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**An initial assessment of the merits of extending  
routine breast cancer screening to women aged 47-49  
years to assist the appraisal of options for extending  
the NHSBSP with appendix considering women  
aged 71 - 73**

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## ***Executive summary***

- We have carried out a model-based preliminary assessment of the cost-effectiveness of adding an extra screening round to the NHSBSP, targeted at the age cohort 47-49. This initial, rapid-response analysis is not intended to produce definitive conclusions, but it does provide useful insights about the likely cost-effectiveness of the proposed intervention, and the relative importance of the various factors influencing the results.
- Our base case model assumes that the psychological impact of screening (particularly from false positive results) is minimal. We find that the mean estimate of the cost-effectiveness of the proposed intervention is c£26,900 per QALY. The probability of cost-effectiveness at a willingness-to-pay threshold of £20,000 per QALY is 19%, rising to 55% at a threshold of £30,000 per QALY.
- Allowing even low levels of anxiety to arise from false positive results has a dramatic impact on the results. Beyond 0.028 QALYs per false positive result, the expected health impact of screening on the relative cohort is negative. Setting the psychological harm from a false positive result at 0.02 per QALY changes the likelihood of cost-effectiveness drastically (1.1% at £20,000 per QALY, 7.5% at £30,000 per QALY).
- Allowing false positive results to influence compliance with subsequent screening rounds has a less marked effect. If 30% of the individuals who receive false positive results change their decision to comply with the main screening programme as a result, this will increase the cost-effectiveness ratio to c£29,000 per QALY, and reduce the likelihood of cost-effectiveness at a willingness-to-pay threshold of £20,000 per QALY to 13% (39% at a threshold of £30,000 per QALY).

- If it is assumed that a negative result from screening is of psychological benefit, and this benefit is included in the analysis, the cost-effectiveness of the intervention improves considerably. Valuing this reassurance at 0.002 QALYs per woman screened improves the point estimate of cost-effectiveness in the base case to c£13,000 per QALY. Even with anxiety from false positive findings set at 0.02 QALYs, the resulting point estimate is c£20,000 per QALY.
- Significant improvements in test technology, such as the adoption of digital techniques, are unlikely to be cost-effective unless the associated increase in cost is modest. The benefit of a relative improvement in test sensitivity of 40% would be offset by an increase in test cost from £42 to £61.
- A 'rough and ready' adaptation of our model to assess an additional screening round targeted at women aged 71-73 estimates the cost-effectiveness of this measure to be c£11,000 per QALY with a 98% probability of cost-effectiveness at a willingness-to-pay of £20,000 per QALY. Even assuming that disutility from false positives is 0.1 QALYs, the probability of cost-effectiveness at that threshold is 10% (32% at £30,000 per QALY).

# 1 Introduction

The breast cancer screening programme operated in the United Kingdom by the National Health Service (NHS) was introduced in 1988 in response to recommendations made by a working group chaired by Professor Sir Patrick Forrest. The programme now has an annual budget of £75 million and screens an estimated 1.5 million women per year in nearly 100 breast cancer screening units established across the United Kingdom. It has been estimated that 119,000 cancers have been detected in women since the introduction of screening and 1400 lives saved per year in England alone.

The initial working group investigated the age related incidence of breast cancer in women in the United Kingdom and concluded that the incidence of breast cancer was greatest amongst women aged over 50. Additionally changes in the density of breast tissue associated with the menopause increase the detection rate of possible breast cancer by mammography. On the basis of this evidence a breast cancer screening programme was introduced that now routinely invites women between the ages of 50 and 70 to screening by mammography every three years, with the first invitation to attend being arranged before her 53rd birthday.

Since the introduction of the programme, the effectiveness of screening is likely to have improved, through greater experience and improved techniques (in particular, the introduction of double view mammography). This raises the question of whether the current programme should be extended. The 2007 NHS Cancer Reform Strategy contains a proposal to add additional rounds to the screening programme, targeted at the lower (47-49) and the upper (71-73) limits of the current cohort. This raises the policy question of how this extension compares to other potential uses of NHS resources.

Evaluating these options is a complex process as there are a number of factors driving the impact of each choice. There are significant differences between each cohort in terms of incidence, compliance, treatment options, relapse rates, competing risks, screening test performance and psychological impact of true and false positives. The evidence base that could be relevant to this question is large, and includes clinical trials, observational studies, qualitative research, and data from the current screening programme. Nevertheless, there are likely to be factors influencing the decision for which the direct evidence is incomplete and inconclusive.

This may explain why attempts to assess the efficacy and cost-effectiveness of extending mammography have shown inconclusive results. Interim analysis of the UK Age trial suggested that screening had a positive effect on mortality in younger women, although results were not statistically significant <sup>1</sup>. The 95% confidence interval for the cost-effectiveness of extending screening to the 40-49 age group was estimated as £9,000 - £infinity per life year saved. For older women, a systematic review has identified a range of estimates for the cost per life-year saved of extending screening to age 75 or 80 of \$34,000 to \$88,000 (2002 US dollars) <sup>2</sup>. These studies do not address exactly the policy question of the appropriate age range for one additional screening round, but they highlight the difficulty of conclusive analysis in this area.

Given the complexity of this decision problem, we believe a useful approach is to carry out a preliminary assessment of each option prior to committing to a lengthy analysis. Such an assessment would involve opportunistic use of available literature rather than a systematic review, and a basic decision model involving a simplified representation of the impact of the intervention. This approach would clearly not give definitive guidance over which option, if either, should be chosen. However, it would give a sense of how likely it is that each option is an appropriate use of resources. If it becomes clear that one option is dominant, or that neither has much chance of being cost-effective, this may save considerable time and research effort. Even if this initial assessment is not conclusive, it will demonstrate the relative importance of the factors influencing the impact of each option. In particular, it will allow us to assess whether factors that are difficult to determine and quantify significantly influence the final results. If they do not, they can be eliminated from the full analysis, simplifying it considerably.

To illustrate this, we have carried out such a pre-assessment looking at the specific option of targeting an additional screening round at the younger cohort. The comparator we have used is the status quo. Whilst the younger cohort was the main focus of the exercise, we present an extension of our modelling to the older cohort in an appendix to this report.

## **2 A description of the decision problem**

We wish to predict the impact of adding an extra screening round, targeted at women aged 47-49, to the current national programme. The impact of this can be divided into three areas: impact on life expectancy, psychological effects, and resource use.

