Breast cancer screening: The latest from the USPSTF

Mammography for women ages <50 years remains controversial except for selected individuals. Data are insufficient to recommend for or against adjunctive screening modalities for women with dense breasts.

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The United States Preventive Services Task Force (USPSTF) recently released draft recommendations on breast cancer screening, which could be finalized within the next few months.[1] The last time the Task Force (TF) weighed in on this topic was in 2009, just as the Affordable Care Act (ACA) was being debated. At that time, the TF recommendations were so controversial that Congress specified in the ACA that they should not be used to determine insurance coverage (more on this later).

The draft recommendations (**TABLE 1**)[1] carry a C grade for women ages 40 to 49 years (ie, offer or provide screening mammography for selected patients depending on individual circumstances) and a B grade for biennial screening of women ages 50 to 74. The proposed recommendations are basically the same as the ones made in 2009, with more detailed wording to explain the rationale for the C recommendation, and to address 2 new issues: tomosynthesis (3-D mammography) and adjunctive screening for women with dense breasts. The previous D recommendation against self breast examination was left unchanged.

Benefit of mammography screening varies by decade of life

Breast cancer is the leading cause of non-skin cancers in women and, after lung cancer, the second leading cause of cancer deaths in women. In 2014 there were 233,000 new cases diagnosed and 40,000 breast cancer deaths.[1,2] While the TF found that mammography reduces deaths from breast cancer in women between the ages of 40 and 74, women ages 40 to 49 benefit the least; those ages 60 to 69 benefit the most.[1,3]

If 10,000 women are screened routinely for 10 years, 4 breast cancer deaths will be prevented in those ages 40 to 49, 8 in those 50 to 59, and 21 in those 60 to 69.[1] And harms appear to be higher in the younger age group. **TABLE 2**[1,3] shows some of the harms resulting from one-time mammography screening of 10,000 women in each age group. Notice the benefits listed previously are from repeated screenings over a 10-year period and the harms in **TABLE 2**[1,3] are from a single mammogram.

The total benefits and harms of biennial screening in 1000 women starting at age 40 (vs age 50) include 8 cancer deaths prevented (vs 7) with a cost of 1529 false positive tests (vs 953); 204 unnecessary breast biopsies (vs 146); and 20 overdiagnoses (vs 18). However, the confidence intervals on these estimates are wide, and in each case, they overlap between the 2 groups.[1]

The TF recommended biennial screening for women between the ages of 50 and 74 because observational studies and modeling show no clear benefit with annual screening vs every 2 years, while annual

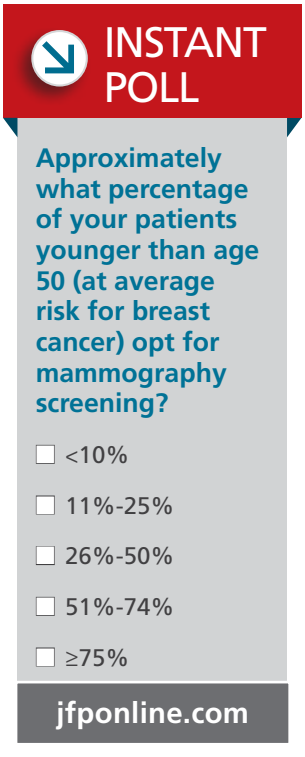

TABLE 1

Summary of USPSTF draft recommendations on breast cancer screening[1]

Population	Recommendation	Grade
Women 50-74 yrs	Screen with mammography every 2 yrs	B
Women 40-49 yrs	Consider starting mammography screening for women in this age range on an individual basis. Women who value its potential benefit above potential harms may choose to start biennial screening before age 50. • Biennial mammography screening for women at average risk for breast cancer most benefits those ages 50-74. Women 60-69 years of age are most likely to avoid breast cancer death with mammography screening. In comparison, far fewer women ages 40-49 years avoid breast cancer death with screening mammography, while false-positive results and unnecessary biopsies occur more often. • For all women, regular mammography increases the risk of diagnosis and treatment of noninvasive and invasive cancer that would otherwise have remained nonthreatening or even undetected in their lifetimes. • Women in this age range who have a mother, sister, or daughter with breast cancer may benefit more than average-risk women by starting screening.	C
Women ≥75 yrs	Current evidence is insufficient to assess the balance of benefits and harms of screening mammography.	I
All women	Current evidence is insufficient to assess the balance of benefits and harms of tomosynthesis (3-D mammography) in screening for breast cancer.	I
Women with dense breasts	Current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using ultrasound, MRI, tomosynthesis, or other modalities in women identified as having dense breasts on an otherwise negative screening mammogram.	I

MRI, magnetic resonance imaging; USPSTF, United States Preventive Services Task Force.

screening results in more false positives and biopsies.

