



American College  
of Radiology™



Submitted Electronically

United State Preventive Services Taskforce  
Agency for Healthcare Research and Quality  
540 Gaither Road  
Rockville, MD 20850

Re: Draft USPSTF Recommendations on Breast Cancer Screening

Dear Dr. Barry and Task Force Members,

The American College of Radiology (ACR)<sup>1</sup> and the Society of Breast Imaging (SBI)<sup>2</sup> promote proven screening methods to save lives. We were encouraged to see that the United States Preventive Services Task Force (USPSTF) draft recommendations on breast cancer screening now align with other national organizations with respect to the recommended start date -- screening mammography beginning at age 40. Including women aged 40-49 in the recommended screening demographic is a substantial improvement given there is a significant reduction in mortality in this age group when women are screened regularly [1]. This will make a meaningful impact on decreasing health care disparities, particularly in Black women and other subgroups of women frequently not equally represented with current follow-up after a screening recall and treatment opportunities. This is especially important as Black women are more likely to be diagnosed at an earlier age, as well as to die from the disease, a point stressed in the draft statement [2].

We have serious concerns, however, with the proposed recommendation for biennial rather than annual screening given the Task Force acknowledgement that annual mammography screening for women forty and older saves the most lives and results in the greatest number of life-years gained – a fact demonstrated through Randomized Control Trials (RCT), Observational Trials and CISNET models. In addition, we are deeply disappointed that the proposed Task Force recommendation continues to perpetuate confusion surrounding when to cease mammographic screening by proposing an “1” recommendation for screening mammography in women 75 and older.

The ACR and SBI are concerned that no breast cancer experts or patient representatives were included on the panel. The Institute of Medicine (IOM) recommends that trustworthy guideline development should include a multidisciplinary panel of experts and representatives from key affected groups [3]. The IOM report suggests that such guideline development cannot assess the evidence in the same way that a multidisciplinary group can. The ACR and SBI believe that having breast cancer experts on the panel would, for example, have avoided the incorrect concept by the USPSTF regarding screening intervals affecting overdiagnosis.

We believe that the draft recommendations overemphasize the potential harms (potential risks) of breast cancer screening and underestimate the benefit of annual mammography starting at age 40 for the average-risk patient in reducing morbidity and mortality. The draft recommendations reflect a biased view of the available evidence, while the Task Force’s own modeling studies conclude annual screening confers a greater benefit. Accordingly, we respectfully urge you to reconsider the evidence as

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<sup>1</sup>ACR is a professional organization representing more than 41,000 radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists

<sup>2</sup> SBI’s core mission is to save lives through early detection, quality education, and trusted information provided to patients, physicians and organizations worldwide

detailed below and adopt final recommendations assigning a B grade for **annual** mammographic screening for all women ages 40 and over who are at average risk for breast cancer.

Finally, we respectfully request, along with the final document, comments submitted during the 30-day review period be addressed individually with explanations included for any comments not incorporated into the final guidelines. The public availability of this information is important for the transparency needed to establish trust. We urge the USPSTF to review the comments herein and seriously reconsider its draft recommendations to better reflect the current and complete evidence available for breast cancer screening.

A detailed review of evidence and analysis of the Task Force draft recommendations is provided below.

### **Annual vs. Biennial Screening – General Comments**

There are two major misconceptions about the differences in outcomes between annual and biennial screening. *Misconception 1:* Annual screening does not provide an advantage because biennial screening finds as many cancers and results in less overdiagnosis. The truth is that an annual screening regimen is more likely to identify smaller, node-negative, and earlier stage cancers, all of which confer more favorable treatment options and are surrogate markers for improved survival and mortality. Additionally, overdiagnosis does not change with longer intervals between screens. Once a cancer is visible on screening, it will remain visible until the next screen, regardless of the interval.

*Misconception 2: Annual screening leads to excessively greater false positives.* It is simplistic to conclude that annual screening doubles the number of false positives compared to biennial screening. Screening recall rates are significantly influenced by the availability of prior mammograms to assess for stability. In addition, there are many factors that may influence recall rate such as breast density, population demographics and family history. Most mammographic screening recalls are determined to be definitively benign after additional diagnostic images. Radiologists' thresholds for screening recalls are designed to maximize cancer detection and minimize false negatives. For abnormalities which warrant a biopsy before pathological confirmation of benignity, they will be detected via either annual or biennial screening regimens as they do not spontaneously regress. It is not clear why the biennial regimen was selected except for it being a value judgment of the panel members with no evidence that patients concur with that value judgment.

