INTRODUCTION — Invasive breast cancer is the most common malignancy in American women, accounting for 26 percent of new cancer cases and 15 percent of all cancer deaths [1]. The lifetime risk of a woman developing invasive breast cancer in the United States is 12.6 percent (one out of eight women). (See "Epidemiology and risk factors for breast cancer").

More women with early stage breast cancer are surviving their disease, at least in part due to advances in adjuvant therapy [2]. Among the issues faced by clinicians caring for these women are who should perform follow-up, how long should surveillance be continued, and what tests are appropriate in this setting. The goals of posttreatment surveillance after primary treatment for breast cancer are early recognition and treatment of potentially curable disease recurrences and second primary breast cancers, screening for therapy-related complications, and detection of symptoms consistent with metastatic disease [3].

The greatest emphasis on surveillance is on the first five years after therapy, since the risk of recurrence is highest during this time [4-7]. However, the threat of a breast cancer recurrence persists for 20 years or longer after primary treatment. In data from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) on breast cancer survival and recurrence rates among women receiving five years of tamoxifen for estrogen receptor (ER)-positive breast cancer, the 15-year probability of death from breast cancer was more than three times as great as the 5-year probability [8].

Recommendations for posttreatment surveillance after primary therapy of localized breast cancer will be reviewed here. They are based upon 2006 guidelines issued from the American Society of Clinical Oncology (ASCO, show table 1) [9]. A detailed discussion of the patterns of relapse (ie, locoregional recurrence, second primary breast tumor, metastatic disease) and the complications of breast cancer therapy are presented separately. (See "Follow-up for breast cancer survivors: Patterns of relapse and long-term complications of therapy").

The guidelines presented here are mainly applicable to women who have been treated for a sporadic breast cancer. The optimal posttreatment surveillance for women who develop breast cancer in the setting of an inherited predisposition (eg, deleterious mutations in BRCA1 or BRCA2) has not been established and practice is variable. Local recurrence rates in women with an inherited predisposition appear to be similar to those of women with sporadic tumors; however, the risks of both contralateral and ipsilateral second breast cancers are higher. Whether the frequency of radiographic surveillance should be greater in these women, and the best way to integrate mammography and breast MRI are unresolved areas of controversy. (See "Options for women with a genetic predisposition to breast and ovarian cancer", section on Management options for high-risk women who develop breast cancer).

INTENSIVE VERSUS LESS INTENSIVE SURVEILLANCE — Routine history and physical examination, and regularly scheduled mammograms are the mainstay of care for the breast cancer survivor [10]. (See "Expert guidelines" below).

Most breast cancer recurrences are heralded by symptoms [11-14]. Diagnosis is then accomplished by tests that are precipitated and guided by the specific symptom complex.

An array of tests may be ordered in the hope of detecting recurrent disease in an asymptomatic patient, including blood chemistries, tumor-associated antigens, chest x-ray, PET scans, liver ultrasound, and bone scans. While these additional tests may detect asymptomatic disease recurrence, two major randomized trials, a Cochrane review, and a meta-analysis all concluded that there is no survival or quality of life benefit from a more intensive surveillance strategy as compared to follow-up programs that are based on regular physical examinations and annual mammography alone [10,11,15-17].

In the absence of a survival benefit, an early diagnosis of distant recurrence prior to onset of clinical signs or symptoms serves only to diminish the disease-free interval, potentially prolonging the time that patients are subjected to the side effects of treatment, and the knowledge that their disease has relapsed and they are incurable. Furthermore, all laboratory and imaging tests evaluated as surveillance tools have significant false positive and false negative rates. Both the anguish and
unnecessary additional testing generated by a false-positive result, and the misleading reassurance generated by a falsely negative test can potentially adversely affect the breast cancer survivor. The extra burden on the cost of health care is also an important consideration.

Thus, for the vast majority of patients, early diagnosis of metastatic disease before it becomes symptomatic provides no discernible benefit. It is speculated that a small percentage of patients with limited metastatic disease (eg, isolated pulmonary or liver metastases) may be approached with multimodality therapy for curative rather than palliative intent. However, whether those patients who stand to benefit from metastatectomy are best identified by intensive posttreatment surveillance is unknown. (See "Chest imaging studies" below and see "Abdominopelvic imaging" below).

This hypothesis must be confirmed in prospective randomized trials before it can be concluded that intensive surveillance monitoring is justified for any patient subgroup. (See "General principles of management of metastatic breast cancer", section on Cure).

EXPERT GUIDELINES — As noted above, 2006 ASCO guidelines for follow-up surveillance after breast cancer treatment are available (show table 1) [9]. Several other groups have published evidence-based clinical practice guidelines for posttreatment surveillance, including the National Comprehensive Cancer Network (NCCN), the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer of Health Canada (show table 2), the National Health and Medical Research Council of Australia, and a separate ASCO panel on tumor markers [9,18-21]. A comparison of these guidelines is presented in Table 3 (show table 3). Although the guidelines differ slightly, history and physical examination and regularly scheduled mammograms form the basis of follow-up care in all.

