higher[100] suggests a level of distress that has clinical significance. The Patient Health Questionnaire-9[101] and the Generalized Anxiety Disorder 7-item scale[102] are validated methods for screening for depression and anxiety, respectively, and are available free online at phqscreeners.com/. For patients with elevated scores on these screeners, further discussion and assessment of the issues are needed, as in the general population. For more information on screening and assessing adults with cancer for psychosocial distress, depression and anxiety algorithms reproduced from the ASCO guidelines are provided online (see online supporting information).[15]

The risk of having major depression after a diagnosis of breast cancer was higher among younger patients, patients with a history of prior psychiatric disease, patients with low socioeconomic status, and those who were unemployed.[103]

Among patients with breast cancer, decreased libido, poor self-image, and relationship issues were common among those who were depressed.[104-106]

Treatment for depression and anxiety in cancer patients and survivors with medication and psychotherapy is comprehensively described in the recent ASCO anxiety and depression guideline adaptation (instituteforquality.org/screening-assessment-and-care-anxiety-and-depressive-symptoms-adults-cancer-american-society).[15] In addition to or instead of pharmacotherapy, mindfulness-based approaches, expression of positive emotions, spiritual interventions, hope therapy, and meaning-making interventions have shown promise in addressing psychosocial needs of breast cancer survivors.[107] Although the methodology used to study the effectiveness of these interventions varied, survivors experienced positive changes, such as enhanced QoL and well-being.[107] If a patient has a clinically significant score on any of the previously discussed instruments, it is recommended that primary care clinicians refer patients to the appropriate psychosocial oncology specialists, mental health professionals, and/or resources in the community.[26] After referring to the appropriate resource(s), primary care clinicians should follow-up with patients to check their adherence to recommended therapies and/or assess the need for additional referrals. If a patient has difficulties with adherence to recommendations, primary care clinicians should identify the challenges with adherence and help the patient overcome these obstacles before discussing alternative interventions.[15] The American Psychosocial Oncology Society website (apos-society.org/) can help primary care clinicians identify resources for their patients.

Fatigue

Where appropriate, these recommendations build upon the recently published ASCO screening, assessment and treatment of cancer-related fatigue guidelines among adult cancer survivors.[25]

Recommendation 3.6. It is recommended that primary care clinicians (a) should assess for fatigue and treat any causative factors for fatigue, including anemia, thyroid dysfunction, and cardiac dysfunction (LOE = 0); (b) should offer treatment or referral for factors that may impact fatigue (eg, mood disorders, sleep disturbance, pain, etc) for those who do not have an otherwise identifiable cause of fatigue (LOE = I); and (c) should counsel patients to engage in regular physical activity and refer for cognitive behavioral therapy as appropriate (LOE = I).

Clinical interpretation. Cancer-related fatigue is very common among those treated for cancer, especially those who undergo treatment with radiation therapy and chemotherapy,[13,25,108] with an estimated prevalence of 28% to 91%.[109,110] Recommendations for how to screen and assess for fatigue are provided online (see online supporting information) and come from the ASCO guidelines.[25] For some, fatigue lasts long after treatment and can significantly interfere with QoL. Treatable causes of fatigue include anemia, thyroid dysfunction, and cardiac dysfunction.[25] For those who do not have an identifiable physical cause of fatigue (anemia), contributing factors, such as mood disorders, sleep disturbance, and pain, should be addressed.[25] Additional information related to distress/depression and pain can be found under Recommendation 4.5.

A regular exercise regimen can reduce fatigue, help survivors feel better physically and emotionally, and help them cope, as has been demonstrated by several RCTs in breast cancer survivors[23,25,111] (see also Recommendation 4.3). Cognitive behavioral therapy may also lessen fatigue.[112,113] There are minimal data to support use of pharmacologic agents for the management of fatigue in this population.[25] Interventions should be tailored to the needs and abilities of the individual breast cancer survivor. ASCO has more detailed information on the management of fatigue for cancer survivors (instituteforquality.org/screening-assessment-and-management-fatigue-adult-survivors-cancer-american-society-clinical[25]).

Bone health

Recommendation 3.7. It is recommended that primary care clinicians (a) should refer postmenopausal breast cancer survivors for a baseline dual-energy x-ray absorptiometry (DEXA) scan (LOE = 0); and (b) should refer for repeat DEXA scans every 2 years for women who are taking an aromatase inhibitor, premenopausal women who are taking tamoxifen and/or a gonadotropin-releasing hormone (GnRH) agonist, and women who have chemotherapy-induced premature menopause (LOE = 0).

Clinical interpretation. The rate and magnitude of bone loss caused by cancer therapy are significantly higher than normal age-related bone loss.[114,115] Up to 80% of breast cancer patients experience bone loss.[116,117] Osteoporosis risk factors unique to patients after cancer therapy include chemotherapy-induced premature menopause, GnRH suppression of gonadal function, antiestrogen therapies, and glucocorticoids.[118] These risk factors are cumulative with other known risk factors, including age, prior fracture history, and family history of fracture.[119,120] Lifestyle-related factors, including smoking, excess alcohol, inadequate exercise, low calcium, and vitamin D deficiency, are common in this population and increase the risk of osteoporosis.[118] Primary care clinicians should manage symptoms as they would in the general population.

