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Validation of a modelling approach to estimating the likely effectiveness of cancer screening using cancer data on prevalence screening and incidence Modelling effectiveness of cancer screening

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Abstract

Purpose—This study aims to validate a biostatistical approach to predict the likely effectiveness of screening in reducing advanced disease in the absence of data on incident screen and interval cancers.

Methods—We derived the predicted relative reduction in advanced stage disease following screening from the expected proportion of advanced disease following screening and the observed proportion of advanced disease detected clinically among the controls. We compared the predicted estimates to those observed in a randomised trial.

Results—Using our method, the predicted estimates of relative reduction in node positive breast cancer following screening were comparable to the observed estimates for the age groups 50–59 and 60–69 in the screening study (predicted 32% vs. observed 40% ($p=0.274$) and predicted 34% vs. observed 45% ($p=0.068$), respectively). However, for the age groups 40–49 and 70–74 the predicted values were overestimates of the likely effectiveness of screening compared to the

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COMPETING INTERESTS

None

observed values (predicted 38% vs. observed 16% ($p=0.014$) and predicted 34% vs. observed 0% ($p=0.001$), respectively).

Conclusion—When the number of cancer cases is more than hundred, the method of prediction using only prevalence screen data may be accurate. Where cancers are less common, for example in small populations or young age groups, further data from interval cancers or incidence screens may be necessary.

Keywords

Screening; prevalence screen; incident cancer; relative reduction; advanced cancer; overdiagnosis; prediction

INTRODUCTION

In the context of demonstration projects and other non-randomised studies of cancer screening, estimation of the effect of screening on clinical outcome is complicated by the absence of comparison group. Although it is less reliable than a randomised trial, the potential effectiveness in terms of reduction in advanced stage cancer and in cancer mortality may also be derived from estimates of disease progression. These estimates can be used to predict the number of cases by stage in a hypothetical control group. By comparing the predicted number of cases to the observed number of cases by stage in the unscreened population, it is possible to estimate the likely relative reduction in advanced stage disease achieved by different screening frequencies (1;2). Estimates of expected reduction in mortality associated with screening can be calculated using stage-specific survival probabilities (1;3-5). Markov chain models have been used to derive estimates of disease progression, based on data on prevalent cases (cancers diagnosed at first screen), incident screen-detected cases (cancers diagnosed at later screens) and interval cancers (cancers diagnosed between screens) (6;7); or data on prevalent and incident cancers (8) or at least using data on interval cancers (9;10). However, these data may not always be available.

We were faced with a particular example of having data only on prevalence prostate specific antigen (PSA) testing in prostate cancer in the UK as part of the ongoing Prostate Testing for Cancer and Treatment (ProtecT) study (11). We devised an approach to estimating the predicted potential relative reduction in advanced stage cancer following screening at different intervals and taking into account overdiagnosis; using data on prevalence PSA testing and incident cancers (cancer diagnosed symptomatically). Here, overdiagnosis is defined as diagnosis of a cancer as a result of screening which would not have led to a clinical diagnosis during the lifetime of the host had screening not taken place (12). We estimated the likely benefit of various screening regimens in terms of the reduction in incidence of advanced stage disease (13). Because of the very specific issues with the prostate screening data (lack of interval cancers, and the likely substantial change in the underlying incidence during the preclinical screen-detectable phase, we had to use rather simple biostatistical approach rather than formal complex modelling to derive estimates of disease progression and to predict the likely reduction in advanced stage disease. While the results were plausible, the accuracy of prediction is by no means guaranteed.

The aim of this paper is to verify the predictive approach by applying it to a randomised trial of mammographic screening of breast cancer, for which the results **are already known**, and comparing the findings predicted by our methodology to those observed in the trial. Thus, here our purpose is not to find the best method of estimation of disease progression parameters, rather to assess the likely accuracy of the method already used to predict the

potential reduction in advanced disease following screening (13). The Swedish Two-County Trial of mammographic screening for breast cancer provided the data for this exercise.

METHODS

The design of the Swedish Two-County Trial has been described elsewhere (14;15). Briefly, in the Swedish Two-County Trial, a cluster randomised controlled trial of mammographic screening for breast cancer in two counties in Sweden, 77,080 women aged 40 to 74 were randomised to screening invitation (Active Study Population, ASP), and 55,985 to no invitation (Passive Study Population, PSP), for 7 to 8 years starting in 1977. Approximately contemporaneously with the last screen of ASP, the PSP had a single screen.

