Breast Cancer Follow-Up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update


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ABSTRACT

Purpose
To provide recommendations on the follow-up and management of patients with breast cancer who have completed primary therapy with curative intent.

Methods
To update the 2006 guideline of the American Society of Clinical Oncology (ASCO), a systematic review of the literature published from March 2006 through March 2012 was completed using MEDLINE and the Cochrane Collaboration Library. An Update Committee reviewed the evidence to determine whether the recommendations were in need of updating.

Results
There were 14 new publications that met inclusion criteria: nine systematic reviews (three included meta-analyses) and five randomized controlled trials. After its review and analysis of the evidence, the Update Committee concluded that no revisions to the existing ASCO recommendations were warranted.

Recommendations
Regular history, physical examination, and mammography are recommended for breast cancer follow-up. Physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter. For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy. Thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed. The use of complete blood counts, chemistry panels, bone scans, chest radiographs, liver ultrasounds, pelvic ultrasounds, computed tomography scans, [18F]fluorodeoxyglucose–positron emission tomography scans, magnetic resonance imaging, and/or tumor markers (carcinoembryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.

INTRODUCTION

In 1997, the American Society of Clinical Oncology (ASCO) published an evidence-based clinical practice guideline on breast cancer follow-up and management in asymptomatic patients after primary, curative therapy. ASCO guidelines are updated periodically by a subset of the original expert panel. The guideline was updated and published in 1999 and again in 2006. In March 2012, the Update Committee reviewed the results of a systematic review of the literature to determine whether the ASCO guideline recommendations needed additional updating.

This clinical practice guideline addresses three overarching clinical questions: (1) What guidance around follow-up and management should be available to women who have been previously treated for breast cancer? (2) What testing is recommended for the detection of breast cancer recurrence in the adjuvant setting after curative-intent primary therapy? (3) What is the optimal frequency of monitoring?

Table 1 summarizes the guideline recommendations. A Data Supplement, a patient guide, and other clinical tools and resources to help clinicians implement this guideline are available at http://www.asco.org/guidelines/breastfollowup.
The Update Committee included academic and community practitioners, medical oncologists, a surgical oncologist, a radiation oncologist, hematologic oncologists, a gynecologic oncologist, a primary care physician, and a patient advocate (Appendix Table A1, online only). A Working Group of the Update Committee completed a review and analysis of evidence published between March 2006 and March 2012 to determine whether the recommendations needed to be updated. The Working Group drafted the guideline update and circulated it to the full Update Committee for review and approval. The ASCO Clinical Practice Guidelines Committee leadership reviewed and approved the final document.

Details of the literature search strategy and the inclusion and exclusion criteria are provided in the Data Supplement (http://www.asco.org/guidelines/breastfollowup). In brief, studies were included if their primary objective was the follow-up and management of patients with breast cancer who had completed primary therapy with curative intent. The outcomes of interest were disease-free survival, overall survival, health-related quality of life, reduced toxicity, and cost-effectiveness. The searches were limited to randomized controlled trials (RCTs), systematic reviews (with or without meta-analyses), and clinical practice guidelines. However, for the search on tumor markers, both randomized and nonrandomized studies were eligible if they directly addressed the clinical utility of one or more tumor markers (ie, carcinoembryonic antigen, CA 15-3, and CA 27.29) by comparing the outcomes of interest for a group of patients monitored with one or more of the listed tumor markers with a group of patients who were not monitored with any tumor marker.

**Guideline Policy**

The practice guideline is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This guideline does not recommend any particular product or course of medical treatment. Use of the practice guideline is voluntary.

**Guideline and Conflicts of Interest**

The Update Committee was assembled in accordance with the ASCO Conflicts of Interest Management Procedures for Clinical Practice Guidelines (summarized at http://www.asco.org/conflictscoi). Members of the Update Committee completed a disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with these procedures, the majority of the members of the Update Committee did not disclose any such relationships.

**RESULTS**

A QUOROM diagram in the Data Supplement reports the results of the literature search. Data were extracted from 14 articles in total. Data Supplement Tables DS3 and DS4 summarize the characteristics of the studies included in the literature review and analysis, along with their findings. These tables, and other clinical tools and resources, can be found at http://www.asco.org/guidelines/breastfollowup.

There were no new RCTs, systematic reviews, or meta-analyses identified in the review that specifically examined history or physical examination, breast self-examination, patient education regarding symptoms of recurrence, or referral for genetic counseling. Additionally, there were no systematic reviews, meta-analyses, RCTs, or observational studies that met the inclusion criteria for breast cancer tumor marker testing.

