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Preschool diet and adult risk of breast cancer

Karin B. Michels[1–3]*, Bernard A. Rosner[3,4], Wm. Cameron Chumlea[5], Graham A. Colditz[2,3] and Walter C. Willett[2,3,6]

[1]*Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
[2]*Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA*
[3]*Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
[4]*Department of Biostatistics, Harvard School of Public Health, Boston, MA, USA*
[5]*Departments of Community Health and Pediatrics, Lifespan Health Research Center, Wright State University School of Medicine, Dayton, OH, USA*
[6]*Department of Nutrition, Harvard School of Public Health, Boston, MA, USA*

Events before puberty may affect adult risk of breast cancer. We examined whether diet during preschool age may affect a woman's risk of breast cancer later in life. We conducted a case-control study including 582 women with breast cancer and 1,569 controls free of breast cancer selected from participants in the Nurses' Health Study and the Nurses' Health Study II. Information concerning childhood diet of the nurses at ages 3–5 years was obtained from the mothers of the participants with a 30-item food-frequency questionnaire. An increased risk of breast cancer was observed among woman who had frequently consumed French fries at preschool age. For one additional serving of French fries per week, the odds ratio (OR) for breast cancer adjusted for adult life breast cancer risk factors was 1.27 (95% confidence interval [CI] = 1.12–1.44). Consumption of whole milk was associated with a slightly decreased risk of breast cancer (covariate-adjusted OR for every additional glass of milk per day = 0.90; 95% CI = 0.82–0.99). Intake of none of the nutrients calculated was related to the risk of breast cancer risk in this study. These data suggest a possible association between diet before puberty and the subsequent risk of breast cancer. Differential recall of preschool diet by the mothers of cases and controls has to be considered as a possible explanation for the observed associations. Further studies are needed to evaluate whether the association between preschool diet and breast cancer is reproducible in prospective data not subject to recall bias.

Key words: breast cancer; nutrition; epidemiology; early life

Factors during early life may play a role in the etiology of chronic disease. Fetal nutrition and infant growth seem to be predictive of adult risk of cardiovascular disease, hypertension, diabetes, and obesity.[1–5] In addition, maternal weight and diet during pregnancy, possibly mediated by fetal malnutrition, have been related to coronary heart disease.[6,7] Similarly, nutrition in early life is linked to later heart disease.[8,9]

A high birthweight has been associated with the risk of breast cancer in a number of studies,[10–20] but whether this association operates through fetal nutrition, hormonal factors or other mechanisms has not been resolved. Breast tissue is largely undifferentiated until puberty and may be particularly susceptible to carcinogenic influences during that age period.[21,22] Migrant studies indicate that rates of breast cancer change after migration primarily affecting the next generation and thus are compatible with modulation of risk during early life.[23–25] The impact of radiation exposure at a young age on breast cancer risk as an adult lends further support to the existence of a susceptible time period in early life.[26–28]

DeWaard and Trichopoulos[29] and Willett[30] have proposed that an energy-rich diet during puberty and adolescence affects the growth of mammary glands and enhances the occurrence of precancerous lesions. The observation that women who experienced the World War II famine in Norway during puberty had a reduced risk of breast cancer later in life supports the importance of diet—whether composition or total energy intake—during early life.[31] A number of breast cancer risk factors, such as tallness,[32] body size,[32,33] rapid growth during childhood[34] and early age at menarche,[35] are affected, at least in part, by childhood diet. Although taller final height,[36] an early age at peak growth[34] and an early age at menarche[35] are associated with an increase in the risk of breast cancer in adulthood, a high childhood body mass is inversely related to the risk of breast cancer.[33,37,38]

Our present study explores the role of diet during preschool age on future risk of breast cancer. Information on preschool diet was gathered from the mothers of participants of the Nurses' Health Study and the Nurses' Health Study II.

