

ORIGINAL PAPER

Number needed to screen: lives saved over 20 years of follow-up in mammographic screening

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Objective: To estimate the number needed to screen with mammography to save one life, based on a stated amount of screening activity and long-term follow-up for breast cancer death.

Setting: A randomised controlled trial of mammographic screening for breast cancer, with 77,080 women invited to screening and 55,985 not invited. The invited group was offered screening for seven years. Follow-up continued for a total of just over 20 years.

Methods: Number needed to screen for seven years to save one life over 20 years was calculated by dividing the number screened (not the number invited) by the total number of lives saved. Similarly, we calculated the number of mammographic examinations required to save one life.

Results: We estimate that the number of women needed to screen for seven years to save one life over 20 years is 465 (95% CI 324-819). The number of mammographic examinations needed to save one life was 1499 (95% CI 1046-2642).

Conclusions: The number needed to screen to save one life is smaller than has been reported in the past. Mammographic screening is effective in absolute terms as well as relative. Long-term follow-up allowed us to estimate the absolute benefit with greater accuracy.

The number needed to treat is a measure of effectiveness sometimes quoted in relation to randomised trial results.¹ If, for example, the trial endpoint is death from the disease in question, absolute death rates in the study and control groups can be used to estimate how many patients would have to be administered the study treatment to save one life more than the control treatment.

In discussion of mammographic screening, estimates of the number needed to screen to save one life from breast cancer have been quoted.²⁻⁴ The basis for the estimates is not always clear. In their summary for the US Preventive Services Task force, Humphrey *et al.* used meta-analysis data from an average of 14 years of follow-up in the breast cancer screening trials to estimate the number needed to invite to screening (not to screen) to save one life.² They arrived at an estimate of 1224 women. Interpretation of their results should be qualified by the following considerations:

1. Number needed to invite is a nebulous entity, dependent as it is on attendance rates among those invited, which vary considerably across environments. In the trials reviewed, attendance rates varied from 50%-90%.
2. The average follow-up of 14 years is not the duration of delivery of screening, but the follow-up time of tumours diagnosed. For some trials, the screening phase was only five years, for others more than a decade.
3. One of the trials was excluded from the analysis

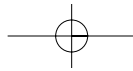
Clearly, the number needed to screen will be more generalisable and will be smaller than the number needed to invite. Also, in view of point two above, the quantity of screening intervention required to produce the estimated benefit is not clear. The estimated numbers needed to invite have subsequently been interpreted as numbers needed to screen and as requiring 14 years of screening to do so.⁴ The number needed to invite is an aid to the political decision as to whether or not to fund a screening programme. The

number needed to screen is of more use to the individual woman in her decision whether or not to be screened. The latter, together with the anticipated attendance rate, is required to calculate the former.

It would be useful to have a measure of the number needed to screen, rather than to invite, over a specified period of time in order to prevent one death in long-term follow-up, including a substantial period after the screening. The last condition relates to the fact that the good survival now observed for breast cancer means that early detection prevents deaths not immediately but up to and probably beyond a decade in the future. It is the purpose of this paper to provide such an estimate. We use data from the Swedish Two-County Trial, a randomised trial of mammography screening, which had a screening phase of approximately seven years, and for which there is follow-up data to just over 20 years after the inception of the trial.

METHODS

The Swedish Two-County Study is a randomized controlled trial of invitation to mammographic screening. The trial took place in the Kopparberg (W), now called Dalarna, and Östergötland (E) counties in Sweden. The trial randomized 77,080 women aged 40-74 years to invitation to screening (active study population, ASP) and 55,985 women to no invitation to screening (passive study population, PSP). The trial started in 1977 in W-county and in 1978 in E-county. Women aged 40-49 years were invited on average every 24 months and women aged 50-74 years on average every 33 months. Approximately seven years after randomisation, a significant 30% reduction in breast cancer mortality was observed in the ASP group,⁵ whereupon the PSP was invited to screening and the screening phase of the trial ended. We have follow-up data for death from breast cancer to the end of 1998.



We estimated the cumulative rate of breast cancer deaths in the ASP and PSP respectively according to the following calculations:

$$r_{ASP} = d_{ASP} / N_{ASP}$$

and

$$r_{PSP} = d_{PSP} / N_{PSP}$$

The phrases d_{ASP} and d_{PSP} are the numbers of deaths from breast cancer, and N_{ASP} and N_{PSP} are the numbers of subjects randomised in the two trial arms. The total number of deaths prevented in the ASP was estimated as in Duffy *et al.*⁶ as

$$D_p = E(d_{ASP}) - d_{ASP} = N_{ASP} r_{PSP} - d_{ASP}$$

D_p was then divided by the number screened (not the number invited) to give the deaths prevented per subject screened. The reciprocal of this is the estimated number needed to screen for seven years to save one life from breast cancer within this seven-year period plus the following 13 years maximum (average total follow-up was just over 17 years). The above procedure means that we estimated the benefit (lives saved) from the intention to treat analysis, but we estimated the screening, rather than invitation, activity required to achieve the benefit.