Subjects eligible for the trial were identified from the Swedish national population registry. Women aged 40-49 at randomisation were invited to screening every 24 months, women aged 50 or more every 33 months, on average. Screening was done using low-dose screen-film mammography with only one view. All films were processed at the central units and read by a radiologist trained in mammography. Tumours were staged by the UICC (International Union against Cancer) classification. Breast cancer cases detected clinically in the interval between screens or clinically in the non-attendees for screening, even among women who had moved out of the counties, were identified through the nationwide cancer registration system.

Estimation of mean sojourn time of breast cancer

We estimated the sensitivity of the mammogram, s , from the number of cases detected by screening during the period of observation of the screening programme, C_s , and the total number of interval cancers arising clinically within one year of a negative screen in the same period of observation, F_i , such that

$$S = \frac{C_s}{C_s + F_i} = \frac{C_s}{C_t} \quad (2.1)$$

This assumes that clinical cancers arising within one year of a negative screen constitute the cancers missed at the screen. This assumption has been shown to be a reasonable approximation (16).

The variance of s , $V(s)$, was calculated as:

$$V(s) = V\left(\frac{C_s}{C_t}\right) = \frac{C_s(C_t - C_s)}{C_t^3} \quad (2.2)$$

Using the prevalence pool concept of Greenland and Rothman (17) we estimated the mean sojourn time (MST), duration of the preclinical screen-detectable period, from the prevalence of screen-detected cases, P , the annual incidence of breast cancer in the control group, I , and the sensitivity of screening mammogram, s , such that

$$P = \frac{I * s}{\lambda} \quad (2.3)$$

where λ is the transition rate from preclinical to clinical disease and the inversion of λ is the MST.

The 95% confidence intervals (CI) on the MST were estimated from the 95% CI on P assuming a Poisson distribution of prevalence.

The variance of $\log P$, $V(\log P) = 1/\text{Number of cancers detected}$

Estimation of relative reduction in advanced stage breast cancer by screening

Using the approach of Launoy et al (1998) (18), we derived the programme sensitivity (ps), probability of diagnosing breast cancer at screening in a population subjected to screening as such

$$ps = \frac{s(1 - e^{-\lambda r})}{\lambda r(1 - (1 - s)e^{-\lambda r})} \quad (2.4)$$

where r = interval length between screens

The 95% CI on the estimated ps was calculated using the Delta method. The variance of ps is calculated as

$$V(ps) = \left(\frac{\delta(ps)}{\delta\lambda}\right)^2 V(\lambda) + \left(\frac{\delta(ps)}{\delta s}\right)^2 V(s) \quad (2.5)$$

$$V(ps) = V(\lambda) \left[-\frac{(s + se^{2(-\lambda r)} + s^2 e^{-\lambda r}) - s^2 e^{2(-\lambda r)} - 2se^{-\lambda r} - rs^2 \lambda e^{-\lambda r}}{r\lambda^2 (se^{-\lambda r} - e^{-\lambda r} + 1)^2} \right]^2 + V(s) \left[\frac{\lambda r e^{-\lambda r} (e^{-\lambda r} - 1)}{[\lambda r(1 - (1 - s)e^{-\lambda r})]^2} \right]^2$$

Derivation of the 95% CI is given in Appendix 1

Here we define advanced stage as node positive (with or without distant metastasis) breast cancer and early stage as node negative and with no other dissemination. Knowing the proportions of prevalent and incident breast cancers in advanced stage and the probability of diagnosing breast cancer at screening (ps), we estimated the expected proportion of advanced disease $E(p_a)$ following screening. $E(p_a)$ is the sum of the proportion of advanced disease detected by screening and the proportion of advanced disease among interval cases, clinical detected cases not picked by the screening programme

$$E(p_a) = (p_{as} * ps) + (p_{ac}(1 - ps)) \quad (2.6)$$

where p_{as} proportion of advanced disease detected by screening; and p_{ac} proportion of advanced disease detected clinically. The relative risk (RR_a) of advanced disease following screening is the ratio of $E(p_a)$ to the observed proportion of advanced disease detected clinically among the controls, $O(p_a)$.

$$RR_a = \frac{E(p_a)}{O(p_a)}$$

$$RR_a = \frac{(p_{as} * ps) + (p_{ac} * (1 - ps))}{p_{ac}}$$

$$RR_a = \frac{(p_{as} * ps)}{p_{ac}} + (1 - ps) \quad (2.7)$$

Assuming that overdiagnosis occurs only in the prevalence screening and only applies to early disease (p_{es}), the relative reduction in advanced disease following screening was estimated after excluding the proportion of overdiagnosed cases, od .