Postmenopausal women treated with aromatase inhibitors are at increased risk of osteoporosis and should have initial and periodic (every 2 years) DEXA scan screening. If major risk factors change, then it is reasonable to consider a

repeat DEXA scan at 1 year.[118] All postmenopausal women or premenopausal women receiving ovarian suppression therapy with GnRH agonists are at risk for developing osteoporosis and should be screened according to the US Preventive Services Task Force[30] and the American Association of Clinical Endocrinologists guide for postmenopausal osteoporosis diagnosis and treatment.[31]

Initial strategies to reduce the morbidity associated with bone loss include education about risk factors and a healthy lifestyle. These should include physical activity and regular weight-bearing exercise, avoiding tobacco use, limiting alcohol intake, and consider supplementation with calcium (to achieve a total intake of 1200 mg/day) and Vitamin D_3 (600-1000 IU/day) for all adults older than 50 years.[118,121-126] In addition to lifestyle and nutritional interventions, pharmacologic options should be considered in patients at high risk for bone loss and/or fracture.[118] Bisphosphonates or denosumab can prevent bone loss and/or treat established osteoporosis.[118,127-129] However, these drugs do have side effects and risks, so that the risk versus benefit of antiresorptive therapy must be carefully considered before starting therapy. Estrogen receptor modulators (raloxifene and tamoxifen) also have antiresorptive properties. However, in one large trial, combining an SERM and an aromatase inhibitor blunted the reduction in breast cancer recurrence compared with an aromatase inhibitor alone. Therefore, SERMs should not be used for the prevention of osteoporosis in women who are taking an aromatase inhibitor.[130]

Musculoskeletal health

Recommendation 3.8. It is recommended that primary care clinicians (a) should assess for musculoskeletal symptoms, including pain, by asking patients about their symptoms at each clinical encounter (LOE = 0); and (b) should offer one or more of the following interventions based on clinical indication: acupuncture, physical activity, referral for physical therapy or rehabilitation (LOE = III).

Clinical interpretation. Breast cancer survivors may report difficulties with the ipsilateral upper extremity after surgery, including decreased range of motion, rotator cuff injury, adhesive capsulitis ("frozen shoulder" with stiffness and pain in the shoulder joint), and axillary web syndrome ("cording" in the skin of the inner arm with sensations of pain and tightness that appear as a web or a corded rope).[131,132] These abnormalities can lead to a decreased ability to perform activities of daily living and can impact employment. Systemic therapies for breast cancer have also been associated with the development of musculoskeletal symptoms.[133] The prevalence of musculoskeletal symptoms among breast cancer patients varies greatly: these include limited shoulder range of motion (range, 1.5%-50% of patients), musculoskeletal pain (range, 12%-51% of patients), upper limb weakness (range, 18%-23% of patients), and numbness (range, 29%-81% of patients).[131,134-136] In particular, up to 50% of postmenopausal women receiving treatment with aromatase inhibitor medications report arthralgias (joint pain) and myalgias (muscle pain) that are severe enough in 20% of women to lead to treatment discontinuation.[137,138] These aromatase inhibitor-associated musculoskeletal symptoms are often not responsive to nonsteroidal anti-inflammatory drugs or acetaminophen. Another option for treatment is to change from one antiestrogen therapy to another. About 40% who discontinue the drug may tolerate a different aromatase inhibitor or a different formulation of the aromatase inhibitor. The rest generally tolerate tamoxifen.[139] Poor compliance/adherence to therapy has been shown to result in an increased risk of breast cancer recurrence, so helping patients manage their symptoms and encouraging drug compliance is important.[140]

Physical therapy, including stretching and other exercises, has been shown to be effective for managing post-surgical musculoskeletal symptoms.[141,142] Recent data from the Hormones and Physical Exercise trial, a prospective cohort study, demonstrated that participation in an intensive exercise regimen resulted in a 20% decrease in aromatase inhibitor-associated pain.[143] To date, only acupuncture[144] and exercise[143] have been demonstrated to result in a statistically significant improvement in aromatase inhibitor-associated symptoms.

Pain and neuropathy

Recommendation 3.9. It is recommended that primary care clinicians (a) should assess for pain and contributing factors for pain with the use of a simple pain scale and comprehensive history of the patient's complaint (LOE = 0); (b) should offer interventions, such as acetaminophen, nonsteroidal anti-inflammatory drugs, physical activity, and/or acupuncture, for pain (LOE = I); (c) should refer to an appropriate specialist, depending on the etiology of the pain once the underlying etiology has been determined (eg, lymphedema specialist, occupational therapist, etc; LOE = 0); (d) should assess for peripheral neuropathy and contributing factors for peripheral neuropathy by asking the patient about their symptoms, specifically numbness and tingling in their hands and/or feet, and the characteristics of that symptom (LOE = 0); (e) should offer physical activity for neuropathy (LOE = IA); and (f) should offer duloxetine for patients with neuropathic pain, numbness, and tingling (LOE = IB).

