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Hi I'm Lillie Shockney, I'm the University Distinguished Service Professor of Breast Cancer at John's Hopkins. In that role I serve as the Administrative Director of the John's Hopkins Breast Center and Director of our Cancer Survivorship Programs in our Cancer Center. I have the rank of being a full professor in surgery and oncology within the John's Hopkins University School of Medicine. I'm also the co-developer of an employee benefit created here with one of my colleagues called John's Hopkins Work Stride Managing Cancer at Work.

And today we're going to be taking a look at Cancer Survivorship E-Learning Series for Primary Care Providers, and its entitled, Summary of Potential Long-Term and Late Effects of Breast Cancer and its Treatment.

I'm really pleased to be able to offer this educational session through the National Cancer Survivorship Resource Center, a collaboration between the American Cancer Society and the George Washington University Cancer Center originally funded by a five year cooperative agreement from the Centers for Disease Control and Prevention.



This work was supported by cooperative agreements from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention. No industry funding was used to support this work.



This presentation was developed from the American Cancer Society and the American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline, which has been cited here.



After completing this lesson, you will be able to:

• Describe potential long-term and late effects of breast cancer and/or it treatments.

The next presentation in this module, which is called Breast Cancer Survivorship Care Guideline for Primary Care Clinicians, will discuss management of the impacts of breast cancer and/or its treatment.



The ACS and ASCO Cancer Survivorship Care Clinical Practice Guidelines is where we're going to begin, by discussing the importance of the American Cancer Society and the American Society of Clinical Oncology Cancer Survivorship Care Clinical Practice Guideline and the process for its development.



Primary Care Clinicians frequently participate in the care of breast cancer survivors. When you realize 1 in 8 women will be diagnosed sometime in their lifetime that means that there's a strong possibility that you will be taking care of women before they are diagnosed as well as after they have been diagnosed.

It is often unclear who has primary responsibility, however, for breast cancer survivorship care and exactly what does that responsibility entail.

The ACS/ASCO guideline provides recommendations on the role of clinicians providing care for breast cancer survivors.



The NCCN, know as the National Comprehensive Cancer Network provides patient and caregiver resources, so we encourage you to visit their website at nccn.org for more information.

You can also go to nccn.com, which is a patient friendly website. It contains the same information, but it has been written solely for the purpose of a lay person being able to understand it.



The guideline featured in this module are based on the American Cancer Society and the American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline, which were published in 2015.

The guideline panel represented a diverse workgroup of providers, which included primary care clinicians, gynecologists, oncologists, nurses and a cancer survivor to both avoid the appearance of professional conflicts and use a multidisciplinary approach to creating a comprehensive guideline representative of the essential elements of high quality clinical follow-up care.

The ACS staff conducted preliminary systematic evidence reviews to develop a foundation for the expert panelists. Additional literature review and analysis to serve as the basis for all guidelines.

Where applicable, existing guidelines for health promotion, screening, surveillance, psychosocial care, and long-term and late effects were leveraged.

237 articles were included in the guideline to ensure that it was evidence-based.

Prior to publication, the draft survivorship care guideline was vetted by the ACS Priority Mission Outcomes Committee and the National Board of Directors, of ASC and ASCO with internal experts, as well as external experts.

Moving forward, the ACS and ASCO survivorship care guideline will be updated every 5 years as new research is available to support revisions.



So onto what do we mean when we say breast cancer survivorship.

Breast Cancer					
Most common non-cutaneous cancer in women					
Estimated new cases in 2018					
Females: 266,120 newly diagnosed and an additional 40,920 deaths					
American Cancer Society, 2018.					

Breast cancer is the most common cancer among women, except for skin cancers. The estimated number of new cases of breast cancer in women in 2018 is 266,120. And I'll emphasize that these are for women who have invasive breast cancer.

There are also an additional 60,000 women with non-invasive breast cancer known as DCIS, ductal carcinoma in situ. So when you add these together and are looking at how many individuals in fact are diagnosed, it exceeds 300,000 a year.

There are also approximately 1,800 men who are also diagnosed, and 40,920 individuals are anticipated to have died in 2018 from their disease and its treatment.



Although non-Hispanic white women have a higher incidence of breast cancer, non-Hispanic black women have a higher mortality.

	Breast	Cancer			
	Median Age at Diagnosis				
	Women	62 years			
Local the	Types of ⁻	Treatment nodes):			
• Breast-c	onserving surgery with radiatio	n or			
Mastector reconstru	omy with or without radiation ar uction	nd with or without immediate/de	ayed		
Systemic	therapy:				
Combina	ations of hormonal, chemothera	apy, targeted therapy, and immu	notherapy		
DeSantis et al., 20	14; Runowicz et al., 2015; American Can	cer Society, 2017.			
ASCC Assertion fockey of Clinic	GW Can	icer Center	American Cancer Society		

The median age at diagnoses is 62 years, and 43 percent are older than 65 at diagnoses. Because of the age breakdown, survivorship must be managed in accordance with comorbidities that are associated with aging. We certainly know that you have a wealth of knowledge when it comes to comorbid conditions of diabetes, heart disease, hypertension, asthma, COPD, etc.

