Screening for breast cancer: Strategies and recommendations

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INTRODUCTION

Breast cancer is the most frequent type of non-skin cancer and the most frequent cause of cancer death in women worldwide, and it is the second most frequent cause of cancer death in United States women. (See "Clinical features, diagnosis, and staging of newly diagnosed breast cancer", section on 'Introduction' and "Clinical features, diagnosis, and staging of newly diagnosed breast cancer", section on 'Epidemiology' and "Diagnostic evaluation of suspected breast cancer", section on 'Introduction'.)

The majority of breast cancers in the United States are diagnosed as a result of an abnormal screening study, although a significant number are first brought to attention by the patient. Findings suggest that screening mammography both reduces the odds of dying of breast cancer and facilitates the use of early treatment. Breast cancer mortality has dropped dramatically since the 1980s, and both earlier detection through screening and improvements in breast cancer treatment are responsible for this reduction in mortality [1-6].

Recommendations for breast cancer screening, taking into account the risk of developing breast cancer, other parameters that might affect screening decisions, and benefits and harms of screening, are discussed here.

Identification and management of 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 "Genetic testing and management of individuals at risk of hereditary breast

and ovarian cancer syndromes" and "Cancer risks and management of BRCA1/2 carriers without cancer" and "Approach to the patient following treatment for breast cancer".)

The evidence for the effectiveness and harms of screening for breast cancer, and performance characteristics of mammography, 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 "MRI of the breast and emerging technologies", section on 'Screening high-risk women'.)

In this topic, we will use the term “woman/en” to describe genetic females. However, we recognize that not all people with breasts identify as female, and we encourage the reader to consider transgender and gender nonbinary individuals as part of this larger group.

BREAST CANCER RISK DETERMINATION

Screening is of greatest value for individuals who are most likely to develop breast cancer and for whom early treatment is more effective than later treatment in reducing mortality. Thus, it is important to determine a person’s risk of developing breast cancer and use that information both to recommend the modality and frequency of screening and also to determine whether referrals are needed for genetic testing and for consideration of chemoprevention and/or prophylactic surgery. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes" and "Cancer risks and management of BRCA1/2 carriers without cancer".)

Initial assessment of risk — The first step in determining a risk category is to assess for major risk factors to identify women at average risk, which is the category for most women, and to identify the smaller number of women at moderate or high risk of developing breast cancer. The risk categories are delineated according to the lifetime risk of being **diagnosed** with breast cancer (not the risk of dying due to breast cancer). Although there is no standardization or consensus about the exact percentages of lifetime risk of developing breast cancer within each risk category, generally they are as follows: average (less than 15 percent), moderate (approximately 15 to 20 percent), or high (greater than 20 percent) lifetime risk.

Most women can be categorized based on history alone; for others, risk prediction models are available for use if needed. (See 'Clinical use of risk prediction models' below and "Factors that modify breast cancer risk in women".)

Major factors used to determine a risk category, based on a patient’s history, are:

- Personal history of breast, ovarian, tubal, or peritoneal cancer

- Family history of breast, ovarian, tubal, or peritoneal cancer
- Ancestry (eg, Ashkenazi Jewish) associated with *BRCA1* or *2* mutations
- Known carrier of a pathogenic mutation for a hereditary breast and ovarian cancer syndrome in self or relative (see "Overview of hereditary breast and ovarian cancer syndromes", section on 'High-penetrance genes')
- Mammographic breast density (see "Breast density and screening for breast cancer", section on 'Breast density and breast cancer risk')
- Previous breast biopsy indicating high-risk lesion (eg, atypical hyperplasia)
- Age of menarche, age at first live birth, number of pregnancies, and menopausal status
- Radiotherapy to the chest between age 10 and 30 years

Women who have none of these risk factors are usually considered at average risk [7,8]. Most women are in this average-risk category, with an average lifetime risk of being diagnosed with breast cancer estimated at 12.4 percent. It is important to remind patients that this is the risk of being **diagnosed** with breast cancer, **not** of **dying** from breast cancer [9]. The approach to screening for average-risk women is discussed below. (See 'Average risk: Screening' below.)

Risk prediction tools are available to stratify the patient's risk (see 'Clinical use of risk prediction models' below). These risk tools take into account multiple concurrent risk factors (eg, family history of cancer, breast density, prior breast biopsy of atypical hyperplasia) and can help assess whether the patient has an elevated risk of breast cancer to determine if referral for more detailed risk analysis is appropriate. Certain tools may be more appropriate than others depending on the strength of the family history. Use of these tools can estimate the risk of developing breast cancer, which can then be used to categorize the risk as average, moderate, or high, as above. Many women who have a family history of breast cancer still have an average risk. Screening recommendations are in part dependent on this categorization. (See 'Average risk: Screening' below and 'Moderate risk: Screening' below and 'High risk: Screening' below.)

Women who have a personal history of breast cancer, a confirmed or suspected genetic mutation known to increase the risk of breast cancer (eg, *BRCA1* or *BRCA2, PTEN, TP53*), or a history of previous radiotherapy to the chest between 10 and 30 years of age are at high risk. As an example, women with a *BRCA1* mutation have a nearly 60 percent absolute risk of developing a breast cancer by the time they are 70 years old [10]. However, because a *BRCA1* or *2* mutation is relatively rare in the general population (1 in 300 to 500), *BRCA1* or *BRCA2* mutation carriers account for only between 5 to 10 percent of all breast cancer cases [11,12].

Information about hereditary breast cancer and indications for testing for genetic mutations are discussed elsewhere. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes", section on 'Criteria for genetic risk evaluation' and "Overview of hereditary breast and ovarian cancer syndromes", section on 'High-penetrance genes'.)

Clinical management of high-risk women, including genetic counseling, indications for prophylactic therapies, and screening, is discussed elsewhere. (See 'High risk: Screening' below and "Cancer risks and management of BRCA1/2 carriers without cancer" and "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes".)

Although there are other factors associated with an increased risk for developing breast cancer, such as use of exogenous estrogen, such features are not necessarily incorporated into the initial risk assessment to determine the appropriate screening approach. These and other risk factors for breast cancer are discussed in detail elsewhere (table 1). (See "Factors that modify breast cancer risk in women".)

Screening considerations specifically regarding dense breasts are discussed in detail elsewhere. (See 'Dense breast tissue' below and "Breast density and screening for breast cancer".)

Clinical use of risk prediction models — There are multiple breast cancer risk models for more specific categorization of breast cancer risk; some models also calculate the risk of being a carrier of *BRCA1* and *BRCA2* [13-24]. Models vary; they may concentrate more on family history or may include personal variables such as history of breast biopsies, parity, and mammographically determined breast density. The models discussed below are available online and are easy to use in general office practice. Other models are not readily available to practicing clinicians.

There are many commonly used tools to calculate breast cancer risk (table 2). Examples of risk calculators for the average woman include:

- The National Cancer Institute's Breast Cancer Risk Assessment Tool (calculator 1) (BCRAT, or Gail Model 2) [25]
- The Breast Cancer Surveillance Consortium's Risk calculator
- Tyrer-Cuzick (IBIS)

Other risk calculators for those with genetic variants/mutations include:

- BRCAPRO
- Claus

- Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA, now called CanRisk)

These are reviewed elsewhere. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes", section on 'Risk assessment models'.)

Clinical judgment must be factored in with the model-based predictions to determine when to refer for genetic counseling, when to refer for consideration of prophylactic therapies including chemoprevention or surgery, and what screening to recommend [26]. This is because the accuracy of risk assessment tools at predicting whether an individual woman will develop breast cancer is only modest, partly because not all important risk factors have been identified, and partly because accurate stratification requires that risk factors be strongly predictive, whereas most risk factors for breast cancer are not very strong risk factors. Risk models are further limited by the fact that they have been created and validated using mostly White individuals. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes", section on 'Pretest genetic counseling' and "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Risk-reducing surgery' and "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Chemoprevention'.)

In addition, risk estimates for other than White and Black individuals may not be as accurate using the risk models, because fewer data have been available and analyzed.

The predictive value of the risk models is limited for an individual woman. For example, the sensitivity of the Gail model to identify women who will develop breast cancer is relatively low, reported as 28 to 44 percent [27,28], using a five-year risk of 1.67 percent as the cut point between "high" and "low" risk. The specificity of the Gail model is also modest, reported as 66 to 88 percent [27,28]. A figure showing the Gail model's estimated risk of developing breast cancer for each of 80,000 women illustrates the limited ability of the Gail model to separate women into groups who will and will not develop breast cancer (figure 1). In the figure, the curve showing the percent of women at each estimated-risk point who did develop breast cancer overlaps substantially with the curve showing the percent who did not develop breast cancer, and there is no point along the estimated-risk continuum that appears to be predictive to separate women who developed breast cancer from those who did not [28].

Efforts to improve on the risk models have mainly centered on adding mammographic breast density to other risk factors [16,17,27], updating the information on race or ethnicity sub-groups [29], focusing on risk of developing advanced cancers or adding information gained from mammography image features using machine-learning algorithms [30].

Models predicting pathogenic BRCA1/2 mutations — Risk prediction models have been developed for patients at increased risk of pathogenic *BRCA1* or *BRCA2* mutations (eg, a personal or family history of breast, ovarian, tubal, or peritoneal cancer, or Ashkenazi Jewish ancestry). These models assess the risk of carrying a pathogenic *BRCA1* or *BRCA2* gene mutation. The approach to genetic testing in individuals at risk of hereditary breast and ovarian cancer syndromes is reviewed in detail elsewhere. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes" and "Overview of hereditary breast and ovarian cancer syndromes".)

AVERAGE RISK: SCREENING

Age-related screening approach — The majority of women are at average risk (less than 15 percent lifetime risk) of developing breast cancer. In these women, age is the most important factor in the decision about when to be screened, because breast cancer incidence rises with age. Breast cancer incidence is quite low under the age of 40 years and then begins to rise as women age. The sensitivity and specificity of mammography are also age-dependent, being higher in older women than in younger women [31,32]. Thus, in younger women, the risk of developing breast cancer over the succeeding 10 years is quite low, and the benefits of screening may not outweigh the costs, inconvenience, emotional stress, occasional direct physical harm, and potential for overtreatment as a result of screening [33].