### ***2.1 Impact on life expectancy***

The rationale for screening is that earlier detection improves survival. The extent to which breast cancer screening can achieve this in the 47-49 cohort will depend first of all on the number of cases that mammography can detect. This in turn will depend on the prevalence of asymptomatic cancer in that cohort, and the ability of the test to pick these cases up.

Whilst it seems self-evident that detecting breast cancer through screening will improve outcomes compared to allowing it to present symptomatically, quantifying this impact is difficult. The extent to which a cancer has developed is often described using staging systems. Data exists to show that mortality is higher in higher-stage cancers, and that screen-detected cancers tend to have a lower stage. Assessing this 'stage-shift' therefore provides one methods for estimating the impact on survival on detecting a cancer early through screening.

A number of trials have been carried out to assess the impact of screening by mammography. For women aged 50-70, there is clear evidence that screening reduces mortality. For women aged 40-49, the evidence is less clear. A trial of annual screening in this age group, recently completed in the UK, found some evidence of benefit, but this was not statistically significant<sup>1</sup>.

There are reasons why it should be difficult to establish benefit in this age group<sup>3</sup>. Incidence of breast cancer increases with age. Also, breast cancer cases tend to be more aggressive in younger women, which suggests a shorter window of opportunity for screen detection. These factors combined imply that the prevalence of asymptomatic screen-detectable cancers in younger women will be low. Not only that, but the proportion of these cases that will be picked up by mammography will also be lower. It is easier to miss the signs of a tumour in the denser breast tissue of younger (in particular, pre-menopausal) women. At the same time, the benefits of detecting these cancers may well be higher; partly because they tend to be more aggressive cancers, and partly because there are more life-years to be gained by preventing breast cancer death in younger women.

## ***2.2 Psychological effects***

If a woman is told that she has, or may have, breast cancer, it will clearly cause considerable distress in the short term. It may be a relief to be eventually diagnosed as disease-free, but the fact remains in this case that a degree of avoidable harm had been directly caused by screening. This harm will be subjective, personal and difficult to measure, which makes its inclusion in any quantitative evaluation of the screening programme problematic. Nevertheless, the anxiety induced in the short term is likely to be marked, and any such evaluation would be strengthened greatly by including it.

Receiving such a false positive diagnosis may also have an impact on the decision to attend further screening rounds. It may lead to a loss of faith in screening, and hence reduced compliance; alternatively, it may lead to greater awareness of the

disease and an increase in compliance. Again, the impact is likely to vary from person to person, and there is evidence that the average impact in a population will be culturally specific. A recent systematic review of this issue found that compliance amongst women who had previously received a false positive diagnosis, compared with those who had not previously been screened, was 20% lower in Canada, comparable in Europe, and 7% higher in the US <sup>4</sup>. A study of women who had received false positive results in the NHSBSP found that their compliance rate fell by 2.7% <sup>5</sup>.

These psychological effects are largely negative, but it is possible that screening can have a positive psychological impact. For example, those who receive a negative screen result may value the reassurance this gives them.

## **2.3 Resource use**

The main resource impact of an additional screening round will derive from the mammography itself. In addition, all positive results will lead to further resource use to establish a definitive diagnosis. These costs are reasonably straightforward to assess. Detecting a tumour early may also change the treatment strategy used, which will have a cost impact. This will be more difficult to estimate, as it will depend on how the values of prognostic factors change over time.

# **3 Model structure and assumptions**

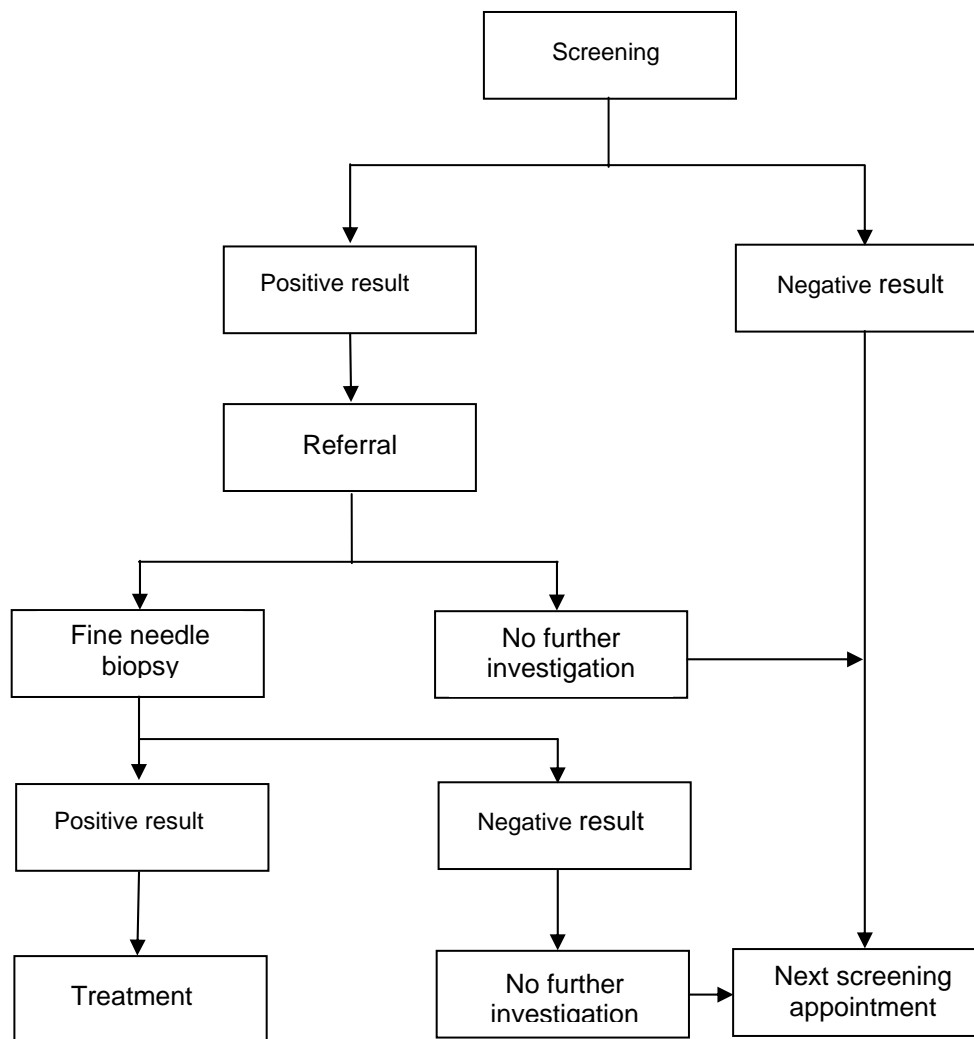
## **3.1 Structure of the model**

The model simulates the experience of a hypothetical cohort of 10,000 women attending a single breast cancer screening appointment between the ages of 47 and

