For more than 25 years, routine screening mammography has been a focal point of efforts to detect and control breast cancer. Following lung cancer, breast cancer remains the second most common cause of cancer death among women. Breast cancer also is the most commonly diagnosed cancer among women aside from nonmelanoma skin cancer. The high incidence and mortality rates related to breast cancer led to increased attention from clinicians, researchers, and policymakers beginning in the 1970s. As a result, breast cancer became a highly publicized public health concern in the United States. In fact, countries around the world established various population-based breast cancer screening programs based on results of mammography screening trials.

Breast cancer screening programs are designed to identify cancer at an earlier stage when it is more treatable. Screening programs attempt to detect disease in individuals who are asymptomatic. Still, screening is not considered of value if it does not advance the time at which clinicians diagnose a cancer that can cause the patient to die without early treatment. Successful screening methods also should be safe and effective.

**History of Screening Mammography**

Guidelines that recommend women begin routine screening for breast cancer at 40 years old have been in place since the early 1990s. However, the age at which women should begin screening mammography has been hotly debated. In October 2015, the American Cancer Society (ACS) amended its breast cancer screening guidelines, including raising its recommended age for beginning screening from 40 to 45 years.

Early in the development of mammography technology, clinicians and the public were excited about the ability to see inside breast tissue and
identify signs of potential cancer. In the early 1960s, radiologist Philip Strax, whose first wife died of breast cancer, proposed the idea of a clinical trial to determine whether mammography would be effective at screening for breast cancer. Randomized clinical trials were new to medicine at that time and represented a more sophisticated and statistically solid way to research effectiveness of diagnostic and therapeutic approaches to care.

In the first trial, which began in 1963, Strax and a group of colleagues selected 62,000 women and randomized the participants into an intervention group that received annual clinical breast examinations and screening mammograms and a control group that received the standard care for the time. Standard care in 1963 consisted of breast cancer screening in only some instances such as more complicated clinical cases. The intervention group received an annual clinical breast examination and a screening mammogram over a period of 4 years. Strax et al found breast cancers at earlier stages among the intervention group, when they were mostly negative in regional lymph nodes. They reported their findings in the Journal of the American Medical Association in 1971.

Eventually, lower-dose film-screen technology reduced concerns previously held about radiation exposure. Digital mammography equipment is now ubiquitous, and new digital breast tomosynthesis technology has been shown to improve detection of small lesions and reduce recall rates.

Breast Cancer Screening Debate

The debate that likely led to changes in breast cancer screening recommendations has been stated in terms not typically seen in professional medical journals. For example, some researchers have criticized studies as questionable or based on faulty science or methodology. The conclusions of studies either touting or vilifying breast cancer screening usually are refuted by subsequent studies, often with authors defending their research methods. In effect, study authors might disagree about the value of screening mammography based on the same data, but with differing interpretations of or judgments about the data.

When one issue in the breast cancer screening debate appears to be resolved, the debate often shifts to another issue or focuses on a particular age of women. Regardless of the rhetoric in the literature, conflicting reports about the value of screening mammography have led to confusion and mistrust among the public.

Most of the debate surrounding mammography depends on balancing its potential harms and benefits. Differing methods and measures used to weigh these make comparisons difficult. A woman’s decision to participate in mammography screening should be approached no differently than decisions about other screening or diagnostic examinations.

At the collective and individual level, cancer screening decisions are affected by uncertain and multiple outcomes. Considerations include defining the best method for judging or measuring value or benefit of screening and determining how to define the risk of harm cited in the literature. Further, in an era that emphasizes patient communication and involvement in care, health care professionals must learn how to communicate benefits and harms in such a way that patients can make informed choices rather than become more confused.

Screening Recommendation Overview

The sentinel research by Strax et al in the 1960s that showed earlier detection and a 40% lower death rate among women receiving breast cancer intervention did not distinguish between the value of clinical breast examination and screening mammography; nonetheless, it suggested that breast cancer screening could lower mortality from the disease. Government funding was generated, and the ACS helped to set the agenda for the Breast Cancer Detection Demonstration Project, which aimed to screen more than 250,000 women in the United States for breast cancer using various methods, including mammography.