Population and methods

The Nurses' Mothers' Study is a case-control study nested in 2 prospective cohort studies, the Nurses' Health Study (NHS) and the Nurses' Health Study II (NHS II). These cohorts consist of 121,700 and 116,678 female registered nurses, respectively, born between 1921–1965. For both cohorts, biennial self-administered questionnaires provide updated information on demographic, anthropometric, and lifestyle factors and on newly diagnosed diseases, including breast cancer.

Documentation of breast cancer

On each biennial questionnaire we ask whether breast cancer has been diagnosed and, if so, the date of diagnosis. We also routinely search the National Death Index for deaths among women who did not respond to the questionnaires. We ask women who report breast cancer (or next of kin, for those who have died without reporting the incident disease) for permission to review the relevant hospital records to confirm the diagnosis. Pathology reports confirmed a breast cancer diagnosis among >99% of participants for whom records could be obtained. The analysis presented in this paper was restricted to cases of invasive breast cancer.

The Nurses' Mothers' Study

Details of the Nurses' Mothers' Study have been described elsewhere.[9] Briefly, in 1993 participants in the Nurses' Health Studies who had been diagnosed with incident breast cancer up to 1993 and had not reported the death of their mother on a previous questionnaire were identified, and 2 participants free of breast cancer at that time who belonged to the same cohort were matched to each case by year of birth. Matching occurred before it was known whether the mother was alive and able to participate. Because some mothers had died or were unable to participate, matching was incomplete for a substantial number of cases and controls. Of mothers still living and able to participate, 91% completed and returned our questionnaire. The study population consisted of 582

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***Correspondence to:** Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, 221 Longwood Avenue, Boston, MA 02115. Fax: +1-617-732-4899.
E-mail: kmichels@rics.bwh.harvard.edu
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nurses with invasive breast cancer and 1,569 nurses free of breast cancer in 1993.

The mothers were asked to complete a mailed, self-administered questionnaire on perinatal and early life events of their nurse-daughter including information on foods consumed by the daughter during preschool years. The mothers were asked how often their nurse-daughter ate or drank an average serving of any of the 30 food items listed on the questionnaire when she was 3–5 years old. The dietary part of the questionnaire was structured like a semiquantitative food-frequency questionnaire (FFQ).[39]

Information on adult breast cancer risk factors was assembled from the large databases already established for each of the two ongoing cohort studies. These variables had been reported by the nurses themselves and included year of birth, age at menarche, parity, age at first birth, height and weight. Data ascertained at baseline before diagnosis of breast cancer among the cases, were used in the analysis (1976 for NHS and 1989 for NHS II). A family history of breast cancer was available from the nurses' reports (mother or sisters with breast cancer) as well as from the mothers' reports (mother herself, grandmothers, or aunts with breast cancer). We created a variable indicating first- or second-degree relative(s) with breast cancer.

Fels Longitudinal Study diet assessment validation

The validity of the dietary information provided by the mothers in the present study could not be directly assessed. To address this problem, we conducted a small validation study in a similar population, the Fels Longitudinal Study. We sampled 33 female Fels participants born between 1929–1950[40] for whom 7-day diet records were kept by their mothers when these participants were 3–6 years old.[41] In 1997, we mailed the food questionnaire used in the Nurses' Mothers' Study to the respective Fels mothers asking them to recall their daughters' diet during preschool age. The mothers' ages in Fels ranged from 60–93 years. We obtained 29 completed diet questionnaires from the mothers. Spearman correlations of mean daily consumption of foods reported by the mothers on the 7-day diet records and on the FFQ were 0.46 ($p = 0.02$) for whole milk, 0.37 ($p = 0.07$) for broccoli and 0.36 ($p = 0.07$) for French fries.

Statistical analysis

Frequencies of intake of the individual foods as specified on the questionnaire were converted into servings/day (*e.g.*, number of glasses of milk per day) or servings/week depending on the food and used as continuous variables.

