United States Preventive Services Task Force Screening Mammography Recommendations: Science Ignored

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OBJECTIVE. The purpose of this article is to examine the scientific evidence considered by the United States Preventive Services Task Force (USPSTF) in recommending against screening mammography in women 40–49 years old and against annual screening mammography in women 50 and older. We use evidence made available to the USPSTF to estimate the benefits and "harms" of screening mammography in women 40 years old and older. We use Cancer Intervention and Surveillance Modeling Network modeling to compare lives saved by different screening scenarios and the summary of evidence prepared for the USPSTF to estimate the frequency of harms of screening mammography by age.

CONCLUSION. Averaged over the six Cancer Intervention and Surveillance Modeling Network models of benefit, screening mammography shows greatest benefit—a 39.6% mortality reduction—from annual screening of women 40–84 years old. This screening regimen saves 71% more lives than the USPSTF-recommended regimen of biennial screening of women 50–74 years old, which had a 23.2% mortality reduction. For U.S. women currently 30–39 years old, annual screening mammography from ages 40–84 years would save 99,829 more lives than USPSTF recommendations if all women comply, and 64,889 more lives with the current 65% compliance rate. The potential harms of a screening examination in women 40–49 years old, on average, consist of the risk of a recall for diagnostic workup every 12 years, a negative biopsy every 149 years, a missed breast cancer every 1,000 years, and a fatal radiation-induced breast cancer every 76,000–97,000 years. Evidence made available to the USPSTF strongly supports the mortality benefit of annual screening mammography beginning at age 40 years, whereas potential harms of screening with this regimen are minor.

Keywords: breast, guidelines, mammography, mortality benefit, screening

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On November 16, 2009, the United States Preventive Services Task Force (USPSTF) released new recommendations for breast cancer screening [1]. Their new recommendations reversed previous 2002 USPSTF recommendations of screening mammography every 1–2 years for women beginning at age 40 years. Their new recommendation instead was for women to begin routine screening biennially, beginning at age 50 and ending at age 74 years.

For women younger than age 50 years, the USPSTF concluded that, "The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms" [1]. For women older than 74 years, they concluded "that the current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older" [1].

The USPSTF considered the following evidence in formulating its recommendations. First, they examined randomized controlled trial (RCT) data on screening mammography, as analyzed and summarized in a detailed report by the Oregon Evidence-Based Practice Center at the Oregon Health and Science University [2]. This publication and a more detailed report [3] were funded by the Agency for Healthcare Research and Quality and were released simultaneously with the USPSTF recommendations on November 16, 2009, having been embargoed to review before that date. A summary of the findings in terms of benefit of screening mammography by age is shown in Table 1.

Second, the USPSTF considered the "harms" associated with screening mammography, as summarized in the publication and more detailed report prepared by the Oregon Evidence-

Based Practice Center at the Oregon Health and Science University [2, 3]. Harms considered included radiation exposure, pain during procedures, patient anxiety and other psychological responses, consequences of false-positive and false-negative test results, and overdiagnosis of breast cancer.

Third, the USPSTF examined age-specific screening results from the Breast Cancer Surveillance Consortium, a National Cancer Institute–sponsored study of longitudinal mammography data collected from seven sites in the United States [4, 5].

Finally, the USPSTF considered modeling of 20 different screening mammography regimens, starting and ending at various ages and including annual and biennial screening. Modeling was conducted independently by six different groups under the Cancer Intervention and Surveillance Modeling Network project funded by the National Cancer Institute. A joint report was made available to the USPSTF in formulating its recommendations and was published simultaneously with the USPSTF recommendations [6].

The evidence not considered by the USPSTF in formulating their recommendations included the following. First, all peer-reviewed studies assessing the benefit of screening mammography that were not RCTs using mortality as the outcome measure were not considered. Omitted studies included all service screening results [7, 8] and studies detailing the improvement in screening mammography over time since the RCTs. Second, all peer-reviewed analyses of the cost-benefit of screening mammography compared with other accepted interventions were not considered. The summary of evidence prepared for the USPSTF listed 112 included studies and 514 excluded studies [3].