When counseling women on screening, we discuss the potential benefits and harms of breast cancer screening and encourage them to consider their own values and preferences. We support women in making a decision that is best for them. We tailor this discussion based on age. (See 'Age under 40 years' below and 'Age 40 to 49 years' below and 'Age 50 to 74 years' below and 'Age 75 years and older' below.)

A number of expert groups have developed recommendations related to age to initiate screening (table 3 and figure 2) [7,8,34-42]. These recommendations can also be useful during discussion and shared clinical decision making.

Age under 40 years — No screening guidelines recommend routine screening for average-risk women who are under 40 years of age. Among women younger than 40, the incidence of breast cancer is low, there are no randomized trials of breast cancer screening, and the performance characteristics of mammography are poor. In a review of results of 73,335 initial screening mammograms in women aged 35 to 39 years, the positive predictive value was only 1.3 percent [43].

Age 40 to 49 years — Many expert groups encourage shared decision-making for women in their 40s because of trade-offs between benefits and harms (table 3 and figure 2); although, the United States Preventive Services Task Force revised preliminary 2023

recommendations suggest starting routine screening at age 40 (with final official recommendations currently pending) [44,45] while both the American Cancer Society and European screening guidelines recommend starting screening at age 45 years [7,46].

For average-risk women in their 40s, we raise the topic of screening for breast cancer to answer any questions the women might have. Raising the topic is different from strongly "recommending" screening; we engage in shared decision-making to encourage women to individualize the decision based on the benefits and harms of screening and their personal values and preferences (see 'Shared medical decision-making' below). For women who decide to initiate screening in their 40s, we typically suggest screening mammography every one to two years. (See 'Frequency of screening with mammography' below.)

Decisions on screening in this age group are highly dependent on a patient's values and preferences. As an example, shared decision-making may result in a 40-year-old woman at average risk choosing to be screened if she has substantial concerns about breast cancer and is willing to accept the possibility of either a false-positive result or overdiagnosis and the resulting evaluation and treatment. On the other hand, a different 40-year-old woman may find that the information gathered during shared decision-making, including the frequency of false positives and overdiagnosis, provides her with a compelling reason to decide to defer mammography screening.

The net benefits of breast cancer screening are less clear for women in their 40s. Although the benefits of screening women in their 40s appear favorable when considering the number of years of life potentially saved [7,37], for the individual average-risk woman, the absolute benefits of screening, when measured by number of breast cancer deaths prevented, are relatively low. A systematic review and meta-analysis of nine randomized trials showed a trend suggesting that for 10,000 women screened over 10 years, three deaths from breast cancer could be prevented [47]. There was an 8 percent relative reduction of breast cancer mortality in women ages 39 to 49 years who were randomly assigned to mammographic screening, which did not achieve statistical significance (relative risk [RR] 0.92, 95% CI 0.75-1.02). Furthermore, in an analysis of the pooled results of four included trials, screening in women aged 39 to 49 years did not impact the risk of advanced breast cancer (RR 0.98, 95% CI 0.74-1.37) [47]. Similarly, 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 mammographic screening at age 40 years, compared with a usual care group, although the difference was not significant (RR 0.83, 95% CI 0.66-1.04) [48]. 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). (See 'Benefits' below.)

Mammography is less sensitive in younger than older women. As an example, mammography is estimated to detect about 73 percent of breast cancers in women in their early 40s compared with 85 percent of breast cancers in women in their early 60s [49].

Given the modest benefits of screening in the 40- to 49-year-old age group, the harms can be relatively more consequential. In particular, false positives are more common in younger than older women. The harms of screening are discussed in detail elsewhere. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Harms from screening'.)

Expert guidelines vary in their recommendations about when to initiate screening and how frequently to screen average-risk women in the 40- to 49-year-old age group (table 3 and figure 2). For example, the American Cancer Society (ACS) recommends that routine mammography screening start at age 45 years based on the finding that the absolute risks of breast cancer occurrence and death for women ages 45 to 49 years are more similar to those for women ages 50 to 54 years than ages 40 to 44 years [7,33,50,51]. The ACS concluded that this similarity in risks of occurrence and mortality outweighs the higher false-positive mammography rates in women under age 50 years. The ACS recommends continuing annual screening until age 55 years, then decreasing to every two years [51].

Age 50 to 74 years — We suggest breast cancer screening with mammography for average-risk women aged 50 to 74 years, consistent with all major United States and international groups (table 3). We typically screen every one to two years depending on an individual woman's risk factors and preference. (See 'Frequency of screening with mammography' below.)

Systematic reviews of multiple randomized trials over the past 50 years found that mammographic screening for women aged 50 to 70 years decreases the risk of breast cancer mortality; however, these results largely reflect trials that used older mammography imaging techniques and did not involve current breast cancer treatment protocols, a factor which may limit the predictive value of the results. Subsequently, a 2016 systematic review of screening mammography found fair-quality evidence that mammography decreases the 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) [47]. Screening mammography 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 benefits are generally thought to outweigh the harms of screening for average-risk women in this age group. (See 'Benefits and harms of screening' below.)

Most expert groups recommend routine screening with mammography for women at average risk who are age 50 or older, and most agree to continue screening through age 74

years (at least) (table 3 and figure 2). However, recommendations on the frequency of mammography screening for this age group vary [8,34,35,52-54].

Age 75 years and older — We suggest that women age 75 years and older be offered screening only if their life expectancy is at least 10 years. For women in this age group who elect to be screened, mammography screening every two years is appropriate. (See 'Frequency of screening with mammography' below.)

There is not a clear upper age limit or ideal frequency for screening in healthy women, since the incidence of breast cancer remains high into the 80s, but the number of life-years saved will decrease with age [33]. A framework that includes life expectancy, risk of dying of cancer, and the number of persons needed to screen over the remaining lifetime to prevent cancer death (table 4) can be useful for guiding decision-making about screening older women for breast and other cancers [55]. It is important to ensure that shared decision-making occurs, with information about both the potential harms and benefits of screening. Providing decision aids to women 75 years and older prior to their preventive visits may help them make more informed decisions [56]. Most potential harms of screening occur relatively soon, whereas a potential benefit may occur up to 10 years later [57]. (See 'Benefits and harms of screening' below.)

Screening mammography may be less beneficial in women age 75 years and older, although data from randomized trials for this age group are limited. In three observational studies, screening mammography was associated with a reduction in mortality due to breast cancer up to age 75 years but not among older women [58-60]. Similarly, a cohort study of 2011 women 80 years and older found no difference in breast cancer rate, stage, or death between women who did and did not undergo screening mammography after age 80 years [61]. However, observational studies may be biased, because older women who participate in screening are likely to be healthier at baseline than those who do not. Furthermore, while screening mammography in older women may result in lower-stage cancer at diagnosis, this may not lead to a decrease in mortality [62-64]. This reflects several factors: a shorter life expectancy decreases the potential that screening will prolong life; the incidence of ductal carcinoma in situ (DCIS) increases with age, but it is not clear that treatment of DCIS affects mortality; and screening-detected cancers are usually lower-stage cancers than those detected clinically, due to lead-time bias [58,59,61].

Several expert group recommendations do not explicitly state at what age breast cancer screening should stop. Some groups take into consideration life expectancy and consider stopping if life expectancy is under 5 or 10 years. Some groups use age 75 years as an age to consider whether or not to continue screening (table 3).

Screening modalities — Mammography (digital 2D, digital breast tomosynthesis [3D], or film) is the primary modality for breast cancer screening in average-risk women. Other

radiologic techniques, including ultrasound and magnetic resonance imaging (MRI), are reserved for further evaluation of findings on mammography or for screening of women at a higher risk for breast cancer. Breast examination by the clinician or by the patient is not recommended as the only screening method, and it is controversial as to whether clinician breast examination (CBE) or patient breast self-examination (BSE) are beneficial as an adjunct to mammography. It is important to educate women about breast awareness and to encourage women to report any breast concerns.

Mammography as preferred screening modality — Among a variety of imaging modalities developed for breast cancer screening, mammography is the best-studied and the only imaging technique that has been shown to decrease breast cancer mortality as demonstrated in multiple randomized trials. However, it is important to know that, even in the best circumstances, mammography may miss up to 20 percent of underlying breast cancers [65]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Mammography'.)

Mammography is available as screen-film mammography, digital mammography, and digital breast tomosynthesis (3D mammography). The choice between them generally depends upon availability. The vast majority of locations in the United States and Europe use digital mammography, but digital breast tomosynthesis is rapidly replacing it as a primary screening modality [66]. For women with dense breasts, digital mammography or digital breast tomosynthesis, if available, is preferred because of higher sensitivity; the sensitivity of mammography is inversely correlated with breast density, especially with older film techniques [67]. The relative benefits of film, digital, and 3D mammography are discussed in further detail elsewhere [68-70]. (See "Breast imaging for cancer screening: Mammography and ultrasonography".)

Prior to the mammogram, it is helpful for women to know that compression of the breasts is transient but important to reduce motion artifact, improve image quality, and reduce the amount of radiation required. Individuals should also provide access to their prior mammograms for comparison if they go to a different mammography facility than they used previously.

Other imaging modalities — For average-risk women, there is a lack of medical evidence to routinely recommend other imaging modalities or supplemental screening with ultrasound, magnetic resonance imaging (MRI), or newer imaging technologies [71]. However, these technologies are useful as adjuncts to screening for certain higher-risk patients and as diagnostic, rather than screening, tools.

- Screening ultrasound is not recommended for screening average-risk women. Ultrasound has not been evaluated as a screening strategy to reduce breast cancer mortality in the average-risk population, including among women with dense breasts.

However, in the United States, some states mandate that ultrasound be mentioned to patients as a potential adjunct to mammography in women with increased breast density [72]. Ultrasound is commonly used for diagnostic follow-up of an abnormality seen on screening mammography to clarify features of a potential lesion. (See "Breast density and screening for breast cancer", section on 'Whole-breast ultrasound screening' and "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Role of ultrasound'.)

- Screening MRI is not recommended for average-risk women, according to supplemental screening MRI guidelines from the ACS [73]. MRI performed in combination with mammography is used primarily to screen high-risk patients with >20 percent lifetime risk. (See "MRI of the breast and emerging technologies", section on 'Indications for breast MRI' and "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Role of ultrasound'.)

Performance specifics of imaging techniques for breast cancer screening are discussed separately. (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".)