Overdiagnosis may occur in nearly 20% of cases

The potential for overdiagnosis and overtreatment is increasingly recognized as a harm of cancer screening. Overdiagnosis results from detecting a tumor during screening that would not have been detected otherwise and that would not have caused death or disease but is treated anyway. This sometimes occurs with the detection of early tumors that would not have progressed or would have progressed slowly, not causing health problems before the woman dies of other causes.

The TF is one of the only organizations that considers the potential harmful effects of this problem. While it is not possible to know for certain the rate of overdiagnosis that occurs with cancer screening, high-quality studies indicate it is close to 20% for breast cancer.[3]

Guidance regarding women ages 40 to 49

The new draft recommendations carefully point out that, while the overall benefit of screening women ages 40 to 49 is small, the decision to begin screening before age 50 should be an individual one, and an informed one. They state that women who value the small potential benefit over the potential for harm may choose to be screened, as might women who have a family history of breast cancer. And the recommendations do not apply to women who have a genotype that places them at increased risk for breast cancer.

Tomosynthesis: Evidence of benefit is insufficient

Tomosynthesis as a primary breast cancer screening tool was studied in a separate evidence report commissioned by the TF.[4] While tomosynthesis, compared with routine mammography, appears to have increased sensitiv-

TABLE 2
Harms of mammography per 10,000 women screened once[1,3]

Harm	40-49 yrs	50-59 yrs	60-69 yrs	70-74 yrs
False-positive mammograms (false alarms)	1212	932	808	696
Number of biopsies needed per case of invasive breast cancer diagnosed	100	60	30	30
False-negative mammograms (missed cancers)	10	11	12	13

ity and specificity in detecting breast cancer, no studies looked at this technology as a primary screening tool and its effect on breast cancer mortality, overall mortality, and quality of life. Sticking to its nationally-recognized methodological rigor, the TF states that information at this time is insufficient to make a recommendation on the use of tomosynthesis.

Dense breasts: Usefulness of adjunctive screening modalities

Breast density is categorized into 4 groups, from category a (breasts are almost all fatty with little fibro nodular tissue) to category d (breasts are extremely dense).[1] About 43% of women ages 40 to 74 are in categories c and d.[1] Dense breasts adversely affect the accuracy of mammography, decreasing sensitivity and specificity. In one study, sensitivity was 87% in category a and 63% in category d; specificities were 97% and 89%, respectively.[5]

Tomosynthesis, magnetic resonance imaging, and ultrasound, when used in addition to mammography, all appear to detect more cancers, but they also yield more false-positive results.[6] The long-term outcome of detecting more tumors is not known. For an individual, there are 3 possibilities when a tumor is detected earlier: a better outcome, no difference in outcome, or a worse outcome resulting from overdiagnosis and overtreatment. The TF felt that the available data are insufficient to judge benefits and harms of an increased frequency of screening or the use of adjunctive screening methods in women with dense breasts.

Benefit for women ≥75 years is inconclusive

There are limited data on the impact of mammography on outcomes for women older than 70. The TF feels that, since women ages 60 to 69 benefit the most from mammography, this benefit is likely to carry over into the next decade. Modeling also predicts this.

However, women ages 70 to 74 who have chronic illnesses are unlikely to benefit from mammography. The conditions specifically mentioned are cardiovascular disease, diabetes, lung disease, liver disease, renal failure, acquired immunodeficiency syndrome, and dementia.

For all women ages 75 and older, the TF feels the evidence is insufficient to make a recommendation.

Insurance coverage

The ACA mandates that 4 sets of preventive services be included in commercial health insurance plans with no out-of-pocket expenses to the patient: immunizations recommended by the Advisory Committee on Immunization Practices; children's preventive services recommended by the Health Resources and Services Administration (HRSA); women's preventive services recommended by HRSA; and recommendations with an A or B rating from the USPSTF.[7]

For children, HRSA opted to use those preventive services listed by the American Academy of Pediatrics in *Bright Futures*, the society's national initiative providing recommendations on prevention screenings and well-child visits.[8] For women, HRSA asked the Institute of Medicine to form a panel to construct a list of recommended preventive services.

