Follow-Up Care for Early-Stage Breast Cancer

Effective Date: December, 2021
Background

At a certain point in time after a patient with resected early-stage breast cancer has completed their adjuvant therapy (either chemotherapy and/or radiation therapy) at the cancer centre, they can be safely transitioned back to the care of their primary health care provider (PHCP) 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 and manage 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.

To meet these surveillance goals, an evidence-based strategy for follow-up should be included in the patient’s overall care plan. Most patients do not require follow-up at the tertiary cancer centres for ongoing routine breast cancer surveillance. Compared to follow-up at the tertiary cancer centre, it is known that follow-up care provided by PHCP is equivalent in terms of long term breast cancer outcomes (recurrence/survival and quality of life). Moreover, patient satisfaction may be higher for some with follow-up care provided in general practice compared to hospital outpatient departments and there are no significant increases in the workload of PHCPs.

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 PHCP. 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. What investigations (i.e., tests and exams) constitute follow-up care for patients who have completed active medical and/or radiation oncology treatment for early-stage breast cancer? How often should these investigations be performed and who is responsible?
2. What are the signs and symptoms to look for regarding a breast cancer recurrence?
3. 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 and Revision History

The original guideline was developed in 2013 and was updated again in 2015. For the 2021 update, evidence was selected and reviewed by a working group of oncologists from Alberta Health Services, Cancer Care Alberta, and the Guideline Resource Unit. A detailed description of the guideline development process used for this update can be found in the Guideline Resource Unit Handbook.
Search Strategy

For the 2021 update, a review of published guidelines listed in the Guideline Resource Unit Handbook were searched and included for review. A systematic search for relevant literature was also conducted of MEDLINE and PubMed (April 2021- June 2021) using 4 independent searches (full details in Appendix A). Only articles available in English were included.

Target Population

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

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. *(Level of Evidence: V, Strength of Recommendation: B)*
- Following completion of active medical and/or radiation oncology treatment (or those receiving ongoing adjuvant endocrine therapy), patients may be discharged from the tertiary cancer center back to their PHCP for ongoing breast cancer surveillance. *(Level of Evidence: V, Strength of Recommendation: B)*
- Guidance on follow-up care and mechanisms for referral back (if required) to tertiary cancer care center should be made available. *(Level of Evidence: V, Strength of Recommendation: B)*
- A written care plan (such as transition letters) recorded by a named health professional from the oncology team with copies sent to the PHCP and the patient should be provided upon discharge. *(Level of Evidence: V, Strength of Recommendation: B)*
- A PHCP, or nurse practitioner working with the PHCP, with experience in clinical breast exam should provide follow-up care to patients who have been treated for early-stage breast cancer. *(Level of Evidence: V, Strength of Recommendation: B)*

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

- Breast self-examination (BSE)
There is no evidence to support the use of BSE as a cancer screening method, and therefore it’s not recommended for the average-risk population. For more information, please refer to Alberta’s Breast Cancer Screening Guideline. *(Level of Evidence: I⁴, V⁵, ⁶, Strength of Recommendation: C)*

- **Clinical Examination**
  - History and physical examination of the breast(s), chest wall +/- reconstructed breast, and supraclavicular and axillary nodes. Also consider assessing arms for lymphedema, especially if axillary nodal dissection or regional nodal irradiation. *(Level of Evidence: II¹, ⁷, ⁸, V⁷, ⁸, Strength of Recommendation: A)*
    - Frequency: every 6 months for 2 years, then annually.

- **Imaging Tests (for patients with breast tissue or who have undergone breast conserving surgery)**
  - 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 indicated. *(Level of Evidence: V⁹, ¹⁰, Strength of Recommendation: C)* Supplemental breast ultrasound can be added to mammography in the setting of extremely dense breast tissue (American College of Radiology category D) and/or at the discretion of the reading radiologist. *(Level of Evidence ¹¹, ¹², Strength of Recommendation: C)* Women at higher risk of breast cancer may benefit from tomosynthesis in addition to regular digital mammography during screening, however, it is not recommended for use on its own. *(Level of Evidence: V⁵, ¹², Strength of Recommendation: C)*
  - Other routine investigations (e.g., computed tomography, bone scan, ultrasound of the abdomen, chest x-ray, tumour markers, and laboratory tests, etc.) are not recommended for asymptomatic patients. *(Level of Evidence: II¹³, V⁸, ¹⁴, Strength of Recommendation: C)*

- **Other**
  - Other cognitive, physical assessments and tests should be completed as required according to general population guidelines (i.e., cardiovascular risk factor assessment, bone density, screening for other cancers such as cervical and colon cancer). *(Level of Evidence V⁴, ⁸, ¹⁵, Strength of Recommendation: A)*

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

- Patients should be counselled on symptoms of potential recurrence and when to report them (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, regional, or metastatic recurrence this should be investigated as clinically indicated.
• For referral back to the Cancer Centre, please contact the appointment booking office at the Cancer Centre 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’s case. To find an oncologist:
  o Specialist Link (Calgary/Southern Alberta)
  o ConnectMD (Edmonton/Northern Alberta)
• For any emergent concerns, patients should be directed to the nearest emergency department for immediate evaluation and intervention.
  o The Oncologic Emergencies Guideline will outline common emergent concerns.