Confidence intervals (CI) were estimated treating the numbers of deaths as Poisson random variables. Thereafter, we estimated the variance and 95% CI of D_p , the number of deaths prevented in the linear scale, to allow for the possibility of a negative number of deaths prevented. CIs of transformations of D_p , such as the number needed to screen, were estimated by transforming the endpoints of the 95% CI on D_p .

RESULTS

The screening activity evaluated here lasted seven years, but total follow-up was for just over 20 years. Table 1 shows the 20-year cumulative deaths from breast cancer in the ASP and PSP with the relative risk and absolute number of deaths prevented. In the ASP, 141 deaths were prevented over the 20-year period. Average attendance for screening in the ASP was 85%, giving 65,518 as the number regularly screened. This in turn means that 2.15 lives were saved per thousand screened, and the number needed to screen to save one life was estimated as 465 (95% CI. 324–819).

As noted above, the screening activity that achieved this reduction in breast cancer deaths took place over seven years. In women aged 40–49 years, most subjects had four rounds of screening but 5% had five rounds at the closure of the screening phase of the trial. In women aged 50–74 years, all subjects had three rounds of screening, 26% had four rounds and 0.5% had five rounds. In total, we estimate that 211,303 screening mammograms were administered, giving 6.7 lives saved per 10,000 mammograms (95% CI 3.7–9.6). The estimated number of mammographic examinations

Table 1 Breast cancer deaths in the ASP and PSP, with measures of relative and absolute benefit in ASP

Quantity	ASP	PSP
Number of subjects	77,080	55,985
Deaths	319	334
Cumulative deaths/1000 randomised	4.14	5.97
RR (95% CI)	0.69 (0.59–0.81)	1.00 (-)
Deaths prevented in ASP (95% CI)	141 (80–202)	-
Number screened in ASP	65,518	-
Deaths prevented/1,000 screened (95% CI)	2.15 (1.22–3.09)	-
Number needed to screen to save one life	465 (324–819)	-

needed to save one life was therefore 1499 (95% CI 1046–2642). That is, to save one life, 465 women needed just over three rounds of screening on average.

DISCUSSION

We estimated that the number needed to screen to save one life from breast cancer was 465. This figure is based on empirical results from a randomised trial of mammographic screening in 133,065 subjects. It pertains to the age group 40–74 years, with screening every 24–33 months for around seven years, and followed up for just over 13 years. It is consistent with the figure of 553 needed to invite in this trial, as calculated by Humphrey *et al.*²

We found a rather smaller number needed to screen to save one life than has been reported by others. The reasons for this are:

1. The Swedish Two-county Study observed a relatively large reduction in mortality (more than 30%) in association with invitation to screening
2. We explicitly estimated the number needed to screen, not the number needed to invite to screening
3. We had data from long-term follow-up reflecting the fact that deaths avoided by early detection include some that would have occurred a considerable time later than the screening.

As regards the first point, we note that the Swedish Two-County Study results are concordant with the broad range of results from all the screening trials.⁷ Even if we substituted the mortality reduction with the lesser reduction of 24% from all the trials combined,⁷ we would arrive at a number needed to screen of 649, which is still considerably smaller than others have quoted.^{2–4} Furthermore, recent evidence from service screening programmes suggests that mortality reductions of at least this magnitude and probably more are being achieved in women attending for screening,⁸ since two-view mammography with a shorter interscreening interval is now used in Sweden, as compared with the single-view technique used every 2–2.75 years in the Swedish Two-County Trial. One should also bear in mind the fact that our estimates pertain to only seven years of screening activity, whereas most organised service screening programmes offer screening for between 15 and 30 years of life, and will hence have a larger absolute benefit (albeit at a greater cost in terms of numbers of mammograms).

The second and third points emphasise the importance of taking care not to confuse invitation with screening, and of inclusion of long-term follow-up in estimation of absolute benefit of screening. This point is particularly important for health economic analyses, which are usually based on absolute benefits. The public health decision as to whether or not to provide screening is arguably more dependent on the number needed to invite. This will vary among societies. However, with an estimate of number needed to screen (N), which is in principle generalisable, and the expected proportion attending (P) the number needed to invite (M) is estimated as

$$M = N / P$$

That is, the number needed to invite is the number needed to screen divided by the expected attendance proportion. Assuming that the logarithm of the relative risk of breast cancer death is a function of the number of years of screening provision (details available from SWD), and estimating the parameters of this from the data in Table 1, the numbers needed to invite for a range of durations of screening and attendance rates are shown in Table 2.