### **Annual vs. Biennial Screening: Decrease in mortality with more frequent screening**

Based largely on CISNET modeling of the benefits and risks of various screening strategies, the USPSTF maintained their 2009 and 2016 recommendation for biennial screening mammography. However, modeling identified five efficient screening strategies resulting in the highest breast cancer mortality reduction and life years gained (LYG) included in the technical report submitted with the current USPSTF draft. The CISNET models show annual screening with Digital Mammography (DM) or Digital Breast Tomosynthesis (DBT) from ages 40-79 (A40) will result in a 41.7% reduction in mortality compared to those not screened. In contrast, biennial screening from ages 40-79 (B40) will reduce mortality by 32.9% for DM and 33.3% for DBT.

To inform women and providers, the USPSTF should provide a clearly labeled benefits table that compares CISNET mortality reduction, LYG, and deaths averted for biennial screening of ages 40-74 versus annual screening ages 40-79. It is clear that the most lives saved, and life years gained, are with an annual screening mammography regimen beginning at age 40. Providing only information on risks without associated benefits demonstrates bias by framing the discussion in a negative light.

CISNET modeling continues to make the basic assumption that the optimal screening protocol is one that maximizes benefit (mortality reduction, breast cancer deaths averted, or life-years gained) per mammography exam performed. The number of mammography exams appears to be a surrogate for cost, and benefit is weighed against this to determine the efficiency of various screening approaches. Such a simplistic assumption ignores the cost borne by women, their families, and society, of not screening: the costs and suffering from more advanced breast cancer treatments and breast cancer deaths. This is especially impactful for younger women who are more likely to be diagnosed with biologically more aggressive, advanced-stage cancer and who often have greater work and family care responsibilities than older women. Another approach to consider instead would be to compare benefits to actual costs, including the costs of screening mammography, follow-up, and biopsies, but also including the costs to women and society of not screening or screening less frequently.

The CISNET modeling includes the risks of screening and follow-up but fails to consider the risks of not screening, including false-positive clinical exams and subsequent benign biopsies. Data are available from the Breast Cancer Surveillance Consortium (BCSC) and other sources on the frequency of diagnostic work-up and benign biopsies in women not participating in screening mammography, yet these risks have not been compared to screening populations.

In addition to the CISNET modeling, the USPSTF reviewed some flawed studies when deciding biennial vs. annual intervals. One included study [4] was conducted in Turku, Finland from 1987 to 2007 which compared mortality rates for annual or triennial screening from women ages 40 to 49. This was a randomized control trial that demonstrated no significant difference in mortality reduction between annual and triennial screening. In fact, there was a notable increase in all-cause mortality in the screened group, which was not addressed by the authors. To date, the only RCT (Canadian National Breast Screening Study) to show an increase in mortality from screening mammography was found to have critical flaws in randomization. It is both conceivable and plausible similar flaws are present in the Finnish study.

#### **Annual vs. Biennial screening: Increase in false positive recalls**

We request that some of the language utilized in the USPSTF recommendations be changed to more accurately reflect the risks associated with screening. Specifically, the term “false positive” suggests that patients are incorrectly diagnosed with breast cancer when they do not have the disease. The “false positives” related to breast cancer screening actually refer to the 10% of women who are recalled from screening for additional diagnostic images. Ninety percent of these women will undergo an additional mammogram or ultrasound and be given direct reassurance that they do not have cancer. Although a screening recall may confer short term anxiety, women are not falsely told they have cancer.

Furthermore, women who are recalled and given assurance that they do not have cancer are more likely to adhere to subsequent screening mammography indicating that there are no long-term deleterious effects and demonstrating the durable influence of reassurance [5]. Given the ambiguity of the term “false positive,” we recommend greater clarity through the qualifier “false positive recalls.” Of note, all medical tests and screening exams may result in false positive recalls of some type.

