Screening for breast cancer: Strategies and recommendations

Author: Joann G Elmore, MD, MPH
Section Editor: Mark D Aronson, MD
Deputy Editor: Sadhna R Vora, MD

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INTRODUCTION — There is more scientific evidence regarding screening for breast cancer, the most common nonskin cancer and second deadliest cancer in women, than for any other cancer. As with all cancer screening, recommendations for breast cancer screening rely on a combination of factors involving evidence about the risk of the condition, the benefits and harms of screening, and the cost.

When considering breast cancer screening, specific issues include determining who should be screened (risk stratification, age to begin screening, age to stop) and what method should be used for screening. As more information has become available about the occurrence of false-positive test results and overdiagnosis, and with increasingly more effective treatment for breast cancer, the trade-offs between benefits and harms of breast cancer screening have received increasing attention.

Recommendations for breast cancer screening, including breast cancer risk and other parameters that might affect screening decisions, are discussed here. These recommendations, based upon the evidence for screening for breast cancer in women, weigh benefits and harms of screening. Benefits and harms, in turn, will depend upon an individual's risk of developing and dying of breast cancer, how good the screening test is, how effective and tolerable the treatment is, and the woman's own personal values. The evidence for the effectiveness and harms of screening for breast cancer in women, performance characteristics of mammography, and patient risk stratification are discussed in detail separately. (See "Screening for breast cancer: Evidence for effectiveness and harms" and "Breast imaging for cancer screening: Mammography and ultrasonography" and "Risk prediction models for breast cancer screening".)

Discoveries of genetic mutations that increase the risk of breast cancer and the development of breast cancer risk prediction models have stimulated efforts to develop screening strategies stratified according to risk level. In tandem with mammography, breast magnetic resonance imaging (MRI) has been studied as a screening method for high-risk women. Management options for women with a genetic predisposition to breast cancer, and surveillance in women with a personal history of breast cancer, are discussed in detail separately. (See "Management of patients at high risk for breast and ovarian cancer" and "Approach to the patient following treatment for breast cancer".)

EPIDEMIOLOGY — Worldwide in 2013 there were about 1.8 million new cases of breast cancer and over 464,000 breast cancer deaths in women [1,2]. About one-half of breast cancer cases, and nearly 60 percent of breast cancer deaths, occur in women in less-developed countries [3]. In the United States, it is estimated that approximately 234,190 women will be diagnosed with invasive breast cancer, and 40,730 women will die from the disease in 2014 [4].

The majority of breast cancers in the United States are diagnosed as a result of an abnormal screening study, although a significant number are also first brought to attention by a patient. In the early 1980s, breast cancer rates rose steeply by 3.7 percent per year over the baseline incidence. Breast cancer incidence rates stabilized or

decreased after 2000 in the United States [5,6] and other developed countries [1]. The increase in breast cancer incidence through the 1990s was seen mostly in early-stage and in situ cancers, and was attributed to increased detection of early stage disease because of screening. However, environmental factors and increased lifetime estrogen exposure likely also contributed to the higher incidence.

A decline in breast cancer incidence may relate, in part, to reduction in postmenopausal hormone therapy since publication of the Women's Health Initiative report in 2002 [7-9]. Findings that the decline leveled off somewhat in 2004, and that the decline was primarily in estrogen receptor positive tumors in women over age 50, support a role for decreased use of hormone therapy in the lower incidence of breast cancer [10,11]. While breast cancer incidence has declined overall, there has been a small increase in the incidence of metastatic breast cancer in young women (25 to 39 years old) in the United States over the past few decades [12].

Breast cancer mortality rates in the United States have also been declining. Mortality rates were remarkably stable during the latter half of the 20th century, at about 30 to 32 per 100,000 [13], and began declining after 1990. The breast cancer mortality rate in 2010 was 21.9 per 100,000 [14]. Most of this decline was in white women. Breast cancer incidence is slightly lower in black women than white women but breast cancer mortality is higher in blacks [14]. This may be due to differences in screening, cancer treatment, tumor biology, or comorbidities.

Differences in the incidence of breast cancer, available medical resources, and health priorities in different populations and geographic areas may influence policies regarding population screening [15-18]. In 2013, the utilization of mammogram screening within two years for women aged 50 to 64 years in the United States was 72.6 percent [19]. Rates were lower for lower socioeconomic groups and for the uninsured.

STRATEGIES FOR SCREENING — Strategies for screening should identify the age to initiate and to discontinue screening and the frequency of examination. Screening decisions should take into account an individual woman's risks of breast cancer and her values and preferences, weighing the potential benefits and harms of screening. Shared decision-making in regard to breast cancer screening has become increasingly more important as evidence emerges that the benefits and harms of screening are more finely balanced than once believed [20,21]. This relates largely to the potential extent of overdiagnosis with screening, which occurs when screening leads to the identification of a breast cancer that would not have caused clinical consequences in a woman's lifetime had it not been detected.

Trade-offs between benefits and harms are summarized in a table (table 1) and in a figure (figure 1). (See 'Informed and shared medical decision-making' below.)

