A Prospective Study of Reproductive, Familial, and Socioeconomic Risk Factors for Breast Cancer Using NHANES I Data

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Synopsis ....

Risk factors for breast cancer in a cohort of women who participated in the first National Health and Nutrition Examination Survey (NHANES) and its followup epidemiologic survey were examined. The analytic cohort consisted of 122 breast cancer cases and 7,304 noncases, with a median followup time of 10 years. We found no appreciable increase in risk among women who reported their onset of menarche as occurring before the age of 13 compared with those reporting onset at ages 13 and older.

Breast cancer risk was progressively elevated with increasing age at first live birth (test for trend, $P < 0.007$). The number of children born to a woman did not influence risk, but the data suggested an increased risk for nulliparous women. A family history of breast cancer in a first-degree relative was the strongest predictor of risk for this cohort of women, with relative risks of 2.2 and 2.4 associated with a mother or sister affected with breast cancer, compared with women having no family history. The age of natural menopause had little influence on breast cancer risk, and the data suggested a slight protective effect of early surgical menopause.

Higher education (compared with less than a high school education) was associated with an increased risk in this cohort of women (relative risk (RR) = 2.1; 95 percent confidence interval (CI) = 0.9–5.1). These results (a) confirm the importance of some well-recognized risk factors for breast cancer in a cohort of women, followed prospectively for 10 years, and perhaps more importantly, (b) uniquely provide risk estimates on a probability sample of women in the United States.

BREAST CANCER remains a leading cause of morbidity and mortality in this country, striking approximately 10 percent of the female population. Epidemiologic studies of breast cancer risk have identified numerous host and environmental determinants (1–13) that presumably play an etiologic role in the development of the disease. While the majority of these studies have used case-control designs (1–6, 8–11), a few cohort studies have been reported, though none have involved an essentially representative sample of women from the United States (7, 12, 13).

We examined the influence of various risk factors in a cohort of women followed prospectively for more than 10 years with the objective of confirming the importance of a number of breast cancer risk factors in a probability sample of U.S. women.

Materials And Methods

Surveys. The first National Health and Nutrition Examination Survey, NHANES I, and its Augmentation Survey were conducted by the National Center for Health Statistics (NCHS) from 1971 to 1975. These surveys provided cross-sectional information on demographic, nutritional, biochemical, clinical, anthropometric, and medical history variables in a sample selected to represent the U.S. noninstitutionalized population. Persons estimated to be at high risk for malnutrition were oversampled: children 1–5 years old, women of childbearing age, the elderly, and the poor. A total of 14,407 subjects 25–74 years old were examined at baseline.

Between 1981 and 1984, after a median interval of 10 years, these subjects were traced and inter-

viewed again for the NHANES I Epidemiologic Followup Study (NHEFS). The followup data included interview information from subjects or proxies, weight and blood pressure measurements, hospital and nursing home records, and death certificate information. Further details of the NHEFS study design have been reported elsewhere (14).

Case ascertainment. Breast cancer cases were identified through either hospital records or death certificates. For the group of confirmed breast cancer cases, the date of the first hospitalization with breast cancer was taken as the onset date. When confirmation was available from a death certificate only, the date of death from breast cancer was taken as the onset date.

Risk factors examined. The risk factors examined were age at the time of the baseline examination, age at menarche, age at first live birth, parity, family history of breast cancer, age at menopause, type of menopause (surgical or natural), education, poverty index ratio (PIR), and relative weight. Age was analyzed both as a continuous and as a categorical variable, and results did not differ; hence, we present the results with age in quintiles in the full model. Information on age at first live birth and family history was available only from questionnaires collected at the time of followup, whereas data for all other risk factors were collected at the time of the baseline interview. Family history was considered positive if the history indicated a mother, sister, or daughter with breast cancer. PIR was based on reported income, which was adjusted for household size (14). Adjustment was also made for alcohol consumption (15). Body mass index (BMI) was used as a measure of weight adjusted for height. In this cohort of women, the measure of weight least correlated with height was defined by weight (kilograms) ÷ height (meters)$^{1.5}$ (16). Information on menopausal status was available only from the baseline interview. Since we did not have data on menopausal status at the time of breast cancer diagnosis, we did not carry out stratified analyses of risk factor by menopausal status. Suitable data were not available on use of oral contraceptives and other exogenous hormones and, therefore, these factors could not be included in the analytic models.

Subject exclusions. Subjects were excluded from the analytic cohort as follows: male sex (*N* =

5,811), women who were lost to followup (*N* = 675), and prevalent cases of breast cancer (*N* = 12). The additional women who were traced— 483—refused a followup interview. The analytic cohort consisted of 122 breast cancer cases and 7,304 noncases. No significant differences exist between the analytic cohort and the total cohort with respect to any of the variables of interest. The median followup period for the cohort was 10 years.

