Frequently Asked Questions about Mammography and the USPSTF Recommendations: A Guide for Practitioners

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What is the goal of breast cancer screening?

The goal is to reduce deaths due to breast cancer by detecting breast cancer early, when treatment is more effective and less harmful. Simply put, the goal of breast cancer screening is to reduce the incidence of advanced disease.

Breast cancer has to reach a certain size to be detected. The benefit of screening mammography is earlier detection and lower risk that the breast cancer will have spread at the time of detection [1]. If a woman waits for her breast cancer to become evident as a palpable lump detected by her or her primary care physician, it will be larger and more likely to have spread to her lymph nodes or elsewhere at the time of detection. This is especially true for premenopausal women.

Breast cancers found with high-quality, two-view screening mammography are relatively small, with median size 1.0 to 1.5 cm (0.4 to 0.6 inches, or the size of a small marble) [2]. Approximately 10% of invasive cancers 1 cm in size or smaller have spread to lymph nodes at the time of detection, compared to close to 35% of those 2 cm in size and 60% of those 4 cm or larger in size [3]. A 2 cm or smaller invasive cancer which has not yet spread to lymph nodes is stage I disease, which has a 5-year disease-free relative survival rate of >98% [3], compared to 86% for stage II disease (1-3 positive axillary lymph nodes and/or primary tumor size 2.1 to 5 cm).

Breast cancers found by clinical breast examination or by a woman herself have a median size of 2 to 2.5 cm [2]. Such cancers are more likely to be later stage breast cancers that are more likely to have already spread to the axillary lymph nodes and are more likely to be lethal. Treatment of women who are node positive (i.e. have a minimum of Stage II breast cancer) usually involves more intensive treatments such as chemotherapy and more radical surgery than is usually needed for Stage 0 (ductal carcinoma in situ, DCIS) and Stage I disease. Despite treatment, women with more advanced breast cancer are more likely to die from it than women diagnosed with early stage disease. Indeed, the 5-year disease-free
relative survival rate is 56% for stage III disease (primary tumor larger than 5 cm and/or 4 or more positive axillary nodes at diagnosis, and/or skin or chest wall involvement, or inflammatory carcinoma) [3, 4].

For a woman in her forties, what is the chance of her being diagnosed with breast cancer during her forties?

About 1 in 69 women will be diagnosed with invasive breast cancer in their forties.

The incidence of newly diagnosed breast cancer increases with age (Figure 1) [5]. There is a very low incidence of breast cancer below age 30. Incidence moderately increases between the ages of 30 and 45, with a steady increase from age 40 through age 75. There is no abrupt change at age 50. Decrease after age 79 is likely due to a combination of death from other causes and decreased detection due to decreased rates of screening (ascertainment bias).

Seventy-five percent of women diagnosed with breast cancer have no special identifiable risk factors: screening only women with risk factors will miss the vast majority of women who will develop breast cancer [6].

![Age-Specific Breast Cancer Incidence Rate per 100,000 Females, SEER 2002-2006](image)

**Figure 1.** Annual U.S. breast cancer incidence rates per 100,000 women as a function of age for invasive + in-situ cancers (orange) and invasive breast cancer only (maroon) [5].
For a woman in her 40s, the chance of having breast cancer detected by mammography in any given year averages 2.18 in 1000 or 1 in 459. Data from the Breast Cancer Surveillance Consortium from 1996 through 2007, across over 3.8 million mammographic examinations show how the breast cancer detection rate with mammography increases as a function of age (Table 1) [7].

Table 1. Breast cancer detection rate from a single mammography exam (per 1,000 examinations) in the Breast Cancer Surveillance Consortium (BCSC) 1996-2007.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cancer detection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-44</td>
<td>1.69</td>
</tr>
<tr>
<td>45-49</td>
<td>2.60</td>
</tr>
<tr>
<td>50-54</td>
<td>3.23</td>
</tr>
<tr>
<td>55-59</td>
<td>4.20</td>
</tr>
<tr>
<td>60-64</td>
<td>4.70</td>
</tr>
<tr>
<td>65-69</td>
<td>5.25</td>
</tr>
<tr>
<td>70-74</td>
<td>5.95</td>
</tr>
<tr>
<td>75-89</td>
<td>6.96</td>
</tr>
<tr>
<td>Any age</td>
<td>4.00</td>
</tr>
</tbody>
</table>

If breast cancer is present, will it be detected by screening mammography?