Role of clinical breast examination — We suggest **not** performing CBE as part of **screening** of average-risk women; however, a diagnostic CBE remains an important part of the evaluation for women with breast complaints or abnormalities. There is a lack of evidence showing any benefit of screening CBE alone or with screening mammography, a lack of data on whether CBE improves patient outcomes, and evidence suggesting an increase in false-positive rates. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Clinical breast examination'.)

Although there is expert consensus that CBE should **not** be the only screening method used, recommendations of major societies differ as to whether or not to include CBE as an adjunctive screening modality [7,8,34,37].

In locations where imaging modalities for breast cancer screening have limited availability, CBE may have a greater screening role. The World Health Organization (WHO) states that CBE may be an appropriate screening approach for women 50 to 69 years of age in low-resource settings with weak health systems [74,75].

Role of breast self-examination — We suggest that average-risk women **not** perform BSE. Several studies have shown a lack of benefit and a higher rate of breast biopsies that showed benign disease with routine BSE. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Breast self-examination'.)

Women who nonetheless choose to perform BSE should receive careful instruction to differentiate normal tissue from suspicious lumps and understand that BSE is an adjunct, but not a substitute, for mammography. Women should be encouraged to bring abnormal breast findings promptly to the attention of their clinician.

Although many expert groups do not encourage BSE, many do encourage educating women about breast self-awareness, general breast health, and the benefits and the limitations of BSE, as well as advising women to seek medical attention soon if they note concerning breast abnormalities [8,34,36,37,76]. The WHO recommends BSE as a way to empower women and raise awareness among women at risk, rather than as a screening method [54,77].

Frequency of screening with mammography — For average-risk women who wish to undergo screening, screening mammography can be performed every one to two years based on patient preference. Although data are limited and mixed on the optimal frequency for performing mammography, annual screening is associated with more harms and costs than screening every two years, and the difference in absolute benefits between annual and biennial screening is small [78]. While some data suggest benefit for annual screening for some women (eg, premenopausal), this benefit needs to be weighed against the increased risk of false-positive mammographic findings and overdiagnosis.

Expert group recommendations for frequency of mammography screening vary between annual and every two years screening, depending mostly upon the patient's age. Specific groups' recommendations are summarized in the attached table (table 3).

Randomized trials have found that screening every two years achieves reduction in breast cancer mortality. In a systematic review for the US Preventive Services Task Force (USPSTF) 2016 update of breast cancer screening recommendations [8], observational studies found that the 10-year cumulative false-positive mammography rates and biopsy rates were more favorable with biennial screening (42 and 5 percent, respectively) than with annual screening (61 and 7 percent, respectively) [79].

The relative benefits of annual versus biennial screening may differ based on a woman's hormonal status (eg, whether they are premenopausal or use menopausal hormone therapy); however, the evidence varies. A 2015 study from the Breast Cancer Surveillance Consortium, which sampled United States mammography registries, evaluated the effectiveness of varied frequencies of screening among women who were later diagnosed with breast cancer [80]. Among premenopausal women and postmenopausal women who used menopausal hormone therapy, biennial screening was associated with higher proportions of cancers that were less favorable (stage IIB or higher) compared with annual screening. However, in postmenopausal women who did not use menopausal hormone replacement therapy, tumor characteristics were similar for those screened annually or

biennially. By contrast, an earlier (2013) Breast Cancer Surveillance Consortium study, using age to stratify women, found that hormonal status did not alter the relative benefit of mammography: screening biennially versus annually for women aged 50 to 74 years did not increase the risk of tumors with advanced stage or large size, regardless of the women's breast density or hormone therapy use [81].

Breast density may also be associated with benefits that vary with different screening frequencies. As an example, in the same Breast Cancer Surveillance Consortium study, among 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 [81]. However, for younger women with dense breasts, frequency of mammography screening did impact the risk of advanced-stage cancer, which was increased for women aged 40 to 49 years with dense breasts who had biennial, compared with annual, mammograms.

Intervals of more than two years between screenings might be appropriate in certain age groups. A 2016 modeling study suggests that annual screening for higher-risk women with high breast density may be indicated, and triennial screening may be the preferred approach for patients aged 50 years and older with average risk for breast cancer and low breast density [82]. Further confirmation is required before adopting this practice [8,83].

MODERATE RISK: SCREENING

For women with moderate risk (ie, approximately 15 to 20 percent lifetime risk of breast cancer), including most women who have a family history of breast cancer in a first-degree relative but do not have a known genetic syndrome, we suggest that the same screening approach, including the age to begin mammography screening, and frequency of screening be used as for women at average risk. (See 'Average risk: Screening' above.)

While some have suggested that screening be initiated at an earlier age if a first-degree relative had premenopausal breast cancer, there are few high-quality data supporting this approach in the absence of a known genetic syndrome. As an example, in a case-control study of breast cancer screening among United States women aged 40 to 65 years, there was only a non-statistical trend towards greater protection in women at moderately increased compared with average breast cancer risk [84].

Many experts suggest that in women at moderate risk, the decision to undergo supplemental screening (with either magnetic resonance imaging [MRI] or ultrasound in addition to mammography) should be determined after a discussion with the patient regarding personal preferences for known risks versus possible benefits, availability, and insurance coverage. Supplemental screening ultrasound may be more widely accessible and

less expensive than supplemental MRI; however, neither modality is routinely covered by insurance for this risk category in most US states. We do not routinely suggest these adjunctive modalities for women at moderate risk, but if women are interested in them, we encourage them to engage in a shared decision-making discussion with their clinician. (See 'Shared medical decision-making' below.)

Screening modalities for women who have dense breast tissue are discussed elsewhere. (See 'Dense breast tissue' below.)

Recommendations for MRI in women with moderate risk are inconclusive. The American Cancer Society (ACS) advises that there is insufficient evidence to recommend for or against supplemental screening MRI as an adjunct to mammography in moderate-risk women (table 5) [73].

HIGH RISK: SCREENING

For high-risk women (eg, those who have *BRCA* or other susceptibility genes, a history of chest radiation, or a calculated lifetime risk of developing breast cancer of greater than 20 percent), it is important both to emphasize the value of appropriate screening, generally with enhanced modalities and at an enhanced frequency (table 5), and to refer to a high-risk screening clinic to screen and to consider risk reduction treatment and intensification of surveillance. Specifics are discussed in detail separately. (See "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Management of female BRCA1/2 carriers without cancer' and "Overview of hereditary breast and ovarian cancer syndromes" and "Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention".)

SPECIAL CONSIDERATIONS

Breast augmentation for benign reasons — Patients who have had breast tissue augmentation with implants for benign reasons warrant routine screening mammography to evaluate the native breast tissue; indications and frequency for screening are the same as in women without implants. However, the implant contents are radiopaque and can obscure small lesions. In addition, the presence of the implant makes it harder to evaluate all parts of the breast and may make compression challenging [85]. This is discussed in detail elsewhere. (See "Implant-based breast reconstruction and augmentation", section on 'Breast cancer detection'.)

Standard imaging technique in women with breast implants involves four views, rather than the usual two views per breast. Positioning is important to include as much breast tissue as

possible by pushing the implant out of view. Standard craniocaudal (CC) and mediolateral oblique (MLO) projections of each breast are obtained with the implant included (image 1). These views permit evaluation of the implant as well as the deep breast tissues adjacent to the implant. The two views are repeated after the implant is displaced back against the chest wall and the breast tissue is pulled forward [86].

The type of implant, as well as its location (prepectoral or retroglandular versus retropectoral or subpectoral) plays a role in the ease of imaging; breasts with implants placed behind the pectoralis muscle (retropectoral or subpectoral) are easier to position.

Breast reconstruction related to malignancy — Mammography is not routinely performed following mastectomy [87,88]. When no native breast tissue is left behind, mammography provides no substantial added benefit to clinical examination in detecting cancer recurrence.

Physical examination is the method of choice in monitoring myocutaneous (eg, transverse rectus abdominis myocutaneous [TRAM] or deep inferior epigastric perforator [DIEP] flap) breast reconstructions. However, it can be difficult to distinguish a palpable area of fat necrosis from recurrent cancer, and diagnostic mammography may be indicated for palpable findings in women with TRAM or DIEP reconstructions [89].

The approach to women who have had mastectomy and reconstruction is discussed elsewhere. (See "Overview of breast reconstruction", section on 'Surveillance of the reconstructed breast'.)

Prior breast biopsy or surgery for benign disease — Women with previous breast biopsy and no other risk factors are considered at average risk and can undergo routine mammography screening.

Breast biopsies are performed in approximately 1 to 2 percent of mammographic screenings in the United States [90], with lower rates in other countries. The effect of a prior breast biopsy on subsequent mammographic interpretation performance was investigated in a review of data involving over two million mammograms in nearly 800,000 women [91]. A history of a prior breast biopsy for benign disease was associated with reduced specificity (odds ratio [OR] 0.75, 95% CI 0.79-0.92) and a lower positive predictive value for a referral for breast biopsy (OR 0.85, 95% CI 0.79-0.92) in subsequent screening mammograms, compared with women who had no prior biopsy history. This may reflect characteristics of the breast tissue (eg, more fibrocystic) that led to the initial biopsy, tissue effects of the biopsy itself, or differing thresholds for mammographic interpretation when a prior biopsy history is provided.

In a study that did not distinguish between removal of benign breast lumps and other benign breast surgery, mammography in women with a history of such surgery had lower sensitivity and slightly lower specificity [92].

Pregnancy and lactation — Screening mammography is not routinely performed in pregnant women, although the American College of Radiology deems screening digital mammography and screening digital breast tomosynthesis usually appropriate for both lactating and pregnant women [93].

By contrast, diagnostic imaging is performed during pregnancy and lactation for patients with a palpable breast mass or abnormal finding on screening mammography. This is discussed in detail separately. (See "Gestational breast cancer: Epidemiology and diagnosis", section on 'Diagnosis and staging' and "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Abnormalities on mammography' and "Diagnostic imaging in pregnant and lactating patients", section on 'Screening mammography'.)

Males — For most biological males, routine screening mammography is not performed. For males who are carriers of *BRCA1/2*, and who have evidence of gynecomastia or parenchymal/glandular breast density, annual screening mammography may be a consideration. (See "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Male breast cancer'.)

The initial mammogram evaluation in a male includes standard bilateral CC and MLO views (image 2 and image 3). Use of narrower paddles may facilitate compression depending on breast size. Similar to females, additional mammographic views and ultrasound may be indicated to characterize abnormalities and facilitate biopsy if indicated.

