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# Breast cancer survivorship ☆

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ABSTRACT

Most individuals diagnosed with breast cancer will experience long-term survival. Following initial active treatment for breast cancer, survivors may experience a variety of medical, physical, and psychosocial consequences that may affect overall health and wellbeing. Clinicians providing care for breast cancer survivors should be comfortable addressing long-term effects of cancer and its treatment, including cardiovascular toxicity, sequelae of estrogen deficiency, chronic pain, fatigue, cognitive concerns, sleep issues, and psychosocial concerns. In addition, providers should promote health maintaining behaviors including healthy lifestyle, treatment adherence, and appropriate surveillance. Survivorship care should be individualized based on treatment received with regular assessment of active symptoms and comorbidities.



## Introduction

As a result of breast cancer early detection and the availability of effective treatments, most individuals diagnosed with breast cancer will experience long-term survival. According to the National Cancer Institute definition, the term Cancer Survivor includes individuals from the time of cancer diagnosis through the balance of their lives [1]. Survivorship care and survivorship services, however, are generally aimed at managing issues that prevail following completion of initial cancer treatment in the absence of active disease. The transition to survivorship care can be thought of as moving from a primary focus on disease treatment to a focus on health maintenance. Areas to consider in breast cancer survivorship care include long-term effects of cancer and its treatment, endocrine therapy adherence, surveillance, subsequent cancer screening, as well as diet and lifestyle recommendations. It should be noted that issues specific to male breast cancer survivors are not well described in the literature, however, men with breast cancer may experience many of the same concerns as women including physical, psychosocial and medical consequences of treatment. Similarly, many aspects of survivorship care for those treated with curative intent will also apply to patients living with advanced breast cancer as a chronic condition. Some of the important adverse health consequences of breast cancer treatment include cardiovascular effects, menopausal symptoms, sexual dysfunction, infertility, bone density loss, chronic pain, lymphedema, fatigue, cognitive changes, sleep problems, psychological symptoms, secondary malignancies, and financial toxicity including loss of employment. Knowledge of these important survivorship concerns allows for the provider to better anticipate and manage treatment related adverse effects, to engage the patient in health promoting behaviors, and to refer as appropriate to specialist care.

## Cardiovascular toxicity

Cardiovascular disease, the leading cause of death in both men and women [2], is a major contributor to morbidity and mortality in breast cancer survivors. Increasing age, alcohol consumption, excess body weight, and low levels of physical activity are common risk factors for both cardiovascular disease and breast cancer. In addition, some treatments for breast cancer, including anthracycline-based chemotherapy, trastuzumab, radiation, and endocrine treatment have been associated with cardiovascular toxicity.

Treatment with anthracycline containing chemotherapy increases long-term risk of cardiomyopathy. Risk factors for this toxicity include higher cumulative dose of anthracycline, concurrent use of trastuzumab, receipt of radiation, older age, increasing body mass index, lower baseline ejection fraction, and pre-existing hypertension, diabetes or tobacco use [3,4]. Anthracycline containing regimens used most commonly in the United States to treat breast cancer typically limit the total dose of doxorubicin to 240 mg/m$^2$. At this dose, the long-term risk of cardiotoxicity should be less than 5% in the absence of pre-existing cardiac disease [5]. Higher cumulative doses of doxorubicin and cardiac risk factors increase this risk. Treatment with trastuzumab, which is typically

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administered for about 1 year in the curative intent setting, is associated with an approximate 0.4% risk of clinical congestive heart failure (CHF) when given without anthracyclines and about a 2% risk of CHF when given following anthracyclines [6]. Reported rates of cardiotoxicity are higher when asymptomatic declines in ejection fraction are included [6-8]. In contrast to what has been observed with anthracyclines, trastuzumab associated cardiotoxicity is commonly reversible after discontinuation of therapy and long-term risk of cardiotoxicity from trastuzumab appears to be relatively low [5,7,8].