Clinical interpretation. A substantial percentage of breast cancer survivors experience long-term, treatment-related chronic pain that can negatively impact QoL. Published reports demonstrate that from 25% to 60% of breast cancer survivors experience chronic pain as a result of the

treatments administered, including surgery, radiation therapy, chemotherapy, and endocrine therapy.[138,145-148]

Patients should also be evaluated for secondary causes of pain, such as lymphedema or tightness of the chest wall or axilla, and should be referred to lymphedema specialists or occupational therapists as indicated. Once the workup and assessment are complete and underlying causes are identified or ruled out, chronic pain after breast cancer surgery is typically treated with standard analgesics, including acetaminophen and nonsteroidal anti-inflammatory drugs.

Acupuncture and physical activity have been shown in meta-analyses of RCTs to improve pain among breast cancer survivors and are typically used to complement traditional cancer care. Treatment-related joint pain among breast cancer survivors is quite commonly treated with acupuncture, and many trials and systematic reviews have demonstrated its efficacy in decreasing pain intensity.[144,149] However, evidence is lacking to show that acupuncture directly benefits breast cancer survivors who are experiencing CIPN. Physical activity has been shown in multiple RCTs to improve pain.[150]

Neuropathy, including numbness, tingling, and burning pain, is also common after a diagnosis of breast cancer and subsequent treatment. It is particularly common after surgery and after treatment with taxane-based or platinum-based chemotherapy regimens and is reported in 30% to 40% of patients.[147] ASCO recently published a clinical practice guideline about the prevention and management of CIPN (instituteforquality.org/prevention-and-management-chemotherapy-induced-peripheral-neuropathy-survivors-adult-cancers),[14] and we endorse that guideline.

Prevention and treatment approaches for the management of CIPN in adult cancer survivors, reproduced from the ASCO guideline, are available online (see online supporting information). In a few small RCTs with breast cancer survivors, physical activity has been shown to improve arthralgias, neuropathy, and neuropathy symptoms.[143,151] Several pharmaceutical agents have been tested for the management of CIPN. In a randomized, placebo-controlled trial, the serotonin-norepinephrine reuptake inhibitor (SNRI) duloxetine was shown to decrease neuropathic pain significantly more than placebo, and it may also improve numbness and tingling. That trial used an initial dose of 30 mg daily for the first week to reduce the likelihood of nausea; then, the dose was increased to 60 mg daily. The associated relative risk benefit was 30% to 50% in pain reduction.[152] Studies of tricyclic antidepressants and anticonvulsants have not demonstrated consistent significant improvements in symptoms. Additional recommendations for the prevention and management of CIPN can be found in the recently published ASCO guidelines.[14]

Infertility

Recommendation 3.10. It is recommended that primary care clinicians should refer survivors of childbearing age who experience infertility to a specialist in reproductive endocrinology and infertility as soon as possible (LOE = 0).

Clinical interpretation. Infertility as a result of cancer treatment is a potential long-term side effect faced by younger breast cancer survivors (younger than age 45 years). When it occurs, it can have a profound impact on a survivor's physical and psychosocial QoL.[47] Breast cancer patients between ages 20 and 45 years represent 10.9% of all new breast cancer cases in the United States,[2] making infertility an issue for many younger survivors.[153]

Chemotherapy can be gonadotoxic, leading to reduced fertility or early menopause secondary to premature ovarian failure.[76,153] Many of the most frequently used chemotherapy agents in the treatment of breast cancer (eg, alkylating agents, platinum agents, and taxanes) are also those that most often lead to premature ovarian failure.[154] The incidence of chemotherapy-related amenorrhea increases with age, as the female ovarian reserve is nonrenewable and diminishes steadily with age. However, there is considerable variation in ovarian reserve among women of similar age.[155] There is limited literature related to the gonadotoxicity of biologics and targeted therapies, and more studies are needed. Primary care clinicians should involve the treating medical oncologist in any potential discussion related to the optimal time for pregnancy after the completion of breast cancer treatment. Premenopausal women who desire pregnancy and are having difficulty conceiving for 6 months or more (or who have had more than one miscarriage) should be referred to a fertility specialist. Timely referral is crucial because of the rapid loss of ovarian reserve in these women.

Sexual health

Recommendation 3.11. It is recommended that primary care clinicians (a) should assess for signs and symptoms of sexual dysfunction or problems with sexual intimacy (LOE = 0); (b) should assess for reversible contributing factors to sexual dysfunction and treat when appropriate (LOE = 0); (c) should offer nonhormonal, water-based lubricants and moisturizers for vaginal dryness (LOE = IA); and (d) should refer for psychoeducational support, group therapy, sexual counseling, marital counseling, or intensive psychotherapy when appropriate (LOE = IA).

