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Short Communication

Screening by Mammography, Women with a Family History of Breast Cancer

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The aim of this study was to describe the experience of screening women under the age of 50 years with a family history of breast cancer. 1259 women attended the Family History Clinic in Manchester for their first and subsequent consultations between 30 September 1992 and 30 April 1997. All women were under the age of 50 years at the initial consultation and had a lifetime risk of breast cancer of 1 in 6 or greater. Seven prevalent, seven incident and two interval cancers were detected. The number of invasive cancers expected to occur if this high risk population had not been screened was 8.45 (in 2722 person years at risk). 12 invasive cancers were detected, giving a ratio of 1.42 (95% confidence interval 0.73–2.48). The overall cancer detection rates in this young, at risk population were similar to those in older women in the National Health Service Breast Screening Programme. The number of cancers detected in the study was greater than expected in this population. As the numbers were small, a national trial needs to be undertaken to confirm these results and to determine the long term effects of screening. © **1998 Published by Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

WOMEN WITH a family history of breast cancer have an increased lifetime risk of developing the disease [1, 2]. If they are found to be carriers of a mutation in the breast cancer predisposition genes, *BRCA1* or *BRCA2*, this risk may be as high as 85% [3]. Most of this increased risk occurs before the age of 50 years [3].

The Family History Clinic (FHC) in Manchester at the Nightingale Breast Screening Centre was established in 1987 in order to provide counselling, risk assessment and screening of women at increased risk of breast cancer by virtue of their family history. It also provides information regarding the potential for genetic testing and preventative mastectomy. Here we report the experience of annual mammographic screening for women under the age of 50 years with a lifetime risk of breast cancer of 1 in 6 or greater.

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PATIENTS AND METHODS

Women with a family history of breast cancer were referred to the clinic by their general practitioner or surgeon and were asked to complete an extensive questionnaire on hormonal risk factors and family history of cancers prior to attending the clinic. Women with an estimated lifetime risk of 1 in 6 or greater were offered an appointment in the FHC. Risks were calculated using data from the Cancer and Steroid Hormone Study reported by Claus and colleagues [4]. In general, a woman's lifetime risk of breast cancer increases with increasing number of relatives affected with breast cancer and decreasing age at diagnosis in the affected case or cases. For example, women with a first degree relative diagnosed with breast cancer before the age of 40 years, or women with a first and a second degree relative diagnosed before the age of 60 years have a lifetime risk of 1 in 6 [4]. This is equivalent to a 4-fold increase in risk under the age of 50 years.

All women accepted into the screening programme were offered annual mammography and breast examination between the ages of 35 and 50 years, or from 5 years younger than the earliest diagnosis of breast cancer in the family.

The initial screen (prevalent) utilised two view mammography (oblique and craniocaudal projections), whilst subsequent screens were single view (oblique) examinations of each breast. All mammograms were read by experienced radiologists working in the National Health Service Breast Screening Programme (NHSBSP).

Screening results were obtained for all women who entered the screening programme between 30 September 1992 and 30 April 1997. The number of cancers expected to develop within this population over this time period, if they had not been screened, was calculated using the age stratified data in Claus and colleagues [4]. The observed incidence of cancer at screening was considered to be a Poisson variable and the 95% confidence interval (CI) calculated for the ratio of cancers observed at screening to the cancers expected without screening. The number of cancers expected in the general population was derived from data held at the North West Regional Cancer Registry. The type, size and grade of malignancies detected at screening were obtained from histopathology reports.

RESULTS

Of 2446 women attending the FHC for the first time, 1259 asymptomatic women were under the age of 50 years and suitable for annual mammographic screening.

The mean age at entry into the screening programme was 39.1 years (range 28–49 years) with a median age of 37 years. These women were followed-up for an average of 30 months (range 1–54; median 33 months). One thousand four hundred and sixty-one subsequent mammograms were performed on this cohort of women. The attendance rates for the first and subsequent screens were 95.2 and 98.9%, respectively.

Fourteen breast cancers were detected at screening, seven at the first (prevalent) screen and seven at repeat (incident) screens. Of the prevalent cancers, three were invasive and four were *in situ* disease. Of the incident cancers, six were invasive and one was *in situ* (LCIS), but this patient was found to have invasive lobular carcinoma at subsequent preventative mastectomy 8 months later. Eight of the 13 screen detected cancers were not palpable on examination and therefore would not be detected on breast examination alone. A further two interval cancers presented between mammographic screens, with palpable lesions a few months after a true negative mammogram. (The mammograms were reviewed following the diagnosis of an interval cancer.) Both tumours were less than 15 mm in size. Table 1 describes the clinical details of each case.

The number of invasive cancers expected to occur, if this high risk population had not been screened, during the period of 2722 person years at risk was 8.45. Twelve cancers were detected during the study period, giving a ratio of cancers observed at screening to those expected in the absence of screening of 1.42, 95% CI 0.73–2.48. Table 2 compares the number of cancers observed in three age groups with the number expected to occur in the absence of screening for the study and general population.

