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For debate

Should healthy populations be screened for breast cancer? A consultant surgeon's perspective

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The intention of screening is to detect cancer early enough so that it reduces mortality. It was only when this intention was proven in randomised trials, and the process considered worthwhile that national screening programmes were introduced. Therefore, the information traditionally provided by well-intentioned government screening programmes was naturally biased in favour of screening. This would have been considered necessary for ensuring that as many women as possible got the benefit of having their cancer detected early so that they had the highest chance of cure.

The results of new analysis of the old randomised trials, as well as widespread recognition of the overdiagnosis that results from screening, suggest that the balance between benefit and harm from screening may not be so clear cut. An extreme example of overdiagnosis by screening is for neuroblastoma in infancy; when this was initiated, a high incidence of such tumours were found – a large proportion of these never progressed and many regressed, which led to a moratorium on screening for neuroblastoma. However, it is not as extreme for breast cancer. Arguably, there can be four possible situations: (1) Screening is clearly beneficial – in that case there is a benevolent reason to promote it. (2) Screening is clearly harmful – in that case there is a benevolent reason to stop the screening programme. (3) There is uncertainty about the benefit or harm – a position of equipoise – in this case, one should only offer screening within a randomised trial. (4) The benefit and harm are not clearly quantifiable and are subject to individual value judgements, which is probably the reality. In this case, one needs to express the benefits and harms in the most comprehensible manner so that an individual woman can make those value judgements and decide about going for screening, whether fully, partly or not at all.

However, there are a few other issues that need to be considered before a policy to stop the screening programme is considered, because this could have significant unintended consequences.

With modern treatments, would the benefit of screening be amplified or diminished? Better surgery, radiotherapy and adjuvant systemic therapy have significantly improved outcomes and there is an argument that the window of opportunity offered by mammographic screening is not relevant, because treatments have become so much better. However, many current treatments are only refinements of older treatments, and this might be a circular argument.

Even though the proportional benefit of most treatments is constant whatever the disease burden, there could be a threshold below which the treatments may be more effective. Also, the good results of these treatments are being seen at a time when screening has become more widespread in recent years, and that begs the question whether the two are synergistic.

Excellent modelling studies suggest that the benefit of treatment may be amplified by the presence of screening (Figure 1).[1] Will all this benefit be reversed if we stop screening and only treat symptomatic cases? If there is any likelihood of this happening, then measures to stop screening could have dangerous unintended consequences. Therefore, any such changes in policy must be first tested in a randomised trial.

Does screening reduce the incidence of symptomatic cancer? It does not appear to reduce the absolute number of symptomatic cases (Figure 2 elegantly demonstrates overdiagnosis of invasive breast cancers). There will of course be some cancers that are picked up early enough so that treatment is life-saving.

The price of overdiagnosis might, today, be at least partially compensated for by less-aggressive treatments that have been proven in randomised trials. Most women who are diagnosed by screening have a lumpectomy rather than mastectomy; they might be treated with single dose-targeted intraoperative radio-