Compliance with published guidelines for surveillance after treatment of localized breast cancer can significantly decrease expenditures for follow-up care. This was illustrated in a French series that examined the number of follow-up tests and consultations for two groups of patients: one cohort started treatment in 1993 prior to the publication of formal surveillance guidelines, while the other started treatment in 1995, after guideline publication [22]. Compared to data from 1993, the mean social security expenditure per patient decreased by 35 percent for the first follow-up year, and 45 percent for the second follow-up year in the patients who were treated after the publication of formal surveillance guidelines.

SURVEILLANCE — The following sections address each of the components of recommended surveillance, as based upon ASCO guidelines (show table 1) [9].

Patient education and referral for genetic counseling — Most breast cancer recurrences are discovered by the patient (71 percent of cases in one series [23]). Patients should be educated regarding the signs and symptoms of recurrent disease, including new lumps, bone, chest, or abdominal pain, dyspnea, cough, or persistent headache (show table 4).

A family history of breast cancer should prompt consideration for an inherited susceptibility to the disease. The most common inherited syndrome is due to mutations in the BRCA 1 or 2 genes; these gene defects account for 5 to 6 percent of all breast cancers and 80 percent of all cases of hereditary breast cancer [24]. Affected women are at increased risk for both breast and ovarian cancer. (See "Genetic testing for breast and ovarian cancer").

Other genetic syndromes are less often implicated in inherited breast cancer (show table 5). (See "Risk assessment and clinical characteristics of women with a family history of breast and/or ovarian cancer", section on Clinical characteristics of hereditary syndromes).

Women at high risk for familial breast cancer syndromes should be referred for genetic counseling in accordance with guidelines recommended by the US Preventive Services Task Force. (See "Genetic testing for breast and ovarian cancer", section on Recommendations: who should be tested). In brief, criteria to warrant referral include:

- Ashkenazi Jewish heritage;
- History of ovarian cancer at any age in the patient or any first- or second-degree relative;
- Any first-degree relative with a history of breast cancer diagnosed before age 50;
- Two or more first- or second-degree relatives diagnosed with breast cancer at any age;
- Patient or relative with a diagnosis of bilateral breast cancer;
- History of breast cancer in a male relative (See "Male breast cancer")

Family history is dynamic, and should be updated annually.

History and physical examination — History and physical examination have been the principal means of detecting a breast cancer recurrence [16,25]. Guidelines from ASCO suggest that patients be seen every three to six months during the first three years after primary therapy, every six to twelve months for the next two years, and then annually (show table 1) [9]. However, this schedule is arbitrary; no studies have evaluated the benefit of less frequent clinical visits in patients with low-risk disease, or more frequent visits in those with higher-risk disease [26].

The history should focus upon signs and symptoms of local recurrence as well as metastatic disease. Evidence of local
recurrence includes newly discovered lumps or skin changes, or axillary discomfort or a mass (show table 4). (See "Follow-up for breast cancer survivors: Patterns of relapse and long-term complications of therapy").

The most common sites of metastatic disease are the bones, liver, lung, brain, and subcutaneous tissues. A review of systems for metastatic disease should include questioning for the following [27,28] :

- Bone metastases (constant, aching pain)
- Liver metastases (anorexia, weight loss, malaise, and occasionally right upper quadrant pain; jaundice is a sign of advanced disease)
- Pulmonary metastases (cough, dyspnea, pleuritic chest pain)
- Central nervous system (CNS) metastases (headache, nausea, vomiting, mental status changes, cranial nerve palsies, motor dysfunction, or spinal cord compression)
- Gastrointestinal (GI) metastases (change in bowel habits, melena)
- Genitourinary metastases (bleeding or pelvic pain)

Guidelines from ASCO suggest that a complete physical examination be performed at each visit [9]. At a minimum, the examination should include [27,28] :

- Thorough examination of both the affected breast (if preserved) and the contralateral side. Diagrams of the affected breast, including postoperative and postradiotherapy changes, can help follow the examination over time.

For women who have undergone mastectomy, the incision site and surrounding skin of the chest wall should be examined visually and palpated for abnormalities.

- Evaluation of axillary supraclavicular lymph nodes
- Examination of arm girth on the affected side to evaluate for lymphedema (see "Arm edema in patients with breast cancer")
- Palpation of the spine, sternum, ribs, and pelvis for bone tenderness
- Lung examination for decreased breath sounds/effusions
- Cardiac examination
- Abdominal examination for right upper quadrant tenderness and hepatomegaly
- Neurologic examination

Local recurrence after breast conserving therapy — Although it is universally recommended in published guidelines (show table 3), physical examination of irradiated breasts has a relatively low sensitivity and specificity for the detection of a local recurrence. In a review summarizing the results of seven randomized clinical trials, the sensitivity and specificity of physical examination for detecting local recurrence after surgery and radiation to a conserved breast ranged from 29 to 74 percent, and 17 to 30 percent, respectively [29].