Additionally, these “**false positive recalls that are ultimately found to be normal breast tissue**” are decreasing with improved mammographic screening technology, especially DBT. In Table 4 in the Draft Recommendations, using Digital Breast Tomosynthesis (DBT) compared to Digital Mammography (DM) reduces likelihood of false positive recalls from screening significantly. A study cited shows the 10-year cumulative probability of a false positive recall was 6.7% lower for DBT vs DM with annual screening and 2.4% lower for DBT vs DM with biennial screening [6]. DBT capability is now widespread in the United States, present in 85% of breast centers as of May 2023.

### **Annual vs. Biennial screening: Risks of not Screening**

The ACR/SBI also believes that the USPSTF underemphasizes the risks of **not** screening patients, especially death. Non-adherence to regular screening intervals increases mortality. Duffy et al. demonstrated that serial participants undergoing an 18-month screening interval had a 49% lower risk of breast cancer mortality (relative risk [RR], 0.51; 95% CI: 0.48, 0.55; P, .001) and a 50% lower risk of death from breast cancer within 10 years of diagnosis (RR, 0.50; 95% CI: 0.46, 0.55; P, .001) than serial nonparticipants [7].

### **Annual vs. Biennial Screening: Interval Cancers**

The USPSTF has now appropriately included surrogate mortality markers like interval cancers to influence their guidelines. Interestingly, this approach was limited to comparing the effectiveness of DBT vs. DM as there are no published mortality data available comparing these two technologies. However, interval cancers can be utilized to compare the effectiveness of selected screening intervals. A study by Moorman et al. [8] analyzed interval cancers in women undergoing various screening intervals. In the annual screening group, there were fewer interval cancers (21 of 200 for annual screening [10.5%] vs 12 of 32 for biennial screening [37.5%;  $p < .001$ ] and 15 of 45 for nonannual screening [33.3%;  $p < .001$ ]) and the cancers were smaller in size ( $1.4 \pm 1.2$  cm for annual vs  $1.8 \pm 1.6$  cm for biennial [ $p = .04$ ] and vs  $1.8 \pm 1.5$  cm nonannual [ $p = .03$ ]).

Furthermore, an analysis of interval cancers in the National Health Service where triennial screening is the standard demonstrates a significant increase in interval cancer rates between (1-12 months (0.55 per 1000 women screened) versus 12-24 months or 24-36 months (1.13 and 1.122 per 100 women screened) [9]. It is not clear why the USPSTF selectively used interval cancer data for determining the effectiveness of DBT and not for determining optimal screening intervals.

### **Overdiagnosis**

The USPSTF recommendation statement does not explain to a sufficient extent or with sufficient clarity the limitations on the quality of data on overdiagnosis. The recommendation statement should be revised to add or expand on the following. It is currently impossible to measure overdiagnosis directly, just as it is currently impossible to determine on a case-by-case basis whether a specific screening-detected cancer would never have been detected or caused health problems in the absence of screening. This causes healthcare providers to treat all detected cancers as actionable, not knowing which cancers may be overdiagnosed and subsequently overtreated.

The recommendation statement should also indicate that overdiagnosis is an issue principally concerning ductal carcinoma in situ (DCIS), especially low nuclear grade DCIS (which accounts for approximately 20% of all DCIS cases) [10]. Evidence of overdiagnosis for invasive carcinoma is sparse, indirect, and often derived from uncommon cancer subtypes, for example, tubular carcinoma, a relatively rare and slow growing form of breast cancer. Given that the current treatment of tubular carcinoma involves no systemic therapy, the harm of overtreatment is also limited. Fundamentally, the concept of overdiagnosis rests upon the assumption that the level of diagnosis absent screening is optimal for women. But this level is not optimal due to the higher breast cancer death rate. Furthermore, breast cancer incidence has exceeded the mortality rate long before screening mammography began in the United States.

### **Overdiagnosis - Frequency of Occurrence**

All current estimates of the frequency of overdiagnosis are imprecise. As described in the USPSTF recommendation statement, estimates of overdiagnosis have ranged widely depending on methodology,

patient population, and other factors. The Task Force's own evidence says that this is an unknown quantity and that although it can be theoretically listed as a harm, no actual weight can be assigned to it since the value is unreliable.