Breast cancer treatment depends on the stage at diagnosis, the size and location of the tumor and its tumor characteristics. Those who have stage II or III disease at the time of their diagnosis may receive more involved cancer treatment, which can result in greater likelihood and severity of the impact of the treatment. Treatment generally includes two key components: treatment of the breast and local lymph nodes with surgery either with or without radiation and drug treatments for cancer cells that may have spread outside of the breast. Surgical treatment includes breast-conserving surgery, known also as lumpectomy, with radiation or mastectomy with or without radiation and with or without immediate or delayed reconstruction. In women with a very high risk of contralateral cancer from inherited susceptibility from mutations such as BRCA1 or BRCA 2 gene mutations, it's very common that contralateral prophylactic mastectomy will be performed also on the healthy breast.

Systemic therapy may precede local therapy as neoadjuvant treatment or follow local therapy as adjuvant therapy. It consists of combinations of hormonal, chemotherapy,

targeted therapy, immunotherapy.

Most women with early stage breast cancer who complete treatment will have endocrine-responsive tumors and will require endocrine therapy for anywhere from 5 to as long as10 years.



There are an estimated 3.5 million breast cancer survivors alive in the United States today. The overall 5-year survival rate is 91 percent. The survival rate for localized-stage cancer is 99 percent. About 61 percent of people with breast cancer have localized-stage disease. However, the 5 year survival rate for distant-stage disease is only 27 percent.

Most also remain at risk indefinitely for local as well as systemic recurrence of their breast cancer.



In this section, I will provide an overview of the physical long-term and late effects of breast cancer and its treatment by treatment type.



Two terms are often used to describe effects of cancer and its treatment. Long-term effects are medical problems that develop during active treatment and persist after the completion of that treatment, whereas late effects are medical problems that develop or become apparent months or years after treatment is completed.



The risk of physical long-term and late effects after therapy is associated with several factors, including:

- The type of treatment that the patient received
- The duration and dosages of treatment
- Specific types of chemotherapy
- Receipt of and type of hormone treatment, also known as endocrine therapy
- The age of patient during treatment

Primary care clinicians should refer to the survivor's cancer treatment summary if available for specific drugs and their dosages.



Potential effects of surgery are listed here. Let's start with long-term effects.

- Lack of skin sensitivity, that the skin can be numb and in some cases remain that way forever
- Body image issues, whether it be that she had a lumpectomy or mastectomy, or mastectomy with reconstruction. Her breast is going to look different than it originally did. If she sees this as her best feature, and it is her erotic zone, she may have more issues and more concerns with body image issues.
- Sexual dysfunction which can also be associated with body image.
- Numbness particularly under the arm, even if only a couple lymph nodes were removed. There is a sensation of numbness there. That can last for a few months but it is quite common to also last for the rest of her life.
- Pain is also an issue. It can be such things as phantom limb sensation and pain. For those that have had mastectomy surgery, the brain really does treat the breast as if it were a limb and so the nerves that went to that breast tissue remain there on the

chest wall. Some of them are also in the underarm area, so patients can have difficulty with pain sensations for a part of their body that isn't even there anymore.

- Limited range of motion, which is a particular issue for women that do need to undergo an axillary node dissection, level one and level two. Most of the time level three nodes are not removed. However, if the patient hasn't followed the rehab medicine instructions of doing range of motion exercises, very soon after the surgery, then they can end up with what are called bands in their armpit area, where they've had scarring tissue that has formed that literally prevents them from being able to raise their arm up. We want to prevent that whenever we can.
- A general feeling of weakness. This can be associated with post-surgery. For some women they just don't bounce back to what their normal physical activity was before they were diagnosed.
- Poor cosmetic outcome. Even with mastectomy with reconstruction, that breast may
 not look the way she was hoping that it would. That's something that needs to be
 dealt with, sometimes revisions of the cosmetic surgery can be done, but sometimes it
 cannot. This is particularly difficult for women who have had radiation to the chest
 wall, where they are going to have very tight skin. If implants are being used, they may
 end up with capsulitis a hardening of the implant and redness around the implant. The
 implant can even ride up her chest. All of these things are quite distressing. If she feels
 like there's not going to be a solution for it or an end to it, it can really play with her
 psychological wellbeing as well.

And then late effects, and I have to emphasize, we don't know all of the late effects yet that breast cancer survivors are dealing with. Two that we do know and know quite well however, lymphedema for those that have had axillary node dissections of their lymph nodes. They are at risk of developing swelling of their arm, which can be permanent. They are going to need to have lymphedema therapy, which can happen, in some cases, 5 days a week. That can be more distressing the patient than ever having gotten a diagnoses of breast cancer and having its treatment.

And then neuropathy again is associated with chemotherapy as a known side effect. Neuropathies of their hands as well as of their feet, which again impacts quality of life in a significant way.