49. The structure of the model is given in figure one, below. The model starts by estimating the number of women who are referred for further investigation. From this group, a proportion of women are diagnosed with breast cancer. Disease severity is classified according to the Nottingham Prognostic Index (NPI) prognostic groups – DCIS, excellent, moderate and poor. The model estimates the split of screen-detected cases between these groups. As a comparator, it also estimates the split that would be observed if screening had not taken place. Using data on the treatment costs and five-year survival for each group, the model estimates the impact of the screening programme on treatment costs and mortality for the cohort.

The model translated improved mortality into Quality Adjusted Life Years (QALYs) gained, using standard tables. This allows a full cost-utility analysis to be carried out. Where appropriate, the parameters used in the model are specified as stochastic variables. This allows us to carry out Probabilistic Sensitivity Analysis (PSA) via Monte Carlo simulation, and produce a cost-effectiveness acceptability curve (CEAC). This allows us to estimate not only the mean cost-effectiveness ratio, but also estimate the probability that the intervention is cost-effective at any given threshold.

In the model base case, we ignore psychological effects and do not include them in the PSA. Instead, we carry out a separate sensitivity analysis for the impact of false positive results on short-term anxiety and on compliance with future screening rounds. We re-ran the model for a range of values for these factors, in order to assess the point at which they made a noticeable difference to the probability that the intervention is cost-effective. If these parameters go beyond plausible values before materially affecting the outcome, then it may not be necessary to include them in a more detailed analysis.



*Figure One: The model process*

## **3.2 Values of key model parameters**

### **3.2.1 Screening test performance**

We modelled the number of positive results in the cohort as the initial parameter, which allowed us to avoid the need to estimate prevalence and test sensitivity separately. We combined this with an estimate of the percentage of women

testing positive that would actually have breast cancer. To construct sampling distributions for these parameters, we drew on two data sources – the UK age trial and the 2001/2 NHSBSP.

Source	Number screened	Referrals	Cancers detected	Referral rate	PPV
NHSBSP 2006/07 1 <sup>st</sup> attenders aged 50-52	201627	17400	1515	8.63%	8.71%
UK age trial – 1 <sup>st</sup> attenders aged 40-41 <sup>6</sup>	35846	1655	37	4.58%	2.2%

*Table one: Source data for modelling test outcomes*

This data does not provide direct evidence of the required parameters for the relevant cohort, but it does allow us to construct a plausible range from which to derive sampling distributions. The UK age trial provides RCT evidence, but from the wrong age group. The age group we are modelling is older, and likely to have significantly more post-menopausal women than those reported in the trial. Therefore, the trial results can be seen as a lower bound on the model parameters. Conversely, the NHSBSP provides data from an older cohort, thus providing an upper bound. Combining upper and lower bounds allows us to define sampling distributions for these model parameters. These sampling distributions are given in table two.

Parameter	Lower bound	Upper Bound	Mean	Standard error
Referral rate	4.58%	8.62%	0.066	0.010
PPV	2.20%	8.71%	0.055	0.017

*Table two: Sampling distributions for screening outcome parameters*

### 3.2.2 Costs related directly to screening

The costs used are given in table three. All costs were obtained from NHS Reference Costs 2005/06, and uplifted to 2006/07 prices using cost indices from the PSSRU.

Activity	2005/06 Cost	2006/07 cost (05/06 + 4.6%)
Initial two-view mammography	£40	£42
Further mammography	£67	£70
Ultrasound examination	£74	£78
Biopsy	£241	£253

*Table three: costs involved in screening and subsequent diagnosis.*

The model assumes that all referrals will undergo either a further mammography or an ultrasound, and uses the average cost of the two procedures. It also assumes that all patients who are ultimately diagnosed with breast cancer receive a biopsy, and 3.5% of those who are referred but subsequently found to be disease-free will also undergo this procedure.

### 3.2.3 Stage shift from screening – with impact on costs and mortality

To predict the impact of screening on costs and outcomes, the model predicts the prognostic category of screen-detected cancers with, and in the absence of, screening. The source data for this is taken from the UK age trial, in combination with analysis from an economic evaluation of the impact of the NHSBSP on treatment costs. This data is given in table four.

Prognosis	10-year Survival	Treatment costs £06/07 <sup>7</sup>	UK age trial – intervention arm	UK age trial – Control arm
DCIS	100	£7,106	69	54
Excellent	98	£8,280	31	28
Good	90	£9,392	84	101
Moderate	79	£10,481	206	422
Poor	47	£12,441	79	173

*Table four: Data on prevalence and outcomes by prognostic group <sup>8</sup>*

We use the data from the UK age trial to simulate the prognosis of cancers detected by the extra screening round, and to simulate their prognosis if they had not been detected early by screening. This allows us to estimate the impact of screening on mortality and costs of treatment. The intervention arm of the UK age trial will not exactly reflect the prognoses one would expect to observe in the cancers detected by screening in our cohort, as it refers to a slightly younger age group, and includes interval cases. However, it provides a reasonable first approximation at this stage.

We use 10-year survival by prognostic group as a proxy for remission/cure. The impact of shift in prognostic group was then translated into life-years gained using standard mortality tables. These were converted into Quality-Adjusted Life Years (QALYs), again using standard tables. All costs and benefits were discounted at the rate recommended by NICE (3.5%).

### **3.2.4 Impact of changes in compliance**

One issue we wish to investigate using the model is the impact of false-positive results in the extra screening round on subsequent compliance with the existing programme. In particular, we wish to explore the level of change in compliance needed to meaningfully alter our estimates of the cost-effectiveness of the proposed intervention. To do this, we need to place a value on the costs and benefits of attending the existing screening programme accruing to an individual participant. For the purposes of this sensitivity analysis, this only needs to be an approximation of the appropriate order of magnitude.