Dense breast tissue — Dense breasts are associated with an increased risk of breast cancer and can decrease the sensitivity of mammography for small lesions. Nevertheless, we do not alter our general approach to age- and risk-based screening based on breast density. However, for women with dense breasts, we do prefer digital mammography over film mammography, due to greater sensitivity [94]; digital mammography (whether 2D or 3D) is the modality typically used for mammography in most locations in the United States.

We suggest that most women with dense breasts and no additional risk factors for breast cancer **not** undergo supplemental screening with other imaging modalities given insufficient evidence demonstrating benefit [8,95]. Nevertheless, some women with dense breasts may reasonably opt to have supplemental screening. For average-risk women who choose to undergo supplemental screening, ultrasound or magnetic resonance imaging (MRI) are options but will likely require out-of-pocket payments (as insurance usually does not cover supplemental screening for average-risk women). (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Breast density' and "Breast density and screening for breast cancer", section on 'Average or low risk (<15 percent lifetime risk)'.)

In moderate-risk women with dense breasts, there are no consensus guidelines to recommend for or against supplemental screening ultrasound. (See "Breast density and

screening for breast cancer", section on 'Intermediate risk (15 to 20 percent lifetime risk)'.)

In the United States, many states have laws requiring that patients be informed about their breast density, that dense breast tissue may be a risk factor for breast cancer, and that dense tissue may interfere with cancer detection [96]. There are risks of supplemental screening including increased false positives, and an increase in the number of biopsies, costs, possible overdiagnoses, and patient anxiety, with no evidence of a reduction of breast cancer specific or overall mortality in average-risk women [97]. The decision to pursue supplemental screening should only be made after shared decision-making between the clinician and the patient.

Recommendations and considerations for screening individuals with dense breast tissue are discussed in detail elsewhere. (See "Breast density and screening for breast cancer".)

Postmenopausal hormone therapy — The normal involution of breast tissue with age appears to be inhibited by postmenopausal hormone therapy (HT), which increases breast density and may decrease the sensitivity of mammography [67,98-100]. However, breast cancer screening recommendations for individuals taking postmenopausal HT are the same as for those not taking HT, including those for women with dense breasts, if applicable. (See "Menopausal hormone therapy and the risk of breast cancer", section on 'Mammographic density' and "Breast density and screening for breast cancer".)

A large prospective cohort study of 329,495 women found that HT prevented the usual improvement in mammographic accuracy with increasing age and that this effect was mediated through increases in breast density [67]. Data from a subset of the Women's Health Initiative (WHI) trial show that among 413 postmenopausal women who were randomly assigned to combination estrogen/progesterone therapy or placebo, mammographic density increased 6 percent at year 1 in the treatment group, compared with a 0.91 percent decrease in the placebo group [101]. Although breast density may not similarly increase with estrogen therapy alone [100], a reduction in mammographic sensitivity and a slight reduction in specificity has been seen in women taking preparations of either combination estrogen/progesterone or estrogen alone [92].

The effect of postmenopausal HT on the risk of breast cancer is reviewed elsewhere. (See "Menopausal hormone therapy and the risk of breast cancer".)

Limited life expectancy — Individuals with significant comorbid illnesses whose life expectancy is less than 10 years are unlikely to benefit from screening, especially when these illnesses might contraindicate effective treatment for breast cancer. Thus, women with less than 10 years of life expectancy do not need routine screening mammography.

Recent COVID-19 vaccination — Axillary adenopathy has been observed after administration of COVID-19 mRNA vaccines [102,103], at rates higher than reported after

other vaccines (ie, Bacillus-Calmette-Guerin [BCG], influenza, and human papillomavirus [HPV]). In a small study, axillary lymphadenopathy after a booster dose of mRNA vaccine had a mean duration of 102 days, shorter than after primary vaccination [104]. While previous recommendations suggested scheduling screening mammography prior to a dose of a COVID-19 mRNA vaccine, or four to six weeks after a dose [105], new research suggests that there should be no delay in scheduling routine screening based on COVID-19 vaccine timing given the very low risk of malignant findings in asymptomatic patients with unilateral axillary lymphadenopathy following recent COVID-19 vaccination and the potential negative effects of delayed screening on breast cancer morbidity and mortality [106,107]. Instead, axillary adenopathy, if detected on screening, will be interpreted by radiologists in the context of patient risk factors. The European Society of Breast Imaging recommends that radiologists classify imaging-detected unilateral lymphadenopathy on the same side as recent COVID-19 vaccination (within 12 weeks) in patients without a breast cancer history and no suspicious breast findings as a benign finding (BI-RADS 2) with no further work-up to be recommended [107].

BENEFITS AND HARMS OF SCREENING

There is more scientific evidence related to screening for breast cancer than for any other cancer. There are both substantial benefits and substantial risks of harm associated with screening (figure 3 and table 6). For that reason, a full discussion between the patient and the clinician about screening is very important. (See 'Shared medical decision-making' below.)

Benefits — The primary benefit of screening with mammography is a decrease in breast cancer mortality. In a 2015 systematic review and a 2012 meta-analysis that each included multiple randomized trials that involved over 600,000 women from several countries [108-115], screening mammography was estimated to reduce the odds of dying of breast cancer by approximately 20 percent [33,116]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Mammography'.)

The absolute benefit of screening depends on the patient's age and is lower in younger women because they have a lower baseline risk of cancer. A 2016 systematic review analyzed risk reduction by age: with at least 11 years of follow-up, the pooled relative risk for breast cancer mortality was 0.92 (95% CI 0.75-1.02) for women 39 to 49 years of age, 0.86 (0.68-0.97) for women 50 to 59 years of age, and 0.67 (0.54-0.83) for women 60 to 69 years of age [47]. Risk reduction by age is discussed in detail elsewhere. (See 'Age 40 to 49 years' above and 'Age 50 to 74 years' above and 'Age 75 years and older' above.)

Confidence in the magnitude of the breast cancer mortality reduction based on these aggregated trial results is reduced for several reasons: the trials were performed in the

setting of older cancer therapies, so the value of screening to find and treat lesions earlier may be reduced, due to the greater efficacy of currently available treatment; some trials did not blind outcome assessors, and thus results may have been biased in favor of screening; and most trials predated advances in breast imaging that would improve the sensitivity of screening. Nevertheless, observational studies continue to support a risk reduction in breast cancer mortality with screening mammography. These studies are discussed elsewhere. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Mammography'.)

Data are limited as to how much of the reduction in mortality seen over time is attributable to advances in imaging techniques for screening and how much is due to improved effectiveness of therapy. In one study of simulation models, about one-third of the decrease in breast cancer mortality in 2012 was attributable to screening mammography, with the balance attributed to treatment [5]. The contribution of screening mammography to mortality reduction varied among different molecular subtypes of breast cancer.

Harms — Harms associated with breast cancer screening include the potential for overdiagnosis leading to unnecessary treatment and its associated risks, false-positive and false-negative findings, radiation exposure, and patient discomfort and anxiety. The risk of harms is substantial (table 6) [117].

- **Overdiagnosis** – Overdiagnosis occurs when screening leads to identification of breast cancer that would not have caused clinical consequences in a woman's lifetime had it not been detected. Estimates for overdiagnosis in breast cancer range from 10 percent or less to over 50 percent of all women diagnosed with breast cancer. Variation in these estimates is likely related to differences in definition (eg, whether ductal carcinoma in situ [DCIS] is included and what age group is studied) and approaches used for study design, measurement, and estimation [118-120]. In the United States, based on Breast Cancer Surveillance Consortium (BCSC) population-based data, about one in seven cases of screen-detected cancers is overdiagnosed [121]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Overdiagnosis' and "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Ductal carcinoma in situ'.)

  Several studies have suggested that many cancers, especially those confined to the mammary ducts (ie, DCIS), are biologically insignificant and would never become clinically evident in the patient's lifetime [122-124]. It is not possible using imaging to distinguish biologically insignificant cancers from those that will proceed to grow, metastasize, and lead to the patient's death at this time. Thus, almost all patients with a diagnosis of breast cancer after abnormal imaging, regardless of its stage, receive some sort of local therapy (eg, surgery, with or without radiation therapy) and

potentially systemic therapy as well. Thus, the overdiagnosis of what may be biologically insignificant cancers leads to substantial treatment that is potentially unnecessary.

- **False-positive mammogram result** – For each woman whose life is saved by mammography, many women will experience false-positive mammograms. The estimated risk of a false positive varies based on a number of factors, including the woman's age and breast density (figure 4) [83]. Factors that increase the possibility of a false-positive mammogram include young age, increased breast density, family or personal history of breast cancer, prior breast biopsies, current estrogen use, three years between screenings, lack of comparison to prior mammograms, and an individual radiologist's tendency to over-read [125-127]. In the United States, about 10 percent of screening mammography exams are false positives [128], and after a decade of annual screening about 50 percent of women have experienced a false positive. The false-positive rate is much lower in other countries [126,129]. Specifics about the incidence of false-positive mammograms and the associated anxiety are discussed elsewhere. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'False-positive tests' and "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Anxiety related to false-positive findings'.)

- **False-negative mammogram result** – There are some screening mammography examinations that are interpreted as negative, but a cancer was present; these cancers (also called interval cancers) may present clinically after that screening examination but prior to the next scheduled screening. These cancers were either missed by the radiologist or were not mammographically visible even on retrospective review [130].

- **Radiation** – Although radiation can increase the risk of breast cancer, radiation from screening mammography is low enough that, for average-risk women over age 40 years, the benefits of screening outweigh the risks of radiation from mammography. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Radiation'.)

  However, there is concern about an increased risk of radiation in women with *BRCA1* or *BRCA2* mutations, which is discussed separately. (See "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Cancer surveillance'.)

- **Discomfort** – Mammographic screening can be temporarily uncomfortable or painful. Techniques to reduce discomfort are discussed elsewhere. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Discomfort'.)

SHARED MEDICAL DECISION-MAKING

The decision to perform mammography should be determined with shared decision-making, in which the clinician helps the patient to make an informed, values-based decision about whether to undergo screening [131,132]. Shared decision-making is an opportunity to indicate that the benefits and harms of breast cancer screening are more finely balanced than once believed [47,79]. (See 'Benefits and harms of screening' above.)

