

Hypothesis/Commentary

Mammography and Women Under 50: Déjà Vu All Over Again?

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“The USPSTF recommends against routine screening mammography in women aged 40 to 49 years. The decision to start regular biennial screening mammography before the age of 50 should be an individual one and take into account patient context, including the patient's values regarding specific benefits and harms.

The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policymakers should understand the evidence but individualize decision making to the specific patient or situation.”

U.S. Preventive Services Task Force Statement (Ann Intern Med 2009;151:716–26).

“The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences. Clinicians should inform women about the potential benefits (reduced chance of dying from breast cancer), potential harms (e.g., false-positive results, unnecessary biopsies), and limitations of the test that apply to women their age. Clinicians should tell women that the balance of benefits and potential harms of mammography improves with increasing age for women between the ages of 40 and 70.”

U.S. Preventive Services Task Force Statement (Ann Intern Med 2002;137:344–6).

The statements above, for women at average risk of breast cancer, seem very reasonable and are not vastly different. However, the leading statement by the 2009 U.S. Preventive Services Task Force (USPSTF) does indeed recommend against routine screening mammography every 1 to 2 years for women ages 40 and older (although the USPSTF also noted that only “fair”

evidence existed for such a recommendation). These statements by the 2002 and 2009 Task Forces are clearly synchronous in terms of clinical considerations for mammography screening, advocating a more personalized approach to decision making (1, 2). What subtle differences do exist are likely driven by two randomized trials published since the 2002 Task Force report which examined the role of mammography screening in women under 50 (3, 4). The 2009 USPSTF recommendations were also informed by the Cancer Intervention and Surveillance Modeling Network studies assessing the effects of mammography screening under different screening schedules and by age groups published since the 2002 recommendations (5). In the case of the trials, neither found a survival advantage among women randomly assigned to screening on measures of all-cause or breast cancer mortality. Are these recommendations so vastly different that they warrant the surge of controversy produced by the 2009 Task Force recommendations? Or is the new recommendation involving screening mammography for women between ages 40 and 49 simply déjà vu all over again?

Although the Task Force recommendations also addressed clinical breast examination and breast self-examination, most of the debate has focused on the Task Force decision not to recommend *routine* annual or biennial mammography screening for women *at average risk* between the ages of 40 and 49. This part of the recommendation is the focus of this commentary. It has clearly been challenging for some cancer organizations, medical professionals, breast cancer advocates, and the lay public to consider the data and to agree on the best course forward. We briefly review the findings of the Task Force, attempt to understand why the recommendations have caused such an uproar, and present a few thoughts on future research needs. Finally, we propose what health care providers and cancer organizations might do *now* to help women between the ages of 40 and 49 make a decision about mammography screening.

Mammography Screening Rationale

There is no debate that breast cancer is a serious health problem for women. In the United States alone, breast cancer is the second leading cause of cancer deaths among women. In 2009, an estimated 192,370 cases of invasive and 62,280 cases of noninvasive breast cancer were diagnosed, with 40,170 women dying of breast cancer (6). The probability of a woman developing breast cancer increases with age and is 1 in 69 in her 40s, 1 in 38 in her 50s, and 1 in 27 in her 60s (7). There is a large

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difference between the outcomes of localized (98% 5-year survival) and advanced disease (27% 5-year survival; ref. 8). Furthermore, annual or biennial mammography among women between the ages of 50 and 70 has consistently been shown in randomized controlled trials to reduce mortality from breast cancer (9). Thus, early detection of breast cancer makes sense, particularly among women ages 50 and older.

The scientific evidence is less clear when determining the value of screening mammography for women between the ages of 40 and 49 (9). It is important to remember that “value” is defined not by the number of breast cancers detected, but whether finding them makes a difference in the outcome of a diagnosis (survival) and whether the benefits of regular mammography screening outweigh the harms. The Task Force recommendation raises a question about whether the survival benefit outweighs the potential harms for women 40 to 49.

