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Assessment of breast screening programme effectiveness

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Keywords

Bias, breast screening effectiveness, mortality reduction, randomised controlled trial

Introduction

The generally held assumption that mammographic screening for breast cancer reduces breast cancer mortality is based on the results of a number of randomised controlled trials and on meta-analysis of these. However, a report published in Sweden last year drew the surprising conclusion that there was no decrease in breast-cancer mortality despite the fact that screening has been recommended in Sweden since 1985. Since screening is a costly public health intervention carried out on seemingly healthy people, it is essential that the true effectiveness of mammographic screening is determined.

Aims

To review the methodology and interpretation of previously reported mammography trials (in New York, Edinburgh, Scotland, Canada, Malmo, Kopparberg, Ostergotland, Stockholm, and Goteborg)and to repeat the meta-analysis of the Swedish trials. To validate the methodology, particularly that of randomisation, and to determine the true impact of screening on mortality.

Comments

The best evidence of the effectiveness of mammographic screening must come from randomised controlled trials. The authors, whose experience comes mainly from small scale therapeutic trials, take the view that inequalities in age between study and control groups in many of the trials carried out to date indicate inadequate randomisation and hence invalid results. They then conclude that screening is ineffective on the basis of results from two supposedly unbiased trials showing lack of effect. However there is no indication that small differences in age between groups would affect the results obtained. Such differences are not unexpected in screening trials involving large numbers of subjects and are unlikely to influence results. However, in the Swedish two-county study (Kopparberg, Ostergotland), the slight age difference would, if anything, have increased the reduction in mortality since the study group was older than the control group and hence at greater risk of breast cancer. Whilst the lesson to be

learned here is that all trial methodology must be robust and reporting must be consistent, open and clear, it is not helpful to throw the baby out with the bathwater by disregarding results from well-run trials where there has been slight inconsistency in methodological reporting.

Methods

Methodology was reviewed focusing on three important sources of bias in randomised trials:

1: suboptimum randomisation methods (was assignment to study or control group during randomisation performed 'blind'?)

2: lack of masking in outcome assessment (was study or control status known when outcome was assessed?)

3: criteria for exclusion after randomisation (were all women in study accounted for?). Original investigators were approached regarding procedural details.

Results

Overall, in only two of eight studies (Malmo, Canada) were the authors confident that randomisation had achieved study and control groups that were comparable with respect to important prognostic characteristics (age, symptoms at entry, family history of breast cancer, socio-economic status etc.). In only three of the eight studies (Malmo, Canada and Edinburgh) was the account of the number of subjects in each group consistent. Masked assessment of cause of death was performed only in Canada, Malmo and in the Swedish meta-analysis.

The two trials with adequate randomisation and baseline comparability found no effect of screening on either breast cancer mortality, or on total mortality. The combined relative-risk estimate for death from breast cancer in study versus control groups was 1.04 (95% CI = 0.84-1.27) and for total mortality was 0.99 (95% CI = 0.94-1.05). The other six trials which showed flawed randomisation and/or lack of baseline comparability showed significant reduction in breast cancer deaths amongst study group women (pooled relative risk 0.75 [0.67-0.83]); thus, these results differed significantly from those for the former two trials ($p = 0.005$). Re-performing of the Swedish meta-analysis showed a decrease in breast cancer mortality, as originally reported, but also an increase in all-cause mortality (relative risk 1.06 [1.04-1.08]) which disappeared after adjustment for an imbalance in age.

Discussion

The authors claim that several factors including, inequality in baseline study and control groups, coupled with lack of masking when assessing outcome and inconsistency in reporting of numbers of women in study and control groups, raise doubts about the validity of these trials. They conclude that there is no reliable evidence that mammographic screening for breast cancer decreases breast cancer mortality and, therefore, screening for breast cancer with mammography is unjustified.

Additional information

An editorial accompanies this paper (de Koning "Assessment of nationwide screening programmes" *Lancet* 2000; **355**: 80-81).

References

1. Gøtzsche PC, Olsen O: Is screening for breast cancer with mammography justifiable?. Lancet. 2000, 355: 129-134.