Eventually, radiography equipment and film designed specifically for breast imaging were developed and in 1974, the National Cancer Institute (NCI) announced an even higher percentage (77%) of early breast cancer detection in a mammography study with 42,000 participants. About the same time, several prominent women, including First Lady Betty Ford, were diagnosed with breast cancer, increasing public interest in detecting and treating
<table>
<thead>
<tr>
<th><strong>Glossary of Mammography Screening and Research Terms</strong></th>
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<tr>
<td><strong>Absolute risk.</strong> The probability that an event will occur during a specific time period such as percent risk that a woman younger than 50 years will develop cancer in her lifetime.</td>
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<td><strong>False-positive result.</strong> A positive result from a screening test or examination that subsequently leads to a negative result for disease. In breast cancer screening, this means the mammogram interpretation suggests further investigation, but no breast cancer is found by the subsequent investigation.</td>
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<tr>
<td><strong>Indolent tumor.</strong> A slow-growing lesion that likely will never produce symptoms or become cancerous during an individual’s lifetime. An indolent tumor might be detected by sensitive breast screening.</td>
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<td><strong>Interval cancer.</strong> A cancer that is diagnosed between successive mammograms.</td>
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<td><strong>Lead time.</strong> Time added to a patient’s survival because of the earlier diagnosis made by screening. This implies that some cancers are diagnosed with screening that might not have been diagnosed otherwise, but also that some cancers are diagnosed at an earlier stage. Lead time bias infers the appearance that screening lengthens or improves survival from breast cancer, even though mammography screening only resulted in an earlier breast cancer diagnosis.</td>
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<tr>
<td><strong>Meta-analysis.</strong> A systematic review of at least 2 research studies on the same question that pools the data from the research. A meta-analysis combines results from several studies to quantify an overall estimate of the question at hand such as a treatment’s effectiveness.</td>
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<tr>
<td><strong>Overdiagnosis.</strong> Detection of lesions during screening that are noninvasive and unlikely to be diagnosed clinically had the patient not been screened. It is a population-based, or epidemiological, measurement, not a judgment based on an individual patient pathology or outcome.</td>
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<td><strong>Population-based screening.</strong> A program aimed at reaching targeted segments of a population to increase screening for a disease among that population.</td>
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<td><strong>Prospective study.</strong> Research conducted by recruiting and monitoring participants who have not already experienced the outcomes of interest in the study. The research is conducted according to criteria described in a study protocol. Some participants are exposed and others are not; both groups are followed over time.</td>
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<tr>
<td><strong>Randomized clinical trials.</strong> Clinical trials consist of research that tests new treatments or examinations by comparing the new method with placebos or existing standards of care (control). Randomization is a method of assigning participants in the trials in such a way that all have the same chances of being assigned to the treatment, or conditions, arm of the study or to the control arm.</td>
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<tr>
<td><strong>Recall rate.</strong> Percentage of screening mammograms for which further diagnostic studies are recommended. Closely related to false-positive rates.</td>
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<td><strong>Relative risk.</strong> A calculation of probability that an event or outcome will occur within a specified time period if a risk factor is present divided by the same risk, or probability, in the absence of the risk factor. The calculation generally is used in randomized clinical trials to compare risk between 2 groups of people.</td>
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<tr>
<td><strong>Retrospective study.</strong> Research conducted after outcomes under study already have occurred. For example, it might include a case study review. In some retrospective clinical trials, data is recalled from memory, which can be problematic.</td>
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<tr>
<td><strong>Selection bias.</strong> An imbalance, or bias, that occurs when choosing participants for a study. Most often, this occurs when control group participants and study group participants come from 2 different populations. In mammography research, this might occur when studying only women who volunteer for screening because they might have different health behaviors.</td>
</tr>
<tr>
<td><strong>Service screening study.</strong> A study based on actual screening, often as a public health initiative. Service screening studies differ from randomized clinical trials, which are conducted with research as the primary goal.</td>
</tr>
<tr>
<td><strong>Statistical significance.</strong> Rejection of a study’s hypothesis. The concept is highly dependent on final sample size of a study’s population to show a level of chance. For example, it suggests that a study question is true if there is a significant enough percentage to avoid rejecting the results.</td>
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the disease. Data from the Breast Cancer Detection Demonstration Project were challenged almost immediately, and the ACS responded by including potential risks of mammography in consent forms for the study’s participants. Much of the debate centered on age for screening and ambiguity of results, which resulted in unnecessary mastectomies for a few women enrolled in the project.10

In the early days of breast cancer screening, age appeared to be the most critical determining factor for screening decision-making. Decades later, evidence has mounted that indicates the decision is more complex than age alone.9 Today, the debate over mammography screening recommendations tends to focus on several primary concerns, including age, frequency, and personal choice.

**Primary U.S. Screening Recommendations**

Consensus on efficacy of early breast cancer detection led to initial agreement across several organizations regarding breast cancer screening.10 The ACS began recommending screening mammograms in 1976 and over the years has modified details of age, frequency, and risk (see Table). In October 2015, the organization amended its recommendations, no longer suggesting annual screening mammograms for women aged 40 to 44 years. Instead, the ACS recommended that these women begin annual screening when they wish to do so after considering potential benefits and risks. Annual mammograms still were recommended for women aged 45 to 54 years, and biennially for those older than 55 years, although the organization recommends giving women a choice to continue screening annually as they wish and as long as they are in good health.15

The changes in the ACS recommendations were announced 6 years after an update to recommendations from the United States Preventive Services Task Force (USPSTF). The USPSTF changed its 2002 recommendations for annual screening mammography in 2009. Previously, the USPSTF recommended beginning at age 40, but in 2009 altered the guidelines to delay screening mammograms for women at average risk until age 50. The update was based on task force members’ review of clinical evidence.1 Most notably, the USPSTF cited 2 studies the group had commissioned. One of these was a systematic review of 6 questions regarding benefits and harms of screening, and the other was a decision analysis based on population modeling techniques. The decision analysis considered age and frequency of screening compared with healthy outcomes and resources required.16 According to Allen et al, the decision was based on studies from other countries in which similar screening recommendations failed to reduce incidence of late-stage breast cancer, and the potential for overdiagnosis and unnecessary exposure to radiation in younger women.1

When the USPSTF made its 2009 changes, the new guidelines conflicted with screening recommendations from other national organizations.15 A hallmark of the changes was the task force’s statement that beginning screening mammography before age 50 is a personal decision.14

**Recommendations vs Clinical Guidelines**

Mammography is perhaps unique among screening practices in the nature of conflicting recommendations from organizations and the fact that those who refer women for screening mammograms or educate and counsel them regarding breast cancer prevention might practice according to different clinical guidelines. Aside from ACS recommendations, the American College of Radiology has practice parameters and appropriateness criteria that guide radiologists,36,37 and the American College of Obstetricians and Gynecologists has its own set of screening guidelines.35

Clinical practice guidelines are evidence-based recommendations developed to help health care professionals make decisions that optimize patient care.38,39 As such, they often are considered the standard of care for physicians within a particular specialty.18 In this way, they differ from task force or nonprofit organization recommendations such as those of the USPSTF or ACS.39 Breast cancer screening guidelines and recommendations primarily are written by groups of physicians and at times include nonphysician members. The make-up of the physicians who write guidelines varies, often depending on the specialty or body of the organization for which the guidelines are being developed.46

When the USPSTF changed its recommendations in 2009, the new guidelines directly conflicted with the ACS at that time, and with guidelines from several
Examinations for women beginning at age 19 and recommend breast self-examination.

