FOLLOW-UP CARE
FOR EARLY-STAGE BREAST CANCER

Effective Date: October 2015

The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

BACKGROUND

Once a patient with resected early stage breast cancer has completed their adjuvant therapy (either chemotherapy and/or radiation therapy) at the cancer center, they can be safely transitioned back to the care of their family physician for ongoing routine breast cancer surveillance.

The goals of follow-up care for patients with early-stage breast cancer are to detect recurrent or new breast cancer, to monitor for side effects of any adjuvant therapy (chemotherapy, endocrine therapy, biologic therapy and/or radiation therapy) and to provide ongoing patient support, including patient education, reassurance, and psychosocial support.

In order to meet these surveillance goals, an evidence-based strategy for follow-up should be included in the patient's overall care plan. All patients are not required to follow-up at the tertiary cancer centers for ongoing routine breast cancer surveillance. Compared to follow-up at the tertiary cancer center, it is known that follow-up care provided by general practitioners is equivalent in terms of long term breast cancer outcomes (recurrence/survival and quality of life).[1] Moreover, patient satisfaction may be higher for some with follow-up care provided in general practice compared to hospital outpatient departments [2] and there are no significant increases in the workload of general practitioners.[3]

Assuming that a shared approach is appropriate for the follow-up care of patients who were treated for early-stage breast cancer, the purpose of this guideline is to provide evidence-based strategies for the care of patients who have been discharged to their referring physician. As such, this guideline should enable physicians to provide follow-up care to their patients and ensure that essential elements are communicated to the patient in a practical format.

GUIDELINE QUESTIONS

1. Who is responsible for follow up care?

2. What investigations (i.e., tests and exams) constitute follow-up care for patients who have completed active medical or radiation oncology treatment for early-stage breast cancer? How often should these investigations be performed?

3. What are the signs and symptoms to look for regarding a breast cancer recurrence?

4. What are the potential complications from breast cancer treatment (surgery, chemotherapy, radiotherapy, endocrine therapy, and/or biologic therapy) that physicians should be aware of? What are the symptoms of these complications and how are they typically managed?

5. What are the more common survivorship concerns and challenges of patients who have been treated for early-stage breast cancer? How can survivorship be improved for these patients? What types of support are available?

DEVELOPMENT

This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team. Members of the Alberta Provincial Breast Tumour Team include medical oncologists, radiation oncologists, surgeons, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and a Knowledge Management

Specialist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

The guideline development panel, including medical oncologists, radiation oncologists, and breast surgeons, originally developed a patient discharge letter to be sent to patients' referring physicians regarding aspects of follow-up care. Recommendations contained in the physician letter were based largely on the 2005 Canadian Medical Association guidelines on follow-up after treatment for breast cancer,[4] as well as other available guidelines. Subsequently, the Alberta Provincial Breast Tumour Team agreed to develop a formal consensus guideline, with updated recommendations based on more recent evidence from the literature. After a review of existing guidelines, consensus recommendations were agreed upon.

SEARCH STRATEGY AND REVISION HISTORY

A systematic search for relevant literature related to breast cancer follow-up was conducted of: MEDLINE and EMBASE. The search included the terms "follow-up" or "surveillance" or "discharge" or "investigation" or clinical examination" AND "breast neoplasm." The MEDLINE and EMBASE search was limited to clinical trials and meta-analyses published in the English language during the previous ten years only (e.g., 2001 to September 2011); a total of 3,812 citations were returned, of which 29 were deemed relevant (i.e., presented data on delivery of follow-up or investigations for follow-up).

A second search was conducted of specific concerns related to follow-up. The MEDLINE and EMBASE databases were searched using the following terms: "lymphedema" or "weight management" or "bone pain" or "sexual functioning" or "psychosocial health" or "fatigue" AND "breast cancer follow-up" and limited to clinical trials and meta-analyses published in the English language during the previous ten years only (e.g., 2001 to September 2011).

The search strategies were repeated just prior to publication of the guideline and covered the period of time from September 2011 through April 2013. An additional 778 studies were identified; of these, 12 were deemed relevant and included in the full literature review.

In addition, the Cochrane Library, Cancerviewcanada, and the National Guidelines Clearinghouse were searched for guidelines and systematic reviews related to breast cancer follow-up. A total of six clinical practice guidelines and two systematic reviews were deemed relevant.

For the 2015 partial update, a review of other existing guidelines was conducted in November 2014 to retrieve updated versions of previously referenced guidelines and any relevant new guidelines. The National Guidelines Clearinghouse and websites of known guideline developers were searched. A total of seven new guidelines were deemed relevant and informed updates of the guideline and discharge letter. A summary of these guidelines is included in the Appendix.

A limited search of the literature was also performed in MEDLINE using the terms "follow-up" or "patient discharge" AND "breast neoplasms". The search was limited to clinical trials, systematic reviews, or meta analyses published in the English language from 2013 – March, 2015. A total of 422 studies were retrieved but none were found relevant to include in the update.

TARGET POPULATION

The recommendations contained in this guideline apply to patients who have completed active medical or radiation oncology treatment for early-stage breast cancer and have been discharged by the cancer care centre for care by the referring physician.

RECOMMENDATIONS

1. Responsibilities regarding follow-up care.

- Cancer surveillance is a shared responsibility between patient and health care provider. It is the health care provider's responsibility to attend to and support the medical and psychosocial needs of the patient, including making appropriate referrals. It is the patient's responsibility to follow through with recommended treatment, book appropriate follow-up appointments, seek help as needed, and report any concerning symptoms to their health care provider.
- Following completion of active medical or radiation oncology treatment, patients may be discharged from the tertiary cancer center back to their primary health care provider for ongoing breast cancer surveillance.
- Guidance on follow-up care and mechanisms for referral back (if required) to tertiary cancer care center should be made available.
- A written care plan recorded by a named health professional with copies sent to the healthcare provider and the patient should be encouraged.
- A health practitioner (i.e. family physician, surgeon, specialist from a breast or gynecologic clinic, nurse practitioner, etc.) with experience in clinical breast exam should provide follow-up care to patients who have been treated for early stage breast cancer.

2. Investigations and surveillance for the follow-up of all patients who have completed active medical or radiation oncology treatment for early-stage breast cancer.

