ELECTRONIC LETTER

Prevalence of family histories of breast cancer in the general population and the incidence of related seeking of health care

C E Jacobi, M A Jonker, N J D Nagelkerke, J C van Houwelingen, G H de Bock

J Med Genet 2003;**40**:e83(http://www.jmedgenet.com/cgi/content/full/40/7/e83)

Breast cancer is the most widespread cancer in women in western countries, currently accounting for one third of all cancers in women.[1 2] The lifetime risk of developing breast cancer is 9% in the United Kingdom,[3] 10% in The Netherlands,[1] and 12% in the United States.[4] About 15%–20% of all cases of breast cancer are thought to be familial,[5 6] and about 5%–10% of all breast cancers are attributed to the known breast cancer susceptibility genes *BRCA1* and *BRCA2*.[7–9]

In most European countries nationwide breast cancer screening programmes are available for women of 50 years and older,[10] whereas comprehensive screening for breast cancer in women under the age of 50 has been found cost ineffective. It is widely acknowledged that women who have relatives with breast cancer have an increased risk of developing breast cancer themselves.[11 12] Consequently, screening for breast cancer might be advisable and cost effective in the subgroup of women under the age of 50 with a familial predisposition to breast cancer. We therefore started a study on the cost effectiveness of breast cancer screening in women under 50 with a familial predisposition to this cancer. For this study we needed information on the distribution of family histories of breast cancer among women under the age of 50 in the general population who might visit a healthcare doctor with concerns about their family history of breast cancer. Several studies have reported information on the percentage of women with a family history of breast cancer among cases of breast cancer and healthy controls.[11] However, no such information is available for the general population. Other researchers have made attempts to gain information on the percentage of women in the general population who might be at an increased risk for breast cancer by using a family history questionnaire.[13] The response rate to the questionnaire was, however, too low to draw useful conclusions. We have chosen to simulate a general population to gain this information.

The aim of this study was to estimate the prevalence of family histories of breast cancer among women aged 30–50 in the general population and to compute the incidence of related seeking of health care.

Key points

- No information is available on the distribution of family histories of breast cancer among women under the age of 50 in the general population. In this study we simulated a population of women aged 30–50 including their first and second degree relatives to gain this information.
- One third of the women aged 30–50 years in the population had at least one relative with breast cancer.
- Of the women with at least one relative with breast cancer, four-fifths had only second degree relatives with breast cancer, and one-fifth had at least one first degree relative with breast cancer.
- Most women who seek health care because of a family history of breast cancer are those who have high risk pedigrees.

METHODS

Design

This study was performed as part of a study on the cost effectiveness of screening women under the age of 50 with a familial predisposition to breast cancer. We needed information on the prevalence and distribution of family histories of breast cancer among women aged 30–50 in the general population. As this information is not directly available, we simulated data with a model and combined them with data available from medical publications.

Simulation of a population including prevalent breast cancer

We simulated a population of 1 million women aged 30–50 and their first and second degree relatives, that is, sibs, parents, maternal and paternal aunts, and uncles and grandparents. Third degree relatives were not included, as previous research has shown that information on breast cancer in third degree relatives gives little additional information on the individual risk of breast cancer.[14] The simulated pedigrees were independent and the structures of the pedigrees were based on actual pedigrees of 256 women under 50 years of age who had visited our hospital in the past seven years. The Dutch population statistics[15] on age and survival were used as input variables in the simulation model to assure that our simulated population was comparable to the general Dutch population. We additionally compared the simulated population and the Dutch population for family structure, by using the mean number of sibs as found in the simulated population and the Dutch population.[15] We found that both populations were comparable, indicating that the 256 actual pedigrees that we used for the simulation may be representative of general Dutch pedigrees.

