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Breast Cancer Screening: An Evidence-Based Update

Mackenzie S. Fuller, BA^{*}, Christoph I. Lee, MD, MSHS^{*†}, and Joann G. Elmore, MD, MPH^{*}

^{*}Department of Medicine, University of Washington, Seattle, WA

[†]Department of Radiology, University of Washington, Seattle, WA

Synopsis

Routine screening mammography is recommended by most groups issuing breast cancer screening guidelines, especially for women 50 years of age. However, both the potential benefits and risks of screening should be discussed with individual patients to allow for shared decision-making regarding their participation in screening, age of commencement and conclusion, and interval of mammography screening.

Keywords

Breast cancer screening; false-positive; false-negative; overdiagnosis; mammography; clinical breast examination; breast self-examination; magnetic resonance imaging; informed decision making

Introduction

Breast cancer screening is used to identify women with asymptomatic cancer with the goal of enabling women to undergo less invasive treatments that lead to better outcomes, ideally at earlier stages before the cancer progresses. There are important considerations for who should be screened, how often women should be screened, and with which imaging modality (or modalities). Ultimately, clinicians need to help women understand the benefits and risks of breast cancer screening in order to make informed decisions.

Who should be screened?

Guidelines for who should undergo breast cancer screening vary within and among countries.¹ In the United States, the U.S. Preventive Services Task Force recommends that breast cancer screening with mammography be offered to women 50 to 74 years of age and that starting screening before age 50 years should be based on the individual woman's

Correspondence to: Joann G. Elmore, MD, MPH, University of Washington, 325 Ninth Avenue, Mailbox 359780, Seattle, WA 98104, Telephone: 206-744-3632, Fax: 206-744-9917, jelmore@u.washington.edu.

Mackenzie S. Fuller, BA 325 Ninth Avenue Mailbox 359780 Seattle, WA 98104 Telephone: 206-744-3632 Fax: 206-744-9917 mfuller2@u.washington.edu

Christoph I. Lee, MD, MSHS 825 Eastlake Avenue East, G3-200 Seattle, WA 98109 Telephone: 206-288-6783 stophlee@uw.edu

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context, including her values regarding the benefits and risks.² The American Cancer Society recommends screening starting at age 40.³ Screening women 40 to 49 years of age is more controversial than older ages, with less evidence available to determine the risk-benefit balance. Analyses using six different breast cancer simulation models of the National Cancer Institute-funded Cancer Intervention and Surveillance Modeling Network (CISNET) found that starting biennial (every two years) screening at age 40 years with mammography, in comparison to age 50 years, was associated with reduced breast cancer mortality by an additional 3%, but at the expense of more false-positives and health care resources.⁴

There is little evidence to support screening women of average risk < 40 years of age. These women have a lower incidence of breast cancer and were largely excluded from randomized controlled trials (RCTs) involving screening mammography. Similarly, there is little evidence regarding screening women more than 75 years of age, as older women were also largely excluded from RCTs. Moreover, elderly women are more likely to have co-morbid medical conditions and may experience less marginal benefit from screening. It is not recommended that people with limited life expectancy (< 5 years) undergo routine screening, as early breast cancer detection and treatment could impair quality of life while not improving survival. However, women with limited life expectancy continue to be screened for breast cancer in the U.S.⁵

How often should women be screened?

Countries vary in how often they recommend women undergo breast cancer screening. In a prospective cohort study of U.S. women, it was found that after 10 years of screening with mammography, the cumulative probability of a woman receiving a false positive recall (of being called back for additional examination after abnormal screening but subsequently found to not have cancer) was lower with biennial screening than with annual screening.⁶ In addition, analyses using six CISNET simulation models found that biennial screening mammography maintained most of the benefit of annual screening while reducing false positive results by almost half.⁴ The United States Preventive Services Task Force, thus, currently recommends that women without additional risk factors undergo screening mammography biennially starting at age 50.

Methods of breast cancer screening

Breast cancer screening modalities include both physical breast exams as well as mammographic imaging. Additional supplemental screening with breast MRI may be considered for special high-risk populations.

Physical Examination

Breast self-examination—Many awareness campaigns encourage women to conduct monthly breast self-examinations. However, the evidence for mortality reduction from breast self-examination is limited. This topic has been investigated in randomized controlled trials, case-control studies, nonrandomized trials, and cohort studies.⁷ While self-examination may lead to detection of lesions at a smaller size, increased false positives and more testing have

been noted with no reduction in mortality. Breast self-exam is no longer recommended by most guidelines.

Clinical breast examination—Clinical breast examination by a health care provider has been studied as a screening method used in conjunction with mammography. In the Canadian National Breast Screening Study of women age 50 to 59 years receiving either mammography and clinical breast examination or only clinical breast examination, the 25 year cumulative mortality from breast cancer diagnosed during the screening period was essentially equivalent between women who received mammography and clinical breast examination versus women who received only clinical breast examination.⁸ Of note, the clinical breast exams were performed by well-trained clinicians, the quality of the clinical breast exams were periodically evaluated, and the clinicians spent 5-10 minutes examining each breast.⁹ Community clinicians may not perform such high quality clinical breast exams, limiting the applicability of these results to general practice.

Imaging

Sample images of a right breast cancer screen-detected by full-field digital mammography and then seen on magnetic resonance imaging and ultrasound are included in Figure 2.

Screen-film mammography—Historically, screen-film mammography had been the standard method of breast cancer screening. In screen-film mammography, images were developed and fixed chemically, a process similar to film photography. Processing errors led to > 20 percent of images being rejected,¹⁰ resulting in repeat imaging which increased examination time, exposure to ionizing radiation, and costs. In the U.S., screen-film mammography has now largely been replaced by full-field digital mammography.