Potential Effe	cts of Radiation	Therapy (RT)
Long-Term Effects ^a Fatigue ^{b,c} Skin sensitivity/pain Sexual dysfunction Pain	Poor cosmetic outcome Breast atrophy/ asymmetrical breast volume Lymphedema ^b	
Pneumonitis ^{b.c} Late Effects	Numbness or weakness of upper extremity ^b	
Skin discoloration Breast may remain smaller and firmer than non-irradiated breast Skin sensitivity/pain Telangiectasia	Lymphedema ^b Shortness of breath (lung pneumonitis or fibrosis) ^{b,c} Cardiovascular disease (i.e. pericardial effusion, pericarditis) ^c	Numbness or weakness of the upper extremity ^{c,d} Second primary cancers (i.e. soft-tissue sarcomas of thorax, shoulder and pelvis; lung cancer) ^{b,c}
Sexual dysfunction ^a Note: Long-term effect starts during treatme ^b Risks are increased in patients who also ha ^c Risks are increased in patients who also ha ^d Need to be careful as these can also be sig <i>Runowicz et al.</i> , 2015.	nt and does not subside. A late-effect develop d RT to supraclavicular nodes d RT to internal mammary nodes ns of recurrent cancer. May need consultatior	os much later n with radiation oncologist
ASCO American Society of Clinical Oncodings	GW Cancer Center	American Canver Society

These are potential effects of radiation therapy to the breast/chest-wall/regional lymph nodes. It is important to note that some of these may be signs of recurrent cancer, however so that's important to be able to differentiate the two.

Primary care clinicians should educate and counsel survivors about the signs and symptoms of local or regional recurrence, including new lumps, particularly those that may be under the arm or on the neck, or underneath the clavicle bone. A rash on the chest 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 the arm.



Common drugs used to treat breast cancer patients include aklylating agents, anthracyclines, platinum agents and taxanes.

And today, we're really at a point in time where more drugs in new categories are being developed and are currently in clinical trials. So, one of the things that will be important for you to be able to do is to periodically get updates about what are these new agents that are now approved, what side effects may they have, what long term effects may they have. And then it's going to require us studying patients longitudinally, for a decade and even longer to then learn what the late effects may very well be.

Potential Effects	of Chemotherapy			
	or enemotierapy			
Cognitive impairment	Infertility			
Fatigue	Weight gain			
Ovarian failure with or without menopausal	Obesity			
symptoms	Neuropathy (especially after taxanes)			
Sexual dysfunction	Oral health issues			
Change in libido	Hair loss			
Late Effects				
Osteoporosis/ osteopenia				
Increased risk of cardiovascular disease (cardio anthracycline-based chemotherapy	omyopathy, congestive heart failure) with			
Increased risk of leukemia and myelodysplastic syndrome with alkylating agents, anthracyclines, other topoisomerase II inhibitors, and other agents with immunosuppressive potential				
Runowicz et al., 2015.				
Referenced with permission from the NCCN Clinical Practice Guidel and NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelin Network, Inc. 2018. All rights reserved. Accessed May 4, 2018. To v to NCCN.org.	lines in Oncology (NCCN Guidelines®) for Breast Cancer V.1.2018. nes®) for Survivorship V.3.2017 © National Comprehensive Cancer riew the most recent and complete version of the guideline, go online			
ASCO GW Can	icer Center			

For potential effects of chemotherapy, here we have long-term effects, cognitive impairment. Chemotherapy can result in hurling a woman into menopause, dealing with all the menopausal symptoms that come along with that diagnosis with vaginal dryness, hot sweats, insomnia at night, etc. So part of this may be associated with a sudden decline of their hormone levels in their body, which is caused by chemotherapy as well as hormone therapy.

Fatigue and fatigue is different than just being tired. This is a fatigue that's even with rest you don't feel like you can really get your energy back.

Ovarian failure with or without menopausal symptoms. With young women that are of child bearing or maybe even aren't of child bearing yet. One of the things that often times will be done is fertility preservation.

Sexual dysfunction. A change in libido.

Infertility which I mentioned.

Weight gain. Obesity. Patient may already be obese and now this is going to make it

worse and that inactivity contributes to that. Obesity is also a leading cause for developing cancer, also a leading cause for cancer recurring. So we do want to inspire her to take better care of her health. And again a motivator is that she doesn't want to get cancer again.

Neuropathies of the hands and feet that are commonly caused by the chemotherapy drugs that are in the taxane category.

Oral health issues—dry mouth, in some cases some of the more severe side effects can result in osteoporosis of their jaw so they can end up losing teeth and having a lot of pain.

Hair loss is very common also, not with all chemotherapy agents for breast cancer but with most.

And late effects, osteoporosis or osteopenia. And again this goes back to the menopausal issues, that these bones are getting more holes in them and we want to make sure we are proactive on her behalf. Having her do exercises that will help her build her bones. Be on a bone building agent, if that's appropriate.

Increased risk of cardiovascular disease, cardiomyopathy, congestive heart failure is also a known late effect that is called by anthracycline-based chemotherapy.

And increased risk of leukemia and the myelodysplastic syndrome that also can happen with a variety of the chemotherapy agents that are given today, including some of the newer agents that are immunosuppressive so we may see this as a growing problem in the future.