Statistical methods. The analytic strategy was to develop a basic model for breast cancer that incorporated currently accepted risk factors. We used Cox proportional-hazard regression techniques (17) to analyze the simultaneous relation between age and other risk factors to the overall risk of developing breast cancer in the analytic cohort. Separate bivariate analyses, including age, were performed to determine each risk factor's contribution to breast cancer risk. In addition, each risk factor's contribution was assessed after adjustment for other covariates in a larger model. Indicator variables were created to model each risk factor, using a variety of categorizations common to other breast cancer analyses. We present results based on the categories presented in the footnote to the table on page 47.

Two approaches were considered to accommodate missing data. The first simply excluded the women with missing covariate data, and the second accounted for missing data with a separate indicator and thus preserved the total sample size. Results were very similar, and we report estimates based on the latter approach. Analyses were performed using the PROC PHGLM procedure available in the SAS statistical package of programs. We report bivariate and multivariate risk-factor adjusted relative risk (*RR*) estimates, the 95 percent confidence intervals (CI) about these estimates, and a *P* value for trend where appropriate.

Results

The average age of the analytic cohort at the time of baseline was 48 years. Women who developed breast cancer were older at baseline (56 years) compared with women without breast cancer (48 years). Mean values for risk factors at baseline for the total cohort were as follows: age at menarche—13 years; age at first live birth—19.5 years; age at menopause—45 years; number of live births—2.8; and BMI—32.6. Approximately 5 percent of the women with breast cancer and 3 percent

Risk factors	Cases of breast cancer	Number of women in sample	Age-adjusted RR	95 percent CI	Multivariate RR [1]	95 percent CI
Age at menarche						
13 years or more......................	76	4,576	[2] 1.0	...	[2] 1.0	...
Less than 13 years....................	46	2,718	1.2	(0.8–1.8)	1.1	(0.8–1.6)
Age at first live birth						
Less than 20 years....................	18	2,030	[2] 1.0	...	[2] 1.0	
20–24 years	47	2,510	2.1	(1.1–3.6)	1.8	(1.0–3.3)
25–29 years	18	1,114	1.6	(0.9–3.0)	1.3	(0.7–2.7)
30 or more years.....................	13	514	2.3	(1.1–5.1)	1.9	(0.9–4.2)
Parity						
Parous women only:						
1 liveborn child	16	1,083	[2] 1.0	...	[2] 1.0	...
2 liveborn children	22	1,638	1.0	(0.5–1.9)	0.9	(0.5–1.6)
3 liveborn children	24	1,333	1.4	(0.8–2.4)	1.2	(0.7–2.2)
4 or more liveborn children...........	35	2,139	1.1	(0.6–2.0)	1.1	(0.6–2.1)
All women:						
Parous...............................	97	6,193	[2] 1.0	...	[2] 1.0	...
Nulliparous	24	1,191	1.1	(0.7–1.7)	1.5	(0.7–3.2)
Family history						
Any history:						
None................................	96	6,735	[2] 1.0	...	[2] 1.0	
History in first-degree relative	17	439	2.4	(1.4–4.0)	2.2	(1.3–3.8)
Detailed history:						
None................................	96	6,735	[2] 1.0	...	[2] 1.0	...
Mother affected only..................	6	191	2.1	(1.1–5.4)	2.2	(1.0–4.9)
Sister(s) affected	10	201	2.6	(1.5–4.7)	2.4	(1.4–4.4)
Age and type of menopause						
Pre and postmenopausal women:						
Premenopausal	46	3,658	[2] 1.0	...	[2] 1.0	...
Post, less than 50 years old...........	38	2,381	0.4	(0.2–0.7)	0.6	(0.3–1.2)
Post, 50 years or older	35	1,255	0.4	(0.2–0.9)	0.7	0.3–1.6)
Postmenopausal women:						
Natural..............................	35	1,726	[2] 1.0	...	[2] 1.0	...
Surgical	14	1,152	0.8	(0.4–1.5)	0.8	(0.4–1.4)
Natural, 45 years old or less	25	1,195	[2] 1.0	...	[2] 1.0	...
Natural, 46 years or older............	10	496	1.0	(0.5–2.0)	0.9	(0.4–1.9)
Surgical, 45 years old or less.........	8	849	1.1	(0.4–2.6)	0.5	(0.2–1.5)
Surgical, 46 years or older	6	289	0.7	(0.3–1.5)	0.9	(0.3–2.5)
Education						
Less than high school	47	3,076	[2] 1.0	...	[2] 1.0	...
High school graduate..................	38	2,756	1.3	(0.9–2.1)	1.2	(0.7–1.9)
College graduate......................	19	845	2.0	(1.2–3.5)	1.6	(0.9–2.7)
More than college	18	710	2.5	(1.4–4.5)	2.1	(0.9–5.1)
Income level						
Poverty index ratio:						
First quartile (lowest)	25	1,442	[2] 1.0	...	[2] 1.0	...
Second quartile	• 17	1,409	0.8	(0.4–1.5)	0.7	(0.4–1.3)
Third quartile	26	1,458	1.2	(0.7–2.1)	1.0	(0.5–1.8)
Fourth quartile (highest)...............	34	1,431	2.5	(1.4–4.5)	2.1	(0.9–5.1)
Relative weight						
First quartile, less than 27.5.............	27	1,856	[2] 1.0	...	[2] 1.0	...
Second quartile, 27.5–31.0..............	32	1,856	1.0	(0.6–1.7)	0.8	(0.6–1.8)
Third quartile, 31.1–36.2................	25	1,856	0.7	(0.4–1.2)	0.8	(0.4–1.3)
Fourth quartile, more than 36.2..........	38	1,856	1.1	(0.6–1.8)	1.3	(0.8–2.1)