Recommendations of the USPSTF carry considerable weight. The U.S. Healthcare Reform Act, in its original form, included a specific recommendation that only USPSTF recommendations with a grade of A or B would receive Medicare or Medicaid funding. The recent USPSTF report gave the recommendation that women 50–74 years should receive biennial screening a B rating. If their recommendations were followed, only women ages 50–74 years would be covered, and then for screening mammography no more frequently than every 24 months. Medicare recipients would not be covered for screening mammography after the age of 74 years.

TABLE 1: Meta-Analysis Results of Randomized Controlled Trials by Age Decade

Variable	Age Range (y)			
	39–49	50–59	60–69	70–74
No. of randomized controlled trials contributing data	8	6	2	1
Relative risk (95% credible interval)	0.85 (0.75–0.96)	0.86 (0.75–0.99)	0.68 (0.54–0.87)	1.12 (0.73–1.72)
No. of subjects needed to invite to prevent one breast cancer death (95% credible interval)	1,904 (929–6,378)	1,339 (322–7,455)	377 (230–1,050)	Not available

Note—Relative risk is defined as the breast cancer mortality rate in the invited-to-screen group divided by breast cancer mortality rate in the control (uninvited-to-screen) group. Data are adapted from [2].

Many third-party insurers follow Medicare's lead in deciding which radiologic studies they will reimburse. Some states, such as Colorado, have tied funding for screening mammography to USPSTF recommendations. The USPSTF recommendations could lead to Medicare and insurers funding only biennial screening and then only for women 50–74 years old.

Historically, the decision to recommend screening mammography has hinged on RCT results showing a statistically significant survival benefit overall or for specific age groups [9–11]. As the meta-analysis prepared specifically for the 2009 USPSTF guidelines shows [2, 3] (Table 1), RCT data show a statistically significant benefit for women 39–49 years old alone, 50–59 years old alone, and 60–69 years old alone. The USPSTF decided to depart from this standard of medical decision making, instead focusing on the "number needed to invite" to screening mammography in justifying its decision against screening women 40–49 years old with mammography. The USPSTF estimated that it would require inviting 1,904 women ages 40–49 years to save one life and concluded that this was too many women screened for one life saved.

We wish to examine in detail the data that the USPSTF used in making the recommendation against screening mammography in women 40–49 years old and against annual screening mammography in women 50 years old and older.

Materials and Methods

We use mean values of the six Cancer Intervention and Surveillance Modeling Network models of screening mammography to compare mortality reduction for women who follow the USPSTF 2009 recommendation (of biennial screening in women ages 50–74 years) to the American Cancer Society (ACS) recommendation (of annual screening starting at age 40 years). For convenience, we assume an ending age of 84 years in the ACS screening regimen because that coincides with data modeled by the National Cancer Institute–funded study that was made available to the USPSTF.

TABLE 2: Potential Harms of Screening Mammography, by Age Decade

Potential Harm	Age Range (y)				
	40–49	50–59	60–69	70–79	≥ 80
False-positive mammogram	10.2	11.5	12.7	14.5	16.8
Additional imaging	11.9	13.2	14.2	15.6	17.8
False-positive biopsy	149	164	196	233	500
Missed breast cancer	1,000	909	714	667	714
Fatal radiation-induced breast cancer due to screening mammography	76,000–97,000	145,000–185,000	293,000–373,000	578,000–736,000	Too large to estimate

Note—Data are average no. of years a woman would undergo annual screening mammography for one occurrence. Results shown in the first four rows are based on tables in [2, 3]. Results in the last row are based on [18–20]. The first number in each column is based on the average dose of screen-film mammography, and the second number is based on the average dose of digital mammography.