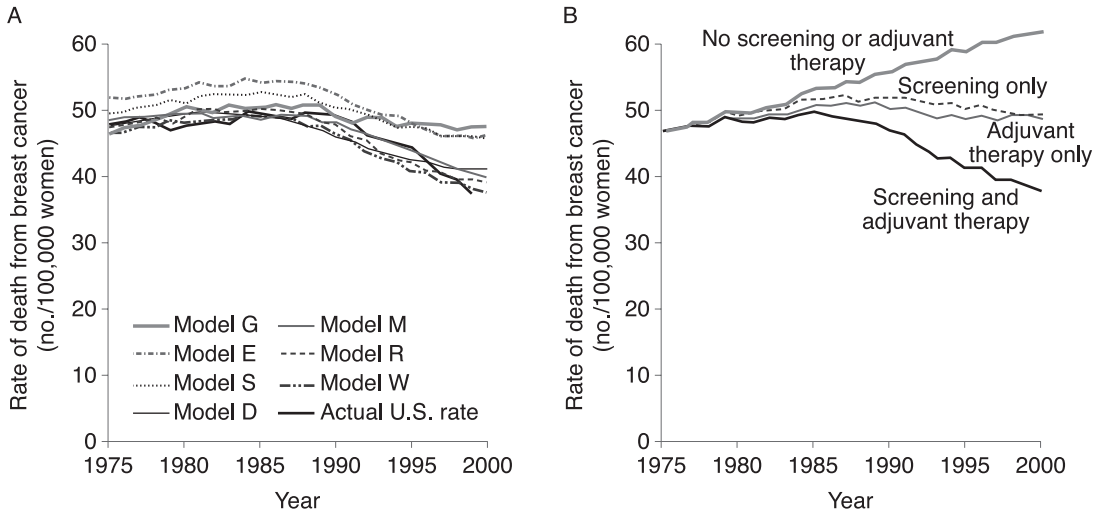

Figure 1 Effect of breast screening and adjuvant therapy on mortality from breast cancer. The estimated combined effect of screening and adjuvant therapy (black line in panel B) appears similar to the actual fall in US breast cancer mortality (black line in panel A)

Estimated and Actual Rates of Death from Breast Cancer among Women 30 to 79 Years of Age from 1975 to 2000 (Panel A); Hypothetical Assumptions about the Use of Screening Mammography and Adjuvant Treatment (Panel B). Panel A, which compares the model-based results with the actual rates in the United States from 1975 to 2000, shows the variability across the model estimates. Some of the models were calibrated according to the observed rate of death from breast cancer in the United States, and some were not. Panel B shows the results from model W (the University of Wisconsin-Madison) of estimated mortality trends for the four scenarios considered: no screening and no adjuvant treatment; base-case screening, but no adjuvant treatment; no screening, but base-case adjuvant treatment; base-case screening and adjuvant treatment. Rates in both panels are age-adjusted to the 2000 US standard.

