

Does mammography protect against death from breast cancer?

The answer isn't clear. This case-control study found that women 40 to 49 years old who had at least one screening mammogram within 2 years before diagnosis of breast cancer had an adjusted odds ratio (OR) for death from breast cancer within 5 years after diagnosis of 0.89 (95% confidence interval [CI], 0.65–1.23), and women aged 50 to 64 years had an OR of 0.47 (95% CI, 0.35–0.63). Among premenopausal women, the adjusted OR for breast cancer death was 0.74 (95% CI, 0.53–1.04), and it was 0.45 (95% CI, 0.33–0.62) among postmenopausal women. However, these findings are unreliable.

EXPERT COMMENTARY

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This article reports a case-control study based on a cohort of 3,886 women aged 40 to 64 years who had a new diagnosis of breast cancer between 1994 and 1998. Of these, 553 died in the subsequent 5 years; these were the cases. The 4,016 women in the control group had no breast cancer and were drawn from the same population as the original cohort.

A much higher percentage of women in the control group had a screening history. Although the ORs reported above are impossibly far from any credible claim about the benefits of screening, the authors concluded that their study supports current screening guidelines.

Why these results are unreliable

Case-control studies have many biases, including selection bias and recall bias. This study is subject to more serious biases that are associated with nonrandomized screening studies: lead-time bias and length bias.

The former is easier to understand. Consider an extreme example: Assume that screening reveals breast cancer 5 years before it would become symptomatic. Then the only women who would die of breast cancer within 5 years (the cases in this study) would be those whose cancer was detected on the basis of symptoms. These women are unlikely to have been screened in the previous 2 years because, if they had been, their cancers probably would have shown up on mammogram. In this scenario, the incidence of screening is lower—much lower—among cases than controls. And this is pure bias, having nothing to do with screening effectiveness.

Of course, not all lead times are 5 years. Some are shorter—possibly even negative—and some are longer than 5 years. But the principle holds for any distribution of lead times among the cases. Length bias is also critical.

The authors try to address lead-time bias by considering follow-up periods of up to 7 years, but this is inadequate to eliminate the bias. Lead-time bias may sometimes be slightly less important with longer follow-up, but both types of bias are real and important for any length of follow-up. That means the conception of this study is fundamentally flawed.

Not only are the estimates biased, the confidence intervals convey an unreasonable sense of accuracy. Anyone who thinks that screening reduces the odds of breast cancer death between 37% and 65% for women aged 50 to 64 years is delusional. The most recent data from randomized trials in Sweden show that reduction in the odds of death is 14% (follow-up analysis).¹ And the Canadian National Breast Screening Study 2, which involved women aged 50 to 59 years, showed an increase of 2%.²

Norman SA, Localio AR, Weber AL, et al. Protection of mammography screening against death from breast cancer in women aged 40–64 years. *Cancer Causes Control*. 2007;18:909–918.

FAST TRACK

A much higher percentage of women in the control group had a screening history, so this comparison was biased

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Difference between age groups is more revealing

One might draw an intriguing conclusion from this study based on the different results for women aged 40 to 49 (OR for screening: 0.89, with a 95% CI of 0.65 to 1.3), compared with older women. It is reasonable to hypothesize that the biases would be similar in the two age brackets. Applying an adjustment in the OR that would be reasonable for women aged 50 to 64 years to the younger women would change the OR of 0.89 to almost 1.00, suggesting little or no benefit for screening women in their 40s.

Issue must be settled by randomized trials

Because the results of this study can be easily explained by biases, it provides no evidence at all about the benefits of screening. Given our present knowledge of cancer biology, observational screening studies are hopelessly flawed. Randomized trials are difficult to run and come with their own inferential baggage—but they offer the only credible evidence about the effectiveness of screening.

This study by Norman and colleagues certainly does not warrant any change in breast cancer screening for women at any age. ■

References

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