The review narrative draft cites rates of 11-22% for trials, 1-10% for observational studies, and 0.4-50% for statistical models. Not included is a systematic review of a large series of service screening experiences that explains the reasons for observed wide variations in estimates of overdiagnosis [11]. To the extent that overdiagnosis exists, estimating its frequency must include methods that adjust for breast cancer risk, lead time, and underlying cancer incidence trends. The systematic review of overdiagnosis studies by Puliti et al. comprehensively and clearly indicates that the most plausible estimates of overdiagnosis range from 1% to 10% (on average, approximately 5%), and that higher estimates of overdiagnosis reported in the literature are due to the lack of adjustment for breast cancer risk and/or lead time [11]. This approach reflects the results from observational studies. Indeed, several published studies also use estimates (or guesses) rather than observed data in determining underlying cancer incidence trends, causing these studies to overestimate, often to a great extent, the true magnitude of overdiagnosis [12].

### **Overdiagnosis - How to Mitigate**

The USPSTF has concluded that overdiagnosis is an important problem, but efforts to mitigate it are not trivial. Some have advocated that overdiagnosis may be reduced by reducing the recall rate or raising the threshold for biopsy [13, 14]. Unfortunately, these approaches cannot be successful because it is currently impossible to differentiate overdiagnosed from non-overdiagnosed cancer at initial diagnosis. Breast cancers can be classified into molecular subtypes based on differences in disease presentation and outcome, but even the less aggressive luminal A cancers still confer a notable breast cancer mortality. Efforts to use radiologist-assessed features from the BI-RADS Atlas or more advanced artificial intelligence-based radiomics features to classify cancers based on retrospective assessments of outcomes (a surrogate for overdiagnosis) are all imprecise with notable overlap in presentation. Simply put, it is impossible to reliably differentiate overdiagnosed and non-overdiagnosed cancer based on imaging, pathology, genomic, or demographic features.

DCIS has been labeled the primary driver of overdiagnosis in breast cancer screening programs, but avoiding a biopsy of potential DCIS is not feasible. Twenty percent of DCIS cases at initial diagnosis will be upgraded to invasive cancer at surgical excision. Estimates of the DCIS overdiagnosis are highly variable and primarily attributable to nuclear grade. However, nuclear grade cannot be determined in the pre-biopsy setting, and there is notable interobserver variability among pathologists in nuclear grading and differentiating DCIS from atypical ductal hyperplasia and invasive cancer. There are already efforts underway to reduce DCIS overtreatment via active surveillance which avoids standard of care surgical excision in favor of imaging follow up, but this requires pathologic confirmation of disease and shared decision-making discussions with patients about the risks of non-standard-of-care treatment.

Many have advocated that overdiagnosis can be mitigated by modifying screening strategies, including delaying the age at which screening starts, and/or lengthening the screening interval from annual to biennial [13]. These strategies may appear viable at first glance but they fail to account for the natural history of cancer which is one of continued, even if slow, growth. Breast cancer does not spontaneously resolve. The same overdiagnosed breast cancer that was detected in a woman screening at age 40 would be detected if she delayed screening until age 50. It would have just shifted the age at diagnosis to later and if it was not overdiagnosed, would have given the cancer additional time to grow. Similarly, there is no difference in the overdiagnosis rate if screening occurs annually or biennially, it just changes when the overdiagnosed cancer is detected.

Overdiagnosis can only be reduced by stopping screening. However, overdiagnosis is highly dependent on life expectancy and other comorbidities which might influence treatment success. These are highly personalized circumstances and cannot be addressed in a one size fits all approach which uses a specific age cutoff. Instead, this should be based on shared decision-making discussion between patients and their providers after cancer diagnosis when the risks and benefits of cancer treatment can be individualized.

Although overdiagnosis is labeled a harm of breast cancer screening programs, all screening programs cause overdiagnosis. Overdiagnosis is not a failure of imaging, but rather a failure in our understanding of the underlying cancer biology. Furthermore, the greatest harm of overdiagnosis is overtreatment which is a failure of personalized treatment rather than diagnosis. Women may choose to undergo less than standard of care or even no treatment for a newly diagnosed breast cancer, but they deserve the right to make that decision themselves with expert consultation from surgeons, oncologists, and input from their family. By seeking to avoid the detection of overdiagnosed breast cancer, the USPSTF risks underdiagnosing clinically relevant breast cancer while taking a paternalistic stance that implies patients cannot be trusted to make their own decisions about whether to act on a newly diagnosed breast cancer. This is directly at odds with the modern patient-centric approach to medical care.