**Breast Imaging**

There were no RCTs of breast imaging that met the inclusion criteria. Several systematic reviews on breast imaging were identified, including one systematic review that evaluated the sensitivity of breast magnetic resonance imaging to detect tumor recurrence and two systematic reviews of the effectiveness of mammography for breast cancer surveillance. Additionally, one meta-analysis of examined...
the sensitivity of positron emission tomography (PET) and PET–computed tomography (CT) to detect tumor recurrence, and one systematic review evaluated the cost effectiveness of PET and PET-CT in breast cancer surveillance.

There were two meta-analyses that addressed multiple modes of surveillance within their reviews and analyses, including ultrasound, mammography, CT scans, magnetic resonance imaging, clinical examinations, frequency of follow-up, or specialist-led or primary care physician–led follow-up.

In general, the systematic reviews and meta-analyses were of varying quality and had significant heterogeneity, particularly in terms of sample characteristics and study designs.

### Coordination of Care

The literature search identified one systematic review and five RCTs that compared various models of care for breast cancer surveillance (Data Supplement Table DS4). These studies and data were of mixed quality—which is important to consider in terms of the reliability and validity of the findings—primarily because of inadequate sample sizes, limited follow-up periods, variations in protocols, and protocol violations. The systematic review examined alternatives to clinical follow-up and frequency or duration of follow-up. Three RCTs evaluated reduced follow-up strategies, including nurse-led telephone follow-up compared with traditional hospital-based follow-up and point-of-need access to specialist care compared with routine hospital-based clinical review. In general, the

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<th>Mode of Surveillance</th>
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<td>RECOMMENDED</td>
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<td>History/physical examination</td>
<td>All women should have a careful history and physical examination every 3 to 6 mo for the first 3 yr after primary therapy, then every 6 to 12 mo for the next 2 yr, and then annually. The history and physical examination should be performed by a physician experienced in the surveillance of patients with cancer and in breast examination.</td>
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<td>Patient education regarding symptoms of recurrence</td>
<td>Physicians should counsel patients about the symptoms of recurrence including new lumps, bone pain, chest pain, dyspnea, abdominal pain, or persistent headaches. Helpful Web sites for patient education include <a href="http://www.cancer.gov">www.cancer.gov</a> and <a href="http://www.cancer.org">www.cancer.org</a>.</td>
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<td>Referral for genetic counseling</td>
<td>Women at high risk for familial breast cancer syndromes should be referred for genetic counseling in accordance with clinical guidelines recommended by the US Preventive Services Task Force. Of all the evidence is lacking, it seems likely that history as well as physical and breast exams may also be conducted by an experienced non-physician provider (eg, Nurse Practitioners, Physician Assistants) under the supervision of an experienced physician.</td>
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<td>Breast self-examination</td>
<td>All women should be counseled to perform monthly breast self-examination.</td>
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<td>Mammography</td>
<td>Women treated with breast-conserving therapy should have their first post-treatment mammogram no earlier than 6 mo after definitive radiation therapy. Subsequent mammograms should be obtained every 6 to 12 mo for surveillance of abnormalities. Mammography should be performed yearly if stability of mammographic findings is achieved after completion of locoregional therapy.</td>
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<td>Pelvic examination</td>
<td>Regular gynecologic follow-up is recommended for all women. Patients who receive tamoxifen therapy are at increased risk for developing endometrial cancer and should be advised to report any vaginal bleeding to their physicians. Longer follow-up intervals may be appropriate for women who have had a total hysterectomy and oophorectomy.</td>
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<td>Coordination of care</td>
<td>The risk of breast cancer recurrence continues through 15 yr after primary treatment and beyond. Continuity of care for patients with breast cancer is recommended and should be performed by a physician experienced in the surveillance of patients with cancer and in breast examination, including the examination of irradiated breasts. Follow-up by a PCP seems to lead to the same health outcomes as specialist follow-up with good patient satisfaction. If a patient with early-stage breast cancer (tumor &lt;5 cm and &lt;4 positive nodes) desires follow-up exclusively by a PCP, care may be transferred to the PCP approximately 1 yr after diagnosis. If care is transferred to a PCP, both the PCP and the patient should be informed of the appropriate follow-up and management strategy. Re-referral for further oncology assessment may be considered, as needed, especially for patients who are receiving adjuvant endocrine therapy.</td>
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NOT RECOMMENDED

| Routine blood tests | CBC testing is not recommended for routine breast cancer surveillance. Automated chemistry studies are not recommended for routine breast cancer surveillance. |
| Imaging studies | Chest x-rays are not recommended for routine breast cancer surveillance. Bone scans are not recommended for routine breast cancer surveillance. Ultrasound of the liver is not recommended for routine breast cancer surveillance. CT scanning is not recommended for routine breast cancer surveillance. FDG-PET scanning is not recommended for routine breast cancer surveillance. Breast MRI is not recommended for routine breast cancer surveillance. |
| Breast cancer tumor marker testing | The use of CA 15-3 or CA 27.29 is not recommended for routine surveillance of patients with breast cancer after primary therapy. CEA testing is not recommended for routine surveillance of patients with breast cancer after primary therapy. |

Abbreviations: CBC, complete blood count; CEA, carcinoembryonic antigen; FDG-PET, [18F] fluorodeoxyglucose–positron emission tomography; MRI, magnetic resonance imaging; PCP, primary care physician.