Clinical interpretation. Sexual complaints are a common problem among breast cancer survivors that should be assessed. They can include sexual desire disorder/decreased libido (range, 23%-64% of patients), arousal or lubrication concerns (range, 20%-48% of patients), orgasmic concerns (range, 16%-36% of patients), and dyspareunia (range, 35%-38% of patients).[76] Patients who receive chemotherapy tend to have more of these sexual concerns than those treated only with surgery and/or radiation.[49] Treatment with aromatase inhibitors may cause vaginal dryness,

dyspareunia (which can be severe), menopausal symptoms, and loss of sexual desire.[156] Radiation therapy can often cause skin fibrosis, loss of sexual sensitivity of the skin, and, uncommonly, cardiac and respiratory damage, all of which negatively impact sexual desire and response.[157]

It is important to counsel patients concerning possible sexual dysfunction remedies, including treatments for vaginal dryness. Nonhormonal, water-based lubricants and moisturizers remain the primary treatment.[158] Silicone-based products may last longer than water-based or glycerin-based products. A combination of therapies may provide additional short-term comfort. Hormonal therapies, such as a low-dose estrogen vaginal tablets or an estradiol vaginal ring, may be recommended for vaginal dryness because of urogenital atrophy, although results commonly take approximately 6 to 12 weeks.[158,159] The safety of these therapies in women with a history of breast cancer is not well established at this time. The level of estrogen absorption is variable, which raises concerns in patients who have a history of breast cancer. Use of hormonal therapies for women on aromatase inhibitors is not recommended.[160] Treating dyspareunia secondary to vaginal atrophy and stenosis with vaginal dilators or pelvic floor relaxation techniques may be helpful.[76]

Referral for interventions, such as brief psychoeducational support, group therapy, sexual counseling, marital counseling or intensive psychotherapy, should be offered to all breast cancer survivors with sexual complaints specifically addressing possible anxiety, stress, unpleasant symptoms including hot flashes, sexual comfort in lovemaking, and mood changes.[49,156,161] Taken together, the trio of counseling, over-the-counter treatments, and pharmacologic treatments can do much to ameliorate the sexual issues caused by breast cancer and its management.[156] See Recommendation 3.1 to address body image concerns.

Premature menopause/hot flashes

Recommendation 3.12. It is recommended that primary care clinicians should offer SNRIs, selective serotonin reuptake inhibitors (SSRIs), gabapentin, lifestyle modifications, and/or environmental modifications to help mitigate vasomotor symptoms of premature menopausal symptoms (LOE = IA).

Clinical interpretation. Women can experience menopausal symptoms if chemotherapy results in premature cessation of ovarian function or as a side effect of endocrine therapies. Vasomotor symptoms are typically more severe in younger survivors because of the abrupt change in hormones[162] and, when present, can have a significant impact on QoL. For younger women on endocrine therapies, 50% to 70% will likely experience hot flashes while on tamoxifen.[76]

Systemic hormone therapy is given rarely, if ever, to patients with breast cancer to control menopausal symptoms. Nonhormonal medications like SNRIs and SSRIs can decrease the intensity and severity of vasomotor symptoms, although they are not approved by the US Food and Drug Administration for this indication. The SNRI venlafaxine has been found to be safe and effective in reducing hot flashes.[163] There is concern that SSRIs that inhibit the CYP2D6 (cytochrome P450 2D6) enzyme pathway, such as paroxetine, may reduce the conversion of tamoxifen to active metabolites, although a negative impact on breast cancer outcomes has not been conclusively demonstrated.[164] Consistent with recommendations by the ASCO and NCCN, patients should not be screened for CYP2D6.[9,165] The anticonvulsant gabapentin has also been shown to be effective in reducing hot flashes.[166-168] Similarly, the antihypertensive clonidine has been used in clinical practice.[169] Antihypertensive medications and modifications in lifestyle and environment may also help decrease the intensity and severity of menopausal symptoms. In a meta-analysis of RCTs among breast cancer survivors, acupuncture reduced menopausal symptoms and hot flashes.[170] Lifestyle interventions, including rhythmic breathing, vitamins, exercise, and avoiding spicy foods, caffeine, and alcohol, have had variable results. Environmental modifications, such as cool rooms and dressing in layers, can also be helpful. Complementary therapies have been studied, and some have been found to be minimally effective.[171]

Health Promotion

Women with breast cancer are likely to have long-term survival.[1] Thus, enhancing the length and quality of life is an important goal in the care of patients with breast cancer and in creating a survivorship care plan (see Recommendations 4.1 and 5.1 for more information on survivorship care plans). Healthy behaviors are paramount to reducing the risk of second cancers, comorbidities, obesity, and possibly recurrence; improving prognosis; ameliorating cancer-related symptoms[172-177]; and decreasing the risk of mortality.[174-184]

Table 7 outlines this information, including physical activity, nutrition, and smoking cessation recommendations for breast cancer survivorship, incorporating existing ACS nutrition and physical activity recommendations[23] (see Table 7: Health Promotion Guidelines).