- Self-examination
  - Patients may perform breast self-examination (BSE) every month. There is no evidence to support the use of BSE as a cancer screening method, but it has been shown to empower women in taking responsibility for their health. The benefits and limitations of BSE should be discussed with patients and BSE can be encouraged to raise breast self-awareness among patients.[5]
- Clinical examination
  - Components: at minimum, history and physical examination of the breast(s), chest wall, and supraclavicular and axillary nodes, auscultation of the chest, and palpation of the liver.
  - Frequency: every 6 months for 2 years, then annually
- Imaging tests (for patients with intact breasts)
  - Mammography: post-treatment mammogram of intact breast(s) 1 year after diagnostic mammogram (or 6+ months post-definitive radiotherapy), then annually; performed at an accredited mammography centre. Mammography of an entirely reconstructed breast (autologous or implant) is not recommended as there is no significant residual natural breast tissue to image. Routine breast cancer screening with breast MRI is not generally indicated [see Magnetic Resonance Imaging in Breast Cancer Guideline (effective 2012-01)].[6]

- Other routine investigations (e.g., computed tomography, bone scan, ultrasound of the abdomen, chest x-ray, tumour markers, and laboratory tests, etc.) are generally not recommended for asymptomatic patients.

3. Signs and symptoms to look for regarding a breast cancer recurrence.

- Patients should be informed on the use / limitations of monthly breast self-exam.
- Patients should be counselled on symptoms of potential recurrence (i.e., new lumps, bone pain, chest pain, persistent headaches, dyspnea, or abdominal pain).
- Table 1 describes signs and symptoms that may suggest recurrence. Patients presenting with any of these symptoms should undergo the appropriate investigations
- If at any time the physician has concerns regarding possible local or metastatic recurrence this should be investigated as clinically indicated.
- For referral back to the Cancer Center, please contact the appointment booking office at the Cancer Center to arrange to see the patient.
- Should the physician have any specific or more pressing concerns, one of the oncologists in radiation oncology or medical oncology can be available to discuss the patient.
- **For any emergent concerns, patients should be directed to the nearest emergency department for immediate evaluation and intervention**

Table 1. Symptoms and appropriate investigations for a local recurrence or metastatic disease.

Symptom	Action / Investigation
new mass in breast	mammography +/- ultrasound +/- needle biopsy
new suspicious rash or nodule on chest wall	refer to surgeon for evaluation and biopsy
new palpable lymphadenopathy	refer to surgeon or interventional radiology for biopsy
new persistent bone pain	plain x-ray of affected site(s) and bone scan
new persistent cough or dyspnea	chest x-ray and/or CT chest
new hepatomegaly or RUQ abdominal pain or jaundice	ultrasound and/or CT scan of abdomen and liver enzymes
new onset seizures	seizure management (as required) and CT/MRI brain
back pain with limb weakness, change in sensation, change in reflexes, or loss of bowel/bladder control	MRI spine
new persistent headache or new concerning neurologic deficits	CT / MRI brain
altered level of consciousness, nausea, vomiting, and/or pain with symptomatic hypercalcemia	IV hydration and bisphosphonate therapy

4. Potential complications from cancer treatment.

General considerations for all patients

- Long-term follow-up care is important for patients after breast cancer therapy, for cancer surveillance, medication adherence, side effect management, and general patient support
- For any patient with a history of previous breast cancer, the use of exogenous estrogens (such as oral contraceptives or hormone replacement therapy) is generally contraindicated.

Endocrine therapy

- Intended treatment duration and/or endocrine therapy treatment plan will be outlined by the oncology team.
- Initial prescription will be written and dispensed at the cancer center.
- Further prescription will be obtained through the patient's family physician. Prescription for endocrine therapy can be faxed to and dispensed by the cancer centre pharmacy (free of charge to the patient) for medications to either be picked up or mailed to the patient.
- Adherence to adjuvant endocrine therapy should be routinely assessed and encouraged on each follow-up visit.

Tamoxifen:

- Patients receiving tamoxifen are at a slightly increased risk of deep vein thrombosis, stroke, and cataracts; investigations should be performed as per signs and symptoms (e.g., sudden swelling or pain in an arm or leg, dyspnea, visual changes, etc.).
    - More common side effects of tamoxifen include hot flashes and vaginal discharge.
    - Ophthalmology exam recommended if patient develops cataracts or vision problems
    - In patients with an intact uterus, monitoring for endometrial cancer should include appropriate gynecologic assessment as indicated.
    - Patients experiencing abnormal vaginal bleeding should be referred to a gynecologist.

Aromatase Inhibitors (AIs):

- Patients receiving AIs (i.e. anastrozole, exemestane, letrozole) may be at increased risk of arthralgia, myalgia, dyspareunia, vulvovaginal atrophy, and hot flashes.
    - All patients initiated on AIs are at risk of developing osteopenia and/or osteoporosis and should have a baseline bone density assessment (DEXA scan) performed.
    - Subsequent follow-up DEXA and management of osteopenia / osteoporosis should be treated as per osteoporosis guidelines.[7]
        - Of note: Raloxifene (Evista®) should not be prescribed for osteoporosis treatment in patients with previous ER+ breast cancer on endocrine therapy.
        - In cases where osteopenia / osteoporosis treatment is indicated, an alternate bone targeted agent (e.g., bisphosphonate or RANK-ligand inhibitor) should be used instead.

- All patients should be encouraged to maintain good "bone health" measures such as:
    - Performing regular weight-bearing, balance and strengthening exercises
    - Smoking cessation
    - Vitamin D: 1000 - 2000 IU per day[7]
    - Calcium (dietary and supplements): 1000-1200 mg per day if postmenopausal (preferably from dietary sources)

Peripheral Neuropathy

- Certain types of chemotherapy may cause peripheral neuropathy. Symptoms vary depending on the type of chemotherapy and whether sensory or motor nerves are involved, but can include paresthesias, numbness, imbalance, pain, and weakness of muscles in the hands and feet.[8,9]
- Work-up should include appropriate history and physical exam, as well as directed neurological exam (e.g., reflexes, muscle strength and tone, sensations, posture, and coordination). In rare severe cases, referral to neurology for other directed evaluation (e.g., electromyography, nerve biopsy, and CT / MRI imaging) may also be indicated.[10]
- Treatments may include analgesics (i.e., acetaminophen, ibuprofen, opiates), certain types of anticonvulsants (i.e., gabapentin, topiramate, pregabalin, carbamazepine, phenytoin), lidocaine (patch), antidepressants (i.e., amitriptyline, nortriptyline) or transcutaneous electrical nerve stimulation.[10]
- Other alternative treatment modalities, such as acupuncture, capsaicin cream, alpha-lipoic acid, and biofeedback have been used to manage the symptoms of peripheral neuropathy; however, these methods have not been tested rigorously.