Full-field digital mammography—In full-field digital mammography, images are immediately displayed on a computer monitor for interpretation, enabling more rapid interpretation than with screen-film mammography.¹¹ The digital display also enables the use of computer-aided detection (CAD) software, which recognizes suspicious image patterns to aid in cancer detection. Full-field digital mammography has been shown to have higher contrast, lower noise, and greater dynamic range than screen-film mammography.¹²

Several clinical trials have found full-field digital mammography to be of similar or greater accuracy than screen-film mammography.¹³⁻¹⁵ The Digital Mammography Imaging Screening Trial (DMIST) found full-field digital mammography to be of similar accuracy to screen-film mammography overall and of greater accuracy than screen-film mammography for three subpopulations: women < 50 years of age, pre- or peri-menopausal women, and women with mammographically dense breast tissue.¹⁶ Given this evidence and the other benefits of full-field digital mammography, including ease of storage and retrieval of images, full-field digital mammography has been progressively adopted as the modality of choice for breast cancer screening in the U.S.¹⁷ and now accounts for > 95% of all functioning mammography units in the U.S.¹⁸

Computer-Aided Detection—Computer-aided detection (CAD) software highlights potentially abnormal image features for radiologists. Early reports suggested that CAD was

associated with improved detection of malignancies when used with either screen-film mammography or full-field digital mammography.^{19,20} However, other reports suggest that CAD results in a significantly higher rate of false positives, as the programs usually add two to five marks per screening case on typical screening exams.^{19,21-23} In addition, CAD's effect on patient outcomes (e.g., mortality) is currently uncertain. CAD has been found to increase detection of ductal carcinoma in situ (DCIS) and, in women without breast cancer, is associated with increased diagnostic testing after screening.²⁴ Results have been mixed regarding the effect of CAD on the stage at which invasive breast cancer is detected.^{24,25} Despite such uncertainty and lack of data on outcomes, CAD is widely used with screening mammography.²⁶

Digital Breast Tomosynthesis—With digital breast tomosynthesis, a rotating gantry takes images of the breast from various angles in order to create a three-dimensional view.²⁷ This FDA-approved technology is now a standard feature in newer digital mammography units and rapidly diffusing into U.S. community practice.²⁸ The radiation dose from digital breast tomosynthesis equals the dose from routine mammography; thus, combined full-field digital mammography and digital breast tomosynthesis currently doubles the radiation dose at screening.²⁹ In May 2013, however, the FDA approved software allowing the reconstruction of the standard two-dimensional mammography image from the three-dimensional tomosynthesis acquisition, negating the doubling of radiation dose.

In two-dimensional full-field digital mammography, fibroglandular tissue directly above or below tumors can mask them, reducing sensitivity. Digital breast tomosynthesis's three-dimensional views enable radiologists to go through breast tissue slice by slice, reducing this masking effect. Two population-based screening studies in Europe and one large retrospective study in the U.S. have shown significantly increased cancer detection rates and decreased false-positive recall rates when digital breast tomosynthesis is added to full-field digital mammography.³⁰⁻³² Digital breast tomosynthesis may therefore reduce both patient morbidity and medical costs by reducing unnecessary diagnostic workups. In addition, digital breast tomosynthesis is less expensive and easier to use than other supplemental breast imaging tests such as screening ultrasound and screening MRI.²⁸

Magnetic Resonance Imaging and Ultrasound—Magnetic resonance imaging (MRI) and ultrasound are useful tools for evaluating abnormalities and diagnosing breast cancer, but they are not recommended as screening modalities for the general population. No studies have shown a mortality benefit for the general population from these imaging modalities. However, there may be mortality benefit for using MRI or ultrasound for supplemental screening in special very high-risk populations such as women with *BRCA1* and *BRCA2* mutations (see below).

Digital Infrared Thermal Imaging—A number of emerging imaging technologies are being developed for breast cancer screening and diagnosis. One that is gaining popularity is digital infrared thermal imaging or breast thermography, which aims to detect malignancy by identifying higher local skin temperature due to increased vascularization and inflammation caused by a developing malignancy.³³ Unfortunately, a recent systematic review concluded that there is currently insufficient evidence to recommend the use of this

technology for breast cancer screening, with significant heterogeneity identified in published studies for both digital infrared thermal imaging's sensitivity (0.25-0.97) and specificity (0.12-0.85).³⁴

Special Populations

Dense breasts—Dense breast tissue reduces screening mammography's sensitivity to detect breast cancer,³⁵ and women with dense breasts have three to five times greater lifetime risk of developing breast cancer than women with mostly fatty breasts,³⁶⁻³⁸ regardless of other risk factors.³⁹ Breast density falls along a spectrum from almost entirely fat, to scattered fibroglandular densities, to heterogeneously dense, to extremely dense (Figure 1). As of September 2014, 19 U.S. states (AL, AZ, CA, CT, HI, MA, MD, MN, MO, NC, NJ, NV, NY, OR, PA, RI, TN, TX, VA) have enacted laws requiring that imaging centers notify patients with heterogeneously or extremely dense breasts that they may be at greater risk of developing breast cancer.⁴⁰ Some states also require, even though there are no supporting data, that women with dense breasts discuss potential benefits from additional screening (e.g., ultrasound) beyond mammography with their physicians.⁴¹

ACRIN 6666, the largest trial comparing the addition of screening ultrasound to mammography in women with dense breasts and at least one other risk factor, demonstrated a detection rate of 4.3 additional cancers per 1000 women screened.⁴² This increased detection was accompanied by an increase in biopsy rates from 2% to 5% of all women screened after adding ultrasound, with only 7.4% of the additional biopsies being positive for cancer – indicating a high false positive rate.⁴² Moreover, the ultrasound exams in ACRIN 6666 were performed by subspecialty-trained breast imagers, raising uncertainty about what the results would be for screening ultrasound performed by general community radiologists and/or technologists.⁴¹

BRCA1 and BRCA2 mutations—Women with *BRCA1* and *BRCA2* gene mutations have a very high risk of developing breast and ovarian cancer during their lifetime. Two meta-analyses estimate cumulative risk of breast cancer by age 70 to be 55% to 65% for women with *BRCA1* and 45% to 47% for women with *BRCA2*.^{43,44} Some carriers elect to undergo prophylactic mastectomy because of this increased risk. For women who don't choose this surgical option, there is debate about the best breast cancer screening strategy.