Information

Recommendation 4.1. It is recommended that primary care clinicians (a) should assess the information needs of the patient related to breast cancer and its treatment, side effects, other health concerns, and available support services (LOE = 0); and (b) should provide or refer survivors to appropriate resources to meet these needs (LOE = 0).

Clinical interpretation. Breast cancer survivors often express unmet needs for information after treatment, including information on the effects of cancer treatment, emotional distress,

TABLE 7. Health Promotion Guideline

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 4.1: Information	
(a) Should assess the information needs of the patient related to breast cancer and its treatment, side effects, other health concerns, and available support services	0 (Assessment)
(b) Should provide or refer survivors to appropriate resources to meet these needs	0 (Referral)
Recommendation 4.2: Obesity	
(a) Should counsel survivors to achieve and maintain a healthy weight	0 (Maintenance)
(b) Should counsel survivors if overweight or obese to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss	IA, III (Weight loss)
Recommendation 4.3: Physical activity	
Should counsel survivors to engage in regular physical activity consistent with the ACS guideline, and specifically	
(a) Should avoid inactivity and return to normal daily activities as soon as possible following diagnosis	III (Avoid inactivity)
(b) Should aim for at least 150 min of moderate or 75 min of vigorous aerobic exercise per wk	I, IA (Aerobic exercise)
(c) Should include strength training exercises at least 2 d per wk; emphasize strength training for women treated with adjuvant chemotherapy or hormone therapy	IA (Strength training)
Recommendation 4.4: Nutrition	
Should counsel survivors to achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; low in saturated fats; and limited in alcohol consumption	IA, III (Nutrition); 0 (Alcohol)
Recommendation 4.5: Smoking cessation	
Should counsel survivors to avoid smoking and refer survivors who smoke to cessation counseling and resources	I

ACS indicates American Cancer Society. [a]Level of evidence: I indicates meta-analyses of randomized controlled trials (RCTs); IA, RCT of breast cancer survivors; IB, RCT based on cancer survivors across multiple sites; IC, RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing fatigue, lymphedema, etc); IIA, nonrandomized controlled trial (non-RCT) based on breast cancer survivors; IIB, non-RCT based on cancer survivors across multiple sites; IIC, non-RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing urinary incontinence, erectile dysfunction, etc); III, case-control or prospective cohort study; 0, expert opinion, observation, clinical practice, literature review, or pilot study.

and lifestyle changes.[185,186] Younger breast cancer patients can be particularly vulnerable to the physical, emotional, and psychosocial late effects of treatment because of the aggressiveness of their disease, the intensity of the treatment plan,[47,187] and their younger age, when a cancer diagnosis is not as common or is unexpected.[188,189] Treatment summaries and individualized survivorship care plans provide survivors with individualized information on their cancer care. However, to date, there is inconsistency in the implementation, comprehensiveness, and perceived helpfulness of such plans for both patients and primary care clinicians.[190-192]

Results from randomized trials of survivorship care plans are mixed,[193-196] making the direct benefits of survivorship care plans less clear. However, the failure of specialists to provide treatment summaries and survivorship care plans is an obstacle to the ability of primary care clinicians to provide relevant information and care to their patients with a history of breast cancer.

The informational needs of breast cancer survivors and caregivers should be routinely assessed, and information about the long-term and late effects of breast cancer treatment, as well as information on risk reduction and health promotion, should be provided. Resources that may be beneficial to share with patients include the ACS Survivorship Center website (cancer.org/survivorshipcenter), the ACS website (cancer.org), Journey Forward (journeyforward.org), the ASCO survivor and caregiver site (cancer.net), and the NCCN patient and caregiver resources (nccn.org/patients).

Obesity

Recommendation 4.2. It is recommended that primary care clinicians (a) should counsel survivors to achieve and maintain a healthy weight (LOE = III); and (b) should counsel survivors, if overweight or obese, to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss (LOE = IA, III).

Clinical interpretation. Approximately 62% of breast cancer survivors are overweight/obese (have a body mass index of least 25 kg/m^2), of which 30% are classified as obese (body mass index, 30 kg/m^2 or higher).[197] Sufficient evidence documents obesity as a risk factor for postoperative complications, second cancers, risk of recurrence, development of diabetes, and other issues. Conversely, weight loss mitigates symptoms

and improves QoL.[198] ASCO issued a position statement underscoring the need for oncology providers to counsel their patients about achieving a healthy weight.[199] Primary care clinicians should also counsel cancer survivors to achieve or maintain a healthy weight[198] and refer to multicomponent obesity treatment programs where appropriate.[200]

Physical activity

Recommendation 4.3. It is recommended that primary care clinicians should counsel survivors to engage in regular physical activity consistent with the ACS guideline[23] and, specifically: (a) should avoid inactivity and return to normal daily activities as soon as possible after diagnosis (LOE = III), (b) should aim for at least 150 minutes of moderate or 75 minutes of vigorous aerobic exercise per week (LOE = I, IA), and (c) should include strength training exercises at least 2 days per week. Strength training should be emphasized for women who are treated with adjuvant chemotherapy or hormone therapy (LOE = IA).

