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EDITORIALS

Benefits and harms of mammography screening

Using evidence from randomised and observational studies is necessary and appropriate

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Discussions over mammography screening began with the view that it does not reduce deaths from breast cancer. More recently this has changed to the view that it probably does reduce mortality but the size of the effect is unclear.[1] This has led to the proposed review of breast cancer screening in the United Kingdom.[2] According to Mike Richards, England's cancer tsar, anyone who has published in this field will be excluded from the panel. However, surely it would be better to include some of the proponents and opponents, who are already aware of key features specific to cancer screening through many years of experience?

Most publications on mammography screening have examined the effects on mortality separately from harms, such as overtreatment and increased anxiety after a false positive result. One of the linked articles attempts to combine benefits and harms (doi:10.1136/bmj.d7627),[3] and the other (doi:10.1136/bmj.d7017) provides an estimate of overdiagnosis (the proportion of women diagnosed with breast cancer through screening who would not have been detected in the absence of screening, and they therefore receive treatment unnecessarily).[4]

It is difficult to examine benefits and harms together but QALYs (quality adjusted life years) provide one approach. Articles reporting QALYs often do so in relation to financial costs. For example, a study from Spain indicated that screening was associated with an incremental cost effectiveness ratio of €4469 (£3741; $5862) per QALY, ignoring overdiagnosis.[5] An analysis based on data from the United States, which incorporated false positives and overdiagnosis, indicated that the cost per QALY gained varies considerably with age, but could be less than $50 000 in women aged 50-79 with high breast density, or less than $100 000 for lower risk women.[6] Others have shown that benefits in relation to harms vary with age and frequency of screening.[7 8] Cancer screening of the whole population will invariably be expensive.

The analysis by Raftery and Chorozoglou focused on factors that directly affect screened women, without incorporating financial costs.[3] The results suggest that benefits from screening tend to appear only several years after starting screening. Three of their five models generated net harms up to four to eight years later, indicated by negative QALYs, and even a few years after this time it could be argued that the gains are not worth while. However, these effects are smaller than the net benefits after 10-12 years and consistent with cancer screening being a long term process.

Like all sensitivity analyses, these results are greatly influenced by the reliability of the parameters used in the modelling (especially at the start of screening), as indicated by the different QALY curves in fig 2 of the article.[3] The reductions in breast cancer mortality were taken from two systematic reviews, but the estimates in one[1] were lower than in another,[9] because some randomised trials were excluded and the observation that mammography is less effective in younger women was not allowed for. Neither review discussed the greater reduction in mortality in screened women (compliers), as opposed to intention to screen analyses. Loss of quality of life in women with false positive results also matters, although the evidence on this is inconsistent.[10] The main potential harm is overdiagnosis (indicated by the relative risk of 1.35 for having surgery in Raftery and Chorozoglou's analysis). Studies report varying estimates of this, but most tend to be less than 10%,[9] suggesting that this may not be a significant factor after all. This is the main conclusion of the second linked study, in which a French population based registry was used to estimate that less than 15% of incident cancers were overdiagnosed.[4] Any benefit-harms analysis must be based on reliable estimates of overdiagnosis, and this can be done only by using carefully considered statistical methods.

No two mammography trials have been identical, so it is unlikely that they would all have reported a reduction in breast cancer mortality if there really were no effect. What is needed now is a comprehensive examination of other types of studies, using appropriate statistical methods, to compare with results from randomised trials, and to repeat the QALY analyses reported in the linked analysis using revised estimates of benefits and harms. For example, case-control studies, based on women who have or have not died from breast cancer but all had access to the same screening programme, generally show reductions in mortality in line with the randomised trials.[11] Similarly, national screening programmes also show reductions in mortality rates over time, which seem to coincide with the implementation and continuation of screening.[12 13] The evidence on cervical screening and mortality comes from observational studies only (no

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randomised trial has looked at screening versus no screening), so using similar evidence in breast screening alongside data from randomised trials should also be appropriate.

New trials of screening versus no screening are unlikely to be conducted, not even in countries where organised programmes are not yet in place. Although health professionals may never completely agree on whether such public health policy is worth while, a comprehensive review of the accumulated data on benefits and harms from a range of study designs over many years should provide a more robust evidence base than focusing on randomised studies only.

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