Generally, women with either of these mutations are advised to consider starting both screening mammography and screening MRI before the age of 40. In 1997, the Cancer Genetics Studies Consortium Task Force recommended that female carriers of *BRCA1* or *BRCA2* initiate annual mammograms between the ages of 25 to 35, using a consistent facility with prior films available for comparison.⁴⁵ Since then, the National Comprehensive Cancer Network has recommended both mammography and MRI screening starting at age 25,⁴⁶ the American College of Radiology recommends starting at age 30,⁴⁷ and the American Cancer Society recommends that individual preferences and circumstances guide the initiation of screening.⁴⁸

Early evidence indicates, however, that mammography is less sensitive for women with *BRCA1* or *BRCA2* mutations than for women without these mutations.⁴⁹ In addition,

tumors in women with these mutations grow rapidly, such that a detectable malignancy could form in between breast cancer screening examinations.⁵⁰

There is mixed evidence concerning whether radiation, including from mammography, increases the risk of breast cancer in women with *BRCA1* and *BRCA2* mutations, with some studies showing that mutation carriers may be more prone to radiation-induced breast cancer than women without mutations⁵¹ and other studies not showing an increased risk from radiation.^{52,53} While it is important to weigh the benefits of mammography against the risks, there is insufficient evidence to suggest that female carriers of *BRCA1* or *BRCA2* should avoid mammography due to radiation exposure.

There have been several limitations on the studies describing outcomes of using MRI to screen women at high risk of breast cancer.⁵⁴⁻⁶² These include limited numbers of screening rounds; lack of clarity regarding prevalent (first round of screening) and incident cancer detection rates; and varied underlying populations, equipment, protocols, and reporting of results. However, studies have consistently demonstrated that breast MRI is more sensitive than mammography or ultrasound in detecting hereditary breast cancer, though MRI has reduced specificity.^{54-56,60,63,64} Some breast cancers are identified with mammography but missed with MRI. Annual MRI screening of women with the *BRCA1* mutation, in conjunction with annual screening mammography, has been shown in simulation modeling to be cost effective.^{65,66} One approach to applying current guidelines to *BRCA1* gene mutation carriers is to alternate MRI and mammography screening in six month intervals beginning at age 30 years.⁶⁷

Women with lifetime risk of breast cancer of >20%—In addition to women with *BRCA* genes, annual MRI screening is recommended for women with a lifetime risk of breast cancer > 20%, which includes women with a strong family history of breast or ovarian cancer and women treated with radiation for Hodgkin lymphoma.⁴⁸ Unlike mammography, MRI does not use ionizing radiation, thus limiting a known risk factor for developing breast cancer.

Potential benefits and risks

Potential benefits

Mortality reduction—Screening mammography has been associated with reduced mortality from breast cancer in women 40 to 70 years of age, with absolute risk reduction increasing with age. Figure 3 shows the breast cancer mortality risk ratios found in RCTs of breast cancer screening. As shown in Table 1, adapted from a systematic review of the benefits and risks of screening mammography,⁶⁸ the number of breast cancer deaths averted with screening mammography in the next 15 years out of 10,000 women undergoing annual screening mammography for 10 years is 1-16 for women aged 40 years, 3-32 women aged 50 years, and 5-49 for women aged 60 years.

Decreased morbidity from therapies for cancers detected at earlier stages—

When screening detects cancer at an earlier stage, a woman can undergo less invasive therapies than she would if the cancer were diagnosed at a later stage. Compared to cancers

detected with physical examination (palpable tumors), breast cancers detected with screening mammography are usually smaller, less likely to have metastasized, more likely to be treated with breast conservation surgery (56% versus 32%), and less likely to receive adjunct chemotherapy (28% versus 56%).^{69,70} Thus, breast cancer screening is associated with increased treatment options and decreased morbidity from invasive therapies such as mastectomy and complete axillary node dissection.⁷¹

Psychological benefit—Another benefit of screening mammography is the peace of mind some women receive from participating in screening and receiving a negative or “normal” mammogram. This benefit has not been well-documented or studied and is often ignored in risk-benefit discussions regarding population-based breast cancer screening.

Potential Risks

Pain and discomfort—During a mammogram, a woman's breasts are compressed in order to create uniform breast density, improve image resolution by reducing motion artifact, and reduce radiation dose. A systematic review of studies evaluating physical pain and discomfort from mammography found that reports of pain were associated with women's menstrual cycles and expectations, rather than from mammographic compression.⁷² While most women experienced some discomfort, few of these women considered compression a deterrent from undergoing screening.

Radiation exposure—Ionizing radiation can increase one's risk of developing breast cancer, as seen in women who have received therapeutic radiation to the chest (e.g., for Hodgkin lymphoma).⁷³⁻⁷⁵ The mean glandular dose from mammography in the U.S. is 1 to 2 mGy (100 to 200 mrad) per view, amounting to 2 to 4 mGy (200 to 400 mrad) per standard two-view examination.^{73,76} There is no way to know if and how many breast cancers are actually being caused by screening mammography. Still, the potential risk has prompted efforts to limit exposure by reducing the amount of radiation required for mammography screening, developing imaging modalities that do not use radiation (e.g., ultrasound and MRI), and modifying screening strategies for subpopulations especially vulnerable to radiation.^{77,78}

False positives—A false positive result occurs when a screening mammogram is interpreted as abnormal in a woman who does not have cancer. In the United States, the false positive rate is estimated to be 10% of women screened with mammography.^{79,80} Table 1 shows estimates that out of 10,000 women screened annually with mammography for 10 years, 4,970 to 6,130 women will receive at least one false positive result in 10 years. It is estimated that 700 to 980 women who receive false positives undergo unnecessary biopsies. In a retrospective study that quantified the cumulative risk of receiving false positive results by following women who were continually enrolled in a U.S. health plan for a decade, the authors estimated the cumulative risk of a woman receiving at least one false positive result as 49.1% (95% CI, 40.3-64.1) after 10 mammograms and 22.3% (95% CI, 19.2-27.5) after 10 clinical breast exams.⁸¹ The cumulative rates of breast biopsies for women without breast cancer were 18.6% (95% CI, 9.8-41.2) after 10 mammograms and 6.2% (95% CI, 3.7-11.2) after 10 clinical breast exams.

The risk of false positives varies depending on the characteristics of women screened, the screening modality used, and the radiologist interpreting the exam.⁸² Risk increases with patient variables (e.g., younger age, higher number of previous breast biopsies, family history of breast cancer, current estrogen use) and interpretive variables (e.g., longer time between screening, failure to compare current with previous mammograms), and the radiologist's tendency to interpret mammograms as abnormal has the greatest effect on false positive risk.

