A Prospective Study of Major Dietary Patterns and the Risk of Breast Cancer[1]

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Abstract

Our aim was to study the broader eating patterns that potentially reflect many dietary exposures working together in their association with breast cancer risk. Using data from a prospective study of 61,463 women with an average follow-up of 9.6 years and 1,328 incident cases of breast cancer, we conducted a factor analysis to identify major dietary patterns. Proportional hazards regression was used to estimate hazard ratios. We found no association between the "Western" dietary pattern (characterized by such foods as red and processed meats, refined grains, fat, and sweets) or the "healthy" dietary pattern (fruit and vegetables, fish and poultry, low-fat dairy, and whole grains) and breast cancer risk. However, women who were in the highest category of the "drinker" dietary pattern (wine, beer, and spirits) had a moderately increased risk (rate ratio = 1.27; 95% confidence interval, 1.06–1.52; *P* for trend, 0.002). The positive association was somewhat weaker among women below 50 years of age, a finding not inconsistent with chance. Our results are in agreement with the majority of previous studies that show alcohol consumption moderately increases the risk of breast cancer, but our results do not support any association between breast cancer risk and the "Western" or "healthy" dietary patterns.

Introduction

Breast cancer is the leading cause of cancer death among women in the United States and other developed countries (1). Diet has been widely studied in relation to breast cancer risk, yet few studies have addressed the broader eating patterns that reflect many dietary exposures working together. The examination of dietary patterns instead of specific foods or nutrients has been discussed in recent years as a potentially important approach in the nutritional epidemiology of chronic diseases (2, 3). Traditional analyses in nutritional epidemiology typically examine diseases in relation to a single or a few nutrients or foods. Foods and food groups that have individually shown potentially important associations with breast cancer risk include alcohol (4, 5), fruit and vegetables (6, 7), fat (8), red meat, (9), sugar (10, 11), low-fat dairy products (10), fish (12), and tea (13). Whereas this type of analysis has been quite valuable, it also has several conceptual limitations. People do not eat isolated foods and nutrients; people eat meals consisting of a variety of foods with complex combinations of nutrients that are likely to be synergistic. One method of identifying and examining broader dietary patterns that may be associated with disease is factor analysis (14), a statistical tool for aggregating inter-related variables into composite "factors." These factors represent eating patterns in the study population and help to distinguish individuals according to the combination of foods they choose to eat. Dietary patterns may go further than individual dietary exposures toward explaining disease occurrence. Therefore, using factor analysis, we identified and examined major dietary patterns and their relation to breast cancer risk in a large prospective cohort study.

Materials and Methods

The Swedish Mammography Screening Cohort. From 1987 to 1990, a population-based mammography screening program was introduced in two counties in central Sweden. In Västmanland County, all women born between 1917 and 1948 received a mailed invitation to be screened by mammography between March 1987 and March 1989 (n = 41,786) together with a 6-page questionnaire; 31,735 women (76%) returned completed questionnaires. In Uppsala County, all women born between 1914 and 1948 were invited to the screening and received the same questionnaire between January 1988 and December 1990 (n = 48,517); 34,916 women (72%) returned completed questionnaires. Hence, questionnaires completed before the mammography were obtained from 66,651 (73.8%) women in the source population. The questionnaire included items about age, weight (kg), height (cm), education, family history of breast cancer, parity age at first birth, and diet.

For the present analyses, we excluded women who were outside the age range 40–76 years (n = 165), those with missing (n = 707) or incorrect identification numbers (n = 415), and those lacking date on the questionnaire (n = 608) or date for moving out of the study area (n = 79) or date of death (n = 16). After further exclusion of 793 women with extreme energy intake estimates, probably reflecting careless completion of the dietary questionnaire (below or above mean ± 3 SD for $\log_e$-transformed calories, cut points of 417 and 3,729 kcal), the cohort was restricted to 63,868 women. By linkage to the Swedish Cancer Registry, we identified and excluded all women with a previous cancer diagnosis other than nonmelanoma skin cancer (n = 2,405). Thus, the study cohort comprised 61,463 women at the start of follow-up.

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Dietary Assessment. The self-administered food frequency questionnaire included 67 commonly eaten foods. Participants were asked how often, on average, they had consumed these foods over the past 6 months. Eight predefined frequency categories, ranging from "never/seldom" to "four or more times per day" were used. For each food item, these frequencies were converted to frequency per week. For energy and nutrient calculations, we used age-specific portion sizes (40–52, 53–65, and 66–74 years) based on mean values from 5,922 days of weighed food records among 213 women randomly selected from the study population.