Radiation treatment for breast cancer has also been associated with an increased risk of cardiovascular toxicity. In a meta-analysis conducted by the Early Breast Cancer Trialists Collaborative Group, receipt of adjuvant radiation was associated with an overall survival benefit but an increased risk of death from cardiovascular causes among women treated prior to 1990 in randomized clinical trials [9]. Since that time, a number of advances in radiation treatment have allowed for reducing the radiation dose to the heart, including modern 3-dimentional treatment planning, heart blocking, patient positioning, active breathing techniques, partial breast irradiation, as well as intensity modulated radiation treatment planning [10]. In a population-based study of women treated in the years 2000–2010, there was no significant excess risk of late cardiotoxicity observed among women who received radiation for early stage breast cancer compared with women who did not receive radiation, supporting the relative cardiac safety of modern radiotherapy techniques [11].

Chemotherapy induced early menopause, oophorectomy, or estrogen lowering medical therapies including gonadotropin releasing hormone agonists and aromatase inhibitors may contribute to cardiovascular risk via effects on weight, lipids, and blood pressure. Aromatase inhibitor use in postmenopausal women has been associated with an increased risk of cardiovascular events when compared with tamoxifen, however, significant increased risk is not observed with 5 years of aromatase inhibitor therapy when compared to placebo [12]. On the other hand, extended use of aromatase inhibitors for up to ten years may modestly increase risk of cardiovascular events [13]. Tamoxifen, which has a favorable effect on lipid profiles [14], has been associated with a reduced risk of cardiovascular events [12]. Tamoxifen use, however, can increase the risk of thromboembolic events including stroke [15].

Cardiovascular risk factors should be assessed in breast cancer survivors. Adherence to general preventive health guidelines including monitoring of lipid levels and cardiovascular risk modification as appropriate is important. There is currently no established role for routine monitoring of cardiac ejection fraction following completion of anthracycline and/or trastuzumab containing therapy or following radiotherapy, however, echocardiography can be considered within a year after completion of anthracycline containing chemotherapy for survivors with risk factors for CHF including diabetes, hypertension, hyperlipidemia or other cardiovascular comorbidities [16]. Patients should be educated on cardiovascular toxicity risk of treatments they have received and instructed to promptly report symptoms of cardiac disease to the appropriate health care provider [17]. In addition, modifiable risk factors should be addressed as indicated through medical management or lifestyle changes including smoking cessation, dietary modification and physical activity.

## Bone health

Bone density loss is another consequence of cancer treatment-related premature menopause and of estrogen lowering therapies including ovarian ablation and aromatase inhibition. Among premenopausal women receiving adjuvant chemotherapy, those who retain ovarian function tend to maintain bone density while those who experience ovarian failure have significant bone density loss in the year following chemotherapy [18]. Compared with placebo, women using aromatase inhibitors experience greater declines in bone mineral density of hip and spine and, at least with extended use of aromatase inhibitors, there is an increased risk of fractures [13,19]. Tamoxifen appears to have differential effects on bone density depending on menopausal status. While premenopausal women taking tamoxifen may experience bone density loss, tamoxifen appears to favorably affect bone density in postmenopausal women [20]. It is recommended that bone density be monitored with dual-energy x-ray absorptiometry every 2 years in postmenopausal women receiving aromatase inhibitors, and in premenopausal women treated with ovarian ablation or tamoxifen [17].

A number of studies have demonstrated that upfront use of bisphosphonates, including intravenous zoledronic acid or oral clodronate, can reduce breast cancer treatment related bone density loss and fracture risk among postmenopausal women receiving aromatase inhibitors and among premenopausal women receiving ovarian ablation and either aromatase inhibitors or tamoxifen [21-25]. Bisphosphonate use in some of these trials was also associated with improved disease related outcomes. In a meta-analysis of clinical trials evaluating the adjuvant use of bisphosphonates in women with early stage breast cancer, statistically significant reductions were observed in distant recurrence of breast cancer and in breast cancer mortality; notably, however, these benefits were not observed among women who remained premenopausal and did not receive ovarian ablative treatments [26]. The adjuvant use of denosumab every 6 months has also been associated with favorable effects on bone density, reduction in fracture risk and improvement in disease-free survival compared with placebo in postmenopausal women receiving aromatase inhibitor therapy for early breast cancer [27].