We assume that the total costs per attendee of each screening round are likely to be similar to those in the proposed intervention, which our model suggests are approximately £45. However, the benefits are likely to be higher in the existing screening programme, for reasons outlined in section two. The cost-effectiveness of the existing programme is likely to be at least £10,000 per QALY, which would imply a benefit of 0.003 QALYs per participant. We assumed that compliance would either be complete or nil, so that all those who comply with the main programme attend seven screening rounds. Discounting at 3.5%, this gave net present costs and benefits of attending the NHSBSP of £208 and 0.014 QALYs. These were assumed to be the costs and benefits foregone by each person who chose not to attend the existing programme.

## **4 Model results and sensitivity analyses**

### **4.1 Base case**

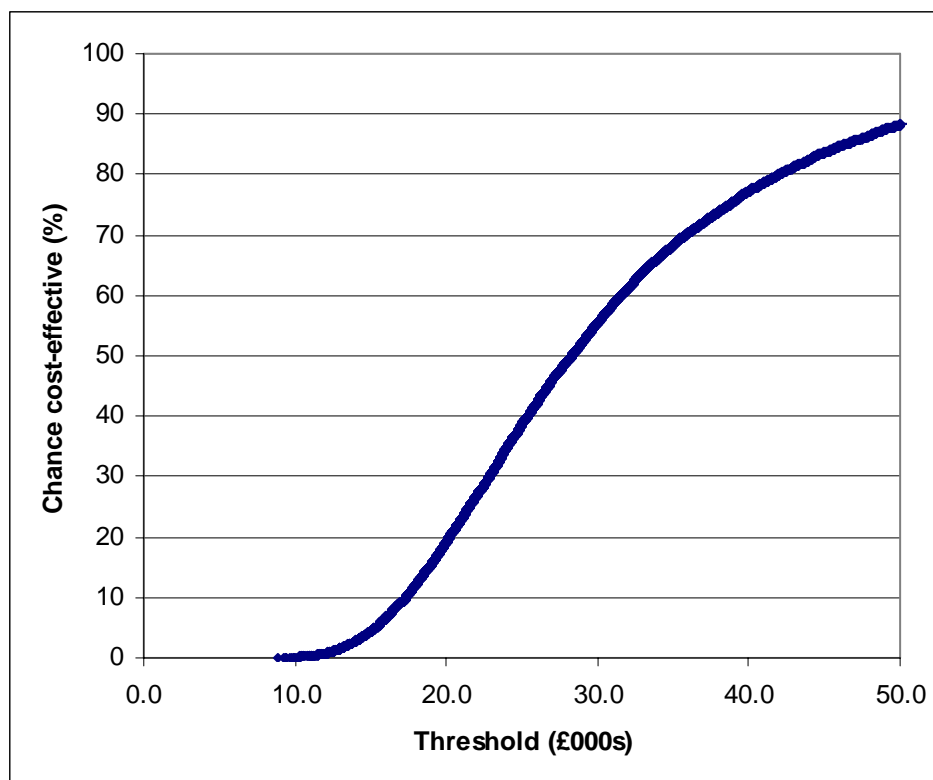
Our initial analysis assumed that the psychological impact of screening is minimal. In this case, the benefits of screening arise from an improvement in mortality. A degree

of saving in treatment costs also arises from early detection. This is offset by the costs of screening and subsequent diagnosis of referred cases, to estimate the overall cost-effectiveness of the extra screening round. We first derived a deterministic (point) estimate of cost-effectiveness by setting all model parameters to their mean values, and then used Monte Carlo sampling of parameters from their distributions to estimate the probability that the extra screening round would be cost-effective.

Cancers detected	QALYs gained through screening	Costs incurred	Cost-effectiveness ratio
36	17.32	£465,489	£26,884

*Table five: Point estimate of the costs and benefits of the intervention (per 10,000 screened)*

Table five gives the deterministic results from the model base case. These results show that the mean estimate of cost-effectiveness from our model lies within the range of commonly used thresholds. Figure two gives the results of the PSA, which quantifies the uncertainty in the results from the model arising from uncertainty in the true value of model parameters. This shows that, for the base case, there is a significant possibility that the intervention actually is cost-effective. At a threshold willingness-to-pay of £20,000 per QALY, there is a 19% probability that the additional screening round is cost-effective, rising to 55% if the threshold is set to £30,000 per QALY.



*Figure Two: Probability of cost-effectiveness by threshold value*

## **4.2 Impact of including psychological effects**

In the base case, we assume that women suffer no anxiety or psychological ill-effects from a false positive screening result. As specific estimates of such effects are difficult to determine, we ran the model a number of times, changing the value used for such an effect each time. We defined short-term anxiety in terms of QALYs lost, and explored the range of 0 to 0.05 QALYs lost per false positive case.

Table six shows the impact on cost-effectiveness within the deterministic model of including short term anxiety. Even if the anxiety caused by the false positive result is assumed to be low, the impact is marked. Beyond 0.028 QALYs per false positive result, the expected impact of screening on the health of the cohort is negative, and the intervention is not cost-effective at any threshold.

Anxiety due to false positive result (QALYs)	0	0.01	0.02	0.03+
Incremental cost-effectiveness ratio (£000s)	27	42	94	Dominated

Table six: Impact of short-term anxiety on deterministic estimate of cost-effectiveness