Food Groupings. The food grouping scheme was based on the similarity of nutrient profiles or culinary usage among the foods and was somewhat similar to that used in previous studies (2, 15). Some individual food items were preserved either because it was inappropriate to incorporate them into a certain food group (*e.g.*, eggs, margarine, tea, and pea soup) or because they were assumed to represent distinct dietary patterns (*e.g.*, wine, liquor, beer, and soda). After the food groupings, 24 variables were retained for the factor analysis (see "Appendix" for details).

Identification of Breast Cancer Cases and Follow-up of the Cohort. We identified incident cases of invasive breast cancer that occurred in our study cohort through December 31, 1998 by matching with the computerized Regional Cancer Register that recorded all breast cancer diagnoses in the two counties. The national Swedish Cancer Registry (that compiles reports from the six Swedish national cancer registries) has been documented to be 98% complete for breast cancer diagnoses (16).

We identified 1328 breast cancers in total. Of these, 420 cases occurred among women 40–49 years of age, and 908 occurred among women 50–76 years of age. Dates of deaths in the cohort were ascertained through the Swedish Death Register, and information about the date of moving out from the study area was obtained by matching the cohort with the computerized and continuously updated Swedish Population Register.

Statistical Analysis. Factor analysis (principal components) was used to derive food patterns based on the 24 food variables in our data. We conducted the analysis using the FACTOR procedure in SAS (SAS). The factors were rotated by an orthogonal transformation (Varimax rotation function in SAS) to achieve simpler structure with greater interpretability. In determining the number of factors to retain, we considered eigenvalues (>1) and the Scree test (14). An overall dietary pattern score was created for each individual by weighting her intake of each food contributing to that pattern by the relative contribution those foods made (factor loadings; Ref. 14). A positive loading indicates that the dietary variable is positively associated with the factor, and a negative loading indicates an inverse association with the factor. All data presented are from the Varimax rotation. Labeling of dietary patterns was based on our interpretation of the data and was arbitrary in that other labels might have been equally suited to the data.

Cox proportional hazards models were used to estimate rate ratios (RR)[3] with 95% CI relating the factors to the occurrence of invasive breast cancer. To stratify women according to younger and older age groups, we used the cut point of either "equal to or above" or "below" the age of 50 years, the mean age of menopause in Sweden (17). Follow-up was censored at date of death, date of migration out of the study area, or at the end of the follow-up period (December 31, 1998). As a basis for the trend tests, scores were constructed from the categorized variables and placed into the model as successive integers.

Table 1 Factor-loading matrix[a] for the three major dietary patterns

	Pattern 1 (healthy)	Pattern 2 (Western)	Pattern 3 (drinker)
Vegetables	0.66	.	.
Fruit	0.55	.	.
Fish	0.54	.	0.24
Whole grains	0.43	0.20	0.36
Low-fat dairy	0.40	.	−0.22
Poultry	0.36	.	0.30
Cereal	0.34	.	.
Eggs	0.32	0.21	0.19
Juice	0.27	.	.
Margarine	0.26	.	−0.22
Tea	0.19	.	0.17
Processed meat	.	0.58	.
Sweets	−0.17	0.54	.
Refined grains	.	0.54	.
High-fat dairy	.	0.46	.
Meat	0.33	0.46	0.20
Soda	.	0.45	.
Potato	.	0.43	−0.20
Pea soup	.	0.30	.
Coffee	.	0.18	.
Wine	.	.	0.67
Liquor	.	.	0.58
Beer	.	.	0.48
Snacks	.	0.16	0.37
Variance explained	9.4%	8.2%	7.0%

[a] For readability, factor loadings below 0.15 are indicated by "."

Results

Three major dietary patterns were discerned (Table 1). Pattern 1 was labeled "healthy" because it reflected the correlated intakes of foods commonly thought to be healthy, such as fruit and vegetables, fish and poultry, cereal and whole grain breads, fruit juice, and low fat dairy products. Pattern 2 was labeled "Western" because it reflected the correlated intakes of foods associated with a Western diet, such as processed meat, soda and sweets, refined breads and potatoes, and high-fat dairy products. Pattern 3 was labeled "drinker" because it reflected the correlated intakes of wine, liquor, and beer. These dietary patterns were distinct in that most food items were important to only one major pattern. The range in median values of factor scores between the lowest and highest quintile of each dietary pattern was −1.16 to +1.24 for the "healthy" pattern, −1.13 to +1.28 for the "Western" pattern, and −1.02 to +1.18 for the "drinker" pattern.

