Annals of Internal Medicine

Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force*

Description: Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for breast cancer in the general population.

Methods: The USPSTF examined the evidence on the efficacy of 5 screening modalities in reducing mortality from breast cancer: film mammography, clinical breast examination, breast self-examination, digital mammography, and magnetic resonance imaging in order to update the 2002 recommendation. To accomplish this update, the USPSTF commissioned 2 studies: 1) a targeted systematic evidence review of 6 selected questions relating to benefits and harms of screening, and 2) a decision analysis that used population modeling techniques to compare the expected health outcomes and resource requirements of starting and ending mammography screening at different ages and using annual versus biennial screening intervals.

Recommendations: The USPSTF recommends against routine screening mammography in women aged 40 to 49 years. The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take into account patient context, including the patient's values regarding specific benefits and harms. (Grade C recommendation)

The USPSTF recommends biennial screening mammography for women between the ages of 50 and 74 years. (Grade B recommendation)

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of clinical breast examination beyond screening mammography in women 40 years or older. (I statement)

The USPSTF recommends against clinicians teaching women how to perform breast self-examination. (Grade D recommendation)

The USPSTF concludes that the current evidence is insufficient to assess additional benefits and harms of either digital mammography or magnetic resonance imaging instead of film mammography as screening modalities for breast cancer. (I statement)

Ann Intern Med. 2009;151:716-726.

www.annals.org

For author affiliation, see end of text.

* For a list of the members of the USPSTF, see the **Appendix** (available at www.annals.org).

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.

It bases its recommendations on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.

See also:

Print

Web-Only

Appendix CME quiz

Conversion of graphics into slides

Downloadable recommendation summary

The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policymakers should understand the evidence but individualize decision making to the specific patient or situation.

SUMMARY OF RECOMMENDATIONS AND EVIDENCE

The USPSTF recommends against routine screening mammography in women aged 40 to 49 years. The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms. This is a C recommendation.

The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. This is a B recommendation.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older. This is an I statement.

Annals of Internal Medicine





The USPSTF recommends against teaching breast self-examination (BSE). This is a D recommendation.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of clinical breast examination (CBE) beyond screening mammography in women 40 years or older. This is an I statement.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer. This is an I statement.

Figures 1 and 2 summarize the recommendations and provide suggestions for clinical practice.

Table 1 describes the USPSTF grades and Table 2 describes the USPSTF classification of levels of certainty about net benefit.

See Clinical Considerations for specific populations at increased risk and for suggestions for practice regarding the I statements.

RATIONALE

Importance

Breast cancer is the second-leading cause of cancer death among women in the United States. Widespread use of screening, along with treatment advances in recent years, have been credited with significant reductions in breast cancer mortality.

Detection

Mammography, as well as physical examination of the breasts (CBE and BSE), can detect presymptomatic breast cancer. Because of its demonstrated effectiveness in randomized, controlled trials of screening, film mammography is the standard for detecting breast cancer; in 2002, the USPSTF found convincing evidence of its adequate sensitivity and specificity.

Benefits of Detection and Early Intervention

There is convincing evidence that screening with film mammography reduces breast cancer mortality, with a greater absolute reduction for women aged 50 to 74 years than for women aged 40 to 49 years. The strongest evidence for the greatest benefit is among women aged 60 to 69 years.

Among women 75 years or older, evidence of benefits of mammography is lacking.

Adequate evidence suggests that teaching BSE does not reduce breast cancer mortality.

The evidence for additional effects of CBE beyond mammography on breast cancer mortality is inadequate.

The evidence for benefits of digital mammography and MRI of the breast, as a substitute for film mammography, is also lacking.

Harms of Detection and Early Intervention

The harms resulting from screening for breast cancer

include psychological harms, unnecessary imaging tests and

www.annals.org

biopsies in women without cancer, and inconvenience due to false-positive screening results. Furthermore, one must also consider the harms associated with treatment of cancer that would not become clinically apparent during a woman's lifetime (overdiagnosis), as well as the harms of unnecessary earlier treatment of breast cancer that would have become clinically apparent but would not have shortened a woman's life. Radiation exposure (from radiologic tests), although a minor concern, is also a consideration.

Adequate evidence suggests that the overall harms associated with mammography are moderate for every age group considered, although the main components of the harms shift over time. Although false-positive test results, overdiagnosis, and unnecessary earlier treatment are problems for all age groups, false-positive results are more common for women aged 40 to 49 years, whereas overdiagnosis is a greater concern for women in the older age groups.

There is adequate evidence that teaching BSE is associated with harms that are at least small. There is inadequate evidence concerning harms of CBE.

USPSTF Assessment

The USPSTF has reached the following conclusions:

For biennial screening mammography in women aged 40 to 49 years, there is moderate certainty that the net benefit is small. Although the USPSTF recognizes that the benefit of screening seems equivalent for women aged 40 to 49 years and 50 to 59 years, the incidence of breast cancer and the consequences differ. The USPSTF emphasizes the adverse consequences for most women—who will not develop breast cancer—and therefore use the number needed to screen to save 1 life as its metric. By this metric, the USPSTF concludes that there is moderate evidence that the net benefit is small for women aged 40 to 49 years.