At the time the ACA was passed, the TF had just made new recommendations on breast cancer screening, which were very

While mammography helps reduce breast cancer deaths, women ages 40 to 49 benefit the least; women ages 60 to 69 benefit the most.

similar to the current draft recommendations. Due to the resulting controversy, Congress mandated that the new recommendations not be used to determine first-dollar insurance coverage, and it cited the TF's pre-2009 recommendations as the applicable standard. Those earlier recommendations included annual mammography starting at age 40.

The wording of the law, however, was not clear as to future mammography recommendations. One interpretation is that the TF recommendations in place before 2009 are the basis for first-dollar coverage until changed by Congress. Another interpretation is that the ACA special provision trumped only the 2009 recommendations and the 2015 recommendations will become the standard. If the latter turns out to be true, it is not clear if commercial insurance plans will begin to charge co-payments for mammography before age 50 or for mammograms ordered more frequently than every 2 years for women ages 50 to 74.

The issue of insurance coverage is important because of the lack of uniformity in recommendations regarding mammography. The American Congress of Obstetricians and Gynecologists,[9] the American Cancer Society,[10] and the American College of Radiology[11] all recommend annual mammography starting at age 40. The American Academy of Family Physicians recommendations[12] mirror those of the USPSTF, and the Canadian Task Force on Preventive Health Care recommends against routine screening for women ages 40 to 49 and recommends mammography every 2 to 3 years for women ages 50 to 74.[13]

Annual mammography screening has shown no clear benefit over screening every 2 years, and it results in more false positives and biopsies.

USPSTF rationale is informed and accessible for review

Breast cancer screening remains a highly controversial and emotional topic. The USPSTF has made a set of recommendations based on extensive and rigorous evidence reports that consider both benefits and harms. There will be those who vigorously disagree. The evidence reports, recommendations, and rationale behind them are easily accessible on the TF Web site (www.uspreventiveservicestaskforce.org) for those who want to read them.[1] JFP

References

1. USPSTF. Draft recommendation statement. Breast cancer: screening. Available at: http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementDraft/breast-cancer-screening1#tab1. Accessed May 25, 2015.
2. National Cancer Institute. SEER Stat Fact Sheets: Breast Cancer. Available at: http://seer.cancer.gov/statfacts/html/breast.html. Accessed June 11, 2015.
3. Nelson HD, Cantor A, Humphrey L, et al. Screening for breast cancer; a systematic review to update the 2009 U.S. Preventive Services Task Force recommendation. Available at: http://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review-screening-for-breast-cancer/breast-cancer-screening1. Accessed May 25, 2015.
4. Melnikow J, Fenton JJ, Miglioretti D, et al. Screening for Breast Cancer with Digital Tomosynthesis. Available at: http://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review-screening-for-breast-cancer-with-digit/breast-cancer-screening1. Accessed May 25, 2015.
5. Carney PA, Miglioretti D, Yaankaskas BC, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. *Ann Intern Med*. 2003;138:168-175.
6. Melnikow J, Fenton JJ, Whitlock EP, et al. Adjunctive screening for breast cancer in women with dense breasts: a systematic review for the U.S. Preventive Services Task Force. AHRQ Publication No. 14-05201-EF-2.
7. 111th Congress Public Law 111-148, section 2713. Available at: http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/html/PLAW-111publ148.htm. Accessed May 25, 2015.
8. American Academy of Pediatrics. *Bright Futures*. Available at: https://brightfutures.aap.org/Pages/default.aspx. Accessed May 25, 2015.
9. American Congress of Obstetricians and Gynecologists. ACOG statement on breast cancer screening. Available at: http://www.acog.org/About-ACOG/News-Room/Statements/2015/ACOG-Statement-on-Breast-Cancer-Screening. Accessed May 25, 2015.
10. Smith RA, Manassaram-Baptiste D, Brooks D, et al. Cancer screening in the United States, 2015: a review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin*. 2015;65:30-54.
11. Lee CH, Dershaw DD, Kopans D, et al. Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J Am Coll Radiol*. 2010;7:18-27.
12. American Academy of Family Physicians. Breast cancer. Available at: http://www.aafp.org/patient-care/clinical-recommendations/all/breast-cancer.html. Accessed May 25, 2015.
13. Canadian Task Force on Preventive Health Care. Screening for breast cancer. Available at: http://canadiantaskforce.ca/ctfphc-guidelines/2011-breast-cancer. Accessed May 25, 2015.