Age was inversely associated with the "drinker" dietary pattern but was not clearly related to the "healthy" or "Western" patterns (Table 2). Energy intake was positively associated with the "healthy" and the "Western" dietary patterns, but not with the "drinker" pattern. The percentage of individuals who had attended university was positively associated with both the "healthy" and the "drinker" dietary patterns but was not clearly related to the "Western" pattern.

There were no clear associations between the "healthy" or "Western" dietary patterns and breast cancer risk (Table 3). In contrast, the "drinker" dietary pattern was positively associated with breast cancer risk in both age- and multivariate-adjusted risk factor models. The association was stronger among women 50 years of age or older at baseline, although tests of interaction by age were not statistically significant (Table 3). Among older

[3] The abbreviations used are: RR, relative risk; CI, confidence interval; BMI, body mass index.

Table 2 Characteristics of dietary patterns in relation to other lifestyle variables

Dietary patterns	Age (median yrs)	Energy (median kcal/day)	BMI (median kg/m^2)	Education (% university)
"Healthy" dietary pattern				
q1 (low)[a]	54	1070	24.3	2.2
q3	52	1279	24.1	5.1
q5 (high)	52	1545	24.2	6.5
P for trend		<0.0001	0.91	<0.0001
"Western" dietary pattern				
q1 (low)	54	990	24.5	4.7
q3	52	1296	24.2	5.0
q5 (high)	52	1660	24.0	3.9
P for trend		<0.0001	<0.0001	0.006
"Drinker" dietary pattern				
q1 (low)	59	1389	24.8	2.7
q3	52	1254	24.3	4.0
q5 (high)	47	1318	23.3	7.3
P for trend		<0.0001	<0.0001	<0.0001

[a] q, quintile.

Table 3 Rate ratios for breast cancer according to the three major dietary patterns[a]

Dietary patterns	Quintiles					*P* for trend[a]
	1 (low load)	2	3	4	5 (high load)	
Ages 40–76 yrs						
Healthy						
Age, Energy	1.00 referent	0.94 (0.79–1.12)	0.96 (0.80–1.13)	0.95 (0.80–1.13)	0.93 (0.78–1.12)	0.56
Multivariate[b]	1.00 referent	0.94 (0.79–1.12)	0.96 (0.80–1.14)	0.95 (0.79–1.14)	0.92 (0.76–1.13)	0.52
Western						
Age, Energy	1.00 referent	1.01 (0.85–1.21)	0.95 (0.79–1.14)	1.05 (0.87–1.27)	1.03 (0.84–1.28)	0.68
Multivariate[b]	1.00 referent	1.01 (0.85–1.21)	0.94 (0.78–1.14)	1.03 (0.85–1.25)	1.00 (0.79–1.26)	0.92
Drinker						
Age, Energy	1.00 referent	1.05 (0.88–1.25)	1.17 (0.99–1.39)	1.25 (1.05–1.49)	1.28 (1.07–1.53)	0.001
Multivariate[b]	1.00 referent	1.05 (0.88–1.25)	1.17 (0.98–1.39)	1.24 (1.04–1.48)	1.27 (1.06–1.52)	0.002
Ages 40–49 yrs (multivariate[b]; *N* cases = 420)						
Healthy	1.00 referent	0.87 (0.63–1.20)	1.12 (0.83–1.53)	0.86 (0.61–1.20)	0.91 (0.63–1.31)	0.68
Western	1.00 referent	1.41 (1.02–1.97)	1.06 (0.74–1.51)	1.24 (0.86–1.78)	1.08 (0.70–1.67)	0.95
Drinker	1.00 referent	1.04 (0.71–1.52)	0.92 (0.63–1.34)	1.10 (0.78–1.57)	1.12 (0.79–1.58)	0.35
Ages 50–76 yrs (multivariate[b]; *N* cases = 908)						
Healthy	1.00 referent	0.97 (0.79–1.19)	0.86 (0.70–1.07)	0.99 (0.79–1.23)	0.91 (0.72–1.16)	0.52
Western	1.00 referent	0.89 (0.72–1.09)	0.92 (0.74–1.14)	0.97 (0.77–1.22)	0.98 (0.74–1.28)	0.89
Drinker	1.00 referent	1.03 (0.85–1.25)	1.25 (1.02–1.52)	1.27 (1.03–1.56)	1.31 (1.05–1.63)	0.002