Let $E(p'_e)$ be the expected prevalence of early disease after excluding the proportion of overdiagnosed cases;

$$\begin{aligned} p'_{es} &= p_{es} * (1 - od), \text{ and} \\ p's &= ps * (1 - od), \text{ then} \\ E(p'_e) &= (p'_{es} * p's) + (p_{ec} (1 - p's)) \end{aligned} \quad (2.8)$$

The expected proportion of advanced disease is $E(p'_a) = 1 - E(p'_e)$.

$$RR'_a = \frac{E(p'_a)}{O(p_a)} \quad (2.9)$$

The 95% CI on the expected RR's of advanced stage disease were calculated using repeated application of the Delta method to the estimated components, assuming that the proportions with advanced stage disease were binomially distributed. The variance of RR is calculated as

$$\begin{aligned} V(RR) &= V\left(\frac{ps * p_{as}}{p_{ac}}\right) + V(ps) + 2 \operatorname{cov}\left[\frac{ps * p_{as}}{p_{ac}}, (1 - ps)\right] \\ V(RR) &= V(ps) \left(1 + \frac{p_{as}^2}{p_{ac}^2} - \frac{2p_{as}}{p_{ac}}\right) + \frac{ps^2}{p_{ac}^2} V(p_{as}) + \frac{ps^2 * p_{as}^2}{p_{ac}^4} V(p_{ac}) \end{aligned} \quad (2.10)$$

Derivation of the 95% CI on RR is given in Appendix 2.

RESULTS

Observed reduction in node positive breast cancer

In the Two-County Trial, 68,770 of the 77,080 women aged 40 to 74 years who were randomised to invitation to screening attended for their first mammographic screen. Of these, 928 had a screen-detected breast cancer. Among the 55,985 women not invited to screening, 757 had clinically detected breast cancer before the screen of the control group at trial closure. Table 1 shows the numbers tested and cases diagnosed by age, and node status. Only 19% of the prevalence screen-detected breast cancers were node positive as compared to 44% of the clinically detected cases.

Table 2 shows the observed relative risk in node positive breast cancer. Participants aged 50-59 and 60-69 years undertaking screening mammogram had 40 percent (RR=0.60, 95%

CI 0.46-0.79) and 45 percent (RR=0.55, 95% CI 0.42-0.71) reduction in node positive breast cancer respectively.

Estimated likely reduction in node positive breast cancer

Table 3 shows the estimates of mean sojourn time, programme sensitivity and the predicted relative risk of node positive breast cancer by age group, considering different scenarios of overdiagnosis. The estimated age-specific mean sojourn time increased with age from 2.0 to 3.6 years for women aged 40-49 and 70-74 years respectively. For interscreening intervals of 24 and 33 months for the age groups 40-49 and 50-74, the programme sensitivity ranged from 55% to 69%. Compared to the control group, the predicted results suggest that screening with mammogram every 24 to 33 months is likely to reduce node positive breast cancer by a third. After adjusting for overdiagnosis, the likely benefit of screening in reducing node positive breast cancer was lower.

Assuming that overdiagnosis was nil, then 32% (RR=0.68, 95% CI 0.63-0.72) reduction in node positive breast cancer would be predicted for the age group 50-59 as compared to the observed reduction of 40% ($p=0.274$) and 34% (RR=0.66, 95% CI 0.60-0.72) predicted reduction as compared to observed reduction of 45% ($p=0.068$) for the age group 60-69. However, under this assumption, the predicted reduction in node positive breast cancer is likely to be overestimate for the age groups 40-49 and 70-74. Assuming 10% overdiagnosis slightly improved the prediction in these age groups, but a cost of poorer prediction for the age groups 50-59 and 60-69. The difference between the observed and expected percent node positive cancers was rather small (Table 3).

In a sensitivity analysis, under the assumption of exponential distribution of MST, using published MST and mammogram sensitivity estimates (15), the relative reduction in node positive breast cancer estimates are shown in Table 4. The results were similar to those from our own estimates, even though our MST estimates were rather different for the age groups 50-59 and 60-69. The differences in the MST were due to our use of the prevalence screen data for estimation, as opposed to the use of interval cancer data by Tabar et al (1992) (15). The predicted estimates of reduction in node positive breast cancer were not statistically significantly different from the observed reductions for the age groups 40-49 to 60-69.