Nonpharmacologic recommendations for maintaining bone health in breast cancer survivors include regular weight bearing exercise, avoiding tobacco use, limiting alcohol consumption, assuring adequate dietary calcium intake and supplementing Vitamin D. For women not already receiving adjuvant bisphosphonates or denosumab for prevention of treatment related bone density loss, either of these (including oral bisphosphonate therapy) can be considered for treatment once a diagnosis of osteoporosis or significant osteopenia is established. The selective estrogen receptor modulator raloxifene, which is approved for the treatment and prevention of osteoporosis in postmenopausal women should be avoided in women on aromatase inhibitors given its similarity to tamoxifen which has been shown to interfere with efficacy of aromatase inhibitors [28]. Raloxifene should also be avoided in women taking tamoxifen given lack of safety or efficacy data for dual selective estrogen receptor modulator therapy.

## Menopausal symptoms, sexuality, and fertility

Other major consequences of endocrine treatment for breast cancer and treatment related ovarian failure are menopausal symptoms, sexual symptoms and loss of fertility. The risk of ovarian failure with chemotherapy is increased with older age at treatment, and with higher cumulative dose of alkylating agent exposure. Vasomotor and sexual symptoms can occur in women receiving endocrine treatment for breast cancer regardless of menopausal status. Their management is complicated by the recommendation to avoid menopausal hormone therapy in women with a history of hormone sensitive breast cancer.

For some women, environmental and dietary modifications such as dressing in layers, using fans and avoiding caffeine or alcohol are adequate for managing hot flashes. Exercise and cognitive behavioral therapy may also be beneficial. Supplementation of

Vitamin E and/or magnesium is often recommended for management of hot flashes, although there is controversy as to whether these are more effective than placebo. There is evidence that plant-based phytoestrogen supplements such as black cohosh or red clover may reduce hot flashes and vaginal dryness [29], however, the safety of these supplements in women with hormone sensitive cancer remains uncertain including a concern that such supplements may interact with the hormonal treatments for breast cancer. Several nonhormonal pharmaceutical options for vasomotor symptoms are available and have been shown to reduce symptom severity in breast cancer survivors. These include selective serotonin reuptake inhibitor and serotonin-norepinephrine reuptake inhibitor antidepressant medications such as citalopram and venlafaxine as well as the anticonvulsant medications gabapentin and pregabalin [30]. Additional nonhormonal options that have been shown to reduce hot flash severity include clonidine and oxybutynin [30], however, these treatments may not be as well tolerated as the antidepressant and anticonvulsant choices. Antidepressant medications that are potent inhibitors of cytochrome P450 2D6 (CYP2D6), such as paroxetine, are preferably avoided in favor of less potent CYP2D6 inhibitors, such as venlafaxine, for women taking tamoxifen since CYP2D6 inhibition may reduce tamoxifen efficacy by interfering with conversion to endoxifen, its active metabolite [31].

Sexual symptoms in breast cancer survivors are often multifactorial. Antiestrogen therapies are a major contributor but concerns with body image and relationship problems brought out by a breast cancer diagnosis also affect sexuality. For management of vaginal dryness, use of nonhormonal lubricants during intercourse and more regular use of non-hormonal vaginal moisturizers can be helpful. In addition, 4% topical lidocaine applied to the vaginal vestibule prior to vaginal penetration can be prescribed for patients experiencing dyspareunia [32]. Patients may also benefit from use of dilators and pelvic floor therapy. For patients with inadequate relief from the above options, topical hormonal treatments including vaginal dehydroepiandrosterone ovules or vaginal estrogen may be considered, although these treatments have been associated with an increase in serum sex hormone levels suggesting the potential for systemic absorption, the clinical significance of which remains uncertain [33]. Patients with sexual concerns should also be referred as appropriate for psychoeducational support services, counseling, and for evaluation by a menopause certified provider.