Both clinical practice guidelines and screening recommendations play important roles in guiding policies that influence health promotion and screening, including referral patterns, policy setting, payer decisions, and patient preventive behavior.

**Age**

A woman’s age at breast cancer screening always has been pertinent to screening recommendations and a prominent source of controversy in the leading medical societies. Changes to the USPSTF and ACS recommendations over the years also have addressed breast self-examination and clinical breast examination, further confusing women and practitioners. In October 2015, the American College of Obstetricians and Gynecologists released a statement regarding the ACS guidelines stating that although the society strongly supports shared decision-making between women and their physicians, it would continue to recommend an annual screening mammogram for women age 40 and older. The statement also emphasized that physicians perform annual clinical breast examinations for women beginning at age 19 and recommend breast self-examination.

Both clinical practice guidelines and screening recommendations play important roles in guiding policies that influence health promotion and screening, including referral patterns, policy setting, payer decisions, and patient preventive behavior.

**Age**

A woman’s age at breast cancer screening always has been pertinent to screening recommendations and a prominent source of controversy in the
Guidelines have differed over the years—or from one another—in terms of the age at which a woman should begin or stop screening. The controversy over the 2009 USPSTF changes to recommendations and the basis of the 2015 change to ACS recommendations revolved mostly around the increased age at which to begin screening. Moss et al reported in September 2015 that most screening programs begin offering mammography screening at age 50.

In its 2009 decision, the USPSTF cited costs of harms from screening in the younger age group as more detrimental than the benefits of screening, along with low incidence of breast cancer in younger women. However, other studies in European countries have shown higher reductions in breast cancer mortality rates (37%) among women younger than 50 years than for those aged 50 to 69 years (21%) when screened with mammography despite the fact that women younger than 50 years rarely receive invitations to screen. Some of the mortality rate reductions in cited studies could have occurred because of improved treatments. It is difficult to determine the precise role played by mammography, particularly when mortality rates also declined among younger women who were not screened. Still, debate continues over the evidence regarding potential harms, including overdiagnosis, vs benefits of screening mammography for women aged 40 to 49 years.

Older age also has been addressed in some guidelines, primarily because of concerns about overuse of mammography or diagnostic tools and overtreatment. The issue is complicated by many individual factors, some of which require considering the woman’s current health and projected future health. In 2009, the USPSTF recommended screening for women aged 50 to 74 years. Older age and projected life span were part of the change made in recent ACS revisions. The organization has been criticized in the past for not incorporating projected life span into its screening recommendations. Although many older women have more limited life spans than those 10 or 20 years younger, incidence of breast cancer rises with age; as many as 40% of breast cancers occur in women who are eligible for Medicare coverage. In addition, mammography sensitivity is better in breasts of elderly women than in younger ones.

**Frequency**

The USPSTF also changed its recommended frequency of mammography screening in 2009 from every 1 to 2 years for all women older than 40 years to biennial screening for women aged 50 to 75 years. Biennial screening now is a more common screening recommendation for women at average risk. The U.K. National Health Service’s program for breast screening recommends routine triennial screening for women aged 50 to 70 years, although invitations to screening sometimes extend to women 3 years older or younger than the upper and lower age limits.

According to Feig, no randomized clinical trial has addressed the issue of screening mammography frequency. Instead, frequency decisions have been based largely on tumor sojourn time, the length of time from when a lesion is detectable on a mammogram to the time it is detected clinically without screening. Some studies have found that women who were screened at intervals of every 3 years or more were more likely to have late-stage breast cancers than those screened annually. Interval cancers not detected by screening mammography can grow quickly and result in lower survival rates. The author stated that optimal screening frequency measures less than calculated lead time.

**Personal Decision-Making**

The age-based recommendations for mammography screening most heavily debated are those developed for women who have no increased risk of breast cancer. When USPSTF guidelines, and then ACS recommendations, recommended that women younger than a certain age and at average risk of breast cancer work with their clinicians to consider potential benefits and harms of screening mammography on an individual basis, the personalized involvement in decision-making represented a shift in mammography screening principles and a gap between the organizations’ recommendations and many medical society and other screening guidelines.

In the United Kingdom, the Independent Breast Screening Review panel also concluded in 2012 that women should receive more information about benefits and harms of screening to support informed decision-making about breast cancer screening. Although the emphasis on personal choice comes at a time when
health care delivery is shifting toward a patient-centered approach, it also has led to a great deal of confusion among the public, media, and referring providers. For the most part, patients are used to participating in screening at the suggestion of their physician without discussion and shared decision-making.

Benefits vs Harms

New guidelines state that patients should receive information about the relative risks, or harms, of mammography to consider along with the benefits of screening as part of their decision. The literature reports that conflicting guidelines and research controversy can make it more confusing and difficult for patients to decide whether to screen. The complex subjects related to screening benefits and harms are made more complicated by past messaging about the value of breast cancer screening, emotion or anxiety caused by false-positive results, and inconsistent statements and guidelines. Research has shown that patients typically do not receive balanced information about benefits and harms of screening, nor are they asked to participate in the decision to be screened.

Randomized clinical trials have been conducted and reviewed to determine how screening mammography helps and potentially harms women, and these analyses have been further segmented into age groups. Balancing benefits and harms of screening mammography has been a controversial topic since the 1990s for women aged 40 to 49 years. Investigators largely agree that the principal benefit of mammography screening is reduced mortality, and many report that the chief potential harms are false-positive results and over-diagnosis. In addition, some investigators continue to discuss concerns about radiation to patients and costs to the health care system or economy as potential harms to consider when balancing benefits.