DISCUSSION

Here we have demonstrated a biostatistical approach to deriving estimates of likely effectiveness of screening in reducing advanced stage cancer using data from prevalence screening and incidence of clinically detected cancer in control population.

Because of the specific issues with prostate cancer screening data (lack of interval cancers and changing underlying incidence over the period of the sojourn time) rather simple methods had to be applied, such as using the prevalence / incidence ratio, to estimate the sojourn time. With more complete data, more formal modelling techniques could be applied (8;9;19). However, the aim of this paper was not to use the best method, but to test the more crude method, already used on the ProtecT data, on a screening study (Swedish Two-County Trial of mammographic screening) for which the effect on advanced disease was already known.

The derived estimates of relative reduction in node positive breast cancer following screening were comparable to the observed estimates for the age groups 50-59 and 60-69 ($p=0.274$ and $p=0.068$, respectively). However, for the age groups 40-49 and 70-74 the predicted values were overestimates of the likely effectiveness of screening as compared to the observed values (predicted 38% and 34% reduction in node positive disease vs. observed

16% and 0% reduction respectively). After accounting for overdiagnosis in the age groups 40-49 and 70-74, the predicted estimates were closer to the observed estimates. The difference between the observed and expected percent node positive cancers, calculated from the model, was rather small.

The estimates depend on the assumed proportion of overdiagnosis. Estimates of overdiagnosis in breast cancer vary, but taking into account complexities such as lead time, the estimates tend to be low, at 10% or less (20;21). This seems a reasonable estimate, considering that breast screening in developed countries is generally offered to middle aged women who have a long life expectancy. Hence, tumours detected by screening would otherwise have had a very long future lifetime in individuals to become symptomatic.

The age groups 40-49 and 70-74 had smaller number of cancers in the data than the 50-59 and 60-69 age groups. It is likely that part of the explanation for poorer prediction at ages 40-49 and 70-74 is instability of the estimates due to smaller numbers.

In this paper, the age-specific MST estimates were derived under the assumption of Poisson distribution of prevalence and binomial distribution of sensitivity. Tabar et al (1992) (15) reported MST estimates under the assumption of exponential distribution of sojourn time. The age-specific MST values differed by 4% to 37% for the age groups 70-74 and 40-49 respectively. The calculated sensitivity values, particularly for the age group 40-49, were different from that of Tabar et al (1992) (15). These differences are likely to be due to different estimation methods and different components of the data used for estimation.

Programme sensitivity depends on the screening sensitivity, the sojourn time and the interval between screens. Estimating programme sensitivity based on the MST and sensitivity values of Tabar et al (1992) (15), gave age-specific programme sensitivity values of 0.33, 0.60, 0.66, 0.67 for the age groups 40-49, 50-59, 60-69, 70-74. Whereas the corresponding age-specific programme sensitivity values, based on Tabar et al (1992) (15) MST values and calculated sensitivity values, were 0.42, 0.63, 0.69, and 0.68 respectively. Except for the age group 40-49, the observed and calculated estimates of programme sensitivity were comparable.

To verify our approach to predict the likely effectiveness of screening in reducing advanced stage disease, we applied the approach to a randomised trial, the Swedish Two County trial of mammographic screening for breast cancer, for which the results, reduction in advanced stage disease, are already known. This enabled us comparing the findings predicted by our methodology to those observed in the trial. To apply our approach we needed data on prevalence screening, incident cancer, and on test sensitivity, which are readily available from published papers on this trial. We have used our approach in prostate cancer screening in the UK (13), and the results were plausible.

This study results suggest that the observed to expected differences are small and when advanced cancer is common (more than hundred cases), the method of prediction using only prevalence screen data may be more accurate. Where cancers are less common, for example in small populations or young age groups, further data from interval cancers or incidence screens may be necessary.

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APPENDIX 1

Estimating 95% confidence interval on programme sensitivity, ps , using the Delta method.