A far preferable approach is for the USPSTF to acknowledge in the recommendation statement that *there is no currently available solution to the problem of overdiagnosis*, and then recommend that as a major direction of future research. Overdiagnosis really has three components: over-detection by the radiologist, overdiagnosis by the pathologist, and overtreatment by the surgeon and oncologist.

### **Women Aged 75 Years and Older: “I” Recommendation**

Screening mammography should continue as long as a woman is in good health with reasonable life expectancy. By ending recommendations at age 74, the Task Force is contributing to the already existing confusion surrounding when to cease mammographic screening. The age of 74 is an arbitrary age, as there is no substantial change that occurs between ages 74 and 75. It is estimated that life expectancy for an 80-year-old woman of any race is 9.1 [15].

The Task Force included far too little data from observational studies presented in the USPSTF recommendation statement on screening mammography outcomes for women age  $\geq 70$ . According to the most current SEER data, approximately 31% of invasive breast cancers in United States women are diagnosed at ages  $\geq 70$ . According to the most recent SEER data, the age-adjusted breast cancer incidence in US women ages 75 and older has demonstrated an annual percentage change of 2% from 2017 to 2019 [16].

The USPSTF did not identify any RCT's designed to assess the comparative effectiveness of different ages to start or stop screening that reported morbidity, mortality, or quality of life outcomes. Given that high-quality (randomized trial) data are too sparse to have the statistical power to indicate a statistically significant mortality reduction, the USPSTF should rely on existing observational data from the United States. There are numerous publications of real-world data on the value of screening in women 75 and over [17-20]. It is wrong to ignore the potentially life extending benefits of screening mammography for 31% of invasive cancers simply because the randomized trials studied too few elderly women. Consider the following table of data on the performance of screening mammography, stratified by age, from over 5 million screening mammogram examinations from the National Mammography Database [21]. These data involve screening mammography from 2008 - 2014, representing actual United States practice.

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### Performance of Screening Mammography

<u>Age</u>	<u>Exams</u>	<u>Cancer Detection Rate</u>	<u>Recall Rate</u>	<u>Positive Predictive Value</u>
50-54	890,701	2.8 per 1000	10.2%	21%
55-59	885,153	3.4 per 1000	8.7%	28%
60-64	801,459	4.3 per 1000	8.3%	35%
65-69	678,274	5.1 per 1000	8.1%	39%
70-74	481,478	5.5 per 1000	7.5%	44%
75-79	304,908	5.6 per 1000	7.1%	47%
80-84	169,808	6.3 per 1000	6.8%	55%
85-89	67,243	6.4 per 1000	6.5%	60%
≥ 90	13,523	6.6 per 1000	6.1%	69%

As demonstrated by the presented data, as well as other U.S. data [22, 23], the high cancer detection rate, sensitivity, and positive predictive value of mammography in middle-aged women continues to increase as women become older. This, combined with the fact that age-specific incidence of breast cancer remains high in elderly women, strongly suggests that screening elderly women will be at least as effective in reducing disease-specific mortality as it is in women aged 50-69, except as affected by limited life expectancy.

Modeling by the 6 CISNET participants did not include modeling results for the benefit or harms for screening scenarios that extended beyond age 79 years even though BCSC and other data sources are available for screening in women beyond age 79.

It is especially troublesome for the USPSTF to suggest (even worse to recommend) a policy of stopping screening at a specific age that applies to *all* women. A recent survey [24] of older women investigated women's willingness to stop screening and found that the majority would not stop screening, indicating even further that it should be the woman's right to choose. More appropriate guidance (and guidelines) would be to advise women and their healthcare providers to consider stopping screening on a case-by-case basis, at whatever age is judged appropriate for each woman. This age will vary widely from woman to woman, because there is great variation in life expectancy and co-morbidity at each age [25]. A woman in the United States who lives to age 75 has an average life expectancy of 12.4 *additional* years [26].

