Dr. Alfred Berg’s counterpoint is gracious and informative. I am grateful that he reinforces the often disregarded but currently best available version of the truth: in women younger than age 50 years, screening benefits take longer to become apparent and absolute benefits are smaller compared with older women. In Dr. Berg’s words, longer means 13–20 years after randomization. My commentary focuses on what happens to women age 40–49 years before the benefits become apparent.

My conviction that, for the first 10 years, breast cancer deaths are increased in women age 40–49 years who receive mammography screening is evidence-based despite Dr. Berg’s assertion that it is not. What is my evidence? The increase in deaths from breast cancer among screened women (compared with that among control women who did not receive screening) is seen very briefly in the Health Insurance Plan of New York study but lasts up to 10 years in the Two-County trial, the Canadian trial, the Stockholm trial, and the Malmö trial.

Furthermore, the meta-analysis performed by Brian Cox in 1997 portrayed the paradox clearly (see Fig. 1 in my commen-
However, statistical significance for the rate ratio was observed only in the third follow-up year. Undeniably, the significance of the third-year twofold excess in risk of death is weakened by the problem of multiple comparisons. However, if the unsuccessfully randomized Edinburgh trial with its 25% excess in all-cause mortality in unscreened control subjects compared with that in screened women (1) had been excluded from the Cox meta-analysis, the mortality paradox might have been more evident. Dr. Berg mentions “only a single reanalysis of the Swedish trials shows a statistically significant difference in the relative risk” for increased early breast cancer mortality in screened women but gave no reference for it.

Viewing the situation as objectively as possible, on the one hand, the possibility that the mortality paradox is real is discounted even though an excess number of deaths in screened women is observed for up to 10 years in trials conducted on two continents over three decades. On the other hand, screening is strongly promoted on the basis of evidence that is not much stronger. The Swedish studies have driven the screening engine in North America and Europe even though, as pointed out in 2002 by Nystrom et al. (2), the reduction in breast cancer mortality in women ages 40–49 years observed in his Swedish meta-analysis was only 9% and was not statistically significant. Objectivity requires that skepticism be applied equally to both sides, not just one.

Research makes huge leaps forward when scientists notice the unexpected, even the “wrong” results, and then think about what could explain them. I hope my commentary successfully argues for the importance of thinking about what might explain the unwelcome observations I have described and prompts others to investigate the causes of the mortality paradox. It will also be wonderful if my concerns are proven baseless when results from the U.K. trial of screening in women in their 40s are finally published.

Dr. Berg and I are clearly in agreement about the most important issue. Women should carefully consider whether screening is the right choice for them. They cannot do that until they are completely informed.

REFERENCES


NOTE

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