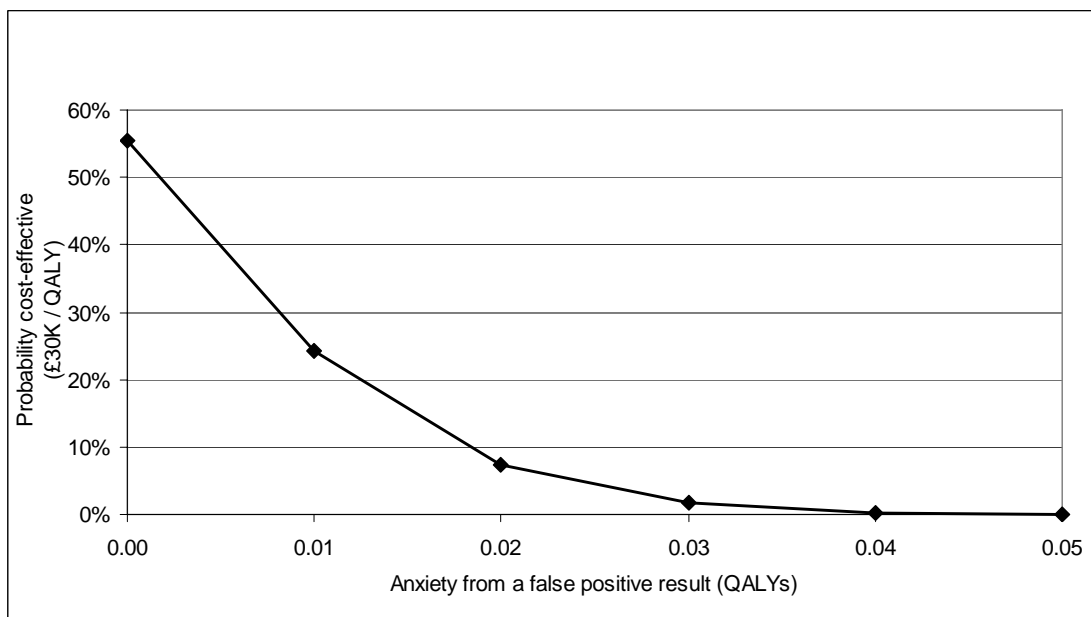
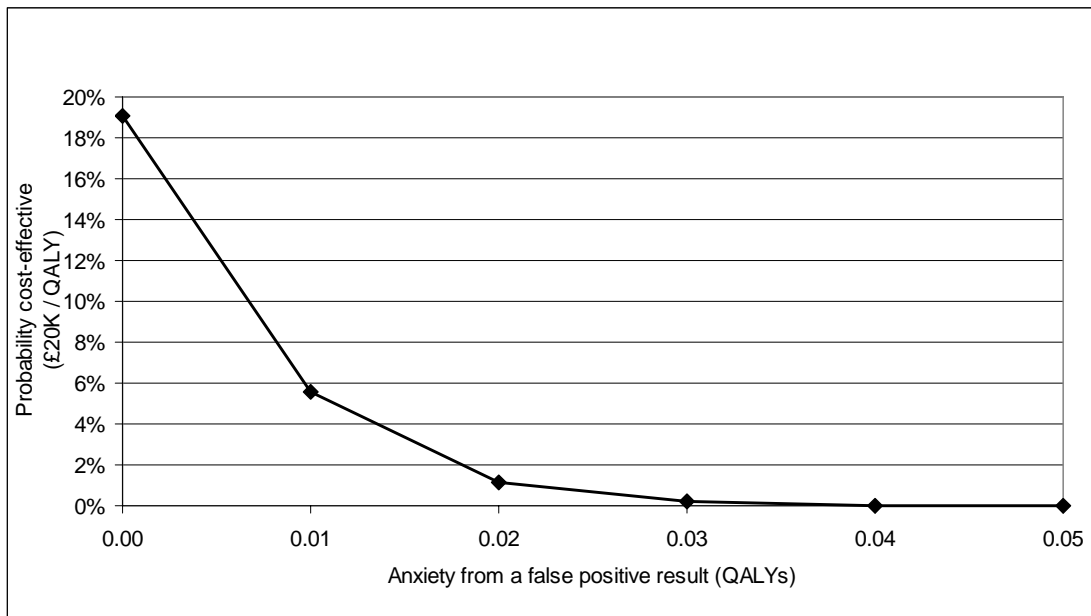


Figure Three: Impact on chance of cost-effectiveness of including false positive anxiety

We carried out a similar sensitivity analysis within the probabilistic model. Figure three shows the impact of increasing values for short-term anxiety on the probability that the intervention is cost-effective at the usual thresholds. Even if quite low values are used, this parameter once more has a noticeable impact on the strength of the model's conclusions. At 0.02 QALYs, the probability that the intervention is cost-effective falls to 1.1% at a threshold of £20,000 per QALY, and 7.5% at a threshold of £30,000 per QALY.

We carried out a separate sensitivity analysis modelling changes in compliance with the existing screening programme linked to false positive results in the additional screening round. As mentioned, there are no definitive data on the extent of the effect, and it is not even certain whether women who receive such false positive findings are more or less likely to attend future screening rounds. We therefore modelled a range of effect sizes. We defined the effect in terms of the proportion of the number of false positive cases that would change their decision to comply with the rest of the screening programme. The interval over which we carried out sensitivity analysis ranged from +50% (for every 100 false positive results, an extra 50 women attend the main programme) to -50% (for every 100 false positive results, 50 women fail to attend the main programme who otherwise would have done).

Change in Compliance	Incremental Cost-effectiveness Ratio (ICER)
-50%	£31,037
-40%	£29,995
-30%	£29,077
-20%	£28,264
-10%	£27,537
Base Case	£26,884
+10%	£26,294
+20%	£25,758
+30%	£25,269
+40%	£24,822
+50%	£24,411

*Table seven: Impact of changes in compliance with the main screening programme on the point estimate of the ICER of the proposed additional screening round.*

Table seven shows the impact of this compliance effect on point estimates of cost-effectiveness. The effect is modest. A change in compliance of 30%, for example, leads to the ratio changing by approximately £2,000 per QALY. Figure four shows the results of the PSA across the range of values analysed. Again, the impact is relatively modest – the change in the likelihood of cost-effectiveness resulting from a compliance effect of 30% is around 6% if the threshold is set at £20,000 per QALY and around 13% at a threshold of £30,000 per QALY.