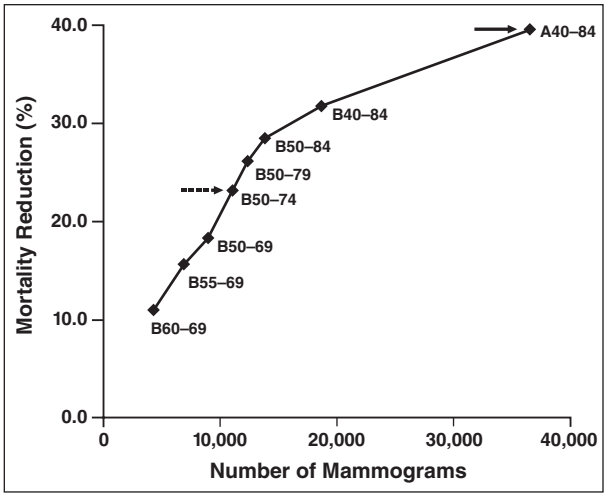

Fig. 1—Percentage mortality reduction from various screening strategies. Note that annual (A) screening from ages 40–84 years (A40–84, *solid arrow*) is estimated to have 71% greater mortality benefit than biennial (B) screening from ages 50–74 years (B50–74, *dashed arrow*). Number of mammograms shown on horizontal axis is per 1,000 women screened. Data shown are mean values of six models from [6].

Mortality reduction is translated into number of women's lives saved per 1,000 women screened with the two competing screening scenarios. Using U.S. population census figures, we compare the number of lives saved for each screening scenario in a representative U.S. population just entering age eligibility for mammographic screening, the cohort of women aged 30–39 years in 2009. U.S. mammography screening compliance rates are used to make a more realistic estimate of the difference in numbers of lives saved by women following the two different screening scenarios. We project the use of these two different scenarios over the mean life span of U.S. women to estimate the difference in numbers of lives saved per year between the two screening scenarios.

"Harms" of screening mammography—specifically, false-positive mammography results, recall for additional workup, recommendation for a biopsy that is negative for cancer, and missed breast cancers—are estimated using Breast Cancer Surveillance Consortium data in terms of number of years a woman would need to undergo annual screening mammography to encounter one such "harm." Surveillance Epidemiology and End Results data on breast cancer incidence in the United States from 2002 to 2006 are used to estimate the frequency of breast cancer in the absence of screening mammography in women 40–49 years old.

Results

The mean results of the six models of screening mammography benefit are summarized in Figure 1. Annual screening for women 40–84 years old is estimated to convey a 39.6% mortality reduction (range in mortality reduction over the six models, 29.4–54%), whereas biennial screening at ages 50–74 years is estimated to convey a 23.2% mortality reduction (range, 20–28%). The mean mortality reduction from annual screening mammography from ages 40–84 years is 71% higher than from biennial screening mammography from ages 50–74 years. Thus, on average, a woman who gets breast cancer has a 71% higher probability of not dying from the disease if she follows ACS mammography screening guidelines rather than USPSTF recommendations.

The Cancer Intervention and Surveillance Modeling Network models used to estimate mortality reduction assume that, starting at age 40 years, 12–15% of women get breast cancer and, in the absence of screening, 3% of women will die of breast cancer (i.e., that 20–25% of women who get breast cancer will die of breast cancer in the absence of screening). Thus, for each 10% mortality reduction from screening, 0.3% or three per 1,000 women's lives would be saved. Therefore, approximately 12 lives per 1,000 women screened would be saved with the annual 40–84 screening regimen (3.96 × 3 per 1,000), whereas approximately seven lives per 1,000 women screened would be saved with the biennial 50–74 USPSTF-recommended screening regimen (2.32 × 3 per 1,000). Thus, the ACS-recommended screening regimen would save five more lives per 1,000 women than the USPSTF-recommended screening regimen.

According to the 2009 U.S. census estimate, there are 19,965,964 women in the 30–39 years age group (i.e., just entering the decade in which they might begin screening) [12]. For women in this 10-year age cohort, over the course of their lifetimes, 99,829 more lives (19,965,964 × 0.005) would be saved by following the ACS-recommended screening regimen rather than by following the USPSTF-recommended screening regimen. Of course, not all women follow screening guidelines. According to recent surveys of compliance with screening mammography guidelines [13, 14], approximately 66% of women 40 years old and older have had screening mammography within the past 2 years. Assuming a 65% compliance rate to each guideline, 64,889 more women's lives would be saved in that single decade cohort (women ages 30–39 years in 2009) by complying with ACS guidelines rather than USPSTF guidelines over the course of their lives.

