COMMENTS AND RESPONSES

The Background Review for the USPSTF Recommendation on Screening for Breast Cancer

TO THE EDITOR: The recent changes to the U.S. Preventive Services Task Force (USPSTF) breast cancer screening recommendations are welcome and reflect the best available current evidence (1). The updated systematic review by Nelson and colleagues (2), which is the basis for the changes, concurs substantially with the relevant Cochrane review on mammography and, indeed, the Cochrane review of breast self-examination or clinical examination (3, 4).

Persons raising concerns about Nelson and colleagues' review should be reassured that the summary breast cancer mortality reduction of 15% from screening mammography is similar to that presented in the Cochrane review, which was performed independently, and leads to similar estimates of the numbers needed to invite for examination to prevent or delay 1 death from breast cancer.

Perhaps the most important addition to the revised USPSTF recommendations is the examination of harms from screening, in particular false-positive results and overdiagnosis. Again, the figures for false-positive results are similar between the 2 reviews and suggest that almost half of U.S. women who have been screened 10 times can expect at least 1 false-positive result with mammography. Both the USPSTF and Cochrane reviews found that overdiagnosis was related to mammography, although the estimation of its frequency varies between the 2 assessments.

Evidence-based decision making requires high-quality reliable reviews. The similar findings of Nelson and colleagues' review and the Cochrane review should be reassuring to women working with their physicians to make evidence-based, informed decisions about screening mammography.

Kay Dickersin, MA, PhD
Johns Hopkins University, Bloomberg School of Public Health
Baltimore, MD 21205

David Tovey, MBChB
The Cochrane Library
London SE1 2LP, United Kingdom

Nicholas Wilcken, MBBS, PhD
University of Sydney
Wentworthville, New South Wales 2145, Australia

Davina Ghersi, MPH, PhD
University of Sydney, Sydney School of Public Health
Sydney, New South Wales 2006, Australia

Potential Conflicts of Interest: All authors are members of the Cochrane Collaboration, which has published related reviews.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]

2. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L; U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37, W237-42. [PMID: 19920273]

3. Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2009:CD001877. [PMID: 19821284]

4. Kösters JP, Gøtzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. Cochrane Database Syst Rev. 2003:CD003373. [PMID: 12804462]

TO THE EDITOR: Two recent USPSTF statements on screening for breast cancer identify the harms of false-positive mammography screening test results, including psychological distress (1, 2). Unfortunately, the reports drift away from published evidence about psychological distress from false-positive mammograms. The summary report dismisses the problem: "Anxiety, distress, and other psychosocial effects can exist with abnormal mammography results but fortunately are usually transient" (1). We believe that this statement mischaracterizes the empirical literature, and indeed what the USPSTF reports to an extent in its own detailed concurrent report (2), which more correctly states that "[f]alse-positive mammography results had no consistent effect on most women's general anxiety and depression but increased breast cancer–specific distress, anxiety, apprehension, and perceived breast cancer risk for some" (2). This statement is consistent with our own recent research, in which we found that false-positive mammography results cause small but reliable elevations in breast cancer–specific distress (3).

The USPSTF summary also comes to a different conclusion about transience of the effects of false-positive mammograms (1, 2) than 2 previous systematic reviews (4, 5). Brett and colleagues state that "[w]omen who have further investigations following their routine mammogram experience significant anxiety in the short-term, and possibly in the long-term" (4). They did not emphasize the transient effects of false-positive results as a general finding. Similarly, our own systematic review concluded that the effects of false-positive mammography results endure over the long term, well after cancer has been ruled out (5). We believe that the correct conclusion is that false-positive mammography results cause small but reliable levels of distress that endure for months and years.

Jessica T. DeFrank, MPH
Noel T. Brewer, PhD
University of North Carolina at Chapel Hill, Gillings School of Global Public Health
Chapel Hill, NC 27599

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]

2. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L; U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37, W237-42. [PMID:

These letters were published at www.annals.org on 16 February 2010.
See editorial comment on page 531.

19920273]

3. Salz T, Richman A, Brewer NT. The long-term consequences of false-positive mammograms on outcomes specific to breast cancer. Psycho-Oncology. 2010. [Forthcoming].

4. Brett J, Bankhead C, Henderson B, Watson E, Austoker J. The psychological impact of mammographic screening. A systematic review. Psycho-Oncology. 2005;14: 917-38. [PMID: 15786514]

5. Brewer NT, Salz T, Lillie SE. Systematic review: the long-term effects of false-positive mammograms. Ann Intern Med. 2007;146:502-10. [PMID: 17404352]

TO THE EDITOR: Nelson and colleagues calculate the reduction in breast cancer mortality on the basis of randomized trials (1) but present no calculations for the most important harm: overdiagnosis. They quote a mixture of observational studies and results from statistical models with unverifiable and doubtful assumptions. Only for the Malmö trial do they quote real data, but these data were obtained 15 years after the trial ended, when many additional cases of cancer had occurred in both groups. When we corrected for this dilution and for the 24% of the women in the control group who were also screened during the trial, we found a 25% overdiagnosis rate (2), rather than the 10% reported by the authors.