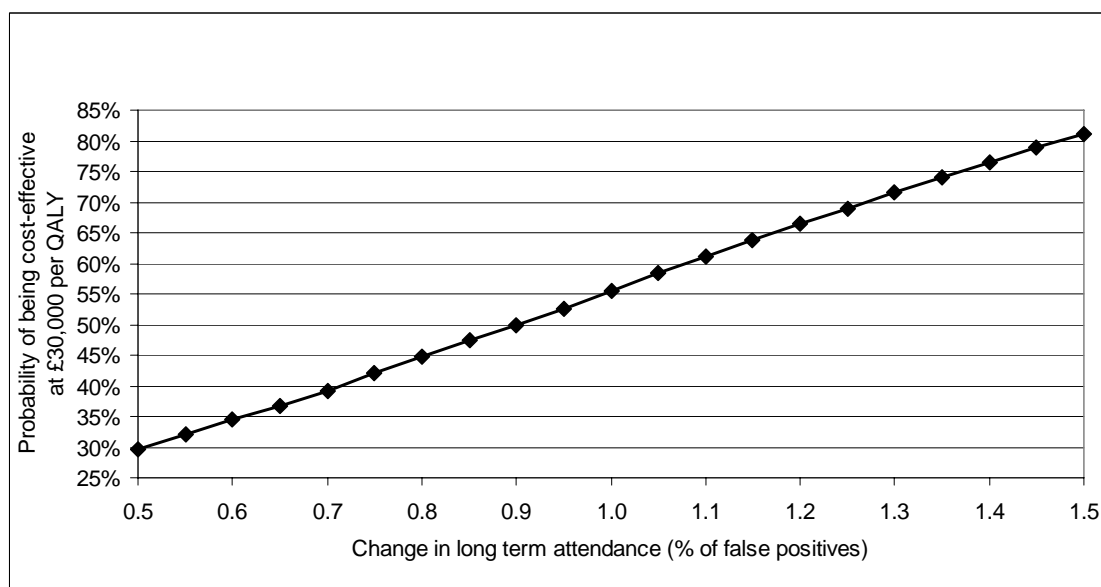
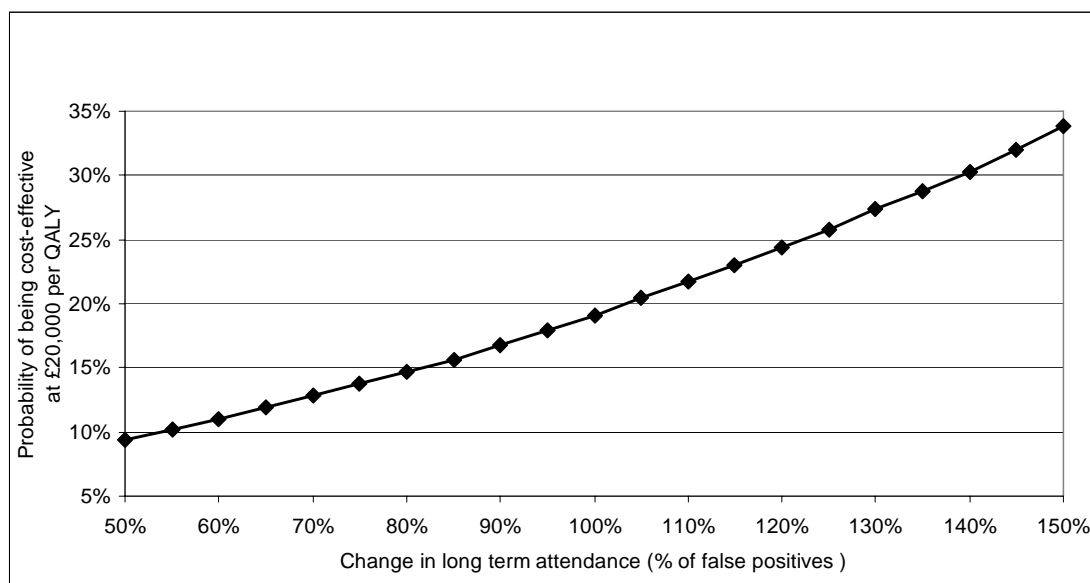


Figure Four: impact of compliance effects on the likelihood of cost-effectiveness.

## 5 Discussion and Conclusions

Our aim in this pre-appraisal was to assist decision-makers in two ways. Firstly, we wanted to explore how likely it was that extending the screening round by one round targeted at the 47-49 cohort would be cost-effective compared to the status quo. Whilst our base case point estimate lies above the cost-effectiveness thresholds commonly applied, we find that there is a meaningful possibility that the true ratio lies below the thresholds. Whilst we are not aware of attempts in the literature to assess the cost-effectiveness of a single screening round in this age group, our results are comparable to, and marginally better than, assessments of the cost-effectiveness of screening programmes targeting the 40-49 age group<sup>9-11</sup>.

Secondly, and perhaps more importantly, we wanted to illustrate the importance of factors that are cumbersome to evaluate and include in the decision analysis, to determine whether their impact on the conclusions made such an effort worthwhile. Our analysis suggests that even modest levels of disutility from false positive results can have a marked affect on the results, so that careful consideration should be given to the issue in deciding on whether to include this option in the full appraisal. Conversely, the impact of changes in compliance with subsequent screening rounds is marginal for plausible values of the effect. The effect is difficult to value and model precisely, and our analysis suggests that it can be ignored in the full appraisal without significantly altering the validity of the results.

If the psychological impact of screening is included in the analysis, and restricted to anxiety resulting from false positive findings, then the additional screening round is unlikely to be cost-effective. However, it might be argued that a negative result from the screening programme provides reassurance, and that this reassurance has a value. We have not fully explored the consequences of including this value in the model. However, we can illustrate the impact of doing so on our point estimates of cost-effectiveness. Assuming that this reassurance has an impact on well-being that can be

valued at 0.002 QALYs is enough to reduce the point estimate of cost-effectiveness from £27,900 per QALY to £12,900 per QALY under the base case, and from £94,000 per QALY to £19,700 per QALY if the anxiety from a false positive result is valued at 0.02 QALYs. The effect sizes used here are purely illustrative; establishing their relevance and value is a complex issue for the judgement of clinical experts. What the analysis does show, however, is that the impact of screening on the psychological well-being of participants is a crucial part of its cost-effectiveness; therefore, a key issue for decision-makers is which effects should be included and what values should be placed on them.

Technological change can affect the performance, and therefore the cost-effectiveness, of a screening test. It has been demonstrated that digital mammography has significantly greater sensitivity (up to 40% relative improvement) than film-based mammography in the under-50s<sup>12</sup>. Our model can be used to explore the likely implications of improved technology on the cost-effectiveness of the proposed intervention. Assuming an ability to detect 40% more cases of breast cancer in the model cohort (50 rather than 36 cases per 10,000 screened) improves the QALYs gained through screening from 17.3 to 24.2 per 10,000 screened. Offsetting this gain will be an increase in the costs of the test itself. We have assumed this to be £42 for the standard test. To restore the cost-effectiveness ratio to that found in the base case, the cost of digital mammography would need to be at most 45% higher (£61). Beyond £69, the overall cost-effectiveness of the extra screening round exceeds £30,000 per QALY, the upper range of commonly quoted willingness-to-pay thresholds. This is only an exploratory analysis, but it does suggest that even a substantial improvement in test performance would be outweighed by fairly modest increases in cost.