Task Force Recommendations: Summary

The comprehensive details of the findings of the Task Force are available elsewhere (2). We summarize here a few key points that pertain to women 40 to 49 years of age:

- Breast cancer mortality was reduced by 15% in favor of screening. This corresponds to 1,904 (95% confidence interval, 929-6,378) women invited to screening to prevent one breast cancer death over several screening rounds that varied by trial (two to nine rounds) and 11 to 20 years of follow-up.
- The cumulative risk for a false positive after 10 mammography screenings is more common in this age group (up to 56%) compared with older age groups.
- False negatives occur less often (1 per 1,000 women per screening round) than in older age groups (1.1-1.5 per 1,000 women per screening round among women 50-89).
- Rates of needed additional imaging are higher (84.3 per 1,000 women per screening round) compared with older age groups (56.3-75.9 per 1,000 women per screening round among women ages 50-89).
- Biopsy rates are lower (9.3 per 1,000 women per screening round) compared with older age groups (10.5-12.2 per 1,000 women per screening round among women 50-89).
- Determining the extent of overdiagnosis (defined as the proportion of cases that would not have clinically surfaced in a woman's lifetime due to lack of progressive potential or death from another cause) is less clear, but estimates vary from <1% to 30%, with most ranging from 1% to 10%. There is suggestive evidence that overdiagnosis is less likely in younger women.

Thus, based on the above, there are clear differences in the benefits and costs of mammography across age groups to be considered when making recommendations for women of average risk between the ages of 40 and 49.

Response to the USPSTF Recommendations

We suspect that there are at least a few reasons for the emotional reaction to the newly released Task Force recommendations. First, for the many women at average risk who face the threat of breast cancer in their lifetime, the perceived postponement of screening mammography to age 50 may be interpreted as a message that they cannot control their own destinies. The belief, promoted for years, that women could indeed catch cancer early *and* prevent death from breast cancer as a result of their own proactive behavior has been challenged. Thus, what may in part be driving the emotional responses to the screening recommendations may be a sense of helplessness about the specter of cancer and our seemingly now decreased ability to prevent or detect cancer early in a way that affects survival. The majority of us have seen friends or family members develop and die from cancer, and now one of our “weapons” against the disease—the use of mammography for women between the ages of 40 to 49—has been called into question.

Second, the fact that many of us have family members or friends living with breast cancer found by screening may bias us towards the belief that early detection prevents death and therefore has solely a beneficial effect. This bias, known formally as the “availability heuristic” involves the tendency to estimate the frequency of a phenomenon by how easily it can be brought to mind. For instance, a smoker may claim that smoking is not unhealthy because his father smoked and lived to be 90 years old. In the case of breast cancer and screening, it is much easier to bring to mind cases of friends, families, or celebrities who have died from breast cancer, which may prompt the perceived need for early detection than it is to recall easily women who have been faced with biopsies or suffered from anxiety associated with “false positive” mammogram results. The media also provides personal stories making it easier to recall examples of women who caught breast cancer early with positive results. Stories of women experiencing the “costs” of mammography are rare occurrences. The flood of letters to the editor in prominent newspapers sent by women diagnosed with breast cancer in their 40s who understandably believe that their lives have been saved by mammography promotes the ease with which this “availability bias” may operate among readers of such testimonials. What is unknown is how many of these breast cancers were clinically aggressive and how many of these would have been lethal without screening mammography between ages 40 and 49.

Third, one national survey found that a large majority (74%) of adults from the United States believe that early detection saves lives “most or all of the time” (10). Seventy-three percent (73%) of respondents in this survey would rather receive a total-body computed tomographic scan instead of receiving \$1,000 in cash, despite the fact that such computed tomographic scans are not endorsed

by any major medical group. The public is clearly enthusiastic about the concept of health screening, although the recent report that exposure to radiation through computed tomographic scans may increase the risk of developing cancer (11, 12) may dampen enthusiasm. In the context of the current recommendations, we may have “oversold” breast cancer screening to a public all too ready to accept such strategies. To date, our “invitations” to women for screening have often read more like a “summons,” with benefits emphasized and potential harms ignored (13). Each detection of cancer by mammography has been hailed as “lifesaving,” when in actuality, this is not necessarily the case. An unknown percentage of these represent overdiagnosis, that is, tumors that, if found later, would not have been lethal. These emotion-laden anecdotes fueled by examples in support of this “lifesaving technology” are powerful tools when this technology is threatened.

