CORRESPONDENCE

Re: Efficacy of Breast Cancer Screening in the Community According to Risk Level

The case–control study of mammography screening by Elmore and colleagues (1) raises some interesting points. We agree with the sentiment in the accompanying editorial by Harris (2) that evaluation of breast screening in the community is challenging and worthy of further research. We see some of those methodologic challenges in the analysis by Elmore et al. The fact that women who died from breast cancer, 75% of whom had tumors larger than 2 cm, had screening exposures similar to those of the population-based control subjects suggests that the screening programs were ineffective and/or there was bias in the study methodology.

The first explanation is possible because a large part of the study pertains to 1980s screening programs, which were dominated by clinical breast examination. How relevant is this kind of screening to good-quality mammography in 2005?

Bias in the study methodology is also possible. The authors’ definition of exposure to screening, i.e., breast cancer screening during the 3 years before diagnosis for the case subjects, is biased in terms of screening opportunity (3). Case subjects had the opportunity to be “screened” during the 3 years before diagnosis if they had symptomatic cancers and had the opportunity to be screen-detected. Control subjects, however, only had the opportunity to be screened in the 3 years before pseudodiagnosis. Depending on the temporal pattern of screening, this bias can be exacerbated by the selection of control subjects who are matched within 1 year of age to the case subjects, as in the Elmore et al. study. Connor et al. (3) showed how the combination of the two biases can cause a true substantial decrease in the mortality associated with screening to be observed as a spurious substantial increase in mortality.

These biases can be addressed by considering screening exposure among the control subjects up to the estimated time that the screen-detected case subjects would have been diagnosed in the absence of screening and by matching on year of birth. The design and analysis of the Elmore et al. study, as it stands, confers a bias against the effect of screening. Thus, Harris’s conclusion (2), that screening has a less than 20% effect on mortality, is probably incorrect. Indeed, the likely extent of the biases (3) suggests that the true benefit of the screening programs evaluated is much larger than 20% and that, if Elmore et al. had been able to measure the effect of modern, regular mammographic screening, it would be greater still.

Other issues raised by the article and the editorial include the narrow range of index periods considered (2–3 years) and the lack of discussion of other findings on service screening. In particular, Harris (2) dismissed our comparisons (4) of mortality before and after screening, referring to confounding with contemporaneous changes in treatment. In fact, we estimated improvements in mortality occurring independently of screening and found a 44% reduction in breast cancer mortality among women who received screening but a 16% reduction in women who did not (4). The effectiveness of service screening is an important task. It is vital to avoid biases in such evaluations, because they can lead to spurious conclusions and to disinformation in press releases.

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REFERENCES

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RESPONSE

I am pleased that Duffy et al. agree that the issue of effectiveness is the next important question for breast cancer screening. Unfortunately, they apparently misunderstood the underlying analysis in my editorial (1) and believe that I concluded that “screening has a less than 20% effect on mortality.”

What I said was that the study by Elmore et al. raises, but does not resolve, important questions about the effectiveness of screening, one of which is whether effectiveness in real life may be less than efficacy in the randomized controlled trials. The real question is: Do we know what contribution breast cancer screening in the United States in 2005 is making to reducing mortality from breast cancer? The truth is that we do not know. I offered two reasons why screening may be having a smaller effect on mortality than one might predict from the results of randomized controlled trials, problems with implementation and changing context, and I suggested ongoing research to provide more information on the issue.

Duffy et al. refer to their previous article (2) as if it answers the issue of effectiveness. In that article, they draw the counterintuitive conclusion that screening in the community has an even greater effect on breast cancer mortality than that found in the carefully conducted randomized controlled trials. In their article, they made comparisons among nonrandomized groups of women who differed by age and by time period. Those groups, of course, differed in many ways other than only screening and treatment. Although a detailed critique of that article is beyond the scope of this letter, suffice it to say that the authors’ attempts to adjust for such differences were insufficient. Their study—like that of Elmore
et al.—raises issues but does not resolve them.

The effectiveness question will not go away soon.

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