Whether the detection of an asymptomatic ipsilateral recurrence or a contralateral second primary breast cancer on routine physical examination benefits survival remains unclear since it has never been the subject of a randomized trial. While it would seem intuitive that early diagnosis would improve the likelihood of successful salvage therapy and improve survival, there are surprisingly few studies which have addressed this question.

The poor quality of the available data is underscored by the results of a meta-analysis of 12 studies involving over 5000 patients undergoing surveillance after treatment of nonmetastatic breast cancer [16]. Of the 378 isolated locoregional recurrences, approximately 58 percent were diagnosed during a routine clinic visit or mammogram (40 percent asymptomatic, 18 percent with symptoms), while the remainder developed symptomatic recurrences in between scheduled visits. The impact of diagnosing a local recurrence while asymptomatic could not be ascertained because none of the studies reported data on localization or size of the locoregional recurrence, subsequent treatment, or survival.
Indirect data regarding the influence of a local recurrence on survival is provided by the EBCTCG meta-analysis described above; in randomized trials, local treatments that resulted in substantially higher local recurrence rates were associated with lower 15-year survival rates [30]. However, these results do not address the question of whether the method by which a local recurrence is detected influences its effect on survival. (See "Introduction" above).

Contralateral breast cancer — Similarly, no randomized trials have examined the survival impact of early detection of a contralateral breast cancer by routine physical examination. Some indirect evidence of benefit was provided in a posthoc analysis of National Surgical Breast and Bowel Project (NSABP) trial B-04 in which the survival of women undergoing mastectomy with or without radiation therapy (RT) was compared [31]. Follow-up of all women included frequent physical examination of the contralateral breast. In a secondary analysis of the 66 women who developed a contralateral breast cancer by 10 years, there was a trend for the metachronous breast cancers to be smaller than the primary tumors (2.4 ± 1.5 versus 3.5 ± 1.8 cm, respectively) [32]. However, there was no difference in survival when women who did and did not develop a contralateral breast cancer were compared.

In summary, although there is a lack of randomized controlled data to support the benefit of this practice, routine physical examination of both breasts during follow-up surveillance visits is recommended in guidelines from expert groups, including ASCO (show table 1).

Pelvic examination — ASCO guidelines suggest regular gynecologic follow-up for all women treated for breast cancer (show table 1) [9]. There is good evidence from multiple observational studies that routine screening with cervical cytology (Pap smears) reduces the incidence of and mortality from cervical cancer. The USPSTF clinical practice guideline for screening for cervical cancer can be accessed through the website for the Agency for Healthcare Research and Quality at www.ahrq.gov/clinic/uspsstfix.htm.

Gynecologic follow-up is particularly important in women who are receiving tamoxifen because of the increased risk for endometrial tumors. (See "Use of selective estrogen receptor modulators in postmenopausal women", section on Adverse effects).

Women receiving tamoxifen should be advised to report any vaginal bleeding immediately to their physicians. However, there are no evidence-based recommendations for uterine cancer screening in asymptomatic women taking tamoxifen. Recommendations from The American College of Obstetricians and Gynecologists for monitoring women taking tamoxifen are discussed elsewhere. (See "Use of selective estrogen receptor modulator in postmenopausal women", section on Screening for uterine tumors).

Although they do not specify the optimal frequency of follow-up for women who retain their uterus, ASCO guidelines suggest longer follow-up intervals for women who have undergone a total hysterectomy and bilateral salpingo-oophorectomy (TAH/BSO) [9]. However, whether routine pelvic examination is indicated at all in women who have undergone a total hysterectomy (ie, cervix excised), and how often it should be performed are unclear. If the procedure was done for benign disease, the only purpose of a routine pelvic examination is to detect a primary vaginal cancer or an asymptomatic vaginal metastasis, both of which are rare. (See "Screening for cervical cancer").

Gynecologists could also address issues related to side effects of hormone therapy such as vaginal dryness or dyspareunia.

Mammography — The purpose of posttreatment mammographic surveillance is to detect ipsilateral local recurrences after breast conserving therapy (BCT), which develop in 1 to 2 percent of patients per year, and to detect second primary breast cancers arising in the contralateral breast. The rate of contralateral breast cancer in women without an inherited predisposition is approximately 0.5 to 1 percent per year; it is much higher among women with deleterious genetic mutations. (See "Follow-up for breast cancer survivors: Patterns of relapse and long-term complications of therapy", section on Second primary breast cancer).