Using a genetic model,[16] ancestors of the simulated pedigrees were assigned breast cancer polymorphisms, which were inherited by their offspring according to mendelian rules. The genetic model was created to describe correctly familial clustering of breast cancer by using the available information on the two known breast cancer susceptibility genes *BRCA1* and *BRCA2* from medical publications, that is, the mutated allele frequencies[17 18] and penetrance functions.[19 20] Because the *BRCA1* and *BRCA2* genes only explain a small proportion of the familial clustering of breast cancer,[7] an additional gene was modelled accounting for the remaining familial clustered breast cancer using relative risks for breast cancer among women with relatives with breast cancer, which were derived from a large meta-analysis.[11] This genetic model assigned the observed breast cancer incidence

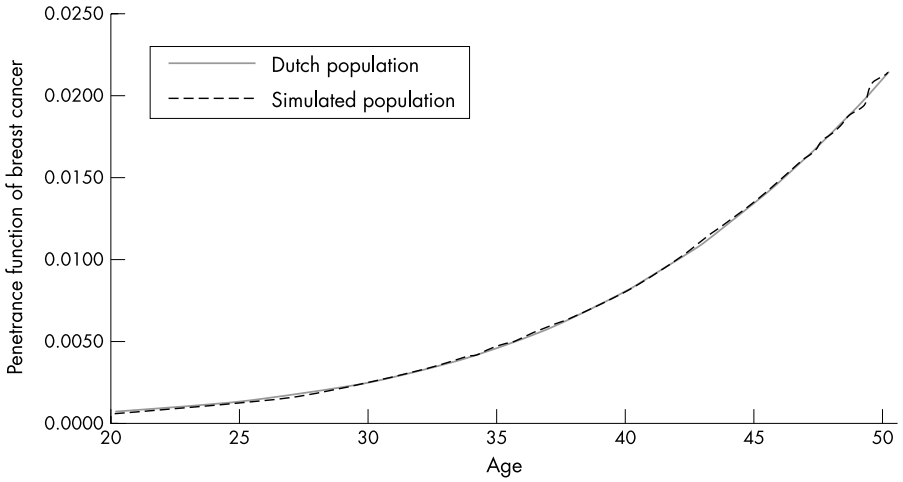

Figure 1 Age specific penetrance of breast cancer among women in the Dutch population and the simulated population.

in The Netherlands[1] to the simulated population (fig 1), and also provided us with information on the familial clustering of breast cancer in the general population.

Prevalence of family histories of breast cancer

In the simulated population, the prevalence of family histories of breast cancer was assessed. For the classification of various risk groups for breast cancer, we determined five different family histories for the women with at least one relative with breast cancer (table 1). Within each of the five groups we determined the percentage of women who had a relative with breast cancer affected under the age of 50 and at the age of 50 or older, to define the family histories more precisely.

Incidence of related healthcare visits

To determine the incidence of seeking health care among women with a certain family history of breast cancer, the following variables were abstracted from the published reports: (1) the distribution of various family histories in general practice and (2) the number of attendees in general practice who newly sought health care because of a family history of breast cancer. Two previous studies reported the variety in family histories of breast cancer in general practice, both from a large primary care centre which corresponded to five general practitioner (GP) practices[21] and from a sample of 200 GP practices.[22] These family histories of breast cancer were registered if a woman visited the GP with concerns about a personal risk of breast cancer. The distribution of the various family histories of breast cancer in general practice, as reported by these studies, is shown in table 2. The number of new attendees with a family history of breast cancer in general practice was obtained through the first study: in the five year period 1997–2001 the number of new attendees in general practice who sought care because of their family history of breast cancer was on average 3.1/1000 women/year (SD 1.8, range 1.4–5.3) (unpublished update to De Bock *et al*[21]). In the Dutch healthcare system, which is similar to that of the United Kingdom, practically every person is registered with a general practice, regardless of his or her medical condition. People who seek care usually start at a general practice.

We computed the average, the minimum, and the maximum incidence of those seeking health care for the various groups of women with a family history of breast cancer by using the distribution of family histories in general practice and the average (3.1), the minimum (1.4), and the maximum (5.3) number of new attendees combined with the distribution of family histories as found in our simulated population. For each group, the incidence of those seeking health care was proportional to the ratio of the distribution of family histories in general practice and the distribution of

Table 1 Family histories of breast cancer in the general population of women aged 30–50 (n=1 000 000)