Benefits

Cancer screening benefits must address individual advantages to screening, particularly as women are given more choice in screening decisions. But population-based screening recommendations also must consider collective benefits and harms. Further, individual and collective decisions about screening must consider the relative degree or magnitude of benefits and harms. For example, if screening mammography saved only one life for every 100 false-positive results, is it worth screening everyone in a target population?

Feig stated that results based on early randomized clinical trials tended to underestimate benefits because of earlier research and mammography protocols such as use of only one mammographic projection in some studies. Yet according to Forbes et al, the public tends to overestimate the benefits of various types of medical screening. It also is possible that individuals achieve a sense of reassurance from attending screening and finding that the examination results are negative. This is particularly true when screening is designed to detect asymptomatic disease. Other illnesses, such as pneumonia, are associated with symptoms. Pneumonia also is easier to treat clinically than is cancer, reducing the justification for screening for such an illness.

Mortality

In general, cancer screening programs aim to reduce mortality from the disease. Mortality from breast cancer has been declining, but reported reduction rates associated with mammography screening can differ by more than 4 times. Published mortality reduction estimates for mammography screening have ranged from 0% to nearly 80%. A randomized controlled trial in Sweden that followed participants for 30 years often is cited in the literature. In the study, 85% of women adhered to recommended screening and had a corresponding mortality rate reduction of 36%. Lengthier follow-up times and large meta-analyses tend to show more statistically significant mortality rate reductions for women who have had screening mammograms. The USPSTF stated a mortality rate reduction of 15% in its 2009 meta-analysis.

It is difficult to determine whether each woman screened or not screened for breast cancer dies from breast cancer or from another cause, and differences in survival rates are influenced by factors other than screening. One study involved 7301 women diagnosed with invasive breast cancer between 1990 and 1999 and followed them through 2007. The study reported 71% of the deaths from breast cancer occurred in women who had not been screened. The authors stated that although effective treatment was contributing to the overall decline in mortality...
from breast cancer, their review showed that death rates were higher among women who were not regularly screened.51

Most of the controversy regarding lowered mortality rates as a benefit from mammography have been noted in screening of women aged 40 to 49 years, leading to guideline changes for this age group. Increasing the follow-up time could show greater benefit, but the reported mortality rates vary markedly among this group.31,46

Morbidity

Screening mammography is meant to help detect breast cancer at its earliest stages, when it is most treatable and more likely to improve morbidity for women.2,5,25 As a result of this goal and improvements in mammography quality, detection of ductal carcinoma in situ (DCIS) has increased from 5% of all findings to between 20% and 40% of nonpalpable lesions detected at screening.31 DCIS often is identified on mammograms when interpreting physicians note suspicious calcifications. A great deal of controversy surrounds whether DCIS is cancer because the lesions have low potential for malignancy.31,43 The National Cancer Institute has recommended that DCIS no longer be called cancer but instead be considered an indolent lesion.16 Debate remains as to whether high-grade types of DCIS can be invasive despite its reclassification.31,43,45 Appropriate treatment of DCIS leads to a survival rate of 99.5%.31

Studies also find that more screened patients who have invasive cancers are likely to have smaller lesions and stage I cancer at the time of diagnosis than are patients who have not been screened. Treatment for DCIS or early-stage breast cancer produces fewer adverse effects than treatment for advanced-stage breast cancer.15,43 Some reports show that missing a screening mammogram even for one year can increase risk of later-stage cancer at diagnosis.15

Harms

Although decreased mortality is a primary benefit of screening mammography, those setting screening recommendations have tried to quantify mortality and other benefits against potential harms. Although investigators might disagree on how to quantify the balance, Paci et al used a decision-making tool to quantify benefits and harms from 1000 women invited to participate in screening with 1000 women who did not participate. Their calculations included absolute number of lives saved, cumulative risks of breast cancer death, and overdia-

False-Positive Results

False-positive screening results prompt recalls, or follow-up imaging, along with office visits or biopsy procedures.18,49 The USPSTF cited unnecessary procedures, psychological harms, and inconvenience from false-positive results as harms of detection and early intervention in breast cancer.31 As a result, women can experience short-term concern and anxiety regarding their health and risk for breast cancer.18

False-positive results often are cited as discouraging women from adhering to screening.4 Some researchers have found, however, that false-positive results do nothing to dampen enthusiasm for screening.4 One study cited by Thomson et al found that false-positive results increased the feeling women had regarding personal responsibility for their health.18 Results vary by study and country, but most report that anxiety from false-positive results lessens over the short term, typically once a negative diagnosis is made.4 A study in Sweden, published in August 2015, found that the negative emotional effects of a false-positive recall could persist for up to 12 months.52

As with other harms, the reported rate of false-positive results from screening mammography varies, often based on the number of years of follow-up. Reported rates range from 0.9% to more than 6%.8 Rates typically are higher for women aged 40 to 49 years than for other age groups and decrease with age.5,21 This stands to reason because mammography tends to be less specific and sensitive in detecting cancer in dense breast tissue, which is common in younger women.4 Ong et al estimated in April 2015 a cumulative

probability that a woman would have a false-positive recall across 10 years of screening mammography at 61%. In 2014, Kopans said the recall rate is approximately 10%, the same as the recall rate for women who have Pap screening for cervical cancer.

False-positive rates can be affected by availability of prior mammograms, an issue that has been debated heavily. Results of a retrospective study presented at the Radiological Society of North America meeting in November 2015 reported that when radiologists have access to more than one prior mammogram, the odds of a recall resulting from the latest screening mammogram decrease by 14%. According to the investigators, it can be difficult for radiologists to compare more than one prior mammogram, particularly if prior studies were not digital mammograms. However, the authors suggest that by comparing multiple mammograms, radiologists can nearly double the positive predictive rate of mammograms and increase the breast cancer detection rate.