For 718 nurses, complete data on the frequencies of food intake were available, but for 1,433 participants, data were missing or the mother did not remember the frequency of intake of one or more food items. On average, mothers marked the ''don't remember'' option for 8.5% of food items and left 3.8% of food items blank. Overall, the proportion of missingness (blanks and don't remember) ranged from 4.5% (for milk) to 21% (for cheese).

Multiple imputation was used to account for dietary data not observed.[42–44] Multiple imputation replaces each missing value with a number of acceptable values representing a distribution of possibilities. We created 5 imputed data sets by replacing missing values with draws from the conditional distribution of the missing values given the observed values. Each of the 5 imputed data sets was analyzed as if it were complete; the results from the 5 data sets were then combined in a manner that takes account of both the between-imputation and within-imputation variability. The multiple imputation method used in the present analysis does not involve sampling of the parameter values in the imputation model but assumes that the parameter estimates are known without error, and are therefore not changed at each imputation by adding error to them.[44]

Nutrients were calculated from nutrient composition tables for the year the nurse was 3 years old; using these tables from 1929–1970 captured changes in the fortification of foods during this time period when calculating nutrient intake. Nutrient residuals were obtained by regressing nutrient intake on the log scale on mean-centered log values of energy intake and exponentiating the resulting residuals. The risk of breast cancer among women in the highest quintile of nutrient intake was compared to that among women in the lowest quintile. Nutrient intake was also considered as a continuous variable, and the risk of breast cancer was estimated per one standard deviation increase in the particular nutrient using continuous residuals divided by their standard deviation.

Odds ratios (OR) were obtained using unconditional logistic regression models. The association between food consumption and breast cancer was estimated for each individual food item, for combinations of foods, and for nutrients. Regression models included adult risk factors for breast cancer obtained from the Nurses' Health Studies' questionnaires: year of birth, age at menarche, parity, age at first birth, family history of breast cancer and body mass index (BMI) in 1976 for NHS and in 1989 for NHS II.

Results

Characteristics of the 582 breast cancer cases and 1,569 controls are listed in Table I. Among cases, 63% were premenopausal at diagnosis, 27% were postmenopausal, and 10% were of uncertain menopausal status. Older age at menarche, higher parity, and younger age at first birth were associated with reduced risk of breast cancer in this population. Higher BMI at baseline was asso-

TABLE I – ADULT CHARACTERISTICS OF PARTICIPANTS OF THE NURSES' HEALTH STUDY AND THE NURSES HEALTH STUDY II WITH BREAST CANCER (CASES) AND WITHOUT BREAST CANCER (CONTROLS) WHOSE MOTHER PARTICIPATED IN THE NURSES' MOTHERS STUDY

Characteristic	Cases (n = 582)		Controls (n = 1,569)	
	No.	%	No.	%
NHSI	461	79	1303	83
NHSII	121	21	266	17
Birth year				
1921–1925	16	3	93	6
1926–1930	68	12	176	11
1931–1935	105	18	307	20
1936–1940	121	21	347	22
1941–1945	136	23	331	21
1946–1950	70	12	169	11
1951–1955	40	7	86	5
1956–1960	20	3	47	3
1961–1963	6	1	13	1
Age at menarche[1]				
<=11	134	23	371	24
12	167	29	427	27
13	179	31	461	30
14	71	12	182	12
15+	27	5	117	8
Parity				
Nulliparous	69	12	174	11
1	59	10	133	8
2	199	34	500	32
3	155	27	405	26
4+	100	17	357	23
Age at first birth				
<=24	290	57	859	62
25–29	183	36	437	31
30+	40	8	99	7
Body Mass Index[1]				
<=21	217	37	437	28
21.1–23	165	28	470	30
23.1–25	99	17	269	17
25.1–29	66	11	232	15
>29	35	6	156	10
Family history of breast cancer				
No	480	82	1395	89
Yes	102	18	174	11

[1]Numbers do not always add up to the entire study population because of missing information on some variables.

ciated with a lower risk of breast cancer among these mostly premenopausal women. Family history of breast cancer was associated with increased breast cancer risk. The median year of birth of the mothers was 1914 for case mothers and 1913 for control mothers.