	No (%)	No (%)	No (%)	No (%)
Total	1 000 000 (100.0)			
Affected with breast cancer	10 166 (1.0)			
Unaffected with breast cancer	989 834 (99.0)	989 834 (100.0)		
And no relatives with breast cancer		643 082 (64.3)		
And at least one relative with breast cancer		346 752 (34.7)	346 752 (100.0)	
One 2nd and no 1st degree relatives		219 634 (22.0)	219 634 (63.3)	219 634 (100.0)
Relative was affected before 50				62 792 (28.6)
Relative was affected at or after 50				156 842 (71.4)
Two or more 2nd and no 1st degree relatives		56 018 (5.6)	56 018 (16.2)	56 018 (100.0)
At least one relative was affected before 50				32 975 (58.9)
All relatives were affected at or after 50				23 043 (41.1)
One 1st and none/one 2nd degree relatives		60 195 (6.0)	60 195 (17.4)	60 195 (100.0)
1st degree relative was affected before 50				26 490 (44.0)
1st degree relative was affected at or after 50				33 705 (56.0)
One 1st and two or more 2nd degree relatives		8 212 (0.8)	8 212 (2.4)	8 212 (100.0)
1st degree relative was affected before 50				4 180 (50.9)
1st degree relative was affected at or after 50				4 032 (49.1)
Two or more 1st degree relatives		2 693 (0.3)	2 693 (0.8)	2 693 (100.0)
At least one 1st degree relative was affected before 50				2 568 (95.4)
All 1st degree relatives were affected at or after 50				125 (4.6)

Table 2 Incidence of seeking health care because of a personal risk for breast cancer among unaffected women aged 30–50 with at least one first or second degree relative with breast cancer

Women with at least one relative with breast cancer	Distribution in the general population (%)	Distribution in general practice[21 22] (%)	Incidence of seeking health care		
			Minimum	Mean	Maximum
New attendees in health care relating to a family history of breast cancer (n/1000 women aged 30–50[21])			1.4	3.1	5.3
One 2nd degree relative	21.96	0.8	0.00005	0.00011	0.00018
Two or more 2nd degree relatives	5.60	14.5	0.00362	0.00802	0.01371
One 1st and no/one 2nd degree relative; 1st ⩾50 at onset	3.37	31.8	0.01324	0.02932	0.05013
One 1st and no/one 2nd degree relative; 1st <50 at onset	2.65	36.2	0.01937	0.04288	0.07331
One 1st and ⩾two 2nd degree relatives or ⩾two 1st degree relatives	1.09	16.7	0.02208	0.04888	0.08357
Total	34.68	100.00			

family histories in the population, by which the sum of the incidence of the various family history groups resulted in the observed number of new attendees.

RESULTS

Prevalence of a family history of breast cancer

The prevalence of family histories of breast cancer in the population of women aged 30–50 (n=1 million) is presented in table 1. Of all the women in this population, 1.0% (n=0 166) had breast cancer, 64.3% (n=643 082) were unaffected and had no relatives with a history of breast cancer, and 34.7% (n=346 752) were unaffected and had at least one relative with breast cancer.

In the population, 12.7% of the women (n=127 118) had at least one first degree relative or at least two second degree relatives affected with breast cancer, of whom 55.9% (n=71 100) had at least one first degree relative with breast cancer.

Incidence of related healthcare visits

In table 2, we calculated the incidence of those seeking health care among women with various family histories of breast cancer. Women with one second degree relative with breast cancer and no affected first degree relatives comprised 21.96% of the general population and 0.8% in general practice and their incidence of seeking health care was 0.00011 (range 0.00005–0.00018). By contrast, women with one first and two or more second degree relatives with breast cancer or at least two first degree relatives with breast cancer comprised 1.09% of the general population and 16.7% in general practice and their incidence of seeking health care was 0.04888 (range 0.02208–0.08357). Thus, the incidence of seeking health care among women with a strong affected family history of breast cancer is higher than of those with a less affected family history.

DISCUSSION

The present study has shown that almost 35% of the women aged 30–50 have at least one first or one second degree relative with breast cancer, of whom most (63.3%) only have one affected second degree relative. In the other groups of women with relatives with breast cancer (12.7% of all women aged 30–50) the family history of breast cancer might represent an increased risk for the disease. The incidence of seeking health care varies from 0.00011 among women with only one second degree relative with breast cancer to 0.04888 among women with one affected first degree relative and two or more second degree relatives and women with two or more affected first degree relatives, resulting in 3.1 new people seeking health care/year/1000 women aged 30–50 in the population.

