Widespread use of screening mammography has been the mainstay of breast cancer prevention in the United States for the past 25 years. An estimated 64% of women aged 40 to 49 years and 72% of women aged 50 to 65 years self-report having mammography within 2 years (1). A total of 63% of U.S. women who have mammography routinely do so every 9 to 20 months—women aged 50 to 69 years are examined on average every 14 months (2, 3). By comparison, women are rarely assessed for risk for breast cancer and rarely receive chemoprevention, even if they are at high risk for breast cancer (4, 5). Major changes to U.S. Preventive Services Task Force (USPSTF) breast cancer screening recommendations (6) and important information about breast cancer prevention (7–9) in this issue should compel clinicians to examine whether current prevention practices in the United States are consistent with the best available evidence.

The first change in the USPSTF screening recommendations is to recommend against universal screening mammography for women aged 40 to 49 years and instead advocate for individualized informed decision making based on specific benefits and harms for women who consider screening before age 50 years (6). This new recommendation is based, in part, on an updated systematic review of screening mammography randomized, controlled trials (RCTs) with 10 or more years of follow-up (7) that includes updated Gothenburg trial data (10) and adds results from the Age trial conducted in the United Kingdom (11). The updated systematic review (7) yields a summary breast cancer mortality reduction of 15%, which is similar to that reported in a previously published systematic review (12). New evidence reported in this issue (8) also contributes to this recommendation by providing estimates of screening outcomes using 6 statistical models that incorporate U.S. population–based breast cancer incidence and mortality information from the Surveillance, Epidemiology, and End Results program and U.S. population–based mammography outcomes from the Breast Cancer Surveillance Consortium (BCSC) (13). These statistical models provide a different method for evaluating screening outcomes and reflect the effectiveness and potential harms of screening mammography in actual community practice in the United States. Model estimates are in agreement with RCT results and show that some reduction in breast cancer mortality occurs by starting screening at age 40 years, but the reduction is modest and has less certainty than mortality reductions observed from screening women aged 50 to 69 years (8). By using summary mortality reductions from RCTs, reviewers estimated that approximately 1 death is averted for every 1900 women aged 40 to 49 years invited to be screened for 10 years compared with approximately 1 death for every 1300 women aged 50 to 59 years and approximately 1 death for every 400 women aged 60 to 69 years (7).

When screening is started at age 40 years, models estimate that about 60% more false-positive results occur per 1000 screening examinations than if screening is started at age 50 years (8). Absolute numbers of important outcomes associated with screening mammography are measured within the BCSC. These outcomes include false-positive results and additional imaging that are most prevalent in women aged 40 to 49 years, with 99 false-positive results per 1000 screening examinations versus 83 false-positive results per 1000 screening examinations in women aged 50 to 69 years (7). Biopsy rates among women aged 40 to 49 years are slightly lower than those of women aged 50 to 69 years (9.3 vs. 11.2 per 1000 screening examinations), but a lower rate of invasive cancer is diagnosed per biopsy (19 vs. 38 per 100 biopsies) (7). Taken together, updated evidence from RCTs and new evidence from statistical models and the BCSC (7, 8) provide consistent results and suggest that the number of additional breast cancer deaths averted by starting screening mammography at age 40 years is small and that earlier screening involves important harms. Thus, universal screening of women aged 40 to 49 years is not recommended.

Should specific subgroups of women aged 40 to 49 years receive screening mammography—if so, at what interval? Notably, the updated USPSTF recommendations do not provide specific recommendations for women at high risk for breast cancer because sufficient evidence does not exist to make such recommendations. Screening recommendations for women aged 40 to 49 years with a first-degree relative with breast cancer could be made on the grounds that risk for disease in these women is similar to that of women aged 50 to 59 years (14). Four of the 6 models show no additional deaths were averted by annual versus biennial screening of women aged 40 to 49 years (8). Randomized, controlled trials that screened women aged 40 to 49 years annually compared with biennially have similar summary breast cancer mortality reductions of 11% (95% CI, −26% to 1%) and 17% (CI, −33% to 3%), respectively (7). Thus, if women aged 40 to 49 years choose to have screening mammography, they can schedule screening biennially, which will limit false-positive results and additional imaging (7, 8).