Table 1. Symptoms and appropriate investigations for a local recurrence or metastatic disease (Level of Evidence: V5, 8, 9, 16, 17, Strength of Recommendation: A)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Action / Investigation</th>
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<td>New mass in breast or armpit, changes in the contour/shape/size of the breast, nipple retraction, or swelling of the breast or arm</td>
<td>Mammography +/- ultrasound +/- needle biopsy</td>
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<td>New suspicious rash, bleeding or nodule on nipple or chest wall, mastectomy scar changes</td>
<td>Refer to surgeon for evaluation and biopsy</td>
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<td>New palpable lymphadenopathy</td>
<td>Refer to surgeon or interventional radiology for biopsy</td>
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<tr>
<td>New persistent bone pain</td>
<td>Plain x-ray of affected site(s) and bone scan</td>
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<tr>
<td>New persistent cough or dyspnea</td>
<td>Chest x-ray and/or CT chest</td>
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<tr>
<td>New hepatomegaly or RUQ abdominal pain or jaundice</td>
<td>Ultrasound and/or CT scan of abdomen and liver enzymes</td>
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<td>New onset seizures</td>
<td>Seizure management (as required) and CT/MRI brain</td>
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<tr>
<td>Back pain with limb weakness, change in sensation, change in reflexes, or loss of bowel/bladder control</td>
<td>MRI spine</td>
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<td>New persistent headache or new concerning neurologic deficits</td>
<td>CT / MRI brain</td>
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<tr>
<td>Altered level of consciousness, nausea, vomiting, and/or pain with symptomatic hypercalcemia</td>
<td>IV hydration and bisphosphonate therapy</td>
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<td>Unexpected constitutional symptoms (severe fatigue, unexplained weight loss)</td>
<td>Workup for any identifiable or treatable causes of fatigue and weight loss (e.g., anemia, liver dysfunction, thyroid, or cardiac dysfunction), imaging investigations according to local symptoms and laboratory abnormalities as appropriate (e.g., liver ultrasound/CT abdomen if abnormal liver enzymes).</td>
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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. *Level of Evidence V, Strength of Recommendation: D*

**Endocrine therapy** *(Level of Evidence V, Strength of Recommendation, B)*:

- 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 centre.
- Further prescription will be obtained through the patient’s PHCP. 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.
- The oncology team may request re-referral to cancer centre after 2-5 years for discussion of potential switch in endocrine therapy (i.e., tamoxifen to an aromatase inhibitor) and/or for discussion of extended endocrine therapy (beyond 5 years). The request for re-referral will be indicated in the note from oncologist or delegate at the time of transition.

*Tamoxifen.*

- Common side effects of tamoxifen include hot flashes and vaginal discharge.
- Patients receiving tamoxifen are at a slightly increased risk of more serious adverse events such as deep vein thrombosis, stroke, endometrial cancer, and cataracts.
- Investigations and referrals should be performed as per signs and symptoms. For example, women with abnormal vaginal bleeding should have a pelvic ultrasound and be referred to gynecology. Concurrent use of CYP2D6 inhibitors can disrupt tamoxifen metabolism. Strong CYP2D6 inhibitors to be aware of include bupropion (Wellbutrin®), fluoxetine (Prozac®), paroxetine (Paxil®), and quinidine (Quinidex®). *Level of Evidence: V<sup>18-20</sup>, Strength of Recommendation, C*

*Aromatase Inhibitors (AIs).*

- Common side effects of AIs (i.e., anastrozole, letrozole, exemestane) include arthralgias, myalgias, dyspareunia, vulvovaginal atrophy, and hot flashes.
• Patients initiated on AIs are at risk of developing osteopenia and/or osteoporosis and should have a baseline bone density assessment (DEXA scan) performed. *(Level of Evidence: V, Strength of Recommendation: B)*

• Subsequent follow-up DEXA and management of osteopenia/osteoporosis should be treated as per osteoporosis guidelines.\(^{21}\)
  - 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.

**Bisphosphonates:**

• Some postmenopausal patients will have had zoledronic acid IV q6 monthly x 2-5 years prior to discharge or be on clodronate as part of their treatment plan (to help reduce risk of recurrence to bone and improve overall survival above and beyond other treatments). *(Level of Evidence: II\(^{22}\), Strength of Recommendation, B)*

• Intended bisphosphonate treatment plan will be outlined by the oncology team.