*All recommendations remain the same as those published in 2006. The Panel concluded that there was no new evidence that warranted changing any of the recommendations. The 2006 guideline provides a detailed discussion and rationale for the recommendations.

**Although the evidence is lacking, it seems likely that history as well as physical and breast exams may also be conducted by an experienced non-physician provider (eg, Nurse Practitioners, Physician Assistants) under the supervision of an experienced physician.**

†Expert consensus-based recommendations are available with criteria specific to patients with cancer (eg, from the National Comprehensive Cancer Network [www.cancer.gov]). These recommendations include similar criteria as those from the USPSTF as well as other criteria such as diagnosis of triple negative breast cancer, or a combination of breast cancer and other specific cancers.
studies found that reduced follow-up strategies did not negatively affect patient-reported outcomes or early detection of recurrence. Another RCT performed a cost-benefit analysis of standard clinical follow-up compared with more intensive follow-up with additional imaging and laboratory tests and concluded that more-intensive follow-up was associated with higher costs without differences in early detection of relapses. However, the analytic methods were not described in the report, and therefore, the validity of this conclusion is difficult to ascertain. Results from one additional RCT found no evidence that survivorship care plans improve patient-reported outcomes, including cancer-related distress and coordination of care, when outcomes of Canadian women randomly assigned to receive a survivorship care plan were compared with those of women who did not receive a comprehensive survivorship care plan. Both groups had follow-up transferred to primary care physicians, which was considered an important strategy to meet the demand for scarce oncology resources.

Clinical practice guidelines for surveillance of breast cancer are available from many national and international organizations other than ASCO. A list of some key guidelines is provided in the Data Supplement (Data Supplement Table DS5). In general, the recommended modes of surveillance are comparable to ASCO’s recommendations. However, there are differences in recommended frequency and duration of surveillance.

**GUIDELINE RECOMMENDATIONS**

After their review and analysis of the evidence for the various modes of surveillance for breast cancer, the Update Committee concluded that the evidence was not compelling enough to warrant changes to any of the 2006 guideline recommendations. Table 1 provides a summary of the guideline recommendations. These recommendations are congruent with the five key opportunities identified by ASCO to improve cancer care and reduce costs.

**CONCLUSION AND FUTURE RESEARCH**

After a systematic review and analysis of the literature for the follow-up and management of patients with breast cancer, the Update Committee concluded that there was no new evidence compelling enough to warrant changes to any of the guideline recommendations. Further research is needed—particularly RCTs—to determine the comparative effectiveness of different modes of breast cancer surveillance and the ideal frequency and duration of follow-up. Research is also needed to establish the clinical utility of breast cancer tumor marker testing for the follow-up and management of breast cancer and ultimately to develop clinical practice guidelines for tumor marker testing that are risk based and/or specific to tumor subtypes (eg, triple-negative breast cancer). More research is also needed to evaluate the effectiveness and quality of different models of survivorship care and to identify subsets of patients who would benefit from the various models of care.

In the meantime, the Update Committee encourages health care providers to have an open dialogue with patients as part of a comprehensive treatment planning process. A useful way to approach treatment planning and ensure a coordinated cancer care plan is through the ASCO Cancer Treatment Plans and Summary templates, available online. The treatment planning discussion should include consideration of scientific evidence, weighing individual risks with potential harms and benefits, and patient preferences. The Update Committee will continue to monitor the literature for new evidence that may warrant revisiting the recommendations for the follow-up and management of breast cancer after primary treatment.

**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

Although all authors completed the disclosure declaration, the following author(s) and/or an author’s immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a “U” are those for which no compensation was received; those relationships marked with a “C” were compensated. For a detailed description of the disclosure categories, or for more information about ASCO’s conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors. Employment or Leadership Position: None Consultant or Advisory Role: None Honoraria: None Research Funding: None Expert Testimony: None Other Remuneration: None

**AUTHOR CONTRIBUTIONS**

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(PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence. Health Technol Assess 15:ii-iv, 1-54, 2011