Clinical interpretation. Approximately 32% of cancer survivors meet the recommendations for physical activity.[201] Numerous systematic reviews and meta-analyses have documented the many health benefits from physical activity in breast cancer survivors, including mitigating treatment side effects (ie, fatigue) and improving QoL and physical functioning. The data suggesting a potential survival benefit of physical activity come from observational data, with the most recent review of this literature citing 16 studies that reported an average relative risk of 0.72 for breast cancer deaths in physically active breast cancer survivors (95% confidence interval, 0.60-0.85) and 0.52 for all-cause mortality (95% confidence interval, 0.42-0.64).[202] Breast cancer survivors should be advised to return to normal daily activities as soon as possible after diagnosis and to continue engaging in regular physical activity. Breast cancer survivors should strive to exercise at least 150 minutes moderately or 75 minutes vigorously per week and should include strength training exercises at least 2 days per week.[23] Additional details regarding the amount of time needed for each strength training session is less clear. However, studies indicate that from 37% to 53% of breast cancer survivors meet the aerobic guideline,[203,204] and 23% meet the strength training guideline.[205] Observational evidence suggests greater amounts of activity may be needed, although the evidence is insufficient to make it a recommendation at this time; aerobic exercise of 3 hours or more per week may be needed to improve breast cancer survival.[184,206]

Nutrition

Recommendation 4.4. It is recommended that primary care clinicians should counsel survivors to achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; low in saturated fats (LOE = IA, III); and limited in alcohol consumption (LOE = 0).

Clinical interpretation. Only 18% to 34% of breast cancer survivors report eating five or more fruit and vegetables daily.[204] Eating a diet characterized by high amounts of vegetables, fruits, whole grains, and legumes (vs a typical Western diet) has been associated with a reduced risk (range, 15%-43%) in all-cause mortality.[207-209] Data from the two large RCTs of diet interventions in breast cancer survivors suggest that dietary change sufficient to result in weight loss may be needed to favorably impact breast cancer recurrence and prognosis.[210,211] According to the ACS Nutrition and Physical Activity Guidelines, alcohol consumption should be limited to no more than one drink per day for women, as in the general population.[212,213] Data are inconsistent but suggest that breast cancer survivors who consume more than three to four drinks per week are at increased risk for breast cancer recurrence.[214]

Studies have shown that the carcinogenic ingredients of alcohol increase the risk of developing many types of cancers[215-217] when alcohol, regardless of the type (ie, wine, beer, etc), is consumed in excess of daily recommended limits.[218] Approximately 7% of breast cancer survivors report excessive drinking.[203] Based on these data, survivors should be counseled to: achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; limit alcohol intake to no more than one drink per day; and follow the ACS Guidelines on Nutrition and Physical Activity for Cancer Survivors[23] with a focus on successful weight management.

Smoking cessation

Recommendation 4.5. It is recommended that primary care clinicians should counsel survivors to avoid smoking and refer survivors who smoke to cessation counseling and resources (LOE = I).

Clinical interpretation. Approximately 10% to 12% of breast cancer survivors smoke.[203,204] Numerous observational studies show that women who smoke at the time of diagnosis have substantially worse breast cancer-specific and overall survival than former and never smokers.[219] A recent meta-analysis of this observational work documents a 33% increased risk of mortality from breast cancer in women who are smokers at diagnosis compared with former smokers.[219] Survivors should discontinue smoking and avoid subsequent tobacco product use. Clinicians should identify smokers and motivate and encourage patients to quit through cessation programs, brochures and pamphlets, counseling, pharmacotherapy, and regular follow-up.[220] These programs should be initiated at the time of initial diagnosis if possible.

Care Coordination/Practice Implications

There are no clear guidelines for the shared care and comanagement of patients with breast cancer after the completion of active treatment (see Table 8). The time to transition is

TABLE 8. Care Coordination Guideline

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 5.1: Survivorship care plan	
Should consult with the cancer treatment team and obtain a treatment summary and survivorship care plan	0, III
Recommendation 5.2: Communication with oncology team	
Should maintain communication with the oncology team throughout your patient's diagnosis, treatment, and posttreatment care to ensure care is evidence-based and well-coordinated	0
Recommendation 5.3: Inclusion of family	
Should encourage the inclusion of caregivers, spouses, or partners in usual breast cancer survivorship care and support	0

