

# The controversy over breast cancer screening

For the last 10 years or so, there has been general agreement, with few dissenters, that screening for breast cancer with mammography reduces mortality from breast cancer. This is based on the results of seven randomized trials worldwide, which found substantially fewer breast cancer deaths in those invited to screening, and on numerous uncontrolled studies. A recent quantitative overview of all the randomized controlled trials of screening showed a significant 24% reduction in breast cancer mortality in association with invitation to screening (Duffy et al, 2002). Evaluation of service screening programmes suggests that the mortality reduction is substantially greater in those who actually attend for screening (Tabar et al, 2001).

This benefit has been called into question by a meta-analysis which claims to find no benefit of breast cancer screening. Indeed, the authors claim that screening causes harm by increasing the rates of radical treatment (Gøtzsche and Olsen, 2000; Olsen and Gøtzsche, 2001). In particular, the authors of the meta-analysis asserted:

1. That only two of the randomized trials are of sufficient quality to be considered in reviewing the evidence
2. That screening leads to more use of radiotherapy which in turn leads to more cardiovascular deaths. These are not counted when breast cancer mortality is compared between groups invited and not invited to screening
3. That, for this reason and others, use of breast cancer mortality as an endpoint is biased in favour of screening
4. That screening increases the rates of mastectomy.

In view of the above, the authors concluded that the case for mammographic screening was not established and that future evaluation should be

based on all-cause (rather than breast cancer) mortality, including deaths in women who never develop breast cancer.

## QUALITY OF THE RESEARCH

The judgment of quality of the trials is based on observed or alleged imbalances between study and control groups and alleged inconsistencies in reported results. It has been shown, however, that the imbalances referred to are either trivial (including a 1-month imbalance in age between study and control groups in the Gothenburg trial), fully adjusted for in the analysis (such as the social class imbalance in the Edinburgh trial), or both (such as the 5-month age imbalance in favour of the control group in the Swedish Two-County Trial) (Alexander et al, 1999; Duffy, 2001).

As regards inconsistencies, these have been shown to be either trivial or not to be inconsistencies at all. For example, alleged inconsistent reporting of deaths was caused by the difference between an expert panel's judgment of cause of death and that recorded on the routine death certificate, or to larger numbers of deaths with longer follow-up (Duffy et al, 2002). The judgment of study quality is therefore at best dubious. Any review of the randomized controlled trials should be even-handed and include all the available evidence.

The assertion that screening leads to more radiotherapy seems to be based on what Gøtzsche and Olsen thought should happen rather than on what did happen. In the Swedish Two-County Trial, treatment with radiotherapy was more common in the control group than in the group invited to screening (Tabar et al, 1999). Also, the increased risk of cardiovascular disease with radiotherapy pertains to archaic forms of radiotherapy which are no longer practised.

The other assertions about cause of death seem similarly ill-founded. Indeed it has been shown that if one considers all causes of death among breast cancer patients (since mammography cannot be expected to affect deaths in women who do not develop breast cancer) there was a reduced risk of death from any cause in the group invited to screening (Tabar et al, 2002). The conclusions of Olsen and Gøtzsche were based on incorrect statistical analysis which failed to take account of lead time.

There is also no convincing evidence that screening increases the rates of radical surgery, in particular mastectomy. Mastectomy rates were lower in the group invited to screening in the Two-County Trial, and indeed have been shown to fall by 40% with the introduction of service screening (Tabar et al, 1999; Paci et al, 2002).

It therefore appears that the consensus of the last decade or so is correct. The vast body of evidence indicates a substantial reduction in mortality from breast cancer from mammographic screening. Whether this reduction justifies the financial and human costs of a screening programme is a judgment which has to be made by individual societies, and will depend on the prevailing rates of breast cancer, availability of facilities and expertise, costs of these, and numerous other considerations. The existence of a benefit in terms of reduced breast cancer deaths, however, is not in question. The UK, along with several other countries and health-care bodies, has already made the decision, correctly in the author's opinion, that such a programme is worthwhile.

## CONCLUSIONS

The time for repeatedly revisiting the trials has gone. The challenge for the future is to evaluate the effects of the service screening programmes which

are springing up around the world, and to pinpoint potential improvements where possible. Great strides have been made in the control of breast cancer in recent years, through both advances in treatment and early detection. Arguing the toss about long-completed trials distracts us from making further progress. **HM**

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### KEY POINTS

- The randomized trials of mammographic screening are generally reliable and much of the recent criticism is ill-founded.
- Breast cancer screening saves lives.
- The challenge for the future is evaluation of the numerous mammographic service screening programmes which have developed worldwide.