

Review: Breast cancer is associated with a family history of the disease in first-degree relatives

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 Oct 27;358:1389-99.

QUESTION

In women with a family history of breast cancer, how does the pattern of breast cancer in first-degree relatives affect the risk for developing the disease?

DATA SOURCES

Studies were identified by searching computerized literature databases, reviewing bibliographies of review articles, and contacting experts in the field.

STUDY SELECTION

Selected studies were cohort or nested case-control studies that included ≥ 100 women with incident invasive breast cancer, and information about reproductive or hormonal factors was sought on each woman.

DATA EXTRACTION

Principal investigators of the included studies were contacted for data on each woman regarding whether any of her first-degree female relatives (mother, sisters, or daughters) had been diagnosed with breast cancer and, if so, their age when the diagnosis was made. Data were also collected on the numbers of sisters and daughters of each woman and the ages of each unaffected first-degree female relative.

MAIN RESULTS

52 published and 2 unpublished studies included 58 209 women with breast cancer

(mean age 52 y) and 101 986 women without breast cancer (mean age 53 y). 7496 women (12.9%) with breast cancer and 7438 women (7.3%) without had ≥ 1 first-degree female relative with a history of breast cancer. The risk for breast cancer increased with an increasing number of affected relatives (Table 1). Age-specific risk ratios (RRs) were not affected by race, age at menarche, education, height, weight, or use of contraceptives or hormone therapy. 27 studies provided data on the age that breast cancer was diagnosed in each first-degree relative. The risk for breast cancer increased as the age of relatives who had been diagnosed with breast cancer decreased (Table 2). The estimates of probability that a woman 20 years of age would develop breast cancer by age 50 were 1.7%, 3.7%, and 8.0% for women with 0, 1,

and 2 affected first-degree relatives, respectively. The corresponding lifetime probability estimates (i.e., age 20 to 80) were 7.8%, 13%, and 21%. The probability estimates for death were 2.3%, 4.2%, and 7.6%.

CONCLUSIONS

Women with first-degree relatives with a history of breast cancer are at increased risk for developing the disease. The risk increases with an increasing number of affected relatives and is higher for younger than for older women.

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For correspondence: ICRF Cancer Epidemiology Unit, Radcliffe Infirmary, Oxford, UK. FAX 44-1865-310-545. ■

Table 1. Relative risk (RR) for breast cancer by number of affected first-degree female relatives

Number of first-degree relatives	RR for women < 50 y (99% CI)	RR for women ≥ 50 y (CI)
1	2.14 (1.92 to 2.38)	1.65 (1.53 to 1.78)
2	3.84 (2.37 to 6.22)	2.61 (2.03 to 3.34)
3	12.05 (1.70 to 85.16)	2.65 (1.29 to 5.46)

Table 2. Relative risk (RR) for breast cancer by age of affected first-degree female relatives

Age at diagnosis of BC in first-degree relatives	RR for women < 50 y (99% CI)	RR for women ≥ 50 y (CI)
< 40 y	13.5 (3.4 to 53.9)	3.9 (1.8 to 8.6)
≥ 40 y	7.8 (2.4 to 25.0)	2.6 (1.8 to 3.7)

COMMENTARY

The review by the Collaborative Group on Hormonal Factors in Breast Cancer (CGHFBC) reported an increased risk for breast cancer according to the number of affected first-degree relatives (mother, sister, or daughter) and the age at which the relatives were diagnosed. This effect was pronounced in women below the age of 50 and was highest when a relative was diagnosed below the age of 40 (RR 13.5, 99% CI 3.4 to 53.9). The review did not discuss women with hereditary breast cancer (e.g., carriers of BRCA1 or BRCA2 mutations) as a separate group who indeed have higher risks for the disease (1).

A family history of breast cancer is one of the few identified and most consistent determinants of breast cancer risk. Nevertheless, it is associated with relatively few cases in the population. In the CGHFBC study, approximately 13% of women with breast cancer had first-degree relatives with the disease compared with 7% of women without the diagnosis. Clearly, a population-wide strategy of early detection aimed at women with a family history of the disease would miss most individuals with breast cancer because 87% would not have a positive family history.

How well do these risks apply to individuals? Rockhill and colleagues

(2) found that the modified Gail model fit well in predicting numbers of breast cancer cases in specific categories of risk but did only slightly better than chance (concordance statistic 0.58, 95% CI 0.56 to 0.60) on the individual level.

The CGHFBC study provides a useful ancillary guide in individual practices for identifying women at relatively high risk for breast cancer who can be counseled and monitored, while emphasizing both the small numbers of women in these high-risk categories and the reassuring fact that most women in these categories will not develop breast cancer.

*Esther C. Janowsky, MD, PhD
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina, USA*

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