Mammography detects most, but not all, breast cancers. Mammographic sensitivity, defined as the fraction of breast cancers that are detected in women who have breast cancer, depends on a variety of factors, but especially on how dense the breast tissue is.

The mammography report issued by the radiologist will describe breast density using one of four categories: 1) fatty; 2) minimal scattered fibroglandular density; 3) heterogeneously dense; and 4) extremely dense. In the first two categories of breast density, from 85 to 90% of breast cancers are easily identified by mammography. In the latter two categories, collectively termed “dense”, only 30 to 55% of breast cancers may be seen on film mammograms [8-10]. Digital mammography produces better tissue contrast, improving cancer detection in dense tissue to up to 70% [10].

Over half of women under age 50 have dense tissue, as do 40% of women in their fifties, and a quarter of women over the age of 60 [11]. Both because of the increasing incidence of breast cancer and the reducing density of the breast tissue, the accuracy of mammography increases as women get older. Although dense tissue is more common in younger women, fatty and dense breasts can be found in some women of all ages. The density of breast tissue can only be established
by imaging such as mammography and cannot be determined by a woman’s age or a physical exam.

**Is there any test other than mammography that will show early breast cancer?**

Magnetic resonance imaging (MRI), ultrasound, and sometimes nuclear medicine techniques, can show small breast cancers, but studies have not yet been performed to show that these techniques reduce mortality from breast cancer. There are some cancers seen only on mammography: MRI and ultrasound can be used to supplement, but not replace, mammographic screening in some groups of women at increased risk of breast cancer [12].

In women with dense breasts, addition of screening ultrasound provides an absolute increase in detection of node-negative breast cancer of 28% [13]. In women at high risk for breast cancer, screening MRI improves detection of early breast cancer by 56% above and beyond the combination of mammography and ultrasound (reviewed in [12]). Such increases in sensitivity come with significant increases in recall rates and needle biopsies. On average, 11% of needle biopsies prompted only by screening ultrasound reveal cancer (reviewed in [14]) and 40% of biopsies prompted only by screening MRI reveal cancer (reviewed in [12]).

**What is the chance that a mammogram will save the life of a woman with breast cancer?**

The overall 5-year relative survival rate (corrected for other causes of mortality) of women with breast cancer is 89% for white women and 78% for black women as of 2001 [3]. Based on the observational studies of modern screening mammography discussed below, there are 30 to 40% fewer deaths due to breast cancer among women screened with mammography than among those who do not undergo screening [15, 16].

Nine prospective randomized controlled trials (RCTs) have been performed to assess whether an invitation to screening mammography decreases deaths due to breast cancer ([17], plus the eight earlier trials reviewed in [18]). In a randomized controlled trial, there is a group *invited* to be screened and a *control* group not invited to be screened.

The simple act of detecting a cancer earlier will bias results in favor of screening, whether or not the natural history of the disease has been altered. For example, a woman’s breast cancer may kill her in the year 2020 either way; if she is screened, it may be detected in the year 2010, and if not screened, in the year 2012. By
screening, she appears to live 10 years after her diagnosis, compared to 8 years without screening, when in fact the natural history of the disease has not been affected. This is called “lead-time bias”. Further, women who participate in screening may be fundamentally healthier than those who do not. This is one type of possible “selection bias”. RCTs correct for such biases by examining breast cancer mortality rates among two groups which in principle are matched except for the screening intervention.

In RCTs, not all women invited to be screened will actually participate, and some women in the control group may undergo screening on their own even though they were not invited to screen. Further, as is consistent with an intention to treat analysis, the comparison of the two groups includes women in the invited group who die from breast cancer but who were not screened (noncompliance) and women in the control group who did not die from breast cancer because they sought screening outside the trial (contamination). At best, only about 70% of women invited to screen will participate. As a result, RCTs underestimate the benefit of screening.

In the first 8 RCTs of screening mammography, women of various ages, ranging from 39 to 74 depending on the trial, were invited to be screened. In the 2002 report of the United Services Preventive Services Task Force (USPSTF)[18], 7 of 8 existing RCTs were analyzed, showing a summary relative risk (RR) of death of 0.84 (95% confidence interval, or CI, of 0.77 to 0.91). A relative risk of 1.0 means there is no difference between the group with the intervention and the group without. Numbers less than one indicate a lower risk. A relative risk of 0.84 means there was an estimated 16% decrease in breast cancer deaths in the groups invited to mammography (as 0.84 is 16% lower than 1.0). A 95% CI expresses that 95% of the time, the results would fall within the given range. A 95% CI which overlaps 1.0 indicates no statistically significant difference. If the 95% CI does not overlap 1.0, results are considered statistically “significant” because there is at most only a 5% chance that the observed difference was due to chance alone.