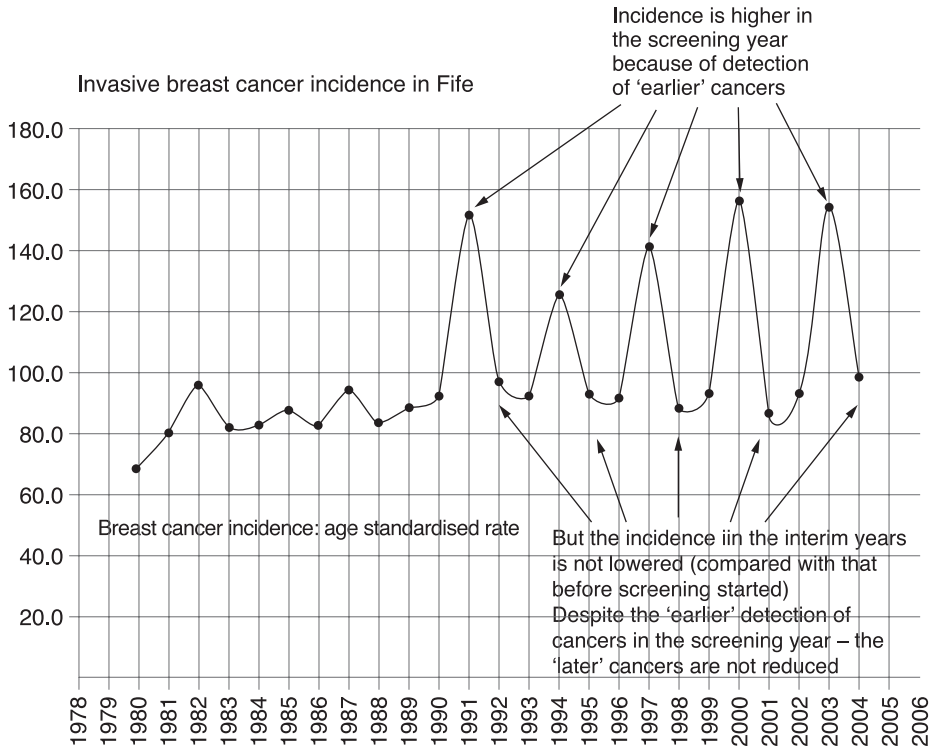

Figure 2 Effect of screening mammography on the incidence of invasive cancer

therapy (TARGIT),[2–4] with which there are fewer non-breast cancer deaths compared with conventional radiotherapy, as suggested by the Marmot committee;[2] they might also have a sentinel node biopsy rather than an axillary clearance. So at least the majority of overdiagnosed cases could have their full surgical and radiotherapy treatment completed within a day-case procedure, reducing the impact of overdiagnosis and the harms that may have occurred by over-treatment. Also, fewer women among these may have systemic chemotherapy. It is conceivable that in those that do require chemotherapy, there will be a few that fall into the overdiagnosed category.

However, there is another point that is probably the most important. The existence of a breast screening programme brings with it the infrastructure and quality assurance mechanisms that improve the treatment of all breast cancers and therefore benefits all women – those with symptomatic and screen-detected cancers. This substantial effect cannot be underestimated. Can that be sustained without actually screening? I doubt it. How do we continue giving high-quality treatment to breast cancer patients without having an infrastructure that supports it? Thus, one of the arguments of stopping screening – reducing opportunity costs – may not work at all, as the resources might be diverted away from breast cancer, and timely treatment of symptomatic breast cancer that is an exemplar for other cancers, might really suffer. Such actions may be more likely in today's times of austerity. One should remember that, unlike manufacturing, provision of health always incurs a net financial loss to the provider: the profit is health, which may or may not translate into wealth, or if it does, it only adds to the world pot of human endeavours – not specifically to the hospital in which they were treated.

Personally, I have a strong prejudice for giving all information about screening to women in a comprehensible manner and have been an active promoter of better information leaflets. However, I should remember that this is a prejudice. If we are adherers to evidence, then we should recognise that there is no evidence to suggest that changing information leaflets such that they are equally balanced between 'accept' or 'refuse' invitation to screening rather than leaning slightly towards screening, is beneficial to a woman's well-being, or the well-being of the population.

At this point, we also need to consider which outcome we are interested in and what is more important – the sum total of happiness/well-being of womankind, or personal length and quality of life of each/most women, or ensuring that the personal autonomy of every woman is preserved? But that is a philosophical question that would need to be discussed in another paper. In any case, if the information is completely balanced then the only ethical action is to do a randomised trial, as one cannot either offer or not-offer screening with such an information leaflet. However, if one has accepted the principle of offering screening, then by definition, the information leaflet would be worded so as to justify screening even though it is not 'balanced'. One has to be internally consistent and, of course there should be no hiding of facts.

The only way we can legitimately challenge 'a screening programme which includes coercive information leaflets to promote screening' is to perform a randomised trial, involving cluster randomisation of regions within a larger community that currently does not currently offer a population screening programme, and assess whether the introduction of a screening programme reduces mortality in a trial design that can differentiate between the benefit from early detection and benefit from infrastructure for delivering high quality care and whether there is any cost-saving, or anxiety reduction.

Such a trial would include modern and less aggressive and equally effective local treatments (such as intraoperative radiotherapy or sentinel node biopsy to reduce the impact of treatment of cancer) as well as more effective and optimised (e.g. targeted) systemic therapies. Then we will have modern evidence to back either of the prejudices. We would also gain important insights into the natural history of breast cancer if the trial design includes imaging studies that are kept unread in those groups randomised to no screening, if that is ethically allowable.

If one has to practice evidence-based policy, then such a trial is essential before making any change in a policy about promoting screening if we are to avoid the unintended consequences of stopping screening.

The insight that screening is not a panacea is now public knowledge. New treatments have become available that are less toxic and/or more effective. Now is the fertile time to do such a randomised trial (rather than either introducing screening or making a decision to not introduce screening) in a community that does not currently offer screening – and this presents an ethical, moral and financial imperative.

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CONFLICTS OF INTEREST

None.

PEER REVIEW

Commissioned; not externally peer reviewed.

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