Counseling a patient — It is important to discuss the patient's risk of developing breast cancer, the potential benefits and harms of screening, and the patient's values [133,134]. Graphics and tables that quantitate benefits and harms can be useful in such discussions (figure 3 and table 6).

Discussion points to help a patient with decision-making can include:

- The vast majority of women are at average risk of breast cancer. Furthermore, the risk of a woman being diagnosed with breast cancer is lower than most women realize.
- There is potential inaccuracy when estimating an **individual's** risk of developing breast cancer, due to the relatively low sensitivity and specificity of the breast cancer risk stratification tools at the individual level. These tools work best for estimating risk of breast cancer for a **group** of women with similar clinical attributes.
- The likelihood is that an individual, even if they are in a high-risk group, will not develop breast cancer, especially over a five-year period, unless they are one of the relatively few people with known high-risk genetic mutations (eg, *BRCA*, *TP53*).
- A woman may, by choosing to be screened, avert death from breast cancer or gain quality-adjusted life-years (QALY). However, gains in QALY from screening are small compared with the larger declines in QALY experienced by all women as they age [78]. We encourage maintaining an open dialogue with women about the relative risks and benefits of continuing screening, particularly as they age, so they can make an informed decision.
- Screening may result in overdiagnosis, which means finding an abnormality that results in further testing and treatment, although had it not been found it would not have caused harm to the patient.
- Screening may produce a false-positive result, for which the sequelae can include further testing and anxiety.
- A patient may experience anxiety about the evaluation, diagnosis, and treatment.

Although women may feel well informed by shared decision-making discussions with clinicians, there may be important components the patient did not learn during the conversation. For example, in a nationwide survey, women reported feeling informed by

their clinician before undergoing breast cancer screening. However, while 96 percent said they were told of the benefits of screening, 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 [135].

Decision aids — Decision aids (eg, leaflets, booklets, videos, and websites) can encourage patients to interpret evidence in the context of their personal goals and concerns. The effect of using decision aids on the length of an office visit varies, ranging from shortening, to no change, to lengthening the visit [136,137].

Decision aids have been noted to reduce the number of patients choosing cancer screening [138,139]. 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 [140]. The breast cancer screening decision aid used in this trial is based on data from Australia; rates of false-positive mammograms are higher in the United States.

FOLLOW-UP OF ABNORMAL MAMMOGRAPHY RESULTS

The evaluation of abnormalities detected by screening is discussed separately. (See "Diagnostic evaluation of suspected breast cancer" and "Clinical manifestations, differential diagnosis, and clinical evaluation of a palpable breast mass", section on 'Clinical evaluation' and "Breast biopsy" and "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Abnormalities on mammography'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Screening for breast cancer".)

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

- **Screening strategies for breast cancer based on risk –** Screening is of greatest value for those patients most likely to develop breast cancer and for whom early treatment is more effective than later treatment in reducing mortality. Thus, screening strategies differ based on the estimated risk of breast cancer. (See 'Breast cancer risk determination' above.)
- **Assessment of risk –** The vast majority of women are at average risk (less than 15 percent lifetime risk) of developing breast cancer. Even women who have some risk factors for breast cancer are still likely to be at average risk, although an established risk assessment tool can be helpful to estimate risk and inform the need for additional testing. Women who have a personal history of breast, ovarian, peritoneal, or fallopian tube cancer, certain genetic mutations (eg, *BRCA1* or *BRCA2, TP53*), or a history of previous radiotherapy to the chest between ages 10 and 30 years are at high risk for developing breast cancer. (See 'Initial assessment of risk' above and 'Clinical use of risk prediction models' above and "Overview of hereditary breast and ovarian cancer syndromes", section on 'High-penetrance genes'.)
- **Screening approach for average-risk women –** Average-risk women have less than a 15 percent lifetime risk of developing breast cancer.
  - **Age-based approach for average-risk women –** In average-risk women, age is the most important factor in deciding when to be screened, because breast cancer incidence rises with age (table 3 and figure 2). (See 'Average risk: Screening' above.)

- For women under age 40 years, screening mammography is not warranted since the incidence of breast cancer is low and the performance characteristics of mammography are lower. (See 'Age under 40 years' above.)

- For women aged 40 to 49 years, we raise the topic of screening and individualize the decision based on patient preferences and values. A woman may opt for screening if she has substantial concerns about breast cancer risk and accepts the possibility of a false-positive result or overdiagnosis and the resulting evaluation and treatment. Another woman may find that the frequency of false positives and overdiagnosis provides a compelling reason to defer screening. Although screening in the 40s is favorable when considering the number of years of life potentially saved, for an average-risk woman, the number of breast cancer deaths prevented is relatively low. (See 'Age 40 to 49 years' above and 'Frequency of screening with mammography' above.)

- For women aged 50 to 74 years, we suggest routine mammographic screening (**Grade 2B**). (See 'Age 50 to 74 years' above and 'Frequency of screening with mammography' above.)

- For women age 75 years and older, we suggest screening mammography only if their life expectancy is at least 10 years (**Grade 2C**). (See 'Age 75 years and older' above and 'Frequency of screening with mammography' above.)

- **Mammography every one to two years recommended** – For average-risk women who decide to be screened, we recommend screening with mammography rather than other modalities (**Grade 1B**). While ultrasound and magnetic resonance imaging (MRI) are useful for diagnostic evaluation of abnormal findings noted on screening mammography, we do not use these modalities to screen average-risk women. We suggest a mammography screening interval of every one to two years based upon the preference of the woman (**Grade 2C**). Although data are limited and evidence mixed on the optimal frequency for performing screening mammography, annual screening is associated with more harms and costs than screening every two years, and the difference in absolute benefits between annual and biennial screening is small. (See 'Other imaging modalities' above and 'Frequency of screening with mammography' above.)

- **Limited value of a screening clinical breast examination (CBE) or breast self-examination (BSE) in average-risk women** – We suggest not using clinical breast examination (CBE) (**Grade 2C**) or breast self-examination (BSE) (**Grade 2B**) as part of screening of average-risk women. Trials evaluating CBE (with or without mammography) and BSE have not demonstrated efficacy in early cancer detection or improved outcomes. Screening CBE may be helpful, however, in resource-limited

settings where there is limited imaging availability. Women should be educated about breast health awareness. (See 'Role of clinical breast examination' above and 'Role of breast self-examination' above.)

- **Screening approach for moderate-risk women** – Moderate-risk women (approximately 15 to 20 percent lifetime breast cancer risk) include most women with breast cancer in a first-degree relative but without a known genetic syndrome. For women with moderate risk, we suggest the same screening approach as for average-risk women (**Grade 2C**). Some practitioners screen earlier if the first-degree relative had premenopausal breast cancer, although there are no data showing a mortality benefit for these women. For women who wish supplemental screening with ultrasound or MRI, for which data are inconclusive, we counsel that harms may outweigh benefits of supplemental screening and that there will likely be out-of-pocket costs, as insurance usually does not cover these tests for moderate-risk women. (See 'Moderate risk: Screening' above and 'Average risk: Screening' above.)

- **Screening approach for high-risk women** – High-risk women (greater than 20 percent lifetime breast cancer risk) warrant referral to a high-risk screening clinic for evaluation, possible intensified screening regimens (table 5), and consideration of genetic testing and risk reduction treatment (eg, chemoprevention and prophylactic surgery). High-risk women include those who have a personal history of ovarian, peritoneal, tubal, or breast cancer; a family history of ovarian, peritoneal, or tubal cancer or a strong family history of breast cancer; an ancestry (eg, Ashkenazi Jewish) associated with *BRCA1* or *2* mutations; a genetic predisposition (eg, known *BRCA* or other susceptibility genes); prior radiotherapy to the chest; or other breast cancer risk factors, resulting in a calculated lifetime risk of developing breast cancer of greater than 20 percent. (See 'High risk: Screening' above and "Cancer risks and management of BRCA1/2 carriers without cancer".)

- **Special considerations for breast cancer screening** – General breast cancer screening recommendations apply to most patients, although there are special considerations for some populations (see 'Special considerations' above):

  - Dense breast tissue is associated with an increased risk of breast cancer and can decrease the sensitivity of mammography. Nevertheless, we do not alter our general approach to age- and risk-based screening based on breast density. (See "Breast density and screening for breast cancer".)

  - Screening mammography is not routinely performed following mastectomy (on the ipsilateral breast; screening mammography is recommended for the contralateral breast). Physical examination is the monitoring method of choice for the ipsilateral

breast. (See 'Breast reconstruction related to malignancy' above and "Overview of breast reconstruction", section on 'Surveillance of the reconstructed breast'.)

- Screening mammography is not routinely performed during pregnancy. (See 'Pregnancy and lactation' above.)
- Individuals with significant comorbid illnesses whose life expectancy is less than 10 years are unlikely to benefit from screening, especially when these illnesses might contraindicate effective treatment for breast cancer. Thus, such individuals do not need routine screening mammography. (See 'Limited life expectancy' above.)
- COVID-19 vaccination with mRNA vaccines may cause transient axillary lymphadenopathy, impacting the interpretation of mammography. Although initial recommendations suggested scheduling screening mammography prior to a dose of a COVID-19 mRNA vaccine, or four to six weeks after a dose, newer research suggests that there should be no delay based on COVID vaccine timing. Instead, axillary adenopathy, if detected on screening, will be interpreted by radiologists in the context of patient risk factors. (See 'Recent COVID-19 vaccination' above.)

- **Shared decision-making** – Shared decision-making should be used in discussing breast cancer screening. Decision aids can be helpful when discussing the patient's risk of developing breast cancer, the potential benefits and harms of screening, and the patient's preferences and values. (See 'Benefits and harms of screening' above and 'Shared medical decision-making' above.)
  - The benefit of screening with mammography is a decrease in breast cancer mortality. However, the absolute benefit is lower in younger women who have a lower baseline risk of cancer.
  - Harms associated with breast cancer screening include the potential for false-negative and false-positive findings, patient anxiety, overdiagnosis, and unnecessary treatment and its associated risks.