The first 6 RCTs were not designed to specifically evaluate screening women of any particular age decade or risk factor subgroup. Nevertheless, results for the subgroup of women aged 39 or 40 to 49 at initial invitation to screen (each of whom could have been anywhere in that decade when first screened) have been analyzed where available. The Canadian trials (NBSS-1 for women in their forties at entry [19] and NBSS-2 [20] for women in their fifties at entry) evaluated screening mammography, but were flawed by poor-quality mammography in both age groups [21]. There was also excess inclusion of women with palpable lumps and advanced breast cancer in the invited group in NBSS-1 [22]. This issue was evident in the first round of screening and led to suspicion that there had been bias in the randomization following clinical breast examination. In the 2002 USPSTF report [18], which included the Canadian trials, the estimated RR of death among those aged 40-49 was 0.85 (95% CI 0.73 to 0.99) among those invited to
screening, i.e. a statistically significant estimated 15% reduction in mortality due to breast cancer.

In the most recent USPSTF analysis [23], again based on review of the RCTs, the summary RR of death was again 0.85 (95% CI, 0.75 to 0.96, which indicates a statistically significant benefit from mammography) for women aged 40 to 49. By comparison, the USPSTF concluded that screening mammography provided women in their fifties a virtually identical 14% reduction in breast cancer deaths (RR of death 0.86 with 95% CI, 0.75 to 0.99) and provided women in their sixties a 32% reduction in breast cancer deaths (RR of 0.68 with 95% CI 0.54 to 0.87).

It is important to note that the vast majority of deaths due to breast cancer occur in women who have never had mammographic screening. In a recent analysis of breast cancer deaths in Massachusetts, 16% of deaths occurred in women whose cancers had been found on mammography, 10% in women who had mammographic screening but no cancer was found, and 70% in women who had never had mammography [24]. Another 5% were in women who had not had a mammogram within 2 years of diagnosis [24]. Thus 75% of deaths were among women not regularly screened with mammography [24].

**Is there new information that prompted a change in mammography recommendations for women aged 40-49?**

There is one new study, which (barely) failed to show a significant benefit to mammography. That study, from the United Kingdom, used a single-view procedure that would be considered incomplete in the United States and used film rather than digital technique. Both of these factors reduced the benefit of mammography, particularly for young women.

This new trial, the only new RCT since the 2002 USPSTF report, was conducted in the United Kingdom and called the “Age” trial [17]. In that protocol, women aged 39 to 41 were randomly assigned to be invited to annual mammography or usual care through age 48. Although the first mammogram included two mammographic views (mediolateral oblique (MLO) and craniocaudal (CC)), each subsequent annual mammogram was performed in the MLO view only [25]. Single-view mammography is less sensitive than 2-view mammography. In the UK National Health Service (NHS), which provides routine screening to women ages 50 and over, sites performing single-view mammography were 19% less successful in detecting breast cancer (76% sensitivity) compared to those using two-view mammography (95% sensitivity) [26]. Changing from one-view to two-view mammography in the UK NHS improved sensitivity by 20%, particularly among cancers smaller than 15 mm, and decreased the recall rate [27], but two-view mammography was not performed in the Age trial after the first round. Among other programmatic factors that may have contributed to lower sensitivity in the
Age trial, only 48% of cancers were screen detected among the invited group attending screening [17]. In the United States, standard screening mammography is always performed using two views. After 10 years of follow-up, the Age trial showed a relative risk (RR) of 0.83, which means a 17% reduction in mortality in women invited to screen compared to the control group of women not invited to screen [17]. The 95% confidence interval (CI) ranged from 0.66 to 1.04, indicating that the mortality reduction just missed being statistically significant [17]. Among women who actually attended screening, the RR was 0.76 (a 24% reduction in breast cancer deaths) with a 95% CI ranging from 0.51 to 1.01 [17]. Because the 95% CI overlapped 1.0, this trial has been used to indicate that there may be no benefit to screening women in their forties, although that conclusion is unlikely.