[a] All *P*s are from two-sided tests.
[b] Multivariate adjustment included age (as a continuous variable), energy intake (as a continuous variable), BMI (as a continuous variable), and education (less than high school, high school, and university), family history (yes, no), parity (0, 1–4, 5+ children), and age at first birth (<35, 35+).

women, those in the highest quintile of the "drinker" dietary pattern, compared with those in the lowest, had a 31% increased risk of breast cancer (95% CI, 5–63%; *P* for trend, 0.002). Among younger women, ages 40–49 years, the corresponding estimate was a statistically nonsignificant 12% increased risk (*P* for trend = 0.35). The "healthy" and "Western" dietary patterns were not associated with breast cancer risk among younger or older women, respectively, and results in the subgroup analyses were similar to the overall results for these patterns (Table 3). Multivariate-adjusted rate ratios estimates were similar to those adjusted only for age and energy intake. We observed no effect modification by family history of breast cancer, BMI, education, parity, and age at first birth.

Discussion

We discerned three major dietary patterns in this population of Swedish women. The "drinker" dietary pattern was positively associated with breast cancer risk, whereas the other two patterns were not associated with risk. The positive association between the "drinker" pattern and breast cancer risk in our data was more evident among women above age 50 years at baseline, the mean age of menopause in Sweden (17).

In an earlier case-control study from the Swedish Mammography Cohort (18) with a more detailed examination of alcohol consumption at various ages obtained from supplementary interviews, the increased breast cancer risk due to alcohol consumption was clearly confined to women above 50 years of age. However, effect modification by age was not detected in an analysis of data from several pooled prospective cohort studies (4), which confirmed the positive association between alcohol consumption and breast cancer risk at various ages. Indeed, formal testing did not reveal a statistically significant interactions between the "drinker" dietary pattern and age in relation to breast cancer risk. Overall, the positive association between

the "drinker" dietary pattern and breast cancer risk is consistent in direction and magnitude with what was observed in previous studies of alcohol consumption (4).

A "Western" dietary pattern has been hypothesized to increase the risk of breast cancer through increased insulin resistance (19), an earlier age at menarche, and decreased estrogen excretion (20). In contrast, a "healthy" dietary pattern has been hypothesized to lower the risk of breast cancer through such mechanisms as the inhibition of the intestinal reabsorption of estrogens excreted through the biliary system (20) and through antioxidative effects (5). In addition, diets that include ω-3 fatty acids contained in fish such as salmon, herring, and mackerel, which are commonly consumed in Sweden (21, 22), might reduce the risk of breast cancer through mechanisms that include the inhibition of cyclooxygenase and *p21* gene expression and the up-regulation of *p53* gene expression (23–25). However, a large study of pooled cohorts did not find an increased risk with high saturated fat intake (8) or a lowered risk with high fruit and vegetable consumption (26). Moreover, prospective cohort studies have not found clear associations between breast cancer risk and intake of dietary fiber (5), several antioxidants (5), or fish and ω-3 fatty acids (27). In sum, the results for dietary patterns in our data do not appear to predict breast cancer risk above and beyond what has been observed separately for the individual dietary items that these patterns comprise.

Factor analysis involves decisions that can be called subjective or arbitrary, decisions that can have some impact on both the results and their interpretation (3). For example, the selection and grouping of foods for analysis from the larger pool of available food items can be guided by existing knowledge about how individual foods may be related to broader dietary patterns, but different investigators may still group foods differently. There are also various criteria for limiting the number of factors to be extracted from the data (3). Some guidelines have been considered useful, such as extracting factors with eignenvalues greater than 1 (14) or by graphing the eigenvalues and extracting factors that visibly explain an important degree of variation beyond what is explained by other factors (14). The methods by which the selected factors are then rotated and the manner in which the factors are ultimately labeled is also based on subjective criteria and is liable to different interpretations (3). Therefore, it is interesting to note that the "Western," "healthy," and "drinker" dietary patterns discerned in our data are similar to those labeled "Western," "moderation," and "alcohol" in the case-control study (2) and those labeled "Western" and "prudent" in a subgroup of the Health Professionals Follow-up Study cohort (15) which suggests that these factors may represent dietary patterns common to several populations.