Multiple large prospective randomized clinical trials, involving over 600,000 women, have been conducted in the United States, Canada, the United Kingdom, and Sweden [22-29]. Combined results suggest that screening mammography reduces the odds of dying of breast cancer by approximately 20 percent [30]. Questions about methodological inconsistencies in these trials have been raised, and the trials predate availability of newer, more effective breast cancer treatments. Mammogram technology has also improved since these studies, and the large number of trial patients who crossed over to be screened (diluting the observed impact of screening) suggests that the mortality reduction may have been higher. Additionally, several epidemiologic studies have found a reduction in breast cancer mortality in selected countries or geographic areas after wide-spread screening programs have been put in place [31]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Mammography'.)

Harms" associated with breast cancer screening include the cumulative risk for false-positive findings (causing anxiety and need for repeat imaging or biopsy) and for "overdiagnosis." Several studies have suggested that many cancers, especially those confined to the mammary ducts (ductal carcinoma in situ; DCIS), are biologically

insignificant, and would never become clinically evident in the patient's lifetime. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Overdiagnosis'.).

It is not possible to distinguish biologically insignificant cancers from those that will proceed to grow, metastasize, and lead to the patient's death. Thus, almost all patients with a diagnosis of breast cancer, regardless of its stage, receive some sort of local therapy (surgery, with or without radiation therapy) and often systemic therapy as well.

Overall, the odds of dying of metastatic breast cancer are roughly one-third of what they were in the 1980s. Statistical modeling suggests that approximately 50 percent of this reduction is due to widespread implementation of adjuvant systemic therapy, and 50 percent to screening and early local therapies [32]. These findings suggest that screening mammography both reduces the odds of dying of breast cancer and facilitates use of early treatment.

Screening mammography is of greatest value for patients who are most likely to develop breast cancer and for whom early treatment is more effective than later treatment in reducing mortality.

- Other than for genetically high-risk women (those with abnormal germline BRCA1 and 2 and other susceptibility genes), the incidence of breast cancer is quite low below the age of 40, begins to rise between 40 to 45, rises more steeply between 45 to 65, and then plateaus with age. The risk of developing breast cancer over the succeeding 10 years in women less than 45 is quite low, and the benefits of screening may not outweigh the costs, inconvenience, emotional stress, occasional direct physical harm, and potential of overtreatment [30].

- Modeling studies suggest that, for groups of women with a two- to fourfold increased risk of breast cancer, annual screening starting at age 40 had effectiveness similar to biennial screening in average risk women aged 50 to 74 years [33].

- Screening women with multiple comorbid illnesses is not likely to provide benefit, especially when illnesses might contraindicate effective treatment for breast cancer or, unrelated to breast cancer, are likely to substantially limit a patient's lifespan. It is not clear that there is a specific age limit for screening in otherwise healthy women, since the incidence of breast cancer remains high into the 80s, but the number of life-years saved will by necessity decrease with age [30].

Different women will assess the benefits of mammography versus the risks with very different perspectives. We discuss screening with all women aged 40 and older, and allow the individual woman to decide whether or not screening is in her best interest. This differs from previous approaches in which women were strongly recommended by their clinicians to have regular mammographic screening. Women should understand that mammography is associated with a small absolute decrease in breast cancer mortality (over 10 years, 8 deaths prevented per 10,000 women aged 50 to 59, 21 deaths per 10,000 women aged 60 to 69 years [21]) but a substantial risk for false-positive findings and overdiagnosis. Some women may choose to forego screening.

Discussions regarding screening should include the benefits and harms, and the patient's own values and preferences. It should be emphasized that the relative benefits and harms of screening change as a woman gets older. The absolute benefits, in terms of numbers of lives saved, are lower for younger women than for older women, because of both decreased incidence of breast cancer and decreased sensitivity of mammography in younger women [34].

For women at average lifetime risk for breast cancer (risk <15 percent), the following approach is advised:

- We discuss the potential benefits and harms of screening with all women aged 40 and older. We encourage women to explore and consider their own values and preferences, and support them in making a decision that is best for them.

- We advise mammography as the screening technique for average-risk women who opt to be screened. (See 'Imaging modalities for screening' below.)
- We suggest breast cancer screening for women aged 50 to 74 years and offer screening to women aged 40 to 49 years who place a higher value on the potential benefits than potential harms of screening.
- For women over the age of 75, we suggest discussing and offering screening if their life expectancy is at least 10 years.
- For average-risk women under age 40, we do not advise breast cancer screening.
- For women who wish to undergo screening, we suggest screening mammography every two years. The ideal interval for screening mammography is not known and some groups recommend annual screening for younger women (eg, to 45 to 55 years) with biennial (every two years) screening after age 55. Randomized trials have found that screening every two to three years achieves reduction in breast cancer mortality, and models find that screening every two years achieves most of the benefit of screening annually without as many harms. (See 'Frequency of mammography' below.)

Imaging modalities for screening — While a variety of imaging modalities have been developed for breast cancer screening, mammography is best studied and the only imaging technique that has shown a mortality benefit. (See "Screening for breast cancer: Evidence for effectiveness and harms" and "Breast imaging for cancer screening: Mammography and ultrasonography" and "MRI of the breast and emerging technologies".)