For biennial screening mammography in women aged 50 to 74 years, there is moderate certainty that the net benefit is moderate.

For screening mammography in women 75 years or older, evidence is lacking and the balance of benefits and harms cannot be determined.

For the teaching of BSE, there is moderate certainty that the harms outweigh the benefits.

For CBE as a supplement to mammography, evidence is lacking and the balance of benefits and harms cannot be determined.

For digital mammography and MRI as a replacement for mammography, the evidence is lacking and the balance of benefits and harms cannot be determined.

CLINICAL CONSIDERATIONS

Patient Population Under Consideration

This recommendation statement applies to women 40 years or older who are not at increased risk for breast cancer by virtue of a known underlying genetic mutation or a history of chest radiation.

17 November 2009 Annals of Internal Medicine Volume 151 • Number 10 717

Assessment of Risk

Increasing age is the most important risk factor for breast cancer for most women. Women without known deleterious genetic mutations (such as BRCA1 or BRCA2) may still have other demographic, physical, or historical risk factors for breast cancer, but none conveys a clinically important absolute increased risk for cancer.

Screening Tests

In recent decades, the early detection of breast cancer has been accomplished by physical examination by a clinician (CBE), by a woman herself (BSE), or by mammography. Standardization of mammography practices enacted by the Mammography Quality Standards Act have led to improved mammography quality. Clinicians should refer patients to Mammography Quality Standards Act-certified facilities, a listing of which is available at www.fda.gov /cdrh/mammography/certified.html.

Screening Intervals

In trials that demonstrated the effectiveness of mammography in decreasing breast cancer mortality, screening was performed every 12 to 33 months. The evidence reviewed by the USPSTF indicates that a large proportion of the benefit of screening mammography is maintained by biennial screening, and changing from annual to biennial screening is likely to reduce the harms of mammography screening by nearly half. At the same time, benefit may be reduced when extending the interval beyond 24 months; therefore the USPSTF recommends biennial screening.

Treatment

Effective treatments, including radiation, chemotherapy (including hormonal treatment), and surgery, are available for invasive carcinoma. Although the standard treatments women receive for ductal carcinoma in situ (DCIS) include surgical approaches as well as radiation and hormonal therapy, considerable debate exists about the optimal treatment strategy for this condition.

Considerations for Practice Regarding I Statements Clinical Breast Examination

Potential Preventable Burden. The evidence for CBE, although indirect, suggests that CBE may detect a substantial proportion of cases of cancer if it is the only screening test available. In parts of the world where mammography is infeasible or unavailable (such as India), CBE is being investigated in this way.

Potential Harms. The potential harms of CBE are thought to be small but include false-positive test results, which lead to anxiety and breast cancer worry, as well as repeated visits and unwarranted imaging and biopsies.

Costs. The principal cost of CBE is the opportunity cost incurred by clinicians in the patient encounter.

Current Practice. Surveys suggest (1) that the CBE technique used in the United States currently lacks a standard approach and reporting standards. Clinicians who are committed to spending the time on CBE would benefit their patients by considering the evidence in favor of a structured, standardized examination (2).

Digital Mammography

Potential Preventable Burden. Digital mammography detects some cases of cancer not identified by film mammography; film mammography detects some cases of cancer not identified by digital mammography. Overall detection is similar for many women. For women who are younger than 50 years or have dense breast tissue, overall detection is somewhat higher with digital mammography. It is not clear whether this additional detection would lead to reduced mortality from breast cancer.

Potential Harms. The possibility of false-positive test results is similar for film and digital mammography. It is uncertain whether overdiagnosis occurs more with digital mammography than with film mammography.

Costs. Digital mammography is more expensive than film mammography.

Current Practice. Some clinical practices are now switching their mammography equipment from film to digital. This may curtail the availability of film mammography in some areas.

Magnetic Resonance Imaging

Potential Preventable Burden. Studies of the use of contrast-enhanced MRI for breast cancer screening have been conducted only in very high-risk populations. In these studies, MRI detected more cases of cancer than did mammography. It is unknown whether detecting these additional cases of cancer would lead to reduced breast cancer

Potential Harms. Contrast-enhanced MRI requires the injection of contrast material. Studies of MRI screening have shown that MRI yields many more false-positive results than does mammography. Magnetic resonance imaging has the potential to be associated with a greater degree of overdiagnosis than mammography.

Costs. Magnetic resonance imaging is much more expensive than either film or digital mammography.

Current Practice. Magnetic resonance imaging is not currently used for screening women at average risk for breast cancer.

Screening Mammography in Women 75 Years or Older

Potential Preventable Burden. No women 75 years or older have been included in the multiple randomized clinical trials of breast cancer screening. Breast cancer is a leading cause of death in older women, which might suggest that the benefits of screening could be important at this age. However, 3 facts suggest that benefits from screening would probably be smaller for this age group than for women aged 60 to 69 years and probably decrease with increasing age: 1) the benefits of screening occur only several years after the actual screening test, whereas the percentage of women who survive long enough to benefit decreases with age; 2) a higher percentage of the type of breast cancer detected in this age group is the more easily treated estrogen receptor-positive type; and 3) women of this age are at much greater risk for dying of other conditions that would not be affected by breast cancer screening.

