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Is the three year breast screening interval too long? Occurrence of interval cancers in NHS breast screening programme's north western region

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See p 229 and editorial by Mitchell

Abstract

***Objective*—To report the detection rate of interval cancers in women screened by the NHS breast screening programme.**

***Design*—Detection of interval cancers by computer linkage of records held by the screening centres in the North Western Regional Health Authority with breast cancer registrations at the regional cancer registry.**

***Setting*—North Western Regional Health Authority.**

***Subjects*—137 421 women screened between 1 March 1988 and 31 March 1992 who had a negative screening result.**

***Results*—297 invasive interval cancers were detected. The rate of detection of interval cancers expressed as a proportion of the underlying incidence was 31% in the first 12 months after screening, 52% between 12 and 24 months, and 82% between 24 and 36 months.**

***Conclusion*—The incidence of interval cancers in the third year after breast screening approaches that which would have been expected in the absence of screening and suggests that the three year interval between screens is too long.**

Introduction

Trials of mass screening show that there is potential for reducing mortality from breast cancer in women.[1-4] Preliminary results from the NHS breast screening programme have been considered satisfactory[5] but no information has been reported on the incidence of interval cancers. The incidence of these cancers must be kept comparatively low if the screening programme is to be successful.[6] We report the incidence of interval cancers in women screened by the programme in the North Western region.

ORGANISATION OF SCREENING IN NORTH WEST

The NHS breast screening programme began screening women in the North Western region in March 1988. Women on family health services authority registers aged 50-64 are invited to be screened by single view mammography every three years. There are five screening centres in the North Western region; two began screening in March 1988, the third began in June 1988, the fourth in January 1990, and the fifth in June 1991. These centres cover estimated target populations of about 49 200, 49 900, 127 400, 46 600, and 36 800 respectively. The uptake rate in the first screening round estimated from Korner returns form KC62 was 73%, and the cancer detection rate was 5·9 per 1000 women screened.

Subjects and methods

The study population included all women in the North Western Regional Health Authority area aged 50-64 routinely screened for the first time as part of the NHS breast screening programme by the region's first four breast screening centres between 1 April 1988 and 31 March 1992.

Definition of interval cancer—A woman was considered to have an interval cancer if there was histological confirmation of a primary breast cancer within three years of her last negative screening assessment. We included women presenting with symptoms while on early recall but excluded women presenting with in situ disease.

Identification of interval cancers—Interval cancers were identified by linking records held by the screening centres and the North West Regional Cancer Registry. The registry has been population based since 1962 and uses multiple sources of registration to ascertain all cancers occurring in residents of the North Western region. The name, date of birth, and screening history of all women screened after 1 April 1988 were down loaded from the breast screening centres' computer systems. Name and date of birth were used to computer match screened women with registrations of primary breast cancer diagnosed after the start of the screening programme. Positive matches were confirmed by using the woman's address. Women with screen detected cancers were excluded. For the remaining women the date of the last negative screen and the date of the histological diagnosis of cancer were compared and probable interval cancers identified. The screening records of these women were examined to verify that they were interval cancers. In order to minimise delay in cancer registration a policy to "fast track" breast cancer registrations was introduced. However, a few interval cancers that had been reported to the screening centres direct were not registered at the cancer registry but are included in the analysis. In all but three cases this was due to the inevitable delay before a cancer is registered.

Statistical methods—The rate of detection of interval

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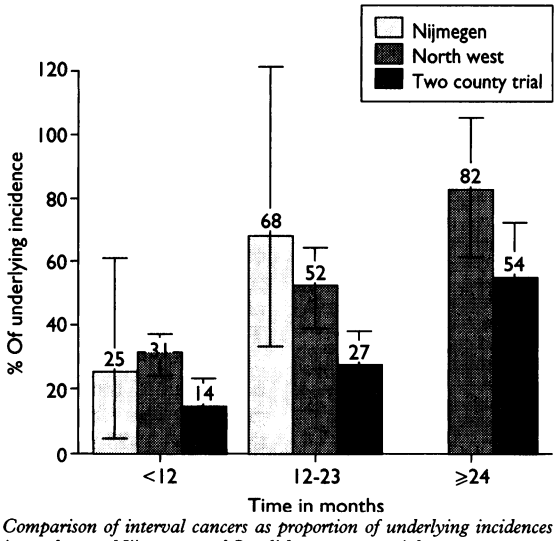
cancers was expressed as a rate per 10 000 women screened. This rate is also presented as a proportion of the underlying incidence. The underlying incidence is defined as the incidence expected in the absence of screening and has been estimated for the north west as the mean annual incidence rates of invasive breast cancer in the three years preceding the introduction of the screening programme (18·3 per 10 000). Ninety five per cent confidence intervals were calculated around the rate of interval cancers as a proportion of the underlying incidence with the assumption that interval cancers are rare events in time following a Poisson distribution. The proportional incidence measure was also used when comparing interval cancer rates across two different screening programmes. Differences are expressed as a ratio of the rate of interval cancers as a proportion of the underlying incidence for the two programmes in each year after screening, and 95% confidence intervals were constructed around these ratios.