- Mammography remains the mainstay of screening for breast cancer, with multiple randomized trials of film mammography finding it decreases breast cancer mortality (figure 2). Digital mammography and breast tomosynthesis are newer mammographic techniques. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Full field digital mammography' and "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Tomosynthesis'.)
- Ultrasonography is commonly used for diagnostic follow-up of an abnormality seen on screening mammography, to clarify features of a potential lesion. Although sometimes advised as an adjunct to mammography in women with increased breast density, ultrasound has not been evaluated as a screening strategy to reduce breast cancer mortality in the average-risk population, including women with dense breasts. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'As adjunct to mammography for screening'.)
- Magnetic resonance imaging (MRI), performed in combination with mammography, is primarily targeted to screening in high-risk patients. (See "MRI of the breast and emerging technologies", section on 'Screening high risk women'.)
- Newer tests are under evaluation [35]. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Newer mammography techniques' and "MRI of the breast and emerging technologies", section on 'Emerging imaging technology for breast cancer detection'.)

Patient age — Benefits (absolute decrease in breast cancer mortality) and harms (false-positive screening tests and overdiagnosis) of breast cancer screening vary by age. (See "Screening for breast cancer: Evidence for effectiveness and harms".)

The sensitivity of mammography is higher in older, compared with younger, women. It has been estimated that mammography can detect about 73 percent of breast cancers in women in their early 40s and 85 percent of breast cancers in women in their early 60s [36]. Breast cancer incidence is also higher in older women than younger. Therefore, age is an important factor in a woman's decision whether or not to be screened.

Age to start — Varying recommendations related to age to initiate screening from a variety of expert groups are discussed separately below (See 'Age to initiate' below.)

Women less than 40 years — We recommend not screening average-risk women who are less than 40 years of age. The incidence of breast cancer is low in women under 40 years of age and there are no randomized trials of breast cancer screening for women less than 40 years. Performance characteristics of mammography are poor for women younger than 40. In a review of results of 73,335 initial screening mammograms in women aged 35 to 39 years, the recall rate was 12.7 percent and positive predictive value was only 1.3 percent [37].

Women over 40 years — Because of the many guidelines with conflicting recommendations for age to start (eg, 40, 45, 50 years), we encourage clinicians in the United States to raise the topic of screening with all women starting in their 40s. Raising the topic with all women is different from "recommending" screening. We do not encourage women to start screening mammography at age 40.

The absolute benefits of screening, in terms of numbers of lives saved, are lower for younger women than for older women both because of decreased incidence of breast cancer, and decreased sensitivity and specificity of mammography in younger women [34,38]. However, benefits for screening younger women (in their 40s) are more favorable when considered from the perspective of years of life saved (figure 3) [39].

Results vary in trials on the effectiveness of screening younger women:

- A systematic review and meta-analysis of nine randomized trials found an 8 percent relative reduction of breast cancer mortality in women ages 39 to 49 who were randomly assigned to mammographic screening, that did not achieve statistical significance (RR 0.92, 95% CI 0.75-1.02) [21]. This trend suggests that per 10,000 women screened over 10 years, three deaths from breast cancer could be prevented.

- Screening in women aged 39 to 49 years did not impact the risk of advanced breast cancer, based on pooled results of four trials (RR 0.98, 95% CI 0.74-1.37) [21].

- The Age trial in the United Kingdom suggested that breast cancer mortality at a mean follow-up of 10.7 years was decreased in the group of women who were invited for mammogram screening at age 40, compared with a usual care group, although the difference was not significant (RR 0.83, 95% CI 0.66-1.04) [40]. Risk reduction for breast cancer mortality was greater, though still not statistically significant, when only those women who actually attended the first screening were compared with the control group (RR 0.76, 95% CI 0.51-1.01). Previous trials of screening women in their 40s for breast cancer had included women who were up to age 49 years at the time of trial entry, and therefore in their 50s during the screening intervention; the Age trial was the first study to assess the effectiveness of screening restricted to women who had not yet passed age 50 years.

The cost-effectiveness of screening mammography for younger women has added to the controversy and difficulty of determining guidelines. One study, as an example, used a Markov model to compare the life expectancy of women undergoing different breast cancer screening strategies [41]. The cost-effectiveness ratios were $21,400 United States dollars per year of life saved for women 50 to 69 years of age and $105,000 for women in their 40s. Thus, the cost of screening mammography in women in their 40s was almost five times that of older women, although both are within a generally accepted range for cost-effectiveness.

Guidelines vary in regard to recommendations for screening women aged 40 to 54 years (table 2). (See 'Age to initiate' below.)

Systematic reviews of multiple randomized trials over the past 50 years found that mammogram screening for women aged 50 to 70 decreases the risk of breast cancer mortality. A 2016 systematic review of screening

mammography found fair quality evidence that mammography decreases the relative risk (RR) for breast cancer mortality for women 50 to 59 years (RR 0.86, 95% CI 0.68-0.97, seven trials), with a more significant reduction for women 60 to 69 years (RR 0.67, 95% CI 0.54-0.83, five trials) [21]. Screening also reduced the risk of advanced breast cancer in women aged 50 years and older (RR 0.62, 95% CI 0.46-0.83). These results, however, largely reflect trials that used older mammography imaging techniques and did not involve current breast cancer treatment protocols.