False positive rates may vary by country as well.⁸³ One review of 32 breast cancer screening programs noted global variation in the percentage of mammograms interpreted as abnormal (ranging from 1.2% to 15%) and the number of biopsies performed (ranging from 5% to 85.5%).⁸⁴ A higher percentage of mammograms interpreted as abnormal in North America was noted, despite cancer rates being similar.⁸⁴ False positive rates may be even higher with the use of additional screening modalities such as CAD and MRI. Studies suggest that 8% to 15% of women who undergo screening MRI are called back for additional evaluation and 3% to 15% will ultimately undergo breast biopsies.^{55,56,85}

Anxiety—Emotional discomfort and anxiety can result from being called back for diagnostic work-up after an abnormal mammogram. Several studies demonstrate that women who receive clear communication about negative screening results experience minimal anxiety about screening, while women who are recalled for additional diagnostic evaluation experience transient to persistent levels of anxiety.⁸⁶ In one study, women who initially received abnormal screening results but were subsequently found not to have cancer still experienced worry that affected their mood or functioning three months after screening.⁸⁷ A systematic review found that women who experience anxiety after a false positive mammography result receive more frequent future screening mammograms.⁸⁸

False negatives—All breast cancer screening modalities can yield a false negative: a negative screening result when the patient does have breast cancer, as proven by biopsy. For example, a lesion may not be viewable on imaging. Both women and their clinicians need to learn to not be falsely reassured by a normal imaging exam in the setting of a clinically detectable mass, as this can lead to delays in diagnosis and treatment.

Cost—In the U.S., mammography is estimated to account for almost \$8 billion in annual health care expenditures.^{89,90} Modeling estimates of screening mammography in the U.S. indicate that screening 85% of women would cost \$10.1 billion with annual screening of women age 40 to 84 years (the American Cancer Society recommendation); \$2.6 billion with biennial screening of women age 50 to 69 years (the European approach); and \$3.5 billion with biennial screening for women age 50 to 74 years, personalized risk-based screening for women < age 50 years, and screening based on comorbid conditions for women age 75 years (USPSTF recommendations).⁸⁹ Other imaging modalities (e.g. MRI) are more expensive than mammography, and they can result in greater recall for diagnostic evaluation.

Overdiagnosis—Overdiagnosis occurs when a woman is diagnosed with a breast cancer that would not have manifested with symptoms during a woman's lifetime; in other words,

she would die of other causes before developing symptoms of breast cancer.⁹¹ Once diagnosed, a woman might undergo treatments such as surgery, radiation, chemotherapy, and hormonal therapy, resulting in unnecessary costs and harms. While it is difficult to determine the magnitude of overdiagnosis, the estimated range of breast cancer cases being overdiagnosed is between 7% to 50%.⁹²⁻⁹⁶ As shown in Table 1, one estimate is that among 10,000 women undergoing screening mammography annually for ten years, 30 to 194 women will be overdiagnosed with either DCIS or invasive breast cancer. Unfortunately, there is currently no way to determine at diagnosis of asymptomatic DCIS or invasive breast cancer whether or not the lesion will manifest symptomatically and ultimately cause harm to the woman; therefore, the current standard is to recommend treating all diagnosed DCIS and invasive breast cancer.

Interpretation of screening mammography results

Clinicians receive screening mammography results for their patients in standardized lexicon using the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS).⁹⁷ Screening mammograms interpreted as normal or benign (BI-RADS assessment categories 1 and 2, respectively) correspond with a clinical management recommendation of continued routine screening, though the decision to continue screening should be based on the woman's preferences. Almost all abnormal screening mammograms are interpreted as BI-RADS assessment category 0, which indicates an incomplete assessment and request for additional diagnostic mammographic views and/or ultrasound. Some radiologists will provide a "probably benign" assessment at screening and recommend short-term follow-up mammography in 6 months. This designation corresponds to a radiologist's belief that the finding harbors < 2% of malignancy. Rarely, radiologists will provide a BI-RADS 4 or 5 category assessment, deeming an imaging finding as suspicious for malignancy; these designations are usually reserved for after a complete diagnostic work-up has been completed.

Communication

Communication with women before screening

Before women begin routine screening, clinicians should address patients' fears, concerns, and desires regarding screening, along with their underlying risk. Women may have an incorrect perception of their risk of dying of breast cancer. While 1 in 8 women will be diagnosed with invasive breast cancer during their lifetime, the majority of women diagnosed will not die from their breast cancer. In addition, the majority of breast cancers are diagnosed in older women.

In terms of discussing breast cancer screening with women in order to facilitate informed decision making, physicians have traditionally been more likely to discuss the benefits than the harms of screening and frequently do not ask about women's preferences.⁹⁸ Therefore, physicians should make an effort to discuss both the benefits and the harms of screening with their patients, as presented in Box 1. In addition, once a woman has decided to undergo screening mammography, her physician should provide her with information to help her prepare for the exam and facilitate clear, useful test result interpretation.

Communication with women after screening

If a woman receives an abnormal screening result, she might be anxious about the possibility of having breast cancer. Clinicians should help women navigate further testing and explain the likelihood that it could be a false positive based on the reported BI-RADS assessment. Women should understand that a positive screening result does not mean that they have cancer, only that they need additional examinations to rule out breast cancer. Similarly, women should understand that it is possible to receive a false negative result, as no screening test is perfect.

Conclusion

Mammography is the best-studied breast cancer screening modality and the only recommended imaging tool for screening the general population of women. Deciding when and how to participate in screening should involve a personalized discussion between a woman and her provider, weighing the individual breast cancer risk factors and competing co-morbidities. In addition, a balanced discussion regarding both the benefits and risks of routine screening is warranted.

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References

1. International Cancer Screening Network. [September 4, 2014] Breast Cancer Screening Programs in 26 ICSN Countries, 2012: Organization, Policies, and Program Reach. 2013. <http://appliedresearch.cancer.gov/icsn/breast/screening.html>
2. U.S. Preventive Services Task Force. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Annals of internal medicine*. 2009; 151(10):716–726. [PubMed: 19920272]
3. Berg AO. Mammography screening: are women really giving informed consent? (Counterpoint). *Journal of the National Cancer Institute*. Oct 15; 2003 95(20):1511–1512. discussion 1512–1513. [PubMed: 14559871]
4. Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. *Annals of Internal Medicine*. Nov 17; 2009 151(10):738–747. [PubMed: 19920274]
5. Royce TJ, Hendrix LH, Stokes WA, Allen IM, Chen RC. Cancer screening rates in individuals with different life expectancies. *JAMA internal medicine*. 2014
6. Hubbard RA, Kerlikowske K, Flowers CI, Yankaskas BC, Zhu W, Miglioretti DL. Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography: a cohort study. *Annals of Internal Medicine*. Oct 18; 2011 155(8):481–492. [PubMed: 22007042]
7. Kusters JP, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. *Cochrane Database Syst Rev*. 2003; (2):CD003373. [PubMed: 12804462]
8. Miller AB, Wall C, Baines CJ, Sun P, To T, Narod SA. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ*. 2014; 348:g366. 2014-02-11. [PubMed: 24519768]
9. Baines CJ, Miller AB, Bassett AA. Physical examination. Its role as a single screening modality in the Canadian National Breast Screening Study. *Cancer*. May 1; 1989 63(9):1816–1822. [PubMed: 2702588]