It is indefensible that Nelson and colleagues base their estimate of overdiagnosis on flawed studies when data from about 600 000 randomly assigned women are available, which we pooled in our Cochrane systematic review in 2009 (3) and before that in 2006 and 2001. We found 31% more lumpectomies and mastectomies. In July, we reported an overdiagnosis rate of 52% in a systematic review of publicly organized mammography screening programs, without using assumptions or statistical modeling (4). It is also curious that Nelson and colleagues do not quote our Cochrane review, as they searched the Cochrane Library.

Nelson and colleagues reported that most studies found an overdiagnosis rate between 1% and 10%. However, systematic reviewing is not a consensus conference—it is a scientific discipline—and Nelson and colleagues overlook that the small estimates of overdiagnosis are based on poor science, mostly produced by researchers with vested interests in screening. If one opens one's eyes, unaided by any statistical tricks, one cannot escape seeing a huge amount of overdiagnosis, such as in the United Kingdom (4, 5).

The Task Force now recommends against breast screening in women aged 40 to 49 years, but the harms may outweigh the benefits in all age groups. An effect of 15% and an overdiagnosis rate of 30% mean that for every 2000 women invited for screening throughout 10 years, 1 woman will have her life prolonged and 10 healthy women, who would not have breast cancer diagnosed if there had not been screening, will be treated unnecessarily (3). Furthermore, about 1000 women in the United States will have had a false-positive diagnosis (3). The psychological strain until one knows whether it was cancer can be severe. The harms caused by overdiagnosis are lifelong.

Karsten J. Jørgensen, MD
Peter C. Gøtzsche, DrMedSci
The Nordic Cochrane Centre
2100 Copenhagen, Denmark

Potential Conflicts of Interest: None disclosed.

References

1. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L; U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37, W237-42. [PMID: 19920273]

2. Gøtzsche PC, Jørgensen KJ. Estimate of harm/benefit ratio of mammography screening was five times too optimistic [Rapid response]. BMJ. Published 27 March 2006. Accessed at http://bmj.bmjjournals.com/cgi/eletters/332/7543/691 on 3 February 2009.

3. Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2009:CD001877. [PMID: 19821284]

4. Jørgensen KJ, Gøtzsche PC. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends. BMJ. 2009;339:b2587. [PMID: 19589821]

5. Jørgensen KJ, Gøtzsche PC. It is time for a new paradigm for overdiagnosis with screening mammography [Rapid response]. BMJ. Published 20 August 2009. Accessed at www.bmj.com/cgi/eletters/339/jul09_1/b2587 on 3 February 2009.

IN RESPONSE: We agree with the comments from Dr. Dickersin and colleagues that the findings of our systematic review and of relevant Cochrane reviews (1, 2) provide corroborative evidence about the benefits and harms of breast cancer screening. When we completed our final literature search in December 2008, the existing Cochrane review had not yet included the Age trial in its meta-analysis of mammography trials. This was added to the 2009 Cochrane meta-analysis, with similar results as our estimate (1).

We also agree with points raised by Ms. DeFrank and Dr. Brewer regarding the transience of the effects of false-positive mammography results. In our article, we state that results of studies are mixed, and in "several studies, women had persistent anxiety, despite eventual negative [biopsy] results, whereas some showed only transient anxiety." Certainly, the long-term adverse effects of false-positive mammography results can be important, and we did not intend to minimize this problem.

Drs. Jørgensen and Gøtzsche raise important issues about studies of overdiagnosis. We did not include the articles they cite because they were published after our review was completed. We also identified many problems with the available studies, including inconsistent methods, use of different outcome measures, lack of reporting results by age, and lack of estimates specific to U.S. populations. As a result, we determined that the studies were too heterogeneous to combine statistically and described them qualitatively. Most agree that overdiagnosis is an important adverse effect of screening, but data to accurately estimate its magnitude and appropriately apply this information to patient decision making in U.S. practice are not yet available.

Heidi D. Nelson, MD, MPH
Arpana Naik, MD
Oregon Health & Science University
Portland, OR 97239

Linda Humphrey, MD, MPH
Portland Veterans Affairs Medical Center
Portland, OR 97239

Kari Tyne, MD
HealthPartners
St. Paul, MN 55114

Potential Conflicts of Interest: None disclosed.