The results of the logistic regression analysis for all individual foods are provided in Table II. Regular consumption of French fries was associated with a significantly increased risk of breast cancer, with an OR of 1.27 for one additional serving/week (95% CI = 1.12–1.44). A slightly decreased risk of breast cancer was apparent for regular consumption of whole milk, although the association was of borderline statistical significance (OR per additional glass of whole milk/day = 0.90; 95% CI = 0.82–0.99). Broccoli consumption was associated with an elevated OR for breast cancer of borderline statistical significance in the unadjusted analysis (OR = 1.24; 95% CI = 0.98–1.57), but the association was attenuated after covariate-adjustment (OR = 1.16; 95% CI = 0.91–1.47).

Among covariates, the most notable correlations with foods were found for year of birth, possibly reflecting time trends in the availability of certain foods (the consumption of ice cream, orange juice, hot dogs, and French fries became more common over time, consumption of other types of potatoes became less common) or changes in habits (margarine partly replaced butter, and cod liver oil became less popular over time and was increasingly replaced by vitamin supplements). Changes in estimates from the covariate-adjusted analysis compared to the unadjusted regression model are accounted for mainly by adjustment for year of birth (Table II).

The estimates changed for some foods considerably after adjusting for all covariates. After controlling for other covariates, primarily year of birth, we found that the association of breast cancer risk with broccoli consumption was attenuated, whereas the estimates for consumption of orange juice, cabbage and ground beef where somewhat strengthened. The strongest changes in the odds ratios after covariate adjustment were for broccoli and liver consumption; these 2 foods were the least frequently consumed during childhood, and therefore these estimates were the least stable. The estimates for French fries (OR = 1.27; 95% CI = 1.12–1.44) and for milk (OR = 0.90; 95% CI = 0.82–0.99) did not change appreciably after covariate adjustment.

Foods associated with breast cancer risk were considered together in a multiple regression model unadjusted for non-dietary covariates to explore the independent contribution of each food. French fries were paired with ground beef to capture a fast food dietary pattern (French fries: OR = 1.27; 95% CI = 1.12–1.43), milk (French fries: OR = 1.27; 95% CI = 1.13–1.43), and broccoli (French fries: OR = 1.27; 95% CI = 1.13–1.43). The results indicated that the association between consumption of French fries and risk of breast cancer was not explained by consumption of any of the other 3 foods. The relation of ground beef consumption with breast cancer risk was somewhat diminished by the inclusion of French fries, indicating that the 2 foods might have been customarily consumed together (ground beef: OR = 1.12; 95% CI = 0.64–1.97). The consumption of milk and French fries was not strongly correlated (whole milk: OR = 0.91; 95% CI = 0.83–1.00) nor was that of broccoli and French fries (broccoli: OR = 1.22; 95% CI = 0.97–1.54).

The distributions of caloric nutrient intake were within the range reasonable for girls of preschool age (Table III). No important relation between intake of any of the calculated nutrients and risk of breast cancer was observed in this study (Table III).

TABLE II – OR AND 95% CI OF ADULT BREAST CANCER AMONG PARTICIPANTS OF THE NURSES' HEALTH STUDY AND THE NURSES' HEALTH STUDY II WHOSE MOTHER PARTICIPATED IN THE NURSES' MOTHERS STUDY[1]