Lymphedema

- Lymphedema of the arm is a possible complication of breast cancer treatment. It occurs more frequently with mastectomy, axillary lymph node dissection, and radiation therapy.
- Treatments may include the following:
    - Exercise: use of muscle contractions of the affected limb to facilitate the drainage of lymph fluid; strenuous exercises should typically be avoided.[11]
    - Manual lymphatic drainage / physiotherapy: use of massage to move lymph fluid out of the affected limb to functioning lymph nodes for drainage[11]
    - Compression therapy: a technique that uses garments, bandages, or gradient pumps to compress the affected limb and move lymph fluid towards the torso.[11] Compression therapy may be combined with manual lymphatic drainage and/or physical therapy.
- If required, dedicated lymphedema management services are available in Calgary and Edmonton:
    - Calgary: www.albertahealthservices.ca/services.asp?pid=service&rid=1026510
    - Edmonton: http://www.albertahealthservices.ca/services.asp?pid=service&rid=1064108

Cardiac Dysfunction

- Cardiac dysfunction is an increasingly rare complication but can still occur in some patients undergoing adjuvant treatment (e.g., anthracycline-based chemotherapy or trastuzumab or left-sided breast/chest wall adjuvant radiation therapy)
- If patient is symptomatic or has clinical signs of congestive heart failure, further cardiac evaluation (with ECG and MUGA or echocardiogram), treatment and referral to cardiology would be warranted.

Acute Leukemia / Myelodysplasia

- This is a rare complication observed in some patients who have undergone adjuvant chemotherapy (typically anthracycline-based treatment).
- If abnormal CBC + differential (with peripheral blood smear) is of clinical concern (i.e. symptoms and/or persistent cytopenias and/or blasts are noted), referral to hematology would be warranted.

5. Common survivorship concerns and challenges.

Fatigue

- Fatigue post breast cancer diagnosis and treatment can be multifactorial.
- Fatigue may be the result of physical and/or psychological factors
  - Physical:
    - Pain
    - Medications (e.g., narcotics or sedatives) and therapies that cause sleep disturbance[12]
    - Direct side effects of treatment (e.g., chemotherapy-induced anemia)
    - Dietary / nutritional deficiencies
    - Other medical comorbidities
    - Recurrent disease
  - Psychological:
    - Depression, anxiety
- A thorough review of the patient should always be performed to determine the underlying cause in order to provide the appropriate directed therapy
- In addition to other directed treatments, appropriate patient education, encouraging exercise, appropriate rest, and cognitive behavior therapy should always be discussed.

Sexual Health and Fertility

***Sexual Intimacy*:** Common issues for patients include intimacy concerns, painful intercourse or loss of sensation, symptoms of menopause, and decreased libido.[13,14] Sexual functioning should be discussed with the patient at follow-up visits and appropriate referrals to sexual health experts made. Patients can be referred to the Oncology and Sexuality, Intimacy, and Survivorship (OASIS) program in Calgary and Edmonton for comprehensive care of physical and psychological sexual health concerns following cancer treatment (http://www.albertahealthservices.ca/frm-19189.pdf).

***Self-Image*:** For some women, breasts are an important part of their self-image. If they are concerned about how a lumpectomy or mastectomy has changed their body, they may be interested in more information regarding an external breast prosthesis or breast reconstruction (referral to plastic surgery). Psychological counselling can also be helpful for improving body image satisfaction, addressing relationship concerns, and reducing sexual dysfunction.

***Menopause Symptoms*:** Endocrine therapies commonly cause menopausal symptoms and chemotherapy may lead to early menopause. Oral estrogens (such as hormone replacement therapy) are not recommended in patients with a history of breast cancer due to concern for increased risk of breast cancer recurrence. Hot flashes which interfere with sleep and daily function can be managed with non-hormone therapies (e.g., venlafaxine or gabapentin). Patients on aromatase inhibitors are more likely to experience dyspareunia, vaginal dryness, and other symptoms of vulvovaginal atrophy than those on tamoxifen.[15] First line treatment includes lifestyle modifications (e.g., smoking cessation, avoidance of scented soaps), vaginal moisturizers and lubricants (e.g., Replens®), and vaginal dilators.[16] Although effective for vaginal atrophy symptoms, the long term safety of topical vaginal estrogen preparations are unknown in patients with a history of prior breast cancer. For refractory vaginal symptoms, referral to gynecology and/or sexual health experts could be considered for a detailed discussion of the potential benefits (local symptom relief) and potential side effects (including theoretical risk of breast cancer recurrence).[17,18]

Fertility and Family Planning: Pregnancy while on endocrine therapy is contraindicated. The absence of regular menses does not equate to menopause in all cases. Non-hormonal contraception is generally recommended (e.g., condoms, IUD). There is an increased risk of sub-fertility / infertility and premature menopause in women who have had previous chemotherapy. There is no evidence that future pregnancy adversely affects recurrence or survival.

Genetic Counselling

- Patients should be informed to report any changes in their family history to their physician. All women from high-risk families should be offered a referral to genetic counselling. For more information, see the Alberta Health Services Genetic Services:
    - Edmonton - http://www.albertahealthservices.ca/services.asp?pid=service&rid=5956
        - Referral form - http://www.albertahealthservices.ca/rf-z4-cancer-genetics-criteria.pdf
    - Calgary - http://www.albertahealthservices.ca/services.asp?pid=service&rid=1026525

Psychosocial Support and Resources

- Patients often struggle with emotional and psychological concerns post-treatment.
- Patients may experience fear of recurrence, stress (family, financial, or work issues), depression, anxiety, loneliness, or anger over their experience with cancer.
- Post-treatment adjustment should be assessed and, if problems are identified, treatment and/or referral to an appropriately trained professional should be ensured.