References

1. Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2009:CD001877. [PMID: 19821284]
2. Kösters JP, Gøtzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. Cochrane Database Syst Rev. 2003:CD003373. [PMID: 12804462]

Comments and Response on the USPSTF Recommendation on Screening for Breast Cancer

TO THE EDITOR: The data search for published evidence from the randomized, controlled trials (RCTs) used by the U.S. Preventive Services Task Force (USPSTF) in its breast cancer screening recommendation (1) ended in December 2008. In June 2009, Holmberg and colleagues (2) presented a review of the data from the Swedish Two-County Trial, which showed that the methods used in the previous overview of the 2 Swedish trials (3) "resulted in a reduction of the estimate of the effect of screening." Unfortunately, these erroneous data from the early overview (3) were used for both the 2002 and 2009 USPSTF evaluations.

The USPSTF evaluation (1) and supporting articles are plagued with ambiguity over the terms "screen" and "screening" when used alone and in conjunction with the term "mammography." Whereas the evidence of benefit has been drawn exclusively from intention-to-treat publications, the numerical conclusions have been directly applied by the USPSTF to the individual woman seeking advice from her physician. If the USPSTF evaluation is taken at face value, women will be told the estimated benefit of receiving an invitation to participate in a mammography screening program. This estimated benefit is considerably lower, by a factor of approximately 1.4, than the actual benefit of mammography (4). On the contrary, the harms estimated by the USPSTF are not calculated on an intention-to-treat basis, which introduced bias into the risk–benefit calculations.

The benefits of regular mammography were measured in Sweden by using the ongoing service screening programs (5), and results for women aged 40 to 49 years have been submitted for publication. These comprehensive service screening data more closely answer the question posed by the USPSTF concerning the benefits resulting from regular mammography versus no mammography than do the historical RCT data, which were designed to answer a different question.

Peter B. Dean, MD
University of Turku Faculty of Medicine and Turku University Hospital
20520 Turku, Finland

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. Holmberg L, Duffy SW, Yen AM, Tabár L, Vitak B, Nyström L, et al. Differences in endpoints between the Swedish W-E (two county) trial of mammographic screening and the Swedish overview: methodological consequences. J Med Screen. 2009;16:73-80. [PMID: 19564519]
3. Nyström L, Andersson I, Bjurstam N, Frisell J, Nordenskjöld B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. Lancet. 2002;359:909-19. [PMID: 11918907]
4. Duffy SW, Tabár L, Chen HH, Holmqvist M, Yen MF, Abdsalah S, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. Cancer. 2002;95:458-69. [PMID: 12209737]
5. Swedish Organised Service Screening Evaluation Group. Reduction in breast cancer mortality from organized service screening with mammography: 1. Further confirmation with extended data. Cancer Epidemiol Biomarkers Prev. 2006;15:45-51. [PMID: 16434585]

TO THE EDITOR: The USPSTF update of screening mammography recommendations (1) created controversy because many people feared it was motivated by cost containment rather than scientific evidence (2). However, neither the Task Force nor the underlying studies considered costs or cost-effectiveness (3, 4). It is tempting to attribute this misunderstanding to unfortunate timing: The USPSTF, a government-appointed body, recommended against routine mammography at a time when the government's role in controlling health spending was being widely debated. However, the true culprit behind misinterpretation may be more subtle. The metric underlying the USPSTF decisions, number needed to screen (NNS), obscures the rationale of subsequent decisions.

A decision based on NNS has many potential rationales. An unfavorably high NNS can argue against screening, because harms exceed benefits; the risk–benefit ratio is "too close to call" (either from a population or from an individual perspective); or benefits exceed harms, but not by enough to justify expenditures. The first 2 rationales do not consider cost, whereas the third rationale does. Because NNS-based decisions can be attributed to many rationales, NNS invites misinterpretation. Furthermore, no NNS threshold is universally favorable or unfavorable. An NNS of 10 (usually favorable) may be unfavorable if the harms and costs of screening are substantial but the benefits are slight. Conversely, an NNS of 10 000 (usually unfavorable) may be favorable if the harms and costs of screening are minimal but the benefits are substantial.

The USPSTF revised recommendations for women aged 39 to 49 years because the NNS of mammography increased to 1904 (1), a number that is usually unfavorable. The likely rationale was that risk–benefit ratio was too close to call, particularly on an individual patient basis. For women who attach great value to avoiding consequences of false-positive results (for example, biopsies and their potential complications or anxiety), harms may exceed benefits. However, for women who attach little value to avoiding these consequences, benefits may exceed harms. Accordingly, the USPSTF advised neither in favor of routine mammography (grades A or B) nor against it (grade D), but rather advised individualized decision making (grade C). However, because the USPSTF's rationale was implicit, it was misinterpreted. Many assumed the USPSTF was using NNS as a backdoor to rationing.

When expert groups invoke NNS to recommend against routine screening, they should specify their rationale, especially given current sensitivities about rationing. Misattributing a recommendation to cost rather than risk–benefit ratio wastes a teachable moment on how screening can cause harms and may erode the toehold of evidence-based medicine in the U.S. health care system.

