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# EDITORIAL

## THE COST-EFFECTIVENESS OF BREAST CANCER SCREENING

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In a moving, reflective survey of the science, politics, and ethics of screening for breast cancer, which was published posthumously, Maureen Roberts asked: "Are we brainwashing ourselves into thinking that we are making a dramatic impact on a serious disease before we brainwash the public?" (2). Such bluntness is unusual in medical journals, particularly when "brainwashing" refers to a widely acclaimed preventive measure that is believed to prevent thousands of women from dying a miserable death. What is unique in this account is that it was written by the clinical director of the Edinburgh Breast Cancer Project and the main organizer of the Edinburgh randomized controlled trial of screening mammography. "We all know," she wrote, "that mammography is an unsuitable screening test: it is technologically difficult to perform, the pictures are difficult to interpret, it has a high false-positive rate, and we don't know how often to carry it out. We can no longer ignore the possibility that screening may not reduce mortality in women of any age, however disappointing this may be" (2).

Maureen Roberts knew that the Edinburgh trial did not achieve a reduction in mortality. She herself developed breast cancer while in charge of the project, and she died of the disease on June 9, 1989, having dedicated her life to screening. She expressed her sorrow that she was critical of her colleagues, but she wrote that she knew that they would recognize that she was telling the truth. "When words are scarce they are seldom spent in vain, for they breathe truth that breathe their words in pain."

Before more countries embark on national breast cancer screening programs, it would be prudent to resist political pressures to "get on with it" and to assess carefully the balance of risks and benefits. Cost-effectiveness analysis should follow only if benefits have been shown to be greater than risks.

Current cost-effectiveness analyses of mammography screening are based on the questionable assumption that screening significantly reduces breast cancer mortality (5). As Anne Elixhauser documents in her review of cost-effectiveness analyses, the estimates of costs vary from $14,000 per life saved (Wald et al.) to $388,000 per extra 10 years of life (Forsyth). Such a range does not inspire confidence in the reliability of the calculations and underlying premises on which these calculations are based.

Another approach to statistical analysis of conflicting trials with weak results is to pool them all by the method of meta-analysis, in the hope that their sum will achieve the Holy Grail of "statistical significance." From the clinician's point of view such an exercise appears futile. If very large numbers of patients, usually hundreds of thousands, must be combined to show that some procedure is worthwhile, it is certain that such a procedure has no clinical usefulness. Furthermore, combining studies that are not comparable in design, sampling, and intervention makes the results of such meta-analyses invalid.

Kit Simpson's and Lyle Snyder's calculations of cost-effectiveness are based on a meta-analysis of six mammographic trials, but they are likely to underestimate the real cost for the following reasons: (a) the meta-analysis is flawed by combining trials that used either mammography alone or mammography combined with physical examination. The contribution of physical examination to breast cancer detection in the HIP trial (in which screening benefit was higher than in other randomized trials, despite use of mammographic equipment that is obsolescent by present standards) was significant, and it is not clear how much of the reported benefit was due to mammography alone (4); (b) the meta-analysis combined "apples" and "pears" by mixing an individually randomized trial (HIP), a trial with randomization by geographic regions (2-county), a trial randomized partly by general practices (Edinburgh) and partly not randomized (Guildford), here subsumed under "the U.K. trial," and three case-control studies (Florence, Utrecht, Nijmegen). As shown by Ranstam, case-control methodology produces invalid results. When the same case-control approach was applied to cases in the Malmö randomized trial, the observed 4% reduction in breast cancer mortality (as established by proper analysis of the randomized sample) was artifactually inflated to 58%, that is to the similar level as the "reductions" reported from Florence, Utrecht, and Nijmegen (1); (c) the exclusion of the Malmö trial from the meta-analysis is peculiar, to say the least, as this trial was exemplary in its planning, execution, documentation, and analysis.

Even with the optimistic assumption that the results of the HIP and 2-county trials are generalizable and reflect the true benefit of screening, Schmidt (3), in a meticulous analysis of the benefits and harms of mammography, concluded that more harm than good would result if women were invited for screening. The harm includes false-positive mammograms with resulting anxiety and fear while awaiting further assessment, overdiagnosis of lesions in the grey area of pathology as "cancer," and further overdiagnosis due to the fact that a proportion of women die with undiagnosed breast cancer that could now be detected by screening, with subsequent unnecessary biopsies, surgical interventions, unnecessary mastectomies, and other iatrogenic damage associated with these procedures. For the majority of women whose cancer was found by mammography, even in trials that claim the largest benefits, the only "gain" is extra years spent living with breast cancer. Schmidt calculated that in the Malmö trial for one death from breast cancer that was prevented or postponed, 90 additional years with cancer had to be suffered by women with breast cancer detected by mammography. "Prevented" or "postponed" may be an academic point, because breast cancer may be a systemic, incurable disease from its inception; furthermore, all mammography trials had a too short follow-up to throw light on this matter.

Screening would make sense only if there existed a wide enough time interval between the time the cancer is diagnosed by screening and the time when the cancer starts metastasizing. This interval ("the cancer control window") is, in the case of breast cancer, probably empty or negative (6). Thus, the search for early breast cancer may be as futile as trying to stop the runaway horse by closing the stable door. Until fundamental questions about the natural history of breast cancer are satisfactorily answered, risk–benefit analysis would be more relevant and more informative than cost-effectiveness analysis.

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