General Support Resources:

- Canadian Cancer Society – http://www.cancer.ca or 1-888-939-3333
- Alberta Health Services – http://www.albertahealthservices.ca
  Click: *Health Information* > *CancerControl Alberta*
  Local sources of help: *CancerControl Alberta* > *Patient Information*
- American Society for Clinical Oncology (patient site): http://www.cancer.net
- CancerBridges – www.cancerbridges.ca

Counselling and Support: Psychosocial support should be encouraged and facilitated, as needed. Some patients may benefit by participating in educational, support, or counselling programs, available through the cancer centres and in the community:

- Calgary: call 403-355-3207; or visit
  www.albertahealthservices.ca/services.asp?pid=service&rid=1047804
- Edmonton: call 780-643-4303; 780-643-4304 or visit
  www.albertahealthservices.ca/services.asp?pid=service&rid=1053260
  www.albertahealthservices.ca/services.asp?pid=service&rid=1003332
- Grande Prairie: 780-538-7372
- Lethbridge: 403-388-6814
- Medicine Hat: 403-529-8817
- Red Deer: 403-343-4485
- Other communities visit http://www.albertahealthservices.ca/Cancer.asp and click *Cancer Programs and Services*
- Peer support: http://cancerconnection.ca/home

General Health Recommendations

According to the American Institute for Cancer Research, once treatment for cancer has been completed, and unless otherwise advised, the patient should aim to follow cancer prevention recommendations for diet, physical activity, and healthy weight maintenance.[19]

Lifestyle factor	Recommendations
Body weight[20,21]	Body mass index (BMI): 18.5-25 kg/m^2 Waist circumference: less than 80 cm for women and less than 94 cm for men
Physical activity[22-25]	Be active 2.5 hours/week, focusing on moderate-vigorous activity spread throughout week
Nutrition[26]	Follow cancer prevention recommendations from the *American Institute for Cancer Research* • Avoid sugary drinks. Limit consumption of energy-dense foods. • Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans. • Limit consumption of red meats (beef, pork and lamb) and avoid processed meats. • Limit consumption of salty foods and foods processed with salt.
Dietary supplements/ bone health[27-29]	Vitamin D: 1000 - 2000 IU per day Calcium: 1000-1200 mg per day if postmenopausal (preferably from dietary/food sources).
Alcohol[30-32]	Ideally limit consumption (<1 drink/day, <3 drinks/week)
Smoking	Practice smoking cessation. For help contact Alberta Quits 1-877-710-QUIT(7848) or www.albertaquits.ca
Sun exposure[33]	Avoid harmful exposure, use sunscreen and wear sunglasses, do not use indoor tanning beds, check skin regularly and report changes to your physician.

DISCUSSION

Responsibility of follow-up

Cancer surveillance is a shared responsibility between the specialist, the family physician (if one is available) or specialty clinic, and the patient. Better coordination between specialists and physicians may be required to ensure that non-oncology services (i.e., influenza vaccination, cholesterol screening, colorectal cancer screening, and bone densitometry) are provided consistently.[34] Following completion of active medical or radiation oncology treatment, patients may be discharged from the tertiary cancer center back to their primary health care provider for ongoing breast cancer surveillance. This is based on evidence that family physician-led follow-up is equivalent to specialist-led follow-up, in terms of patient satisfaction and recurrence outcomes.[35]

Ideally a health practitioner (e.g., family physician, nurse practitioner, specialist from a breast or gynecology clinic, etc.) with experience in clinical breast exam should provide follow-up care to patients who have been treated for early stage breast cancer. Due to the increasing burden of breast cancer on hospital clinics, means other than specialists or physicians have been investigated for delivering follow-up

care. Data comparing nurse-led telephone follow-up with hospital-based follow-up has been shown to be equivalent in terms of patient satisfaction[36] and detection of recurrences,[37] with reduced hospital clinic burden.[38] Moreover, as compared to physician-led follow-up, nurse-led follow-up has demonstrated high patient satisfaction, no differences in terms of time to recurrence or death, and greater cost-effectiveness.[39,40]

A written care plan recorded by a named health professional with copies sent to the healthcare provider and the patient may be useful.[41,42]

According to the New Zealand Guidelines Group, guidance on follow-up care and mechanisms for referral back to the tertiary cancer care center should be made available, if required.[43] In Alberta, the appointment booking offices at the Cancer Centers may be utilized if referral back is necessary (i.e. cancer recurrence). Reasons for a re-referral back to the cancer center have been outlined previously (see Recommendation 3).

Follow-up investigations

Clinical examination for breast cancer outpatients should include, at minimum, patient history and physical examination of the breast(s), chest wall, and lymph nodes, auscultation of the chest, and palpation of the liver. The frequency of clinical examination should be every six months for two years, then annually. Similar recommendations have been developed elsewhere.[4,44,45] A randomized controlled trial comparing specialist-led versus family physician-led follow-up utilized a similar strategy that included examination of the breasts, chest, lymph nodes, and liver with similar frequency (e.g., three to six months for three years, then every six months for two years, then annually), but with the addition of assessment for bone pain/tenderness and neurological abnormalities; regardless of the way follow-up was delivered, the rate of death (all causes) was just six percent.[35] A cost analysis that included 472 breast cancer patients without distant metastasis after primary treatment and compared four strategies (e.g., three versus six months and routine versus clinical examinations) showed, after a mean follow-up of 4.2 years, that there was no difference in disease-free or overall survival, regardless of strategy. Cost, however, was more than two times greater for more frequent routine follow-up.[46]

Regarding imaging, only mammography is routinely recommended (i.e., annually). The sensitivity of annual mammography in patients with metachronous contralateral breast cancer was shown to be 70.8% (95% CI: 61.7-80.0) and was associated with better survival rates than detection by other means (HR: 3.18; 95% CI: 1.59-6.34).[47] Other investigations, such as bone scan, ultrasound of the abdomen, chest x-ray, and breast MRI are not recommended for asymptomatic patients. Furthermore, tumour markers and laboratory tests are also not recommended for asymptomatic patients. Although these recommendations are largely supported elsewhere,[4,44,45,48] there is some variation in the recommendations for mammography. The European Society for Medical Oncology (2013 guideline) recommends ipsilateral (after breast conservation surgery) and contralateral mammograms every one to two years.[49] The National Institute for Health and Care Excellence (2014 guideline) recommends that, after five years, patients be stratified and screened according to risk category.[41] Nevertheless, the recommendations on other imaging and blood work are in favor of signs and symptoms-based investigation only. This is based on lack of evidence from randomized controlled trial data and retrospective data that these tests lead to earlier detection of recurrences or survival differences.[35,50-54]