R. Scott Braithwaite, MD, MS
New York University School of Medicine
New York, NY 10016

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. A breast cancer preview: the mammogram decision is a sign of cost control to come. Wall Street Journal. 19 November 2009. Accessed at http://online.wsj.com/article/SB10001424052748704204304574543721253688720.html on 3 February 2010.
3. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L; U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37, W237-42. [PMID: 19920273]
4. Mandelblatt JS, Cronin KA, Bailey S, Berry DA, de Koning HJ, Draisma G, et al; Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151:738-47. [PMID: 19920274]

TO THE EDITOR: The USPSTF (1) recommended against "routine screening mammography in women aged 40 to 49 years," writing that the decision should be based on "patient context, including the patient's values regarding specific benefits and harms." These criteria do not explicitly include risk assessment. Indeed, the recommendation seems to dismiss risk assessment based on "demographic, physical, or historical risk factors for breast cancer," stating that "none conveys clinically important absolute increased risk for cancer."

Although age is the most important risk factor over long age intervals, it is not as important as other risk factors at the ages of 40 to 50 years. In 1998, Gail and Rimer (2) suggested that a woman in her 40s should consider mammography screening if her absolute risk was as great as that of a 50-year-old woman without other risk factors. Benefits are believed to outweigh risks in a 50-year-old woman, and Gail and Rimer say the same should be true for a younger woman with similar risk. The ratio of incidence rates of a 50-year-old white woman with no risk factors versus a 40-year-old white woman with no risk factors is 2.46 (2). If the 40-year-old woman has risk factors that increase her risk at least 2.46 times above baseline, she has at least the absolute risk of the 50-year-old woman. Many risk factors, such as having 2 affected first-degree relatives, atypical hyperplasia, and at least 75% dense tissue on mammography, have relative risks that exceed 2.46, as do many combinations of weaker risk factors (2, 3). For a 48-year-old woman, risk factors need to increase baseline risk by only 6% to put her at the risk of a 50-year-old woman with no risk factors (2).

Recent data (1) show that screening reduces breast cancer mortality by 15% in women aged 39 to 49 years and by 14% in women aged 50 to 59 years. These data only strengthen arguments (2) that a woman in her 40s with the same absolute risk as a 50-year-old woman has a similar ratio of benefits to adverse effects, such as false-positive results requiring further evaluation. Thus, risk factors in addition to age should be considered when counseling a woman in her 40s on whether to have screening mammography. Of course, "the patient's values regarding specific benefits and harms" should also be considered, as recommended by the USPSTF (1).

Mitchell H. Gail, MD, PhD
Catherine Schairer, PhD
National Cancer Institute
Bethesda, MD 20892

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. Gail M, Rimer B. Risk-based recommendations for mammographic screening for women in their forties. J Clin Oncol. 1998;16:3105-14. [PMID: 9738582]
3. Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989;81:1879-86. [PMID: 2593165]

TO THE EDITOR: In its evaluation of mammography, the USPSTF (1) recommends screening for breast cancer biennially starting at age 50 years. The USPSTF has stressed that this recommendation depends solely on the tradeoff between medical benefits and harms, with no consideration of costs. Editorials in the *Wall Street Journal* (2) and *New England Journal of Medicine* (3), however, suggest that the recommendation was in fact motivated by cost considerations. A careful examination of the data analyses by Mandelblatt and colleagues (4), presented in support of the recommendations, seems to confirm the view that costs were indeed pivotal in informing the USPSTF recommendation.

The USPSTF states that its recommendation involves trading off the mortality benefit of screening against medical "harms," such as provoked anxiety, the adverse consequences of false-positive results (such as unnecessary biopsies and treatment), and the adverse effects of overdiagnosis. But how did the Task Force use the evidence about these effects to reach its recommendation? No analyses in the report or supporting articles (4, 5) simultaneously consider both benefits and harms and lead directly to the specific recommendation to begin screening at age 50 years and to do it biennially. Only the Figure in Mandelblatt and colleagues' article (4) includes an analysis that aligns clearly with the USPSTF recommendation.

This figure shows the results of independent analyses by 6 investigative groups of the projected mortality reduction for a range of screening strategies, covering various starting ages, and including options to screen annually or biennially. The critical feature of these analyses is that the population mortality benefit is contrasted solely with the number of mammograms required, a surrogate for resource utilization and thus for costs. The authors do not use the term *harms*. These analyses search for an optimum strategy at the point where the graphs plateau, representing a point of diminishing returns from additional screening. Biennial screening strategies starting at age 50 years are close to the optimum inflection point in all 6 of these analyses, which seems to be the crucial finding that motivated the USPSTF recommendation.

The number of mammograms in these analyses does not represent "harm." Rather, it is a measure of the societal investment in mammography (that is, the societal cost). In other words, this is, in effect, a thinly disguised assessment of cost relative to effectiveness, something most experts would label a cost-effectiveness analysis.