Potential Harms. Screening detects not only cancer that could lead to a woman's death but also cancer that will not shorten a woman's life. Women cannot benefit from but can be harmed by—the discovery and treatment of this second type of cancer, which includes both cancer that might some day become clinically apparent and cancer that never will. Detection of cancer that would never have become clinically apparent is called overdiagnosis, and it is usually followed by overtreatment. Because of a shortened life span among women 75 years or older, the probability of overdiagnosis and unnecessary earlier treatment increases dramatically after about age 70 or 75 years. Overdiagnosis and unnecessary earlier treatment are important potential harms from screening women in this age group.

Current Practice. Studies show that many women 75 years or older are currently being screened.

Useful Resources

Other USPSTF recommendations on screening for genetic susceptibility for breast cancer and chemoprevention of breast cancer are available on the Agency for Healthcare Research and Quality Web site (www.preventiveservices .ahrq.gov).

OTHER CONSIDERATIONS

Implementation

www.annals.org

The Task Force on Community Preventive Services has reviewed the evidence on methods to increase breast cancer screening, including reminder systems and other interventions (3-5).

Explanation of Change in Recommendation

The 2002 USPSTF issued a B recommendation for screening mammography for women 40 years or older. However, it went on to say:

The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences. Clinicians should inform women about the potential benefits (reduced chance of dying from breast cancer), potential harms (for example, false-positive results, unnecessary biopsies), and limitations of the test that apply to women their age. Clinicians should tell women that the balance of benefits and potential harms of mammography improves with increasing age for women between the ages of 40 and 70 (6).

The updated USPSTF recommendation endorses this approach to deciding when to start screening. However, the current USPSTF is now further informed by a new

systematic review (7), which incorporates a new randomized, controlled trial that estimates the "number needed to invite for screening to extend one woman's life" as 1904 for women aged 40 to 49 years and 1339 for women aged 50 to 59 years. Although the relative risk reduction is nearly identical (15% and 14%) for these 2 age groups, the risk for breast cancer increases steeply with age starting in Thus, the absolute risk reduction from the 40s. screening (as shown by the number needed to invite to screen) is greater for women aged 50 to 59 years than for those aged 40 to 49 years.

The current USPSTF statement is also informed by the Cancer Intervention and Surveillance Modeling Network (CISNET) modeling studies (8) that accompany this recommendation. The Task Force considered both "mortality" and "life-years gained" outcomes. In this case, given that the age groups (40 to 49 years and 50 to 59 years) are adjacent, the Task Force elected to emphasize the mortality outcomes from the modeling studies. Of the 8 screening strategies found most efficient, 6 start at age 50 years rather than age 40 years. The frontier curves for the mortality outcome show only small gains but larger numbers of mammograms required when screening is started at age 40 years versus age 50 years.

In conclusion, the USPSTF reasoned that the additional benefit gained by starting screening at age 40 years rather than at age 50 years is small, and that moderate harms from screening remain at any age. This leads to the C recommendation. The USPSTF notes that a "C" grade is a recommendation against routine screening of women aged 40 to 49 years. The Task Force encourages individualized, informed decision making about when to start mammography screening.

RESEARCH NEEDS AND GAPS

A series of randomized clinical trials that would compare the results of stopping breast cancer screening at different ages (by first comparing stopping screening at age 75 years with continued screening, and then further comparing stopping screening at earlier ages, depending on the results of the first study) would be ethical and informative.

Extended follow-up of this type of study might also provide useful information about overdiagnosis in this age group. In general, more studies of overdiagnosis, including comparisons of lifetime breast cancer incidence among similar screened and unscreened women, would be helpful. Studies on overdiagnosis might also include long-term follow-up of women with probable missed cases of DCIS on the basis of microcalcifications that were missed in an earlier mammogram. Such studies could provide the percentage of these women who develop invasive breast cancer over the next 10 or more years.

Randomized clinical trials of film versus digital mammography among women with dense breast tissue, with sufficient follow-up to detect stage shifts (reductions of late-stage cancer) or decreases in clinical interval cases, would also be ethical and helpful.

Better understanding of certain facets of tumor biology is needed, particularly how age, race, breast density, and other factors may predispose certain women toward tumors with faster growth rates and greater lethality. This would improve the ability to determine at diagnosis which patients can be treated minimally.

DISCUSSION

Burden of Disease

Breast cancer is the most frequently diagnosed cancer in women in the United States, not including skin cancer, and is second only to lung cancer as a cause of cancer deaths. In 2008, an estimated 182 460 cases of invasive cancer and 67 770 cases of in situ breast cancer were diagnosed and 40 480 breast cancer deaths occurred (9). The National Cancer Institute, on the basis of Surveillance Epidemiology and End Result data, estimates the lifetime risk for a woman to develop breast cancer at 12% (10). The risk for breast cancer increases with age. The 10-year risk for breast cancer is 1 in 69 for a woman at age 40 years, 1 in 42 at age 50 years, and 1 in 29 at age 60 years (11). The incidence rate of breast cancer has increased since the 1970s; however, recent data show that this rate seems to be decreasing, both overall and on an age-adjusted basis. The incidence rate in 2003 was 124.2 per 100 000 women, a 6.7% decrease from the previous year (12). Discontinuation of hormone replacement therapy may be largely responsible for this observed decrease (12, 13), although slowed growth or even a decline in screening mammography also may have contributed (14). Breast cancer mortality has been decreasing since 1990 by 2.3% per year overall and by 3.3% for women aged 40 to 50 years. This decrease is largely attributed to the combination of mammography screening with improved treatment (15).