There were other problems with the Age trial that resulted in disappointing results. Only 41% of the invited group attended all screening rounds, with diminished attendance occurring in the later years, when incidence was increasing due to advancing age of the patient population. While the trial produced results similar to the early trials of mammography because it used a 1970's protocol and had significantly diminished statistical power at the conclusion of the study (60% power to detect a 20% mortality reduction) [17], these important limitations affecting the study’s end results have not been described by the USPSTF. Rather, they have cited the observed mortality reduction as additional evidence that there is only marginal benefit to screening women in their forties.

When the Age trial was included in the recent USPSTF analysis of RCTs [23], the conclusion was again that mammographic screening reduces breast cancer mortality by 15% for women invited to screen from age 39 to 49 years [RR 0.85, 95% CI 0.75 to 0.96]. Thus, there is no change in the conclusion that, for breast cancer occurring in the forties, regular screening mammography will prevent premature death from breast cancer for at least 1 in 6 to 1 in 7 women who would otherwise be expected to die without screening.

**Why is the benefit of mammography measured by a meta-analysis of all the trials?**

The logic for doing meta-analysis is not described in the evidence report [23] or the USPSTF recommendations. There is no methodological rule that says when more than one study exists, they must all be combined in meta-analysis. The first meta-analyses of mammography screening for women in their forties were done because none of the trials had been designed to study women in this age group, and consequently, none was adequately powered to measure age-specific benefit from a single decade of screening. With additional years of follow-up, the relative risk of dying from breast cancer in the group invited to screening increased, and eventually meta-analysis demonstrated a statistically significant mortality reduction for women randomized in their forties. However, two second generation trials, each designed with shorter screening intervals based on the high interval cancer rates
observed in the earlier trials, showed statistically significant mortality reductions similar to those observed in women 50 years of age and older [28, 29]. Further, among women under and older than age 50, all trials that succeeded in reducing the risk of being diagnosed with an advanced breast cancer also observed a significant reduction in the risk of dying from breast cancer [1]. Those trials that failed to reduce the relative risk of being diagnosed with advanced disease also did not observe a significant reduction in breast cancer deaths associated with an invitation to screening [1]. Since we understand that an effective mammography program will reduce the incidence rate of advanced disease, conducting meta-analysis of studies with different rates of performance related to that fundamental goal only diminishes the true approximation of benefit.

If the RCTs are limited in important ways, what can we expect from modern mammography?

The risk of death from breast cancer is decreased by 30 to 48% by routine mammographic screening. Once the efficacy of a screening test has been determined with a RCT, observational studies offer a better study design to measure effectiveness among women who actually underwent routine mammography, rather than just analyzing results from women who were invited. Such results were not included in the USPSTF analysis.

Some of the best such analyses come from evaluations of service screening in Sweden and British Columbia. In Sweden, counties can decide whether to start inviting women to mammographic screening at age 40 or age 50. Since treatments are the same across counties, this provides an ideal opportunity to evaluate the impact of screening mammography. Across all age groups, at 20 years of follow-up, women who participated in screening had a 44% decrease in risk of death from breast cancer [RR 0.56 (95% CI 0.49 to 0.64)] compared to those who were not screened [16]. In Sweden, once a woman begins screening, she is screened every 18 months from age 40 through 54. Women in their forties who actually participated in routine screening mammography had a 48% lower risk of death from breast cancer [RR 0.52 (95% CI 0.40 to 0.67)] than those not screened [16]. Compared to historical controls, there was an estimated 18% reduction in mortality attributed to improved treatment, increased breast awareness, and other clinical factors in the period 1978 to 1997 compared to 1957 to 1977 [16]; a 30% mortality reduction was attributed to screening mammography alone. In British Columbia, there was a 40% decrease in deaths among women screened annually between ages 40 and 79 during the period 1988 to 2003, and a 39% reduction among women aged 40 to 49 at first screen [15].
If women are screened, is it necessary for women to undergo mammography every year?

To achieve the greatest possible benefit from mammography, yes. If a woman chooses to have mammography, it is especially important that it be performed at least every year from ages 40 to 49 and in the early 50’s, when cancers can grow more rapidly.

Part of the answer to this question depends on how fast a breast cancer grows and whether or not it spreads to lymph nodes. Some breast cancers spread to lymph nodes when they are very small. It has been estimated that for every invasive breast cancer cell, there is a 1-in-one-billion chance of spread to cause lethal distant metastasis [30]. By the time a breast cancer is 1 cm in size (and usually detectable on mammography), it is typically composed of over one million cells. Some breast cancers double in volume in as little as one month. Others may take many months or even many years to double. At this time, we usually cannot reliably predict how quickly a given cancer will grow.