Colin B. Begg, PhD
Memorial Sloan-Kettering Cancer Center
New York, NY 10065

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. Editorial. Liberals and mammography: Rationing? What rationing? Wall Street Journal. 24 November 2009. Accessed at http://online.wsj.com/article/SB10001424052748704779704574552320222125990.html on 3 February 2010.
3. Truog RD. Screening mammography and the "r" word. N Engl J Med. 2009;361:2501-3. [PMID: 19940292]
4. Mandelblatt JS, Cronin KA, Bailey S, Berry DA, de Koning HJ, Draisma G, et al; Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151:738-47. [PMID: 19920274]
5. U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37, W237-42. [PMID: 19920273]

TO THE EDITOR: Although the USPSTF breast cancer screening recommendations (1) are meant to provide guidance to clinicians and their patients, these and other USPSTF recommendations are released in a public health arena and may have unintended or unforeseen effects on public health. Unfortunately, current practices of the USPSTF seem not to take this into account.

For example, I believe that the recommendation against clinicians teaching breast self-examination (BSE) was related to a particular form of BSE, and that the recommendation, as communicated, may have unintended negative consequences. First, it assumes that most such education occurs through interaction with clinicians. Although the recommendation is only to clinicians, the USPSTF does not explain how it may or may not apply to other settings or persons (for example, health educators and public health departments). Nor does the lack of specificity regarding this recommendation account for the possibility that women may be taught how to be more aware of BSEs and how to conduct them for other reasons, such as finding cysts.

In addition, the language of the recommendations indicates that the only concern is for clinicians and their patients. However, the recommendations are also widely disseminated in the media to women who do not have health care coverage or clinicians to interact with on a regular basis—or if they do, only in emergency situations. The recommendations as perceived by these populations could have the unintended effect of not only decreasing the use of breast cancer detection services (including public health services) but also conveying the impression that these issues are not important for persons without regular health care. Furthermore, there is little consideration about the effect on other health behaviors at a time when the entire health community is urging people to be more aware of and to take a more active role in their health and health behaviors, as well as to shift toward prevention and early intervention before tertiary intervention is required.

Although the USPSTF properly tries to address 1 clinical issue at a time, it operates in an arena in which clinical and public health concerns and effects naturally intermingle and in which persons apply what they have learned about one health behavior to another. As much as the USPSTF may assume otherwise, the recommendations are disseminated not only to clinicians but also to persons who might be patients but in reality have little regular interaction with clinicians and to nonclinicians who regularly address the same or similar health concerns with the patients of others.

Richard Yoast, MA, PhD
American Medical Association
Chicago, IL 60654

Potential Conflicts of Interest: None disclosed.

Reference

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]

TO THE EDITOR: The USPSTF (1) recently recommended against routine mammography screening in women aged 40 to 49 years. The recommendation was based on the relative probability of unscreened women dying of breast cancer and the reduction in mortality provided by mammographic screening. On the basis of these studies, the USPSTF issued a blanket recommendation against routine screening mammography in all women aged 40 to 49 years.

The USPSTF study lacks evidence to support a reduction in mammography screening in African-American and Latino women who are younger than 50 years (1). The USPSTF study analyzed the risk–benefit ratio of mammography as a function of a woman's age but did not consider the potential contributions of race and ethnicity (1). Investigators did not state the racial and ethnic composition of study participants and did not analyze the risk–benefit ratio of mammography in African-American and Latino women (1). It is concerning that the USPSTF issued a one-size-fits-all recommendation on breast cancer screening without considering whether the recommendation is appropriate for all women.

Our current recommendations for mammography screening are based on studies in European, European-Canadian, and European-American women. Eight randomized trials (2) studied the effectiveness of mammography in the United States, Sweden, Canada, and the United Kingdom. These studies balance the relative contributions of mammographic density (sensitivity and specificity of mammography) and the mortality rate from breast cancer (2). To our knowledge, there has been no large-scale analysis of the effectiveness of mammographic screening in African-American and Latino women.

Studies of mammography screening in women aged 40 to 49 years are complex because younger women have a lower incidence of breast cancer; denser breast tissue (which can lower sensitivity); and on average, faster growing, biologically aggressive cancer. Relative to European-American women, African-American women have lower breast density, faster-growing cancer, and a higher likelihood of dying to breast cancer (3–5). Because the mortality rate from breast cancer in African-American women is higher and mammographic density is typically lower, the benefit from mammography screening is probably higher in African-American and perhaps Latino women

than in European-American women. So where is the evidence to recommend against routine mammography screening of African-American and Latino women younger than 50 years?

We agree with the USPSTF that change is needed. But the change we call for is the end of one-size-fits-all recommendations and the inclusion of African-American and Latino women in clinical trials testing the benefit of mammographic screening.