DISCUSSION

Many women attending the FHC have initiated the referral via their general practitioner. The high attendance of women for both initial and subsequent screening is an indication of their strong motivation. For comparison, the attendance rates in the NHSBSP are approximately 70–75% [5]. In this study, the overall detection rates of non-invasive and invasive

Table 1. *Malignancies detected by screening of the study population*

Case no.	Age at first screen (years)	Lifetime risk	Age at diagnosis (years)	Histology	Size (mm)	Grade	Node status	Palpable	Screening round
1	45	1 in 4	45	DCIS	n/r	High grade comedo	–	No	Prevalent
2	47	1 in 6	47	DCIS	–	–	–	Yes	Prevalent
3	35	1 in 3	35	IDC	10	II	0/16	No	Prevalent
4	45	1 in 4	45	DCIS	7	Comedo and cribiform type	–	No	Prevalent
5	37	1 in 6	37	IDC	Size of carcinoma n/r	II	2/19	No	Prevalent
6	48	1 in 6	48	LCIS	20	–	–	No	Prevalent
7	37	1 in 4	37	IDC	8	II	0/13	Yes	Prevalent
8	48	1 in 6	49	Tubular carcinoma	8	I	n/a	No	First incident
9	46	1 in 5	50	LCIS*	–	–	–	Yes	First incident
10	27	1 in 2–3	28	IDC	10	III	1/12	No	First incident
11	47	1 in 3	49	IDC	10	III	3/20	Yes	First incident
12	48	1 in 6	50	IDC	10	I	n/a	Yes	First incident
13	44	1 in 4	48	Mixed IDC and ILC	12	II	0/10	No	Fourth incident
14	40	1 in 2–3	43	IDC	45	III	3/6	Yes	Third incident
15	41	1 in 5	44	IDC	10	I	0/15	Yes	Interval (after second incident screen)
16	43	1 in 3	45	IDC	12	III	2/16	Yes	Interval (after first incident screen)

*This patient at preventative mastectomy following diagnosis was shown to have invasive lobular carcinoma. IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*; n/r, not recorded; n/a, not available.

Table 2. The expected number of cancers within the study population compared with the observed

Age (years)	Population years at risk	Invasive cancers expected in general population without screening	Invasive cancers expected in study population without screening	Invasive cancers observed in study population with screening
< 29	36	0.0003	0.005	1
29–39	1380	0.55	2.81	3
39–49	1306	1.83	5.64	8
	2722	2.38	8.45	12

cancers was 5.6 per 1,000 for prevalent screens and 4.8 for incident screens. Similar detection rates are reported in the older population screened by the NHSBSP (5.7 per 1,000 for prevalent screens and 3.8 for incident screens) [5]. However, the proportion of ductal carcinoma *in situ* (DCIS) was greater in our younger population.

The significance of detecting non-invasive malignancy (DCIS and LCIS) in mass screening programmes is unknown. It is estimated that the risk of invasive cancer developing following untreated DCIS in the general population is 30–50% and this usually occurs within 10 years [6]. In the context of a family history, we believe detection of these non-invasive lesions may become more important. As with invasive malignancies, family history is a risk factor for DCIS [7, 8], especially in younger women and LCIS also appears to be more frequent in women with a family history of breast cancer [9]. In addition, all DCIS detected in this study were of high grade and Lampejo and colleagues report an association between high grade DCIS and high grade invasive carcinomas [10]. Furthermore, in one of two cases of LCIS detected at screening, contralateral invasive lobular carcinoma was found at subsequent mastectomy a few months later.

In the absence of screening, it was estimated that 8.45 invasive cancers would have occurred in the study period. A total of 12 invasive cancers occurred, of which 10 were detected at screening. This suggests that the lead time gained from detecting cancer at screening is unlikely to be on average greater than 1 year in this population and suggests that screening high risk younger women requires an annual screening policy. Although the lead time gained does not appear that long, most of the invasive malignancies were less than 20 mm and thus small in size. These tumour sizes compare favourably with the size distribution of cancers occurring in the North West of England in unscreened women of a similar age in the general population [11].

Women with a strong family history of breast and/or ovarian cancer have a high probability of being *BRCA1* or *BRCA2* mutation carriers. It has been shown that *BRCA1*-associated tumours are highly proliferating [12] and therefore probably fast growing. Recent work [12–14] has demonstrated a greater prevalence of higher grade breast tumours in mutation carriers. Some reports suggest that these tumours behave in a different manner to sporadic tumours [14] and may have a better prognosis [15]. Case 10 has been shown to be carrying a mutation in *BRCA2* and the other cases are still under investigation.

Annual screening under the age of 50 years in the general population can be shown to offer a mortality advantage [16]. The cost of introducing such a programme is, however, expensive. In younger women it may be more effective to focus screening on a high risk population. Women with a family history are such a population and this small study shows that these women will attend annual screening and that non-palpable small cancers can be detected. It is probable, however, that the proportion of women in this population with *BRCA1/2* mutations is still low. Our findings are similar to a previous study by Houlston and associates [17], but to establish fully the effectiveness of screening young high risk women long term studies are required. The numbers of women attending any one family history clinic are insufficient for this type of study and therefore national collaboration between a number of centres is required.

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