Age to stop — Varying recommendations related to age to stop screening from a variety of expert groups are discussed separately below. (See 'Age to discontinue' below.)

For women who opt to undergo breast cancer screening, we suggest that breast cancer screening with mammography be continued as long as a woman has a life expectancy of at least 10 years.

Screening mammography may be less beneficial in women aged 75 and older, although there are less data available. While screening mammography in older women may result in lower-stage cancer at diagnosis, this may not lead to a decrease in mortality [42-44]. Several factors can explain this:

- A shorter life expectancy decreases the potential for screening to prolong life (increases the risk of overdiagnosis).
- The incidence of ductal carcinoma in situ (DCIS) increases with age and it is not clear that treatment of DCIS affects mortality in older women. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis".)
- Screen-detected cancers are usually lower-stage than cancers detected clinically, due to lead time bias.

Data from randomized trials in women older than 70 years are limited. In one analysis, breast cancer mortality was unchanged for women 70 to 74 who were randomly assigned to mammogram screening (pooled RR 1.12, 95% CI 0.73-1.72), but few women actually underwent screening in the studies [38]. In another meta-analysis involving three trials of women aged 70 to 74 years, there was a trend toward decreased breast cancer mortality (pooled RR 0.80, 95% CI 0.51-1.28), which would account for 13 deaths prevented per 10,000 women over 10 years [21].

Observational studies may be biased, because older women who participate in screening are likely to be healthier at baseline than those who do not. Two case-control studies involving the same population in Holland, but done slightly differently, found that screening women aged 65 to 74 was associated with a decrease in breast cancer mortality of 55 percent (RR 0.45, 95% CI 0.20-1.02) or 66 percent (RR 0.34, 0.12-1.41); there was no protective effect beyond age 75 [45,46]. A cohort study of 2011 women 80 years and older found no difference in breast cancer rate, stage, or death comparing women who did and did not undergo mammography after age 80; 11 percent of the 1034 older women who underwent mammography screening had a false-positive result [47].

In one meta-analysis pooling data from multiple populations, it took 10.7 years on average to prevent one death among 1000 women screened for breast cancer [48]. One group presented a framework for guiding decision-making in screening older women for various cancers that included life expectancy, risk of dying of cancer, and the number needed to screen over the remaining lifetime to prevent cancer death (table 3) [49].

Frequency of mammography — Although data are limited on the optimal frequency for performing mammography, annual screening is associated with more harms and costs than screening every two years (biennial), and the difference in absolute benefits between annual and biennial screening is small. In particular, while some data suggest benefit for annual screening for some women (eg, premenopausal), this needs to be weighed against the increased risk of false-positive mammogram findings.

- A modeling study using United States data evaluated screening strategies that varied by age and frequency of mammography and found that, per 1000 women screened, biennial (every two years) screening for women aged 50 to 74 years avoided seven breast cancer deaths compared to no screening, while annual screening for this age group had similar benefits but caused more harms [33]. Annual screening in women 40 to 74 years avoided 10 breast cancers, but led to nearly 2000 more false-positive results and 11 more overdiagnoses per 1000 screened women.

- In a systematic review for the US Preventive Services Task Force (USPSTF) 2016 update of breast cancer screening recommendations, the 10-year cumulative rates of false-positive mammography results and biopsies were 61 percent and 7 percent, respectively, for annual screening compared with 42 percent and 5 percent, respectively, for biennial screening [20].

- A 2015 analysis of data from the Breast Cancer Surveillance Consortium, a nationwide sample of mammography registries in the United States, compared annual and biennial screening among women with breast cancer, stratified by menopausal status and use of menopausal hormone therapy, rather than by age [50]. Premenopausal women who underwent biennial screening had higher proportions of cancers that were less favorable (stage IIB or higher) than women who had annual screening. Biennial screening was also associated with less favorable cancers in women who used menopausal hormone therapy, but not for other postmenopausal women in whom tumor characteristics were similar for those screened annually or biennially.

- A Breast Cancer Surveillance Consortium study found that mammography screening biennially versus annually for women aged 50 to 74 years does not increase the risk of tumors with advanced stage or large size, regardless of women's breast density or hormone therapy use [51]. For women 50 to 74 years of age with scattered fibroglandular or fatty breasts, biennial or triennial mammography screening lowered false-positive results, compared with annual screening. However, the risk of advanced stage cancer was increased for women aged 40 to 49 years with dense breasts who had biennial, compared with annual, mammograms.

While one modeling study suggests that triennial screening may be the preferred approach for patients aged 50 years and older with average risk for breast cancer and low breast density, further confirmation of this finding is required before adopting this practice [52].