As with physical examination, there is a lack of high-quality evidence to support the optimal timing and survival benefit of mammographic surveillance for detecting ipsilateral recurrence or a contralateral breast cancer [33,34]. (See "History and physical examination" above).

Local recurrence — There are no prospective trials that address the utility of mammography in the detection of local recurrence. Data from retrospective series suggest that mammography detects earlier lesions with a more favorable prognosis, and that survival is improved in women whose lesions are detected mammographically as compared to those detected by other means [35-37]. (See "Management of locoregional recurrence of breast cancer after breast conserving therapy").

Contralateral breast cancer — Likewise, there are no randomized trials that address the role of mammography or its impact on survival in detecting contralateral breast cancers. However, recommendations for mammographic surveillance are based upon the benefits seen in the general population without a history of breast cancer. In general, breast cancer survivors are higher-risk women than the general population, and it would seem reasonable to infer that they derive as much or even more benefit from mammography of the contralateral breast. (See "Screening average risk women for breast cancer").
Overall, 40 cancers were discovered. The addition of US to mammography increased the diagnostic yield from 7.6 to 11.8 per 1000 women (that is, 4.2 additional cancers were discovered by the addition of US for every 1000 high-risk women 95% CI 1.1 to 7.2). However, it also increased the false positive rate (10.4 versus 4.4 percent for US plus mammography versus mammography alone). After mammography plus US and a full diagnostic workup, 31 of 276 participants who had undergone biopsy had cancer, resulting in a positive predictive value of both mammography and US of only 11.2 percent (95% CI 7.8 versus 15.6 percent). The corresponding value for mammography alone was 22.6 percent (95% CI 14.2 to 33 percent).

Thus, adding a single screening US to mammography will yield an additional 1.1 to 7.2 cancers per 1000 high-risk women, but it will also substantially increase the number of unnecessary biopsies.

Surveillance of reconstructed breasts — Posttreatment follow-up guidelines from expert groups do not explicitly give recommendations for women who have undergone breast reconstruction [9,18,19]. Postmastectomy surveillance for reconstructed breasts has usually been performed by physical examination. Routine mammographic imaging is technically limited in patients who have prosthetic implants, and is generally not advocated.

However, mammography is technically feasible following autogenous myocutaneous flap reconstruction, particularly following TRAM (transverse rectus abdominis musculocutaneous) or perforator flap reconstruction, because abdominal adipose tissue forms the bulk of the reconstructed breast. Although the available data are sparse, and there is no consensus on this issue, some institutions image TRAM-reconstructed breasts using mammography ("TRAMogram"). This topic is addressed in detail elsewhere. (See "Breast reconstruction in women with breast cancer" and see "Management of locoregional recurrence of breast cancer after mastectomy", section on Findings on imaging).

Summary — Despite the lack of high quality evidence, all expert groups, including ASCO recommend mammography as a component of posttreatment surveillance (show table 3). Despite this general consensus, mammography utilization in breast cancer survivors declines over time [42-44].

ASCO guidelines suggest that women treated with BCT have their first posttreatment mammogram no earlier than six months after definitive RT (show table 1) [9]. Subsequent studies should be obtained every 6 to 12 months. Once stability of mammographic findings is achieved after completion of locoregional therapy, mammography may be performed annually.

The age at which annual mammography should be discontinued is controversial, and most guidelines do not make a specific recommendation. Most decisions are individualized, based upon life expectancy and the likelihood that an abnormal result would be pursued.

However, at least some data suggest that surveillance mammography is beneficial for older breast cancer survivors [34] and that potentially treatable local recurrences occur at a constant rate for at least 10 years after BCT [37]. Since most recurrences are diagnosed by routine screening mammography, it can be argued that long-term follow-up based on regular mammography is warranted, even among older survivors. (See "Management of locoregional recurrence of breast cancer after breast conserving therapy", section on Diagnosis and pretreatment evaluation).

Breast self examination — As previously noted, most recurrences are detected by patients rather than health care providers [23]. The utility of breast self examination (BSE) is controversial in women at average risk for breast cancer, mainly because randomized studies have failed to show a survival benefit from this practice. (See "Screening average risk women for breast cancer", section on Breast self examination).

However, there are no randomized trials examining the effect of BSE in conjunction with regular screening mamograms for women who have been treated for breast cancer. ASCO guidelines suggest that breast cancer survivors be encouraged to perform BSE monthly (show table 1) [9], although this is not a universal recommendation (show table 3).

Additional topics of concern — In addition to the above, updated Canadian guidelines also recommend periodic screening for cognitive dysfunction, fatigue, osteoporosis, and sexual functioning, as well as counseling for weight management (show table...
Recommendations for maintaining bone health in women with breast cancer are also available from ASCO [45]. (See "Side effects of adjuvant chemotherapy for early stage breast cancer" and see "Cancer-related fatigue: Assessment and treatment" and see "Various rehabilitation issues in patients treated for cancer").