The economic cost of false-positive results and recalls underlies much of the discussion of their collective harm. Ong et al reported that up to 30% of women have a biopsy following a false-positive screening mammogram. In total, recalls can cost more than $1.6 billion. Cost also is important to individual women when making medical decisions. In a 2014 survey of 3501 women, investigators found that only slightly more than 50% followed through with attending regular mammography screening, even though 75% strongly agreed that mammography screening is important. One of the primary reasons women cited for failing to appear for screening mammograms was cost. This was true even though the survey was conducted following implementation of the Patient Protection and Affordable Care Act, which provides annual mammograms at no cost.

When the ACS announced its October 2015 update to screening recommendations, 2 radiologists and a breast surgeon responded with an editorial in The New York Times addressing the changes. The physicians noted that no ideal test exists for cancer detection, including mammograms for breast cancer, and that false-positive results are a reality for all types of screening examinations. They also reported that only 2% of screening cases cannot be resolved by additional imaging and require a biopsy. In addition, they said biopsies are safe procedures.

In December 2015, Henderson et al reported that women who have a history of false-positive screening mammograms or recommendations for biopsy have increased risk of developing breast cancer for at least 10 years following the false-positive result. Women who were recommended for additional imaging had a 39% higher risk of breast cancer, and those recommended for biopsy had a 76% higher risk. The authors suggested that radiologists’ findings served as markers for future breast cancer risk.

Overdiagnosis

According to Allen et al, evidence supporting the 2009 screening recommendations from the USPSTF included a propensity for radiologists interpreting screening mammograms of women younger than 50 years to overdiagnose at a rate of 20% to 40%. The topic has been hotly debated since the first report suggesting the harm was published in 1982. In 2014, at least 45 peer-reviewed articles were published regarding overdiagnosis in breast cancer, and the topic has become one of the most highly publicized breast cancer screening risks.

Overdiagnosis is not a harm that can be observed directly by investigators. It can be measured only in incidence and inferred as a harm. It is not possible to examine an individual patient’s cancer and determine a case of overdiagnosis; the incidence must be calculated at the population level. Frequency often is calculated by estimating data from clinical trials on screening, service screening studies, and trends in breast cancer incidence and stages of breast cancer in the general population.

Mentions of overdiagnosis often include breast cancer incidence detected on screening mammograms without accounting for the actual types of breast cancer detected. Still, data continue to emerge indicating widespread overdiagnosis, which weighs heavily in favor of small, early-stage lesions instead of late-stage, more invasive cancers. The debate continues regarding potential bias in calculations of the data and quantification of harm.

Although an argument can be made that detecting DCIS is a benefit of screening mammography, DCIS
also is frequently indicated in overdiagnosis and overtreatment as a harm.\textsuperscript{2,24} Of approximately 64,000 new cases of in situ breast cancer detected in 2013, 85% were diagnosed as DCIS.\textsuperscript{2} Ong et al estimated the average annual cost of DCIS overdiagnoses in the United States at $243 million.\textsuperscript{21}

Overtreatment is cited as a harm that results from overdiagnosis, particularly when treating DCIS.\textsuperscript{2,24} The USPSTF has cited harms associated with treating cancer that would not become clinically evident or require treatment during a woman’s lifetime, and unnecessary early treatment of cancer that might have been diagnosed but would not have shortened a patient’s life.\textsuperscript{14} However, little evidence exists regarding the natural history of DCIS when left untreated. Research is ongoing to assist clinicians in determining which DCIS tumors might progress to invasive breast cancer. Reports have shown that up to 30% of the lesions treated only by local excision will recur.\textsuperscript{1} Still, treating DCIS that would not otherwise progress to invasive cancer is a genuine harm related to breast cancer screening and management.\textsuperscript{28}

Opponents of the overdiagnosis argument point out that pathology also plays a role in diagnosis, and that decisions regarding treatment of DCIS and early-stage cancer are made separate from screening and by other medical specialists.\textsuperscript{53} In addition, Morris et al proposed that underdiagnosis poses greater harm than does overdiagnosis. Still, underdiagnosis of breast cancer is difficult to measure. Researchers can measure how many late-stage cancers are detected, particularly following alterations in age or frequency recommendations. These types of studies take years to complete, however.\textsuperscript{28}

Other

According to Thomson et al, the relatively short duration of anxiety and other psychosocial effects of receiving a false-positive mammogram result should be taken into account when citing the effects as harms of screening.\textsuperscript{18} When patients visit their physician or an imaging department for a diagnostic examination, they likely have signs or symptoms of disease and a corresponding understanding or expectation of a potentially positive result. In screening, however, individuals are asymptomatic and taking preventive measures. A positive result suddenly changes their health status from well to ill. With a false-positive finding, patients undergo additional examinations, only to discover they were well all along. The anxiety and economic cost of additional testing and possible breast cancer diagnosis can be considered harms related to breast cancer screening.\textsuperscript{23}

Radiation exposure is cited less in the literature than it once was as a harm for screening mammography because the absolute radiation exposure from mammography is minimal.\textsuperscript{1} Still, radiation exposure remains a potential harm, particularly if a patient has several recalls for follow-up imaging that involve ionizing radiation. Radiation exposure was mentioned as a minor consideration, but nonetheless a harm, by the USPSTF in its 2009 recommendations.\textsuperscript{34,49}

Reports in the literature also have mentioned pain from breast compression and false-negative results in addition to the harms listed above. Pain and associated anxiety are considered short-term or transient harms.\textsuperscript{2} Adverse effects of unnecessary treatment can produce greater, longer-term harm.\textsuperscript{46}

Research and Methodology Debate

Discussions in the literature and among policymakers regarding the benefits and harms of breast cancer screening typically focus on clinical trials and interpretation of research. Some authors dispute results of the same trials simply by debating the methods used to calculate the results or by interpreting data differently.\textsuperscript{13,14} At times, rhetoric has turned to accusations regarding faulty science, questioning of methods, and accusation of incorrect conclusions.\textsuperscript{12,31}