Special discussion topic: complications from endocrine therapy

Aromatase Inhibitors. In brief, short-term use of aromatase inhibitors appears to be safe; however, there is currently no long term data for cardiovascular, musculoskeletal, and central nervous system side effects. Switching from tamoxifen to exemestane may be associated with unfavorable changes in lipid profiles;[55] however, these changes may be due to the removal of tamoxifen rather than the aromatase inhibitor. Regarding musculoskeletal toxicity, some patients have reported non-inflammatory musculoskeletal symptoms or local inflammation in the tenosynovial structures.[56] Cognition, however, does not appear to be affected, at least in the short term.[57,58] Other side effects of aromatase inhibitors may include arthralgia and joint stiffness (especially among those with history of taxane use), bone pain, hot flashes, fatigue, myalgia, and insomnia.[59-62] The continued use of endocrine therapy should be encouraged and side effects managed, as possible. Guidance on the use of aromatase inhibitors can be found in the CancerControl Alberta quick reference guideline, *Systemic Therapy for Early Stage (Lymph Node Negative and Lymph Node Positive) Breast Cancer.*[63]

Tamoxifen. Patients receiving tamoxifen may be at a slightly increased risk of deep vein thrombosis, strokes, and visual disturbances;[64-66] investigations should be performed as per signs and symptoms (e.g., sudden swelling or pain in an arm or leg, dyspnea, visual changes, etc.). More common side effects of tamoxifen include hot flashes and vaginal discharge. In patients with an intact uterus, monitoring for endometrial cancer should include a gynecologic assessment, in addition to clinical examination. Patients experiencing abnormal vaginal bleeding should be referred to a gynecologist. Regarding drug-drug interactions, there is some concern with the concurrent use of CYP2D6 inhibitors, which can disrupt tamoxifen metabolism. Strong CYP2D6 inhibitors to be aware of include bupropion (Wellbutrin®), fluoxetine (Prozac®), paroxetine (Paxil®), and quinidine (Quinidex®).[67-69] Patients should discuss any concerns about interactions between prescription drugs with their cancer pharmacist. As compared the aromatase inhibitor anastrozole, tamoxifen resulted in more treatment-related adverse events (61% vs. 68%; p<.0001) and treatment-related serious adverse events (5% vs. 9%; p<.0001), among postmenopausal women in the ATAC trial. Among these adverse events were gynecological events (3% vs. 10%; p<.0001) and muscle cramps (4% vs. 8%; p<.0001); however, patients in the anastrozole group reported more frequent osteopenia or osteoporosis (11% vs. 7%; p<.0001), carpal-tunnel syndrome (3% vs. 1%; p<.0001), and hypercholesterolemia (9% vs. 3%; p<.0001).[70] The continued use of endocrine therapy should be encouraged and side effects managed, as possible. Guidance on the use of tamoxifen can be found in the CancerControl Alberta quick reference guideline, *Systemic Therapy for Early Stage (Lymph Node Negative and Lymph Node Positive) Breast Cancer.*[63]

Endocrine therapies commonly cause menopausal symptoms, and chemotherapy may lead to early menopause. Hot flashes which interfere with sleep and daily function can be managed with non-hormone therapies (e.g., venlafaxine or gabapentin). Aromatase inhibitors may are more likely than tamoxifen to cause significant vulvovaginal atrophy (VVA), vaginal dryness, and sexual dysfunction.[15] Vaginal dryness may be alleviated with vaginal moisturizers and lubricants.[16] Vaginal dilators can be used to manage some symptoms of VVA. In severe cases when non-hormonal therapies have not improved symptoms, the use of low-dose topical vaginal estrogens is controversial; more information about their long-term safety in this population is needed. Studies on the use of intravaginal estrogens among breast cancer survivors have produced conflicting results and there have been no long-term randomized controlled trials looking at the risk of breast cancer recurrence with the use of vaginal estrogens. Studies have shown that the rate of vaginal absorption of estrogen through topical application varies, but it is unclear whether or not short-term increases in serum estrogen levels increase the risk of recurrence.[16] Conjugated estrogen creams result in the highest degree of systemic absorption and are contraindicated in breast cancer survivors.[16] Estriol

likely has the lowest risk as it is not transformed into estradiol or estrone.[16] Until more research is done on the long-term impact of topical vaginal estrogen on breast cancer recurrence risk, non-hormonal options should remain as first-line treatment for women with a history of hormone receptor-positive breast cancer.[16,17,71] However, the use of topical vaginal estrogen therapies (lowest amount for the shortest duration required to treat symptoms) could be discussed in severe cases after thorough discussion with the patient about the unknown risk of breast cancer recurrence.[17,71]

Special discussion topic: lymphedema

Lymphedema of the arm is a possible complication of breast cancer treatment. The prevalence of lymphedema among female breast cancer patients with no sign of disease four or more years after surgery (n=355) was 17.5% in a cross-section study.[72] This study, as well as a meta-analysis,[73] both showed that lymphedema was more common among patients who had undergone mastectomy (versus breast conserving surgery). The meta-analysis also showed that lymphedema increased among patients who had undergone axillary lymph node dissection and patients who had received radiotherapy.[73] Several treatments exist for lymphedema, and have been used as monotherapy or in combination. These include manual lymphatic drainage therapy, compression therapy, physical therapy, surgery, and low level laser therapy; each is discussed below.

Manual lymphatic drainage (MLD), or massage therapy, may represent a minimally invasive technique for relieving swelling of the arm. A randomized controlled trial (Martin et al., 2011) among 58 women with post-mastectomy lymphedema is underway and will compare four weeks of daily standard treatment (e.g., skin care, exercise, and compression) with four weeks of daily standard treatment plus manual lymphatic drainage, at one, three, and six months. Results are pending.[74] Earlier research by Williams et al. (2002) showed that MLD reduces excess limb volume and dermal thickness in the upper arm and improves quality of life (e.g., emotional function, dyspnea, and sleep disturbance) and pain and heaviness.[75] The addition of compression therapy to MLD was shown, among a prospective cohort of 537 patients with breast cancer-related lymphedema, to reduce the mean volume by more than 400 ml; by one year, approximately half of patients experienced an increase above 10% of their value at the end of intensive therapy.[76] Overall, there appears to be some evidence of benefit for MLD, with or without compression therapy; however, given the relative paucity of literature, more data on this technique is required. The results of the pending randomized controlled trial by Martin et al. should add to the body of evidence on MLD.