INFORMED AND SHARED MEDICAL DECISION-MAKING — Guidelines for cancer screening increasingly address the importance of individuals making informed decisions about participating. Shared decision-making, in which the provider helps the patient to make an informed, values-based decision about whether to undergo screening [53,54], is especially important when the tradeoff between harms and benefits is a close call. Unbiased and balanced information on the potential benefits and harms of breast cancer screening plays an important part in this decision-making.

The decision to perform mammography should be determined with shared decision-making about patient risk, the benefits and harms of screening, and by individual patient values [55,56]. The discussion should be noted in the medical record.

In a nationwide survey of women about their discussions with their care providers before undergoing breast cancer screening, women reported feeling informed, but often were not knowledgeable about the risks and benefits of breast cancer screening [57]. Most women reported that their provider did not ask them about their screening preferences, and only 20 percent said their provider discussed the potential harms of screening, while 86 percent said they were told of the benefits of screening.

Trade-offs between benefits and harms — A table summarizes the findings of an estimate of mammography screening consequences, while varying frequency and age at which screening starts and ends (table 4) [58].

The trade-off between benefits and harms of breast cancer screening are best understood when they are expressed in absolute terms. Estimates of what happens over time to 1000 women who undergo mammography screening in terms of breast cancer deaths avoided, false-positive mammograms (false alarms), and overdiagnosis or unnecessary treatment are shown in figures (figure 1) and a table (table 1). The table and figures make explicit the fact that many women will experience harms, especially false-positive mammograms, for each woman whose life is saved by mammography. Overdiagnosis is a serious harm because it means that some women diagnosed with breast cancer are treated for lesions that would not have caused them harm if the cancers had never been identified. The incidence of overdiagnosis related to breast cancer screening is uncertain, with estimates varying from 10 percent or less to over 30 percent, depending on the methodology used to study overdiagnosis [59,60]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Overdiagnosis'.)

Decision aids — Patient decision aids can be useful in providing information and assisting patients to make a decision. Decision aids should encourage patients to interpret evidence in the context of their personal goals and concerns. Decision aids can come in many different formats, including leaflets, booklets, videos, and websites. A systematic review of 115 randomized trials of shared decision-making related to a variety of clinical treatment or screening decisions indicated that, in general, decision aids improve patient knowledge regarding options and harms, reduce decisional conflict related to feeling uninformed or unclear about personal values, and stimulate patients to take more active roles in decision-making [61]. The effect of using decision aids on the length of consultation varies, ranging from shortening to no change to lengthening consult time.

Decision aids have been noted to reduce the number of patients choosing cancer screening [62]. In an Australian randomized trial of breast cancer screening decision aids for women 48 to 50 years of age, compared with control women whose decision aids did not include information on overdiagnosis, more women who were informed about overdiagnosis met the threshold for adequate overall knowledge, and fewer expressed positive attitudes toward screening or intent to be screened in the future [63]. A sample breast cancer screening decision aid used in this trial (using data from Australia; rates of false-positive mammograms are higher in the United States) is available for clinicians.

STRATIFYING SCREENING BY RISK — In women with a lifetime risk of breast cancer, less than 15 percent are considered to be at "average risk," and those with a lifetime risk greater than 20 to 25 percent are considered to be at "increased risk." Major risk factors for breast cancer in women are age, genetic predisposition, and estrogen exposure (table 5). Breast density is also a significant risk factor, particularly in women aged 40 to 49 years (table 6) [64]. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Breast density'.)

A detailed discussion of the risk factors for breast cancer is presented elsewhere. (See "Factors that modify breast cancer risk in women".)

Several breast cancer risk prediction tools have been developed that combine major risk factors. The purpose of the models is to stratify women into risk categories that can be used to determine optimal screening strategies and indications for prophylactic therapies, including chemoprevention. (See "Risk prediction models for breast cancer screening".)

The most widely used tool to calculate breast cancer risk is the Breast Cancer Risk Assessment Tool, sometimes called the Gail Model after Dr. Mitchell Gail, its developer at the National Cancer Institute [65,66]. The Gail Model tool takes into consideration race and ethnicity as well as age, history of breast disease, age at onset of menses, parity, and family history, and is available online at www.cancer.gov/bcrisktool/. Cancer risk assessment tools can be helpful in clarifying a patient's risk group. However, their accuracy for predicting whether an individual woman will develop cancer is modest, partly because not all important risks have been identified and partly because accurate stratification requires strong risk factors, and most risk factors for breast cancer are relatively small.

Family history of breast cancer — If a woman has a strong family history of breast, ovarian, tubal or peritoneal cancer, a more detailed family history is recommended, using one of several available risk tools to determine if she is a candidate for genetic testing [67,68]. (See "Risk prediction models for breast cancer screening" and "Management of patients at high risk for breast and ovarian cancer".)

For women without a known genetic syndrome, there are no data from randomized controlled trials on the effectiveness of mammography in reducing mortality in younger women with a family history of breast cancer. A case control study showed a nonstatistical trend towards greater protection among women in their 40s at increased risk, but no trend among older women [69]. For most women with a family history of breast cancer in a first-degree relative, but without a known genetic syndrome, we suggest that screening be performed as for women at average risk. Some have suggested that screening be initiated at an earlier age if the family member had premenopausal breast cancer.

