Chapter 8
Evaluation

Evaluation of the efficacy of breast cancer screening

There is *sufficient evidence* for the efficacy of screening women aged 50–69 years by mammography as the sole screening modality in reducing mortality from breast cancer.

There is *limited evidence* for the efficacy of screening women aged 40–49 years by mammography as the sole screening modality in reducing mortality from breast cancer.

There is *inadequate evidence* for the efficacy of screening women under 40 or over 69 years by mammography in reducing mortality from breast cancer.

There is *inadequate evidence* for the efficacy of screening women by clinical breast examination in reducing mortality from breast cancer.

There is *inadequate evidence* for the efficacy of screening women by breast self-examination in reducing mortality from breast cancer.

Overall evaluation

Effect of screening with mammography on mortality from breast cancer

There is *sufficient evidence* from randomized trials that inviting women 50–69 years of age to screening with mammography reduces their mortality from breast cancer; the best current estimate of the average reduction is 25%. There is only *limited evidence* for this effect in women 40–49 years of age, in whom the reduction, if real, is estimated at 19% but could be less, depending on the extent to which it is due to screening of the women after they reached the age of 50. No direct conclusions can be drawn about the efficacy of inviting women younger than 40 or older than 69 years of age to screening with mammography.

The reduction in mortality from breast cancer in women 50–69 years of age who accept an invitation to screening has been estimated to be about 35%, by adjustment of the results of the trials for the effect of non-acceptance of the invitation by some women.

Both apparent and real deficiencies of the randomized trials that were considered in making this evaluation of the efficacy of invitation to screening were carefully assessed for their impact on its validity. They were judged not to invalidate the trials' findings and therefore the evaluation.

Influence of inter-screening interval on effect of screening by mammography

There is little evidence on which to base recommendations on the frequency with which women should be offered mammographic screening. In most of the randomized trials on which the evidence of efficacy of screening was based, women were invited to be screened at intervals of about 24 months. Modelling has suggested that about a further 5% reduction in mortality is gained for women 50–69 years of age for each reduction in the inter-screening interval of one year, between three years and one year. These estimates are compatible with the results of a randomized trial of the effects of annual compared with three-yearly screening, which predicted breast cancer mortality on the basis of the prognostic characteristics of breast cancers at the time of diagnosis.

Effect of breast screening by clinical breast examination on mortality from breast cancer

There is *inadequate evidence* that breast screening with clinical breast examination, whether alone or in addition to screening mammography, can reduce mortality from breast cancer.

Effect of breast screening by breast self-examination on mortality from breast cancer

There is *inadequate evidence* that breast self-examination can reduce mortality from breast cancer.

Effectiveness in practice of breast cancer screening with mammography

There is some evidence for the effectiveness of programmes of screening with mammography, with or without clinical breast examination, in reducing mortality from breast cancer in targeted populations. Estimates made in some European countries with organized breast screening programmes suggest that reductions of some 20% can be expected in the long term in the target populations of screening. Estimates of the actual reduction achieved so far have ranged between 5% and 20%. The lower early figures are probably due to the length of time taken to achieve full implementation of national programmes, a substantial proportion of the breast cancer deaths in the first 5–10 years after implementation being due to cancers diagnosed before screening began or lower quality screening in the early years of implementation.

Changes in breast cancer mortality due to screening are difficult to distinguish from other trends in breast cancer mortality in many populations. An alternative would be to measure intermediate indicators of the effectiveness of screening programmes, such as participation rate, rate of detection of small cancers, rate of interval cancers and the incidence rate of later-stage cancers, to show whether the programme is adequate to achieve the desired long-term outcomes. These indicators will also be valuable for improving the quality of service.

Adverse effects of breast screening

Between 50% and 90% of women who are referred for assessment after a positive screening mammogram will prove not to have breast cancer. These false-positive mammograms generate anxiety, additional physician visits and diagnostic tests, and some excision biopsies. If a false-positive result is not recognized as such during assessment, some such referrals may also lead to unnecessary treatment for breast cancer.

Some 20% of women in whom breast cancer is diagnosed have ductal carcinoma *in situ*, a cancerous change that has not extended beyond the tissue lining the breast ducts. Treatment of some forms of this lesion will prevent development of an invasive cancer in the affected tissue. In a currently unknown, but possibly high, proportion of women in whom ductal carcinoma *in situ* is diagnosed as a result of breast cancer screening, invasive cancer would not develop in the in-situ cancer within the lifetime of the woman. Some of these women, however, will be treated for breast cancer, with little prospect of long-term benefit from the therapy.

In some women in whom an abnormality is detected by breast cancer screening, an invasive cancer may be diagnosed that would never have progressed to produce symptoms and be diagnosed clinically in their lifetime. This possibility is suggested by the persistence of the increased incidence rates of breast cancer that occurs with the introduction of screening to a population and, initially at least, can be attributed to earlier detection of cancers that would otherwise be incident in a later period. No population into which breast screening has been introduced has yet been reported to show an unequivocal return of incidence rates to the baseline expected from pre-screening trends; but there have been no rigorous analyses.

As irradiation of the breasts with X-rays is known to increase a woman's risk for breast cancer, the exposure of women from mammography should be the lowest compatible with adequate image quality. In women 50–69 years of age, the increase in risk for breast cancer due to this exposure is extremely small and is substantially outweighed by the benefits of mammography. This balance is probably not as favourable, however, for women 40–49 years of age. In women under 40 years of age, the risk for radiation-induced breast cancer is higher, and there is no evidence of benefit for this age group.

Cost–effectiveness of a programme of screening with mammography

A recent summary of analyses of the cost–effectiveness of breast cancer screening programmes in a number of countries, done with similar methods, has shown costs per year of life saved varying from 3000 to 8000 euros for two-yearly screening of women 50–69 years of age. If, in addition, the impact of screening on quality of life is considered and account is taken, on the negative side, of the longer period of life with a diagnosis of breast cancer and of the the consequences of false-positive diagnoses, the costs per quality-adjusted year of life saved may, depending on the assumptions, be up to 23% higher or 3% lower than those stated above.

Implications for public health

Health policy-makers can make decisions about the screening services they offer women, and women themselves can take decisions about whether to seek or accept an offer of breast cancer screening, in the knowledge that quality screening mammography done every two years in women 50–69 years of age should reduce their risk for death from breast cancer by about 35%.

When such a programme is offered and there is a high participation rate, it would be reasonable for a health service to expect a fall in the mortality rate from breast cancer in the target population for screening of some 20% in the long term. This reduction may be less if there is a high level of opportunistic screening before an organized programme is introduced.

The cost–effectiveness of a programme of screening mammography is comparable to that of other cancer screening programmes. As in all screening programmes, there are adverse consequences. For breast cancer screening, these include costs to the quality and, to a very small extent, the quantity of a woman's life due to false-positive diagnoses, and the diagnosis of some in-situ and possibly invasive breast cancers that would not otherwise have been diagnosed. A few rare cases of breast cancer may be caused by mammographic radiation, but this adverse effect is substantially offset by the net reduction in mortality due to screening.

When mammographic screening cannot be offered, for practical or economic reasons, or women cannot afford to accept it, there is no other method of screening that is known to reduce the risk for death from breast cancer. Specifically, it is unlikely on present evidence that a programme to encourage breast self-examination alone would reduce mortality from breast cancer. Women should, however, be encouraged to seek medical advice immediately if they detect any change in a breast that suggests breast cancer.