For young women wishing to avoid menopause as a consequence of chemotherapy, including those with hormone receptor-negative breast cancer and those wishing to preserve fertility, ovarian function suppression with gonadotropin releasing hormone agonists during chemotherapy treatment can reduce the risk of early ovarian failure and improve prospects for fertility [34,35]. It is also recommended that young women interested in future childbearing consult with a fertility specialist prior to initiation of systemic cancer treatment if possible, as assisted reproductive technologies are more likely to be successful when initiated prior to chemotherapy treatment. Even among young women who do not receive chemotherapy, a delay in childbearing while taking endocrine therapy may reduce fertility prospects so it is important to assess family planning goals and provide appropriate referrals for all young women treated for breast cancer.

## Lymphedema and chronic pain including arthralgias and neuropathy

Lymphedema is a common complication of breast cancer and its treatment in which interruption of lymphatic drainage by axillary surgery, radiation or by cancer involved lymph nodes results in excessive accumulation of interstitial fluid and swelling of the affected extremity. Risks factors for developing lymphedema include higher body mass index, post-operative infection, receipt of radiation and axillary dissection [36,37]. Newer surgical techniques including axillary reverse lymphatic mapping and lymphaticovenous bypass may allow for preservation of important lymphatic channels in patients at high risk for lymphedema [38]. Data do not support that lymphedema risk can be reduced by avoiding blood draws, injections or blood pressure measurements on the affected arm or by avoiding airplane travel [39,40]. Awareness of lymphedema risk can allow for early intervention with physical therapy and compression garments which may be more effective when applied before symptoms are severe. In addition, there is evidence that exercise, including weight lifting, is not only safe but actually reduces lymphedema [37].

Chronic pain is another highly prevalent symptom among breast cancer survivors and may be a consequence of surgery and/or radiation treatment or a result of systemic treatment including chemotherapy induced neuropathy or endocrine therapy related arthralgias. Pain concerns in breast cancer survivors often worsen rather than improve with time and appear to be more prevalent in those who are overweight or obese and in those with lower levels of physical activity [41]. In addition to the previously discussed treatments for managing lymphedema, and to analgesics such as acetaminophen and nonsteroidal anti-inflammatories, a number of options are available for managing various pain syndromes.

Hormonal treatments and hormonal consequences of breast cancer treatment can result in musculoskeletal symptoms including arthralgias which can be severe enough to affect treatment adherence. Some patients may experience fewer symptoms upon switching to a different medication of the same class (such as from anastrozole to letrozole or exemestane) or to a different endocrine therapy (such as from an aromatase inhibitor to tamoxifen). Often joint pain and stiffness from aromatase inhibitors improves with activity. There is evidence that a combination of aerobic and resistance exercise can improve musculoskeletal pain and quality of life in women taking aromatase inhibitors [42]. Other interventions that appear to help with aromatase-inhibitor associated arthralgias include acupuncture [43], omega-3 fatty acids [44], and duloxetine [45] with the latter two treatments having seemingly greater benefit in obese patients [44,46].