Tamoxiten	Aromatase Inhibitors				
Hot flashes	Vaginal dryness				
Changes in menstruation	Decreased libido				
Increased triglycerides	Musculoskeletal symptoms/pain				
Mood changes	Cholesterol elevation				
Late Effects					
Tamoxifen	Aromatase Inhibitors				
Increased risk of stroke	Increased risk of osteoporosis				
Increased risk of endometrial cancer	Increased risk of fractures				
Increased risk of blood clots					
Osteopenia in pre-menopausal women					
Runowicz et al. 2015.					
Referenced with permission from the NCCN Clinical Practice Guide and NCCN Clinical Practice Guidelines in Oncology (NCCN Guideli Network, Inc. 2018. All rights reserved. Accessed May 4, 2018. To	lines in Oncology (NCCN Guidelines®) for Breast Cancer V.1.2018. nes®) for Survivorship V.3.2017 © National Comprehensive Cancer view the most recent and complete version of the guideline, go onlin				

The potential effects from hormonal therapy, also known as endocrine therapy, and they fall into two categories: SERMS—selective estrogen receptor modulators of which tamoxifen is the leader in that group. The other category are aromatase inhibitors— and aromasin, arimidex and other similar drugs. They carry similar side effects, but how they work within the body is different. Tamoxifen more commonly used with pre-menopausal women. Aromatase inhibitors used for post-menopausal women.

So if we look at tamoxifen, hot flashes, changes in menstruation or menses completely stopping. Increase in tryclcyerides, again that's an area that you know far better than we do. Mood changes again associated with menopause.

And for late effects from that drug, an increased risk of stroke, increased risk of endometrial cancer. Again, it's a very low risk, less than 2 percent, but we certainly do need to pay attention to it and if she has abnormal bleeding while receiving tamoxifen then we want her GYN to examine her and do a endometrial biopsy to see how thick is the endometrium.

Increased risk of blood clots. We certainly don't want anyone on this drug, either who has a personal history already with blood clots or who is a smoker or has already experienced a cardiovascular incident.

And osteopenia in premenopausal women. And that's a tough road to hough. These women literally feel like their bodies have aged by decades and to some degree they're correct.

Now for aromatase inhibitors vaginal dryness, decreased libido, musculoskeletal symptoms and pain, particularly knee pain, joint pain, hip pain. And then elevation of their cholesterol levels.

And for late effects with Als, increased risk of osteoporosis, increased risk of fractures. We know, as you so very well know, that getting for example, a hip fracture, can really be a serious situation today, even resulting in an earlier death for a woman.



Potential effects of targeted therapy, and we're going to be specifically talking about trastuzumab. There is an increased risk of cardiac dysfunction when using this drug. This drug is given on average for a year so the patient is getting many doses of this drug.



The psychosocial long-term and late effects of treatment.



When we take a look at these, ongoing difficulties in recovery and returning to normal. Sometimes we misspeak to patients and say, "go back to your normal life again." This is a life altering experience. Their old normal is gone. We need to help them with their new normal and ideally help them design their new normal.

They're very fearful that the cancer's going to come back. Fear of recurrence contributes to significant mental health problems including that distress, depression, and anxiety.

30.5 percent prevalence of depression in breast cancer survivors for urban and 19.8 percent for rural residents.

Decreased libido, poor self-image, and relationship issues are common among those who are depressed.

We try our best to educate family members about this and educate the patient about this. However, it is still going to happen to some degree and that's when she is going to be back in your arms.

Potential General Psychosocial Effects			
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 and self image			
Relationship(s) and other social role difficulties			
Return-to-work concerns			
Financial challenges			
Runowicz et al., 2015.			
ASCO CW Control Control			
American Society of Clinical Overlagy			

Potential general psychosocial effects, long-term as well as late effects: clinical depression, distress, which can be multifactorial unpleasant experience of psychosocial, social and/or spiritual nature, worry and anxiety, fear of recurrence, fear of pain.

They will meet other people who are breast cancer survivors that will describe, I was doing fine until...blah, blah, blah, and then post radiation my skin got so tight I've been seen in a pain treatment center.

End of life concerns, death and dying.

Loss of sexual function and/or loss of desire. Their partner or spouse may not understand this. They're just upset by it and say, "I don't understand what's wrong with you, you're all done with your breast cancer." That means also educating the partner, the spouse. But also hopefully be able to provide some solutions to it as well.

Challenges with body image and with self image. We may think she looks fine, if she doesn't think she looks fine, then she doesn't look fine. This is all about her. We need to treat her in a truly patient-centered way.

Other relationships, not just the spouse or partner, but social relationships. Her friends may not understand why she does act differently or think differently. Her coworkers may not understand also why things just don't seem to be the way they were before.

And last but not least are financial issues, what we call financial toxicity. Cancer treatment is expensive. If you have a survivor who is dealing with financial challenges associated with their—the bills that are coming in from their cancer treatment. Something to consider would be to connect them up with the Patient Advocate Foundation. The national organization that has financial resources for cancer patients and also can direct them to other financial resources. We all need to work together to support her and have her also feel comfortable in discussing her financial situation.



Now let's take a look at a case study.