$$ps = \frac{s(1 - e^{-\lambda r})}{\lambda r(1 - (1 - s)e^{-\lambda r})}$$

Assuming independence of λ (instantaneous transition rate from preclinical screen detectable phase to clinical phase) and s (test sensitivity), then variance of ps , $V(ps)$ is:

$$V(ps) = \left(\frac{\delta(ps)}{\delta_\lambda} \right)^2 V(\lambda) + \left(\frac{\delta(ps)}{\delta_s} \right)^2 V(s)$$

$$\frac{\delta}{\delta_x} \left(\frac{f}{g} \right) = \frac{f'g - g'f}{g^2}$$

where,

$$\frac{\delta(ps)}{\delta_\lambda} = \frac{\left\{ rse^{-\lambda r} [\lambda r(1 - (1 - s)e^{-\lambda r})] - s(1 - e^{-\lambda r})\lambda r(1 - s)(-r)e^{-\lambda r} \right\}}{[\lambda r(1 - (1 - s)e^{-\lambda r})]^2}$$

$$\frac{\delta \left(\frac{s(1 - e^{-\lambda r})}{\lambda r(1 - (1 - s)e^{-\lambda r})} \right)}{\delta_\lambda} = - \frac{(s + se^{2(-\lambda r)} + s^2e^{-\lambda r} - s^2e^{2(-\lambda r)} - 2se^{-\lambda r} - rs^2\lambda e^{-\lambda r})}{r\lambda^2(se^{-\lambda r} - e^{-\lambda r} + 1)^2}$$

and

$$\frac{\delta(ps)}{\delta_s} = \frac{\left\{ (1 - e^{-\lambda r})(\lambda r(1 - (1 - s)e^{-\lambda r}) - \lambda re^{-\lambda r}s(1 - e^{-\lambda r})) \right\}}{[\lambda r(1 - (1 - s)e^{-\lambda r})]^2}$$

$$\frac{\delta(ps)}{\delta_s} = \frac{\lambda re^{-\lambda r}(e^{-\lambda r} - 1)}{[\lambda r(1 - (1 - s)e^{-\lambda r})]^2}$$

$$V(ps) = V(\lambda) \left[-\frac{(s + se^{2(-\lambda r)}) + s^2 e^{-\lambda r} - s^2 e^{2(-\lambda r)} - 2se^{-\lambda r} - rs^2 \lambda e^{-\lambda r}}{r\lambda^2 (se^{-r} - e^{-\lambda r} + 1)^2} \right]^2 + V(\lambda) \left[\frac{\lambda r e^{-\lambda r} (e^{-\lambda r} - 1)}{[\lambda r (1 - (1 - s) e^{-\lambda r})]^2} \right]$$

$$SE(ps) = \sqrt{V(ps)}$$

$$95\% CI = ps \pm 1.96 SE(ps)$$

APPENDIX 2

Estimating 95% confidence interval on relative reduction in advanced disease, RR , using the Delta method.

$$RR = \frac{ps * p_{as}}{p_{ac}} + (1 - ps)$$

$$\begin{aligned}
V(RR) &= V\left(\frac{ps * pas}{pac}\right) \\
&+ V(ps) \\
&+ 2 \operatorname{cov}\left[\frac{ps * pas}{pac}, (1 - ps)\right] \\
&= \left(\frac{ps * pas}{pac}\right)^2 V\left[\ln\left(\frac{ps * pas}{pac}\right)\right] \\
&+ V(ps) \\
&- 2 \frac{pas}{pac} V(ps) \\
&= \left(\frac{ps * pas}{pac}\right)^2 [V(\ln ps) + V(\ln pls) + V(\ln plc)] \\
&+ V(ps) \left(1 - \frac{2pas}{pac}\right) \\
&= \left(\frac{ps * pas}{pac}\right)^2 \left[\frac{V(ps)}{ps^2} + V\left(\frac{pas}{pas^2}\right) + V\left(\frac{pac}{pac^2}\right) \right] \\
&+ V(ps) \left(1 - \frac{2pas}{pac}\right) \\
&= \frac{pas^2}{p_{ac}^2} V(ps) \\
&+ \frac{ps^2}{pac^2} V(pas) \\
&+ \frac{ps^2 * pas^2}{pac^4} V(pac) \\
&+ V(ps) \left(1 - \frac{2pas}{pac}\right) \\
&= V(ps) \left(1 + \frac{pas^2}{pac^2} - 2 \frac{pas}{pac}\right) \\
&+ \frac{ps^2}{pac^2} V(pas) \\
&+ \frac{ps^2 * pas^2}{pac^4} V(pac)
\end{aligned} \tag{1}$$

$$\text{So } 95\% \text{CI} = RR_{\pm}^{\times} e^{\left(\frac{1.96 \sqrt{V(RR)}}{RR}\right)}$$

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Table 1

Number of women screened, breast cancers by age group and detection mode, and percentages of node positive cases among the prevalence screen-detected and clinically-detected breast cancers; the Swedish Two-County Trial

