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Progress Toward Consensus on Breast Cancer Screening Guidelines and Reducing Screening Harms

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Abstract

IMPORTANCE—Breast cancer is a leading cause of premature mortality among US women. Early detection has been shown to be associated with reduced breast cancer morbidity and mortality.

OBJECTIVE—To update the American Cancer Society (ACS) 2003 breast cancer screening guideline for women at average risk for breast cancer.

PROCESS—The ACS commissioned a systematic evidence review of the breast cancer screening literature to inform the update and a supplemental analysis of mammography registry data to address questions related to the screening interval. Formulation of recommendations was based on the quality of the evidence and judgment (incorporating values and preferences) about the balance of benefits and harms.

EVIDENCE SYNTHESIS—Screening mammography in women aged 40 to 69 years is associated with a reduction in breast cancer deaths across a range of study designs, and inferential evidence supports breast cancer screening for women 70 years and older who are in good health. Estimates of the cumulative lifetime risk of false-positive examination results are greater if screening begins at younger ages because of the greater number of mammograms, as well as the higher recall rate in younger women. The quality of the evidence for overdiagnosis is not sufficient to estimate a lifetime risk with confidence. Analysis examining the screening interval demonstrates more favorable tumor characteristics when premenopausal women are screened annually vs biennially. Evidence does not support routine clinical breast examination as a screening method for women at average risk.

RECOMMENDATIONS—The ACS recommends that women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years (strong recommendation). Women aged 45 to 54 years should be screened annually (qualified recommendation). Women 55 years and older should transition to biennial screening or have the opportunity to continue screening annually (qualified recommendation). Women should have the opportunity to begin annual screening between the ages of 40 and 44 years (qualified recommendation). Women should continue screening mammography as long as their overall

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health is good and they have a life expectancy of 10 years or longer (qualified recommendation). The ACS does not recommend clinical breast examination for breast cancer screening among average-risk women at any age (qualified recommendation).

CONCLUSIONS AND RELEVANCE—These updated ACS guidelines provide evidence-based recommendations for breast cancer screening for women at average risk of breast cancer. These recommendations should be considered by physicians and women in discussions about breast cancer screening.

The American Cancer Society (ACS) and US Preventive Services Task Force (USPSTF) updated their breast cancer screening guidelines.^{1,2} The guidelines differ in their recommendations on key questions, but there appears to be progress toward consensus in reducing screening harms.

The ACS guidelines are developed by a group of public health professionals, practitioners, and laypersons who used the Grades of Recommendation, Assessment, Development, and Evaluation system to score the evidence and strength of recommendations.¹ Guidelines are given a *strong recommendation* when the benefits of adherence to the intervention outweigh the undesirable effects and a *qualified recommendation* when there is clear evidence of benefit but less certainty about either the balance of benefits and harms or about patients' values and preferences. The ACS gave a strong recommendation to starting screening at age 45 years, but qualified recommendations for annual screening from ages 45 through 54 years, biennial screening starting at age 55 years, and continued screening as long as women are healthy and have a life expectancy of 10 years or more.

The group that developed the USPSTF guidelines has expertise in primary care medicine and in evidence-based medicine and/or research and assigns a letter grade to guidelines based on the strength of the evidence on the harms and benefits of the intervention. An *A recommendation* indicates a high certainty that the net benefit is substantial. *B recommendations* indicate a high certainty that the net benefit is moderate or a moderate certainty that the net benefit is moderate to substantial. *C recommendations* indicate that the service should be selectively offered or provided to individuals based on professional judgment and patient preferences. The USPSTF members recommended starting screening at age 50 years and screening biennially until age 74 years (B recommendation); the decision to start screening mammography in women younger than 50 years should be an individual one because there is at least moderate certainty that the net benefit is small (C recommendation).²

In addition to differences in guideline member composition and evidence grading systems between the ACS and the USPSTF, there are also differences in the evidence considered and what constitutes a favorable benefit to harm ratio to recommend screening. For example, the ACS recommendation to start screening at age 45 years is based, in part, on lower breast cancer mortality in a cohort of women aged 40 to 49 years invited to receive mammography vs another cohort not offered mammography.¹ Such cohort results are affected by differences in disease incidence in the populations and lead- and length-time bias, and for these reasons, the USPSTF does not consider such evidence.

Both guideline reviews cite evidence from randomized clinical trials and mathematical modeling to conclude that there is no or little added benefit to annual vs biennial screening in women 50 years or older, and there are more harms with annual screening. Nonetheless, the ACS guidelines gave a qualified recommendation for biennial screening of women 55 years or older, and the USPSTF gave such screening a B recommendation. For women 75 years or older, the USPSTF concluded that the current evidence is insufficient to assess the benefits and harms of screening mammography, while the ACS recommended continued screening with no upper age limit. There are no randomized clinical trials of women 75 years or older to assess mammography efficacy in this group, and observational data of older age groups are biased. The magnitude of screening mammography harms is similar in women aged 75 to 89 years and those aged 66 to 74 years.³ Yet the risk of screening harms is not incorporated into the ACS guideline for continued screening, only the criterion of having a life expectancy of 10 years or more.

Following the ACS strong and qualified recommendations, a woman would undergo 20 mammograms in her lifetime (Table). Compared with previous ACS guidelines, the new guidelines will result in fewer screening examinations and false-positive test results and less detection and treatment of noninvasive and invasive cancer that would otherwise not affect life expectancy, improving the benefit to harm ratio for screened women.⁴ On the other hand, since most of the new recommendations are qualified, a woman might continue annual screening beginning at age 40 years resulting in 35 mammograms or more in her lifetime. Of note, while the new ACS guidelines provide the opportunity to reduce screening harms, they have little added benefit in reducing lifetime risk of breast cancer death compared with the USPSTF guidelines because most of the benefit of mammography screening results from screening women aged 50 to 74 years, when breast cancer incidence and mortality are highest and mammography most efficacious (Table).

Research is under way to evaluate risk-based approaches to breast cancer screening with the goal to improve the benefit to harm ratio beyond what is possible by using age alone.⁵ By better understanding which women are at increased breast cancer risk, and for what type of breast cancer, and what imaging test will most likely detect the cancer, we can target screening to those most likely to benefit. Advancing the discussion on how best to identify women at increased risk who are most likely to benefit from breast cancer screening will improve and individualize care for women and hopefully lead to consensus across guideline-producing organizations.

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Table

ACS and USPSTF 2015 Breast Cancer Screening Guidelines

Mammography Screening Parameter	Recommendation	
	ACS	USPSTF
Starting age, y	45	50
Screening frequency	Annually to age 54 years, then biennially	Biennially
Stopping age, y	As long as healthy and with life expectancy of at least 10 years	75
Total lifetime mammograms if screening continued to age 74 years, No.	20	13
Lifetime risk of dying from breast cancer, %	1.8–1.9 ^a	2.0 ^a

^aLifetime risk of dying from breast cancer with no screening is 2.7%.