You are seeing a 42 year old woman who completed adjuvant chemotherapy for a stage II breast cancer 18 months ago. She is no longer menstruating, has insomnia and fatigue, and complains that she can no longer manage her work as a third grade teacher.

The medications that she is on currently are tamoxifen, calcium and vitamin D. She has mild hypertension and arthritis. For her social history, she's married and has two children who are young, ages 5 and 7. She's recently gained weight, and quite a bit, 25 pounds, and her BMI is 32. And she's dealing with hot flashes and night sweats.



Question #1. What insomnia symptom management strategy would you recommend to this patient?

Prescribe a sleep medication

Discuss her pattern of sleep difficulties and consider CBT-Insomnia

Prescribe venlafaxine to help control hot flashes and night sweats

Propose a weight loss program



C is the correct answer. This particular drug is likely to be effective in managing vasomotor symptoms from tamoxifen and should be prescribed

A is incorrect. While this could have been considered, it is unlikely to address the root cause of her insomnia, which is likely from vasomotor symptoms. B is incorrect. And that is because this type of insomnia is an effective treatment but it would be best to manage symptoms that are causal first and D is incorrect because obesity could be associate with sleep apnea and this patient could certainly benefit from weight loss for her overall health, but it would not be the first recommendation for someone with insomnia.


In this lesson, you've learned to describe potential long and late effects of breast cancer and/or its treatments.



We are grateful for the support of CDC.

We would also like to acknowledge Dr. Patricia Ganz as lead author of this presentation and the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline.

This concludes the presentation, please continue to explore the remaining sections of the cancer survivorship e-learning series for primary care providers.









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This presentation was developed from the American Cancer Society / American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline cited here.

I would like to turn the session over to our presenter: Dr. Louise Chang, a primary care clinician and director of cancer information at the American Cancer Society.



After completing this lesson, you will be able to:

Describe how to care for breast cancer survivors as outlined in the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline.

Demonstrate understanding of a primary care clinician's role in providing follow-up care to breast cancer survivors.



The guideline was developed based on evidence review and assigning levels of evidence ranging from the highest level being one, which is meta-analysis of randomized controlled trials to level 3, case study and finally 0, which is based on expert opinion, observational study, clinical practice, literature review or pilot study.



The American Cancer Society / American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline provide recommendations to primary care clinicians for the care of breast cancer survivors in the following areas:

- Surveillance for Breast Cancer Recurrence and Genetic Counseling
- Early Detection of Cancer in Average Risk, Asymptomatic Individuals
- Assessment & Management of Physical & Psychosocial Long-Term & Late Effects of breast cancer and/or its treatment
- Health Promotion and
- Care Coordination/Practice Implications

And we will discuss each of these.



In this section, we will discuss surveillance for recurrence and recommendations for primary care clinicians to conduct surveillance for recurrence of breast cancer in survivors who have completed treatment for stage I, II or III cancer, and who have no evidence of disease.



The surveillance recommendations are based on level 2a evidence, which means they are leveraged from the NCCN breast cancer guideline where a 2A rating indicates that, based on lower level evidence, there is uniform consensus that the intervention is appropriate. The guiding principle of surveillance is that it should consider a survivor's risk of recurrence in the context of functional status and survivor's preferences. Care should be i



Clinical follow-up care provided to breast cancer survivors is based on age, specific diagnosis, and treatment protocol as recommended by the treating oncology team.

For the first 3 years after primary therapy, the survivors should receive a detailed cancer-related history and physical exam every 3-6 months.

Then every 6-12 mo for the next 2 years, and annually thereafter by the treating oncology team.



Survivors at a higher risk for local recurrence should have appropriate screening. 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. After mastectomy, the site of the reconstructed breast does not require imaging.

You should not refer survivors for routine screening with MRI because of an increased risk of false-positives. In women who have not undergone bilateral mastectomy, the use of MRI should be restricted to women who meet high-risk criteria. High risk is defined as a woman with a lifetime risk of greater than 20%, such as a woman with a BRCA1/BRCA2 mutation or a very strong breast cancer history.



Primary care clinicians should not offer routine laboratory tests of imaging, except if mammography is indicated for the detection of disease recurrence in the absence of symptoms. Chest x-rays and advanced body imaging should be ordered only if disease recurrence is suspected.

It is also recommended that primary care clinicians should counsel survivors to adhere to adjuvant endocrine therapy, which is used for 5 to 10 years and reduces the risk of recurrence and second primary breast cancers and improves overall survival. Reported adherence to a 5-year course of therapy ranges from 50% to 92% of breast cancer survivors.



It is also recommended that primary care clinicians assess the survivor's cancer family history and offer genetic counseling if potential hereditary risk factors are suspected. Genetic counseling should be recommended for survivors with the following characteristics:

At least 1 grandparent of Ashkenazi Jewish heritage

Younger than age 50 at diagnosis

History of ovarian cancer at any age or in any first-degree or second-degree relative

First-degree relative who had breast cancer before age 50

2+ first- or second-degree relatives diagnosed with breast cancer at any age

Diagnosis of bilateral breast cancer

History of breast cancer in a male relative

Any survivor diagnosed at age 60 or younger with triple-negative breast cancer

It is important to periodically review these issues with the survivor, because some survivors may not have been offered genetic counseling or testing at diagnosis and/or new cancer events may have occurred in the family after initial diagnosis and treatment. 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 are considered. 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 primary care clinician.