According to 2006 life tables, the life expectancy of a woman in her 40th year of life (39 years) in the United States is 42.6 years [15]. Including all U.S. women ages 40–82.6 years, a total of approximately 85 million women would be eligible for screening mammography at any given time. If all women were following screening recommendations, approximately 10,000 more lives per year would be saved following ACS recommendations rather than USPSTF recommendations. Using more realistic estimates of compliance with screening recommendations (a 65% compliance rate), approximately 6,500 more women's lives would be saved per year following ACS recommendations. In terms of women-years of life saved, the benefit of following ACS recommendations is even greater because of the added life expectancy gained by saving the lives of younger women.

Table 2 estimates the harms of mammography that are focused on by the USPSTF by estimating the average number of years of annual screening a woman of a given age would need to undergo to encounter a specific harm [2, 4, 5]. On average, a woman in the age range 40–49 years who attends annual screening mammography will have a false-positive screening mammogram once every 10 years, get recalled for additional imaging once every 12 years, undergo a false-positive biopsy once every 149 years, and have a missed breast cancer once every 1,000 years.

For an older woman, the likelihood of a false-positive screening mammography result, recall, and false-positive biopsy is less than that for a woman 40–49 years old, whereas the likelihood of a missed breast cancer would increase (from an average of once every 1,000 years for a woman 40–49 years old to once every 667 years for a woman 70–79 years old), as shown in Table 2.

According to Surveillance Epidemiology and End Results breast cancer incidence data [16], in the absence of screening mammography,

a woman in the age range 40–49 years will get breast cancer, on average, once every 506 years of life, or over the entire decade, has about a one in 51 chance of being diagnosed with breast cancer, in situ or invasive, and a one in 66 chance of being diagnosed with invasive breast cancer.

The USPSTF made two fundamental errors in estimating radiation dose (and risk) to the breast. First, they based their estimates of radiation doses on screen-film mammography phantom results [17] rather than on actual average patient exposures [18]. Patient doses are 26% higher than phantom doses for screen-film mammography because the average U.S. woman's compressed breast during mammography is thicker than the standard phantom. Second, the USPSTF incorrectly combined the mean glandular dose to the left breast to the mean glandular dose to the right breast, doubling their dose estimate.

When correctly estimated, the mean glandular dose for bilateral two-view mammography averages 3.72 mGy for digital mammography and 4.74 mGy for screen-film mammography [18]. On the basis of the most recent Biologic Effects of Ionizing Radiation report [19], the risk of a fatal radiation-induced breast cancer for a woman 40–49 years old is approximately one in 100,000 for a bilateral two-view digital mammography examination and 1.3 in 100,000 for a bilateral two-view screen-film mammography examination [20]. As shown in Table 2, these radiation risks decrease when screening older women [19, 20].

Discussion

The publication of the USPSTF guidelines immediately led to national controversy. Many have voiced the opinion that the USPSTF's "new data" showed mammography to be ineffective for women in their 40s and that there is no real difference between annual and biennial screening intervals for older women. Furthermore, the harms associated with screening mammography, such as unnecessary biopsies, have been thought to occur frequently. Our review and analysis of the published data available to the USPSTF refute these opinions.

The meta-analysis of RCT data made available to the USPSTF in formulating their screening recommendations showed a statistically significant benefit from invitation to screening in each of three subdivided age cohorts: 39–49, 50–59, and 60–69 years [2, 3]. Available RCT data showed no benefit in women older than 69 years, primarily because of limited study data for older women. Yet the USPSTF failed to recommend screening in younger women, 40–49 years old, while recommending screening every 2 years for women 70–74 years old. Clearly, the USPSTF was not using statistical significance of invitation to screening in RCTs as their criterion for selecting the age ranges for which they recommended screening.

The USPSTF's focus on "number needed to invite" to screening to prevent one breast cancer death was misguided and has been frequently misinterpreted as "number needed to screen." Number needed to invite is relevant to RCTs, but not to service screening [21]. The potential harms considered by the USPSTF, such as radiation dose and cancer risk [19, 20], false-positive and false-negative mammograms, and recall for further imaging workup, accrue only to women who actually attend screening mammography, not from an invitation to screening. The "number needed to invite" estimated from screening trials is greater than the "number needed to screen" to save one life. Nonattendance rates and contamination rates in screening trials cause the "number needed to invite" to be at least 25–30% greater than the number needed to screen to prevent one breast cancer death.