Finally, the timing of the recommendations relative to the health care reform discussions has provoked concern about whether economic costs and politics played a role in the Task Force recommendation not to endorse routine mammography for women 40 to 49 years of age. The fact that the Task Force recommended routine screening be extended from 70 to 74 years of age argues against this monetary cost interpretation of the USPSTF recommendations. In addition, Task Force members are impartial, independent senior scientists and clinicians. Since the creation of the USPSTF in 1984, the selection process and deliberations have been expressly designed to be insulated from politics, involving cross-disciplinary scientists and a system of revolving membership. Politics and monetary costs are expressly not part of the deliberation process. Task Force members should be applauded for their dedication to science and “evidence-based medicine” as it applies to breast cancer screening. The “easier” approach would have been to adhere to the language of the 2002 Task Force recommendations and note “fair” evidence for mammography screening in women ages 40 to 49. However, their assessment of the scientific evidence did not support this recommendation. Instead, they attempted to move the science of cancer control forward by acknowledging the potential harms of mammography in women 40 to 49 and offering women the option of postponing the initiation of screening.

It is important to stay focused on the *science* of this issue, be accurate in our communications, and present a balanced view of the risks and benefits. Some responses by cancer patient advocacy organizations have focused almost exclusively on the benefits. Dr. Otis Brawley (American Cancer Society) commented “With its new recommendations, the USPSTF is essentially telling women that mammography at age 40 to 49 saves lives; just not enough of them” (14, 15). Nancy Brinker (Susan G. Komen for the Cure) noted “I am not willing to lose that one woman in 1,900” (16). All of us want to save lives, and we agree with the sentiment of such statements. However, such language simplifies the issue by implying

that the decision involves looking *only* at benefits (lives saved) without assessing costs. The public should recognize that *all* medical decisions involve an analysis of benefits *and* costs, whether it is at the population or at the clinical level. This is particularly the case when the scientific evidence is unclear about the balance between the benefits and costs and when the costs affect quality of life. For example, as noted above, screening 1,904 (95% confidence interval, 929-6,378) women over several screening rounds and following them for 11 to 20 years results in one life saved by mammography among women ages 40 to 49. If we compare that with prostate cancer screening, 1,410 (95% confidence interval, 1,142-1,721) men would need to be screened with the prostate screening antigen test to prevent one prostate cancer death (17). Yet, routine prostate screening antigen screening on a national basis is *not* recommended because of lack of evidence for a benefit in terms of mortality reduction *combined with* a consideration of the costs related to false positives, uncertainty, and unnecessary treatment. Rather, the recommendation related to prostate screening antigen testing is to engage men in a discussion of benefits and costs and encourage them to make a decision based on their values and other considerations. Likewise, although mammography starting at age 40 (or even younger) could save *some* lives, there are costs entailed that should be considered when a woman makes a decision about when and how often screening should occur. In sum, costs should be considered along with the benefits before population-based recommendations are made for or against any health screening on a national basis.

So Where Are We Now?

We hope that the debate energizes new research in a host of needed domains: what is the magnitude of overdiagnosis in breast cancer? Studies of women with untreated ductal carcinoma *in situ*, found only by mammography, show progression to invasive disease in half or fewer of diagnosed cases (2). What could we learn about the natural history of ductal carcinoma *in situ* that might affect issues related to overtreatment and the cost-benefits of mammography among younger women? Might we better measure the magnitude and effect of radiation risk among younger women undergoing annual or biennial mammography? How do we better present information to women at low to average risk to facilitate the understanding of benefits and costs and personalized risk factors as part of a truly informed decision making process?

More globally, even under the most optimistic assumptions about the benefits of mammography, this technology cannot prevent the vast majority of breast cancer deaths. We agree with the recent call (18) to shift strategy in breast cancer screening, focusing on work to develop and validate markers that identify aggressive versus minimal risk disease and reduce treatment for minimal risk disease. Such work need not preclude research that

focuses on available strategies for the early detection of breast cancer and on what we can do now to detect breast cancer early that may have a favorable effect on type of treatment and survival.