Let's next review the recommendations for screening for second primary cancers in breast cancer survivors. These are according to American Cancer Society Guideline for the Early Detection of Cancer in Average Risk, Asymptomatic Individuals.



Women should be advised to follow the ACS early detection guidelines for cervical, colorectal, endometrial, and lung cancers. Discuss the risks, benefits, and limitations of screening modalities with patients.

Postmenopausal women who are taking selective estrogen receptor modulators (SERMs), such as tamoxifen or raloxifene, 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.



In the first presentation, you learned about long-term and late effects experienced by breast cancer survivors. In this next section, we will review recommendations for primary care clinicians to assess and manage the effects of breast cancer and its treatment.



The body image recommendations are based on level 0 and 1a evidence ratings, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study and randomized controlled trials of breast cancer survivors. Body image or appearance changes affect 31-67% of breast cancer survivors and can be a major area of concern. Factors such as the loss of a breast, scarring and/or lymphedema after surgery, hair loss, 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 quality of life. These body image implications are especially relevant for young breast cancer survivors.

Women who are sexually active tend to have greater body image concerns that are associated with mastectomy (with or without reconstruction), hair loss from chemotherapy, concern with weight change, decreased self-esteem prior to the time of cancer diagnosis, poorer mental health, and a partner's difficulty understanding one's feelings.

Survivors with radiation-associated breast/soft-tissue fibrosis should be considered for therapy with oral pentoxifylline (Trental) and vitamin E.



The guideline recommends that primary care clinicians assess for survivor body image/appearance concerns. They should also offer the option of adaptive devices and/or surgery when appropriate. Breast forms or prostheses, bras, special lingerie, attachable nipples and other resources are available. Also, wigs, hats, scarves and other accessories are available for survivors who experience permanent hair loss or changes in hair color or texture. Clinicians should also refer survivors with body image concerns to psychosocial care. Support groups, psychotherapy, cognitive behavioral therapy, couple-based interventions or sex therapy may be helpful.



The lymphedema recommendations are based on a level 0 evidence rating. All breast cancer survivors who undergo breast surgery and/or radiation are at risk for lymphedema. It is estimated that over 40% of survivors will experience lymphedema to some degree. It can occur immediately after treatment or develop after many years. Radiation treatment can cause or exacerbate lymphedema.

Generally lymphedema is limited in extent and not disabling, but in some cases the swelling is extensive and leads to significant disability. Symptoms can range from mild discomfort to overt pain. Survivors with lymphedema are also at greater risk for the development of cellulitis of the breast, arm, or chest, which may exacerbate lymphedema if not treated promptly with antibiotics.

It is recommended that clinicans counsel survivors on how to prevent/reduce the risk of lymphedema, including weight loss for those who are overweight or obese and refer survivors 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.



The cardiotoxicity recommendations are based on level 0 and I evidence ratings, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study, and meta-analysis of randomized controlled trials. Several factors increase the risk of cardio toxicity, including treatment with radiation, chemotherapy, or hormonal/endocrine therapy with aromatase inhibitors, being post-menopausal, having had epirubicin; doxorubicin; or trastuzumab (especially if given with or after anthracycline). Additionally, aromatase inhibitors can raise cholesterol, and significant weight gain may lead to hypertension and insulin resistance, which further elevate the risk of cardiovascular disease.

So primary care clinicians should monitor lipid levels and provide cardiovascular monitoring, as indicated, as well as educate breast cancer survivors on healthy lifestyle modifications, potential cardiac risk factors, and when to report relevant symptoms (shortness of breath or fatigue).

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.



The cognitive impairment recommendations are based on a level 0 and 1a evidence level ratings indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study, and RCT of breast cancer survivors. Impairment in cognitive function can lead to distress and impaired quality of life. Up to 35% of breast cancer survivors report cognitive impairment after treatment, including problems with concentration, executive function and memory. It can also impact roles and relationships with family, co-workers, and the community.

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, surgery/anesthesia, endocrine therapy as well as cancer itself. Older adults and/or those with lower cognitive reserves may be more susceptible. The treatment of cognitive impairment in breast cancer survivors is not well established.

The guideline recommends that primary care clinicians 1) ask survivors if they are experiencing cognitive issues, 2) assess for reversible contributing factors of cognitive impairment and optimally treat when possible, and 3) refer survivors with signs of cognitive impairment for neurocognitive assessment and rehabilitation, including group cognitive training if available.



Recommendations for distress, depression and anxiety are based on evidence level ratings of 1 and 3, indicating meta-analysis of RCTs and case-control and prospective cohort studies. Many cancer survivors report ongoing difficulties in recovery and returning to "normal" after treatment. Some survivors experience fear of recurrence, which contributes to significant mental health problems for which they may already have an increased risk, including distress, depression, and anxiety. Prevalence estimates vary widely because of inconsistent use of measurement tools and differences in methodological approaches. In a systematic review of observational studies, the prevalence of depression and anxiety specifically among breast cancer survivors ranged from 10-22%.