	Age group			
	40-49	50-59	60-69	70-74
No. of women screened	18495	21559	20579	8137
No. of prevalence screen-detected cancers (ASP- first screen)	39	105	184	101
No. of screen-detected cancers (ASP- first screen, & ASP- later screen)	149	259	367	153
No. of interval cancers 12 months	33	18	24	3
Prevalence /1000 of screened participants-	2.11	4.87	8.94	12.41
Incidence /1000 PY in women with clinically detected breast cancer	1.30	2.23	2.95	3.56
Percentage node positive among prevalence screen-detected cases (%)	16	19	19	23
Percentage node positive among clinically-detected cases (%)	51	45	40	45

ASP – active study population

Table 2

Breast cancer screening test sensitivity, and relative risk of node positive breast cancer as observed in the Swedish Two -County Trial

	Age group			
	40-49	50-59	60-69	70-74
Test sensitivity *	0.82	0.94	0.94	0.98
Undertook screening (prevalence, incidence and interval cancers)				
Node positive breast cancer	64	88	91	61
Observed % node positive breast cancer	27	26	20	27
Population	18495	21559	20579	8137
Control group				
Node positive breast cancer	64	114	132	55
Observed % node positive breast cancer	42	38	34	44
Population	15604	16805	16269	7307
RR (Node positive among the screened)	0.84	0.60	0.55	1.00

Note: the number of breast cancer cases in the screened group exclude non-attendees

* Test sensitivity = Screen-detected cancers / (Screen-detected cancers + interval cancers 12 months)

Table 3

Estimates of mean sojourn time, screening programme sensitivity and predicted relative risk (RR) of node positive breast cancer following screening by age group, with and without accounting for overdiagnosis; and 95% confidence intervals around these estimates

	Age group			
	40-49	50-59	60-69	70-74
Mean Sojourn time (years)	1.98	2.34	3.23	3.56
95% CI	1.95 -2.01	2.30-2.37	3.19-3.27	3.48-3.63
Estimated Programme sensitivity	0.55	0.56	0.65	0.69
95% CI	0.54-0.57	0.55-0.57	0.64-0.66	0.68-0.70
RR -observed				
Observed RR of node positive	0.84	0.60	0.55	1.00
95% CI	0.60-1.19	0.46-0.79	0.42-0.71	0.69-1.43
RR-predicted				
<i>Assuming no overdiagnosis</i>				
Estimated RR of node positive	0.62	0.68	0.66	0.66
95% CI	0.56-0.64	0.63-0.72	0.60-0.72	0.67-0.80
(Observed - Expected) % node positive *	1	0	-2	-2
<i>Assuming 10% overdiagnosis</i>				
Estimated RR of node positive	0.68	0.73	0.72	0.73
95% CI	0.65-0.71	0.69-0.77	0.67-0.78	0.68-0.79
(Observed - Expected) % node positive *	-2	-2	-4	-5

* The percent of node positive tumours in the screened group minus the percent calculated from the model

Table 4

In sensitivity analysis, under the assumption of exponential distribution of MST, based on based on MST and mammogram sensitivity findings reported by Tabar et al 1992, estimates of the predicted relative risk (RR) of node positive breast cancer following screening by age group, with and without accounting for overdiagnosis; and 95% confidence intervals around these estimates

	Age group			
	40-49	50-59	60-69	70-74
Mean Sojourn time (years)	1.25	3.03	3.89	3.41
95% CI	0.87-2.15	2.37-4.19	3.11-5.19	2.21-7.48
Mammogram sensitivity	0.60	0.86	0.86	0.95
Estimated Programme sensitivity	0.33	0.60	0.66	0.67
95% CI (corrected for sensitivity variance)	0.32-0.33	0.59-0.61	0.65-0.67	0.66-0.68
RR-observed				
Observed RR of node positive	0.84	0.60	0.55	1.00
95% CI	0.60-1.19	0.46-0.79	0.42-0.71	0.69-1.43
RR - predicted				
<i>Assuming no overdiagnosis</i>				
RR of node positive	0.78	0.65	0.65	0.67
95% CI	0.75-0.80	0.61-0.71	0.59-0.72	0.62-0.74
(Observed -Expected) % node positive *	-6	1	-2	-2
<i>Assuming 10% overdiagnosis</i>				
RR of node positive	0.81	0.71	0.72	0.74
95% CI	0.79-0.83	0.67-0.76	0.67-0.77	0.69-0.79
(Observed -Expected) % node positive *	-7	-1	-4	-6

* The percent of node positive tumours in the screened group minus the percent calculated from the model