Scope of Review

The systematic evidence review undertaken in support of this recommendation (7) addressed the efficacy of 5 breast cancer screening methods for reducing breast cancer mortality—film mammography, CBE, BSE, digital mammography, and MRI—by using published reports of randomized, controlled screening trials and specifically updated information from mammography trials among women in the age groups of 40 to 49 years and 70 years or older. Information on harms of breast cancer screening, such as false-positive test results, pain, anxiety, and biopsy rates, were sought from multiple sources, including systematic reviews, meta-analyses, and recently published literature. To assess the follow-up testing and other outcomes of a mammography screening program, the reviewers included data from the Breast Cancer Surveillance Consortium from 2000 to 2005.

In addition to the systematic review of screening tests, the USPSTF requested a report from the CISNET Breast Cancer Modeling Group to provide data from comparative decision models on optimal starting and stopping ages and intervals for screening mammography (8).

Accuracy of Screening Tests

Mammography, CBE, and BSE are recognized approaches for breast cancer screening. Since the 2002 USPSTF recommendation statement, digital (as opposed to film-based) mammography has been increasingly used, and MRI is being used with greater frequency for screening women at increased risk for breast cancer. The sensitivity of mammography screening is 77% to 95%, whereas specificity is 94% to 97% (16). Multiple factors, including age, time since last examination, breast tissue density, equipment, and the skill of the interpreting radiologist can affect sensitivity and specificity (17). A single, large comparison study of film and digital mammography (18) demonstrated similar diagnostic accuracy for the 2 methods, although digital mammography was better at detecting lesions in women who were younger than 50 years or premenopausal or had radiographically dense breasts. Studies of MRI in high-risk women without cancer (19) showed that MRI has a sensitivity of 71% to 100% and a specificity of 81% to 97%; MRI is therefore recommended by the American Cancer Society for women at high risk for breast cancer. However, no studies have been done on using MRI to screen women at average risk.

Clinical breast examination has a sensitivity of 40% to 69% and a specificity in the range of 88% to 99%. For BSE, sensitivity ranges from 12% to 41%, lower than that of CBE and mammography, and is age-dependent (16).

Effectiveness of Early Detection

The newly updated meta-analysis by Nelson and colleagues (7) confirms an earlier finding (16) that screening mammography reduces mortality. Improvements in the relative risk (RR) for death due to breast cancer for women aged 39 to 49 years and 50 to 59 years are similar at 0.85 (95% CI, 0.75 to 0.96) and 0.86 (CI, 0.75 to 0.99), respectively. An even greater improvement was found for women aged 60 to 69 years (RR, 0.68 [CI, 0.54 to 0.87]). Results were uncertain for older women, with a new report from a previously included trial with longer follow-up data showing an RR of 1.12 (CI, 0.73 to 1.72) for breast cancer death associated with screening women aged 70 to 74 years (based on a small number of participants). At the time of the previous meta-analysis, data from 2 trials showed an RR of 0.78 (CI, 0.62 to 0.99) for breast cancer death in screened women aged 65 to 74 years (16). Mortality reduction and life-years gained (8) were both considered important outcomes of screening in forming this recommendation; in the end, mortality reduction as observed in trials was the metric chosen to express the benefits of screening in each age group. Digital mammography has been shown to perform similarly to film mammography, although it

720 17 November 2009 Annals of Internal Medicine Volume 151 • Number 10

has never been studied in relation to health outcomes. Magnetic resonance imaging has not been evaluated for its potential benefit in screening average-risk women. Clinical breast examination is inexpensive and easy to perform; however, few studies have compared the effectiveness of CBE with that of no screening and none has examined CBE and mammography versus mammography alone. Two large trials of teaching BSE outside the United States (7) demonstrated no mortality benefit in the intervention groups.

Potential Harms of Screening Mammography

False-positive results are common with mammography and can cause anxiety and lead to additional imaging studies and invasive procedures (such as biopsy or fine-needle aspiration). False-positive results and accompanying additional imaging studies are more common in younger women. Biopsies may occur as a consequence of falsepositive mammography results; biopsy rates are more common among older women. Anxiety, distress, and other psychosocial effects can exist with abnormal mammography results but fortunately are usually transient, and some research suggests that these effects are not a barrier to screening. False-negative results occur at a relatively low rate for all ages, but are slightly higher in women older than 70 years. Other potential harms, such as pain caused by the procedure, exist but are thought to have little effect on mammography use.

Overdiagnosis can occur when screening detects earlystage invasive breast cancer or DCIS in a woman, typically older, who is likely to die from another cause before the breast cancer would be clinically detected. Overdiagnosis can also occur in younger women if a detected DCIS or other early-stage lesion never progresses to invasive cancer. Methods for estimating overdiagnosis at a population level are not well established, and thus the proportion of all detected DCIS lesions that constitute overdiagnosis is uncertain (7). Similarly, unnecessary earlier treatment can occur at any age when screening detects a slower-growing cancer that would have eventually become clinically apparent but would never have caused death.