Food	Unadjusted		Adjusted[2]	
	OR	95% CI	OR	95% CI
Servings/day				
Whole milk	0.91	0.83–1.00	0.90	0.82–0.99
Skim or lowfat milk	1.04	0.83–1.29	1.06	0.84–1.33
Cheese	1.07	0.77–1.49	1.04	0.78–1.39
Margarine	1.03	0.94–1.13	1.03	0.94–1.14
Butter	0.93	0.86–1.01	0.94	0.87–1.02
Apples	0.94	0.65–1.36	0.97	0.67–1.42
Oranges	1.09	0.75–1.58	1.02	0.70–1.49
Orange juice	0.95	0.74–1.22	0.85	0.65–1.10
Eggs	0.98	0.62–1.57	1.11	0.69–1.80
Ground beef	1.33	0.76–2.32	1.44	0.81–2.57
Meat as main dish	0.76	0.47–1.22	0.75	0.46–1.22
Meat as sandwich or mixed dish	0.81	0.48–1.36	0.85	0.49–1.46
Bread	0.96	0.88–1.06	0.98	0.89–1.08
Potatoes	0.98	0.63–1.54	1.06	0.66–1.69
Cereal	1.03	0.73–1.45	0.97	0.67–1.42
Cookies	1.06	0.95–1.19	1.06	0.94–1.19
Multiple vitamins	0.89	0.66–1.21	0.77	0.55–1.06
Cod liver oil	0.90	0.62–1.33	1.03	0.68–1.55
Servings/week				
Ice cream	1.06	0.98–1.15	1.04	0.96–1.13
Cabbage/coleslaw	1.03	0.87–1.22	1.10	0.92–1.31
Broccoli	1.24	0.98–1.57	1.16	0.91–1.47
Raw carrots	1.01	0.95–1.08	1.00	0.94–1.08
Cooked carrots	1.05	0.97–1.14	1.05	0.97–1.15
Cooked spinach	0.95	0.84–1.07	0.96	0.88–1.04
Hot dogs	0.95	0.83–1.09	0.96	0.83–1.10
Chicken	0.99	0.89–1.09	0.99	0.89–1.09
Fish/tuna	1.09	0.97–1.22	1.08	0.96–1.21
Liver	0.91	0.61–1.37	1.07	0.70–1.63
Rice	1.02	0.91–1.14	1.03	0.92–1.15
French fries	1.27	1.13–1.43	1.27	1.12–1.44

[1]Per serving increase of foods/day or week consumed at preschool age. OR, odds ratio; CI, confidence interval.–[2]Adjusted for year of birth, age at menarche, parity, age at first birth, family history of breast cancer, and adult body mass index.

Discussion

In our study, which was embedded in the 2 Nurses' Health Studies, we found a significant association between frequent consumption of French fries during preschool age as reported by the mothers of the study participants and breast cancer risk later in life. For one additional serving of French fries per week during their preschool years, women had a 27% increased risk of breast cancer when they were adults. Although consumption of milk and broccoli were marginally associated with adult breast cancer risk, no other food or nutrient appeared as strongly correlated with adult breast cancer risk as did French fries. As consumption of potatoes themselves was not associated with the risk of breast cancer, the preparation of French fries, namely the use of frying fat high in saturated fats and trans-fatty acids, may be of relevance. During the period of exposure spanning the years 1924–1970, preparation of French fries changed: solid shortening was used in the earlier years, and hydrogenated oils were used in later years. French fries have also been found to contain acrylamide, an industrial chemical that has been classified as a likely human carcinogen due to its DNA-reactive mechanism but was not related to breast cancer in a Swedish study.[45,46]

Frequent consumption of French fries did not seem to be a marker of ''fast food'' habits, because we did not observe a similar association of breast cancer risk with frequent consumption of hot dogs or ground beef. Consumption of French fries, however, could be a marker of a dietary pattern that we might not have been able to detect because we assessed only a limited number of foods with our diet questionnaire.