Comparison of interval cancers as proportion of underlying incidences in north west, Nijmegen, and Swedish two county trial

Results

A total of 297 interval cancers were identified in the 137 421 women screened between 1 April 1988 and 31 March 1992. A further 12 cases were registered as ductal carcinoma in situ but are not included in subsequent analyses. The study population was stratified into four cohorts according to the year in which screening occurred (table). Two hundred and seventy six (93%) cancers occurred in the interval between a first and second screen and 21 (7%) occurred in women aged 64 and over within three years of a negative screen. In the 37 749 women screened before 1 April 1990 (for which interval cancer registrations were considered complete), 23 (20%) interval cancers occurred within one year of screening, 37 (32%) occurred between 12 and 24 months, and 57 (49%) occurred between 24 and 36 months. The yearly occurrence of interval cancers in all cohorts and the rates per 10 000 women screened are shown in the table.

COMPARISON WITH OTHER SCREENING PROGRAMMES

We compared these results with those from another screening programme (Nijmegen)[7] and from randomised controlled trials (Swedish two county trial[6] and Stockholm[8]). All employed single view mammography. The Nijmegen programme and Stockholm trial screened women aged 50-64 at intervals of 24 and 28 months respectively. The two county trial screened women aged 50-69, with an average screening interval of 33 months.

Comparison with other series was not appropriate because either multiple modalities of screening (health insurance plan trial, 1963; United Kingdom early detection trial, 1979; diagnostisch onderzoek mammacarcinoom project, 1974) or double view mammography (Florence, 1970; Malmo, 1976; Gothenburg, 1982) were used or the screening interval was one year (Canadian trials).

Rates of detection of interval cancers per 10 000 women in the first 24 months after the first screen were 15·8 in the north west, 15·7 in the Nijmegen programme, 19·2 in the Stockholm trial, and 9·4 in the Swedish two county trial.

Published data permit us to compare rates of detection only as a proportion of the underlying incidence for the north west, Nijmegen, and Swedish two county trial. For the Nijmegen programme the underlying incidence was assumed to be that of the adjacent population of Arnhem, which has been cited as a control group.[3] The incidence of breast cancer for women aged 50-64 in Arnhem between 1975 and 1982 was 17·0 per 10 000. For the Swedish trial the underlying incidence was derived from the control group, and the published figures for women aged 50-59 and women aged 60-69 were used[9] to calculate an estimate for the age group 50-69. The proportional incidence rates of interval cancers for each year after screening in the north west, two county trial, and Nijmegen's first screening rounds are shown in the figure.

The risk of an interval cancer for women screened in the north west was significantly higher than for women screened in the Swedish two county trial. The ratio of interval cancer rates as a proportion of the underlying incidence was 2·25 (95% confidence interval 1·37 to 4·91), 1·94 (1·28 to 3·27), and 1·52 (1·02 to 2·34) in the first, second, and third years after screening.

Distribution of interval cancers by screening cohort

Screening year	No of women screened	<12 Months: No of cancers	<12 Months: Rate per 10 000	12-23 Months: No of cancers	12-23 Months: Rate per 10 000	24-36 Months: No of cancers	24-36 Months: Rate per 10 000
1 April 1988 to 31 March 1989	13 359	5	3·7	14	10·5	24	18·0
1 April 1989 to 31 March 1990	24 390	18	7·4	23	9·4	33	13·5
1 April 1990 to 31 March 1991	40 891	26	6·4	38	9·3	43†<	
1 April 1991 to 31 March 1992	58 781	30	5·1	40†		3†	

†Numbers may increase with new cancer registrations and rates were not calculated.

Discussion

An accurate estimate of the incidence of interval cancers occurring in a mass screening programme is dependent on the availability of a population based cancer surveillance system and requires the collaboration of personnel in regional breast screening quality assurance teams, screening centres, and cancer registries.