## Appendix – Analysis of the cost-effectiveness of an additional screening round targeted at women aged 71-73

### Adaptation of parameter distributions

Our model can be used to generate an initial estimate of the cost-effectiveness of extending the current NHSBSP to older women. To do this, we need appropriate estimates, with uncertainty, of the following parameters:

- recall rate
- positive predictive value
- impact of screen detection on survival.

Data from the current screening programme can help with estimating these parameters. Table eight shows data from the 2006-07 NHSBSP on those who had been screened within the past five years.

Age range	No. Screened	No. Recalled (%)	True positives (%)
55-59	388,872	12,284 (3.16)	2,439 (19.9)
60-64	338,872	11,070 (3.27)	2,727 (24.6)
65-69	227,850	7,475 (3.28)	2,019 (27.0)
70	14,778	498 (3.37)	145 (29.1)

*Table eight: Sampling distributions for screening outcome parameters*

The rates we would expect to see for the age range 71-73 is likely to be similar to that observed for ages 65-69 and for age 70. For both parameters, there appears to be an upward trend with age. Therefore, we decided to use the rates for age 65-69 as lower bounds for our model. Using the results for age 70 as a mid-point, and invoking symmetry, gave us the following sampling distributions:

Parameter	Lower bound	Mid-point	Mean	Standard error
Referral rate	3.28%	3.37%	0.034	0.0006
PPV	27.0%	29.1%	0.291	0.011

*Table nine: Sampling distributions for screening outcome parameters*

To estimate the impact of early detection on survival, we used data reported by the Breast Cancer Clinical Outcome Measures (BCCOM) project. Their first annual report compared the clinical nature of screen-detected and symptomatic invasive cancers in the West Midlands. The results for the age group 65-79 are given in table nine.

Prognosis	Screen-detected No. (%)	Symptomatic No.(%)
Excellent	35 (30.4)	47 (8.7)
Good	48 (38.3)	119 (20.2)
Moderate	41 (28.7)	244 (36.3)
Poor	6 (2.5)	120 (10.6)

*Table ten: Prognostic group of invasive cancers in women aged 65-79*

Applying the survival data given in table four to the results in table nine allowed us to estimate the probability that screen-detection would allow a woman to survive a cancer that would otherwise have killed her. This we calculated to be 10.8%. Unlike the data used for the younger cohort, this is not based on matched arms of an RCT. Also, the mortality calculation uses survival data for the younger cohort. Therefore, to reflect the additional uncertainty, we set the equivalent probability for the younger cohort (4.5%) to be the lower bound of the sampling distribution for the older cohort. As the BCCOM data relates directly to the relevant age group, it is likely to be closer to the true figure. To account for this, we set the upper bound to be one standard deviation above the mean, and the lower bound to be two standard deviations below. The resulting sampling distribution was normal with mean 7.6% and standard deviation 1.6%.

The data from table nine was used to estimate the impact of screening on subsequent treatment costs in the same way as the data from table four was used with the younger cohort.

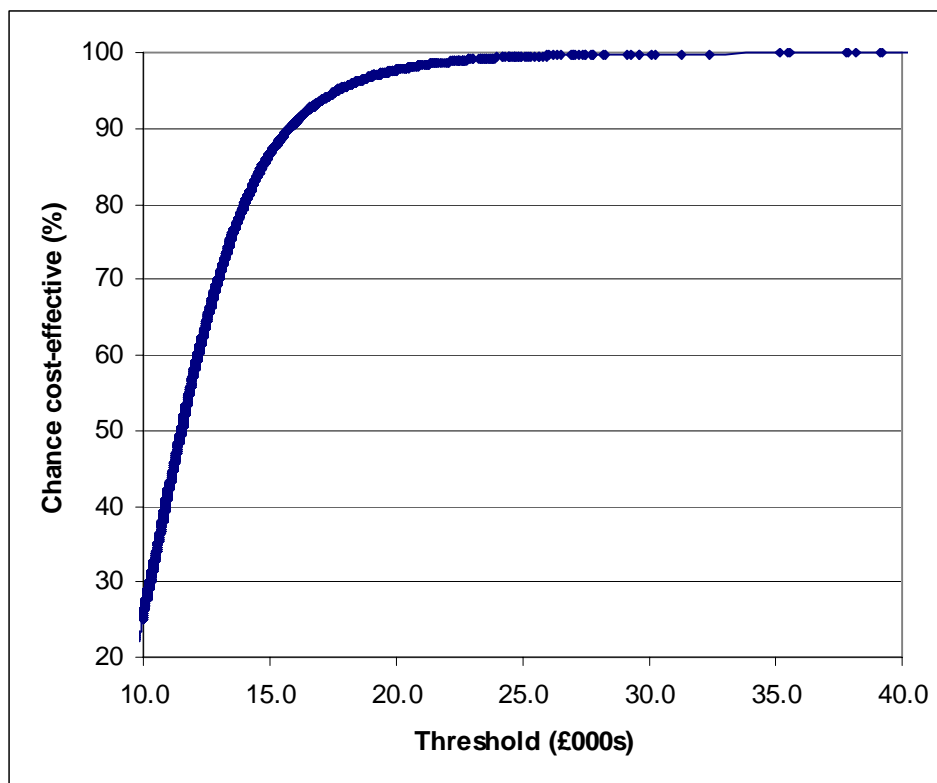
## Results

Table five shows the expected costs and benefits of screening 10,000 women aged 71-73. The ICER is comfortably below the ICER for the younger cohort, and commonly-quoted thresholds. The main reason is that substantially more cancers are detected (98 vs. 36), and the impact of screening on the chance of surviving the cancer is greater.