There likely is no single “right” answer in depicting the degree of harms or benefits from screening mammography. All research studies have some degree of variables and uncertainty such as the population chosen to participate or skills and nuances in radiologist interpretation. Investigators typically strive, however, to design and conduct clinical trials and reviews that follow standard conduct methods and ethics and avoid introducing bias into the study’s results when possible. A lack of data should lead to additional research, as in the level of recommendations associated with
mammography and older women. As a result, organizations fall short of absolute statements regarding screening in this population in the absence of clear trial data.9,49

**Interpretation**

The ongoing debate over screening of women aged 40 to 49 years provides an example of data judgment and interpretation. Early discussions centered on whether screening mammograms led to statistically significant fewer deaths among the younger age group. The debate then began over cost-effectiveness of mammography for women in their 40s, and eventually to the balance of harms and benefits. In essence, those debating the issue once again were discussing benefits, such as reduced mortality, and harms, such as false-positive results, but in a new context.14

An often-cited statistic, particularly surrounding the USPSTF recommendation change, is the number of women who must be invited to screening to save only one life with screening mammography. Using meta-analyses, various authors have conducted reviews and produced absolute risk estimates on which to base “number of lives saved” statements. According to Smith, each of these absolute risk measures depends on different data, such as mortality benefit, reference population, screening duration, follow-up duration, and whether the data involve women invited to screen or women who actually were screened. The information used by the USPSTF that produced an absolute risk of one life saved included the shortest observation period of trials Smith studied (10 years) and included mostly trials involving women younger than 50 years.14

**Methods and Limitations**

Flaws in study methodology often are cited in the literature, particularly in contradicting breast cancer screening harm or benefit results.16,18 Letters to editors and studies designed to contradict previous research cite issues or flaws in methodology or design such as the population included or the years of study.97

Seigneurin et al stated in 2015 that methodological issues likely explained the wide variations in over-diagnosis estimates from screening mammography published in the literature. In particular, the authors explained that increases in a disease’s incidence can be expected following implementation of a screening program, partly because of earlier diagnosis, or lead time, along with overdiagnosis. When studies report on overdiagnosis, the most reliable information is from randomized controlled trials that compare cumulative incidence of breast cancer between women who are screened and those who are not screened. If the follow-up period after screening is not adequate, typically a minimum of 10 years, the incidence estimate must be adjusted to account for lead time.26,60 Breast cancer incidence increases with age, but detecting cancers earlier because of introduction of a screening program increases the number detected and shifts the age of incidence forward. Lead time also shifts forward the calendar year in which a breast cancer is detected.28

To correctly estimate overdiagnosis, a study should allow sufficient follow-up time after invitation to screening, and the longer the follow-up, the better.31,44 Some women opt for screening upon completion of a study’s screening period, however. Indeed, the longer the follow-up period, the more likely women who were not screened will have breast screening that might detect cancer. This intersection of screening and control groups can skew results.26,61 Harding et al agreed that more breast cancers are detected when a cancer screening program is initiated, causing a temporary increase in incidence. They report, however, that lead-time effects on breast cancer incidence should decrease and eventually disappear once screening has reached a steady state, so that lead time no longer accounts for overdiagnosis.44

Other studies regarding overdiagnosis have been questioned for noncompliance of women participating in the study or contamination of results in control groups.57 Examples could include women in control groups who have screening mammograms outside the study or women in the study group who do not adhere to scheduled screening.57 A retrospective review of mortality for women undergoing annual mammography by Engel et al demonstrated this methodological issue when both screening and diagnostic mammograms were included for analysis as mammograms within each studied 1-year period. Including women with symptoms most likely skewed mortality data to some extent by including women with more aggressive, symptomatic cancers.5
Reported and quoted data on overdiagnosis can be flawed if it was calculated using incorrect assumptions, does not correct for risk factors in populations studied, or does not have sufficient follow-up time. According to Feig, an example of an assumption is basing overdiagnosis estimates on changes in incidence rates rather than on actual screening studies. This data can be repeated in the media and persuade policymakers against or dissuade women from screening. Another assumption that often affects screening mammography study results is use of hormone replacement therapy. Effects of hormone replacement therapy on breast cancer incidence were likely highest in the mid-1990s through 2006, but it is difficult to measure the exact effect, and researchers must estimate how the therapy affected incidence when studying data from that time period.

The 1992 Canadian National Breast Screening Study reported no benefit from screening mammography but was limited to women who were screened between 1980 and 1985. Critics of the study denounced the mammography quality used to reach the results, which included a reportedly higher mortality rate among women invited to screening than among those in the control group. Specifically, the study’s breast cancer detection rate was 3 cases per 1000, compared with a rate of about 6 cases per 1000 in 2014. Yaffe pointed to additional problems in the trial’s design and methods, including some potential problems with randomization to the mammography arm that might have been based on results of clinical breast examinations before assignment to the screening or control groups.

Bias

In 2014, Juni and Zwahlen suggested that bias occurs in studies reporting mortality from breast cancer screening because effective screening mammography helps to reduce deaths from breast cancer but does not affect mortality from other causes. As a result, mammography should not contribute to increased mortality unless the examination causes extreme harm. Biases and chance also affect mortality results. After analyzing consistent and nonconsistent trials in the literature, the authors questioned whether published trials reporting reductions in breast cancer deaths attributed to screening have diluted results, or even whether some study participants’ deaths actually are from other causes. They suggested conducting a new trial with more contemporary mammography technology and therapy.

The concept of bias in data also can be debated. For example, when examining the effects of false-positive results on subsequent screening behavior, Johns et al used data over a number of screens. Doing so could have introduced selection bias because the results from women who accept all or nearly all of their invitations to screening mammography might be different from those who do not, or perhaps from a woman who has her first mammogram. The authors found, however, that their results were independent of participants’ previous experiences with false-positive mammograms.