Radiation exposure may increase the risk for breast cancer, but usually only at much higher doses than those used in mammography, although regular mammography could contribute to cumulative radiation doses from additional imaging for other reasons (7).

Digital Mammography and Magnetic Resonance Imaging

Digital mammography can be expected to have harms similar to those of film mammography. No studies have evaluated MRI screening of average-risk women; in theory, because MRI could be considerably less specific than mammography screening, it could potentially be associated with higher biopsy rates and greater degrees of overdiagnosis if used in low-risk populations.

www.annals.org

Clinical Breast Examination

A theoretical harm of CBE is that its lower specificity than that of mammography may result in more women undergoing biopsy. Few data are available to evaluate harms associated with CBE.

Breast Self-Examination

One study indicated that anxiety was not a concern with BSE. The 2 available trials (20, 21) indicated that more additional imaging procedures and biopsies were done for women who performed BSE than for control participants.

Estimate of Magnitude of Net Benefit

In 2002, the USPSTF concluded that there was fair evidence that mammography screening every 12 to 33 months could significantly reduce breast cancer mortality. The evidence was strongest for women aged 50 to 69 years, with weaker evidence supporting mammography screening for women aged 40 to 49 years. Since that recommendation, 1 new trial and updated data from an older study have been published that specifically address screening in women in the younger age group. These findings were combined in an updated meta-analysis, which resulted in an RR for breast cancer death of 0.85 (CI, 0.75 to 0.96; 8 trials) and a number needed to invite for screening of 1904 (CI, 929 to 6378) to prevent 1 breast cancer death in women aged 39 to 49 years. A meta-analysis of 6 trials among women aged 50 to 59 years and 2 trials among women aged 60 to 69 years provided pooled RRs for breast cancer death in the screened group of 0.86 (CI, 0.75 to 0.99; number needed to invite, 1339 [CI, 322 to 7455]) and 0.68 (CI, 0.54 to 0.87; number needed to invite, 377 [CI, 230 to 1050]), respectively. Only 1 study provided data on women older than 70 years, yielding an RR of 1.12 (CI, 0.73 to 1.72), although an RR of 0.78 (CI, 0.62 to 0.99) was found for women aged 65 to 74 years by combining the results of 2 studies used in the 2002 review.

A decision analysis performed for the USPSTF projected that biennial screening produced 70% to 99% of the benefit of annual screening, with a significant reduction in the number of mammograms required and therefore a decreased risk for harms. Screening between the ages of 50 and 69 years produced a projected 17% (range, 15% to 23%) reduction in mortality (compared with no screening), whereas extending the age range produced only minor improvements (additional 3% reduction from starting at age 40 years and 7% from extending to age 79 years) (8).

The USPSTF noted with moderate certainty that the net benefits of screening mammography in women aged 50 to 74 years were at least moderate, and that the greatest benefits were seen in women aged 60 to 69 years. For women aged 40 to 49 years, the USPSTF had moderate certainty that the net benefits were small. Because of the uncertainties related to harms of screening, particularly overdiagnosis, and the near total lack of trial data for older women, the USPSTF had low certainty about the net benefits of screening mammography for women 75 years or

How Does Evidence Fit With Biological Understanding?

Current knowledge about the development of breast cancer is limited. The effectiveness of screening mammography seen in trials presumably results from the early detection of smaller, earlier-stage tumors, which are more responsive to available treatments. Although the most common breast cancer occurs in the epithelial cells that line the duct system of the gland (ductal carcinoma), the sequence of development of invasive cancer is not entirely known. For example, DCIS does not always represent a precursor to invasive ductal cancer. Studies of women with untreated DCIS showed progression to invasive disease in half or fewer of the cases. Because DCIS is often found only by mammography, its incidence has increased steadily since the advent of widespread screening mammography. In 1983, 4900 cases of DCIS were diagnosed; by 2008, that number was expected to be 67 770 (22). Because the likelihood that DCIS will progress to invasive cancer is unknown, surgical removal—with or without adjuvant treatment may represent overdiagnosis or overtreatment. Lobular carcinoma in situ, in contrast, is not considered a true precursor lesion but connotes a higher risk for subsequent invasive lobular or ductal cancer in either breast. Lobular carcinoma in situ is often multifocal, appearing in several distinct locations. Knowledge of what determines the rapidity with which invasive cancer can spread (tumor characteristics, host factors, hormonal triggers) is limited (23). Because of these elements of biological uncertainty, it is clear that lesion sensitivity alone is not a sufficient metric for assessing effectiveness of new screening methods (24).

UPDATE OF PREVIOUS USPSTF RECOMMENDATION

This recommendation updates the 2002 recommendation by providing specific recommendations for mammography screening by age. The previous recommendation statement recommended screening mammography every 1 to 2 years for all women older than 40 years. The USPSTF now recommends against routine screening of women aged 40 to 49 years (C recommendation), recommends biennial screening mammography for all women aged 50 to 74 years (B recommendation), and provides an I statement regarding screening of women older than 75 years. The USPSTF now recommends against teaching BSE (D recommendation), replacing the previous statement of insufficient evidence. The evidence for CBE continues to be assessed as insufficient. Digital mammography and MRI as screening tools were not addressed in the 2002 recommendation statement; the USPSTF concludes that the evidence is insufficient to assess the harms or benefits of these methods for screening.