Cancers detected	QALYs gained through screening	Costs incurred	Cost-effectiveness ratio
98	33.5	£381,574	£11,402

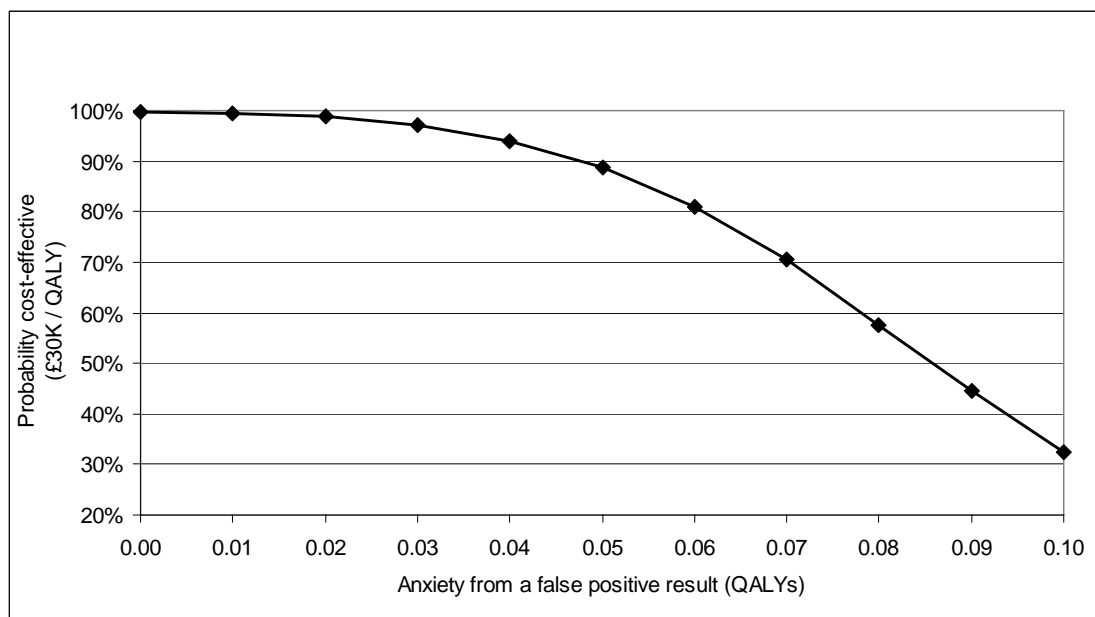
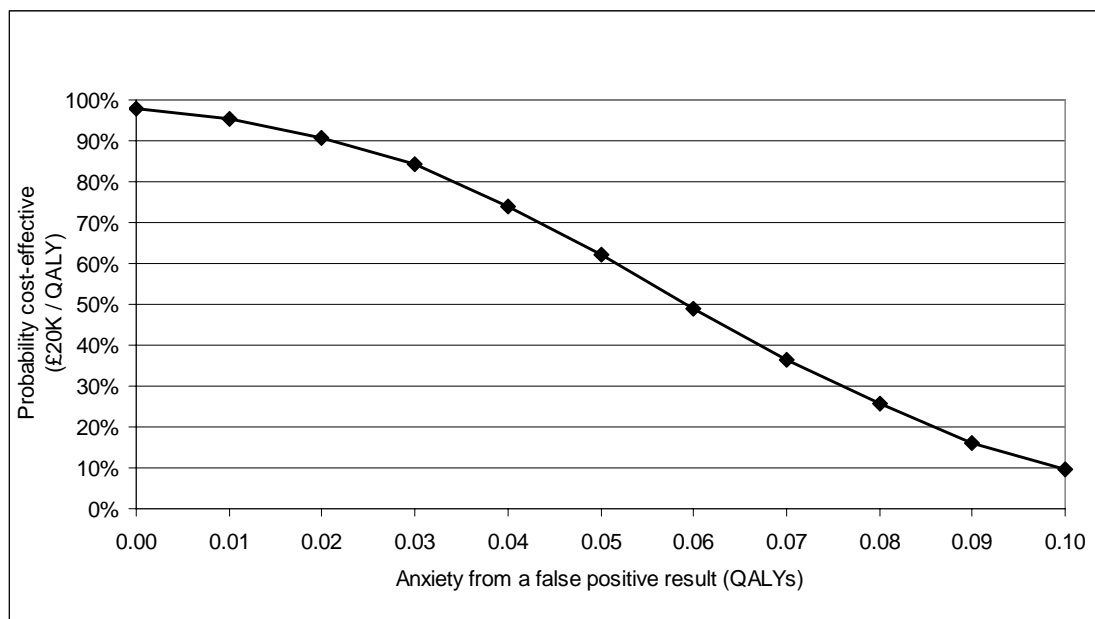
*Table eleven: Point estimate of the costs and benefits of the intervention (per 10,000 screened)*

Specifying sampling distributions for the model parameters allowed us, as before, to carry out a probabilistic sensitivity analysis and estimate the CEAC given in figure five. This analysis suggested that the probability that screening is cost-effective in the older cohort is 98% at a willingness to pay threshold of £20,000 per QALY.



*Figure five: Cost-effectiveness Acceptability Curve for screening ages 71-73*

We described above how we carried out a sensitivity analysis of the impact on the cost-effectiveness of screening in the 47-49 cohort of including anxiety from false positives. We repeated this analysis for the 71-73 cohort. Including this anxiety once more had an impact on cost-effectiveness, but it was less pronounced in the older age group. The net expected impact of screening on health outcomes was still positive when the anxiety was valued up to 0.14 QALYs (for the younger women, this figure was 0.028 QALYs). Figure six shows the impact of false positive anxiety on the PSA. Even attaching a value of 0.1 QALYs to the anxiety from a false positive result, there is a moderate chance that screening the older cohort is cost-effective (10% at a threshold of £20,000 per QALY, 32% at a threshold of £30,000 per QALY).



*Figure six: Impact on chance of cost-effectiveness of including false positive anxiety (71-73 cohort)*

Our initial assessment of screening the older cohort suggests that it is more likely to be cost-effective than screening the younger cohort, and the benefits are less sensitive to the impact of anxiety caused by false positive results. This may seem surprising, as the QALY gain of preventing a breast cancer death is much larger for younger women. The result is driven by two factors. Firstly, there are likely to be many more cases detected in the older women, and fewer false positives. There is strong evidence for this from the current screening programme. Secondly, the impact of screen detection on avoiding breast cancer death is stronger in older women. There is some evidence for this from a comparison of screen-detected and symptomatic cancers. Through our choice of sampling distribution, we have allowed for a reasonable possibility that the benefit for older women of screen detection is in fact no higher than for younger women. Even so, we still estimate that screening is markedly more likely to be cost-effective in the older cohort.

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