Victoria L. Seewaldt, MD
Duke University
Durham, NC 27708

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. Elmore JG, Armstrong K, Lehman CD, Fletcher SW. Screening for breast cancer. JAMA. 2005;293:1245-56. [PMID: 15755947]
3. Stuedal A, Ma H, Bernstein L, Pike MC, Ursin G. Does breast size modify the association between mammographic density and breast cancer risk? Cancer Epidemiol Biomarkers Prev. 2008;17:621-7. [PMID: 18349279]
4. Ursin G, Ma H, Wu AH, Bernstein L, Salane M, Parisky YR, et al. Mammographic density and breast cancer in three ethnic groups. Cancer Epidemiol Biomarkers Prev. 2003;12:332-8. [PMID: 12692108]
5. Elledge RM, Clark GM, Chamness GC, Osborne CK. Tumor biologic factors and breast cancer prognosis among white, Hispanic, and black women in the United States. J Natl Cancer Inst. 1994;86:705-12. [PMID: 7908990]

TO THE EDITOR: The recommendation statement by the USPSTF (1) sensibly concludes that the decision about mammography should be an individual one, reflecting the patient's values regarding specific benefits and harms. However, the USPSTF did little to enable women to understand these risks and benefits and did not help them to make sound choices about screening. For women in their 40s, the USPSTF considered a 55% chance of a false-positive result (2) to prevent 1 breast cancer death for every 1900 women screened to be unacceptable. Curiously, they reached the opposite conclusion for women in their 50s, in whom "only" a 46% chance of a false-positive result to prevent 1 breast cancer death for 1300 women screened is acceptable. The difference between 1 in 1300 and 1 in 1900 (0.053% vs. 0.077%) is so small that it is difficult to imagine a woman for whom it would matter, which makes this an odd policy distinction. This is a classic "close call" or "toss-up," and either choice should be acceptable (3).

Other factors to consider are the psychological stress of treatment and the reassurance of having done everything possible by being screened. Women are entitled to know the chances that mammography will uncover a treatable cancer and the chances that screening will lead to useless, risky treatment. Reasonable women could make different choices, depending on how they feel about these risks and benefits. Rather than having numbers dictate their decision, women should decide how high of a risk they want to take for how much potential benefit.

The public debate sadly veered to whether the USPSTF served the interests of bureaucrats, eager to ration medical care, and insurance companies, eager to deny coverage. But history is repeating itself. A dozen years ago, a National Institutes of Health consensus panel (4) created similar guidelines and also suggested that women in their 40s decide for themselves about screening. Public reaction was similar: widespread concern that the recommendations were driven by health care costs, not science (5). We should have learned that the motivation behind guidelines is easily misconstrued and that the public does not trust expert panels.

Patients cannot make informed medical decisions without adequate information that is clearly communicated. The difference between rationing health care and rational health care lies in who makes the decision. If policymakers or insurers limit the availability of tests, it feels like rationing. However, if informed patients choose to forgo tests that are less effective, it becomes rational decision making.

Nananda F. Col, MD, MPP, MPH
Moritz H. Hansen, MD
Maine Medical Center
Portland, ME 04101

Baruch Fischhoff, PhD
Carnegie Mellon University
Pittsburgh, PA 15213

Steven G. Pauker, MD
Tufts University School of Medicine
Boston, MA 02111

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]
2. Christiansen CL, Wang F, Barton MB, Kreuter W, Elmore JG, Gelfand AE, et al. Predicting the cumulative risk of false-positive mammograms. J Natl Cancer Inst. 2000;92:1657-66. [PMID: 11036111]
3. Kassirer JP, Pauker SG. The toss-up [Editorial]. N Engl J Med. 1981;305:1467-9. [PMID: 7300866]
4. NIH Consensus Statement. Breast cancer screening for women ages 40-49. NIH Consens Statement. 1997;15:1-35. [PMID: 9267441]
5. Woloshin S, Schwartz LM, Byram SJ, Sox HC, Fischhoff B, Welch HG. Women's understanding of the mammography screening debate. Arch Intern Med. 2000;160:1434-40. [PMID: 10826455]

TO THE EDITOR: The USPSTF (1), regarded by many medical professionals as a premier source of information on preventive services (2), was blind-sided by the recent controversy regarding its recommendation against routine screening mammography for asymptomatic women younger than 50 years. Although the evidence-based panel prides itself on being independent of advocacy groups or managed care organizations, the controversy can be better understood if we consider the sociopolitical context of women's health and health care reform. Historically, women have had substantially less access to some of the major diagnostic and therapeutic interventions than men (3), were more likely to delay or forgo necessary medical care, and expressed more concerns about the quality of health care they received (4). The panel's recommendations may have prompted many to perceive, correctly or incorrectly, that the guidelines were a setback in the promotion of women's health.