A second change is to recommend biennial screening mammography for women aged 50 to 69 years. Mandelblatt and colleagues (8) report that in all 6 models, biennial screening of women aged 50 to 69 years averts 70% to 99% of breast cancer deaths attributable with mammography screening. About 2 additional breast cancer deaths are
Evidence-Based Breast Cancer Prevention

Editorial

Tailored recommendations for prevention based on individual risk. There is some precedent for risk-based recommendations in use of screening mammography from 2 studies (20, 27) that suggest that the age to start screening and continue screening past age 70 years should be dependent on the pretest risk for disease. We urgently need risk models with better discriminatory accuracy (than that of current models) (26, 28, 29) that can correctly identify persons at all levels of risk. We also need research to determine the best prevention strategies for levels of risk to maximize prevention benefits while minimizing harms. In addition, to accomplish widespread use of risk assessment, health care systems would need to develop mechanisms for routinely assessing risk factors, calculating breast cancer risk, and reporting risk to women and providers in an easily understandable format. Health professionals will need education about how to communicate breast cancer risk to women, potential benefits and harms of prevention interventions, and how to assist women in understanding which factors might influence their choice to have an intervention or not (30). Women should have the opportunity to make informed choices about primary and secondary breast cancer prevention on the basis of their risk for disease and the potential benefits and harms of prevention interventions.

Karla Kerlikowske, MD
San Francisco Veterans Affairs Medical Center
San Francisco, CA 94121

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Requests for Single Reprints: Karla Kerlikowske, MD, San Francisco Veterans Affairs Medical Center, General Internal Medicine Section, 111A1, 4150 Clement Street, San Francisco, CA 94121; e-mail, karla.kerlikowske@ucsf.edu.


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A third change is to extend screening mammography to women aged 70 to 74 years. Data from RCTs are inadequate to draw conclusions about the benefits of screening in this age group; therefore, the primary evidence about whether to extend screening mammography comes from models. Models estimate that approximately 2 additional breast cancer deaths are averted per 1000 women screened by continuing screening mammography from ages 70 to 74 years (8). More deaths are not averted because cardiovascular disease is the leading cause of death, and more women die of other causes after a breast cancer diagnosis regardless of whether they have screening mammography (19). Thus, decisions about offering screening mammography to women aged 70 to 74 years should be based on her general health, presence of comorbid conditions, and willingness to have additional tests and treatment of clinically insignificant breast lesions that may have no effect on mortality but are fairly common in this age group (8, 20, 21).

Both tamoxifen and raloxifene have been shown to reduce the risk for invasive breast cancer, as reported in recent systematic reviews (9, 22). Two studies have reported that the benefits of chemoprevention outweigh the harms for women aged 35 to 60 years, with a 5-year Gail risk of 5% or more (23, 24). Despite strong evidence that it is efficacious, chemoprevention has been underused in eligible women. The reasons include adverse effects, medical costs (23, 25), lack of reasonably accurate and feasible methods for assessing risk (26), and lack of established risk thresholds that maximize benefit and minimize harms. To increase chemoprevention use, analyses are needed to establish thresholds of breast cancer risk according to a woman’s age and development of better methods are needed to assess breast cancer risk.

We can improve primary and secondary breast cancer prevention effectiveness by implementing risk assessment in primary care and mammography facilities and providing averted per 1000 women who receive screening annually (8). Model results are consistent with 3 other lines of evidence found in women aged 50 to 74 years. A systemic review of RCTs shows that screening every 18 to 33 months versus annually results in the same 23% reduction in breast cancer mortality (15). A population-based screening program reports similar 10-year breast cancer–specific survival rates for women who have annual and biennial screening mammography (16). A community-based study found the likelihood of late-stage disease at diagnosis to be the same for 2- and 1-year screening intervals (17). Annual screening increases costs (18), which includes doubling the number of mammography examinations, false-positive results, and breast biopsies, and increases the chance of over-diagnosis (8). Thus, new evidence from statistical models (8) and published studies (15–17) show consistent results and demonstrate that biennial screening for women aged 50 to 69 years maximizes the potential benefits of screening while minimizing harms.

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We can improve primary and secondary breast cancer prevention effectiveness by implementing risk assessment in primary care and mammography facilities and providing tailored recommendations for prevention based on individual risk. There is some precedent for risk-based recommendations in use of screening mammography from 2 studies (20, 27) that suggest that the age to start screening and continue screening past age 70 years should be dependent on the pretest risk for disease. We urgently need risk models with better discriminatory accuracy (than that of current models) (26, 28, 29) that can correctly identify persons at all levels of risk. We also need research to determine the best prevention strategies for levels of risk to maximize prevention benefits while minimizing harms. In addition, to accomplish widespread use of risk assessment, health care systems would need to develop mechanisms for routinely assessing risk factors, calculating breast cancer risk, and reporting risk to women and providers in an easily understandable format. Health professionals will need education about how to communicate breast cancer risk to women, potential benefits and harms of prevention interventions, and how to assist women in understanding which factors might influence their choice to have an intervention or not (30). Women should have the opportunity to make informed choices about primary and secondary breast cancer prevention on the basis of their risk for disease and the potential benefits and harms of prevention interventions.

Karla Kerlikowske, MD
San Francisco Veterans Affairs Medical Center
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