Based on data from Sweden, tumors in younger women tend to be more biologically aggressive, i.e. they tend to grow and spread more quickly. It has been estimated that a preclinical node-negative tumor has a 16% chance of spreading to lymph nodes within one year at age 40-49 vs 7% for women in their fifties and 5% for women in their sixties [31]. To achieve optimal benefit from mammographic screening, women in their forties need to be screened annually (Table 2).

Table 2: Expected percent of women with breast cancer whose lives will be saved by mammographic screening (compared to not screening) for different age groups and screening intervals (adapted from [31]).

<table>
<thead>
<tr>
<th>Interval</th>
<th>40-49 year old</th>
<th>50-59 year old</th>
<th>60-69 year old</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>36%</td>
<td>46%</td>
<td>44%</td>
</tr>
<tr>
<td>2 year</td>
<td>18%(^a)</td>
<td>39%</td>
<td>39%</td>
</tr>
<tr>
<td>3 year</td>
<td>4%</td>
<td>34%</td>
<td>34%</td>
</tr>
</tbody>
</table>

\(^a\) Actual observed for this age group and screening interval was 13%

These results suggest that the majority of benefit from mammographic screening can be achieved with biennial screening in women aged 50 and older, but that annual screening is especially important for women aged 40 to 49 years. It may be that biologic aggressivity decreases after menopause: annual screening may be appropriate until menopause is reached, though this has not been directly studied.
At what age should a woman stop getting regular mammograms?

There is a potential benefit to screening mammography as long as a woman is in good health, expects to live at least 5 to 10 years, and would seek treatment if a cancer is found.

None of the RCTs of mammography invited women older than 74 to be screened. Because the USPSTF report [23] only considered RCTs, they concluded that there was insufficient evidence to recommend screening women over age 74. Multiple observational studies have shown that regular mammography continues to depict early breast cancer in older women and continues to decrease the risk of death from breast cancer. For all ages, the mortality benefit from mammographic screening begins to be seen five to seven years after the onset of screening. Annual mammographic screening can be continued as long as there is reasonable expectation of a life expectancy of at least seven years, and only if treatment would be pursued if a diagnosis is made. A downward shift in the stage distribution has been observed among women diagnosed with breast cancer who have continued mammographic screening [32, 33]. In one study, each mammogram obtained produced a 37% reduction in risk of being diagnosed with late-stage breast cancer among women aged 80 and older [32]. Average life expectancy for an 80 year-old woman is 8.6 years [34], which means that the healthiest quartile can be expected to live considerably longer. As long as a woman doesn’t have life-limiting health problems, periodic mammographic screening can be beneficial.

What is the “number needed to screen (NNS)”?

This is a calculation of the number of women needed to screen to prevent one death due to breast cancer. It can be expressed in terms of a period, i.e., “the number of women needed to be screened annually over a period of 10 years to prevent one death,” or in terms of the absolute number of exams that need to be done once to prevent one death.

The number needed to screen will be higher in younger women because there is a lower incidence of breast cancer (Figure 1). This number will also vary based on the estimated mortality reduction, with higher numbers needed to screen if the estimate of the mortality benefit is low. The duration of follow-up is especially influential, and analyses commonly err in estimating the NNS with contemporaneous screening and follow-up periods.

Since the USPSTF derived their estimates from the RCTs, they only estimated the number needed to invite to screening (NNI) to save one life [23], which has been described as a nebulous concept [35]. Since an average of only 70% of women in the RCTs participated in screening when invited, the NNI will overestimate the number needed to screen to save one life. The USPSTF used a 15% decrease in breast cancer deaths among women in their forties invited and estimated 1904
women in their forties would need to be invited to screen to prevent one death due to breast cancer [23]. Using the same algorithm, but invoking direct measures of benefit from service screening such as in Sweden and British Columbia (RR 30-40%) the NNI to screen to save one life among women in their forties drops to 952 (using a 30% benefit) and to 714 (using a 40% benefit). In an analysis of Swedish data, the number of women in their forties needed to be screened 5 to 6 times in a 10-year period to save one life for 20 years was 726 [16]. The USPSTF estimate for number of women aged 50-59 needed to invite to save one life was 1300, which was considered worthwhile [23].

What are the downsides to mammography?

Mammography is not perfect, and it will not benefit all women equally. There are downsides to mammography that most women will experience if they get regular mammograms, and these are most commonly the need for additional imaging when an abnormality is suspected, or the need for biopsy for findings that may not be cancer. As with all x-ray examinations, there is some radiation exposure, although the radiation dose from mammography is minimal. As discussed above, there is a risk that breast cancer, even when present, will not be seen on mammography. The additional possibility of overdiagnosis is discussed below.