A critical practical issue is what to do *now* for women ages 40 to 49 as we face much confusion about when and how often women in this age group should undergo mammography. This issue is not, as noted previously, simply about “benefits.” There are indeed real costs involved, including false positives, radiation risk, anxiety, and worry as women face a mammogram or follow-up visits for diagnostic mammography, biopsy, or possible unnecessary treatment. As noted above, for women ages 40 to 49, the likelihood of experiencing a “cost” is very likely a more frequent occurrence than accruing a “benefit.”

A first step is returning to the clear statements made by the USPSTF at the top of this commentary. Let's neither “summon” women to have mammograms, our outcome data based solely on how many women complete screening, nor dismiss women ages 40 to 49 who are now seemingly in limbo. It seems reasonable for our early detection discussions to focus not on uptake of screening but on ensuring informed choice. We suggest that health care providers discuss this decision and inform women about the costs and benefits of waiting until age 50 before beginning routine screening mammography and about annual versus biennial screening in a clear and understandable manner to help them make a decision that is best for them. Major cancer organizations and advocacy groups should offer material to women that provides the benefits and costs in a “transparent” manner. “Transparency” in this case means describing the benefits and risk in terms women can understand. For example, there is evidence that people are more likely to understand risk when it is presented as “natural frequencies” or in absolute terms, as opposed to relative risk (e.g., 15% reduction in breast cancer deaths by use of mammography among women ages 40-49; ref. 19). An example of such transparency for a single screening might be as follows, (9) and a similar style of presenting information could be accomplished for a 10-year period of screening between the ages of 40 and 49:

Imagine 1,000 women ages 40-49 having a single mammogram. Of these 1,000 women, about 900 (or about 90%) will not have breast cancer and the mammogram will be “negative,” accurately showing that they do not (i.e., true negatives). About 100 of these 1,000 women (or about 10%) will not have breast can-

cer, but the mammogram will be read as “positive” for breast cancer (i.e., false positives). About 2 of these 1,000 women (or about 0.2%) will have mammograms that accurately show they have invasive breast cancer and 1 of these women (or about 0.1%) will have a mammogram that accurately shows that they have a noninvasive type of breast cancer (i.e., true positives). Finally, 1 of 1,000 (or about 0.1%) of these women will have breast cancer, but the mammogram will miss it (i.e., a false negative).

Mammography may also lead to “overdiagnosis.” This means that a mammogram may find cancers that grow so slowly that, if left alone, would not cause symptoms or cause any other problems in your lifetime. This may result in unnecessary surgery, radiation treatment, or chemotherapy. It is not yet possible to provide a reliable estimate on the likelihood of overdiagnosis, but it appears to be less in the 40- to 49-year-old age group than in older women.

Conclusion

As noted in the 2002 Task Force recommendations, and consistent with the current ones “The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences... Clinicians should tell women that the balance of benefits and potential harms of mammography improves with increasing age for women between the ages of 40 and 70.” (1). We argue strongly for more discussion between health care providers and women of average risk between the ages of 40 and 49 about the costs and benefits of mammography, and encourage informed decision making. For this age group, we also endorse the sentiment that: “It should be clear to potential participants (in mammography screening) that there are both important benefits and important harms and that the decision *not* to participate is *as sensible* as the decision to do so” (20).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Correction**Correction: Mammography and Women Under 50: Déjà Vu All Over Again?**

In this article (1), which was published in the March 2010 issue of *Cancer Epidemiology, Biomarkers & Prevention*, prostate specific antigen (PSA) testing was incorrectly referred to as “prostate screening antigen,” “prostate screening antigen screening,” and “prostate screening antigen testing” (lines 14,16, 21 respectively in the right column of page 637). In all cases, the authors are referring to prostate specific antigen (PSA) testing.

Reference

1. Stefanek M, Gritz E, Vernon S. Mammography and women under 50: déjà vu all over again? *Cancer Epidemiol Biomarkers Prev* 2010;19:635–9.

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