Coordination of care — The follow-up of breast cancer survivors may potentially be divided among the primary care provider (PCP), medical oncologist, surgeon, and radiotherapist. At least two randomized trials suggest that less intensive, generalist-directed follow-up care seems to lead to the same health outcomes as specialist-directed care [46,47]:

- In a British trial in which 296 women with stage I to III breast cancer in remission were assigned to follow-up by specialists or by their general practitioner, there was no significant difference between the two groups in measured outcomes including time to diagnosis of recurrence, anxiety, or health-related quality of life [46]. Women presented with symptoms of recurrence between regularly scheduled follow-up visits in 69 percent of cases; in 44 percent of the recurrences that developed in women assigned to specialist care, the women presented first to their general practitioner.

A subsequent economic analysis of this study found that the quality of care as measured by frequency and length of patient visits was superior in the primary care setting [48]. Costs to patients and to the health service were also lower in the generalist setting. One important aspect of this trial was the provision of specialized training in the follow-up of breast cancer survivors that was provided to the participating generalist physicians.

- This study was replicated in Canada by the same investigators in a larger population of 968 selected women with tumor size less than 5 cm, and fewer than four positive nodes [47]. Again, there were no significant differences between the groups assigned to follow-up by specialists or generalists in terms of any recurrence-related serious clinical event or in health-related quality of life. Furthermore, in a later analysis, patients' costs to follow-up (travel costs, out-of-pocket expense, lost earnings) were significantly less to 24 months [49]. Although costs were also less between 36 and 48 months, the difference was not significant.

These studies were conducted before the widespread use of adjuvant selective aromatase inhibitors (SAIs). In the larger trial, approximately 50 percent of the patients in each arm of the study received five years of tamoxifen alone [47].

The increasing use of SAIs in the adjuvant setting raises a number of issues that are relevant to posttreatment follow-up:

- Recommendations for adjuvant hormone therapy are evolving, particularly in postmenopausal women. Current guidelines recommend that an SAI be administered as a component of adjuvant hormone therapy for postmenopausal women with hormonally responsive breast cancers. However, whether it is better to start with an SAI or to start with tamoxifen and sequence to an SAI after two to three or five years of tamoxifen, and the optimal duration of therapy when both drugs are used in sequence remain unsettled issues.

- SAIs are not effective in premenopausal women. Some guidelines suggest sequential administration of SAIs for younger women who have become menopausal following adjuvant chemotherapy and tamoxifen. However, concerns have been raised that a subset of women may have recovery of menstrual function and hence be on ineffective therapy. Thus, if this approach is used, monitoring of ovarian function is needed, and a menstrual history must be continuously reelicited at each follow-up visit to be sure that there has been no recovery of ovarian function. (See "Adjuvant systemic therapy for hormone receptor positive early stage breast cancer in premenopausal women", section on Recommendations of expert groups).

Oncology specialists are best positioned to advise patients on issues relevant to the selection and optimal duration of adjuvant hormone therapy and the particular side effects to monitor for. (See "Adjuvant systemic therapy for hormone receptor positive early stage breast cancer in postmenopausal women", section on Aromatase inhibitors).

A variety of care models have been proposed to coordinate follow-up between specialists and PCPs. A report from the Institute of Medicine contains recommendations for improving care of cancer survivors, including a shared-care model that could be integrated across different specialties [50]. If agreed upon by the patient and the treating oncologist, a shared-care model would provide treatment summary information and a plan for follow-up care to both the patient and the PCP. The level of shared follow-up by the oncology specialist and PCP could depend upon patient and provider preferences.

Summary — A variety of physicians may adequately follow women after the primary therapy of breast cancer provided they are experienced in the surveillance of these patients, the complications that may arise from treatment, and in breast examination, including the examination of irradiated breasts.

ASCO guidelines suggest that if a patient with early stage breast cancer (tumor <5 cm and fewer than four positive nodes) desires follow-up exclusively with a PCP, care may be transferred approximately one year after diagnosis. In such cases, both the patient and the PCP should be advised of the appropriate follow-up and management strategy.

Due to the fact that endocrine strategies are evolving over time, informed decisions regarding long-term options for adjuvant...
hormone therapy for individual patients may necessitate periodic referral for oncology assessment.

TESTS NOT ROUTINELY RECOMMENDED — As noted previously, two well-designed major randomized trials involving a total of 2563 women failed to show a significant survival advantage to intensive surveillance (clinical visits, bone scans, liver ultrasonography, chest x-rays and laboratory testing) versus regular clinical visits alone [11,15]. (See "Intensive versus less intensive surveillance" above).