722 17 November 2009 Annals of Internal Medicine Volume 151 • Number 10

RECOMMENDATIONS OF OTHERS

Numerous organizations have provided breast cancer screening recommendations. These recommendations are summarized below. All recommendations are for women not at increased risk for breast cancer.

In 2003, the American Cancer Society recommended annual mammography beginning at age 40 years, annual CBE after the age of 40 years (25). It does not recommend MRI for women at average risk for breast cancer and states that there is insufficient evidence to recommend BSE.

The American Medical Association, in 2002 (26), and the National Comprehensive Cancer Network, in 2009 (27), have made recommendations similar to those of the American Cancer Society, except for the inclusion of a positive recommendation for BSE.

The American Academy of Family Physicians has endorsed the USPSTF recommendation on breast cancer screening in the past (28). The American College of Physicians recommended in 2007 that screening mammography decisions in women aged 40 to 49 years should be based on individualized assessment of risk for breast cancer; that clinicians should inform women aged 40 to 49 years about the potential benefits and harms of screening mammography; and that clinicians should base screening mammography decisions on benefits and harms of screening, as well as on a woman's preferences and breast cancer risk profile (29).

According to the Canadian Task Force on Preventive Health Care in 2001:

Current evidence . . . does not suggest the inclusion of the manoeuvre in, or its exclusion from, the periodic health examination of women aged 40-49 years at average risk of breast cancer (grade C recommendation). Upon reaching the age of 40, Canadian women should be informed of the potential benefits and risk of screening mammography and assisted in deciding at what age they wish to initiate the manoeuvre (30).

In 2003, the American College of Obstetrics and Gynecology recommended mammography every 1 to 2 years for women aged 40 to 49 years and annually after the age of 50 years (31). It recommended CBE for all women and noted that BSE can be recommended.

In 2009, the World Health Organization recommended mammography every 1 to 2 years for women aged 50 to 69 years, but does not recommend CBE or BSE (32).

Addendum: On 4 December 2009, the U.S. Preventive Services Task Force (USPSTF) voted unanimously to update the language of its recommendation regarding women younger than 50 years to clarify its original and continued intent. The USPSTF omitted the first sentence of the recommendation. The recommendation for women younger than 50 now reads: "The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms."

From the U.S. Preventive Services Task Force, Agency for Healthcare Research and Quality, Rockville, Maryland.

Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Financial Support: The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Potential Conflicts of Interest: None disclosed.

Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.preventiveservices.ahrq.gov).

References

- 1. Saslow D, Hannan J, Osuch J, Alciati MH, Baines C, Barton M, et al. Clinical breast examination: practical recommendations for optimizing performance and reporting. CA Cancer J Clin. 2004;54:327-44. [PMID: 15537576]
- 2. Barton MB, Harris R, Fletcher SW. The rational clinical examination. Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? JAMA. 1999;282:1270-80. [PMID: 10517431]
- 3. Baron RC, Rimer BK, Breslow RA, Coates RJ, Kerner J, Melillo S, et al; Task Force on Community Preventive Services. Client-directed interventions to increase community demand for breast, cervical, and colorectal cancer screening a systematic review. Am J Prev Med. 2008;35:S34-55. [PMID: 18541187]
- 4. Baron RC, Rimer BK, Coates RJ, Kerner J, Kalra GP, Melillo S, et al; Task Force on Community Preventive Services. Client-directed interventions to increase community access to breast, cervical, and colorectal cancer screening a systematic review. Am J Prev Med. 2008;35:S56-66. [PMID: 18541188]
- 5. Baron RC, Rimer BK, Coates RJ, Kerner J, Mullen PD, Chattopadhyay S, et al; Task Force on Community Preventive Services. Methods for conducting systematic reviews of evidence on effectiveness and economic efficiency of interventions to increase screening for breast, cervical, and colorectal cancers. Am J Prev Med. 2008;35:S26-33. [PMID: 18541185]
- 6. U.S. Preventive Services Task Force. Screening for breast cancer: recommendations and rationale. Ann Intern Med. 2002;137:344-6. [PMID: 12204019]
- 7. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37.
- 8. Mandelblatt JS, Cronin KA, Bailey S, Berry DA, de Koning HJ, Draisma G, et al. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151:
- 9. American Cancer Society. How Many Women Get Breast Cancer? Overview: Breast Cancer. Atlanta, GA: American Cancer Society; 2009. Accessed at www .cancer.org/docroot/CRI/content/CRI_2_2_1X_How_many_people_get_breast _cancer_5.asp on 25 September 2009.
- 10. National Cancer Institute. Surveillance Epidemiology and End Results (SEER) Stat Fact Sheets: Breast Cancer. Bethesda, MD: National Cancer Institute; 2009. Accessed at http://seer.cancer.gov/statfacts/html/breast.html on 25 September 2009.
- 11. Horner MJ, Ries LAG, Krapcho M, Neyman N, Aminou R, Howlader N, et al, eds. SEER Cancer Statistics Review, 1975-2006, National Cancer Institute. Bethesda, MD: National Cancer Institute; 2009. Accessed at http://seer.cancer .gov/csr/1975_2006 on 25 September 2009.
- 12. Ravdin PM, Cronin KA, Howlader N, Berg CD, Chlebowski RT, Feuer EJ, et al. The decrease in breast-cancer incidence in 2003 in the United States. N Engl J Med. 2007;356:1670-4. [PMID: 17442911]
- 13. Kerlikowske K, Miglioretti DL, Buist DS, Walker R, Carney PA; National Cancer Institute-Sponsored Breast Cancer Surveillance Consortium. Declines in invasive breast cancer and use of postmenopausal hormone therapy in a screening mammography population. J Natl Cancer Inst. 2007;99:1335-9. [PMID:
- 14. Chagpar AB, McMasters KM. Trends in mammography and clinical breast examination: a population-based study. J Surg Res. 2007;140:214-9. [PMID: 174188621