The strengths of our study include the relatively large sample size of our cohort, its population-based character, completeness of follow-up in the Swedish cancer registry system, and a large number of cases. The prospective assessment of exposure in our study eliminates information bias from selected recall, which is a potential threat to the validity of case-control studies. To the best of our knowledge, this is the first study to examine dietary patterns in relation to breast cancer risk.

We could not adjust rate ratios for the potentially confounding effect of physical activity because this information was not collected at baseline. Energy intake, a rough indicator of physical activity (28), was not associated with breast cancer in our data, and our results were not altered by adjustment for the effects of energy intake or BMI. Moreover, physical activity was not associated previously with either the "Western" or the "alcohol" dietary pattern (2) and is therefore unlikely to have confounded our results. However, we cannot rule out the possibility of residual confounding due to physical activity. We also did not have information on smoking. Previous studies of smoking and breast cancer risk generally do not show an association (29), although recent studies have reported a positive association (30, 31), an inverse association (32, 33), or no association (34, 35). Thus, the association between smoking and breast cancer risk remains unclear, but most studies to date suggest that there is no important association. Furthermore, the 30% increased risk among women in the highest category of our "drinker" dietary pattern is similar in magnitude to what has been observed with alcohol consumption in prior studies where smoking was considered in the analysis (4). However, we cannot rule out the possibility of some confounding due to smoking.

Our data were further limited by the likelihood of measurement error of the individual dietary exposures, and nondifferential misclassification of exposure would tend to attenuate rate ratios (36). Therefore, we cannot rule out the possibility of a stronger association between "drinker" dietary pattern and breast cancer risk than what was found in our data. Similarly, we cannot rule out weak associations in either direction with the "healthy" or "Western" dietary pattern.

In conclusion, three major dietary patterns were discerned in the study population. The "drinker" pattern, characterized by consumption of wine, beer, and spirits, was significantly positively associated with breast cancer risk. The positive association between the "drinker" dietary pattern and breast cancer risk is consistent with the results of previous studies of alcohol consumption, which may increase the risk of breast cancer by increasing endogenous estrogen levels (7). Neither the "healthy" nor the "Western" dietary pattern was associated with breast cancer risk.

Appendix

Table 4 Food groupings used in the dietary pattern analyses

Foods or food groups	Food items
Vegetables	Beets, carrots, cabbage, lettuce, spinach, tomatoes, and cucumbers
Fruit	Apples, pears, oranges, grapefruit and bananas
Whole grains	Whole grain soft bread, crisp bread, oatmeal, and other whole grain hot cereals
Refined grains	White bread, rice, spaghetti, waffles, and pancakes
Cereal	Assorted breakfast cereals and musli
Low-fat dairy	Low-fat milk, reduced-fat (medium) milk, and low-fat yogurt
High-fat dairy	Butter, cheese, whole milk, whole yogurt, and ice cream
Fish	Salmon, mackerel, sardines, tuna, herring, other fish, lobster, shrimp, crab, and mussels
Poultry	Chicken
Meat	Beef, chopped meat, minced meat, liver, and liver pate
Processed meat	Bacon, sausage and blood pudding
Eggs	Eggs
Margarine	Margarine
Pea soup	Pea soup and bean soup
Potato	Boiled potatoes, fried potatoes, and french fries
Snacks	Potato chips, other snack chips, popcorn, and fried and salted nuts
Sweets	Assorted candy, caramels, chocolate, cookies, sugar (*e.g.*, sugar cubes), sweet soups, marmalade, and jams
Juice	Juice
Soda	Carbonated and uncarbonated sweetened drinks
Tea	Tea
Coffee	Coffee
Beer	Beer
Wine	Wine
Liquor	Liquor

References

1. Parkin, D. M., Pisani, P., and Ferlay, J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int. J. Cancer, *80:* 827–841, 1999.

2. Slattery, M. L., Boucher, K. M., Caan, B. J., Potter, J. D., and Ma, K. N. Eating patterns and risk of colon cancer. Am. J. Epidemiol., *148:* 4–16, 1998.