Some remarks on our results should be made. Firstly, we have based our estimates on the age specific incidence of breast cancer in The Netherlands. As this varies between countries, the estimates could be slightly different for other populations. Secondly, we have not included ovarian cancer or other related cancers in the family history. This may have resulted in an underestimation of the number of women at increased risk, but is in line with the current guidelines for general practice, which only include breast cancer among family relatives.[23 24] Thirdly, the number of new attendees with a family history of breast cancer in general practice was retrieved over a five year period from one large primary care centre, which corresponds to five GP practices. By using a relatively small sample of GP practices, some underestimation of the consultation rate might be introduced. We, however, think that these figures are representative of the general population as other researchers found a slightly higher rate in a sample that included women at all ages over 16[25] instead of ages 30–50 as in our population.

Our results indicate that about 13% of women aged 30–50 have at least one first degree relative or at least two second degree relatives with breast cancer, which may relate to an increased risk for the disease. Future studies should assess whether screening these women or subgroups is worthwhile and cost effective. The estimates from the current study could be used to plan management strategies in health care for these women and to compute the cost effectiveness of various treatment strategies in this subgroup of women. In addition, future studies should also be directed at gaining insight into the sensitivity and specificity of preventive strategies for women under the age of 50 to decide if the currently available preventive strategies are effective in these women.

In conclusion, about 13% of the women aged 30–50 have a family history of breast cancer that may relate to an increased risk for breast cancer and most of the women who seek health care because of a family history of breast cancer are those women who have higher risk pedigrees. The estimates that we provided may be used in future studies that investigate management strategies and compute the cost effectiveness of monitoring women aged 30–50 who might be at an increased risk for breast cancer.

ACKNOWLEDGEMENTS

We gratefully acknowledge Job Kievit and Perla Marang-van de Mheen for their valuable contribution to an earlier draft of this paper, and Wilbert van den Hout and Margot de Waal for their contribution to the estimation of data. This study was financially supported by the National Health Insurance Board of The Netherlands (College voor Zorgverzekeringen).

Authors' affiliations

C E Jacobi, G H de Bock, Department of Medical Decision Making, Leiden University Medcial Centre, Leiden, The Netherlands

M A Jonker, N J D Nagelkerke, J C van Houwelingen, Department of Medical Statistics, Leiden University Medical Centre, Leiden, The Netherlands

Correspondence to: C E Jacobi MSc, Leiden University Medical Centre, Department of Medical Decision Making (J10-S), PO Box 9600, 2300 RC Leiden, The Netherlands; c.e.jacobi@lumc.nl