In the midst of discussions on health care reform, the public's response may also reflect its skepticism of scientists' claim of value neutrality in evidence-based medicine and their social authority based therein. After all, even if scientific evidence is the most important factor in the panel's recommendation, choosing which conditions create a large enough burden of suffering on society to warrant the USPSTF's investigation is partly a value judgment (5). Because the USPSTF's ratings influence insurance coverage of various preventive services, the public's flat-out rejection of the panel's conclusion may be a result of its distrust in the social authority of expert opinion, confusion about the panel's decision-making process, and concern about how rationing and funding priorities are determined by these experts.

In responding to accusations that its recommendations were politically and economically driven, the USPSTF adamantly denied any financial considerations. Instead of convincing the public of its neutral stance, the USPSTF may have inadvertently perpetuated the impression that financial considerations in health care are never legitimate. As the country continues its debate on health care reform, the USPSTF and government officials may want to use this controversy as a new opportunity to facilitate more informed and responsible discussions among citizens regarding the planning and funding of health care programs. Rather than simply denying that economic or social context plays any role in scientific review, it may be more useful for the USPSTF to clearly explain what values were part of the consideration, how such values were chosen, and why such values were appropriate in determining its guidelines.

Anita Ho, PhD
University of British Columbia
Vancouver, British Columbia V6T 1Z4, Canada

Acknowledgment: The author thanks Dave Unger, MD, and Suze Berkhout for their critical and constructive comments on an earlier draft.

Potential Conflicts of Interest: None disclosed.

References

1. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151:716-26, W-236. [PMID: 19920272]

2. Eisenberg JM, Kamerow DB. The Agency for Healthcare Research and Quality and the U.S. Preventive Services Task Force: public support for translating evidence into prevention practice and policy. Am J Prev Med. 2001;20:1-2. [PMID: 11306223]

3. Segev DL, Kucirka LM, Oberai PC, Parekh RS, Boulware LE, Powe NR, et al. Age and comorbidities are effect modifiers of gender disparities in renal transplantation. J Am Soc Nephrol. 2009;20:621-8. [PMID: 19129311]

4. Salganicoff A, Beckerman JZ, Wyn R, Ojeda V. Women's Health in the United States: Health Coverage and Access to Care. Washington, DC: Henry J. Kaiser Family Foundation; 2002. Accessed at www.kff.org/womenshealth/20020507a-index.cfm on 3 February 2010.

5. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21-35. [PMID: 11306229]

IN RESPONSE: We thank the readers for their many comments and welcome the opportunity to clarify our processes and recommendations. Dr. Dean, by focusing on estimates of the number needed to invite for screening, implies that these estimates were the sole determinant of the USPSTF's conclusion that the net benefit of starting mammography screening in women in their 40s is small compared with starting at a later age. In fact, such information was only one of several lines of evidence that we considered. The analysis of Breast Cancer Surveillance Consortium (BCSC) data, information about the risks of radiation and overdiagnosis, and the Cancer Intervention and Surveillance Modeling Network (CISNET) study also contributed. Dr. Braithwaite may be correct that the USPSTF's rationale for when to start screening was left too open to interpretation; however, it is incorrect for anyone to assume that the USPSTF used (or has ever used) NNS as a backdoor means of rationing care.

The USPSTF appreciates Drs. Gail and Shairer's points about risk assessment. To be useful for decision making, risk-prediction instruments must be feasible for use in clinical practice and must accurately discriminate between women who will develop breast cancer and those who will not. One proposed instrument is a risk calculator based on the Gail model and developed by the National Cancer Institute (available at www.cancer.gov/bcrisktool). We note that this calculator requires the input of information that most women do not necessarily know and that one of the stronger risk factors for breast cancer in women aged 40 to 49 years—dense breast tissue—actually presupposes that the woman has had at least 1 mammography performed at an institution that measures and reports breast density, which is not common. This calculator has limited value for helping women in the general population decide when to start mammography screening.

Dr. Begg expresses disbelief concerning the USPSTF's statement that cost is not a factor in its recommendations. He implies that false-positive results and their consequences were used by the USPSTF as cost surrogates or "opportunity costs." The USPSTF has repeatedly rejected calls to use cost-effectiveness analysis in its recommendations and did not use them for this recommendation. The model used by the USPSTF was not a cost model, and the analysis was not a cost-effectiveness analysis in disguise. The USPSTF used false-positive mammograms in the same way that colonoscopy was used as a counter for screening-associated risk in the decision analysis (1) that supported the recommendation on screening for colorectal cancer. The USPSTF specifically asked Mandelblatt and colleagues (2) to present an analysis comparing the benefits of annual versus biennial screening. The BCSC data show how harms accrue with each screening. Although there is no "equation" displaying the simultaneous consideration of harms and benefits for a particular population, the USPSTF has elsewhere (3) described the judgment required in making its recommendations.

