I was confused by these two articles. Should we or should we not invest resources in screening the currently unscreened? Resolution of this issue requires a critical review of the arguments used to support the two opposing viewpoints. Two points seem noteworthy.

First, the three biases cited by Baum (2) are irrelevant to the findings of Taplin et al. (1). As stated by Taplin et al., their goal was to evaluate screening implementation and not screening efficacy. Indeed, the study participants were aged 50 years and older, an age group for which the benefits of screening are generally accepted (thanks to several randomized trials of screening and mortality). The three biases do not invalidate the observed association between absence of screening and late-stage cancers, nor do they invalidate the observed associations between absence of screening and the participants’ demographic characteristics.

Second, the study by Taplin et al. (1) is flawed by its use of cancer size as an endpoint for investigation. Translating the findings to public health policy requires a leap of faith from “screening leads to smaller cancers at diagnosis” to “screening reduces mortality.” This leap cannot be taken with confidence, as evidenced by the results of the Canadian National Breast Screening Study, a randomized trial of breast cancer mortality in women aged 40–49 years (3). The participants were assigned to either the treatment arm (screening with annual mammography, clinical breast evaluation, and instructions on breast self-examination) or the control arm (community care after a single breast physical examination and instructions on breast self-examination). Data on the sizes of breast cancers diagnosed during 9 years of follow-up in that study (3, Appendix Table 2), shows that only 47% of the cancers among women in the screened group were greater than 2 cm in diameter, compared with 55% of those among women in the control group (odds ratio = 1.37, two-tailed P = .03). Yet after 11–16 years of follow-up, screening had not reduced breast cancer mortality below that of the control group (cumulative mortality risk ratio = 1.06, 95% confidence interval = 0.80 to 1.40).

Thus, we cannot assume that efforts to screen currently unscreened women will lead to lower breast cancer death rates. The study by Taplin et al. (1) would have been more informative had prediagnostic screening practices been compared in breast cancer patients who had and had not died from the disease.

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REFERENCES


RESPONSE

We thank Dr. Whittemore for her observations and hope that our explanation below reduces confusion about our work.

Dr. Whittemore states that our findings require a leap of faith from “screening leads to smaller cancers” to “screening reduces mortality” and cites evidence from the Canadian National Breast Screening Study, a randomized trial in women aged 40–49 years, that mammography does not reduce mortality. She notes that, in the Canadian trial, the proportion of large tumors decreased among women who received screening but that mortality did not. However, the proportion of large tumors can be deceiving because the proportion of all cancers detected is influenced by the propensity of screening to find early cancer, which inflates the denominator of that proportion (i.e., all invasive cancers) (1). Instead, we believe that the population-based incidence of large tumors is a better indicator of screening’s impact, and in studies that have shown a reduction in mortality associated with screening the incidence of large tumors decreased before mortality decreased (2,3). Dr. Whittemore also...
notes the important fact that our study did not include women aged 40–49 years and that our study did not evaluate the efficacy of screening. Therefore, the results of the Canadian trial are not directly relevant to our results.

We restricted our evaluation to women aged 50 years or older because the strongest evidence for a screening benefit is in this age group, as recently affirmed by the U.S. Preventive Services Task Force and others (4,5). Our definition of late-stage disease included large tumors and the presence of metastases because the incidence of large tumors declines with screening implementation (6) and because a reduction in late-stage disease is an indicator of screening success in a population (3,7). With our definition of late-stage disease as the indicator, we showed that the largest proportion of late-stage cancers occurred among unscreened women. We therefore concluded that the best chance for further mortality reduction was to reach the unscreened women. Although we did not make it clear in our article, “reaching the unscreened” simply means making sure that women without screening have access to mammography, understand what the test has to offer, and are making an informed choice about their care.

Dr. Whittemore describes a valid concern that our definition of late-stage disease, which includes large tumors, could influence our conclusions. Among women with late-stage disease, the proportion of women with tumors at least 3 cm in greatest diameter (n = 1112) and of those with metastases (n = 235) differed among the “absence of screening,” “absence of detection,” and “potential breakdown in follow-up” groups (3 cm, no metastases: 49%, 43%, and 8%, respectively; metastases: 67%, 25% and 8%, respectively). However, this difference reinforces the priorities for improvements in screening implementation reported in our paper because the proportion without screening is even higher among metastatic cases.

Dr. Whittemore suggests that mortality would have been a better endpoint. A nested case–control study of screening efficacy in which breast cancer deaths are used as the endpoint has been undertaken within the Cancer Research Network, but the results have not yet been published. We did not evaluate the efficacy of mammography, which is best done in a randomized trial, but assumed that mammography is efficacious and demonstrated that there are opportunities to improve the screening process. We agree that the mortality impact of improvements in the screening process will need evaluation, but we do not think that women and health plans need to wait for that evaluation before pursuing those improvements.

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**REFERENCES**