3. Martinez, M. E., Marshall, J. R., and Sechrest, L. Invited commentary: factor analysis and the search for objectivity. Am. J. Epidemiol., *148:* 17–19, 1998.

4. Smith-Warner, S. A., Spiegelman, D., Yaun, S. S., van den Brandt, P. A., Folsom, A. R., Goldbohm, R. A., Graham, S., Holmberg, L., Howe, G. R., Marshall, J. R., Miller, A. B., Potter, J. D., Speizer, F. E., Willett, W. C., Wolk, A., and Hunter, D. J. Alcohol and breast cancer in women: a pooled analysis of cohort studies. J. Am. Med. Assoc., *279:* 535–540, 1998.

5. Willett, W. C. Diet and breast cancer. J. Intern. Med., *249:* 395–411, 2001.

6. Gandini, S., Merzenich, H., Robertson, C., and Boyle, P. Meta-analysis of studies on breast cancer risk and diet: the role of fruit and vegetable consumption and the intake of associated micronutrients. Eur. J. Cancer, *36:* 636–646, 2000.

7. Hunter, D. J., and Willett, W. C. Nutrition and breast cancer. Cancer Causes Control, *7:* 56–68, 1996.

8. Hunter, D. J., Spiegelman, D., Adami, H. O., Beeson, L., van den Brandt, P. A., Folsom, A. R., Fraser, G. E., Goldbohm, R. A., Graham, S., Howe, G. R., *et al.* Cohort studies of fat intake and the risk of breast cancer—a pooled analysis. N. Engl. J. Med., *334:* 356–361, 1996.

9. Toniolo, P., Riboli, E., Shore, R. E., and Pasternack, B. S. Consumption of meat, animal products, protein, and fat and risk of breast cancer: a prospective cohort study in New York. Epidemiology, *5:* 391–397, 1994.

10. Witte, J. S., Ursin, G., Siemiatycki, J., Thompson, W. D., Paganini-Hill, A., and Haile, R. W. Diet and premenopausal bilateral breast cancer: a case-control study. Breast Cancer Res. Treat., *42:* 243–251, 1997.

11. Favero, A., Parpinel, M., and Franceschi, S. Diet and risk of breast cancer: major findings from an Italian case-control study. Biomed. Pharmacother., *52:* 109–115, 1998.

12. Braga, C., La Vecchia, C., Negri, E., Franceschi, S., and Parpinel, M. Intake of selected foods and nutrients and breast cancer risk: an age- and menopause-specific analysis. Nutr. Cancer, *28:* 258–263, 1997.

13. Franceschi, S., Favero, A., La Vecchia, C., Negri, E., Dal Maso, L., Salvini, S., Decarli, A., and Giacosa, A. Influence of food groups and food diversity on breast cancer risk in Italy. Int. J. Cancer, *63:* 785–789, 1995.

14. Kim, J. O., and C. W., M. Factor analysis: statistical analysis and practice. C. A.: Sage. Publication Inc., 1978.

15. Hu, F. B., Rimm, E., Smith-Warner, S. A., Feskanich, D., Stampfer, M. J., Ascherio, A., Sampson, L., and Willett, W. C. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. Am. J. Clin. Nutr., *69:* 243–249, 1999.

16. Mattsson, B., and Wallgren, A. Completeness of the Swedish Cancer Register. Non-notified cancer cases recorded on death certificates in 1978. Acta Radiol. Oncol., *23:* 305–313, 1984.

17. Weiderpass, E., Baron, J. A., Adami, H. O., Magnusson, C., Lindgren, A., Bergstrom, R., Correia, N., and Persson, I. Low-potency oestrogen and risk of endometrial cancer: a case-control study. Lancet, *353:* 1824–1828, 1999.

18. Holmberg, L., Baron, J. A., Byers, T., Wolk, A., Ohlander, E. M., Zack, M., and Adami, H. O. Alcohol intake and breast cancer risk: effect of exposure from 15 years of age. Cancer Epidemiol. Biomark. Prev., *4:* 843–847, 1995.

19. Stoll, B. A. Western diet, early puberty, and breast cancer risk. Breast Cancer Res. Treat., *49:* 187–193, 1998.

20. Goldin, B. R., Adlercreutz, H., Gorbach, S. L., Warram, J. H., Dwyer, J. T., Swenson, L., and Woods, M. N. Estrogen excretion patterns and plasma levels in vegetarian and omnivorous women. N. Engl. J. Med., *307:* 1542–1547, 1982.

