Breast Screening Subgroup of EUSOMA

E4. Current issues in breast cancer screening

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Abstract: The debate about the overall benefits and harms of breast cancer screening continues. Sceptics continue to question the likely breast cancer mortality reduction and emphasise the potential harms, including over-diagnosis and over-treatment. These issues will be debated following presentations on the current evidence. There is also continuing interest in the benefits and harms of targeting screening to women at increased risk. Current thoughts and evidence on this will be presented.

1. The Benefits and Risks of Screening Mammography – A Debate

Update on the evidence for breast cancer screening in 50–70-year-old women (L. Nyström)

Population-based breast cancer screening programmes (BSPs) using mammography have been implemented in most counties in West Europe in accordance with the European Guidelines using the results of the various randomised controlled trials (RCTs) as the justification. The efficacy of these RCTs has been questioned, and as a result the effectiveness of the BSPs has been re-evaluated. A number of different approaches has been applied. Initially, simple analysis of the trends in breast cancer mortality before and after the introduction of the BSP was used. This approach has significant limitations as the majority of those dying from breast cancer in the early years after the start of the BSP were diagnosed before the introduction of the BSP. Several more sophisticated approaches have since been applied. A crucial issue is being able to link the cancer registry data with the cause-of-death registry on an individual basis to be able to calculate the incidence-based breast cancer mortality, making comparisons over time or between geographical areas with and without BSPs. The results from studies based on incidence-based mortality, case-referent approach and trend analysis using Poisson regression and/or joinpoint analysis will be presented, summarised and discussed.

Evidence for screening women under 50 and over 70 years (H.J. de Koning)

While the majority interpret the results of the screening trials as showing a significant breast cancer mortality benefit for women aged 50–70 years, there is much less agreement about the benefits of screening in older and younger women. The evidence that is available from both trials and trial-based modelling studies suggests that there is a benefit, although at a significantly lower level. In younger women earlier diagnosis appears to have less benefit because of the greater likelihood of aggressive characteristics of the cancer typical in younger women; in older women the opposite is true and the exponential increase in competing causes of death becomes more important. The data will be presented and discussed.

A randomised trial in one million UK women to assess the benefits of adding one extra screening visit (R. Peto)

Continuing with the theme of screening older and younger women and the lack of data from randomised trials in the UK a population-based trial of offering screening to half of all women in the age ranges 47–50 and 70–73 has been started. This is the largest randomised trial in the world. The aims, methodology and means of assessment of the results will be discussed.

The adverse effects of screening (E. Paci)

With medical interventions such as screening there is always a need to balance the benefits and harms. This issue has been taken into consideration particularly in the evaluation of the performance of breast cancer screening, with special attention being given to the risk of false-positive results.

Excess in cancer diagnosis (over-diagnosis) in screened compared to unscreened populations is well known in breast, lung and prostate screening. This over-diagnosis is recognised only at the population level. Estimates of over-diagnosis were possible in the few RCTs that did not offer screening to the control group and is reported to be between 7 and 14%. Estimates of over-diagnosis from

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observational studies vary widely, in the UK programme for example varying from the 4% reported by Duffy to the 52% estimated by Jørgensen and Gøtzsche. Considering only the studies which have taken into consideration adjustment for underlying incidence and lead time, the range of the estimates of observational studies which considered underlying trends and lead time adjustment in Europe are between 0 and 11%.

Recall rate is one the most important performance parameters in breast screening. In the European Guidelines positive and negative predictive value and the level of false positive assessment are the subject of quality evaluation of screening programmes. The cumulative risk of false positives in women undergoing biennial screening has been estimated at 20.8% in Norway and 15.2% in Italy, substantially different from that in the United States where up to 50% of women screened may experience a false-positive recall.

2. Screening Higher-Risk Groups?

Pathological risk factors and screening (A. Salomon)

Much more attention has been given to the increased risks of breast cancer associated with family history than to other factors – such as lifestyle, hormone therapy and breast density – and pathological risk factors. Pathological risks associated with entities such as atypical ductal hyperplasia (ADH) and lobular neoplasia (lobular carcinoma in situ, LCIS, and atypical lobular hyperplasia, ALH) have risks that are equal to and higher than family history, and strategies for screening should always include these. The range of pathological risk factors and the mechanism for this underlying risk will be discussed.

The evidence for mammography screening after breast cancer treatment? Health technology assessment (F. Gilbert)

Following treatment for primary breast cancer disease can recur either following conservation surgery – ipsilateral breast tumour recurrence (IBTR) or in the opposite breast – metachronous contralateral breast cancer (MCBC). Recurrence rates are between 0.4 and 0.8% each year and are higher than the rate of breast cancer in the normal unaffected population. Young age (<50), large tumours, node-positive disease, high-grade disease, incomplete tumour excision, ductal carcinoma in situ (DCIS), and no radiotherapy treatment are all risk factors for recurrence. Previous studies have suggested that ipsilateral recurrence has an adverse effect on survival. Early detection of metachronous disease has been shown to be beneficial. The large numbers of women who develop and survive breast cancer mean that the cost and resources required to follow up these women are considerable. The results of two systematic reviews show that magnetic resonance imaging (MRI) has the best diagnostic accuracy and is the most effective method of detecting further disease. However, there was a paucity of evidence in this area. The cost effectiveness of different mammography regimens after the treatment of primary breast cancer was estimated, and this shows that the cost/benefit equilibrium is seen at between yearly and 18-monthly surveillance. Modelling of data from two cancer registries was undertaken to ascertain the survival benefit. This showed that no recurrence or recurrence detected at less than 1 cm had a significantly improved survival compared to tumours more than 2 cm in size. Alternative methods of surveillance will be considered, such as MRI, comparing the diagnostic accuracy of the various imaging techniques.

The effective use of MRI in screening (R. Mann)

MRI screening studies in patients with increased risk (>15% LTR) reported sensitivities ranging from 71 to 93%. This is twice as high as the sensitivity of mammography. Although breast MRI also detects more benign disease, the positive predictive value of MRI-induced biopsies is 0.35–0.45 and is not different from mammographic screening.

However, there are some substantial drawbacks to screening with breast MRI. We do not know if all of the extra cancers detected are clinically relevant, although retrospective comparisons suggest that they might be, and recent screening trials indicate better disease-free survival and overall survival for MRI-screen-detected breast cancer. There is also uncertainty about the cost effectiveness of MRI as a breast screening tool. Current recommendations are to reserve MRI screening for women with substantially increased risk, but in the future we might select women for MRI screening when the performance of mammographic screening is expected to be poor (e.g. in women with very dense breasts).

Evidence-based higher-risk screening (L. Holmberg)

The Department of Health in the UK has decided to introduce breast screening for younger women (<50 years), and to define the basis for such screening commissioned a specialist group to review and define the various risks and recommend screening strategies. This group has considered all the potential risks and has recommended that women at very high risk (RR > 8) should be offered screening with MRI from the age of 30, while those at moderate risk should be offered mammographic screening from the age of 40. The data analyses and rationale for these recommendations will be discussed.

Conflict of interest statement

None declared.

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