To our knowledge, no other data on the association between preschool diet and breast cancer risk are available. The role of childhood or adolescent diet recalled by the participants themselves has been explored in four case-control studies and two

TABLE III – OR AND 95% CI OF ADULT BREAST CANCER AMONG PARTICIPANTS OF THE NURSES' HEALTH STUDY AND THE NURSES' HEALTH STUDY II WHOSE MOTHER PARTICIPATED IN THE NURSES' MOTHERS STUDY[1]

Nutrient[2]	Parameter	Q1	Q2	Q3	Q4	Q5	OR/I SD increase in intake
Total calories	Mean intake	558	830	1,019	1,198	1,466	
	Unadjusted OR	1.0	1.11 (0.82–1.51)	0.9 (0.67–1.22)	1.15 (0.84–1.57)	1.02 (0.75–1.39)	1.06 (0.96–1.17)
	Covariate–adjusted OR	1.0	1.15 (0.84–1.59)	0.91 (0.67–1.25)	1.19 (0.87–1.65)	1.06 (0.77–1.46)	1.07 (0.97–1.19)
Protein (g)	Mean intake	23.3	35.6	44.1	51.8	63.8	
	Unadjusted OR	1.0	1.19 (0.87–1.62)	1.09 (0.81–1.48)	1.02 (0.76–1.38)	1.15 (0.85–1.56)	1.02 (0.93–1.13)
	Covariate–adjusted OR	1.0	1.21 (0.89–1.66)	1.12 (0.82–1.52)	1.05 (0.78–1.43)	1.21 (0.88–1.64)	1.03 (0.93–1.14)
Carbohydrates (g)	Mean intake	53.9	81.3	101.3	120.1	150.0	
	Unadjusted OR	1.0	0.90 (0.66–1.22)	0.97 (0.71–1.32)	0.89 (0.65–1.20)	0.94 (0.69–1.28)	0.99 (0.90–1.09)
	Covariate–adjusted OR	1.0	0.88 (0.64–1.22)	0.96 (0.69–1.34)	0.91 (0.66–1.26)	0.97 (0.70–1.35)	1.01 (0.92–1.12)
Vegetable fat (g)	Mean intake	2.5	4.7	7.1	11.0	18.7	
	Unadjusted OR	1.0	1.03 (0.75–1.40)	1.04 (0.76–1.42)	0.97 (0.71–1.32)	0.92 (0.68–1.25)	0.99 (0.89–1.09)
	Covariate–adjusted OR	1.0	1.03 (0.75–1.42)	1.09 (0.79–1.50)	0.98 (0.71–1.36)	0.92 (0.67–1.27)	0.99 (0.89–1.10)
Animal fat (g)	Mean intake	19.3	31.6	40.2	48.7	62.3	
	Unadjusted OR	1.0	0.94 (0.70–1.30)	1.11 (0.81–1.51)	1.04 (0.76–1.41)	1.09 (0.80–1.49)	1.05 (0.95–1.15)
	Covariate–adjusted OR	1.0	0.93 (0.68–1.28)	1.07 (0.77–1.48)	1.03 (0.74–1.43)	1.05 (0.75–1.48)	1.04 (0.94–1.15)
Saturated fat (g)	Mean intake	10.7	17.8	22.9	27.6	35.4	
	Unadjusted OR	1.0	1.09 (0.81–1.48)	1.35 (0.99–1.84)	1.07 (0.79–1.45)	1.18 (0.87–1.61)	1.04 (0.95–1.15)
	Covariate–adjusted OR	1.0	1.19 (0.86–1.65)	1.38 (0.97–1.95)	1.14 (0.87–1.78)	1.24 (0.87–1.78)	1.05(0.95–1.16)
Linoleic acid (g)	Mean intake	1.5	2.4	3.2	4.1	6.4	
	Unadjusted OR	1.0	0.93 (0.68–1.27)	0.81 (0.59–1.10)	1.18 (0.86–1.62)	0.85 (0.63–1.16)	0.99 (0.90–1.09)
