

Review of USPSTF 2009 Study

By Julie Ohnemus, M.D.

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In November 2009 the U.S. Preventative Services Task Force (USPSTF) released new recommendations regarding mammogram screening. Their recommendation changed from starting routine mammograms when a woman turns 40 to when she turns 50, and then to screen only every two years instead of annually. For my response to women who are confused about what to do, see the newsletter of the Humboldt Community Breast Health Project, Spring, 2010. There is no simple answer that fits everyone. This is my summary of the USPSTF report to supplement that newsletter article.

The USPSTF used two processes to come to their conclusions. The first was a Meta-analysis, a systematic analysis of evidence-based and Medline studies, which was evaluated by the Oregon Evidence-based Practice Center¹. The second process was statistical modeling of 20 different screening scenarios by six universities in the US.

Several things surprised me about the USPSTF study. The task force itself was composed of primary care physicians and did not include oncologists or cancer specialists. Six out of eight of the studies utilized are from the 1960s, 70s & 80s (TABLE 1) – older studies are likely to involve equipment and techniques by pathologists that are now considered outdated. The statistical modeling groups did not even look at the same features and outcomes. Only two of these groups looked at mortality related to breast cancer, and yet that was part of the USPSTF's grounds for the conclusions they drew (TABLE 2).

Four key questions were considered. In order to help us make our own personal decisions, the USPSTF recommendations² were graded to reflect the strength of the evidence they reviewed. The tables from the USPSTF report and the footnotes of sources are included here.

QUESTION 1: Does screening with mammography (film and digital) or MRI decrease breast cancer mortality among women ages 40 to 49 years and 70 years and older?

USPSTF ANSWERS:

- The USPSTF found "fair" evidence to recommend against routine screening mammography in women aged 40 to 49 years who have no abnormal breast findings. The decision to start regular, biennial screening mammography before the age of 50 should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms (Grade C recommendation, see TABLE 3).
- This recommendation statement applies to women 40 years or older who are not at increased risk for breast cancer with a known underlying genetic mutation or a history of chest radiation.
- The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or MRI instead of film mammography

as screening modalities for breast cancer.

- Results indicated that the overall diagnostic accuracy of digital and film mammography was similar, although digital was more accurate in women under age 50 years, women with radiographically dense breasts, and premenopausal women³.

WHAT THE META-ANALYSIS CONCLUDED:

Breast cancer has an asymptomatic, non-palpable phase that can be identified by mammography. Breast cancer can be more effectively treated in the early stages.

Recent data shows us that approximately 17% of breast cancer deaths occurred in women who were diagnosed in their 40s, and 22% occurred in women diagnosed in their 50s.

NCI 2005 data showed breast cancer mortality has decreased since 1990 at a rate of 2.3% per year overall^{4,5}. Women age 40-50 years had a decline in breast cancer mortality of 3.3% per year. An evaluation of mortality trends from 1990 through 2000 from seven studies attributed 28-65% of the decline to mammography screening, while the remainder of the decline was due to improved adjuvant treatments⁶.

The "fair" evidence was an independent rating out of good, fair or poor. It was rated fair because 1) some studies were old and didn't utilize the current technology we have today; 2) the most current study analyzed, the AGE trial, which was specific to the age group of 40-50, came from Europe where screening is performed differently than in the US (e.g. the baseline mammogram is two views and the biennial follow-up screening is one view); and 3) the AGE trial and the other studies pooled for mortality for women 39-40 year old was not statistically significant which means its results could have been secondary to chance (TABLE 4).

There was a 15% reduction in dying from breast cancer for women in their 40s when screening was used, which means that the "number needed to invite" (NNI) was 1,904 women to have a mammogram to prevent one breast cancer death. This was contrasted to a 21% reduction in mortality for all age groups. (NNI 1,339 women in their 50s; NNI 377 women in the 60-70 age group – which at 32% was the greatest mortality reduction). The prevention of death from screening mammograms improves with aging due to the decline in the amount of glands vs. fat in the breast tissue (TABLE 5).

If a woman had all three characteristics – under age 50 years, premenopausal, and determined "dense breasts" on their mammogram – the detection of cancer by film was 54% vs. 79% for digital.

A screening mammogram plus MRI detects twice as many cancers in dense breasts, but the supplemental MRI leads to two times as many unneeded additional exams and three times as many unneeded biopsies⁷.

QUESTION 2: What are the harms associated with screening with mammography (film and digital) and MRI?