For every 1000 women screened,
- 80 to 100 will be called back (“recalled”) [36] for additional evaluation, usually consisting of additional mammographic views and often ultrasound
- 45 to 65 of those recalled will have nothing of concern (“false positive”)
- 20 may be asked to return in six months just to be careful, with the area being followed having less than a 2% chance of being cancer
- 15 will be recommended to have a biopsy
- 2 to 5 will be found to have breast cancer (10 to 13 biopsies will not show cancer, also “false positives”).

What is involved in a breast biopsy?

Nearly all findings found on breast imaging can be biopsied in an office procedure called a “needle” biopsy.

About 1 in 4 to 1 in 5 biopsies for calcifications seen on mammograms will prove to be cancer. About 1 in 3 biopsies of suspicious masses will prove to be cancer. If the area of concern can be seen on ultrasound, the needle biopsy is usually done with ultrasound guidance which is a simple, 15 minute procedure. Local anesthetic (usually lidocaine) is given, which may cause a burning sensation for about 15 seconds, but otherwise there is very little discomfort. It is similar to going to the dentist. A clip may be placed to help communicate with other doctors where the area of concern is/was within the breast. A stereotactic needle biopsy is similar but
requires positioning on a special table while the breast is compressed as with a mammogram. A stereotactic biopsy takes about 30 minutes, though you will likely be in the department for up to several hours. After a needle biopsy, you can resume your normal activities the same day. Results are typically available within a few days.

**Is there reason to worry that the radiation exposure from mammograms will cause breast cancer?**

The risk of causing breast cancer from the radiation of mammography is far lower than the likelihood of mammography detecting breast cancer for women aged 40 years and older.

Mammography uses low energy ionizing x-rays at low radiation doses to create an image. There is a slight risk of ionizing radiation inducing a breast cancer eight or more years after exposure. The best evidence available comes from women who received radiation doses hundreds or thousands of times higher than that from mammography, such as Japanese women who survived the atomic bomb explosions at Hiroshima and Nagasaki. In the interest of radiation protection, the high radiation doses that occurred in those explosions and the subsequent excess breast cancers that occurred are extrapolated to the low radiation doses that occur in medical procedures such as mammography using a linear risk-to-dose model. Results indicate that there is a low risk of radiation-induced breast cancer, that is higher at earlier ages of exposure. Assuming that 100,000 women receive a typical (4 milligray) total breast dose from mammography, the best estimate of their risk of a resulting radiation-induced breast cancer occurring (incidence) or breast cancer death (mortality) is given by Table 4, based on age at exposure.

**Table 4. Estimated lifetime risk of breast cancer induced by the radiation from a 2-view bilateral mammogram (incidence), and estimated lifetime risk of excess breast cancer deaths (mortality) due to that radiation exposure, per 100,000 women, as a function of age at exposure (based on BEIR-VII [37]).**

<table>
<thead>
<tr>
<th>Age at Exposure (yrs)</th>
<th>Lifetime Incidence of Excess Breast Cancers per 100,000</th>
<th>Excess Breast Cancer Mortality per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>30</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>40</td>
<td>5.6</td>
<td>1.4</td>
</tr>
<tr>
<td>50</td>
<td>2.8</td>
<td>0.8</td>
</tr>
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</table>
The table above shows that the risk of radiation exposure at age 40 or above is quite low compared to the likelihood of naturally-occurring breast cancer. Among 100,000 women in their forties, there are over 200 naturally-occurring breast cancers diagnosed per year (over 150 of which will be seen on mammography), compared to fewer than 6 potentially induced over their entire lifetime by the radiation exposure from mammography. The few cancers possibly induced by radiation exposure typically occur a minimum of 8 years later, and would be expected to be detected through continued screening.

Average natural background radiation per year in the United States, excluding medical exposures, is a whole-body exposure of about 3 milliSieverts. The radiation exposure to the breasts from annual natural background radiation is about ¾ that of the exposure to the breasts from 2-view bilateral mammography. The effective dose (and total risk of detriment) from natural background radiation, however, is about 6 times higher than the effective dose (total risk of detriment) from mammography, because natural background radiation exposes the entire body, while mammography exposes only breast tissue.