[a]Level of evidence: I indicates meta-analyses of randomized controlled trials (RCTs); IA, RCT of breast cancer survivors; IB, RCT based on cancer survivors across multiple sites; IC, RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing fatigue, lymphedema, etc); IIA, nonrandomized controlled trial (non-RCT) based on breast cancer survivors; IIB, non-RCT based on cancer survivors across multiple sites; IIC, non-RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (eg, managing urinary incontinence, erectile dysfunction, etc); III, case-control or prospective cohort study; 0, expert opinion, observation, clinical practice, literature review, or pilot study.

variable and depends on medical, geographic, and resource restraints. Some patients return to their primary care clinician immediately after treatment is completed.[221-223] Others may choose to transition to their follow-up care only after they are considered at little or low risk for disease recurrence or late effects of cancer treatment.[224,225] Several RCTs show that care led by primary care clinicians is as effective as hospital-led or specialist-led care, including similar rates of recurrence-related, serious clinical events; levels of health-related QoL[226]; and patient satisfaction with care.[227]

Breast cancer survivors may continue to see their oncology team for follow-up disease surveillance; however, they should also be seen by their primary care clinician for health maintenance and management of comorbidities that may or may not be related to their cancer diagnosis and treatment.[222,228]

Survivorship care plan

Recommendation 5.1. It is recommended that primary care clinicians should consult with the cancer treatment team and obtain a treatment summary and survivorship care plan (LOE = 0, III).

Clinical interpretation. Survivorship care plans are recommended as an important tool to facilitate communication and allocation of responsibility during the transition from active treatment to survivorship care.[4,229] A summary of a patient's diagnosis and treatment received should be provided by the oncology care team when a patient with breast cancer transitions care to other providers; a treatment summary should describe the type and stage/side of the cancer, type of surgery, the name of the chemotherapy/hormones/biologics and cumulative doses of chemotherapy, and the types and cumulative doses of radiation therapy, including the fields and extent of the radiation.[4,190] Patients can initiate the building of a survivorship care plan process on the ASCO website (cancer.net/survivorship/follow-care-after-cancer-treatment/asco-cancer-treatment-and-survivorship-care-plans; at journeyforward.org/ or livestrongcareplan.org/).

Ideally, the oncology team should also work with the patient to develop an individualized cancer survivorship care plan for breast cancer survivors. This care plan guides recommendations for the type and timing of follow-up imaging, laboratory tests, and office visits. The care plan should include information on the risk for late effects of treatment and what to watch for specifically based on the type of cancer and treatment received. Survivors should be assessed for the presence of these physical effects (eg, cardiovascular issues, musculoskeletal issues) as well as psychosocial effects (eg, cognitive dysfunction, depression, FOR, body image, and sexual dysfunction) and should be referred to the appropriate providers and services.

However, the field of oncology is broadly struggling with how to best meet this recommendation and in identifying the specific benefits of such care plans. Various tools and strategies to facilitate the creation and distribution of these care plans are being actively considered for all tumor sites, including breast cancer. Currently, challenges in workflow and tools make this difficult, but the field is working toward a sustainable solution.

Communication with oncology team

Recommendation 5.2. It is recommended that primary care clinicians should maintain communication with the oncology team throughout your patient's diagnosis, treatment, and post-treatment care to ensure care is evidence-based and well-coordinated (LOE = 0).

Clinical interpretation. Communication and cooperation among providers and survivors are critical, with the oncology team providing concrete recommendations for care when needed or requested by other providers.[229] Clear communication regarding the respective roles of different members of the health care team is critical to a successful transition to survivorship care.

The primary care clinician should serve as a general medical care coordinator throughout the spectrum of breast cancer detection and aftercare, focusing on evidence-based preventive care and the management of pre-existing comorbid conditions; regularly addressing the

patient's overall physical and psychosocial status; making appropriate referrals for psychosocial, rehabilitative, or other specialist care as needed; and coordinating those components of survivorship care that are agreed upon with the treating clinicians. Treatment of breast cancer is complex and rapidly changing; therefore, decisions about and coordination of cancer treatment should be left to the oncology team.

Inclusion of family

Recommendation 5.3. It is recommended that primary care clinicians should encourage the inclusion of caregivers, spouses, or partners in usual breast cancer survivorship care and support (LOE = 0).

Clinical interpretation. Caregivers have to cope with the physical aftermath of the survivors' treatment and manage their long-term and late effects in addition to their own psychosocial and physical unmet needs.[230] Research has shown that, for 14 to 24 months after a survivor's cancer diagnosis, caregivers provide consistent, continuing care involvement[231] for patients after breast cancer treatment. Successful coordination of care involves not only a comprehensive care team, including primary care clinicians, but also the informal caregivers (usually the spouse/partner/family member) who provide ongoing care to cancer survivors in the home.[232] Furthermore, most caregivers are older adults who are also managing their own health problems. When possible, primary care clinicians should include caregivers of breast cancer survivors in all follow-up care appointments to optimize survivor wellness.