The following tests are specifically not recommended as a component of the posttreatment surveillance strategy for asymptomatic women with normal examinations in 2006 guidelines from the American Society of Clinical Oncology (ASCO, show table 1) [9].

CBC and automated chemistry studies — Routine liver function tests are elevated in 32 to 95 percent of patients with liver metastases; however, they can be falsely elevated in up to 60 to 80 percent of women without metastases [51-53]. Thus, a single abnormal value is not a helpful predictor of distant metastases. Serially rising tests are more suggestive of the possibility of metastatic disease, but routine measurement is generally not recommended in the absence of symptoms because of the lack of a survival benefit shown in randomized trials.

Breast cancer tumor markers — A number of serum markers are available that can detect early breast cancer recurrence, including CA 15-3, CEA (carcinoembryonic antigen), and CA 27.29 [54-57]. These biochemical markers of breast cancer increase in conjunction with advancing primary disease stage, and reflect the total body burden of disease (show table 6) [6,58-60]. As such, they are potentially more sensitive than radiographic imaging to detect early disease recurrence. Consistent with this concept, combined analysis of three separate studies involving more than 9000 patients demonstrates that when elevated, these markers can predict breast cancer relapse with an average lead time of five to six months [55,56].

However, several limitations argue against the routine use of serial tumor marker measurements in the posttreatment surveillance of women with breast cancer:

- These serum tests are neither sensitive nor specific for breast cancer relapse [6,57].
- Significant fluctuations in CEA and CA 15-3 make it difficult to interpret changing serum levels.
- There are no prospective randomized trials to demonstrate whether detection and treatment of asymptomatic metastases using tumor markers impacts on the most significant outcomes (disease-free survival overall survival, quality of life, toxicity or cost-effectiveness)
- The lack of potentially curative salvage therapy for women with metastatic breast cancer negates the potential benefit of a five to six month lead time in the diagnosis of metastatic disease.

Serial assay of serum tumors marker levels is not recommended as a component of the posttreatment surveillance strategy in guidelines from any expert group, including ASCO (show table 3) [9,18-21]. (See "Expert guidelines" above). An ASCO expert panel on tumor markers in breast cancer concluded that the only recommended use of circulating tumor markers was in monitoring response to treatment in the absence of readily measurable advanced disease [21]. (See "General principles of management of metastatic breast cancer", section on Monitoring therapy).

Chest imaging studies — Neither chest x-ray nor chest CT is recommended for routine surveillance of women following treatment of breast cancer in guidelines from any major group, including ASCO [9,18-20]. (See "Expert guidelines" above).

Chest x-rays are rarely useful for detecting asymptomatic recurrence because of limited sensitivity [23,61-63]. One retrospective review concluded that 1091 posttreatment chest x-rays were required to detect eight patients with asymptomatic disease recurrence [62]. As noted above, at least two randomized trials, a Cochrane review, and a meta-analysis concluded that intensive surveillance strategies that include chest x-ray do not provide any benefit in terms of either survival or quality of life as compared to follow-up programs that are based on regular physical examinations and annual mammography alone. (See "Intensive versus less intensive surveillance" above).

Although they provide a more specific method of detecting asymptomatic pulmonary metastases than does chest x-ray, few retrospective studies have evaluated the utility of routine thoracic chest CT scans during posttreatment surveillance:

- One report consisted of 250 patients with early stage breast cancer who had either chest x-ray (74 percent) or CT scans (26 percent) performed over a two-year period, either for screening purposes or for symptom evaluation [61]. Of the 10 patients who developed metastatic disease (4 percent), only two (0.8 percent of the total) were diagnosed by chest x-ray, and none were found by routine chest CT.
- Furthermore, in series in which chest CT has been used to find occult metastatic disease in patients with newly diagnosed breast cancer, or in which scans obtained for radiation treatment planning have been reviewed for occult
metastatic disease, the yield of chest CT has been low, with high rates of false-positive findings [64-66]. (See "Diagnostic evaluation and initial staging work-up of women with suspected breast cancer", section on Metastatic work-up).

Identifying candidates for pulmonary metastatectomy — Resection of isolated pulmonary metastases has resulted in prolonged disease-free survival in highly selected patients with limited pulmonary metastases from breast cancer. Surgical outcomes are most favorable for those who have a complete resection, solitary rather than multiple metastases, and a long disease-free interval between the diagnosis of the primary tumor and the development of metastatic disease. This topic is addressed in detail elsewhere. (See "The role of surgery in metastatic breast cancer", section on Lung metastases).

While this issue has not been addressed prospectively, it is unlikely that routine use of chest CT as a component of posttreatment surveillance would help to identify women who are appropriate candidates for pulmonary metastatectomy. Breast cancer survivors are unlikely to present as the first site of metastatic disease with isolated lung (ie, without bone or liver) metastases that could be approached surgically for curative intent. This issue was addressed in a series of 416 patients who were undergoing surveillance with routine chest imaging after completing primary treatment for breast cancer [67]. Only nine of the 148 relapsing patients had isolated pulmonary metastases; six were solitary, five of whom had evidence of progressive disease within five months.