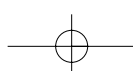


Table 2 Estimated numbers needed to invite to save one life, by attendance rate and years of screening

Years of screening	Attendance rate	Number needed to invite
10 (e.g. 50–59 years)	100*	350*
	80	438
	60	583
20 (e.g. 50–69 years)	100*	221*
	80	276
	60	368
30 (e.g. 40–69)	100*	181*
	80	226
	60	302

* 100% attendance corresponds to number needed to screen

As regards the individual decision whether or not to be screened, the number needed to screen is the important quantity. Previous estimates of approximately 1000 suggest to the individual that if she is screened for 10 years, there is a one in 1000 chance that it will prevent her premature death from breast cancer. Our results show that the correct estimate is closer to one in 350. Whether this will make a substantial difference to individual choice in practice is not clear, but it is evident that the previous figure was misleading.

Despite the fact that our estimate of the number needed to screen is lower than that reported by others, it may seem large in comparison with numbers needed to treat in trials of therapy as opposed to primary or secondary prevention. This points up a paradox in attitudes to prevention. There is a general tendency to pay verbal homage to prevention. The proposed application of preventive measures, however, frequently raises concerns, notably about applying an intervention to large populations in order to benefit the small minority destined to develop or die of the disease. If we consider other, well-accepted preventive interventions, the figure of 465 needed to screen appears modest. For example, how many people need to be exposed to health education campaigns against smoking to save one life from lung cancer? How many infants need to be vaccinated to prevent one death from measles? How many people need to be compelled by law to wear seat belts to save one life from road traffic accidents?

A point made in the past by those who express concern about the absolute benefit of mammography is that the resources might be better spent on treatment.^{9,10} There are two problems with this position. Firstly, if breast cancer patients are not being treated optimally, this is a matter for oncological practice and has nothing to do with screening. There is no evidence that the advent of screening has detracted from therapy, and indeed in the UK the introduction of screening was contemporaneous with many improvements in therapy.¹¹ Moreover, screening in the UK has been shown to be associated with more complete pathology.¹² Screening is therefore likely to be contributing to better staging and more informed treatment decisions.

The second problem with this thinking is that in economic terms the smaller numbers needed to treat when comparing therapy with prevention do not automatically confer a better cost-benefit ratio. Our figure of 1499 mammograms per life saved, taking into account the average 4% leading to assessment, suggests a total cost of US \$109,427 per life saved, on the basis of around \$65 per mammogram and \$200 per assessment (in year 2000 costs).¹³ This corresponds to around \$11,000 per year of life saved. These are over-estimates of the costs, as some of these costs, with others, will be incurred in an unscreened group. Taking poly-chemotherapy treatment for breast cancer as an example, combining the results of the Early Breast Cancer Trialists'

Collaborative Group¹⁴ with the treatment costs¹⁵ of a combination chemotherapy regime including an anthracycline, we arrive at almost exactly the same figures.

It should be mentioned that with the availability of both early detection and adjuvant therapies, the marginal benefit of both in terms of years of life saved will be smaller than the estimates from the randomised trials from the pre-mammography, pre-adjuvant therapy epoch, since each confers an increased length of life, leaving fewer life-years for the other to save.

The above is not an argument against multi-agent chemotherapy, it merely serves to illustrate that the higher number needed to treat in primary or secondary prevention is not necessarily indicative of lesser efficiency. Others have advised caution in interpretation of absolute benefit measures such as number needed to treat.^{16–18}

Ideally it would be of value to have age-specific estimates of number needed to screen. Although it is something of an artificial division, there is particular interest in comparing the benefits of screening women under 50 years with those of screening women older than 50 years. We were unable to do so here, partly because our screening regime was based on age at randomisation rather than at each screen, but principally because the screening regime for women aged 40–49 years at randomisation in the Swedish Two-County Trial was biennial single-view, single-reader mammography. Although this was understandable in the late 1970s and early 1980s when less was known about age-specific effects in mammography screening, it is not optimal to say the least. In the present day, no one would consider such a regime for women under 50 years. Inclusion of women aged 40–49 years probably renders our results slightly conservative. When the UK trial of annual screening in women aged less than 50 years throughout the period of the trial reports, estimation of the absolute benefit in this age group will be possible.

In conclusion, therefore, we estimate that it is necessary to screen 465 women an average of three times over seven years to save one life from breast cancer. In routine population screening – for example the UK programme, which offers screening for 15 years and is soon to expand to 20 years – a greater absolute benefit is to be expected. Long-term observation will provide an estimate of the full benefit.

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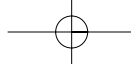
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