10. Iared W, Shigueoka DC, Torloni MR, et al. Comparative evaluation of digital mammography and film mammography: systematic review and meta-analysis. *Sao Paulo medical journal = Revista paulista de medicina*. 2011; 129(4):250–260. [PubMed: 21971901]
11. Pisano ED, Yaffe MJ. Digital mammography. *Radiology*. Feb; 2005 234(2):353–362. [PubMed: 15670993]
12. Shtern F. Digital mammography and related technologies: a perspective from the National Cancer Institute. *Radiology*. Jun; 1992 183(3):629–630. [PubMed: 1584908]
13. Skaane P. Studies comparing screen-film mammography and full-field digital mammography in breast cancer screening: updated review. *Acta radiologica (Stockholm, Sweden : 1987)*. Jan; 2009 50(1):3–14.
14. Skaane P, Hofvind S, Skjennald A. Randomized trial of screen-film versus full-field digital mammography with soft-copy reading in population-based screening program: follow-up and final results of Oslo II study. *Radiology*. Sep; 2007 244(3):708–717. [PubMed: 17709826]
15. Skaane P, Skjennald A, Young K, et al. Follow-up and final results of the Oslo I Study comparing screen-film mammography and full-field digital mammography with soft-copy reading. *Acta radiologica (Stockholm, Sweden : 1987)*. Nov; 2005 46(7):679–689.
16. Pisano ED, Gatsonis CA, Yaffe MJ, et al. American College of Radiology Imaging Network digital mammographic imaging screening trial: objectives and methodology. *Radiology*. Aug; 2005 236(2):404–412. [PubMed: 15961755]
17. Houssami N, Ciatto S. The evolving role of new imaging methods in breast screening. *Preventive Medicine*. Sep; 2011 53(3):123–126. [PubMed: 21605590]
18. U.S. Food and Drug Administration. [September 26, 2014] Mammography Quality Standards Act and Program (MQSA) National Statistics. 2014. http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/FacilityScorecard/uc_m113858.htm.
19. Warren Burhenne LJ, Wood SA, D'Orsi CJ, et al. Potential contribution of computer-aided detection to the sensitivity of screening mammography. *Radiology*. May; 2000 215(2):554–562. [PubMed: 10796939]
20. Brem RF, Baum J, Lechner M, et al. Improvement in sensitivity of screening mammography with computer-aided detection: a multiinstitutional trial. *AJR. American journal of roentgenology*. Sep; 2003 181(3):687–693. [PubMed: 12933460]
21. The JS, Schilling KJ, Hoffmeister JW, Friedmann E, McGinnis R, Holcomb RG. Detection of breast cancer with full-field digital mammography and computer-aided detection. *AJR. American journal of roentgenology*. Feb; 2009 192(2):337–340. [PubMed: 19155392]
22. Yang SK, Moon WK, Cho N, et al. Screening mammography-detected cancers: sensitivity of a computer-aided detection system applied to full-field digital mammograms. *Radiology*. Jul; 2007 244(1):104–111. [PubMed: 17507722]
23. Freer TW, Ulissey MJ. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. *Radiology*. 2001; 220(3):781–786. [PubMed: 11526282]
24. Fenton JJ, Xing G, Elmore JG, et al. Short-term outcomes of screening mammography using computer-aided detection: a population-based study of medicare enrollees. *Ann Intern Med*. Apr 16; 2013 158(8):580–587. [PubMed: 23588746]
25. Fenton JJ, Abraham L, Taplin SH, et al. Effectiveness of computer-aided detection in community mammography practice. *J Natl Cancer Inst*. Aug 3; 2011 103(15):1152–1161. [PubMed: 21795668]
26. Rao VM, Levin DC, Parker L, Cavanaugh B, Frangos AJ, Sunshine JH. How widely is computer-aided detection used in screening and diagnostic mammography? *J Am Coll Radiol*. Oct; 2010 7(10):802–805. [PubMed: 20889111]
27. Diekmann F, Bick U. Breast tomosynthesis. *Seminars in Ultrasound, CT and MR*. Aug; 2011 32(4):281–287.
28. Gur D. Tomosynthesis: potential clinical role in breast imaging. *AJR. American journal of roentgenology*. Sep; 2007 189(3):614–615. [PubMed: 17715108]