What is “overdiagnosis”? A cancer that would not have progressed within a woman’s lifetime does not require treatment. Detecting such cancers is “overdiagnosis” and will result in unnecessary testing and procedures, often including surgery and radiation treatment. There is a real possibility that some overdiagnosis exists, but because an indolent tumor can not be distinguished from a progressive tumor, estimates of overdiagnosis must be derived from observed vs. expected incidence rates. In the presence of an on-going screening program, there will always appear to be an excess of cancers due to the lead time gained by screening. Reasonable estimates of overdiagnosis suggest it is a very small fraction of all breast cancers.

There are no formal studies where breast cancer has been diagnosed and deliberately not treated. The closest direct evidence on the natural history of breast cancer that may not require urgent treatment comes from retrospective review of excisional surgical pathology where the initial interpretation was not cancer, but where cancer was actually present. Typically such cancers are low-grade DCIS. In these series, where most of the cancer was typically removed, but the patient did not receive further treatment for cancer, 11 to 60% developed invasive cancer in that quadrant over follow-up periods ranging from 10 to 30 years.
(reviewed in [38]), with one death from breast cancer reported [39] among 130 women collectively studied.

In an ongoing trial where patients with 2.5 cm or smaller low- or intermediate-grade DCIS and 1 cm or smaller high-grade DCIS (with no residual calcifications mammographically) were randomized to surgery only or surgery plus radiation, the five-year recurrence risk in the group having only surgery was 6.1% in women with low- to intermediate-grade DCIS and 15% for those with high-grade DCIS [40]. These findings suggest that selected women with low-grade DCIS may not require radiation treatment, though longer follow-up is needed.

High-grade DCIS requires treatment. In 20-year follow-up results from the Swedish screening trials, 73% of deaths in women with “early” breast cancer (< 1 cm, node negative) can be attributed to those with casting type calcifications on mammography [41] (representing a 42% fatality rate in this group), usually due to high-grade DCIS with a small invasive component.

Because invasive cancers can spread to lymph nodes and to the rest of the body and cause death, they are not usually considered among potential cases of overdiagnosis. Potentially, detection of a very slowly growing invasive cancer in an elderly woman could be overdiagnosis for that woman. One of the ways we infer the biologic behavior of a cancer is change from a prior mammogram. A new finding on a mammogram that proves to be an invasive cancer is unlikely to be indolent, as it has shown itself to be growing.

The first mammogram may show some disease which is indolent and would not progress. Yen et al [42] estimated that 37% of DCIS seen on the first (prevalent screening) mammogram may be nonprogressive. At subsequent (incidence screening) mammography, only 4% of DCIS was estimated to be nonprogressive [42]. We do not know which cancers will progress based on a single time point. It may be more dangerous to delay treatment of even slowly-growing cancers in a younger woman as there are more potential years ahead during which the cancer could progress (and more potential years of life lost if she dies of breast cancer). Early identification of even high-risk precursors of cancer such as atypical ductal hyperplasia, which often have a similar mammographic appearance to low-grade DCIS, may prove advantageous in that a woman and her doctor can discuss risk reduction strategies and possibly more intensive screening.

As breast imagers, it is our duty to make the correct diagnosis. This is usually readily accomplished by a needle biopsy, in concert with the pathologist. Decisions about treatment and reducing harms from treatment are those of the surgical, radiation, and medical oncology communities, and clearly merit further study.
Are recommendations to reduce mammographic screening based on saving money?

The USPSTF does not specifically consider monetary costs, though its recommendations are often used to determine insurance and Medicare coverage. That said, cutting mammographic screening is not fiscally prudent.

When making health care policy decisions, the cost per (quality-adjusted) year of life saved (QALY) is often considered. A commonly accepted threshold is that a procedure or test that costs $100,000 per year of life saved is deemed “cost effective” [43]. While there are fewer cancers in younger women, there are more potential years of life to be saved. The estimated marginal cost per year of life saved by screening mammography in 1998 in women aged 40 to 79 was $18,800 [44]. Looking at only women aged 40 to 49, using a 30% estimated reduction in mortality such as seen in Sweden, the estimated marginal cost per year of life saved was $26,200 [44]. For women aged 80 to 85, the estimated marginal cost per year of life saved was $35,000 [44]. Targeted use of digital mammography in women with dense breasts is estimated to cost $97,000 per QALY [45], assuming early detection carries the same benefit regardless of film or digital technique. Seat belts and air bags were in the range of $32,000 per QALY [46]. Just as a seatbelt is only of benefit if you get into an accident, a mammogram is only of potential benefit if you have breast cancer.