Neuropathy is a potential chronic complication from breast cancer chemotherapy, particularly taxane-containing chemotherapy and is associated with pain and disability. As with chronic pain in general, neuropathy symptoms are more commonly reported among survivors with higher body mass index and those who do not exercise regularly [47]. Currently no pharmacologic interventions have conclusively been shown to prevent taxane associated peripheral neuropathy. Placebo controlled studies of group B vitamins, glutathione and acetyl-*L*-carnitine have failed to show a neuroprotective effect from these supplements and in fact acetyl-*L*-carnitine use during taxane chemotherapy was associated with worse neuropathy symptoms than placebo [48-50]. Similarly, electro-acupuncture was associated with no benefit over a sham acupuncture procedure in attenuating taxane-induced peripheral neuropathy [51]. There is some evidence that cryotherapy with use of frozen gloves and socks during chemotherapy administration can reduce paclitaxel associated peripheral neuropathy [52]. Exercise may provide benefit in both the prevention and treatment of chemotherapy-induced peripheral neuropathy [53,54]. Additional options for patients with established chemotherapy-associated peripheral neuropathy include duloxetine and pregabalin which have each been shown to improve pain and quality of life scores [55,56]. There is, however, a lack of pharmacologic interventions shown to reverse numbness, tingling and functional impairment from peripheral neuropathy.

## Fatigue, sleep problems, cognitive changes and psychological effects

Causes of fatigue, sleep problems, cognitive changes and psychological concerns may be multifactorial and more than one of these issues often coexist. Cognitive changes can result from fatigue which may be a consequence of sleep problems. Psychological distress may affect sleep. Breast cancer treatments can affect any of these.

In the evaluation of a breast cancer survivor with fatigue, it is important to assess for treatable causes such as anemia, thyroid disease, cardiac dysfunction, other medical issues, or medication effects. Fatigue is an expected side effect of chemotherapy which typically resolves within a year or two of treatment completion, however, some individuals may have longer-lasting fatigue. Factors that may increase the risk of long-term fatigue in breast cancer survivors include sedentary lifestyle, obesity, aromatase inhibitor use, and certain pre-existing medical issues including migraines, arthritis, peripheral arterial disease and depression [57]. Exercise may improve fatigue in cancer survivors, particularly within the first few years after diagnosis [58], as can cognitive behavioral therapy aimed at reducing insomnia [59].

Sleep problems can have a major impact on quality of life for breast cancer survivors. Factors associated with sleep disturbances in breast cancer survivors include hot flashes, menopause, pain, depressive symptoms, and fatigue [60]. Treating hot flashes, pain, and depression as appropriate may help with sleep. While sleep medications may improve sleep in the short-term, they can be habit-forming and are often not a suitable long-term solution to chronic sleep disturbance. Patients should be educated on sleep hygiene and some will benefit from formal cognitive behavioral therapy for insomnia which can having durable effects over time [61,62].

Cognitive changes can also result from fatigue, sleep issues, anxiety, and depression, as well as from various cancer treatments. Patients with less cognitive reserve due to age, comorbidity or lower education may be more susceptible to declines in objective measures of cognitive function while patients with greater cognitive reserves may perform relatively well on objective cognitive tests yet still experience subjective concerns regarding cognitive function [63]. Pharmacologic interventions have not proven to be particularly helpful in the management of cancer treatment associated cognitive dysfunction but exercise, cognitive behavioral therapy and cognitive rehabilitation appear to provide some benefit [63]. It is also important to assess for reversible factors, such as medications that might affect cognition. Patients with significant cognitive change can be referred for formal neurocognitive assessment.

Mood changes and other psychological symptoms are also common in breast cancer survivors. Fear of recurrence, body image concerns, changes in physical function, relationship concerns and financial difficulties related to a breast cancer diagnosis can all contribute to psychological distress. Depressed mood in breast cancer survivors has been associated with lower physical activity level, more fatigue, pain and other treatment related side effects [64]. Fatigue, arm morbidity, cognitive problems, and depressive symptoms have been associated with a lower likelihood of returning to work following treatment for breast cancer [65]. Survivors with more education, those who participate in regular exercise, and those who following treatment report better body image, physical function, and existential well-being appear more likely to return to work [66]. Loss of employment, hospital bills and relationship changes may all contribute to the financial toxicity of a breast cancer diagnosis. Over a third of survivors may experience financial strain following breast cancer treatment, with a substantially higher likelihood of financial strain in those who are younger, unmarried and without a college education [67]. Breast cancer survivors should be regularly assessed for mood disorders and psychological distress and should be offered psychosocial support services, counseling, and/or pharmacotherapy for depression as appropriate.