Clinicians should 1) assess survivors for distress, depression, or anxiety, using a validated tool such as the NCCN Distress Thermometer, 2) conduct a more probing assessment for survivors at higher risk pf depression, such as those who are younger, those with history of prior psychiatric disease, and survivors with low socioeconomic status, and 3.) offer in-office counseling and/or pharmacotherapy and/or refer to appropriate psycho-oncology and mental health resources if signs of distress, depression, or anxiety are present.



Recommendations for fatigue are based on an evidence level rating of 0 and 1, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study, and meta-analysis of RCTs. Cancer-related fatigue is very common among cancer survivors, especially those who have had radiation and chemotherapy. Prevalence is estimated at 28-91%. Recommendations for how to screen and assess for fatigue come from the ASCO guideline.

Fatigue can be caused by factors such as anemia, thyroid dysfunction, and cardiac dysfunction, so primary care clinicians should assess for causative factors. For survivors who do not have an otherwise identifiable cause of fatigue, offer treatment or referral for factors that might impact fatigue, such as mood disorders, sleep disturbance, and pain. Regular exercise and cognitive behavioral therapy may lessen fatigue, so clinicians should counsel survivors to engage in regular physical activity and refer them for cognitive behavioral therapy as appropriate. There are minimal data to support use of pharmacologic agents for the management of fatigue in this population.



Recommendations for bone health are based on a level 0 evidence rating, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study. Up to 80% of breast cancer survivors experience bone loss. Risk factors unique to survivors include chemotherapy-induced premature menopause, GnRH suppression of gonadal function, antiestrogen therapies, and glucocorticoids. Lifestyle factors, including smoking, excess alcohol, inadequate exercise, low calcium, and vitamin D deficiency are common in this population and increase the risk of osteoporosis. Initial strategies to reduce the morbidity associated with bone loss include education about risk factors and a healthy lifestyle, including physical activity and regular weight-bearing exercises, avoiding tobacco, limiting alcohol intake, and calcium and Vitamin D3 supplementation for all adults older than 50.

Clinicians should 1) refer post-menopausal survivors for a baseline DEXA scan and 2) refer for repeat DEXA scans every 2 years for women taking aromatase inhibitors; premenopausal women who are taking tamoxifen and/or a gonadotropic-releasing hormone agonist; and women with chemo-induced menopause.

Pharmacologic options should be considered in survivors at high risk for bone loss and/or fracture. Bisphosphonates or denosumab can prevent bone loss and/or treat established osteoporosis. However, these drugs do have side effects and risks that must be considered first. Selective estrogen receptor modulators (SERMs) should not be used in the prevention of osteoporosis in women who are taking an aromatase inhibitor.



Recommendations for musculoskeletal health are based on a level 0 and 3 evidence rating, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study and casecontrol and prospective cohort studies. Breast cancer survivors may report difficulties with the ipsilateral upper extremity after surgery. Prevalence of symptoms varies. These can lead to a decreased ability to perform activities of daily living and can impact employment.

Primary care clinicians should assess for musculoskeletal symptoms, including pain, by asking survivors about their symptoms at each encounter. Aromatase-inhibitor joint and muscle pain can be severe enough for women to discontinue treatment. In these women, 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. Because poor adherence to therapy can increase risk for recurrence, so helping survivors manage their symptoms and encouraging drug compliance is important.

Clinicians should also offer one or more of the following interventions based on clinical indication: acupuncture, physical activity, referral for physical therapy or rehabilitation.



Pain and neuropathy recommendations are based on level 0, 1, 1a and 1b evidence ratings, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study, and case-control and prospective cohort studies; meta-analyses of RCTs; RCT of breast cancer survivors; and RCTs based on cancer survivors across multiple sites. A substantial percentage of breast cancer survivors experience long-term, treatment-related chronic pain that can negatively impact quality of life. 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. Follow ASCO's clinical practice guideline on prevention and management of chemotherapy-induced peripheral neuropathy.

Clinicians should :

Assess for pain and contributing factors for pain with the use of a simple pain scale and comprehensive history of the survivor's complaint

Offer interventions, such as acetaminophen, non-steroidal anti-inflammatory drugs, physical activity, and/or acupuncture, for pain

Refer to an appropriate specialist, depending on the etiology of the pain once the underlying etiology has been determined

Assess for peripheral neuropathy and contributing factors for peripheral neuropathy by

asking the survivor about their symptoms, specifically numbness and tingling in hands/feet, and the characteristics of that symptom

Offer physical activity for neuropathy

Offer Duloxetine for survivors with neuropathic pain, numbness, and tingling



Infertility recommendations are based on level 0 evidence rating indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study. Infertility can have a profound impact on physical and psychosocial quality of life. 10.9% of all new breast cancer cases are in women <45, making infertility an issue for many younger survivors. Chemotherapy can be gonadotoxic, leading to reduced fertility or early menopause secondary to premature ovarian failure. Most of the frequently used chemotherapy agents used are also those that most often lead to premature ovarian failure.