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Topic 7564 Version 106.0

GRAPHICS

Factors significantly associated with increased breast cancer risk for women aged 40 to 49 years

Risk factor	Breast cancer risk ratio (95% CI)	Source (reference)
≥2-fold increased risk		
First-degree relatives with breast cancer		
1	2.14 (1.92-2.38)	1
2	3.84 (2.37-6.22)	1
Age of first-degree relative with breast cancer		
<40 years	3.0 (1.8-4.9)	1
<50 years	2.17 (1.86-2.53)	BCSC
Breast density BI-RADS category 4	2.04 (1.84-2.26)	2*
1.5- to 2.0-fold increased risk		
Prior benign breast biopsy result	1.87 (1.64-2.13)	3*
Second-degree relative with breast cancer	1.7 (1.4-2.0)	4
Breast density BI-RADS category 3	1.62 (1.51-1.75)	2*
1.0- to 1.5-fold increased risk		
Current oral contraceptive use	1.30 (1.13-1.49)	BCSC
Nulliparity¶	1.25 (1.08-1.46)	5-9
Age at first birth ≥30 yearsΔ	1.20 (1.02-1.42)	5-9

BCSC: Breast Cancer Surveillance Consortium; BI-RADS: Breast Imaging Reporting and Data System.

* BCSC estimates from published analyses.

¶ Nulliparity was calculated in two ways. Estimates indicating significantly increased risk for nonparous compared with parous women were similar for the meta-analysis and the BCSC data. Estimates comparing ages at first birth that included nonparous women provided significant results for the meta-analysis only.

Δ Results were not statistically significant for the BCSC data.

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Graphic 83694 Version 16.0

Breast cancer risk prediction tools

Model	Characteristics and limitations
Gail model 2 (BRCAT)[1]	Considers nongenetic risk factors such as age at menarche, first term birth, and biopsy history, including atypical hyperplasia. Not appropriate for females with DCIS, LCIS, prior chest radiation due to Hodgkin lymphoma, or for females with *BRCA 1/2* mutations.
	Does not consider family history beyond first-degree relatives with breast cancer. It does not factor in any other cancers or any paternal relatives with cancer.
	Calculates 5-year and lifetime invasive breast cancer risk.
Breast cancer surveillance consortium Risk Calculator[2]	Considers age, race, family history of breast cancer in a first-degree relative, breast biopsy history, and mammographic breast density.
	Does not consider family history beyond first-degree relatives with breast cancer. It does not factor in any other cancers or any paternal relatives with cancer.
	Calculates 5- and 10-year invasive breast cancer risk.
Tyrer-Cuzick (IBIS)[3]	Considers nongenetic risk factors such as age at menarche, first term birth, biopsy history, height and weight, age at menopause, etc.
	Considers a family history of breast and ovarian cancer beyond first-degree relatives.
	Although it considers the contributions of other low-penetrance genes to breast cancer risk,[4] some evidence suggests it overestimates the risk of subsequent breast cancer, except in those with personal or family history of *BRCA 1/2* mutations.[5]
	Not used in patients with a history of breast cancer.
	Often predicts breast cancer risks that are higher than other mathematic models.
	Calculates 10-year and lifetime invasive breast cancer risk and the risk of carrying a *BRCA 1/2* mutation.
Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA, now called CanRisk)[6]	Considers age, BMI, alcohol consumption, number of children and age at first birth, mammographic breast density, personal cancer history, results of genetic testing (if available), and family history.
BRCAPRO (part of CancerGene)[7]	Considers race, Ashkenazi Jewish ancestry, as well as extensive family history of breast, ovarian, and other cancers and constructs a pedigree.
	Considers history of oophorectomy and bilateral oophorectomy.
	Contains the Chen-Gail model, which estimates breast cancer risk on Gail model factors plus weight and mammographic density; however, this

	model is not well validated.[8]
	Assumes that *BRCA 1/2* mutations account for all hereditary breast and ovarian cancers.[7,9]
	In the highest-risk families (eg, with multiple cases of ovarian cancer and early breast cancer), the model may generate high residual risks for carrying a *BRCA* mutation (ie, the chance of carrying an undetected pathogenic variant). Thus, it may generate high risks for primary or contralateral breast cancer and ovarian cancer, even with an uninformative negative result.
	Calculates probability of having a *BRCA 1/2* mutation.

DCIS: ductal carcinoma in situ; LCIS: lobular carcinoma in situ; BRCA: breast cancer susceptibility genes.

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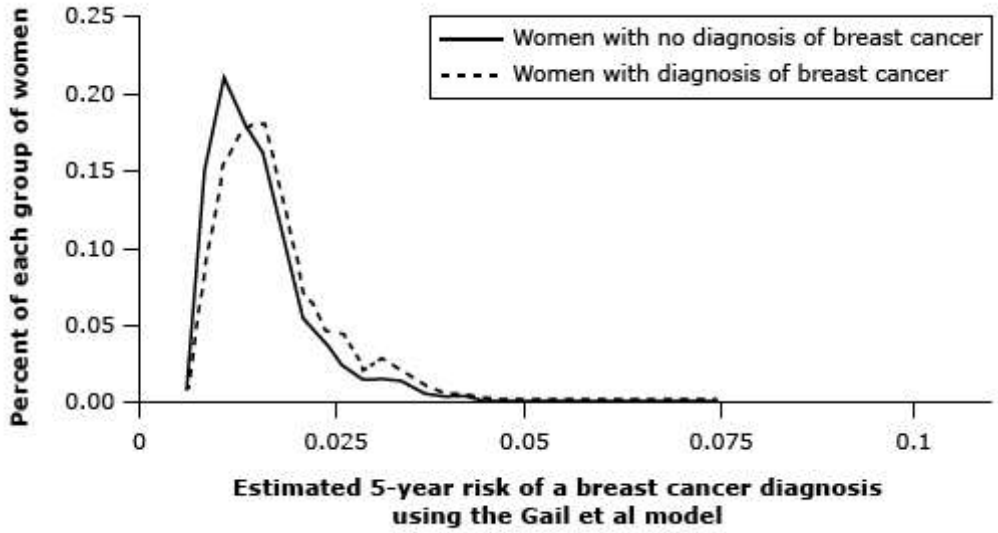
Graphic 118958 Version 4.0

Gail model accuracy



Ability of the Gail breast cancer risk prediction model to discriminate among women who did and did not develop breast cancer in the Nurses' Health Study. Concordance statistics = 0.58 (95% CI 0.56-0.60).

Graphic 54619 Version 9.0

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

Group (date)	Frequency of screening (years)	Initiation of screening for women at average risk		
		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 (2018)[2]	2 to 3	Recommend against*	Yes	Yes, to age 74
National Health Service, United Kingdom (2018)[3]	3	Yes, start age 47	Yes	Yes, to age 73
Royal Australian College of General Practitioners (2018)[4]	2	No	Yes	Yes, to age 74
Medical societies				
American College of Obstetricians and Gynecologists (2017)[5]	1 to 2*	Individualize*	Yes	Yes, to at least age 75¶
American College of Physicians (2019)[6]	2	Individualize*	Yes	Yes, to age 74
American Cancer Society (2015)[7]	1 year age 45 to 54	Individualize* through age 44	Yes	Yes△
	1 to 2 years age ≥55	Yes, start age 45		
American College of Radiology and Society of Breast Imaging (2021)[8]	1	Yes	Yes	Yes◇
Coalitions				
National Comprehensive Cancer Network (2018)[9]	1	Yes	Yes	Yes

* Women should be counseled about the harms and benefits of mammography; individualized decisions should include shared decision-making based on risks, benefits, patient values and preferences.

¶ Decision to discontinue screening mammography should be based on a shared decision-making process informed by the woman's health status and longevity.

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

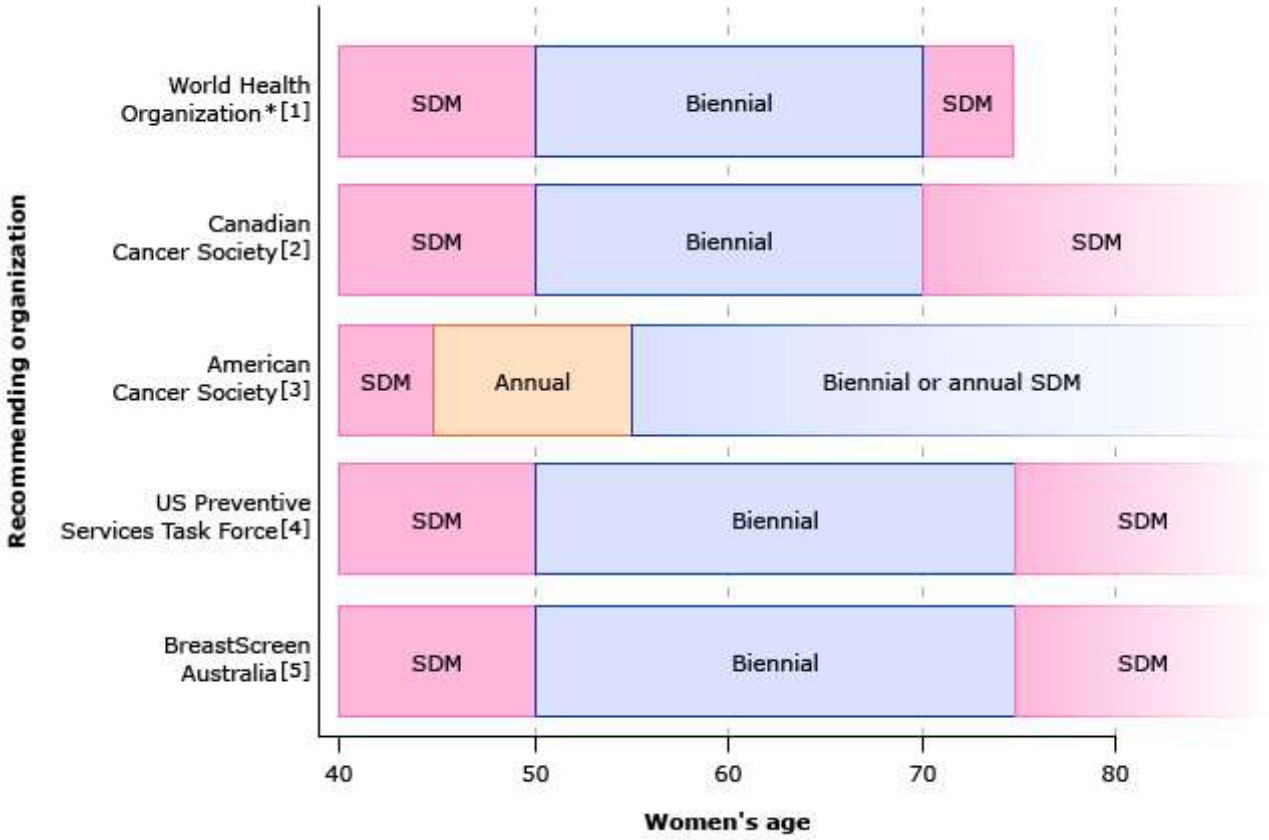
◇ Individualize to current health and life expectancy; if a woman is in reasonably good health and would be a candidate for treatment, then should continue screening.