	Covariate–adjusted OR	1.0	0.96 (0.69–1.34)	0.83 (0.59–0.16)	1.18 (0.83–1.68)	0.83 (0.58–1.19)	0.99 (0.89–1.09)
Dietary fiber (g)	Mean intake	2.7	4.5	5.8	7.3	12.2	
	Unadjusted OR	1.0	0.92 (0.68–1.26)	0.97 (0.72–1.32)	1.03 (0.76–1.41)	0.87 (0.64–1.18)	0.93 (0.85–1.02)
	Covariate–adjusted OR	1.0	0.92 (0.67–1.27)	0.94 (0.68–1.29)	0.98 (0.71–1.37)	0.85 (0.62–1.18)	0.91 (0.83–1.01)
Sucrose (g)	Mean intake	3.3	6.4	9.0	12.9	19.6	
	Unadjusted OR	1.0	1.03 (0.75–1.41)	0.92 (0.67–1.25)	0.97 (0.71–1.33)	0.78 (0.58–1.06)	0.95 (0.86–1.04)
	Covariate–adjusted OR	1.0	1.08 (0.78–1.49)	0.96 (0.70–1.32)	1.03 (0.74–1.43)	0.81 (0.59–1.12)	0.97 (0.88–1.07)
Folate (μg)	Mean intake	59.2	96.2	125.6	157.9	208.7	
	Unadjusted OR	1.0	1.04 (0.76–1.41)	0.93 (0.68–1.26)	1.07 (0.78–1.47)	0.79 (0.59–1.08)	0.94 (0.85–1.03)
	Covariate–adjusted OR	1.0	1.04 (0.75–1.44)	0.95 (0.69–1.32)	1.17 (0.84–1.63)	0.96 (0.63–1.18)	0.96 (0.87–1.06)
Vitamin A (IU)	Mean intake	2,086	4282	6555	8927	13,597	
	Unadjusted OR	1.0	0.98 (0.72–1.34)	0.87 (0.64–1.19)	1.00 (0.73–1.37)	0.85 (0.63–1.15)	0.96 (0.87–1.06)
	Covariate–adjusted OR	1.0	1.00 (0.72–1.37)	0.89 (0.65–1.22)	0.96 (0.69–1.33)	0.86 (0.62–1.17)	0.95 (0.86–1.05)
Carotene (IU)	Mean intake	678	1623	2596	3926	6848	
	Unadjusted OR	1.0	1.00 (0.73–1.37)	0.82 (0.60–1.11)	0.84 (0.61–1.14)	0.82 (0.60–1.11)	0.90 (0.82–0.99)
	Covariate–adjusted OR	1.0	1.02 (0.74–1.42)	0.82 (0.60–1.13)	0.85 (0.62–1.17)	0.85 (0.61–1.17)	0.91 (0.83–1.00)
Vitamin C (mg)	Mean intake	15.7	41.4	69.0	94.3	146.7	
	Unadjusted OR	1.00	1.04 (0.76–1.42)	1.06 (0.77–1.45)	0.82 (0.60–1.11)	0.82 (0.60–1.11)	0.91 (0.83–1.00)
	Covariate–adjusted OR	1.00	1.10 (0.79–1.53)	1.25 (0.89–1.75)	0.92 (0.66–1.30)	0.92 (0.67–1.28)	0.94 (0.85–1.04)
Vitamin E (mg)	Mean intake	1.19	1.94	2.55	3.23	4.81	
	Unadjusted OR	1.00	1.09 (0.80–1.49)	1.03 (0.76–1.39)	0.89 (0.66–1.20)	1.04 (0.77–1.41)	0.96 (0.87–1.06)
	Covariate–adjusted OR	1.00	1.09 (0.83–1.58)	1.01 (0.73–1.41)	0.84 (0.60–1.18)	0.94 (0.67–1.39)	0.93 (0.84–1.03)
Iron (mg)	Mean intake	2.54	3.89	4.83	5.70	7.23	
	Unadjusted OR	1.00	0.78 (0.57–1.07)	0.87 (0.63–1.19)	0.98 (0.71–1.35)	0.71 (0.52–0.97)	0.93 (0.84–1.02)
	Covariate–adjusted OR	1.00	0.82 (0.59–1.14)	0.92 (0.65–1.30)	1.07 (0.74–1.52)	0.79 (0.55–1.13)	0.97 (0.87–1.07)