Cancer Intervention and Surveillance Modeling Network models used by the USPSTF show large differences in mortality reduction and life-years gained between ACS and USPSTF recommended guidelines. A 71% improvement in mortality reduction and similar improvement in life-years gained is predicted for women who elect ACS guidelines over the USPSTF guidelines of biennial mammography between ages 50 and 74 years. Unfortunately, the USPSTF chose not to delineate these differences in their publication, resulting in confusion regarding the magnitude of the difference. The 71% mortality reduction improvement derives from cumulative smaller gains in three areas: screening women in their 40s, annual versus biennial screening in women 50–74 years old, and screening beyond age 74 years.

Missed breast cancers were considered one of the serious harms of mammography screening, and correctly so. Nothing is potentially more harmful than letting a breast cancer evolve from its preclinical mammographically detectable potentially curable stage to a larger clinically detectable stage. That missed breast cancers are the second highest cause of medical malpractice lawsuits in the United States attests to their importance. Yet according to the Cancer Intervention and Surveillance Modeling Network modeling data averaged over all six models, the USPSTF-recommended screening regimen misses 20–25 more cancers per 1,000 women screened than the ACS-recommended screening regimen and by our own analysis, costs approximately 6,500 more women's lives per year. If missed breast cancers are one of the greatest harms of mammography, then are not USPSTF recommendations doing greater harm? Is not the point of medical intervention to save the most lives?

Although harms associated with screening exist, they compare favorably to the harms associated with many medical interventions. There are also harms of not screening that must be compared with the harms of screening. To provide some perspective for women and their health care providers contemplating the USPSTF screening harms information, we have expressed the potential harms of annual screening mammography in individual patient terms in Table 2. The risk of a false-positive biopsy once every 149 years for annually screened women in their 40s is less frequent than commonly assumed. The USPSTF did not enumerate the false-positive biopsy rate for nonscreened women for comparison with the rate for screened women. The harms of unnecessary recall for additional imaging were emphasized. On average, women will be recalled only once every 11.9–17.8 years to gain the mortality reduction benefits described above. This harm can be mitigated if women elect real-time screening interpretation with same-visit diagnostic imaging offered at many U.S. facilities. This option was not mentioned by the USPSTF report. The USPSTF did not delineate the rate of diagnostic mammography for women not screened for comparison.

The USPSTF recommendations have done potential damage to women's health by failing to seize the singular opportunity to both improve mammography in the United States and to increase screening mammography compliance. Their recommendations have dissuaded some women from undergoing mammography. Equally important, the USPSTF failed to make any recommendations to implement a population-based screening program in the United States. The USPSTF could have recommended establishment of an organized screening program and a national mammography database tracking system for women undergoing mammography in the United States [22].

The irony of screening mammography is that it is one of the most studied of medical interventions. Over three-quarters of a million women have participated in RCTs of screening mammography, over half of them in women 39–49 years old. Millions more women have been followed longitudinally through databases such as the Breast Cancer Surveillance Consortium, Swedish, and Canadian screening programs. Mammography is one of the few medical screening interventions that has been shown to have statistically significant mortality benefits, even when broken down into age subgroups never intended by the original RCT investigators. Rather than following the established criterion for evaluating medical screening interventions (i.e., the presence of a statistically significant mortality benefit), the USPSTF chose to ignore the science available to them and overemphasized the potential harms of screening mammography, to the serious detriment of U.S. women who follow their flawed recommendations.

Analyses done to support the USPSTF in making recommendations for mammography screening show that lives saved and life-years gained are maximized by screening annually starting at age 40. This regimen saves 71% more lives than the USPSTF-recommended regimen of biennial screening from ages 50–74 years. These analyses also show that the individual harms from the additional screening, including the risks of recall for additional testing, biopsy, and radiation-induced breast cancers, are minimal compared with the life-saving benefit of early detection for women electing screening.

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