

# Breast cancer screening causes more harm than good

## NO

### Screening substantially reduces mortality from breast cancer

Recent debate on mammography has focused on the balance of benefits and harms to women who participate in screening.<sup>1,2</sup> The debate has been fuelled by publications of observational analyses, the most prominent recent example being that of Bleyer and Welch,<sup>3</sup> suggesting that screening has only a small effect on mortality or incidence of advanced disease, but confers a high risk of over-diagnosis. These publications have in turn been criticised for misclassification of screening exposure, failure to account for underlying incidence trends, and failure to distinguish between cancers diagnosed early and cancers over-diagnosed.<sup>4,5</sup>

We shall return to the observational studies, but first consider the more important randomised controlled trials evidence. The combined trials show a 20% reduction in breast cancer mortality with the offer of screening.<sup>1</sup> All major reviews find an empirical result close to this, although some prefer a conjectured 15% reduction to the 20% observed.<sup>2,5</sup> Despite this relative uniformity, the absolute benefits concluded by various reviews differ substantially, with the number of women needed to screen (or invite to screening) to prevent one death ranging from 111 to 2000.<sup>5</sup>

Surprisingly, this disparity is largely artificial, arising from the different populations and timescales used in the various estimates. Duffy et al.<sup>5</sup> expressed the results of each of the UK Review, the Nordic Cochrane Review, the US Preventive Services Task Force and Euroscreen, relative to the same population and timescale as the UK Independent review: the effect of 20

years' screening at ages 50–69 years on UK breast cancer mortality at ages 55–79 years. This yielded numbers needed to screen to prevent one breast cancer death ranging from 64 in Euroscreen to 257 in the Nordic Cochrane review. Thus, all major reviews imply a benefit of similar magnitude, and one that is comparable to other prevention or screening programmes.

In terms of mortality, it has been speculated that advances in systemic therapies, occurring after the screening trials, may have rendered earlier detection redundant. This question is reasonable, but it could just as reasonably be put the other way round: since diagnosis precedes treatment, has screening rendered some advances in therapy redundant in screened populations? In fact, neither is the case. Duffy et al.<sup>5</sup> present survival by node status of 9040 breast cancer cases diagnosed in the east of England in the years 1998–2003, unequivocally in the systemic therapy epoch. In these data, node positive cases still have substantially and significantly poorer survival than node negative cases. This result holds for screen-detected and symptomatic cancers separately, so it is not a product of lead time, length bias or over-diagnosis. Thus, there is still a clear role for screening in this epoch of effective systemic therapy. Colleagues in oncology and radiology should each acknowledge the efforts of the other in achieving the excellent survival that prevails in breast cancer today.

In response to recent observational studies giving rise to assertions that screening has failed to reduce mortality or incidence of advanced disease, two points arise: firstly, when the totality of observational studies are reviewed, these negative findings constitute a small minority of the evidence.<sup>6</sup> Secondly, whatever observational studies might find to qualify the randomised controlled trial evidence, they cannot replace it. And the trial evidence shows conclusively that breast

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cancer mortality is substantially and significantly reduced by mammographic screening.

### Harms of screening are limited

There are a number of potential harms, but the one that most occupies public debate is over-diagnosis. Over-diagnosis is defined as the diagnosis as a result of screening of cancer that would not have been diagnosed in the lifetime of the woman had screening not taken place.<sup>1-5</sup> For any individual tumour, this is not ascertainable, since we cannot know what would have happened to a treated cancer if it had been left untreated.

Researchers therefore estimate rates of over-diagnosis by comparison of incidence of breast cancer in screened populations, with that expected in the absence of screening, using either trial or observational data,<sup>1,3,4</sup> both of which are limited. For such comparisons to be valid, they must take into account contemporaneous changes in incidence independent of screening, and have sufficient follow-up or appropriate analysis to remove the effect of lead time (to exclude from over-diagnosis estimates that excess incidence which is due to bringing forward in time the diagnosis of cancers that would have been diagnosed later in any case).

Estimates of over-diagnosis vary widely, some suggesting that as many as 50% of cancers detected in the context of a screening programme are over-diagnosed. This is implausible, particularly when one considers the typical clinical outcome of untreated breast cancer. Puliti et al.<sup>4</sup> found that the very high estimates of over-diagnosis result from analyses that fail to take adequate account of independent effects on incidence, or of lead time.<sup>4</sup> Studies that control for these phenomena yield estimates of 10% or less, which are substantially outweighed by the mortality benefit.<sup>4,5</sup>

Concern has been expressed about over-diagnosis of ductal carcinoma in situ (DCIS). While the benefits and risks of diagnosis and treatment of DCIS remain to be fully quantified, there is evidence from screening trials that detection of DCIS forestalls future diagnoses of invasive disease,<sup>7</sup> and from treatment trials that a substantial

proportion of DCIS cases recur or progress to invasive disease despite complete local excision.<sup>8</sup> The current policy of detection and treatment of DCIS is therefore prudent.

Other harms of screening, including discomfort, and the physical and psychological effects of false positives are generally well tolerated and fairly short-lived; while these, together with radiation exposure, should not be ignored, they can be minimised with proper training of staff.

### Conclusion

Breast cancer screening prevents large numbers of breast cancer deaths. While there are harms associated with screening, these have been exaggerated by inappropriate analyses, and are outweighed by the benefit in terms of lives saved. The independent UK review concluded that one breast cancer death is prevented for every 180 women screened regularly.<sup>1</sup>

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