- 15. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al; Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med. 2005;353:1784-92. [PMID: 16251534]
- 16. Humphrey LL, Helfand M, Chan BK, Woolf SH. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2002;137:347-60. [PMID: 12204020]
- 17. Breast Cancer Surveillance Consortium. Evaluating Screening Performance in Practice. Bethesda, MD: National Cancer Institute; 2004. Accessed at http: //breastscreening.cancer.gov/espp.pdf on 25 September 2009.
- 18. Pisano ED, Gatsonis C, Hendrick E, Yaffe M, Baum JK, Acharyya S, et al; Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group. Diagnostic performance of digital versus film mammography for breastcancer screening. N Engl J Med. 2005;353:1773-83. [PMID: 16169887]
- 19. Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al; Magnetic Resonance Imaging Screening Study Group. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med. 2004;351:427-37. [PMID: 15282350] 20. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, et al. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst. 2002;94:1445-57. [PMID: 12359854]
- 21. Semiglazov VF, Manikhas AG, Moiseenko VM, Protsenko SA, Kharikova RS, Seleznev IK, et al. [Results of a prospective randomized investigation [Russia (St.Petersburg)/WHO] to evaluate the significance of self-examination for the early detection of breast cancer]. Vopr Onkol. 2003;49:434-41. [PMID: 14569932]
- 22. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Nygren P, et al. Screening for Breast Cancer: Systematic Evidence Review Update for the U.S. Preventive Services Task Force. Evidence Synthesis No. 74. AHRQ Publication No. 10-05142-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2009.
- 23. National Cancer Institute. Effect of Screening on Breast Cancer Mortality. Atlanta, GA: National Cancer Institute; 2009. Accessed at www.cancer .gov/cancertopics/pdq/screening/breast/HealthProfessional/page6 on 25 September 2009.
- 24. Lord SJ, Irwig L, Simes RJ. When is measuring sensitivity and specificity sufficient to evaluate a diagnostic test, and when do we need randomized trials? Ann Intern Med. 2006;144:850-5. [PMID: 16754927]
- 25. American Cancer Society. American Cancer Society Guidelines for the Early Detection of Cancer. Atlanta, GA: American Cancer Society; 2009. Accessed at www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer _Detection_Guidelines_36.asp on 25 September 2009.
- 26. American Medical Association. H-525.993. Mammography Screening in Asymptomatic Women Forty Years and Older. Chicago: American Medical Association; 2002. Accessed at www.ama-assn.org/ama/no-index/about-ama/9060 .shtml on 25 September 2009.
- 27. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer, v.1.2009 [Registration Required]. Fort Washington, PA: National Comprehensive Cancer Network; 2009. Accessed at www .nccn.org/professionals/physician_gls/f_guidelines.asp on 25 September 2009.
- 28. American Academy of Family Physicians. A-E: Recommendations for Clinical Preventive Services. Leawood, KS: American Academy of Family Physicians; 2009. Accessed at www.aafp.org/online/en/home/clinical/exam/a-e.html on 25
- 29. Qaseem A, Snow V, Sherif K, Aronson M, Weiss KB, Owens DK; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2007;146: 511-5. [PMID: 17404353]
- 30. Ringash J; Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer. CMAJ. 2001;164:469-76. [PMID: 11233866]
- 31. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 42, April 2003. Breast cancer screening. Obstet Gynecol. 2003;101:821-31. [PMID:
- 32. World Health Organization. Screening for Breast Cancer. Geneva: World Health Organization, 2009. Accessed at www.who.int/cancer /detection/breastcancer/en/index.html on 8 September 2009.

Table 1. What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
Α	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
В	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
С	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Table 2. USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies inconsistency of findings across individual studies limited generalizability of findings to routine primary care practice lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies important flaws in study design or methods inconsistency of findings across individual studies gaps in the chain of evidence findings that are not generalizable to routine primary care practice a lack of information on important health outcomes.
	More information may allow an estimation of effects on health outcomes.