29. Lee CI, Lehman CD. Digital breast tomosynthesis and the challenges of implementing an emerging breast cancer screening technology into clinical practice. *J Am Coll Radiol*. Dec; 2013 10(12): 913–917. [PubMed: 24295940]
30. Ciatto S, Houssami N, Bernardi D, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. *Lancet Oncol*. 2013; 14(7):583–589. [PubMed: 23623721]
31. Skaane P, Bandos AI, Gullien R, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology*. Apr; 2013 267(1):47–56. [PubMed: 23297332]
32. Friedewald SM, Rafferty EA, Rose SL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. *Jama*. 2014; 311(24):2499–2507. [PubMed: 25058084]
33. Anbar M. Clinical thermal imaging today. *IEEE engineering in medicine and biology magazine : the quarterly magazine of the Engineering in Medicine & Biology Society*. Jul-Aug;1998 17(4): 25–33.
34. Vreugdenburg TD, Willis CD, Mundy L, Hiller JE. A systematic review of elastography, electrical impedance scanning, and digital infrared thermography for breast cancer screening and diagnosis. *Breast Cancer Res Treat*. Feb; 2013 137(3):665–676. [PubMed: 23288346]
35. Ciatto S, Visioli C, Paci E, Zappa M. Breast density as a determinant of interval cancer at mammographic screening. *British journal of cancer*. Jan 26; 2004 90(2):393–396. [PubMed: 14735182]
36. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. *Cancer Epidemiology, Biomarkers and Prevention*. Jun; 2006 15(6): 1159–1169.
37. Byrne C, Schairer C, Wolfe J, et al. Mammographic features and breast cancer risk: effects with time, age, and menopause status. *Journal of the National Cancer Institute*. Nov 1; 1995 87(21): 1622–1629. [PubMed: 7563205]
38. Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. *New England Journal of Medicine*. Jan 18; 2007 356(3):227–236. [PubMed: 17229950]
39. Vachon CM, van Gils CH, Sellers TA, et al. Mammographic density, breast cancer risk and risk prediction. *Breast cancer research : BCR*. 2007; 9(6):217. [PubMed: 18190724]
40. Are you dense advocacy Inc.. [September 8, 2014] D.E.N.S.E. State Efforts. <http://www.areyoudenseadvocacy.org/dense/>.
41. Lee CI, Bassett LW, Lehman CD. Breast density legislation and opportunities for patient-centered outcomes research. *Radiology*. Sep; 2012 264(3):632–636. [PubMed: 22919037]
42. Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA*. Apr 4; 2012 307(13):1394–1404. [PubMed: 22474203]
43. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet*. May; 2003 72(5):1117–1130. [PubMed: 12677558]
44. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. *J Clin Oncol*. Apr 10; 2007 25(11):1329–1333. [PubMed: 17416853]
45. Burke W, Daly M, Garber J, et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. II. BRCA1 and BRCA2. Cancer Genetics Studies Consortium. *JAMA*. Mar 26; 1997 277(12):997–1003. [PubMed: 9091675]
46. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 2 ed. National Comprehensive Cancer Network; Jenkintown, PA: 2011.
47. Lee CH, Dershaw DD, Kopans D, et al. Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J Am Coll Radiol*. Jan; 2010 7(1):18–27. [PubMed: 20129267]

48. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA: a cancer journal for clinicians*. Mar-Apr;2007 57(2):75–89. [PubMed: 17392385]
49. Tilanus-Linthorst M, Verhoog L, Obdeijn IM, et al. A BRCA1/2 mutation, high breast density and prominent pushing margins of a tumor independently contribute to a frequent false-negative mammography. *International Journal of Cancer*. Nov 1; 2002 102(1):91–95. [PubMed: 12353239]
50. Tilanus-Linthorst MM, Kriege M, Boetes C, et al. Hereditary breast cancer growth rates and its impact on screening policy. *European Journal of Cancer*. Jul; 2005 41(11):1610–1617. [PubMed: 15978801]
51. Andrieu N, Easton DF, Chang-Claude J, et al. Effect of chest X-rays on the risk of breast cancer among BRCA1/2 mutation carriers in the international BRCA1/2 carrier cohort study: a report from the EMBRACE, GENEPSO, GEO-HEBON, and IBCCS Collaborators' Group. *J Clin Oncol*. Jul 20; 2006 24(21):3361–3366. [PubMed: 16801631]
52. Narod SA, Lubinski J, Ghadirian P, et al. Screening mammography and risk of breast cancer in BRCA1 and BRCA2 mutation carriers: a case-control study. *Lancet Oncol*. May; 2006 7(5):402–406. [PubMed: 16648044]
53. Goldfrank D, Chuai S, Bernstein JL, et al. Effect of mammography on breast cancer risk in women with mutations in BRCA1 or BRCA2. *Cancer Epidemiology, Biomarkers and Prevention*. Nov; 2006 15(11):2311–2313.
54. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA*. Sep 15; 2004 292(11):1317–1325. [PubMed: 15367553]
55. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *New England Journal of Medicine*. Jul 29; 2004 351(5):427–437. [PubMed: 15282350]
56. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet*. May 21-27; 2005 365(9473):1769–1778. [PubMed: 15910949]
57. Lehman CD, Blume JD, Weatherall P, et al. Screening women at high risk for breast cancer with mammography and magnetic resonance imaging. *Cancer*. May 1; 2005 103(9):1898–1905. [PubMed: 15800894]
58. Lehman CD, Isaacs C, Schnall MD, et al. Cancer yield of mammography, MR, and US in high-risk women: prospective multi-institution breast cancer screening study. *Radiology*. Aug; 2007 244(2):381–388. [PubMed: 17641362]
59. Sardanelli F, Podo F, D'Agnolo G, et al. Multicenter comparative multimodality surveillance of women at genetic-familial high risk for breast cancer (HIBCRIT study): interim results. *Radiology*. Mar; 2007 242(3):698–715. [PubMed: 17244718]
60. Kuhl C, Weigel S, Schrading S, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. *J Clin Oncol*. Mar 20; 2010 28(9):1450–1457. [PubMed: 20177029]
61. Shah P, Rosen M, Stopfer J, et al. Prospective study of breast MRI in BRCA1 and BRCA2 mutation carriers: effect of mutation status on cancer incidence. *Breast Cancer Research and Treatment*. Dec; 2009 118(3):539–546. [PubMed: 19609668]
62. Rijnsburger AJ, Obdeijn IM, Kaas R, et al. BRCA1-associated breast cancers present differently from BRCA2-associated and familial cases: long-term follow-up of the Dutch MRISC Screening Study. *J Clin Oncol*. Dec 20; 2010 28(36):5265–5273. [PubMed: 21079137]
63. Weinstein SP, Localio AR, Conant EF, Rosen M, Thomas KM, Schnall MD. Multimodality screening of high-risk women: a prospective cohort study. *J Clin Oncol*. Dec 20; 2009 27(36):6124–6128. [PubMed: 19884532]
64. Sardanelli F, Podo F, Santoro F, et al. Multicenter surveillance of women at high genetic breast cancer risk using mammography, ultrasonography, and contrast-enhanced magnetic resonance imaging (the high breast cancer risk italian 1 study): final results. *Investigative Radiology*. Feb; 2011 46(2):94–105. [PubMed: 21139507]