REFERENCES

1 **Visser O**, Coebergh JWW, van Dijck JAAM, Siesling S. *Incidence of cancer in the Netherlands 1998. Tenth report of the Netherlands Cancer Registry*. Utrecht: Association of Comprehensive Cancer Centres, 2002.
2 **McPherson K**, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. *BMJ* 2000;**321**:624–8.
3 **Eccles DM**, Evans DG, MacKay J. Guidelines for a genetic risk based approach to advising women with a family history of breast cancer. UK Cancer Family Study Group (UKCFSG). *J Med Genet* 2000;**37**:203–9.
4 **American Cancer Society**. *Cancer facts and figures*. Atlanta: American Cancer Society, 1995.
5 **Colditz GA**, Willett WC, Hunter DJ, Stampfer MJ, Manson JE, Hennekens CH, Rosner BA. Family history, age, and risk of breast cancer. Prospective data from the Nurses' health study. *JAMA* 1993;**270**:338–43.
6 **Slattery ML**, Kerber RA. A comprehensive evaluation of family history and breast cancer risk. The Utah population database. *JAMA* 1993;**270**:1563–8.
7 **Nathanson KN**, Wooster R, Weber BL. Breast cancer genetics: what we know and what we need. *Nat Med* 2001;**7**:552–6.
8 **Coughlin SS**, Khoury MJ, Steinberg KK. BRCA1 and BRCA2 gene mutations and risk of breast cancer. Public health perspectives. *Am J Prev Med* 1999;**16**:91–8.
9 **Claus EB**, Schildkraut JM, Thompson WD, Risch NJ. The genetic attributable risk of breast and ovarian cancer. *Cancer* 1996;**77**:2318–24.
10 **Shapiro S**, Coleman EA, Broeders M, Codd M, de Koning H, Fracheboud J, Moss S, Paci E, Stachenko S, Ballard-Barbash R. Breast cancer screening programmes in 22 countries: current policies, administration and guidelines. International breast cancer screening network (IBSN) and the european network of pilot projects for breast cancer screening. *Int J Epidemiol* 1998;**27**:735–42.
11 **Collaborative Group on Hormonal Factors in Breast Cancer**. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58 209 women with breast cancer and 101 986 women without the disease. *Lancet* 2001;**358**:1389–99.
12 **Pharoah PD**, Stratton JF, MacKay J. Screening for breast and ovarian cancer: the relevance of family history. *Br Med Bull* 1998;**54**:823–38.
13 **Leggatt V**, MacKay J, Yates JR. Evaluation of questionnaire on cancer family history in identifying patients at increased genetic risk in general practice. *BMJ* 1999;**319**:757–8.
14 **Jonker MA**, De Bock GH, Hoogendoorn WE, Van Asperen CJ, van Houwelingen HC. Little value from including cousins in individual risk assessment of hereditary breast cancer. A simulation study. *J Med Genet* 2003;**40**:e25.
15 **Statistics Netherlands**. *Online statistics of The Netherlands*. http://statline.cbs.nl. 2002.
16 **Jonker MA**, Jacobi CE, Nagelkerke NJD, Hoogendoorn WE, De Bock GH, van Houwelingen JC. Modeling familial clustered breast cancer using published data. Submitted.
17 **Ford D**, Easton DF, Peto J. Estimates of the gene frequency of BRCA1 and its contribution to breast and ovarian cancer incidence. *Am J Hum Genet* 1995;**57**:1457–62.
18 **Peto J**, Collins N, Barfoot R, Seal S, Warren W, Rahman N, Easton DF, Evans C, Deacon J, Stratton MR. Prevalence of BRCA1 and BRCA2 gene mutations in patients with early-onset breast cancer. *J Natl Cancer Inst* 1999;**91**:943–9.
19 **Easton DF**, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *Am J Hum Genet* 1995;**56**:265–71.
20 **Ford D**, Easton DF, Stratton M, Narod S, Goldgar D, Devilee P, Bishop DT, Weber B, Lenoir G, Chang-Claude J, Sobol H, Teare MD, Struewing J, Arason A, Scherneck S, Peto J, Rebbeck TR, Tonin P, Neuhausen S, Barkardottir R, Eyfjord J, Lynch H, Ponder BA, Gayther SA, Zelada-Hedman M. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. *Am J Hum Genet* 1998;**62**:676–89.
21 **De Bock GH**, Perk DC, Oosterwijk JC, Hageman GC, Kievit J, Springer MP. Women worried about their familial breast cancer risk: a study on genetic advice in general practice. *Fam Pract* 1997;**14**:40–3.
22 **De Bock GH**, Vliet Vlieland TP, Hakkeling M, Kievit J, Springer MP. GPs' management of women seeking help for familial breast cancer. *Fam Pract* 1999;**16**:463–7.
23 **De Bock GH**, Vliet Vlieland TP, Hageman GC, Oosterwijk JC, Springer MP, Kievit J. The assessment of genetic risk of breast cancer: a set of GP guidelines. *Fam Pract* 1999;**16**:71–7.
24 **De Bock GH**, Beusmans GHMI, Hinloopen R, Roelfsma WJ, Wiersma Tj. NHG-standaard Dignostiek van mammacarinoom (NHG-Standaard M07). *Huisarts en Wetenschap* 2002;**45**:466–72.
25 **Hyland F**, Kinmonth AL, Marteau TM, Griffin S, Murrell P, Spiegelhalter D, Todd C, Walter F, Berrington B, Bobrow M, MacKay J. Raising concerns about family history of breast cancer in primary care consultations: prospective, population based study. Women's Concerns Study Group. *BMJ* 2001;**322**:27–8.