References:

1. *US Preventive Services Task Force. Screening for Breast Cancer: US Preventive Services Task Force recommendation statement. Ann Intern Med 2016; 164:279.*
2. *Canadian Task Force on Preventive Health Care, Klarenbach S, Sims-Jones N, Lewin G, et al. Recommendations on screening for breast cancer in women aged 40-74 years who are not at increased risk for breast cancer. CMAJ 2018; 190:E1441.*
3. *National Health Service. When it's offered: Breast cancer screening. Available at: https://www.nhs.uk/conditions/breast-cancer-screening/when-its-offered/ (Accessed on June 18, 2019).*
4. *The Royal Australian College of General Practitioners. Guidelines for preventive activities in general practice, 9th ed, East Melbourne, RACGP 2018.*
5. *American College of Obstetricians-Gynecologists. Practice bulletin no. 179: Breast cancer risk assessment and screening in average-risk women. Obstet Gynecol 2017; 130:e1-16.*
6. *Qaseem A, Lin JS, Mustafa RA, et al. Screening for breast cancer in average-risk women: A guidance statement from the American College of Physicians. Ann Intern Med 2019; 170:547.*
7. *Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. JAMA 2015; 314:1599.*
8. *Monticciolo DL, Malak SF, Friedewald SM, et al. Breast cancer screening recommendations inclusive of all women at average risk: Update from the ACR and Society of Breast Imaging. J Am Coll Radiol 2021; 18:1280.*
9. *National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in oncology: Breast cancer version 2. 2018.*

Graphic 53551 Version 30.0

Professional societies' breast cancer screening recommendations



Comparison of breast cancer screening recommendations.

SDM: shared decision-making is recommended; biennial: biennial mammography is recommended; annual: annual mammography is recommended.

* Recommendation applies in well-resourced settings.

References:

1. *World Health Organization. WHO Position Paper on Mammography Screening. World Health Organization, Geneva 2014.*
2. *Canadian Cancer Society. Screening for breast cancer. Screening mammography. http://www.cancer.ca/en/cancer-information/cancer-type/breast/screening/?region=on. Accessed 16 Feb 2017.*
3. *Oeffinger KC, Fontham ET, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. JAMA 2015; 314:1599.*
4. *Siu AL. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2016; 164:279.*
5. *Australian Government Department of Health. About breast screening. BreastScreen Australia Program. http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/about-breast-screening. Published March 2015. Accessed 16 Feb 2017.*

Graphic 113796 Version 8.0

Breast cancer screening in women >50 years, according to life expectancy

Age (years)	Life expectancy (years)*	Risk of dying from breast cancer (%)¶	Number needed to screen over remaining lifetime
50	40	4.4	95
	33	3.1	133
	24.5	2	226
70	21.3	3.3	142
	15.7	2.2	242
	9.5	1.2	642
75	17	2.8	176
	11.9	1.8	330
	6.8	0.9	1361
80	13	2.4	240
	8.6	1.5	533
	4.6	0.7	-
85	9.6	1.9	417
	5.9	1.2	2131
	2.9	0.6	-
90	6.8	1.4	1066
	3.9	0.8	-
	1.8	0.4	-

* Life expectancy is depicted as the upper, middle, and lower quartiles of life expectancy for the United States population; placing an individual into the appropriate quartile depends upon a number of factors, including the number and severity of comorbid conditions and functional impairments.

¶ Risk of dying refers to the risk of dying of breast cancer during the remaining lifetime.

Data from: Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. JAMA 2001; 285:2750.

Graphic 61593 Version 6.0

ACS recommendations for breast MRI screening as an adjunct to mammography

Recommend annual MRI screening (based on high risk of breast cancer and high sensitivity of MRI*)
BRCA mutation
First-degree relative of *BRCA* carrier, but untested
Lifetime risk >20 to 25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history
Recommend annual MRI screening (based on high risk of breast cancer)
Radiation to chest between age 10 and 30 years
Li-Fraumeni syndrome and first-degree relatives
Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives
Insufficient evidence to recommend for or against MRI screening[Δ]
Lifetime risk 15 to 20%, as defined by BRCAPRO or other models that are largely dependent on family history
Lobular carcinoma in situ or atypical lobular hyperplasia
Atypical ductal hyperplasia
Heterogeneously or extremely dense breast on mammography
Women with a personal history of breast cancer, including ductal carcinoma in situ
Recommend against MRI screening (based on expert consensus opinion)
Women at <15% lifetime risk

ACS: American Cancer Society; MRI: magnetic resonance imaging.

* Evidence from nonrandomized screening trials and observational studies.

Δ Payment should not be a barrier. Screening decisions should be made on a case-by-case basis, as there may be particular factors to support MRI.

Graphic 54270 Version 5.0

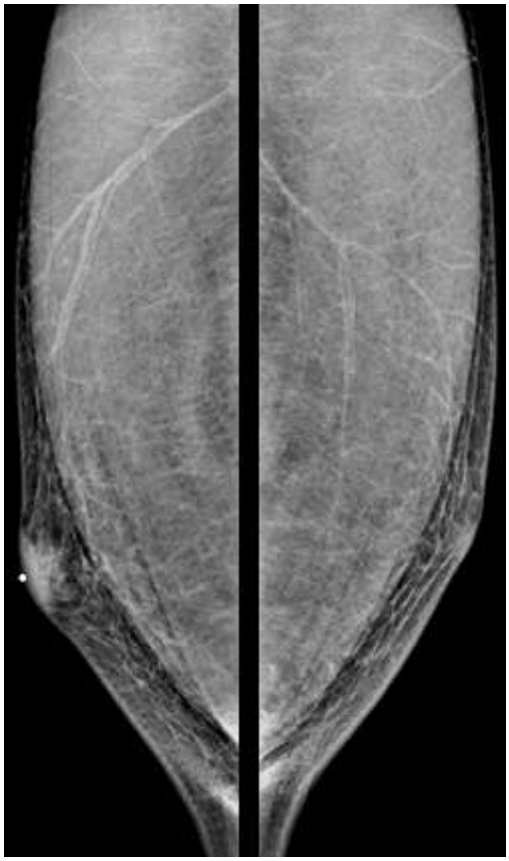
Normal saline implants

Bilateral CC (panels A and B) and MLO (panels C and D) mammographic views obtained with a saline implant in place. The implant capsule is intact. Normal folds (thin arrow) and implant valve (thick arrow) can be seen.

CC: cradiocaudal; MLO: mediolateral oblique.

Graphic 58154 Version 7.0

Normal male breast

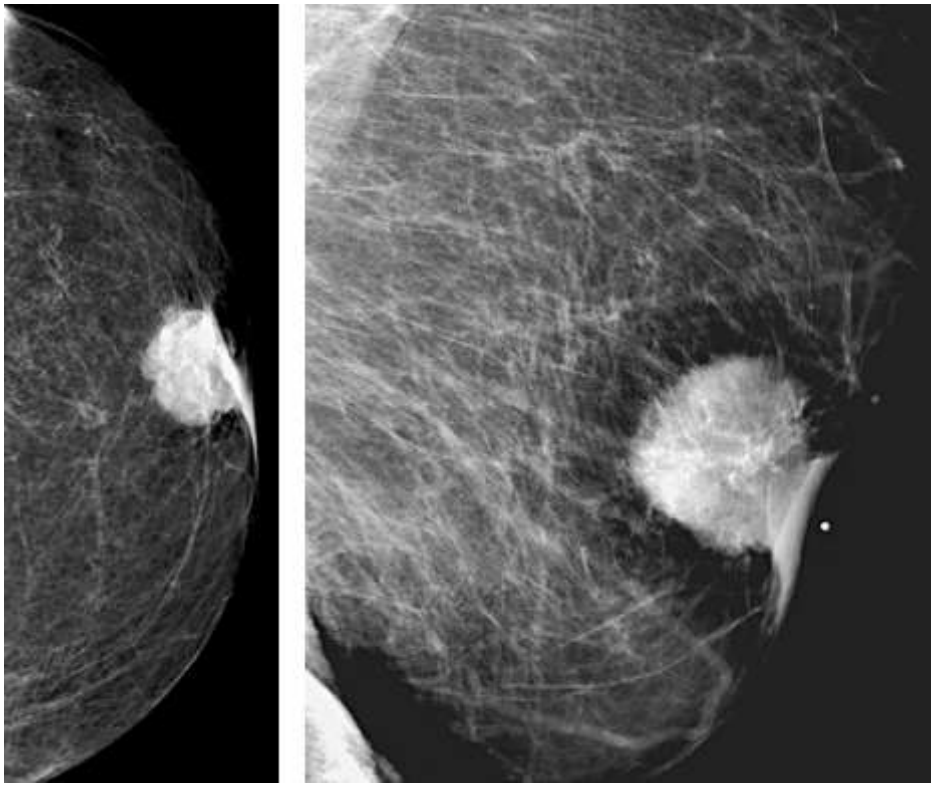


Bilateral MLO views of a normal male breast showing small amount of fatty breast tissue.

MLO: mediolateral oblique.