Even when investigators are analyzing previous trials, they can introduce issues with methodology or selection bias. Studies examining the relationship between screening mammography and mortality in which investigators combined results of randomized clinical trials have been criticized for the trials the investigators chose to select or exclude from their analyses.

Ethics and Conduct Bias

Bias also can occur—or be accused—in breast cancer screening research as a result of the people investigating a question or the specialty in which they work and publish their results. Although investigators must reveal conflicts of interest in research studies, such as funding, conflicts do not always preclude them from publishing. Nor are conflicts of interest necessarily clear to women who might hear about results of studies from the media or friends. Even when investigators do not have conflicts of interest, they still can have a vested interest in the results. For example, a surgery specialty journal has an interest in research involving biopsy procedures, and radiologist societies have an interest in mammography and other imaging specialties. Of course, the same authors who have a vested interest also are experts on the topics under consideration.

Rasmussen et al analyzed articles discussing 3 specific and major comprehensive reviews that questioned the value of screening mammography. The authors’ analysis aimed to determine whether general and specialty medical journals differed in how they approached...
Confusing guidelines and research supporting or denying benefit from screening mammography contribute to a climate of confusion among women and their clinicians. Up to one-third of women surveyed following the USPSTF guideline changes in 2009 said the new recommendations increased their confusion about when to get a mammogram; women aged 40 to 49 years were the most confused. The updates made by the ACS in October 2015 helped bring 2 primary recommendations of these 2 bodies closer in line with one another, paving the way toward a more consistent future approach, particularly if professionals on either side of the issue begin to accept some changes and cease defending polarized positions for the good of patients.

Confusion and Adherence
Numerous studies have been conducted about patients’ adherence to screening guidelines, including those for mammography. Decision-making and odds of adhering to cervical and breast cancer screening guidelines improve with higher education level and health literacy.

Patients’ providers also have been confused by recent changes in screening recommendations and the ongoing debate. In 2012, Corbelli et al surveyed physicians in family and internal medicine and obstetrics/gynecology to determine their screening recommendations following the 2009 USPSTF age change. The authors found that nearly 70% of the physicians still recommended that women begin screening at age 40 instead of 50 and that nearly 80% recommended annual rather than biennial screening for their patients. Mammography screening rates did not immediately decrease for any age group following the 2009 updates to screening recommendations, but reports in 2013 and 2014 vary about the ripple effects of the changes on screening rates.

The fear and anxiety associated with a false-positive result also can deter a woman from screening, at least temporarily. Despite worry, most women with a history of false-positive results recognize the importance of screening mammography, however. This could be associated with the relief that ensues when ultimately no cancer is found.
Communication
Current levels of understanding from women regarding breast cancer screening typically weigh in favor of benefits, regardless of a woman’s age or risk for the disease.14 Public education and enthusiasm for mammography has helped improve adherence to screening but also should strive to present balanced information for all age groups or targeted populations.19 The concepts that explain risks and benefits of screening are complex and a challenge to explain regardless of disagreement.16 The challenge is exacerbated by the public’s tendency to find information online.19,65 As many as 80% of U.S. adults use the Internet for medical information, and patients often consult the Internet before and after visiting their physicians.65 Scholarly journals are not written at patient literacy levels and materials that are written at lay level might not undergo any clinical review.19 Women also seek or receive information from friends, family members, or others.66

Studies suggest that women need information on all of the harms, particularly overdiagnosis, to make an informed decision about screening mammography. They also suggest that these are difficult concepts for patients to understand, and that overdiagnosis is particularly complex.23,66

Transition to Patient-Centered Care
Several new guidelines recommend that women and their physicians take a personalized or individualized approach to mammography screening in particular age groups. In general, health care is trending toward a more patient-centered approach, and many patients want to be more involved in decisions about their care.18,66 Recent ACS guidelines suggest that women aged 40 to 44 years consider the potential benefits and risks of screening if they want to begin annual screening before age 45. These decisions have been more straightforward for women who have risk factors for breast cancer, but less so for women at average risk.67

Primary care physicians often have limited time with patients for educating and assisting with informed decisions. Physicians have received conflicting information from literature and colleagues; moreover, they must carve and shape this information into understandable and concise messages for their patients.15

To assist patients in making the decision regarding mammography screening, the clinician must first inform a woman that she has a choice or decision to make. Next, the physician should present information about options, benefits, and harms. The clinician can guide the patient in making a decision that best matches the patient’s health and personal values.17,68

Studies have shown that up to 20% of cancer screening decisions were made without the patients’ involvement in discussion. Further, information that was presented to the patient often was not balanced.17 The transition to patient-centered care and tailoring management is a new direction for patients and their providers.2,16 Even as patient-centered care and an emphasis on involving women in screening decisions have advanced, little has been done to help women understand the risks and benefits of breast cancer screening or to engage them more actively in decision-making.18

Support of this new approach to the patient-provider relationship and health care delivery model requires careful consideration and clear, trustworthy information.2,16 No evidence suggests that patients or providers assisting with their screening decisions are prepared to discern whether benefit outweighs risk when presented with figures such as number of lives saved per 1000 women invited to screen.19 Physicians and other health care professionals can engage patients in discussions only when the professionals have at hand solid and balanced consensus from experts in the specialty.2 The information must then be made comprehensible and relevant to their patients.29

Further, patient-centered care emphasizes culturally sensitive information. If women are to make informed personal decisions about the benefits and potential harms of screening mammography, the information should consider culture and be provided in context when possible. For all women, this requires a certain degree of cultural change in the patient-provider relationship from past directives from advocacy groups, media, and providers to “get a mammogram,” to becoming informed consumers who make the best choice with the help of current screening recommendations, their providers, and their values.1,17
Role of the Radiologic Technologist

Breast cancer screening decisions involve complex information that has been made more confusing by the breast cancer screening controversy. If women must rely solely on the media, Internet, and patient information or education materials, they risk receiving incomplete or imbalanced information. For adequate informed consent and patient-centered care approaches, health care professionals must provide information women can better understand.