Bone scan and serum alkaline phosphatase — Neither bone scan nor serial testing of serum alkaline phosphatase levels is recommended for routine surveillance of women following treatment of breast cancer in guidelines from any major group, including ASCO [9,18-20]. (See "Expert guidelines" above).

Metastases to bone are almost always diagnosed by symptoms, even when patients undergo routine surveillance with bone scans [14,68-70]. Furthermore, when metastases have been detected by serial studies in asymptomatic women, there is no evidence that this discovery changes the clinical course of the disease, the prognosis, or alters the therapeutic approach. (See "Intensive versus less intensive surveillance" above).

Some physicians use routine screening measurement of serum alkaline phosphatase to help guide the decision as to when an asymptomatic patient should undergo bone scanning. However, alkaline phosphatase is neither sensitive nor specific for bone metastases. In a series of 1601 patients with node-positive breast cancer, alkaline phosphatase was only elevated in one-half of those patients who had known skeletal metastases, while the test was abnormal in 28 percent of those without bone (or liver) metastases [70].

Abdominopelvic imaging — Neither liver ultrasound nor abdominopelvic CT scans is recommended as a routine component of posttreatment surveillance in guidelines from any expert group. [9,18-20]. (See "Expert guidelines" above).

The value of routine abdominopelvic imaging as a component of routine posttreatment surveillance has been addressed in the following studies:

- In a retrospective study in which 414 asymptomatic survivors underwent serial right upper quadrant ultrasound, only 28 of 2657 examinations (1 percent) revealed the presence of liver metastases [71].

- One large randomized trial [11], a Cochrane review, and a meta-analysis concluded that intensive surveillance strategies that included liver ultrasound do not provide any benefit in terms of either survival or quality of life as compared to follow-up programs that are based on regular physical examinations and annual mammography alone (See "Intensive versus less intensive surveillance" above).

- In a report of 6628 pelvic CT scans performed in 2426 patients with breast cancer over a nine-year period, pelvic metastases were the only site of metastatic disease in 13 (0.5 percent) [72]. However, the findings led to over 200 additional radiographic and 50 surgical procedures, of which 84 percent yielded benign or negative results.

Identifying candidates for hepatic metastatectomy — Hepatic resection is a standard procedure for patients with isolated hepatic metastases from colorectal cancer, providing long-term disease control in up to 58 percent of cases. (See "Management of potentially resectable colorectal cancer liver metastases").

The liver is involved in over one-half of patients with metastatic breast cancer. However, in contrast to colorectal cancer, liver metastases are usually a late development in breast cancer, and generally considered to represent disseminated disease with a poorer prognosis than bone or soft tissue metastases. Fewer than 10 percent of cases will have isolated liver involvement. (See "The role of surgery in metastatic breast cancer", section on Liver metastases).

Thus, while this issue has not been addressed prospectively, it is unlikely that routine use of abdominal CT as a component of posttreatment surveillance would help to identify women with limited, isolated hepatic metastases who are appropriate candidates for hepatic metastasectomy.
Thus, at present, the optimal use of ductal lavage in women with a prior history of breast cancer remains to be determined.

There is no evidence that breast MRI improves outcomes when used as a breast cancer surveillance tool during routine posttreatment follow-up in asymptomatic women. Breast MRI is not recommended for routine posttreatment surveillance in women treated for an apparently sporadic primary breast cancer in guidelines from any expert group, including ASCO [9,18-20,73]. (See "Expert guidelines" above).

PET scanning — The role of PET scanning in the diagnostic evaluation of women with breast cancer is evolving. There are no prospective trials that address the value of PET scanning as a component of the posttreatment surveillance strategy. In retrospective cohort studies and a meta-analysis of 16 reports, PET scanning has been consistently more sensitive than conventional imaging and serum tumor markers for early diagnosis of recurrent disease [74-76]. However, the impact on survival and quality of life has not been addressed, and it seems unlikely that this approach would provide a survival or quality of life benefit when many other approaches have failed to do so.

The use of PET scan for routine posttreatment surveillance in women treated for early stage breast cancer is not recommended in guidelines from any major group, including ASCO [9,18-20].

Ductal lavage — Most breast cancers originate from ductal epithelium that undergoes progressive molecular and morphologic change. An intermediate step in the progression from normal duct epithelium to invasive cancer is atypical ductal hyperplasia (ADH). It is postulated that the identification of ADH may identify women at risk for invasive breast cancer (including a second primary tumor). (See "Overview of benign breast disease").