Compression therapy involves the use of garments, bandaging or wrapping, or a gradient pump to relieve lymphedema. Among 23 patients who had not previously been treated for lymphedema, the addition of intermittent pneumatic compression to decongestive therapy (DT) further reduced the mean volume by nearly 20% as compared to DT alone (45.3% vs. 26%; p<.05).[77] However, a larger study by Haghighat, et al. (2010), among 112 patients with mastectomy-related lymphedema, compared intermittent pneumatic compression plus DT with DT alone demonstrated better results with single modality therapy, in terms of volume reduction following treatment (43.1% vs. 37.5%; p=.036) and after three months (16.9% vs. 7.5%).[78] The efficacy of compression therapy was shown *not* to be related to the pressure of the bandage: low pressure (20-30 mm Hg) and high pressure (44-58 mm Hg) bandages resulted in equivalent reductions in edema after 24 hours (9.2% vs. 4.8%, respectively; not significant) in patients with breast cancer-related lymphedema resistant to other treatments.[79]

Physical therapy and exercise has been researched more extensively in the setting of breast cancer-related lymphedema. Complex decongestive physiotherapy (CDP) generally consists of a combination of modalities including lymph drainage, multi-layer compression bandage, elevation, remedial exercises, and

skin care. Liao, et al. (2004) found that daily CDP reduced the limb circumference, calculated volume, and edema ratio (p<.000) versus pretreatment values, with a mean reduction of excess volume of 67.8 +/- 33.2%, among patients (n=30) with unilateral upper or lower limb chronic lymphedema after breast or pelvic cancer therapy.[80] Kim et al. (2007) demonstrated reductions in volume along with increases in quality of life at six months, among breast cancer with lymphedema patients who underwent CDP.[81]

Exercise was previously thought to contribute to additional lymphedema in patients who had undergone treatment for breast cancer. However, a systematic review showed that exercise does not increase the risk of lymphedema and, in fact, appears to be beneficial for those with upper-limb dysfunction.[82] Twice-weekly progressive weight lifting has been shown, in a randomized controlled trial setting, to reduce the incidence of lymphedema in those at high breast cancer-related risk by 6% (p=.04); among those with five or more lymph nodes removed, the incidence was reduced by 15% (p=.003).[83] The authors also showed that this weight lifting regimen improved self-reported severity of lymphedema symptoms (p=.03) and lowered the incidence of lymphedema exacerbations (14% vs. 29%; p=.04), among breast-cancer survivors with stable lymphedema of the arm.[84] Despite these findings of a positive effect of exercise on lymphedema, there is also data to the contrary. A randomized controlled trial comparing moderate resistance exercise plus no activity restrictions with usual care plus activity restrictions showed no differences in the development of lymphedema after two years, among patients treated with breast cancer surgery with axillary node dissection.[85] Furthermore, another randomized controlled trial comparing supervised, group, aerobic, and resistance exercise sessions (20 over 12 weeks) with habitual activities showed no change among the intervention group at three-month follow-up.[86] Clearly additional data is required to determine the most effective exercise regimen, in this setting.

There is limited evidence regarding the efficacy of surgical interventions for the treatment of breast cancer-related lymphedema. A small prospective study among ten patients who were unresponsive to 12-weeks of non-operative treatment and were treated with lympho-venous anastomosis demonstrated a 4.8% reduction of lymphedema at three months and a 2% reduction after one year. Improvement in reported quality of life was minimal.[87] The LYMPHA technique (lymphatic-venous anastomoses at the time of axillary dissection) was prospectively compared to axillary dissection alone in 46 women with breast cancer. At 6 months, lymphedema occurred in one patient in the treatment group (4.34%) versus seven patients (30.43%) in the control group; no statistically significant differences in the arm volume were observed in the treatment group during follow-up, while the arm volume in the control group showed a significant increase after 1, 3, and 6 months from operation. There was significant difference between the 2 groups in the volume changes with respect to baseline after 1, 3, 6, 12, and 18 months after surgery (every timing P value < 0.01).[88] Despite these promising results, prospective randomized controlled trial data is lacking and there is a large variation in the selection of patients, classification of lymphedema, and indications and types of anastomosis procedures described in retrospective studies. Additional research is needed to better understand the efficacy of surgery as a treatment modality for breast cancer survivors with lymphedema.

Low level laser therapy (LLLT) is used for the management of several conditions, including arthralgia, tendinopathy, and back pain. The use of LLLT for the management of lymphedema is still considered experimental, as the optimal wavelengths, durations, and doses are yet to be defined. Nevertheless, it has shown some promise. Carati et al. (2003) conducted a double-blind randomized controlled trial comparing LLLT (one cycle or two cycles to the axillary region) with placebo, which showed a reduction in the mean affected limb volume at three months of follow-up after two cycles of active laser treatment; approximately 31% of subjects had a clinically significant reduction in the volume (>200 mL).[89] Lau, et al. (2009) demonstrated, among 21 patients with breast cancer-related lymphedema in a randomized controlled trial setting, that LLLT (12 sessions over four weeks) reduced arm volume by 28% and increased tissue

softening by 33% at four weeks post-treatment.[90] Although these results are promising, more prospective data on efficacy and safety is needed before this modality can become an accepted approach.

GLOSSARY OF ABBREVIATIONS

Acronym	Description
CDP	complex decongestive physiotherapy
CT	computed tomography
DEXA	dual-energy x-ray absorptiometry
DT	decongestive therapy
IU	international units
LLLT	low level laser therapy
MLD	manual lymphatic drainage
MRI	magnetic resonance imaging
U/S	ultrasound

DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

MAINTENANCE

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2016. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

CONFLICT OF INTEREST

Participation of members of the Alberta Provincial Breast Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Breast Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

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APPENDIX: Summary of guidelines for follow-up care of breast cancer (BCa) patients.