Discussion

A significant limitation of this guideline is the limited evidence base with which to provide clear and specific recommendations for the prevention and management of long-term and late effects of cancer survivors. There are few prospective, RCTs testing interventions among breast cancer survivors, although studies in breast cancer survivors dominate the survivorship literature. The majority of the citations characterizing the risk and magnitude of risk of late effects and management recommendations relied predominantly on case-control studies with fewer than 500 participants and reviews that combined studies with various outcome measures. There were several cohort studies that used population-based data to estimate the risk of late effects.

Another limitation is the reliance on previous guidelines for surveillance and symptom management. In addition, the literature review was not managed by a clinical epidemiologist because of limited resources and, instead, was conducted by project staff and an ACS librarian. Furthermore, the guidelines did not result directly from the development of specific clinical questions asked before the literature review; and guidelines included in the literature review were not evaluated through an instrument such as the Rigor of Development subscale of the Appraisal for Guidelines for Research and Evaluation (AGREE II). Recommendations are based on current evidence in the literature, but most evidence is not sufficient to warrant a strong recommendation. Rather, recommendations should be largely seen as possible management strategies given the current limited evidence base.

Health Disparities

Although the ACS/ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients have limited access to medical care. Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients with cancer who are members of racial/ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving poor-quality care than other Americans.[233-236] Many other patients lack access to care because of their geographic location and distance from appropriate treatment facilities. Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

The ACS and ASCO believe that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

Multiple Chronic Conditions

Creating evidence-based recommendations to inform the treatment of patients with additional chronic conditions, a situation in which the patient may have two or more such conditions—referred to as multiple chronic conditions (MCCs)—is challenging.[237] Patients with MCCs are a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials in which study selection criteria may exclude these patients to avoid potential interaction effects or confounding of results associated with MCCs. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous patient population.

Because many patients for whom guideline recommendations apply present with MCCs, any treatment plan needs to

take into account the complexity and uncertainty created by the presence of MCCs and should highlight the importance of shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for the target index condition, clinicians should review all other chronic conditions present in the patient and take those conditions into account when formulating the treatment and follow-up plan.

In light of these considerations, practice guidelines should provide information on how to apply the recommendations for patients with MCCs, perhaps as a qualifying statement for recommended care. This may mean that some or all of the recommended care options are modified or not applied, as determined by best practice in consideration of any MCCs.

External Review

After finalization by the workgroup, the guideline was sent to additional internal experts (ACS and ASCO) and external experts for review and comment before submission for publication. Review comments were reviewed by the expert panel and integrated into the final article before approval by the Clinical Practice Guideline Committee.

Guideline Implementation

ACS/ASCO guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box (Table 1) was designed to facilitate the implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ACS/ASCO guidelines are posted on the ACS and ASCO websites. This joint ACS-ASCO guideline is published in both *CA: A Cancer Journal for Clinicians* and in the *Journal of Clinical Oncology*.

Summary

Breast cancer survivors face potentially significant impacts of cancer and its treatment and deserve high-quality, comprehensive, coordinated clinical follow-up care. Primary care clinicians must consider each patient's individual risk profile and preferences of care to address physical and psychosocial impacts. Survivors should be provided support to address FOR, depression, anxiety, cognitive impairment, body image issues, sexual concerns, functional changes and physical impairments, relationship changes, other social role difficulties, employment concerns, and financial challenges, among others. Breast cancer survivors also need to be counseled on health promotion strategies to minimize and mitigate long-term and late effects, to ameliorate comorbid health conditions, and to potentially increase survival.

To clarify the roles of all clinicians working with cancer survivors, we concur with the Institute of Medicine that survivors and primary care clinicians should receive a survivorship care plan that includes a concise summary of treatment as well as a clinical follow-up care plan. Ideally, this plan would be constructed in partnership with the survivor to identify and prioritize goals for survivorship care and would be communicated to the patient to ensure their understanding of individual risks; recommended tests, procedures, and supportive care strategies; and how to optimize wellness. Survivorship care should be coordinated with treating cancer specialists.

Additional Resources

In addition to this guideline, tools and resources are available to assist primary care clinicians in implementing these recommendations. *CA* offers a Patient Page (onlinelibrary.wiley.com/doi/10.3322/caac.21322/pdf) to help patients understand how to use this guideline to talk to their doctor about surveillance and screening, symptom management, healthy behaviors, and care coordination. *CA* also offers free continuing medical education and free continuing nursing education for this article at acsjournals.com/ce as an additional resource for physicians and nurses. The Survivorship Center also offers The GW Cancer Institute's Cancer Survivorship E-Learning Series for Primary Care Providers (The E-Learning Series), a free, innovative, online, continuing education program to educate primary care clinicians about how to better understand and care for survivors in the primary care setting. Continuing education credits are available at no cost to physicians, nurse practitioners, nurses, and physician assistants for each 1-hour module. Learn more about The E-learning Series at cancersurvivorshipcentereducation.org. Visit asco.org/guidelineswiki to provide comments on the guideline or to submit new evidence. ■

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