The incidence of interval cancers in the north west is higher than predicted in the NHS breast screening programme guidelines and after 24 months approaches that which would be expected in the absence of screening. The programme's prediction of the expected incidence of interval cancers is based on the Swedish two county trial. The incidence of interval cancers in that trial was significantly lower than in the north west. Some of this difference can be explained. The Swedish estimate of the number of interval cancers occurring in the third year is derived from screening rounds with an average interval of 33 months. In the NHS breast screening programme women are screened at intervals of three years and consequently our third year estimate reflects a complete 12 month period.

It is more difficult to explain the difference observed in the first and second years after screening. The Swedish trial included older women, up to 69 years of age, in whom cancers may have been easier to detect or slower growing and therefore not apt to present in the screening interval. However, this explanation seems unlikely, as the incidence of interval cancers was similar in the 50-59 and 60-69 age groups. We may be underestimating the underlying incidence of breast cancer in the screened population in the north west and consequently overestimating the incidence of interval cancers as a proportion of the underlying incidence. This is almost certainly the case because the incidence of invasive breast cancer in this age group had been rising before the introduction of the screening programme. The estimated annual percentage change for the period 1975 to 1987 was 2·25%. However, adjustment of the underlying incidence based on an extrapolation of this trend had only a modest impact on the proportional incidence of interval cancers.

EFFECT OF SCREENING QUALITY

Can a difference in the quality of screening explain the variation in incidence of interval cancers? The programme in the north west has met all other quality assurance standards set for the NHS breast screening programme.[10] The breast cancer detection rate at the prevalent screen is over three times the expected rate, which is similar to that achieved in the Swedish two county trial. The greater number of interval cancers in the north west is therefore surprising. Possibly radiologists in the two county trial may have been more successful in identifying small aggressive cancers that if missed would grow quickly and present as interval cancers.

The incidence of interval cancers in the first two years after screening in the north west is, however, comparable to that reported by the Nijmegen programme and the Stockholm trial. In the Stockholm trial the interval cancer rate between 18 and 24 months after screening was 80% of the incidence in the control group. The authors suggested that were the screening interval lengthened from 24 to 36 months the incidence of interval cancers in this period would be almost the same as in the control group.[8] A similar conclusion was reached by the investigators in the two county trial.[6,9]

Interval cancers may occur as a result of the failure to detect an abnormality at the time of screening (false negative interval cancers) or may occur as a new event after a negative screen (true interval cancers). A few of these true interval cancers are considered mammographically occult and cannot be detected with mammography at the time of diagnosis. The relative proportion of each type of interval cancer can be ascertained only by reviewing both the screening and diagnostic mammograms. In the Stockholm trial 45% of invasive cancers occurring within 24 months of screening in women aged 50-64 were true interval cancers.[8] In the Nijmegen programme 58% of all interval cancers were true interval cancers.[7] Inevitably the incidence of true interval cancers increases with time from screening, and the screening interval in the north west is longer than in either the Nijmegen programme or the Stockholm trial.

The NHS breast screening programme is firmly established but still new. The first screening round is not yet complete in all parts of Britain. Increasing experience may reduce the number of false negative interval cancers, but it is disconcerting that improvements in the radiologists' reading of films and in the technical quality of mammography have not been followed by a reduction in the incidence of interval cancers in the first seven screening rounds of the Nijmegen programme.[11] Further reductions in the incidence of false negative interval cancers may be dependent on improvements in the sensitivity of the screening test, and this has been reported with the use of two view mammography.[12,13] The outcome of the national randomised controlled trial of single versus two view mammography is awaited with interest.

Improvements in screening sensitivity will reduce the number of false negative interval cancers, but with a three year screening interval most interval cancers are likely to be true interval cancers. The incidence of these cancers can be reduced only by shortening the screening interval. This would have substantial resource implications. If, however, these findings are replicated throughout the programme a three year screening interval would seem no longer tenable.

Key messages

- Trials of breast cancer screening show that earlier detection of cancer can lead to a 25% mortality reduction from breast cancer in screened women
- The NHS breast screening programme invites all women aged 50-64 to be screened every three years
- To be successful, the incidence of cancers presenting with symptoms between screening appointments—that is, interval cancers—must be kept low
- More interval cancers than predicted are occurring, and after 24 months the incidence approaches that expected in the absence of screening
- To reduce the incidence of interval cancers it may be necessary to shorten the screening interval

We thank the staff of the North Western region's NHS breast screening services who helped in the identification and verification of the women with interval cancers. This work formed part of the NHS breast screening quality assurance programme.

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