Topic	Cancer Care Manitoba, 2014[1]	American Society of Clinical Oncology, 2012[2]	National Comprehensive Cancer Network, 2014[3,4,5]	European Society for Medical Oncology, 2013[6]	New Zealand Guidelines Group, 2009[7]	National Institute for Health & Care Excellence, 2012[8]
Responsibility for follow-up	Not addressed	A physician with experience in cancer surveillance & CBE, including irradiated breasts. The HCP and pt should be informed of the follow-up plan.	Follow-up is optimally performed by members of the treatment team.	Specialized breast nurses are crucial and health authorities should make them available within the multidisciplinary team.	A clinician (e.g., breast specialist, breast physician, nurse practitioner) with experience in BCa surveillance & CBE, including irradiated breasts.	Discuss with pts where they would like to be followed up (primary, secondary, or shared care). All pts with BCa should be assigned to a named breast nurse specialist to support them throughout treatment and follow-up.
Involvement of general practitioners	*Follow-up described in the guidelines is meant to be carried out by GPs or primary care nurse practitioners.*	Early BCa pts may be transferred back to PC ~1 year after diagnosis. Follow-up in PC seems to lead to the same health outcomes with good pt satisfaction.	Screening for 2nd primary cancers should be a shared responsibility between the PCP and oncologist.	Not addressed.	Care may be shared with GP as appropriate (i.e., with ready access to specialist support); in this case, guidance on management and referral back to secondary care to be provided.	Pts should have an agreed, written care plan recorded by a named health professional with copies sent to the GP and the patient.
Self-care	*Gives list of symptoms to see HCP about (for patients)* Encourage pts to seek medical attention for any worrisome symptoms without waiting for next regular appointment.	Counsel women to perform monthly breast exam. Counsel on symptoms of recurrence: new lumps, bone, chest, or abdominal pain, persistent headaches, dyspnea. Provide helpful websites.	If lymphedema, use compression garments while exercising and work with professional if considering weight training	Not addressed.	Not addressed.	Give advice on how to prevent infection or trauma that may cause or exacerbate lymphedema.
Clinical trial	Not addressed.	Not addressed.	NCCN believes best management of any pt is in a clinical trial. Participation is encouraged.	Not addressed.	Pts should be the given opportunity to participate in clinical trials where eligible and available.	Not addressed.

Topic	Cancer Care Manitoba, 2014[1]	American Society of Clinical Oncology, 2012[2]	National Comprehensive Cancer Network, 2014[3,4,5]	European Society for Medical Oncology, 2013[6]	New Zealand Guidelines Group, 2009[7]	National Institute for Health & Care Excellence, 2012[8]
Laboratory and imaging tests	Annual mammogram starting 1 year after diagnostic mammogram, but not earlier than 6 months post RT. Abnormal signs should be investigated with exam, imaging, or lab as appropriate. *Not recommended:* X-Rays, CT-U/S-MRI-Bone-PET scans, tumour markers, CBC, or biochemistry if asymptomatic.	Post-treatment mammogram 1 year after diagnostic mammogram (or 6+ months post-definitive RT); subsequent mammograms annually if findings stable. *Not recommended:* Routine CBC, LFTs, chest x-ray, DEXA scan, liver U/S, CT scan, FDG-PET scan, breast MRI, tumour markers.	Annual mammography (or 6-12 months post-RT if breast conserved). Breast MRI may be considered in women at high risk for bilateral disease, such as *BRCA1/2* mutation carriers. *Not recommended:* LFTs, tumour markers, routine bone scans, CT, MRI, or PET scans, or U/S in asymptomatic patients.	Annual ipsilateral (after BCS) and contralateral clinical mammogram. Breast MRI may be indicated for young pts, especially if dense breast tissue or genetic or familial predispositions. Routine blood tests usually indicated for pts on ET due to side effects (mainly lipid profile). *Not recommended:* Other lab or imaging tests (e.g., CBC, routine chemistry tests, chest x-rays, bone scans, liver U/S, CT scans or tumour markers if asymptomatic.	Regular mammography to detect recurrence or new BCa at an early stage. Post-treatment mammogram 1 year after diagnostic (or 6+ months after RT); annually thereafter. For high risk of contra-lateral BCa (e.g., BRCA 1/2) mammogram of contralateral breast should be done by 12 months after the diagnostic mammogram; other imaging can also be considered.	Annual mammogram for all pts with early BCa, including DCIS, for 5 years. After 5 years, stratify screening frequency in line with pt risk category. *Not recommended:* Mammography of the ipsilateral soft tissues after mastectomy; U/S or MRI for routine post-treatment surveillance.
Clinic visits/ physical exam	Every 6 months for years 1-5, then annually. *To be included:* 1. Exam of breast(s), chest wall, axillae, supraclavicular nodes, lungs, bones, abdomen, CNS, arm for lymphedema. 2. If Tamoxifen, regular gynecologic exams (pap smears in accordance with guidelines). 3. If AI, monitor cholesterol and blood pressure.	Every 3-6 months for years 0 to 3, every 6-12 months for years 4 to 5; then annually. *To be included:* 1. Regular pelvic exam for all women. 2. If Tamoxifen: advise to report any vaginal bleeding to physician.	Every 4-6 months for 5 years, then every 12 months. *To be included:* 1. History, physical exam 3. Assess and encourage adherence to adjuvant ET. 4. If Tamoxifen: annual gynecologic exam if uterus intact and rapid evaluation of any vaginal spotting. 5. Assess sexual health/function at regular intervals.	Every 3-4 months for years 0-2, every 6 months for years 3-5, then every 12 months. *To be included:* 1. History, eliciting of symptoms 2. Physical exam 3. If Tamoxifen, annual gynecologic exam. Initiate appropriate tests immediately if any abnormal findings or symptomatic.	Not addressed.	Clinic visit frequency not addressed. Ensure that all pts with early BCa who develop lymphedema have rapid access to a lymphedema specialty service.