Treating early breast cancer is not only less harmful and more effective than treating advanced breast cancer, it is also less expensive. In a study of nearly 180,000 members of a health maintenance organization in southeastern Pennsylvania, women who had undergone mammographic screening were much more likely to have earlier stage disease than those who had not [47]: 12% were stage 0 (ductal carcinoma in situ, DCIS), 62% were stage I (invasive cancer 2 cm in size or smaller with negative nodes), and 28% were stage II (invasive tumor 2.1 to 5 cm in size and/or metastatic axillary nodes (details of staging can be found in [4])) among women with breast cancer who had had mammography. Among women who did not undergo screening mammography, 2% were stage 0, 29% stage I, and 44% stage II. Among those not screened, 14% of women presented with advanced breast cancer (stage III or IV), compared to 2% among those who had been screened [47]. The cumulative costs of treating stage III to IV breast cancer were $50,000 to $60,000 (in 1989 dollars) compared to $18,000 to $25,000 for stage 0 to I breast cancer [47]. These figures do not consider pain and suffering or effects of chemotherapy, more extensive surgery, lost productive time from work and family that often accompany treating more advanced breast cancer but which are minimized when cancer is diagnosed early. Such harms from cutting back mammographic screening were not considered in the USPSTF review [23].
**Women are getting the message not to examine their breasts. Is this correct?**

The USPSTF now recommends against *teaching* breast self examination, but awareness of changes in one’s breasts is still important.

Since 2002, results from two large prospective RCTs have been published where women were systematically taught breast self examination (BSE, reviewed in [48]). There was no difference in breast cancer death rates among women taught BSE compared to those who were not. There was a nearly two-fold increase in benign biopsies among those women who performed BSE (false positives).

If a woman notices a new lump or other suspicious change in her breast (bloody nipple discharge, nipple retraction, skin dimpling or skin thickening), she should seek medical attention. If cancer is present, you don’t want to watch it grow.

**Should a woman’s doctor still examine her breasts?**

It is not wrong for a doctor to examine the breasts, but it is unlikely to be of benefit to the woman.

About 3 cancers will be found only on clinical breast examination (CBE) for every 10,000 women examined (about tenfold lower than cancer detection rates of mammography) [49]. There are many more false positives with clinical examination than with mammography, with 1% of women with a finding suspicious only on clinical breast examination proving to have cancer (compared to about 7% of women recalled for a mammographic finding and 20-30% of those biopsied based on mammography having cancer) [49]. Most of these require mammography and/or ultrasound for further evaluation, and some even require biopsy. If there is no suspicious finding on either mammography or ultrasound, the chance of a clinical abnormality being cancer is under 3% [50]. Cancers found only on mammography are 10 times more likely to be node negative than those found only on clinical examination [49]. Thus, clinical breast examination produces many false positives with very little additional cancer detection yield, and finding such cancers is less likely to be life-saving. At present, the USPSTF indicated there was insufficient evidence of a benefit to recommend clinical breast examination [23].

**SUMMARY**

In summary, mammography is the only method proven to reduce deaths due to breast cancer. This benefit is observed for women aged 40 through 74 years, and likely extends to older women as long as reasonable health is maintained. The so-called “harms” due to mammography are mostly minor, consisting of additional mammographic views or ultrasound in about 8 to 10% of women screened (per
screening round). About 15 women per 1000 women screened will be recommended for a needle biopsy because of mammography, and from 10 to 13 of those biopsies will show that cancer is not present (false positives). For the one in 69 women who will develop invasive breast cancer in her forties, and more than one in 40 women who will develop breast cancer in her fifties or older, potential harms of delayed diagnosis if mammography is not performed regularly include diagnosis with advanced breast cancer requiring chemotherapy and often more extensive surgery, and an increased risk of death from breast cancer. Not all breast cancer is seen with mammography: further research and validation of supplemental methods to detect early breast cancer is needed. Use of supplemental screening with ultrasound or magnetic resonance imaging may be appropriate in addition to mammography in women at increased risk of breast cancer [12]. Since 75% of women who develop breast cancer have no known risk factors, annual mammography should be offered to all women aged 40 and older.

Disclosures

WAB is a consultant to Naviscan, Inc., and an uncompensated member of the medical advisory board of Medipattern, Inc. REH is a consultant to General Electric Healthcare, and is on the medical advisory boards of Koning Corporation and Bracco, SpA. DBK receives research support from General Electric Healthcare. RAS has nothing to disclose.

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