^{*} The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

724 | 17 November 2009 | Annals of Internal Medicine | Volume 151 • Number 10

Women Aged 50–74 Years

Women Aged ≥75 Years

Population

Women Aged 40–49 Years

Figure 1. Screening for breast cancer using film mammography: clinical summary of USPSTF recommendation.

Annals of Internal Medicine







CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION
--

east cancer are available at	susceptibility for breast cancer and chemoprevention of brownwn.preventiveservices.ahrq.gov.	USPSTF recommendations on screening for genetic susceptibility for breast cancer and chemoprevention of breast cancer are available at www.preventiveservices.ahrq.gov.	Relevant USPSTF Recommendations
Among women 75 years or older, evidence of benefit is lacking.			Rationale for No Recommendation (I Statement)
	romen; treatment of cancer that would not become nosis) is an increasing problem as women age.	False-positive results are a greater concern for younger women; treatment of cancer that would not become clinically apparent during a woman's life (overdiagnosis) is an increasing problem as women age.	
	nal medical visits, imaging, and biopsies in women ening results, harms of unnecessary treatment, and noderate for each age group.	Harms of screening include psychological harms, additional medical visits, imaging, and biopsies in women without cancer, inconvenience due to false-positive screening results, harms of unnecessary treatment, and radiation exposure. Harms seem moderate for each age group.	
	.mmography reduces breast cancer mortality, with a 50 to 74 years than for younger women.	There is convincing evidence that screening with film mammography reduces breast cancer mortality, with a greater absolute reduction for women aged 50 to 74 years than for younger women.	Balance of Harms and Benefits
	biennial schedule preserves most of the benefit of ulf. A longer interval may reduce the benefit.	Evidence indicates that biennial screening is optimal. A biennial schedule preserves most of the benefit of annual screening and cuts the harms nearly in half. A longer interval may reduce the benefit.	Timing of Screening
	ed quality. Refer patients to facilities certified under dards Act (MQSA), listed at ography/certified.html.	Standardization of film mammography has led to improved quality. Refer patients to facilities certified under the Mammography Quality Standards Act (MQSA), listed at www.fda.gov/cdrh/mammmography/certified.html.	Screening Tests
	l ≥40 years who are not at increased risk on or history of chest radiation. nt risk factor for most women.	This recommendation applies to women aged ≥40 years who are not at increased risk by virtue of a known genetic mutation or history of chest radiation. Increasing age is the most important risk factor for most women.	Risk Assessment
Grade: I (insufficient evidence)	Grade: B	Grade: C	
•	-	-	
No recommendation.	Screen every 2 years.	Do not screen routinely. Individualize decision to begin biennial screening according to the patient's context and values.	Recommendation

documents, please go to www.preventiveservices.ahrq.gov. For a summary of the evidence systematically reviewed in making these recommendations, the full recommendation statement, and supporting

www.annals.org

17 November 2009 Annals of Internal Medicine Volume 151 • Number 10 **725**

Figure 2. Screening for breast cancer using methods other than film mammography: clinical summary of USPSTF recommendation.

Annals of Internal Medicine





SCREENING FOR BREAST CANCER USING METHODS OTHER THAN FILM MAMMOGRAPHY CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population		Women Aged ≥40 Years	≥40 Years		
Screening Method	Digital Mammography	Magnetic Resonance Imaging (MRI)	Clinical Breast Examination (CBE)	Breast Self-Examination (BSE)	
Recommendation	· ·	Grade: I (insufficient evidence)		Grade: D	

Adequate evidence suggests that BSE does not reduce breast cancer mortality.			Harms of BSE include the same potential harms as for CBE and may be larger in magnitude.	Costs of BSE are primarily opportunity costs to clinicians.	The number of clinicians who teach BSE to patients is unknown; it is likely that few clinicians teach BSE to all women.
Evidence of CBE's additional benefit, beyond mammography, is inadequate.	tice	Indirect evidence suggests that when CBE is the only test available, it may detect a significant proportion of cancer cases.	Harms of CBE include false-positive results, which lead to anxiety, unnecessay visits, imaging, and biopsies.	Costs of CBE are primarily opportunity costs to clinicians.	No standard approach or reporting standards are in place.
Evidence is lacking for benefits of digital mammography and MRI of the breast as substitutes for film mammography.	Considerations for Practice	Contrast-enhanced MRI has been shown to detect more cases of cancer in very high-risk populations than does mammography.	Contrast-enhanced MRI requires injection of contrast material. MRI yields many more false-positive results and potentially more overdiagnosis than mammography.	MRI is much more expensive than mammography.	MRI is not currently used to screen women of average risk.
Evidence is lacking for benefit MRI of the breast as substit		For younger women and women with dense breast tissue, overall detection is somewhat better with digital mammography.	It is not certain whether overdiagnosis occurs more often with digital than with film mammography.	Digital mammography is more expensive than film.	Some clinical practices are now switching to digital equipment.
Rationale for No Recommendation or Negative Recommendation		Potential Preventable Burden	Potential Harms	Costs	Current Practice

For a summary of the evidence systematically reviewed in making these recommendations, the full recommendation statement, and supporting documents, please go to www.preventiveservices.ahrq.gov.

726 | 17 2009 | Annals of Internal Medicine | Volume 151 • Number 10 www.annals.org