65. Plevritis SK, Kurian AW, Sigal BM, et al. Cost-effectiveness of screening BRCA1/2 mutation carriers with breast magnetic resonance imaging. *JAMA*. May 24; 2006 295(20):2374–2384. [PubMed: 16720823]
66. Lee JM, McMahon PM, Kong CY, et al. Cost-effectiveness of breast MR imaging and screen-film mammography for screening BRCA1 gene mutation carriers. *Radiology*. Mar; 2010 254(3):793–800. [PubMed: 20177093]
67. Cott Chubiz JE, Lee JM, Gilmore ME, et al. Cost-effectiveness of alternating magnetic resonance imaging and digital mammography screening in BRCA1 and BRCA2 gene mutation carriers. *Cancer*. Nov 26.2012
68. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. *Jama*. 2014; 311(13):1327–1335. [PubMed: 24691608]
69. Barth RJ Jr, Gibson GR, Carney PA, Mott LA, Becher RD, Poplack SP. Detection of breast cancer on screening mammography allows patients to be treated with less-toxic therapy. *AJR. American journal of roentgenology*. Jan; 2005 184(1):324–329. [PubMed: 15615996]
70. Leung JW. Screening mammography reduces morbidity of breast cancer treatment. *AJR. American journal of roentgenology*. May; 2005 184(5):1508–1509. [PubMed: 15855106]
71. Freedman GM, Anderson PR, Goldstein LJ, et al. Routine mammography is associated with earlier stage disease and greater eligibility for breast conservation in breast carcinoma patients age 40 years and older. *Cancer*. Sep 1; 2003 98(5):918–925. [PubMed: 12942557]
72. Armstrong K, Moye E, Williams S, Berlin JA, Reynolds EE. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. *Annals of Internal Medicine*. Apr 3; 2007 146(7):516–526. [PubMed: 17404354]
73. Elmore, JG.; Lee, CI. [Nov 21, 2012] Radiation-related risks of imaging studies. UpToDate. 2012. <http://www.uptodate.com/contents/radiation-related-risks-of-imaging-studies>.
74. Olsson H, Baldetorp B, Ferno M, Perfekt R. Relation between the rate of tumour cell proliferation and latency time in radiation associated breast cancer. *Bmc Cancer*. Apr 9.2003 3:11. [PubMed: 12697074]
75. Janjan NA, Zellmer DL. Calculated risk of breast cancer following mantle irradiation determined by measured dose. *Cancer Detection and Prevention*. 1992; 16(5-6):273–282. [PubMed: 1473117]
76. Suleiman OH, Spelic DC, McCrohan JL, Symonds GR, Houn F. Mammography in the 1990s: the United States and Canada. *Radiology*. Feb; 1999 210(2):345–351. [PubMed: 10207413]
77. Helzlsouer KJ, Harris EL, Parshad R, Fogel S, Bigbee WL, Sanford KK. Familial clustering of breast cancer: possible interaction between DNA repair proficiency and radiation exposure in the development of breast cancer. *International Journal of Cancer*. Feb 20; 1995 64(1):14–17. [PubMed: 7665242]
78. Swift M, Morrell D, Massey RB, Chase CL. Incidence of cancer in 161 families affected by ataxia-telangiectasia. *New England Journal of Medicine*. Dec 26; 1991 325(26):1831–1836. [PubMed: 1961222]
79. Johns LE, Moss SM, Age Trial Management G. False-positive results in the randomized controlled trial of mammographic screening from age 40 (“Age” trial). *Cancer Epidemiology, Biomarkers and Prevention*. Nov; 2010 19(11):2758–2764.
80. Breast Cancer Surveillance Consortium (NCI). [Nov 20, 2012] 2012. <http://breastscreening.cancer.gov/>.
81. Elmore JG, Barton MB, Mocer VM, Polk S, Arena PJ, Fletcher SW. Ten-year risk of false positive screening mammograms and clinical breast examinations. *N Engl J Med*. Apr 16; 1998 338(16):1089–1096. [PubMed: 9545356]
82. Christiansen CL, Wang F, Barton MB, et al. Predicting the cumulative risk of false-positive mammograms. *Journal of the National Cancer Institute*. Oct 18; 2000 92(20):1657–1666. [PubMed: 11036111]
83. Smith-Bindman R, Chu PW, Miglioretti DL, et al. Comparison of screening mammography in the United States and the United kingdom. *JAMA*. Oct 22; 2003 290(16):2129–2137. [PubMed: 14570948]

84. Elmore JG, Nakano CY, Koepsell TD, Desnick LM, D'Orsi CJ, Ransohoff DF. International variation in screening mammography interpretations in community-based programs. *J Natl Cancer Inst.* Sep 17; 2003 95(18):1384–1393. [PubMed: 13130114]
85. Kuhl CK, Schrading S, Leutner CC, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol.* Nov 20; 2005 23(33):8469–8476. [PubMed: 16293877]
86. Brett J, Bankhead C, Henderson B, Watson E, Austoker J. The psychological impact of mammographic screening. A systematic review. *Psychooncology.* Nov; 2005 14(11):917–938. [PubMed: 15786514]
87. Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. Psychological side effects of breast cancer screening. *Health Psychology.* 1991; 10(4):259–267. [PubMed: 1915212]
88. Brewer NT, Salz T, Lillie SE. Systematic review: the long-term effects of false-positive mammograms. *Annals of Internal Medicine.* Apr 3; 2007 146(7):502–510. [PubMed: 17404352]
89. O'Donoghue C, Eklund M, Ozanne EM, Esserman LJ. Aggregate Cost of Mammography Screening in the United States: Comparison of Current Practice and Advocated Guidelines. *Annals of internal medicine.* 2014; 160(3):145–153. [PubMed: 24658691]
90. Elmore JG, Gross CP. The cost of breast cancer screening in the United States: a picture is worth ... a billion dollars? *Ann Intern Med.* Feb 4; 2014 160(3):203. [PubMed: 24658697]
91. Welch HG, Black WC. Overdiagnosis in cancer. *Journal of the National Cancer Institute.* May 5; 2010 102(9):605–613. [PubMed: 20413742]
92. Gotzsche PC, Jorgensen KJ, Maehlen J, Zahl PH. Estimation of lead time and overdiagnosis in breast cancer screening. *British journal of cancer.* Jan 13; 2009 100(1):219. author reply 220. [PubMed: 19127274]
93. Duffy SW, Lynge E, Jonsson H, Ayyaz S, Olsen AH. Complexities in the estimation of overdiagnosis in breast cancer screening. *British journal of cancer.* Oct 7; 2008 99(7):1176–1178. [PubMed: 18766185]
94. Gotzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database Syst Rev.* 2006; (4):CD001877. [PubMed: 17054145]
95. Zackrisson S, Andersson I, Janzon L, Manjer J, Garne JP. Rate of over-diagnosis of breast cancer 15 years after end of Malmo mammographic screening trial: follow-up study. *BMJ.* Mar 25; 2006 332(7543):689–692. [PubMed: 16517548]
96. Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. *New England Journal of Medicine.* Nov 22; 2012 367(21):1998–2005. [PubMed: 23171096]
97. American College of Radiology. Breast Imaging Atlas. 5th ed.. American College of Radiology; Renton, VA: 2013. ACR Breast Imaging Reporting and Data System (BIRADS)..
98. Hoffman RM, Lewis CL, Pignone MP, et al. Decision-making processes for breast, colorectal, and prostate cancer screening: the DECISIONS survey. *Medical Decision Making.* Sep-Oct; 2010 30(5 Suppl):53S–64S. [PubMed: 20881154]
99. Welch H, Passow HJ. Quantifying the benefits and harms of screening mammography. *JAMA internal medicine.* 2014; 174(3):448–454. [PubMed: 24380095]
100. Miller AB, To T, Baines CJ, Wall C. The Canadian National Breast Screening Study-1: breast cancer mortality after 11 to 16 years of follow-up. A randomized screening trial of mammography in women age 40 to 49 years. *Annals of Internal Medicine.* Sep 3; 2002 137(5 Part 1):305–312. [PubMed: 12204013]
101. Miller AB, To T, Baines CJ, Wall C. Canadian National Breast Screening Study-2: 13-year results of a randomized trial in women aged 50-59 years. *Journal of the National Cancer Institute.* Sep 20; 2000 92(18):1490–1499. [PubMed: 10995804]
102. Tabar L, Vitak B, Chen TH, et al. Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades. *Radiology.* Sep; 2011 260(3):658–663. [PubMed: 21712474]
103. Braithwaite D, Zhu W, Hubbard RA, et al. Screening outcomes in older US women undergoing multiple mammograms in community practice: does interval, age, or comorbidity score affect