## Adherence, recurrence, and subsequent primary cancers

Financial stress and concerns about side effects may lead to non-adherence to treatment and therefore potentially increase risk of metastasis. Some of the factors associated with reduced adherence to adjuvant endocrine treatment include higher out-of-pocket medication costs, lower patient-perceived benefit from endocrine therapy, and side effects impacting quality of life [68,69]. Management of treatment-related side effects, providing support resources and educating patients on the rationale for recommended treatments may help improve adherence and, as a result, breast cancer outcomes.

While adjuvant treatment aims to improve cure rates through preventing metastases, screening for metastatic disease in those with a history of early stage breast cancer has not been shown to improve long-term outcomes. Radiographic studies to evaluate for distant recurrence are generally symptom directed and, per the current American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline, routine use of laboratory or imaging studies in patients without symptoms is not recommended [17]. Regular assessment with history and physical examination with follow-up testing based on any signs or symptoms of recurrent disease is recommended. Screening for local recurrence and for new breast primary cancers is recommended and typically consists of clinical breast examination and annual mammography of remaining breast tissue. The addition of breast MRI screening may be considered in subsets of survivors at particularly high risk for a new primary breast cancer including those with BRCA1, BRCA2, or other high-risk gene mutations who have not undergone bilateral mastectomy.

Some cancer treatments can increase the risk for nonbreast subsequent malignancies. Rarely, acute leukemia or myelodysplasia can occur following chemotherapy for breast cancer. Risk is increased with receipt of anthracycline-containing chemotherapy, particularly when more dose intensive regimens are used and when patients also receive radiation treatment [70]. Tamoxifen has been associated with an approximately 3-fold risk of endometrial cancer with 5 years of therapy with a cumulative 7-year rate of about 1.5%; risk appears to be largely limited to women over age 50 [15]. Risk of uterine cancer is further increased with extension of therapy to 10 years [71]. Radiation treatment has also been associated with the development of secondary malignancies including angiosarcoma which typically occurs in the skin of a previously radiated breast and may or may not be associated with a history of lymphedema [72]. While no specific screening is indicated for treatment associated leukemia, endometrial cancer or sarcoma, providers should be aware of these risks and appropriately investigate suggestive signs and symptoms. For most breast cancer survivors, cancer screening recommendations are similar to standard age-appropriate cancer screening for the general population, including screening for colorectal, and cervical cancers. Discussion of additional screening and prevention options is appropriate for survivors found to be at increased genetic risk for subsequent malignancies. For instance, women with BRCA mutations are at increased risk for ovarian cancer and should be counseled on the option of risk-reducing surgery versus screening and its limitations. Because screening and prevention recommendations differ from the general population for those with hereditary cancer syndromes, it is important assess survivors regarding indications for genetic testing, including regular updating of family history. Factors that increase the likelihood of identifying a hereditary cause

of breast cancer and that should prompt consideration of referral for genetic testing include a diagnosis of triple-negative breast cancer at or prior to age 60, any breast cancer diagnosis under age 50, bilateral breast cancer, male breast cancer, Ashkenazi Jewish heritage, a personal history of ovarian cancer, or a significant family history of breast or ovarian cancer [17].

## Diet and lifestyle recommendations

Health promoting behavior has the potential to improve outcomes through direct effect on cancer recurrence risk as well as by indirect effects of attenuating comorbidities and treatment related toxicities with resultant improved adherence. Exercise in particular appears reduce fatigue, arthralgias, neuropathy and depressive symptoms in addition to improving cardiopulmonary fitness, bone health and helping to maintain a healthy weight. In the Health, Eating, Activity, and Lifestyle Study, survivors with higher levels of physical activity in the 2 years following breast cancer diagnosis had a substantially lower risk of death compared with inactive survivors; these findings held whether survivors were physically active prior to diagnosis or increased activity following breast cancer diagnosis [73]. National Comprehensive Cancer Network Survivorship Guidelines recommend a minimum of 150–300 minutes of moderate intensity activity or at least 75 minutes of vigorous physical activity or an equivalent combination of the two weekly, spread out over each week along with strength training and stretching [16].