In prior studies, cytologic specimens for evaluation of atypia have been collected by either nipple aspiration [77] or random periareolar fine needle aspiration [78]. Ductal lavage is a new procedure for the detection of epithelial atypia that is designed to overcome the problems of scant cellularity in aspirated nipple fluid and to sample the entire ductal tree rather than those ducts that are closest to the nipple. Ductal cells are collected by lavage using a microcatheter that is inserted into individual ducts [79].

Ductal lavage appears to detect abnormal cells more often than does nipple aspiration [80]. However, the actual risk of breast cancer in patients who are found to have ADH as determined by ductal lavage has not been determined, and diagnostic and treatment algorithms have not been widely accepted.

Although it would seem intuitive that ductal lavage might be beneficial for early detection of recurrent breast cancer, there are insufficient data to justify its use for this purpose, either alone, or as an adjunct to mammography. A major problem is the limited sensitivity for malignancy or marked atypia (as low as 17 percent in one series [81]).

Thus, at present, the optimal use of ductal lavage in women with a prior history of breast cancer remains to be determined [79]. It should not be considered as a component of routine surveillance.

SUMMARY AND RECOMMENDATIONS — The goals of posttreatment surveillance after primary treatment for breast cancer are early recognition and treatment of potentially curable disease recurrences and second primary breast cancers, evaluation for therapy-related complications, and detection of symptoms consistent with metastatic disease. (See "Follow-up for breast cancer survivors: Patterns of relapse and long-term complications of therapy").

The greatest emphasis on surveillance is on the first five years after therapy, since the risk of a disease recurrence is highest during this time. However, the threat of a disease recurrence persists for 20 years or longer after primary treatment. (See "Introduction" above).

General surveillance guidelines following treatment of breast cancer are available from several groups, including the American Society of Clinical Oncology (ASCO, show table 1) [9,18-20]. History and physical examination and routine mammography form the cornerstone of posttreatment surveillance in all guidelines. (See "Expert guidelines" above).

Generalist versus specialist care — Follow up care performed by a primary care physician (PCP) seems to lead to the same health outcomes as specialist-directed care, provided they are experienced in the surveillance of these patients, the complications that may arise from treatment, and in examination of irradiated breasts. ASCO guidelines suggest that if a patient with early stage breast cancer (tumor <5 cm and fewer than four positive nodes) desires follow-up exclusively with a PCP, care may be transferred approximately one year after diagnosis [9]. However:

- Both the patient and the PCP should be advised of the appropriate surveillance and management strategy.
Due to the fact that endocrine strategies are evolving over time, patients receiving adjuvant endocrine therapy should be referred for periodic oncology assessment (See "Coordination of care" above).

Recommendations for surveillance — The following recommendations for posttreatment follow-up are consistent with the 2006 ASCO guidelines, and are outlined in the following table (show table 1) [9].

Women should be informed of the signs and symptoms of breast cancer recurrence (show table 4). Those at high risk for familial breast cancer syndromes should be referred for genetic counseling in accordance with guidelines recommended by the US Preventive Services Task Force. (See "Genetic testing for breast and ovarian cancer", section on Recommendations: who should be tested).

Criteria for referral include the following (see "Patient education and referral for genetic counseling" above):

- Ashkenazi Jewish heritage;
- History of ovarian cancer at any age in the patient or any first- or second-degree relative;
- Any first-degree relative with a history of breast cancer diagnosed before age 50;
- Two or more first- or second-degree relatives diagnosed with breast cancer at any age;
- Patient or relative with a diagnosis of bilateral breast cancer;
- History of breast cancer in a male relative.

Although others disagree, we suggest that women with a history of breast cancer be encouraged to perform breast self-examination monthly (Grade 2C). (See "Breast self examination" above).

We suggest that patients be seen for a history and complete physical examination every three to six months during the first three years after primary therapy, every six to twelve months for the next two years, and then annually (Grade 2C). (See "History and physical examination" above).

We suggest regular gynecologic follow-up, including a Pap smear, particularly if women are receiving tamoxifen (Grade 2B). (See "Pelvic examination" above).

We suggest posttreatment surveillance mammography (Grade 2B). Women treated with breast conserving surgery should have their first posttreatment mammogram no earlier than 6 months after definitive radiation therapy. Subsequent mammograms should be obtained every 6 to 12 months for surveillance of abnormalities. Once stability of mammographic findings is achieved after completion of locoregional therapy, mammography may be performed annually. (See "Mammography" above).

Tests not recommended — We recommend not obtaining the following tests for routine surveillance (Grade 1C) (see "Tests not routinely recommended" above):

- Liver function tests
- Complete blood count
- Chest x-ray
- Bone scans
- CT scans of the chest, abdomen, or pelvis
- Liver ultrasound
- Serum tumor markers
- Breast MRI
- PET scanning
- Ductal lavage

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