21. Swedish Board of Agriculture. Food consumption, 1994–1997: Report 1988:8. Jönköping, Sweden: Statens Jordbruksnämd, 1998.

22. Hursting, S. D., Thornquist, M., and Henderson, M. M. Types of dietary fat and the incidence of cancer at five sites. Prev. Med., *19:* 242–253, 1990.

23. Rose, D. P., and Connolly, J. M. Regulation of tumor angiogenesis by dietary fatty acids and eicosanoids. Nutr. Cancer, *37:* 119–127, 2000.

24. Rose, D. P., and Connolly, J. M. Omega-3 fatty acids as cancer chemopreventive agents. Pharmacol. Ther., *83:* 217–244, 1999.

25. Ip, C. Review of the effects of trans fatty acids, oleic acid, *n*-3 polyunsaturated fatty acids, and conjugated linoleic acid on mammary carcinogenesis in animals. Am. J. Clin. Nutr., *66:* 1523S–1529S, 1997.

26. Smith-Warner, S. A., Spiegelman, D., Yaun, S. S., Adami, H. O., Beeson, W. L., van den Brandt, P. A., Folsom, A. R., Fraser, G. E., Freudenheim, J. L., Goldbohm, R. A., Graham, S., Miller, A. B., Potter, J. D., Rohan, T. E., Speizer, F. E., Toniolo, P., Willett, W. C., Wolk, A., Zeleniuch-Jacquotte, A., and Hunter, D. J. Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. J. Am. Med. Assoc., *285:* 769–776, 2001.

27. Willett, W. C. Specific fatty acids and risks of breast and prostate cancer: dietary intake. Am. J. Clin. Nutr., *66:* 1557S–1563S, 1997.

28. Willett, W. C., Howe, G. R., and Kushi, L. H. Adjustment for total energy intake in epidemiologic studies. Am. J. Clin. Nutr., *65:* 1220S–1228S; discussion 1229S–1231S, 1997.

29. Palmer, J. R., and Rosenberg, L. Cigarette smoking and the risk of breast cancer. Epidemiol. Rev., *15:* 145–156, 1993.

30. Ambrosone, C. B., Freudenheim, J. L., Graham, S., Marshall, J. R., Vena, J. E., Brasure, J. R., Michalek, A. M., Laughlin, R., Nemoto, T., Gillenwater, K. A., and Shields, P. G. Cigarette smoking, *N*-acetyltransferase 2 genetic polymorphisms, and breast cancer risk. J. Am. Med. Assoc., *276:* 1494–1501, 1996.

31. Johnson, K. C., Hu, J., and Mao, Y. Passive and active smoking and breast cancer risk in Canada, 1994–97. The Canadian Cancer Registries Epidemiology Research Group. Cancer Causes Control, *11:* 211–221, 2000.

32. Gammon, M. D., Schoenberg, J. B., Teitelbaum, S. L., Brinton, L. A., Potischman, N., Swanson, C. A., Brogan, D. J., Coates, R. J., Malone, K. E., and Stanford, J. L. Cigarette smoking and breast cancer risk among young women (United States). Cancer Causes Control, *9:* 583–590, 1998.

33. Ghadirian, P., Lacroix, A., Perret, C., Maisonneuve, P., and Boyle, P. Sociodemographic characteristics, smoking, medical and family history, and breast cancer. Cancer Detect. Prev., *22:* 485–494, 1998.

34. Delfino, R. J., Smith, C., West, J. G., Lin, H. J., White, E., Liao, S. Y., Gim, J. S., Ma, H. L., Butler, J., and Anton-Culver, H. Breast cancer, passive and active cigarette smoking and *N*-acetyltransferase 2 genotype. Pharmacogenetics, *10:* 461–469, 2000.

35. Wartenberg, D., Calle, E. E., Thun, M. J., Heath, C. W., Jr., Lally, C., and Woodruff, T. Passive smoking exposure and female breast cancer mortality. J. Natl. Cancer Inst. (Bethesda), *92:* 1666–1673, 2000.

36. Rothman, K. J., and Greenland, S. Modern Epidemiology. Philadelphia: Lippincott-Raven, 1998.

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