[1] Adjusted for age in quintiles, age at first birth (less than 20 years, 20–24, 25–29, 30 or more), parity (less than 3, 3 or more, nulliparous), menopause (natural, surgical, premenopausal), family history (yes, no), education (high school or less, high school, beyond high school), weight in kilograms ÷ height in meters$^{1.5}$ body mass index (less than 36.2, 36.2 or more), alcohol use (yes, no), poverty index ratio (less than 3.3, 3.3 or more). Total number of cases = 122, missing information accounts for different sample sizes.

[2] Reference category.

NOTE: RR = relative risk; CI = confidence interval.

'. . . we found that a late age at first live birth, nulliparity, positive family history, and high educational achievement were associated with an increased risk to breast cancer. Age at menarche, number of live born children, and relative weight did not appreciably affect a woman's risk.'

without were nulliparous, and 39 percent of the women with breast cancer and 42 percent without had completed less than 12 years of education at baseline. The ratio of observed to expected number of breast cancer cases (based on the age, sex, race-adjusted rates from the Connecticut Tumor Registry) was 1.08 (CI = 0.90–1.29).

The table shows the relation of age at menarche (less than 13 years versus 13 or more years) to breast cancer risk. Menarche was not associated with an increased risk of breast cancer in this cohort of women ($RR = 1.1$; CI = 0.8–1.6). We examined a variety of age ranges for menarche; no relation was observed.

For the relation between age at birth of the first live born child and breast cancer risk, there was a significant trend ($P < 0.007$) in risk with increasing age at first live birth for parous women; women who gave birth for the first time after age 30 were at the highest risk.

For the relation of parity to breast cancer risk in this cohort, we analyzed the data by both including and then excluding women who had had a miscarriage or stillborn child ($N = 5$ cases, 205 noncases), but there were no appreciable differences in the relative risks; hence, we excluded them from the analysis. Among parous women, there was no evidence of a protective effect as parity increased. The data suggest that women who remained nulliparous, compared with those who had at least one liveborn child, were at increased risk ($RR = 1.5$; CI = 0.7–3.2).

A positive family history for breast cancer in either a mother, sister, or daughter was reported by 14 percent of the women with breast cancer and 6 percent without breast cancer. Having any family history in a first-degree relative placed a woman at more than twice the risk of developing breast cancer compared with those women free of a family history ($RR = 2.2$ CI = 1.3–3.8). Women were at increased risk if they reported that their mother ($RR = 2.2$; CI = 1.0–4.9) or sister ($RR = $

2.4; CI = 1.4–4.4) developed breast cancer (compared with women reporting no family history).

Both the age and type of menopause had an influence on breast cancer risk in this cohort. Premenopausal women were at an increased risk compared with postmenopausal women. Among women who were menopausal, those who had a surgical menopause were at a slightly lower risk compared with women having a natural menopause ($RR = 0.8$), although the confidence interval about this result included 1.0. Also, relative to women with natural menopause, women who had an earlier surgical menopause (at less than 45 years of age) had a slightly lower risk than those with a later menopause.

Two measures of socioeconomic status, education and income, were also examined for their association with breast cancer risk. Risk was elevated with increasing educational level in this cohort (P for trend, < 0.0006). Compared with women completing less than a high school education, the relative risks associated with graduating from high school were 1.2, with graduating from college 1.6, or with attending some graduate or professional school 2.1.

A positive association of income to risk was noted in this data set (P for trend, < 0.015). Women with high relative income, PIR > 3.3, were at a two fold risk. When age, education, and PIR were examined in a reduced model (not shown), risk was not associated with income level ($RR = 1.04$), while the risk increased for women completing high school ($RR = 1.2$), completing college ($RR = 1.9$), and attending some graduate school ($RR = 2.1$). Only the association for college remained statistically significant.