USPSTF ANSWERS:

- The USPSTF recommends biennial screening mammography for women aged 50 to 74 years to lessen harms (Recommendation Grade B, TABLE 3).
- The current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older (Recommendation Grade I, TABLE 3).
- The harms resulting from screening for breast cancer include psychological harms, unnecessary imaging tests and biopsies in women without cancer and inconvenience due to false-positive screening results.
- Detection of cancer that would never have affected the woman's health is called over-diagnosis, and it is usually followed by over-treatment. Over-diagnosis and unnecessary earlier treatment are important potential harms from screening women in the age group older than 74.
- Radiation exposure, although a minor concern, is also a consideration.
- Adequate evidence suggests that the overall harms associated with mammography are moderate for every age group considered. Although false positive results are more common for women aged 40 to 49 years, over-diagnosis is a greater concern for women in the older age groups.
- The potential harm or risks of film mammography are insufficient to recommend digital or MRI screening. (Recommendation Grade I, Table 3)

WHAT THE META-ANALYSIS / STATISTICAL MODELS¹ SHOWED:

Biennial screening is likely to lessen the harms by half and still prevent 80% of the deaths achieved by annual screening. TABLE 6 shows the comparison of the harms and benefits for biennial vs. annual screening and stopping ages as determined by the statistical models used by USPSTF. TABLE 7 shows the percentage of the reduction of mortality maintained when moving from an annual to a biennial screening. So for example if 100 women's lives were saved by annual mammography only 80 of those lives would be saved with screening every other year.

Several recent reviews include older studies of untreated DCIS cases that were diagnosed on going back and reviewing biopsy specimens that were previously reported benign^{8,9,10}. In these studies, untreated DCIS progressed to invasive cancer in 14-53% of cases over mean periods of 8-22 years. In a case series of 775 women diagnosed with DCIS who underwent breast-conserving therapy, 66 eventually developed invasive cancer, and 71 developed recurrent DCIS at a mean follow-up of 5.4 years¹¹.

Many patients would consider quality of life as an important outcome but it is difficult to measure and report in trials – more research is needed. Harms of mammography screening have been identified, but their magnitude and effect are difficult to measure.

The absolute level of radiation exposure and corresponding radiation risk from mammography is very low. Special considerations may be needed, however, for women exposed to additional radiation for other purposes or women particularly susceptible to breast cancer such as BRCA mutation carriers.

Patient adverse experiences, such as pain during procedures and anxiety and other psychosocial responses, are common but seem to be transient and do not discourage future screening practices. This may differ for individual women.

The magnitude of over-diagnosis is based on estimates. These estimates are difficult to apply because, for individual women, it is not known which types of cancer will progress, how quickly cancer will advance, and expected lifetimes.

No women 75 years or older have been included in the multiple randomized clinical trials of breast cancer screening. And yet breast cancer is a leading cause of death in older women, which might suggest that the benefits of screening could be important at this age.

One must also consider the harms associated with treatment of cancer. Screening detects not only cancer that could lead to a woman's death but also cancer that will not shorten a woman's life.

Because of a shortened life span among women 75 years or older, the probability of over-diagnosis and unnecessary earlier treatment increases dramatically after about age 70 or 75 years.

Harms also include downstream consequences of false-positive mammography results, such as additional imaging and biopsy.

In order to diagnose one case of invasive cancer 556 women aged 40-49 must be screened, 294 women aged 50-59, 200 women aged 60-69, and 148 women aged 70+ (TABLE 8).

In women age 40-49 years for one case of invasive breast cancer detected by mammography screening, 556 women have a screening mammography, 46-48 women have additional imaging, and 5-8 women have biopsies. (TABLE 9).

So women age 40-49 years have higher rates of additional imaging but lower rates of biopsy than older women – suggesting that additional imaging for an abnormal finding upon screening may be particularly useful in selecting biopsy candidates among premenopausal women, who have denser breast tissue and more fibrocystic changes than postmenopausal women.

QUESTION 3: Does clinical breast exam (CBE) screening decrease breast cancer mortality? Alone or with mammography? What are the harms associated with CBE?

USPSTF ANSWER:

- There is insufficient evidence to assess the additional benefits and harms of CBE beyond screening mammography in women 40 years or older (Recommendation Grade I).

WHAT THE META-ANALYSIS SHOWED:

The potential harms of CBE are thought to be small but include false-positive test results, which lead to anxiety and worry, as well as repeated medical visits and unwarranted imaging and biopsies.

QUESTION 4: Does breast self-examination (BSE) practice decrease breast cancer mortality? What are the harms associated with BSE?

USPSTF ANSWER:

- The USPSTF recommends against clinicians teaching women how to perform breast self-examination. There is adequate evidence that teaching BSE is associated with harms that are at least small (Recommendation Grade D).

WHAT THE META-ANALYSIS SHOWED:

Results indicate no significant differences in breast cancer mortality when utilizing BSE or not^{12, 13, 14}.

All the evidence garnered from the USPSTF meta-analysis is summarized in TABLE 10. Interpretation of the evidence varies, however, and TABLE 11 shows the differences in recommendations of each evaluating organization.

Sources:

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