Based upon the CISNET modeling data presented by the USPSTF, annual screening mammography with digital breast tomosynthesis in women ages 75-79 results in a 4.7% mortality reduction compared to 3.3% for biennial screening DBT, representing a 42% improvement in mortality reduction (derived from Table 5). Similarly, annual screening DBT in women ages 75-79 results in 13.1 LYG per 1000 women screened compared to 8.7 for biennial screening DBT, representing a 51% improvement in LYG (derived from Table 5). The CISNET modeling data show continued substantial benefit in mortality reduction and LYG when healthy women are screened past age 74.

The USPSTF draft recommendation states that "Collaborative [CISNET] modeling suggests that screening in women aged 75 years or older is of benefit, but a trial emulation found no benefit with breast cancer screening in women ages 75 to 84 years. Thus, there is insufficient evidence to recommend for or against screening mammography in women aged 75 years or older." Given the extensive observational data, as well as the CISNET modeling results, the panel should re-consider its conclusion that there is insufficient evidence based on a single trial emulation, with only 8 years of follow up which demonstrated no benefit in women ages 75-84.

The USPSTF should qualify use of the “B” rating for elderly women by indicating that this is meant for women without substantial comorbid conditions or limited life expectancy, as already done for women ages 70-74, but instead apply this recommendation to elderly women of all ages.

### **Supplemental Screening in Women with Dense Breasts: “I” Recommendation**

The USPSTF concludes that there is insufficient evidence to assess the balance of benefits and harms of supplemental screening with MRI (Magnetic Resonance Imaging) or ultrasound in women with dense breast tissue, giving an “I” grade. This is problematic as literature has proven that women with dense breast tissue have an increased risk for the development of breast cancer, and in addition, are at risk for a cancer being masked on screening mammography. Patients with extremely dense breasts are approximately two times as likely to develop breast cancer as patients with average density and 4-6 times as likely as patients with fatty breasts [27, 28]. The Task Force does note this. Breast density is recognized as a significant risk factor and has been included in the most up-to-date risk assessment tools. Additionally, the sensitivity of mammography is decreased in patients with dense breasts, which is a fact that is also acknowledged by the Task Force. Sensitivities for mammography are reported to be significantly lower in patients with dense breasts compared to patients with fatty breasts [29, 30, 31].

Currently, 43%-46% of US women aged 40 or over have dense breasts [2]. In a case-controlled analysis of the Dutch mammography screening data, a 41% mortality reduction in women with non-dense breasts was demonstrated compared to a 13% reduction in women with dense breasts [32], likely reflecting both the effect that breast density has on risk and its cancer masking effect (sensitivity). Therefore, if an equitable screening approach is desired (as conveyed in the Task Force document), patients with dense breasts should have access to supplemental screening so they can achieve screening benefits in a manner more fully in keeping with those of patients with less dense breasts.

The Task Force did not consider that annual screening mammography is especially important in women with dense breasts. Annual screening in this population reduces the chance of an interval cancer. By increasing the time between screenings, interval cancers are given more time to develop and grow, which tend to be more aggressive with worse outcomes.

The Task Force incorrectly lumps women with dense breast tissue into recommendations for average risk women, but women with dense tissue are at a higher-than-average risk. In addition, the Task Force did not consider the combination of risk factors; women with dense breasts and a family history of breast cancer or other risk factors currently meet the criteria for supplemental screening with MRI, in addition to mammography, as stated by the ACS, NCCN and ACR.

### **Screening Breast MRI**

A review of literature to date confirms that for women with dense breasts who are otherwise considered at average to intermediate risk for breast cancer (i.e., breast density is their only risk factor) MRI is an optimal supplemental imaging modality, with cancer detection rates and positive predictive values (PPVs) favorable to US or DBT [2]. The cancers found with MR screening tend to be small, node negative and “dedifferentiated” (high grade), even in women at average risk [33].

Detection efficiency can be increased using effective abbreviated MRI (AbMR) techniques, which increase access and decrease cost while maintaining high incremental cancer detection rates in women with dense breasts (11.8/1000 CDR for AbMR vs 4.8 for DBT) [34]. AbMR shows comparable sensitivity and superior specificity to full protocol MRI techniques, addressing false positivity concerns [35]. While randomized controlled studies assessing mortality effect are historically the gold standard for determining efficacy, they require exceptionally large cohorts and long follow up, and may not be practical to study all ongoing questions. Surrogate outcomes should be recognized and used as we move



forward. One such surrogate is the interval cancer rate. Interval cancer rates are decreased with the use of supplemental MRI screening. A 50% decrease in interval cancers was noted in women with very dense tissue when surveilled with supplemental MRI compared to mammography alone [36]. This randomized controlled study also showed a cancer detection rate with MRI to be 16.5/1000 (far higher than that found with mammographic screening) and the false positive rate to be 8% among those undergoing MRI, in line with or lower than typical recall rates for screening mammography in the United States. In average-risk women, Kuhl demonstrated no interval cancers to be found among her study cohort when MRI was used for supplemental screening [33].