Alternative or adjunctive screening modalities for younger women at significantly increased risk for breast cancer, including magnetic resonance imaging (MRI) and ultrasound, may improve screening sensitivity, but there are no data on mortality reduction [70-73]. The combination of MRI and mammography is recommended by the American Cancer Society in women at high risk of breast cancer (≥20 to 25 percent lifetime risk), as defined by risk prediction models based primarily on family history [70]. (See "MRI of the breast and emerging technologies", section on 'Screening high risk women'.)

Germline predisposition (BRCA1 or BRCA2) — Although a family history of breast cancer is common in women who develop breast cancer, only 5 to 6 percent of all breast cancers are associated with germline (inherited) genetic mutations. The majority of these involve two genes, *BRCA1* and *BRCA2*, and testing for mutations in these genes is commercially available. (See "Genetic counseling and testing for hereditary breast and ovarian cancer".)

Women who test positive for *BRCA1* or *BRCA2* mutations are at increased risk of both breast and ovarian cancer. Such women should be referred for appropriate counseling to consider options for reducing risk and intensified surveillance. For women with an inherited predisposition, guidelines from major groups (including the National Comprehensive Cancer Network [NCCN] [74] and the American Cancer Society [70]) recommend a combination of annual mammography and breast MRI for breast cancer surveillance in women who are BRCA mutation carriers. (See "Management of patients at high risk for breast and ovarian cancer", section on 'Women'.)

Other genetic risk — The strategy of incorporating genetic profiling, to evaluate combinations of genes contributing to cancer risk and thereby determine screening parameters (age to initiate screening, screening frequency, and type of screening), remains theoretical at this time for women who do not have a strong family history or specific genetic mutations [75]. Several breast cancer susceptibility loci have been found. In isolation they confer far lower risk than BRCA mutations, but in combination they could identify subgroups of women at moderate to high risk. As more such alleles are identified, the precision of risk estimates will improve.

RECOMMENDATIONS FOR SCREENING BY EXPERT GROUPS — Multiple guidelines have been published regarding breast cancer screening, with varying recommendations (table 2).

Screening with mammography

Age to initiate — Major groups making recommendations about breast cancer screening all endorse routine screening with mammography for women at average risk age 50 and older. There is controversy, however, about routine screening for younger women at average risk, with most groups encouraging shared decision-making because of trade-offs of benefits and harms (table 2):

- The American College of Radiology [76,77], the American College of Obstetricians and Gynecologists [39], and the National Comprehensive Cancer Network (NCCN) [78] recommend starting routine screening at age 40.

- The American Cancer Society recommends initiating screening at age 45 [79].

- Other groups, including the US Preventive Services Task Force (USPSTF), [80-84] advise individual risk assessment and shared decision-making regarding screening for women 40 to 49 years of age, and routine screening for women age 50 and older [82,83,85], while the Canadian Task Force revised its recommendations in 2011 to recommend against screening for women under age 50 [80].

Age to discontinue — Several groups do not explicitly state at what age breast cancer screening should stop. The USPSTF, the Canadian Task Force of Preventive Health Care, the American Academy of Family Physicians and the American College of Physicians recommend mammography screening to age 74 [80-84]. They state that there is insufficient evidence beyond age 74. The American College of Radiology recommends screening until life expectancy is less than five to seven years, on the basis of age or comorbidities [77]. The American College of Obstetricians and Gynecologists recommend that women aged 75 years and older should consult with their clinician to decide whether to continue screening [39]. The American Cancer Society recommends screening as long as a woman's health is good and life expectancy is 10 years or longer [79].

Frequency — The recommended frequency of mammography is variable among organizations (table 2). The USPSTF recommends mammography screening every two years for women who are screened. Most other North American groups recommending screening for younger women (eg, <55 years of age) have tended to shift towards annual examinations because of the evidence of more rapid tumor growth in younger women [39,50,86]. The American Cancer Society recommends annual screening for women ages 45 to 54, and screening every two years for women 55 and older [79]. However, the benefit of detecting more tumors in earlier stage for younger women needs to be balanced against the increased harms associated with an increased rate of false-positive mammograms [87].

The World Health Organization recommends mammography every one to two years for women aged 50 to 69 years [88,89]. There has been a tendency for recommendations to extend the interval to two years for older women. In 2011, the Canadian Task Force recommended screening intervals of two to three years, whereas previous recommendations had been for one to two years [80].

Screening with clinical breast examination — In 2015, revising previous guidelines, the American Cancer Society recommends not performing clinical breast examination, given the potential for false-positive findings and lack of evidence for improved outcomes [79]. The American College of Obstetricians and Gynecologists recommends clinical breast examination every one to three years from age 20 to 39, and annually thereafter [39]. The USPSTF did not revise its earlier (2009) finding that evidence is insufficient to assess additional benefits of clinical breast examination beyond mammography [84], and the Canadian Task Force on Preventive Health Care recommends against clinical breast examination [80]. The World Health Organization states that clinical breast examination may be an appropriate screening approach for women 50 to 69 years of age in low-resource settings with weak health systems, pending when evidence from ongoing studies becomes available [88,89]. No group recommends clinical breast examination alone.