Because 2 large studies (4, 5), including one of exceptional quality, failed to show a benefit from teaching women BSE techniques, the USPSTF could not recommend that clinicians spend time teaching it. When communicating this, the USPSTF should have more clearly emphasized the word "teach." Other approaches to public education, including those suggesting that women be "aware of their bodies," seem to be more promising ways to promote public health.

Dr. Seewaldt raises several important points. Minority women have not been included in most trials assessing the benefits of mammography. Evidence is growing that cancer incidence differs by age in African-American and white women, and that breast cancer in young African-American women has particularly high malignant po-

tential. Much needs to be learned about how to prevent breast cancer mortality in African-American women. However, even if mammography is universally and frequently performed, it is not likely to address the problem of triple-negative tumors in women, regardless of racial or ethnic background. New early-detection technologies, such as serum markers, coupled with enhanced targeted treatments should be pursued to address this problem.

We agree with Dr. Col and colleagues that more work must be done to understand how women and men make decisions when balancing the benefits and harms of medical tests and to create materials to support such informed decision making. Accomplishing these aims will require cooperative efforts by voluntary agencies (such as the American Cancer Society), governmental agencies (such as the National Institutes of Health), and the Agency for Healthcare Research and Quality, in collaboration with behavioral scientists, medical clinician-researchers, and communication experts.

Finally, we believe that Dr. Dean's assertions are incorrect. An RCT based on number needed to invite is the best design to yield an unbiased estimate of the effectiveness (as opposed to efficacy) of a screening program. Estimates of the effect of mammography on breast cancer mortality from observational studies vary widely: 6.5% in the United Kingdom (6), 19.9% in the Netherlands (7), and 25% in Denmark (8). Separating the effect of screening on breast cancer mortality from the effect of improved treatment is methodologically challenging.

The attention attracted by this recommendation has given the USPSTF an opportunity to examine its processes and messages. Although the language of the recommendation was intended for primary care clinicians, we recognize that it was poorly communicated to the broader health care community and public. Despite this, we reaffirm our finding that periodic mammography starting at age 40 to 49 provides small net health benefit compared with starting at age 50. We recommend that physicians and patients discuss the potential harms and benefits when making the individual, personalized decision about when to start screening.

Diana Pettiti, MD, MPH
Ned Calonge, MPH
U.S. Preventive Services Task Force
Rockville, MD 20850

Potential Conflicts of Interest: None disclosed.

References

1. Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, Wilschut J, van Ballegooijen M, Kuntz KM. Evaluating test strategies for colorectal cancer screening: a decision analysis for the U.S. Preventive Services Task Force. Ann Intern Med. 2008;149:659-69. [PMID: 18838717]

2. Mandelblatt JS, Cronin KA, Bailey S, Berry DA, de Koning HJ, Draisma G, et al; Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151:738-47. [PMID: 19920274]

3. Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D; U.S. Preventive Services Task Force. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med. 2007;147:871-5. [PMID: 18087058]

4. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, et al. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst. 2002;94:1445-57. [PMID: 12359854]

5. Semiglazov VF, Manikhas AG, Moiseenko VM, Protsenko SA, Kharikova RS, Seleznev IK, et al. [Results of a prospective randomized investigation [Russia (St. Petersburg)/WHO] to evaluate the significance of self-examination for the early detection of breast cancer]. Vopr Onkol. 2003;49:434-41. [PMID: 14569932]

6. Blanks RG, Moss SM, McGahan CE, Quinn MJ, Babb PJ. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990-8: comparison of observed with predicted mortality. BMJ. 2000;321:665-9. [PMID: 10987769]

7. Otto SJ, Fracheboud J, Looman CW, Broeders MJ, Boer R, Hendriks JH, et al; National Evaluation Team for Breast Cancer Screening. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. Lancet. 2003;361:1411-7. [PMID: 12727393]

8. Olsen AH, Njor SH, Vejborg I, Schwartz W, Dalgaard P, Jensen MB, et al. Breast cancer mortality in Copenhagen after introduction of mammography screening: cohort study. BMJ. 2005;330:220. [PMID: 15649904]

Editors' Note on the USPSTF Recommendation on Screening for Breast Cancer

In response to media reports that imply otherwise, *Annals of Internal Medicine* did not schedule the publication of the U.S. Preventive Services Task Force recommendations about breast cancer screening to coincide with a particular date or event. The background papers underwent several rounds of revision over about 5 months, based on comments by independent peer reviewers and an *Annals* statistical editor. The background papers and the recommendation statement were all in final, accepted form by 10 September 2009. *Annals* scheduled them for the next available print issue, which was the 17 November 2009 issue. Our routine print production process takes about 2 months from final acceptance to print.

—*The Editors*

Potential Conflicts of Interest: None disclosed.