Graphic 54355 Version 2.0

Male with palpable lump

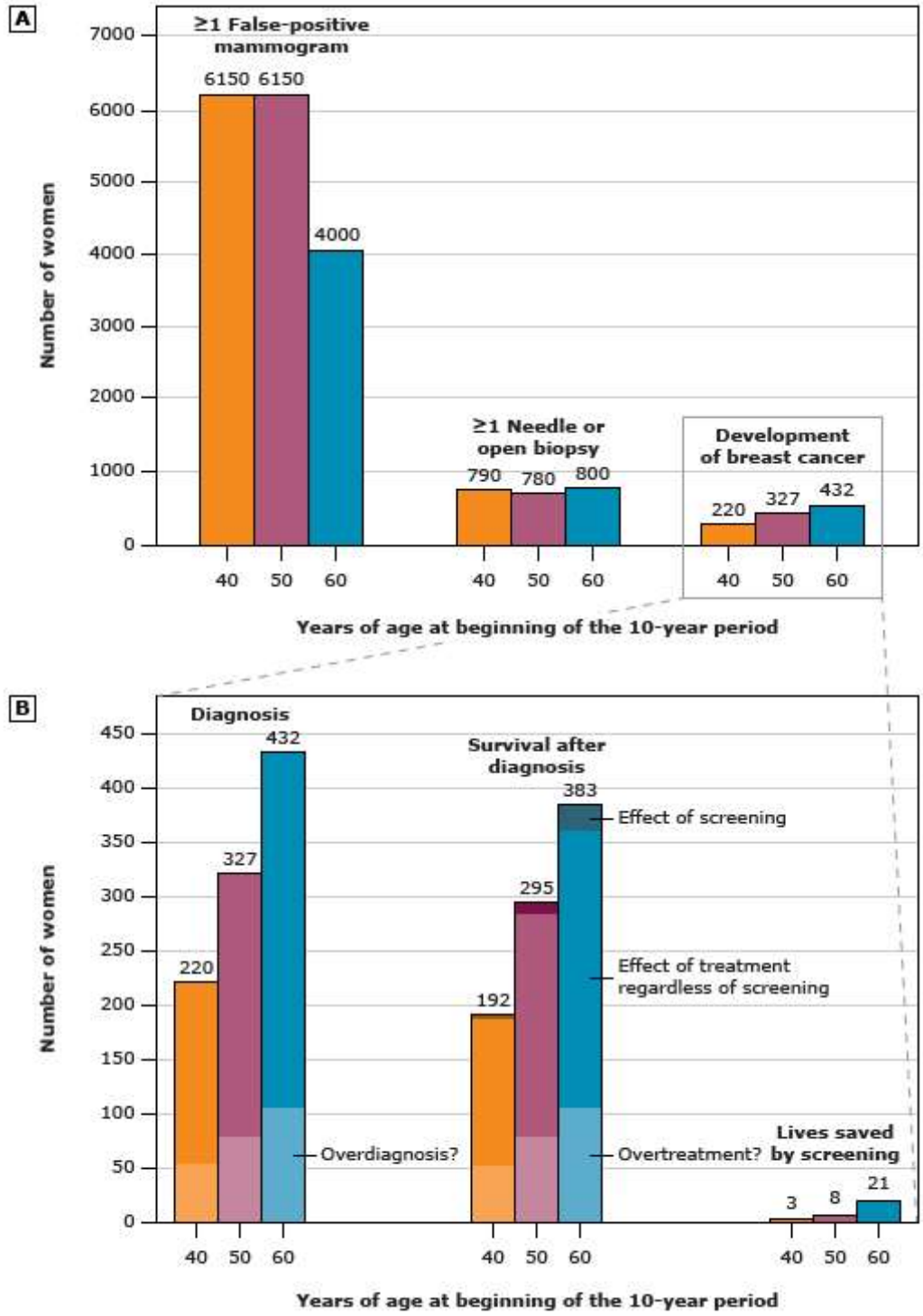


CC and MLO views in a male with a palpable lump behind the nipple. The mammograms show an irregular, dense, spiculated mass. The mammographic appearance of breast cancer in a male is similar to that in a female.

CC: craniocaudal; MLO: mediolateral oblique.

Graphic 70483 Version 2.0

Weighing the benefits and harms when deciding about a preventive activity: Comparing estimated benefits and harms of screening mammography[1-3]



Chances among 1000 women who undergo annual screening mammography for 10 years: (A) of experiencing a false-positive mammogram, undergoing a breast biopsy, and developing breast cancer; and (B) of being cured of breast cancer regardless of screening, and averting death from breast cancer because of screening mammography.

References:

1. *Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2016. Bethesda, MD: National Cancer Institute. Available at: https://seer.cancer.gov/csr/1975_2016/& based on November 2018 SEER data submission, posted to the SEER website, April 2019.*
2. *Nelson HD, Fu R, Cantor A, et al. Effectiveness of breast cancer screening: systematic review and meta-analysis to update the 2009 U.S. Preventive Services Task Force recommendation. Ann Intern Med 2016; 164:244.*
3. *Hubbard RA, Kerlikowske K, Flowers CI, et al. Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography. Ann Intern Med 2011; 155:481.*

Graphic 89378 Version 7.0

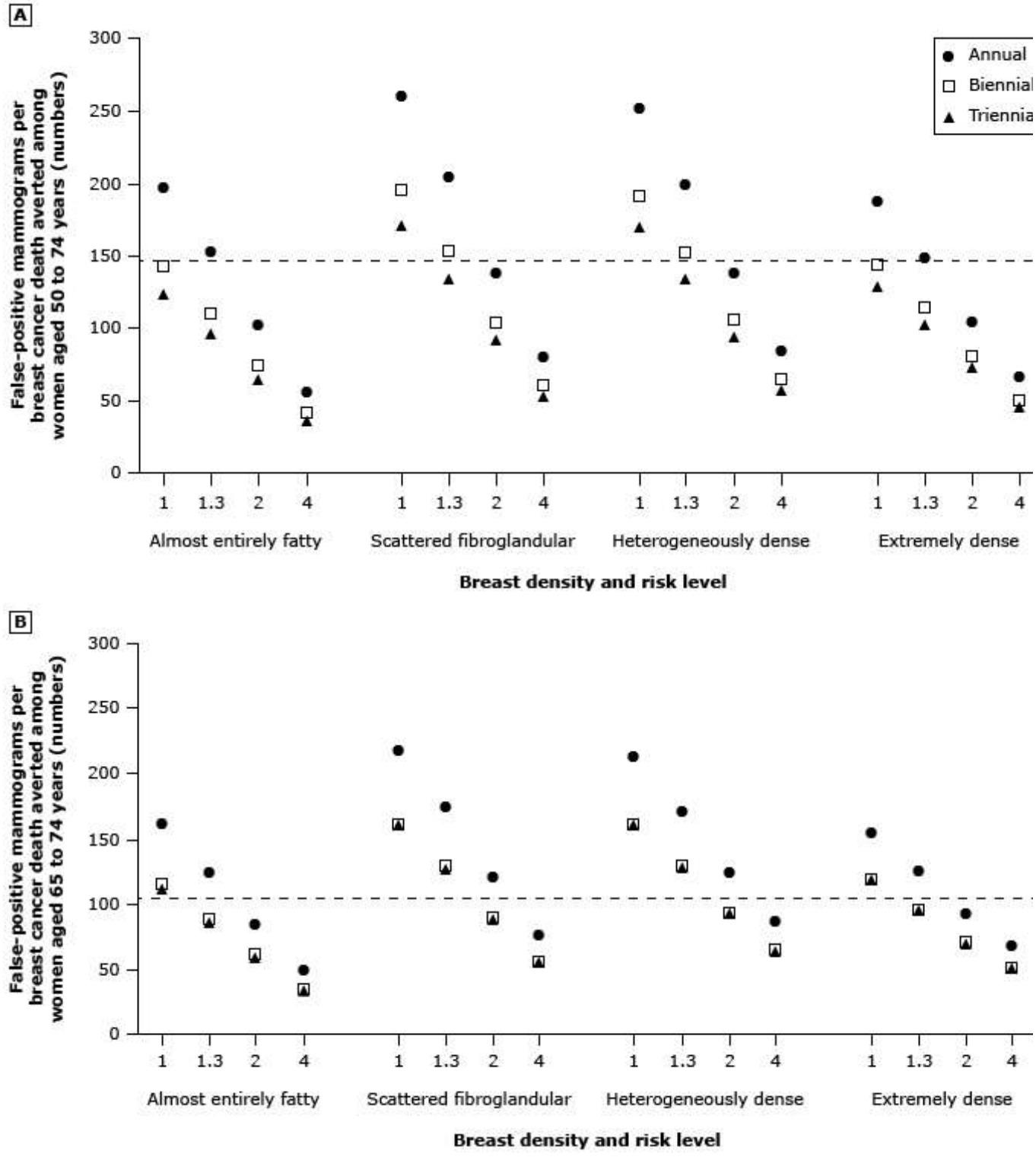
Chances of breast cancer-related outcomes among 1000 women screened annually or biennially, starting at age 40 or 50 and continuing through age 69 or 74

Screening program			Cumulative consequences of screening program			
Mammogram frequency	Starting age	Ending age	Lives saved (number)	Life-years gained (number)	False-positive mammograms (number)	Unnecessary biopsies (number)
Annual						
	40	69	8.3	164	2250	158
	50	69	7.3	132	1350	95
	40	74	10.5	188	2470	173
	50	74	9.5	156	1570	110
Biennial						
	40	69	6.1	120	1250	88
	50	69	5.4	99	780	55
	40	74	8.2	142	1410	99
	50	74	7.5	121	940	66

Adapted and calculated from: Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of Mammography Screening Under Different Screening Schedules: Model Estimates of Potential Benefits and Harms. Ann Intern Med 2009; 151:738.

Graphic 69681 Version 5.0

Breast density, risk level, and false-positive results



Data for women aged 50 to 74 years (A) and 65 to 74 years (B) are shown according to screening frequency and risk level (relative risk group and breast density level) using an exemplar model (Model E* Values for all screening frequencies were compared with the scenario of no mammography screening. Values for women aged 65 to 74 years assume all women received biennial screening during ages 50 to 64 years. Dashed lines show this value for women with average density and average risk receiving biennial screening (147.7 for women aged 50 to 74 years and 105.8 for women aged 65 to 74 years). Having fewer false-positive mammograms per breast cancer death averted than this level—in other words, a value below the dashed line—would be more favorable.

* Model E: microsimulation model (Erasmus Medical Center, Rotterdam, Netherlands).

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Joann G Elmore, MD, MPH No relevant financial relationship(s) with ineligible companies to disclose. **Christoph I Lee, MD, MS** Consultant/Advisory Boards: GRAIL [Cancer screening]. Other Financial Interest: McGraw-Hill [Textbook royalties]; Oxford University Press [Textbook royalties]. All of the relevant financial relationships listed have been mitigated. **Mark D Aronson, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Gary J Whitman, MD** Consultant/Advisory Boards: Siemens [Digital mammography, tomosynthesis, breast cancer]. All of the relevant financial relationships listed have been mitigated. **Jane Givens, MD, MSCE** No relevant financial relationship(s) with ineligible companies to disclose.

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