Screening with breast self-examination — There is general consensus among expert groups **not** to recommend breast self-examination (BSE). Many groups encourage educating women about general breast health and encourage women to seek medical attention soon if they note concerning breast abnormalities.

- The Canadian Task Force on Preventive Health Care recommends not advising women to routinely practice self-breast examination on the basis of no evidence of a reduction in mortality, but evidence of increased

harm with BSE [80]. The USPSTF did not revise its 2009 recommendation against teaching women the procedure [84].

- In 2003, the American Cancer Society (ACS) changed its previous recommendation in favor of monthly BSE to a recommendation that women be educated about the benefits and limitations of BSE [90]. Updated guidelines in 2015 identified no new studies of outcomes related to BSE, and thus did not revise their 2003 recommendations [79].

- The American College of Obstetricians and Gynecologists recommends breast self-examination be considered for high-risk patients and that breast self-awareness be encouraged, which "can include breast self-examination" [39].

- The World Health Organization recommends BSE as a way to empower women and raise awareness among women at risk, rather than as a screening method [85,91].

- The National Comprehensive Cancer Network (NCCN) recommends that women maintain "breast awareness" but revised 2009 guidelines no longer recommend instruction in breast self-examination [78].

Screening with breast MRI — In general, screening with breast MRI as an adjunct to mammography should be restricted to women at increased risk for breast cancer. Criteria for defining these risk groups differ somewhat between guidelines:

The 2007 American Cancer Society (ACS) recommends offering annual MRI, in addition to mammography, to women within certain high-risk groups, including [70]:

- Known BRCA mutation carriers

- First-degree relatives of known BRCA mutation carriers

- Women with an approximate lifetime risk of breast cancer from 20 to over 25 percent, according to risk prediction models primarily using family history (table 7)

- Radiation to the chest between age 10 and 30

- Genetic mutation in genes causing the Li-Fraumeni syndrome or Cowden and Bannayan-Riley syndromes (see "Li-Fraumeni syndrome" and "PTEN hamartoma tumor syndrome, including Cowden syndrome")

National Comprehensive Cancer Network (NCCN) criteria are similar [78].

The National Institute for Health and Care Excellence (NICE) guidelines recommend offering annual MRI in addition to mammography to the following high-risk groups [92]:

- *BRCA1* and *BRCA2* mutations carriers, and untested women with >30 percent probability of BRCA carrier, starting at age 30, until age 49; for women with a dense breast pattern, continue until age 69

- TP53 mutation carriers, starting at 20 until age 49, and consider offering through age 69

- Untested women with >30 percent probability of TP53 carrier, starting at age 20, until age 49; for women with a dense breast pattern, continue until age 69

The USPSTF concluded that evidence is insufficient to determine benefits and harms of digital mammography or MRI for breast cancer screening [84].

FOLLOW-UP OF DETECTED ABNORMALITIES — The evaluation of abnormalities detected by screening is discussed separately. (See "Diagnostic evaluation of women with suspected breast cancer" and "Clinical

manifestations and diagnosis of a palpable breast mass", section on 'Evaluation' and "Breast biopsy".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Breast cancer screening (The Basics)")
- Beyond the Basics topic (see "Patient education: Breast cancer screening (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS — Recommendations for screening vary by country and even within country, as noted by the conflicting recommendations of different United States groups (table 2). The ideal age to start, age to stop, screening interval, and method to define risk is not known.

Although randomized trials have shown that breast cancer screening in average risk women decreases breast cancer mortality, these trials do not reflect the improved outcomes for breast cancer with newer treatment strategies, and the current applicability of these trials is uncertain. The absolute benefit of screening is less than we had hoped, and harms such as false-positive exams accumulate as women are repeatedly screened. Additionally, screening detects some cancers that would not have clinical consequences in a woman's lifetime (overdiagnosis) and thus may lead to overtreatment and harms associated with such treatment. Given these limitations, decisions about screening need to balance the potential benefits and harms of screening in the context of a woman's individual risks for breast cancer and her personal values and preferences related to screening. (See 'Strategies for screening' above.)

An approach to breast cancer screening should incorporate an individual's level of breast cancer risk, established by history and by use of a risk prediction model. The model most commonly used is the Breast Cancer Risk Assessment Tool (Gail model). If the patient has a family history of breast or ovarian cancer, a risk tool that assesses the probability of genetic mutations should be used. (See "Risk prediction models for breast cancer screening" and 'Stratifying screening by risk' above.)

Average-risk women (lifetime breast cancer risk below 15 percent)

- The benefit of screening increases as women age (eg, the absolute benefit is more for women in their 50s and 60s than 40s). Screening should be available to all women over age 40 who opt to be screened after shared decision-making. For healthy women over age 40, we suggest that decisions about screening for breast cancer be individualized, based on discussion of the benefits and harms of screening and personal values and preferences; we do not encourage women to begin screening at age 40. We suggest breast cancer screening with mammography for women aged 50 to 74 years (**Grade 2B**). (See 'Women over 40 years' above.)
- We suggest that women over the age of 74, and younger women who have comorbid medical problems, be offered screening only if their life expectancy is at least 10 years (**Grade 2C**). (See 'Age to stop' above.)