[1]According to quintiles (Q) of nutrient intake at preschool age. Adjusted for age, age at menarche, parity, age at first birth, family history, adult body mass index, and total caloric intake. OR, odds ratio; CI, confidence interval.–[2]Nutrient residuals obtained by regressing nutrient intake on the log scale on mean-centered log values of energy intake and exponentiating the resulting residuals.

cohort studies of breast cancer.[47–52] In a study conducted in British Columbia, Canada, a reduced breast cancer risk was associated with self-reported frequent consumption of whole milk and vegetable oils before age 13 and an increased risk with frequent consumption of visible fat on meat.[7] In a case-control study in Utah, women with postmenopausal breast cancer reported higher intake of dietary fiber, whereas women with premenopausal breast cancer reported lower intake of fiber from grains.[48] In that study, fat intake from dairy products was associated with lower breast cancer risk.[48] Potischman *et al*. reported no strong influence of adolescent diet on breast cancer risk among women younger than age 45 years.[49] High meat consumption was reported more frequently among women with breast cancer.[49] In a cohort study conducted in Norway, participants were asked to recall their milk consumption during childhood and were then followed prospectively.[51] A non-significant inverse association between milk consumption during childhood and breast cancer incidence in adulthood was observed.[51]

Information on eating patterns during adolescence has also been retrospectively obtained from a subgroup of participants of the Nurses' Health Study.[50] In a case-control study (of a different population than that included in the present analyses), women with breast cancer were marginally less likely than women without breast cancer to report high consumption of eggs during adolescence but somewhat more likely to report high butter consumption.[50] In a retrospective study among 47,355 participants of the Nurses' Health Study II, high school diet was assessed in 1998 using a 131-item FFQ and incident cases of breast cancer between 1989–1998 were included.[52] A high intake of vegetable fat and of vitamin E was associated with a reduced risk of breast cancer, whereas a high glycemic index was associated with an increased risk.

Information concerning exposure to the Dutch hunger winter was used in a case-cohort analysis from the Netherlands Cohort Study.[53] No important association was found between residence in the western part of the Netherlands during adolescence and breast cancer risk, but individual data on energy intake or dietary composition were not available.

Validity of maternal recall of diet could not be tested in our population. A number of studies have explored the validity of parental reporting of their child's preschool diet using an FFQ.[54] Although mothers generally seemed to be able to report their preschool children's diet with acceptable accuracy, the most notable concern was overreporting of caloric intake, as well as fruits and vegetables, dairy products, meat and fat, on the FFQ. We evaluated the validity of recall of preschool diet among mothers of participants of the Fels Longitudinal Study, which used 7-day diet records the mothers had kept decades earlier and found adequate validity for some foods of interest in the current study. To our knowledge, no other data are available on the validity or reproducibility of maternal or parental recall of children's diet decades later.

The observed association between consumption of French fries and breast cancer risk may have resulted from bias or chance. Nondifferential misclassification would probably have obscured any true association. Because mothers were asked to recall their daughter's preschool diet after her case status was known, differential recall has to be considered as a possible explanation of the observed association. If case mothers overestimated the foods consumed that were considered ''unhealthy,'' consumption of hot dogs and ice cream would be expected to have been overestimated along with consumption of French fries. Reports by case mothers of high consumption of French fries by their daughters, however, stand out among all ''unhealthy'' foods.

Additional research is needed, particularly prospective studies that eliminate the potential for recall bias, to confirm our findings and to investigate further the role of diet during early life in breast cancer etiology.

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