As long as the Affordable Care Act continues to cover screening mammography, breast care centers and their staff should be sure that women know they can receive annual screening mammograms based on current coverage levels. Women who receive false-positive screening results fare better when they have plenty of information to reassure them about their individual situation. In a series of structured interviews with women who experienced recent false-positive results from screening mammograms, Thomson and Siminoff reported that women wanted trusted information to help ease their anxiety. Specifically, they felt this information should come from "health care providers recommending or performing screening." Many authors also report that current breast cancer patient education materials do not mention overdiagnosis but should include information about the issue.

Whether a woman makes the decision to screen or not to screen for breast cancer under new guidelines, it is important that she feels comfortable having conversations about screening and making informed decisions. Radiologic technologists can support women in their decision-making efforts without bias or judgment.

Conclusion

Any screening program that aims to reduce incidence of advanced disease and resulting mortality by detecting cancer earlier will, by its very nature, be somewhat inefficient. Imaging women who have no symptoms to identify breast cancer at the earliest possible stage means most women will leave a breast imaging center or department with a negative result and a reassured mind. A minority of women face inconclusive results and the harms associated with mammography screening.

Patients and the public are helped when the professionals who investigate and set policy in breast cancer screening and management come together to address problems related to controversies over screening guidelines. Initiatives, such as the 2003 Appraisal of Guidelines for Research and Evaluation, aim to assist in providing a framework for the methodology used in research that serves as the basis for guideline development, assessing the quality of guidelines, and assessing the information reported in guidelines.

Several steps also are in place to provide new, evidence-based tools to help women and their clinicians weigh the benefits and potential harms of breast cancer screening. Future tools might be able to better predict individual breast cancer risk. Decision aid instruments can assist in validating personal risk and benefit from screening but cannot replace education and personal discussions patients have with health care professionals.

This article does not take sides in the debate about breast cancer screening nor any particular issue regarding the harms or benefits of screening mammography. It is intended as an educational article for radiologic technologists only and is a summary of research conducted by the author in fall 2015. Because of the extensive amount of information, highly mixed and divisive opinions on the subject, and continuous flow of emerging information, the author recognizes that some information might have changed between the time the article was submitted and the date of publication, as well as expiration of the Directed Reading. Readers are encouraged to use this summary and its references as a starting point from which to learn more about the topic.

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References


Breast Cancer Screening Benefits: Research and Controversies


1. In October 2015 changes to its breast cancer screening program, the American Cancer Society:
   a. lowered the recommended age for beginning screening to 40.
   b. raised the recommended age for beginning screening to 45.
   c. halted annual screening for all women older than 70 years.
   d. changed screening from annual to biennial for women aged 45 to 54 years.

2. A cancer diagnosed between successive mammograms is called a(n):
   a. indolent tumor.
   b. interval cancer.
   c. false-positive result.
   d. lead-time tumor.

3. In the 1960s, research showed earlier detection and a ____% lower death rate among women receiving breast cancer screening intervention.
   a. 10
   b. 20
   c. 30
   d. 40

4. A hallmark of the 2009 update to U.S. Preventive Services Task Force (USPSTF) screening guidelines for breast cancer was the:
   a. statement that beginning screening mammography before age 50 is a personal decision.
   b. recommendation that no woman younger than age 50 should have screening mammography.
   c. decision to make primary care physicians completely responsible for decisions regarding mammography.
   d. suggestion that mammography is more harmful than helpful for women of all age groups.
5. Which of the following statements about mammography screening frequency is true?
   a. The most common screening recommendation for women at average risk is annual screening.
   b. The most common screening recommendation for women at average risk is biennial screening.
   c. The U.K. National Health Service program for breast screening recommends routine annual screening.
   d. The U.K. National Health Service program for breast screening recommends routine biennial screening.

6. Ductal carcinoma in situ (DCIS):
   1. often is identified when interpreting physicians note suspicious calcifications.
   2. should be reclassified as an indolent lesion according to the National Cancer Institute.
   3. has decreased in incidence because of screening mammography.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

7. Reported rates for false-positive results on mammograms typically are higher for women aged 40 to 49 years and decrease with age.
   a. true
   b. false

8. Which of the following statements is true regarding overdiagnosis from screening mammograms?
   a. Several observational studies have been conducted to better study the matter.
   b. Radiologists are encouraged to begin noting and tracking overdiagnosis in each patient.
   c. Overdiagnosis data favors small, early-stage lesions.
   d. DCIS is not included in overdiagnosis figures.

9. In 2015, Seignuerin et al stated that ______ likely explained the wide variations in overdiagnosis estimates from screening mammography published in the literature.
   a. poor mammography quality in past years
   b. radiologist caution
   c. methodological issues
   d. researcher bias

10. One assumption that often affects screening mammography study results is use of:
    a. hormone replacement therapy.
    b. digital radiography.
    c. survival rates.
    d. flawed calculations.

11. A survey following the 2009 USPSTF recommendations for breast cancer screening found that nearly 80% of physicians still recommended:
    a. screening beginning at age 40.
    b. a baseline mammogram before age 40.
    c. annual, rather than biennial, mammograms.
    d. monthly breast self-examination only.

12. In a series of structured interviews with women who had experienced recent false-positive results from screening mammograms, women said they felt information to ease their anxiety should come from:
    a. primary care physicians.
    b. providers who recommend and perform screening.
    c. family and friends.
    d. the Internet.

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