Clinicians should refer survivors of childbearing age who experience infertility to a specialist in reproductive endocrinology and infertility as soon as possible.



Sexual health recommendations are based on level 0 and 1a evidence ratings, indicating expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study and RCT of breast cancer survivors. Sexual complaints are a common problem among breast cancer survivors that should be assessed. These include sexual desire disorder and decreased libido, arousal or lubrication concerns, orgasmic concerns, and dyspareunia.

Clinicians should

- Assess for signs and symptoms of sexual dysfunction or problems with sexual intimacy
- Assess for reversible contributing factors to sexual dysfunction and treat when appropriate
- Offer nonhormonal, water-based lubricants and moisturizers for vaginal dryness
- Refer for psychoeducational support, group therapy, sexual counseling, marital counseling, or intensive psycho-therapy when appropriate


Recommendations for premature menopause and hot flashes are based on a 1a evidence level rating, indicating RCT of breast cancer survivors. Premature menopause is caused by premature cessation of ovarian function due to chemotherapy or as side effect of endocrine therapies. 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.

To help mitigate vasomotor symptoms of premature menopausal symptoms, clinicians should offer SNRIs and SSRIs, gabapentin, clonidine, acupuncture, lifestyle modifications, and/or environmental modifications to help mitigate vasomotor symptoms of premature menopausal symptoms.



For health promotion recommendations, primary care clinicians are encouraged to follow the ACS Nutrition and Physical Activity Guideline for Cancer Survivors. Let's review them now.



Primary care clinicians should:

Address information needs of the survivor related to breast cancer and its treatment, side effects, other health concerns and available support services; clinicians should also provide or refer survivors to appropriate resources to meet these needs.

Clinicians should counsel survivors to achieve and maintain a healthy weight and should counsel overweight or obese survivors to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss.

Clinicians should counsel survivors to engage in regular physical activity consistent with the ACS guideline, and specifically survivors should avoid inactivity and return to normal daily activities as soon as possible following diagnosis, aim for at least 150 minutes of moderate or 75 minutes of vigorous aerobic exercise per week, and include strength training exercises at least 2 days per week, emphasizing strength training for women treated with adjuvant chemotherapy or hormone therapy.

Survivors should be counseled to achieve a dietary pattern that is high in vegetables, fruits, whole grains and legumes; low in saturated fats; and limited in alcohol consumption.

Finally, survivors should be counseled to avoid smoking and survivors who smoke should be referred to cessation counseling and resources.



The BRC guideline provides clear recommendations to primary care clinicians on their role in the care coordination of survivors.



Primary care clinicians play an important role on the care team. The guideline recommends that clinicians consult with the cancer treatment team and obtain a treatment summary and survivorship care plan. A summary of a patient's diagnosis and treatment received should be provided by the oncology team when a breast cancer survivor transitions to other providers. The oncology team should also work with the patient to develop an individualized cancer survivorship care plan that guides recommendations for the type and timing of follow-up imaging, lab tests, and office visits. 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.

Primary care clinicians should also maintain communication with the oncology team throughout the patient's diagnosis, treatment, and posttreatment care to ensure care is evidence-based and well-coordinated. 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; making appropriate referrals as needed; and coordinating those components of survivorship care that are agreed upon with the treating clinicians.

Finally, primary care clinicians should encourage the inclusion of caregivers, spouses, or partners in usual breast cancer survivorship care and support.



Let's review what you've learned with a case study.



Mrs. C is a 68 year old woman scheduled for a routine primary care visit. She is 2 years s/p radiation treatment following lumpectomy for stage 1 breast cancer which was detected from a screening mammogram. She offers no complaints.

Additional PMH: type 2 diabetes, hypertension

Current meds: letrozole, metformin, losartan, OTC calcium with vitamin D

BP 112/70 BMI 28



During the visit, you order lab tests to check her A1C, chemistry, and lipids. What additional testing may be needed to evaluate for complications related to AI use?



Use of aromatase inhibitors has been associated with bone loss. A breast cancer survivor taking AIs should be referred for DEXA scan every 2 years. A cardiac stress test or chest x-ray would not be indicated because of AI use. AI use is also linked to elevation in cholesterol which can contribute to cardiac risk, but it is not necessary to order a cardiac stress test routinely with AI use.



What testing is recommended to screen for local recurrence or new primary breast cancer in Mrs. C?



BRCA1/BRCA2 mutation or

Very strong history of breast cancer)



Which one the statements is not true?



primary care clinicians should screen for other cancers as they would for patients in the general

population; and they should provide an annual gynecologic assessment for postmenopausal women on selective estrogen receptor modulator therapies.



In this lesson you learned to:

Describe how to care for breast cancer survivors as outlined in the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline.

Demonstrate understanding of the primary care clinician's role in providing clinical follow-up care to breast cancer survivors.



Thank you Dr. Chang for your presentation and for sharing your expertise on this important topic.

This concludes the webinar, please continue to explore the remaining sections of the cancer survivorship e-learning series for primary care providers. Thank you.