Finally, we found that the highest quartile for relative weight was associated with a slight increase in risk of breast cancer in this study ($RR = 1.3$; CI = 0.8–2.1). However, the test for a trend of increasing risk with increasing relative weight was not significant.

Discussion

In this study, we report relative risks associated with reproductive factors which are in general agreement with those found previously. An early age at menarche did not affect the risk of breast cancer, which agrees with some, but not all (5, 8–10, 18, 19), of the studies that we examined. We did find evidence for a significant trend in risk for breast cancer as age at first live birth increased, though relative risk estimates were not strictly

monotonically increasing. Perhaps small numbers prevented us from observing the progressive increase in risk found in many studies (4, 7–9, 20, 21). In parous women, the number of liveborn children had no significant influence on breast cancer risk and this, again, agrees with several studies (5, 8, 21). Others have shown, however, a clear linear trend with decreasing risk as the number of live born children increased (6, 7, 9, 11). We also found, in accordance with several recent investigations (4, 8, 11, 18), that remaining nulliparous was associated with an increased risk.

Our findings on the influence of family history of breast cancer in a female first-degree relative concur with the large majority of the studies we examined on the association of family history with breast cancer risk (2, 6, 9, 11, 20, 22–24). We should note, however, that since data on family history were available only from the followup interview, our results may be affected by a slight recall bias (which would tend to inflate the relative risk).

Overall, premenopausal women were at a higher age-adjusted risk of breast cancer than postmenopausal women. Having a surgical rather than natural menopause (particularly when the surgical procedure was performed early), was associated with a reduced risk to breast cancer in this study. These results are consistent with two earlier studies (25, 26) and, most notably, the recent work of Brinton and her colleagues (19). Our findings further suggest that a surgical menopause confers protection only if performed earlier than a natural menopause would occur.

The strength of the relation between educational level and breast cancer risk in this study was somewhat surprising. It is possible that our data contain a sufficient range of variability for educational level, which would increase the chances of observing an association. Nonetheless, Paffenbarger and coworkers in 1980 (8) and Helmrich and coworkers in 1983 (9) showed similar results in their series of women whose level of education exceeded high school. This relation did not disappear after adjustment for PIR in our study. It remains to be determined what correlate of education places a woman at an increased risk for breast cancer. In summary, we found that a late age at first live birth, nulliparity, positive family history, and high educational achievement were associated with an increased risk to breast cancer. Age at menarche, number of live born children, and relative weight did not appreciably affect a woman's risk. This study, based on a probability sample of U.S. women who were followed prospectively for 10 years, confirms the etiologic significance of a variety of risk factors for the development of breast cancer.

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Baby Bottle Tooth Decay in Native American Children in Head Start Centers

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Synopsis ....

Baby bottle tooth decay is a unique pattern of dental caries (tooth decay) affecting the dentition of young children. It is associated with the practice of putting the child to sleep with a nursing bottle filled with liquid that contains sugar. Practitioners who treat Native American children have noted that this population suffers from a high prevalence of the condition.

In order to establish specific program priorities and treatment needs for this segment of the Native American population, additional information is required on both prevalence and severity of baby bottle tooth decay. In this survey, an overall prevalence of 70 percent was observed when Navajo and Cherokee Head Start students ages 4–5 years were examined. Of the children affected by baby bottle tooth decay, 87 percent displayed the most severe manifestation of the disease.

The prevalence of this disease in these Native American children appears to be substantially higher than in other populations. Further study is needed to identify the factors contributing to this difference in prevalence and to identify effective measures for reducing the occurrence of baby bottle tooth decay among Native Americans.

MANY TERMS HAVE BEEN applied to a specific pattern of dental caries (tooth decay) observed in young children: nursing caries, nursing bottle caries, nursing bottle syndrome, nursing bottle mouth, baby bottle caries, and bottle mouth. Most recently, the term baby bottle tooth decay (BBTD) has been adopted by the Healthy Mothers/Healthy Babies Coalition, a consortium representing organizations interested in the health of children. The term was selected to emphasize the frequent association of this form of dental caries with improper feeding practices.

Dental caries is a complex, multifactorial disease. Causative bacteria adhere to tooth surfaces in dental plaque and ferment carbohydrate to produce acid, which then demineralizes adjacent tooth enamel. At the earliest stages, this process can be interrupted. Remineralization depends on many factors, including the availability and concentration of fluoride. For clinical dental caries to develop, four factors are essential: acid-producing bacteria; a suitable substrate, particularly refined carbohydrate; enamel that is susceptible to demineralization; and time for repeated and undisturbed interaction of the first three factors.

While the process that produces BBTD is identical to the one just described, the resulting pattern of dental caries is unique to very young children. McDonald and Avery (1) explain that the pattern involves primary maxillary incisors, followed sequentially by the maxillary and mandibular primary first molars and the mandibular primary cuspids.