Topic	Cancer Care Manitoba, 2014[1]	American Society of Clinical Oncology, 2012[2]	National Comprehensive Cancer Network, 2014[3,4,5]	European Society for Medical Oncology, 2013[6]	New Zealand Guidelines Group, 2009[7]	National Institute for Health & Care Excellence, 2012[8]
Endocrine Therapy	If AIs: 1. Hot flashes: try bedtime dosing; add venlafaxine, gabapentin, or clonidine; consider change of AI. 2. Arthralgias / myalgias: use of pain killers, exercise, change of AI or to Tamoxifen. 3. Vaginal dryness: moisturizers/ lubricants; use of intravaginal estrogens contraindicated. If Tamoxifen: 1. Hot flashes: try bedtime dosing; add venlafaxine, gabapentin, or clonidine. Avoid SSRIs. 2. Vaginal dryness: moisturizers & lubricants, use of intravaginal estrogens relatively contraindicated. 3. Risk of uterine cancer 1% for post-menopausal women. Bleeding requires U/S and/or biopsy and referral to gynecology if concerned. 4. VTE: Risk is 0.2% per year. Encourage smoking cessation, watch for VTE symptoms. 5. Cataracts: exam every 1-2 years.	Not addressed.	Symptom management may include treatment for hot flashes and depression; Venlafaxine effective for hot flashes (other SSRIs may decrease effectiveness of Tamoxifen). Ophthalmology exam recommended if cataracts or vision problems.	If Tamoxifen: 1. Risk of thromboembolic complications and endometrial hyperplasia / cancer. Exercise caution in pts with predisposing factors and carry out appropriate tests if symptoms occur. 2. Avoid use of moderate and strong CYP2D6 inhibitors or switch to alternative (i.e. consider AIs) if they cannot be avoided. If AIs: 1. Pts on AIs or ovarian suppression at increased risk of bone loss. Assess BMD and ensure vitamin D3 intake adequate.	Tamoxifen is associated with: hot flushes, vaginal bleeding or discharge, endometrial hyperplasia and rarely cancer, risk of thromboembolic events, and less commonly arthritis, myalgia, cataracts, and stroke. AIs associated with: hot flushes, vaginal dryness, arthralgia and arthritis, decreased BMD, osteoporosis, increased fracture risk, loss of libido, diarrhea, increased cholesterol, and rarely insomnia and hair thinning.	SSRIs paroxetine or fluoxetine may be used to treat menopausal symptoms (not if on Tamoxifen) with informed consent. Clonidine, venlafaxine, or gabapentin may be used for hot flushes with informed consent. *Not recommended for treatment of menopausal symptoms:* Tibolone, progestogens, soy (isoflavone), red cloven, black cohosh, vitamin E, magnetic devices.

Topic	Cancer Care Manitoba, 2014[1]	American Society of Clinical Oncology, 2012[2]	National Comprehensive Cancer Network, 2014[3,4,5]	European Society for Medical Oncology, 2013[6]	New Zealand Guidelines Group, 2009[7]	National Institute for Health & Care Excellence, 2012[8]
Lifestyle	Smoking cessation, limit alcohol consumption to no more than 1 drink per day (women), reduce harmful sun exposure, maintain healthy body weight, eat a healthy diet, do moderate exercise for at least 30 minutes per day (increase time and intensity as fitness improves).	Not addressed.	Active lifestyle, achieving and maintaining an ideal body weight (20-25 BMI) may lead to optimal BCa outcomes. Smoking cessation and alcohol limitations may also reduce risk of recurrence (<1 drink per day for women).	Weight gain affects prognosis and should be discouraged; nutrition counselling if necessary. Regular long-term moderate/strenuous activity associated with favourable prognosis and functional and psychological benefits; aerobic & weight training do not cause lymphedema.	Obesity associated with decreased survival and increased complication rates.	Not addressed.
Fatigue / other side effects	Exercise can help reduce fatigue.	Not addressed.	Screen all patients for fatigue as a vital sign at regular intervals. If patient reports moderate/severe fatigue, assess treatable contributing factors, consider labs based on other symptoms, and treat as appropriate.	Depression and fatigue often occur after treatment. Pts should have unlimited access to rehabilitation services.	Not addressed.	Not addressed.
Psychosocial support	BCa can be a traumatic event. *Counselling available through patient and family support services.*	Not addressed.	Not addressed.	Follow-up should address long-term psychological effects of living with BCa.	Follow-up should address psychosocial issues of BCa survivorship.	Not addressed.
Sexual and reproductive health	It is not safe to become pregnant while taking Tamoxifen. Hormonal birth control not recommended.	Not addressed.	Hormonal birth control methods discouraged. Breast feeding on chemotherapy or ET not recommended. Pts should not become pregnant while on RT, ET, or chemotherapy.	Not addressed.	No evidence that pregnancy increases relapse risk. Tamoxifen associated with fetal abnormalities. Breast feeding on chemotherapy or ET not recommended	Not addressed

Topic	Cancer Care Manitoba, 2014[1]	American Society of Clinical Oncology, 2012[2]	National Comprehensive Cancer Network, 2014[3,4,5]	European Society for Medical Oncology, 2013[6]	New Zealand Guidelines Group, 2009[7]	National Institute for Health & Care Excellence, 2012[8]
Genetic counselling	If concerned, pts can discuss with their doctor or contact the HBOC Clinic.	Offer counselling if: 1. Ashkenazi Jewish 2. OvCa in pt (any age) or 1st /2nd degree relative 3. BCa in a 1st degree relative before age 50 4. BCa in two or more 1st - or 2nd degree relatives at any age 5. BCa (bilateral) in pt or relative 6. Male BCa.	If high risk due to strong family history or early onset disease, genetic counselling should be offered.	Not addressed.	All women from high risk families should be offered referral to GC.	Not addressed.

Abbreviation	Definition	Abbreviation	Definition
BCa	Breast cancer	HBOC	Hereditary breast and ovarian cancer
BCS	Breast conserving surgery	HCP	Health care provider
BMD	Bone mineral density	LFT	Liver function test
CBE	Clinical breast exam	MRI	Magnetic resonance imaging
CBC	Complete blood count	OvCa	Ovarian cancer
CT	Computed tomography	PC	Primary care
DEXA	Dual-energy x-ray absorptiometry	PET	Positron emission tomography
DVT	Deep vein thrombosis	Pt(s)	Patient(s)
ET	Endocrine therapy	RT	Radiotherapy
FDG-PET	Fluorodeoxyglucose-positron emission tomography	SSRIs	Selective serotonin reuptake inhibitors
FRAX	Fracture risk algorithm	U/S	Ultrasound
GP	General practitioner	VTE	Venous thromboembolism

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