• While zoledronic acid would have been administered at the cancer center, clodronate is an outside prescription that is filled in the community pharmacies.

**Peripheral Neuropathy:**

• Certain types of chemotherapy may cause peripheral neuropathy. Visit the [Chemotherapy Induced Peripheral Neuropathy](#) guideline for more information on screening, assessing, and managing peripheral neuropathy.

**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.

• Physicians should counsel survivors on how to prevent/reduce the risk of lymphedema, including weight loss for those who are overweight or obese. *(Level of Evidence V\(^{\oplus}\), Strength of Recommendation, B)*

• The Alberta Lymphedema Association recommends Combined Decongestive Therapy (CDT) as best practice for the treatment of lymphedema\(^{23}\). CDT consist of manual lymph drainage, compression therapy, education, exercise, and skin care. *(Level of Evidence V\(^{23, 24}\), Strength of Recommendation: B):*
  - Manual lymph drainage: A specialized type of massage. The use of massage helps to move lymph fluid out of the affected limb to functioning lymph nodes for drainage.\(^{24}\)
  - Compression therapy: a technique that uses garments, bandages, or gradient pumps to
compress the affected limb and move lymph fluid towards the torso. Compression therapy may be combined with manual lymphatic drainage and/or physical therapy.

- **Exercise:** To promote lymphatic flow. Use of muscle contractions of the affected limb to facilitate the drainage of lymph fluid; strenuous exercises should typically be avoided.

- **Skin care:** to prevent infection.

- **There is no current evidence to support the use of medical therapies such as diuretics.** *(Level of Evidence: V, Strength of Recommendation: C)*

- **Referral should be considered to lymphedema management services.**
  - For primary lymphedema, refer to the Calgary Ambulatory Lymphedema Service in Calgary and the CRIS Lymphedema Clinic in Edmonton.
  - For secondary lymphedema caused by cancer and/or cancer treatment, refer to Rehabilitation Oncology.

### 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. *(Level of Evidence: V, Strength of Recommendation: A)*

### 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), urgent referral to hematology is indicated. *(Level of Evidence: V, Strength of Recommendation: A)*

### Additional Resources:

- [Sample End of Treatment Physician Letter: Early Breast Follow-up](#)
- [Sample End of Treatment Patient Letter: Early Breast Follow-up](#)
- [Sample Transfer of Care Physician Letter: Early Breast Follow-up](#)
- [Sample Transfer of Care Patient Letter: Early Breast Follow-up](#)
References


19. Horn JR, Hansten PD. Beware of CYP2D6 Inhibitors in Patients Taking Tamoxifen. *Pharmacy Times.* 2009;0(0)
https://www.breastcancer.org/treatment/hormonal/serms/tamoxifen
https://www.physiotherapyalberta.ca/xchange/evidence_based_practice_resources/physiotherapy_works/lymphedema
## Appendix A: Full Search Strategy and Results

### Search for Research Question 1:

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<tr>
<th>Other articles added</th>
<th>SURVIVORSHIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
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Development and Revision History
This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team. Members include surgical oncologists, radiation oncologists, medical oncologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Tumour Teams, external participants identified by the Working Group Lead, and a methodologist 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.

This guideline was first developed in 2011 and updated in 2015 and 2021.

Levels of Evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity</td>
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<tr>
<td>II</td>
<td>Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity</td>
</tr>
<tr>
<td>III</td>
<td>Prospective cohort studies</td>
</tr>
<tr>
<td>IV</td>
<td>Retrospective cohort studies or case-control studies</td>
</tr>
<tr>
<td>V</td>
<td>Studies without control group, case reports, expert opinion</td>
</tr>
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Strength of Recommendations

<table>
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<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>Strong evidence for efficacy with a substantial clinical benefit; strongly recommended</td>
</tr>
<tr>
<td>B</td>
<td>Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended</td>
</tr>
<tr>
<td>C</td>
<td>Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.): optional</td>
</tr>
<tr>
<td>D</td>
<td>Moderate evidence against efficacy or for adverse outcome; generally not recommended</td>
</tr>
<tr>
<td>E</td>
<td>Strong evidence against efficacy or for adverse outcome; never recommended</td>
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</tbody>
</table>

Maintenance
A formal review of the guideline will be conducted in 2026. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations
BCa, Breast cancer; PHCP, Primary Health Care Practitioners. CDT, Complex Decongestive Therapy; ECG, Electrocardiogram; MUGA, Multiple Gated Acquisition scan; CBC, complete blood count.

Disclaimer
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.

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Conflict of Interest Statements
Dr. Petra Grendarova reports grants from the Canadian Strategic Clinical Network and Alberta Health Services. Madison Bischoff reports financial interest from the University of Calgary.