- We recommend that screening be performed with mammography, rather than other modalities, when a decision is made to screen (**Grade 1B**). (See 'Imaging modalities for screening' above.)

- The ideal interval for screening mammography is not known. We suggest screening every two years (**Grade 2B**). Alternative intervals for younger women may be preferred by some clinicians, patients, or national policies. (See 'Frequency of mammography' above.)

- We suggest not performing clinical breast examination as part of screening (**Grade 2C**). However, clinical breast examination remains an important part of the evaluation for women with breast complaints or abnormalities. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Clinical breast examination'.)

- We suggest that women not perform breast self-examination (BSE) (**Grade 2B**). Women who nonetheless choose to perform self-examination should receive careful instruction to differentiate normal tissue from suspicious lumps and recognize that BSE is an adjunct, but not a substitute, for mammography. Women should be encouraged to bring abnormal breast findings to the attention of their caregiver. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Breast self-examination'.)

High-risk women (lifetime breast cancer risk 20 to 25 percent or higher)

- Women at high risk for breast cancer (lifetime risk ≥20 to 25 percent) should be referred for genetic counseling to determine the likelihood of a BRCA mutation and to decide on management options. (See "Overview of hereditary breast and ovarian cancer syndromes" and "Management of patients at high risk for breast and ovarian cancer".)

Women with mild-to-moderately increased lifetime breast cancer risk

- It is not known whether increased screening, either by beginning at an earlier age or by adding breast MRI, would result in greater benefits than harms for women with mild- to moderately-elevated lifetime breast cancer risks (15 percent or greater and less than 20 to 25 percent). We suggest that women with mild- to moderately-increased breast cancer risk follow the recommendations for women at average risk (**Grade 2C**). (See 'Family history of breast cancer' above.)

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GRAPHICS

Benefit-harm trade-off for a 10-year course of annual screening mammography for women starting at age 40, 50, and 60 years

Benefits (lower- and upper-bound estimates)	Harms (lower- and upper-bound estimates)
Among 1000 *40-year-old* women undergoing annual mammography for 10 years:	
0.1 to 1.6 women will avoid dying from breast cancer	510 to 690 women will have at least one "false alarm" (60 to 80 of whom will undergo a biopsy)
	? to 11 women will be overdiagnosed and treated needlessly with surgery, radiation, and/or chemotherapy
Among 1000 *50-year-old* women undergoing annual mammography for 10 years:	
0.3 to 3.2 women will avoid dying from breast cancer	490 to 670 women will have at least one "false alarm" (70 to 100 of whom will undergo a biopsy)
	3 to 14 women will be overdiagnosed and treated needlessly with surgery, radiation, and/or chemotherapy
Among 1000 *60-year-old* women undergoing annual mammography for 10 years:	
0.5 to 4.9 women will avoid dying from breast cancer	390 to 540 women will have at least one "false alarm" (50 to 70 of whom will undergo a biopsy)
	6 to 20 women will be overdiagnosed and treated needlessly with surgery, radiation, and/or chemotherapy

Reducing the frequency from annual to every two years has been demonstrated to substantially reduce the harm of false alarms and would be expected to reduce the harm of overdiagnosis.

Graphic 94497 Version 5.0

Society and expert recommendations for routine mammographic screening in women at average risk

Group (date)	Frequency of screening (years)	Initiation of screening		
		40 to 49 years of age	50 to 69 years of age	≥70 years of age
Government-sponsored groups				
US Preventive Services Task Force (2016) [1]	2	Individualize*	Yes	Yes, to age 74
Canadian Task Force on Preventive Health Care (2011) [2]	2 to 3	Recommend against*	Yes	Yes, to age 74
National Health Service, United Kingdom (2013) [3]	3	Yes, start age 47	Yes	Yes, to age 73
Royal Australian College of General Practitioners (2012) [4]	2	No (eligible but not targeted)	Yes	No (eligible but not targeted)
Medical societies				
American College of Obstetricians and Gynecologists (2011) [5]	1	Yes	Yes	Yes ¶
American College of Physicians (2015) [6]	1 to 2	Individualize*	Yes	Yes, to age 74
American Academy of Family Physicians (2009) [7]	2	Individualize*	Yes	Yes, to age 74
American Cancer Society (2015) [8]	1 year age 45 to 54 2 years age ≥55	Yes, start age 45	Yes	Yes Δ
American College of Radiology (2013) [9]	1	Yes	Yes	Yes ◇
Coalitions				
National Comprehensive Cancer Network (2014) [10]	1	Yes	Yes	Yes

* Women should be counseled about the harms and benefits of mammography; individualized decision based on risks and patient preference.

¶ Discuss with doctor and individualize decision after age 75.

Δ If in good health and life expectancy >10 years.

◇ Individualize to current health and life expectancy; if a woman is in reasonably good health and would be a candidate for treatment, then should continue screening.

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