Dietary interventions aimed at achieving a healthy weight may also be beneficial to cancer survivors. Obesity has been associated with a higher risk of breast cancer recurrence and death, particularly among those with hormone receptor positive disease [74]. There is controversy as to optimal diet for cancer survivors and large randomized trials of dietary intervention are difficult to conduct. The Women's Healthy Eating and Living randomized trial was unable to demonstrate a significant impact on breast cancer outcomes with increasing vegetable, fruit, and fiber intake along with reducing fat intake [75]. On the other hand, in the randomized Women's Intervention Nutrition Study a dietary intervention aimed at reducing fat intake was associated with a reduction in breast cancer recurrence [76]. One important difference in these studies is that participants in the Women's Healthy Eating and Living study did not achieve weight loss with the dietary intervention; in Women's Intervention Nutrition Study, participants assigned to the intervention achieved sustained weight loss while controls did not. In counseling breast cancer survivors, it is appropriate to recommend diets that have been associated with achieving a healthy weight and with overall mortality reduction. Diets emphasizing whole grains and plants, including vegetables, nuts and fruit, while limiting intake of saturated fats, simple sugars, red meats, and processed meat have been associated with a reduction in all-cause mortality and specifically in cardiovascular and cancer associated mortality [77].

Breast cancer survivors often seek advice regarding dietary supplements and about the need to avoid dietary phytoestrogens. National Comprehensive Cancer Network Guidelines recommend obtaining nutrients predominantly from a variety of food sources rather than routine use of dietary supplements [16]. Recommendations to take dietary supplements should generally be limited to instances of dietary insufficiency (such as B12 supplementation for those following a vegan diet), known deficiency, or comorbidity (such as Vitamin D supplementation in the setting of bone density loss). Supplemental forms of soy isoflavones, such as red clover and black cohosh, aimed at treating symptoms of estrogen deficiency, have not been well tested for safety in women with hormone sensitive cancers and it is unknown if they may interact with endocrine treatments for breast cancer [78]. Intake of soy isoflavones through food sources, on the other hand, has been shown in several studies to be safe for breast cancer survivors, and their avoidance need not be recommended [78-80].

Breast cancer survivors should be encouraged not to smoke and to limit consumption of alcohol. Tobacco use may be associated with an increased risk for developing breast cancer [81] and has been associated with worse breast cancer mortality as well as worse all-cause mortality among women with breast cancer [82-84]. These risks can be attenuated with smoking cessation following diagnosis [84]. Alcohol consumption has been associated with an increased risk of developing breast cancer with higher levels of consumption associated with higher risk [85,86]. Data are mixed regarding effect of alcohol on risk of recurrence in women with a history of breast cancer, but consumption of more than 20 g/d has been associated with an increased risk of breast cancer mortality [87,88].

## Discussion

Caring for the breast cancer survivor includes addressing a variety of health issues, many of which are interrelated and may be attenuated by lifestyle changes. Some symptoms may improve with relatively simple pharmacologic or non-pharmacologic interventions while others may require referral to specialty care for ongoing management. Certain survivorship concerns, such as fertility, are most successfully addressed early on during initial treatment planning. For all breast cancer survivors, care should be individualized based on treatment received, active symptoms and comorbidities with regular reassessment of survivorship needs. Survivorship care goes well beyond a one-time treatment summary and care planning visit. Ongoing management can be provided by oncologists, mid-level providers or primary care providers. Patients should be encouraged to be proactive in their own health maintenance.

## Declaration of Competing Interest

None.

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