tumor characteristics or false positive rates? Journal of the National Cancer Institute. Monographs. Mar 6; 2013 105(5):334–341.

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Box 1 Topics to discuss with patients when deciding whether to participate in screening

Most Women Are at Lower Risk of Breast Cancer Diagnosis Than May Be Perceived

- Most women have a lower risk of breast cancer death than they might think. The “1 in 8” statistic refers to how many women will be *diagnosed* with breast cancer over their lifetime, with most women diagnosed in their 70s and 80s, not how many women will *die* of breast cancer over a certain period of time.

Mammography Is Not a Perfect Screening Test

- While mammography will detect most cancers, some cancers will be missed, and some women will die of breast cancer regardless of whether they are screened.
- Often, women are called back for further testing because of an abnormality that is not cancer; this is called a “false-positive” result.
- Most women diagnosed with breast cancer will be cured regardless of whether the cancer was found by a mammogram.
- Some cancers that are found would have never caused problems (i.e., symptoms). This is called “overdiagnosis.”

Making a Decision about Mammography

- Some expert groups, including the United States Preventive Services Task Force, recommend that women aged 50 to 74 years undergo a screening mammogram every 2 years. Other expert groups recommend screening mammograms beginning at age 40 every 1-2 years.
- Whether you are likely to benefit from starting mammograms earlier or having them more frequently depends on your risks for breast cancer and your values and preferences.
- Each woman may feel differently about the possibility of having a false-positive result or being diagnosed with and treated for cancer that might not have caused problems. It is important for you to consider what these experiences might mean for you. It is also important to consider how you might feel if you decide not to undergo screening mammography and you are later diagnosed with breast cancer, even if the likelihood that mammography would have made a difference is small.

(Adapted from Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. *JAMA*. 2014;311(13):1327-1335; with permission.)

Key points

- Mammography is the best-studied breast cancer screening modality and the only recommended imaging tool for screening the general population of women.
- Overall, there is a modest mortality benefit from routine breast cancer screening with mammography at the population level.
- Potential harms of routine screening include false negative results, false positive results with undue anxiety and benign biopsies, and overdiagnosis.
- Efforts should be made to help women make more informed decisions about participating in breast cancer screening.

Figure 1. Mammograms of varying breast densities from a craniocaudal view: (a) almost entirely fat, (b) scattered fibroglandular densities, (c) heterogeneously dense, and (d) extremely dense.

Figure 2.
Invasive cancer as seen by the following modalities: (a) screening mammogram, (b) ultrasound, and (c) MRI.

Figure 3. Breast Cancer Screening RCTs

Results of a meta-analysis of randomized clinical trials of breast cancer screening. From Glasziou P, Houssami N. The evidence base for breast cancer screening. *Prev Med.* 2011 Sep;53(3):100-2; with permission.

Table 1

Estimated benefits and risks of mammography screening for 10,000 women who undergo annual screening mammography over a 10-year period.

Age of women, years	No. of Breast Cancer Deaths Averted With Mammography Screening Over Next 15 Years ^a	No. of Women (95% CI) With 1 False-Positive Result During the 10 Years ^b	No. (95% CI) With 1 False Positive Resulting in a Biopsy During the 10 Years ^b	No. of Breast Cancers or DCIS Diagnosed During the 10 y That Would Never Become Clinically Important (Overdiagnosis) ^c
40	1-16	6130 (5940-6310)	700 (610-780)	?-104 ^d
50	3-32	6130 (5800-6470)	940 (740-1150)	30-137
60	5-49	4970 (4780-5150)	980 (840-1130)	64-194

(Adapted from Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. *JAMA*. 2014;311(13):1327-1335; with permission.)

^aNumber of deaths averted are from Welch and Passow;⁹⁹ the lower bound represents breast cancer mortality reduction if the breast cancer mortality RR were 0.95 (based on minimal benefit from the Canadian trials^{100,101}), and the upper bound represents the breast cancer mortality reduction if the RR were 0.64 (based on the Swedish 2-County Trial¹⁰²).

^bFalse-positive and biopsy estimates and 95% CIs are 10-year cumulative risks reported in Hubbard et al⁶ and Braithwaite et al.¹⁰³

^cOverdiagnosed cases are calculated by Welch and Passow;⁹⁹ the lower bound represents overdiagnosis based on results from the Malmö trial,⁹⁵ whereas the upper bound represents the estimate from Bleyer and Welch.⁹⁶

^dThe lower bound estimate for overdiagnosis reported by Welch and Passow⁹⁹ came from the Malmö study.⁹⁵ The study did not enroll women younger than 50 years.