For women with dense breasts who cannot undergo breast MRI due to cost or technical considerations, other supplemental modalities can be offered, such as contrast enhanced mammography (CEM) or ultrasound. CEM is shown to have similar sensitivity and improved specificity compared to MRI [37].

### **Other general comments**

In the United States, compliance with screening guidelines is far less than 100%, whether those of the USPSTF or those of other national organizations. Therefore, a major thrust of the USPSTF recommendation statement should acknowledge this lack of compliance and urge those women and healthcare providers who choose to accept USPSTF recommendations to follow them as presented, specifically not to consider a biennial recommendation as being equivalent to screening every 2½ or 3 years, and not to consider the annual recommendation for those women at ages 40-49 who choose to be screened as being equivalent to screening every 1½ to 2 years.

### **Tables and Figures**

Below are comments related to concerns with the Tables and Figures in the Draft Modeling Report:

The wide range of overdiagnosis estimates among the CISNET models: for DBT, from 6 to 32 overdiagnosed cases per 1,000 screened for B40-74, and from 9 to 49 overdiagnosed cases per 1,000 screened for A40-79, both greater than a 5-fold difference among the models (see Table 13 for DM and Table 14 for DBT). Not only do their overdiagnosis median values fail to recognize that overdiagnosis does not increase when comparing biennial to annual screening, but this wide range of overdiagnosis estimates for each protocol suggests that median overdiagnosis estimates are likely unreliable and should not be used to decide on the most appropriate screening protocol.

Comparing median model results, which CISNET chooses to report, shown in Table 4 (for DM) and Table 5 (for DBT), DBT consistently shows higher (or in one case, equal) median breast cancer mortality reduction and higher (except for one case) life-years gained than DM, but DBT in every case is reported to have fewer breast cancer deaths averted than DM. These results appear to be inconsistent.

Table 25 does not specify whether these changes in estimated screening outcomes are for DM, DBT, or both.

Figure 3 states that the upper (dashed) black curve depicts the SEER18 invasive breast cancer incidence rate starting in 1992, but SEER18 does not report breast cancer incidence rates until 2000. Also, the age ranges for which breast cancer incidence rates are reported for both SEER data and the 6 CISNET models are not stated.

Figure 4: The age ranges for which breast cancer mortality rates are reported for both SEER data and the 6 CISNET models are not stated.

## Summary

We recognize and appreciate that this comment period is designed to receive comments about concerns with the draft guidelines on screening for breast cancer. As there were no breast cancer experts in the guideline development, we hope that those of us who are content experts in this field will shed light, through this document, that some of the conclusions of the USPSTF are incorrect. Please consider our comments seriously as we strongly feel that some of the conclusions and recommendations of the Task Force may negatively impact public health.

Since the biennial screening recommendations are based on the judgment of the panel, we suggest that it be made very clear to women in the United States that the greatest number of lives saved is derived from a strategy of annual screening beginning at age 40 for the average risk woman. Women should be informed that there are risks of not screening or delayed screening which include death. We suggest that the appropriate recommendation should read, "Since the most lives are saved, women should start annual screening at the age of 40, unless they put a higher value on the potential risks of screening, and that choice should be an individual one (B recommendation)."

Respectfully Submitted,

*Stamatia Destounis*

Stamatia V. Destounis, MD, FACR  
Chair, Commission on Breast Imaging  
American College of Radiology (ACR)

A handwritten signature in blue ink that reads "Mary S. Newell". The signature is written in a cursive style with a large, sweeping flourish at the end.

Mary S. Newell, MD, FACR  
President, Society of Breast Imaging (SBI)

ACR Breast Commission USPSTF Work Group  
Lars J. Grimm, MD  
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